William Harvey Research Institute

PhD

The Challenges of Designing and Implementing a Pilot Study of Ovarium Compositum in Infertile Women

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Abstract

Introduction

This thesis reports a research project with a mixed methods research design and a pragmatist worldview. It documents, analyses and reflects upon the evolution of a project, that over nine years, examined the challenges of designing and implementing a clinical trial design that could capture the effect of using Ovarium compositum to support the outcomes of women undergoing infertility treatment at Jersey General Hospital.

Aims

The initial aim of the research project was to design and conduct a randomised clinical trial of a homeopathic product, Ovarium compositum, as an additional treatment for women undergoing infertility treatment at Jersey General Hospital. When the trial did not meet it's recruitment target the focus of the project switched to an investigation of the reasons for trial failure. The need for a pragmatist philosophical worldview to bring structure and understanding to the process of writing and rewriting the thesis became increasingly clear as the project evolved.

The aims are divided into two categories, methodological and outcomes.
Methodological aims include:

- To explore the appropriate methodology for designing a clinical trial of a homeopathic product.
- To understand the role of a pragmatist worldview in clinical trial design and in rewriting a thesis.
- To understand the use of Mixed Methods Research in healthcare research.

Outcome aims include:

To understand the conceptualisation of infertility and its treatment by homotoxicologists in the UK

To explore the effectiveness of using Ovarium compositum to treat infertility in women.

To understand the perspective of the women who are being recruited and therefore aid trial recruitment.

Trial Design:

The four strands of the study follow a sequential design that was firstly exploratory and then explanatory; a schematic diagram is included after this abstract for the overview and for each strand.

Strand 1: Qualitative review of homotoxicology treatment for Infertility in the UK.

Strand 2: Qualitative study of the feasibility of working with patients and staff, based at The Bridge Centre London

Strand 3: An RCT of Ovarium compositum. A double blind placebo controlled trial seeking to recruit 90 women undergoing infertility treatment at Jersey General Hospital.

Strand 4: Qualitative investigation into work related concerns of infertile women:

Results: The results from strand one led to a greater understanding of how homotoxicologists conceptualise infertility and their responses were used to select the trial medication and to check the model validity of the planned RCT. The results from strand 2 were used to check the feasibility of running a trial at an infertility unit. The results highlighted areas such as patient distress, the role of nurses as a link between CAM and conventional medicine, the additional time needed during appointments.

Strand 4 led to a conceptual model of the comparative risks and benefits of disclosing treatment status at work. The ethical use of data from Internet forums is explored as a source of qualitative data.

Conclusion: Pragmatism and MMR were suitable as an approach for the investigation of the two research objectives and the rewriting of a thesis. There is a need to consider both qualitative and quantitative data when planning and conducting a clinical trial of CAM in order to ensure model

validity, successful recruitment and retention of patients and meaningful, useful results. Qualitative data may also include data sourced from patient forums on the Internet and there are unique ethical considerations when using this kind of data that need to be taken into account.

Infertile women have to balance the risks and benefits of treatment disclosure. Future trials including women undergoing infertility treatment should consider providing flexible appointment times, support for their psychological identity and use a participatory approach towards including nursing staff and patients during trial design.

Homotoxicology as a form of complex homeopathy is suitable for evaluation using an RCT model as long as there is an appropriate blinding, control groups and randomisation. It is only suitable if there is a homogeneous patient pool with a clinical diagnosis that matches the indications for the remedy being tested.

Limitations: It was not possible to assess the effectiveness of Ovarium compositum in the treatment of women undergoing infertility treatment. The failure of strand 3 (RCT of Ovarium compositum) to meet it's recruitment target can largely be attributed to the fact that the researcher did not take sufficient account of the perspectives of staff at the unit and the pressures faced by the women attending as patients. The differences between a clinic in London and a clinic in Jersey were not adequately explored. The importance of using both qualitative and quantitative data to plan a trial and attaching equal value to both approaches is acknowledged to be one of the major lessons of this thesis. The need for a systematic approach to the literature review was also highlighted during viva examination and addressed as part of the corrections submitted.

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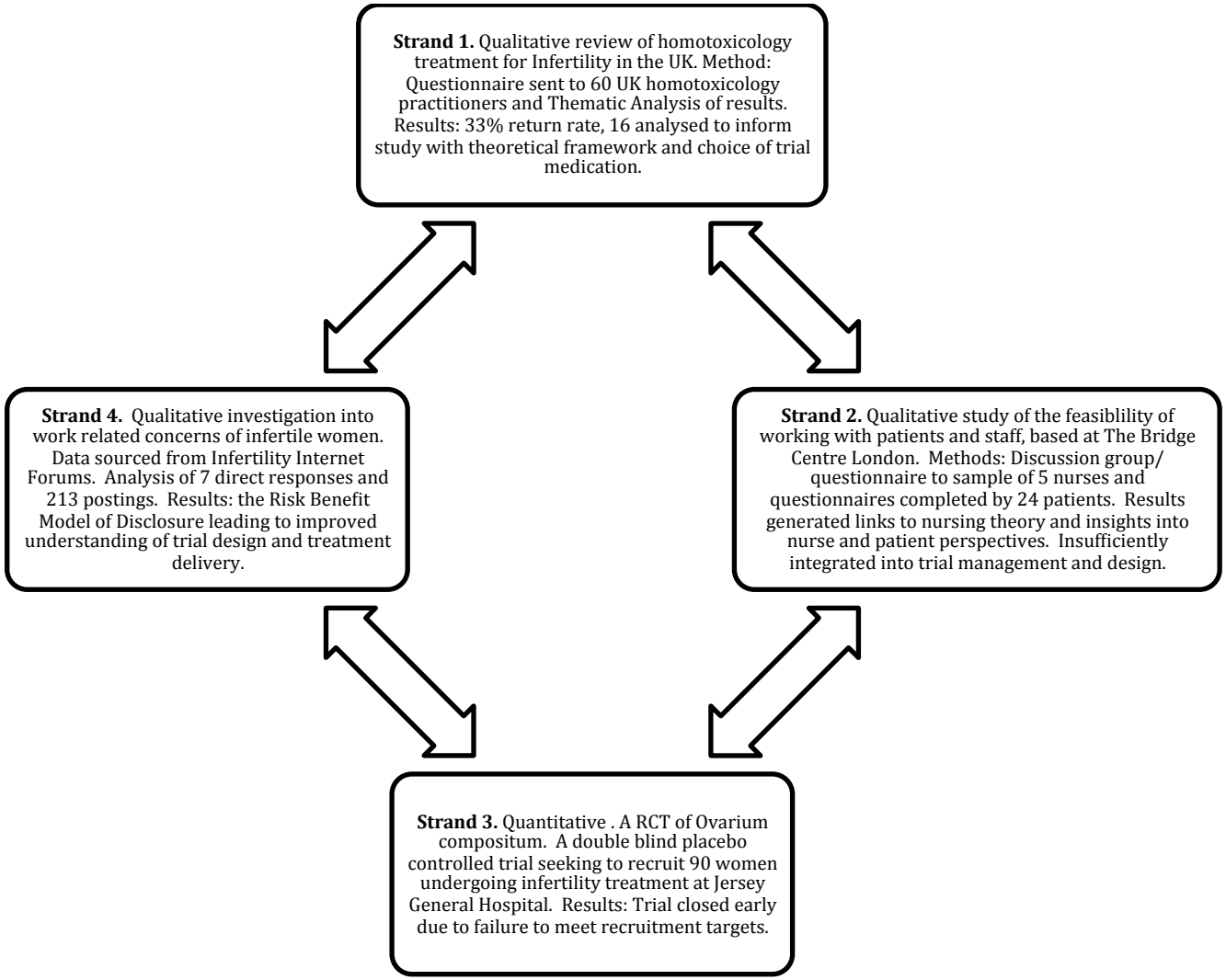
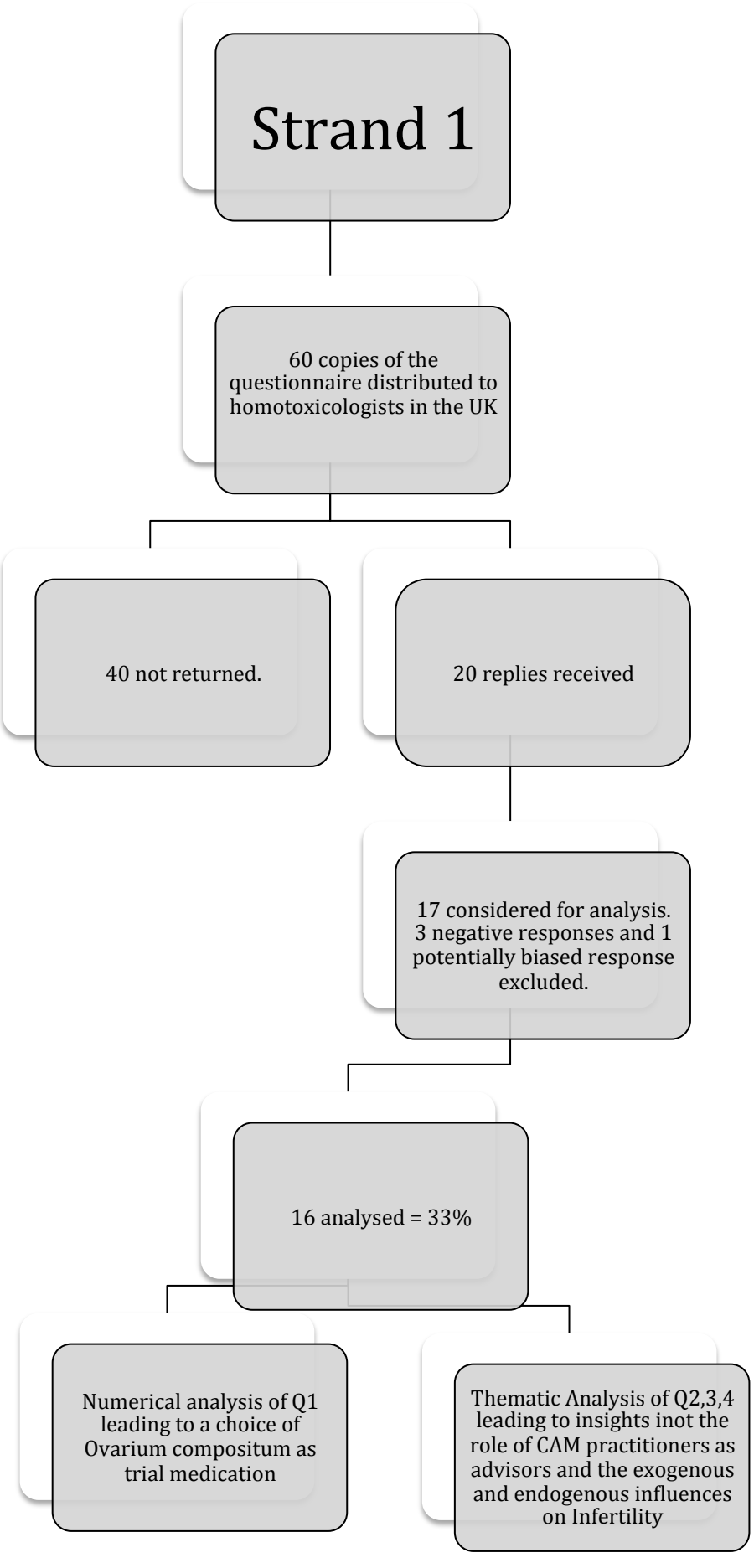
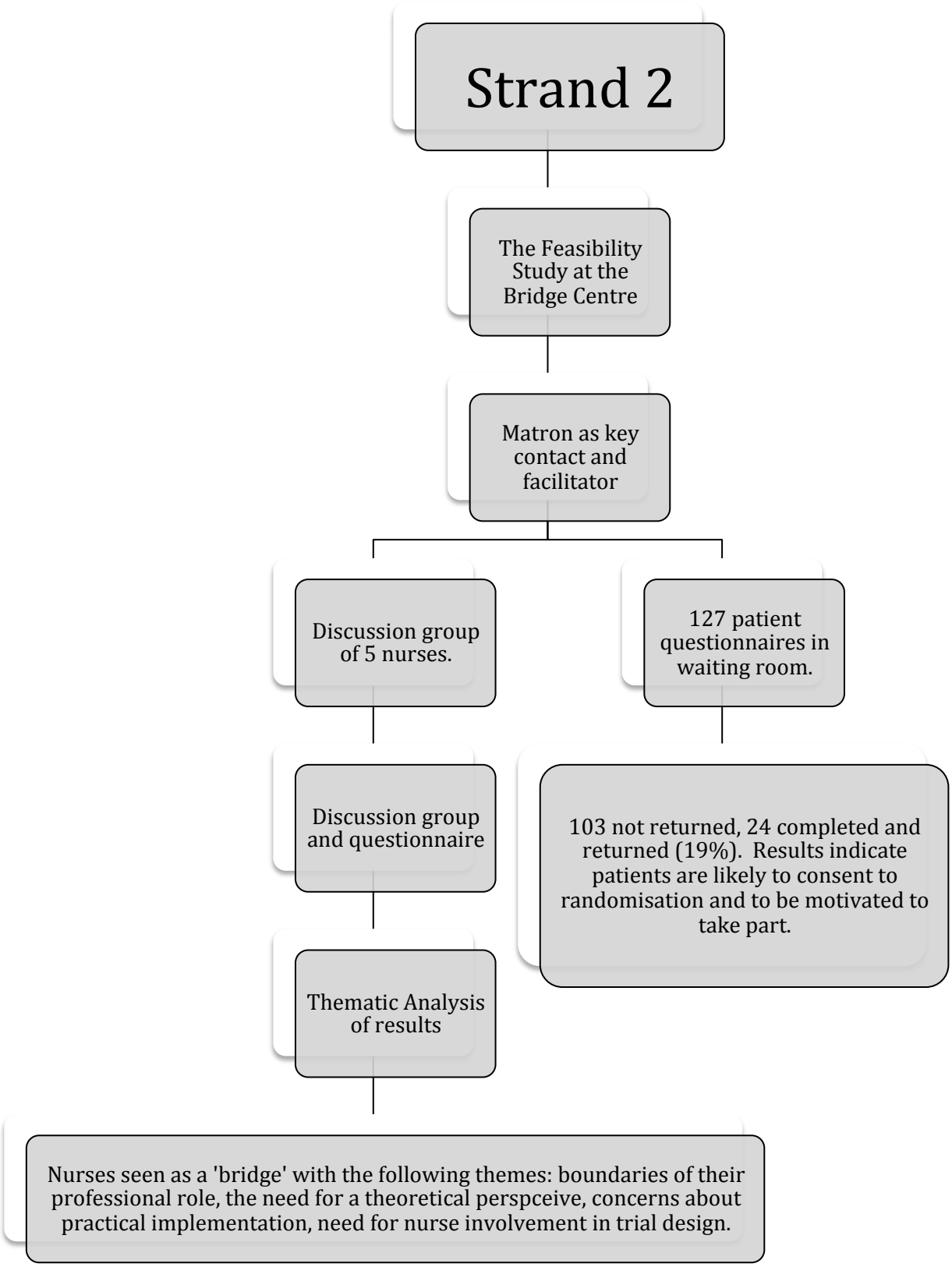
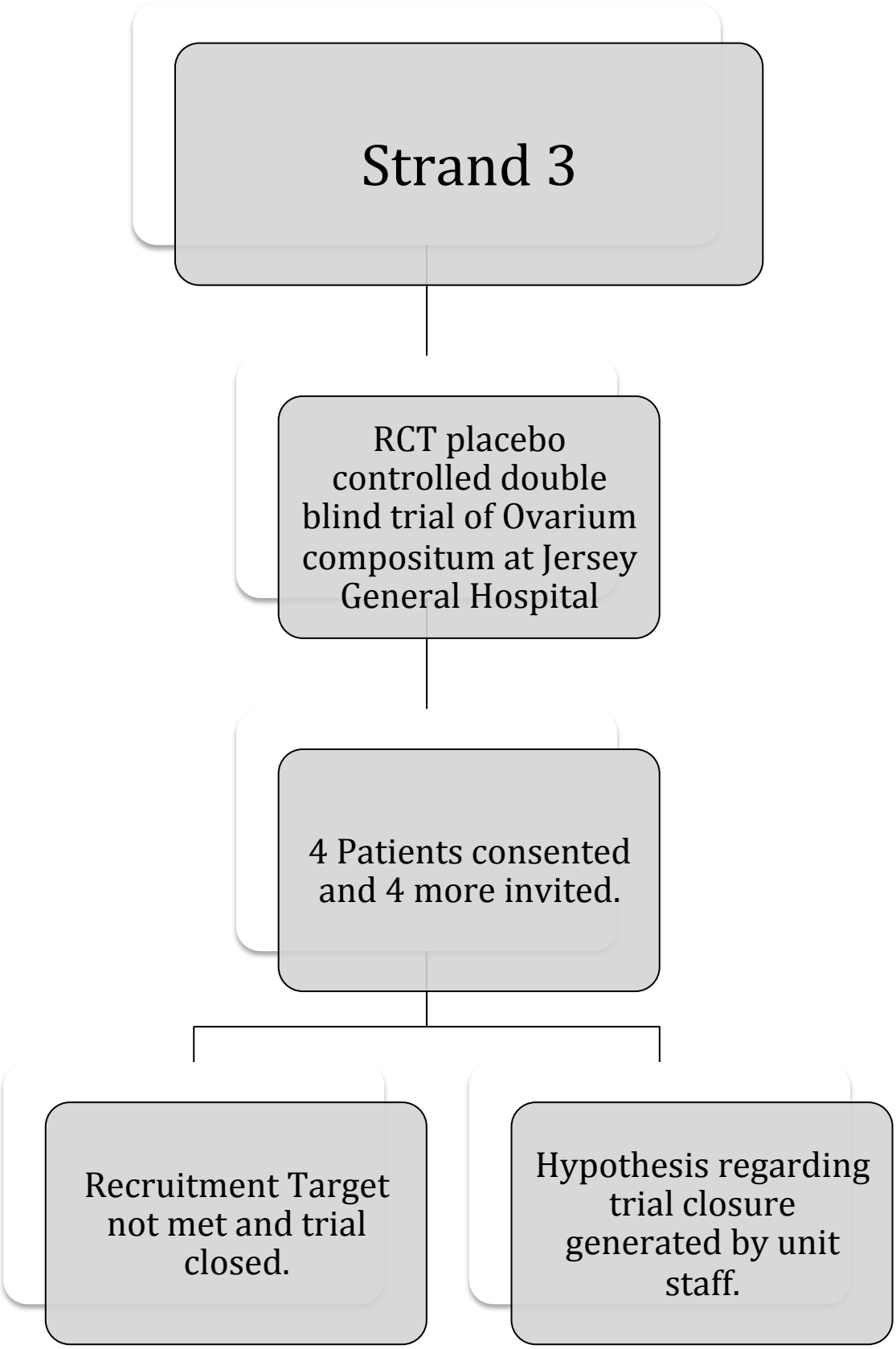
Road Map for Thesis: A Schematic Overview of the Thesis.

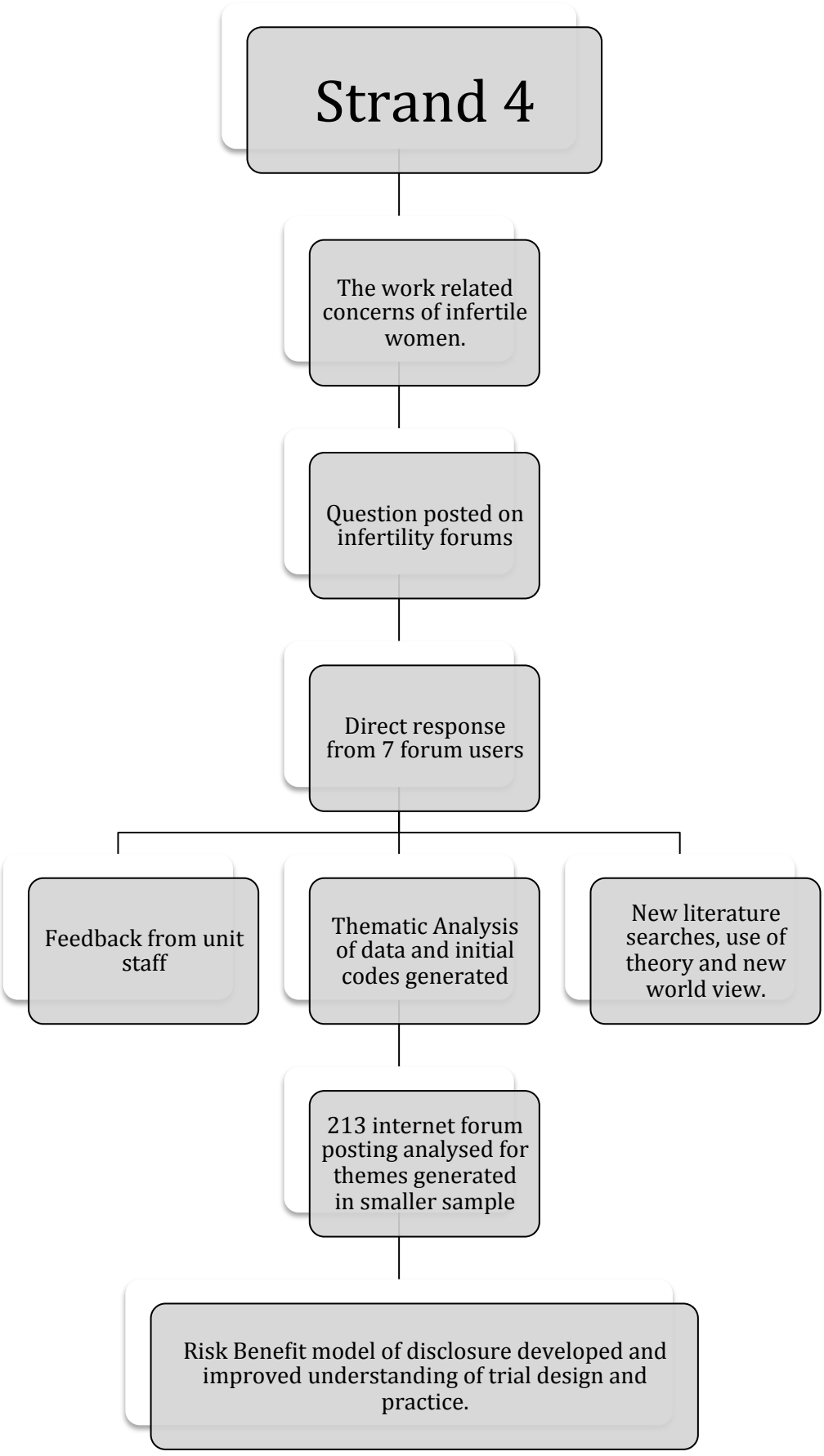


INTRODUCTION


Strand 1
60 copies of the questionnaire distributed to homotoxicologists in the UK
40 not returned.
20 replies received
17 considered for analysis. 3 negative responses and 1 potentially biased response excluded.
16 analysed = 33%
Numerical analysis of Q1 leading to a choice of Ovarium compositum as trial medication
Thematic Analysis of Q2,3,4 leading to insights inot the role of CAM practitioners as advisors and the exogenous and endogenous influences on Infertility


Strand 2
The Feasibility Study at the Bridge Centre
Matron as key contact and facilitator
Discussion group of 5 nurses.
127 patient questionnaires in waiting room.
Discussion group and questionnaire
103 not returned, 24 completed and returned (19%). Results indicate patients are likely to consent to randomisation and to be motivated to take part.
Thematic Analysis of results
Nurses seen as a 'bridge' with the following themes: boundaries of their professional role, the need for a theoretical perspceive, concerns about practical implementation, need for nurse involvement in trial design.


Strand 3
RCT placebo controlled double blind trial of Ovarium compositum at Jersey General Hospital
4 Patients consented and 4 more invited.
Recruitment Target not met and trial closed.
Hypothesis regarding trial closure generated by unit staff.


Strand 4
The work related concerns of infertile women.
Question posted on infertility forums
Direct response from 7 forum users
Feedback from unit staff
Thematic Analysis of data and initial codes generated
New literature searches, use of theory and new world view.
213 internet forum posting analysed for themes generated in smaller sample
Risk Benefit model of disclosure developed and improved understanding of trial design and practice.

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Introduction

The aim of this thesis is to explore the need for high quality evidence that respects the unique features of homotoxicology and the holistic needs of the infertile female patient. The study is also located in the debate around homeopathy and the challenge it represents to the traditional model of medicine. Pragmatism is explored as a foundation for reconciling traditional dualisms between conventional and humanistic approaches to providing medical care and a mixed methods research (MMR) approach chosen as suitable for combining the data from qualitative and quantitative sources.

The PhD serves two main objectives. The first is made quite explicit by PhD Handbooks (e.g., QUT, 1993, p. 2): the student researcher is required to produce "an original and substantial contribution to knowledge." The second, which is less explicit, but which is nevertheless implied in the type of thesis examination required, is to investigate and become proficient in the process of doing research in an ethical manner in one's chosen area (Phillips & Pugh, 1990).
(Hanrahan et al., 1999)

Objective One

This is a mixed methods research project looking at the design of and recruitment to a placebo controlled, double blind trial of a complex homeopathic product, Ovarium compositum, to treat infertile women at Jersey General Hospital.

When recruitment failed to enrol enough women to run the trial, the focus of the project moved to a qualitative investigation into the possible reasons for trial recruitment failure. This project therefore is composed of four discrete strands and these are explained in more detail in the methodology chapter.

The researcher had successfully used homotoxicology (complex homeopathy) in her own practice, with women who had been diagnosed with

failure to ovulate, treatment resulting in live births (n= 3) and the PhD study grew out of an interest in investigating the apparent efficacy of this approach.

Earlier studies (Gerhard I, 1997, Lai, 2000), (Bergmann et al., 2000) had also tried to reproduce their clinical successes as trials but had failed due to difficulties with recruitment or are of such poor methodological quality that they cannot be used as evidence of a specific effect. They are discussed in more detail in the Literature Review Chapter.

The initial aim of this project was therefore to improve on the existing published trials and design a trial that could provide evidence of the specific effects of Ovarium compositum. The first three strands of this study focus on the design of a suitable randomised controlled trial (RCT) that also fulfils the criteria of model validity for a homeopathic product (Mathie et al., 2012). One aim was to find out if homotoxicology as a complementary and alternative medicine (CAM) intervention could be evaluated using scientific methods of investigation in a positivist framework of evaluation.

The failure of trial recruitment and feedback from the site staff led to a second hypothesis, that the social and work concerns of the infertile women prevented them participating and so the fourth strand of this study is a qualitative investigation of the experiences of infertile women.

It was not possible to have access to the original patient group and as no specific support group or forum exists for infertile women in Jersey the leading UK infertility websites were used as a source of data. The specific responses of 7 women and the online postings of 213 women were analysed thematically (Braun and Clarke, 2006a) to investigate their concerns about their work and their treatment. The researcher takes a constructionist approach to both the selection of the data, the analysis of the data and the approach to writing the thesis and this is consistent with both the worldview and the methodology adopted.

Objective Two

I saw my individual production of knowledge as being necessarily shaped by my personal place in my own cultural context. This seemed a natural extension of the notion that knowledge is context-dependent, and thus should be reported in relation to that context (with myself being part of the context).
(Hanrahan et al., 1999)

The researcher moved from an unconscious acceptance of the positivist worldview of her social environment towards a more pragmatist understanding of using a mixed methods research approach (MMR) and in turn to an appreciation of the underlying philosophical worldview and the theoretical approach known as constructionism.

The constructed knowledge of the researcher was formed in an iterative cycle of action, feedback and reflection leading to a new world view with strong pragmatic characteristics and this study therefore makes a contribution to the literature on the role of philosophical foundations in trial design and in particular how such a world view can emerge from the processes of action and reflection, with writing and rewriting as an integral part of that cycle.

The study also illustrates how methodology can change in order to address an evolving research question, and makes a contribution to the knowledge about the use of MMR to investigate a homoeopathic product as treatment for infertility. A recent review found that only 4% of CAM research journals articles included MMR studies and noted that the quality could be improved (Bishop and Holmes, 2013).

The integration of both the qualitative (1 & 2) and quantitative strands (3) was made possible by the philosophical worldview. Pragmatism which is a pluralistic philosophy provides a framework for reconciling the dualistic views originating from quantitative and qualitative research traditions (Mesel, 2013).

This thesis values the knowledge that can be gained from conducting both quantitative and qualitative methods in order to gain a wider, more complete perspective on the research question.

The need to report philosophical orientation when writing up a mixed methods study was highlighted by (Bishop and Holmes, 2013) who reviewed articles from the field of CAM and found that only 5% of studies acknowledged or reflected on the limitations of their mixed methods design. None of the studies they reviewed acknowledged or addressed the philosophical tensions involved in a mixed methods research project. This study seeks to make a contribution to the field by reporting with transparency both the pragmatic philosophical framework and the process through which it was developed.

The World View Adopted In This Study

I hold that both qualitative and quantitative forms of knowledge are of value and importance and that they need to be judged on their own terms and within their own logic.

The worldview adopted in this study underwent transformation as the study progressed through the different strands identified in the diagram and discussed in more detail in the Methodology Chapter. It encompasses both the philosophy of how we come to know the world (epistemology) and the practice of how we come to know the world (ontology).

The transformation was driven by the research questions which changed from ‘can we show that this remedy makes a difference? To ‘why is it difficult to recruit women to this trial?’

The initial starting point was a post-positivist worldview characterised by reductionism, empirical observation, measurement and theory verification (Creswell and Clark, 2007a). The researcher was inherently biased by the cultural experience of studying in a medical school, which has a positivist

view of medicine and knowledge. This is a form of critical realism where the researcher believes that there is a form of reality independent of our thinking about it that science can study. However it is recognised that all observation is fallible and that all theory is revisable. In other words the researcher is critical of their ability to know reality with certainty. This emphasises the need for multiple measurements and observations that can be triangulated to try and get a better idea of 'reality' (William M.K. Trochim, 2006).

The intention was to design a clinical trial that allowed the effect of a medicinal product to be investigated under controlled conditions. This is a top down, or deductive, methodology in which the researcher works from theory to hypothesis to data, which adds to or problematizes the theory.

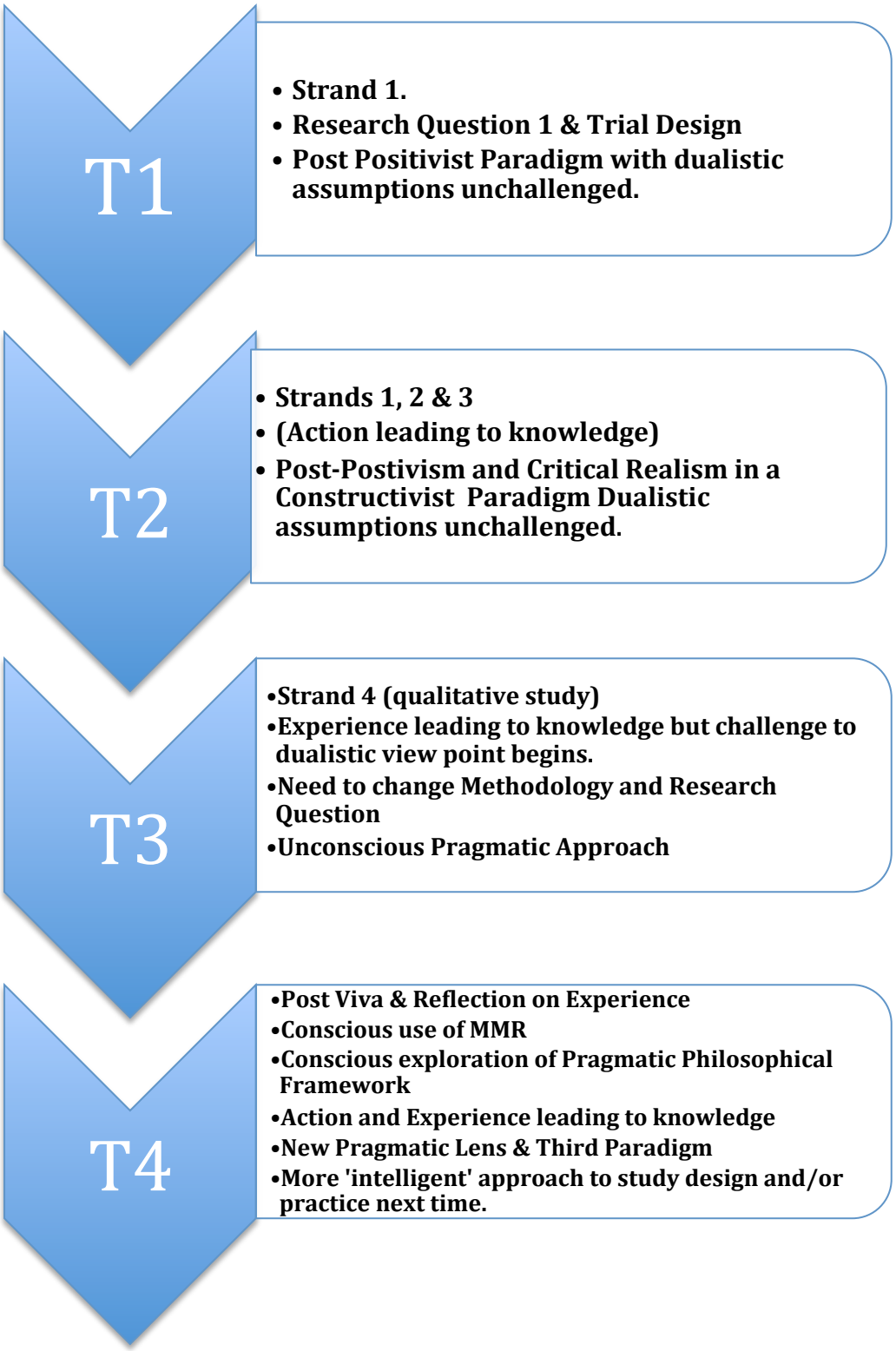
Full integration of qualitative and quantitative methods came about after trial recruitment failed and the necessity of solving the problems associated with changing the direction of the study led to a Pragmatist worldview characterised by a pluralistic approach to research. This meant that a bottom up approach was adopted in order to use the participants' views to build themes and generate a theory. In the process of writing and rewriting the thesis the researcher's knowledge was constructed, deconstructed and reconstructed.

The Researcher's view of knowledge changed to acknowledge that:
One might say that as a consequence that there is no single hierarchy of knowledge, nor should we give up on hierarchies, but that we should acknowledge that there are hierarchies of knowledge for each object of knowledge, or there is one world but multiple hierarchies of knowledge. (Nairn, 2012)

The other realisation was that inquiry has a sequential nature, this has been described (Dewey, 1925) as having its root in conditions of life itself. There is no absolute end to inquiry, it does not solve problems by returning to a stable position but creates a new position each time, therefore the learning

process in this thesis is summarised and described as a four step model (Time point 1 – Time point 4) below:

Figure 1 Model to show the development of the researcher world view



Time point 1 (T1)

First Research Question Formulated and Trial Design

- **Strand 1.**
- **Research Question 1 & Trial Design**
- **Post Positivist Paradigm with ddualistic assumptions unchallenged.**

Research denotes the deliberate instigation of intelligent experimental problem solving in order to generate knowledge and understanding (Biesta and Burbules, 2003)

This is the natural starting point where theory (e.g. often from literature review in medical research) shapes practice (e.g. trial design) and collection of facts of the case, which both help to define the terms of the problem. The research question arises out of a problem in lived professional practice. The research question at time point 1 of this project was 'Can Ovarium compositum make a difference to the fertility outcomes of women undergoing treatment at Jersey General Hospital?' The researcher was working in a positivist environment where the expectation of a good trial design was that it would create quantitative data for analysis; any qualitative data was intended to inform the design of a rigorous quantitative study.

According to pragmatism, the lived experience becomes the 'cognitive' mode or 'experience' when we start inquiry. The stages of inquiry were described by Dewey (Dewey, 1925) as:

The occurrence of the problem

i. *Its specification*
ii. *Occurrence of a solving suggestion, supposition, hypothesis*
iii. *Elaboration of suggestions or reasoning*
iv. *Experimental testing.*

The process of inquiry consists of the cooperation of two kinds of operations: *existential operations* (the actual transformation of the situation for example

the setting up of a control group in a randomised trial) and *conceptual operations* (reflecting or thinking) in order to transform an indeterminate situation into a situation where the elements are recognisable as part of a unified whole (Dewey, 1925).

Time point 2 (T2)

- **Strands 1, 2 & 3**
- **(Action leading to knowledge)**
- **Post-Positivism and Critical Realism in a Constructivist Paradigm Dualistic assumptions unchallenged.**

The need for a qualitative aspect to the study was seen as contributing to the validity of the quantitative study design rather than generating answers to the research question. The dualism between qualitative and quantitative forms of knowledge was not being challenged as each domain was seen as contributing separately to the inquiry. Thus, the first qualitative strand was the review of homotoxicology treatment for infertility in the UK in order to make sure that the protocol chosen for the clinical trial was an accurate representation of how homotoxicologists would prescribe for infertile women.

The researcher was conscious of operating simultaneously in two paradigms, both the medical and the CAM paradigm of health and disease, but had not found a way to reconcile these two aspects of the study. The study of placebo and non-specific effects was contemplated as a link between these two paradigms during this phase resulting in a published paper (Haresnape, 2013b).

The researcher had not yet made the link with pragmatism and the continuity between the material world and the world of consciousness, meaning, interaction and communication (Dewey, 1928). Dewey rejected the idea that the universe consists of two completely difference substances, ‘mind and matter’ (Biesta and Burbules, 2003), taking instead a naturalistic approach which claimed there is a continuity between the material and social domains

that we experience…*In the social world the physical world is taken up into a wider and more complex and delicate system of interactions so that it takes on new properties* (Dewey, 2008).

The second qualitative strand was a feasibility study with patients and staff at The Bridge Centre, a private infertility clinic in London. Here the staff and patient perceptions of two paradigms of treatment (CAM and conventional medicine) for infertility were explored. The perception of the two paradigms as separate led to the failure of the researcher to fully integrate the qualitative findings into the quantitative trial design and probably contributed to the eventual failure of the trial recruitment in strand 3 for an RCT of the use of Ovarium Compositum as an adjunct treatment for infertile women in an assisted reproduction unit.

Time point 3 (T3)

- **Strand 4 (qualitative study of work related concerns of infertile women)**
- **Experience leading to knowledge but challenge to dualistic viewpoint begins.**
- **Need to change Methodology and Research Question**
- **Unconscious Pragmatic Approach**

Dewey's analysis of the process of inquiry distinguishes between two outcomes or types of knowledge: an 'actual' and a 'conceptual' outcome (Biesta and Burbules, 2003).

By recognising that the conceptual outcome is related to the specific situation in which it was achieved we recognise that the knowledge gained in this way is provisional not absolute. Dewey preferred to use the expression *warranted assertion* to denote the conceptual outcomes of inquiry rather than *knowledge or truth (Biesta and Burbules, 2003)*

In this case the RCT trial led to an *actual* outcome in that women were reluctant to take part in the trial and a *conceptual* outcome - an understanding that qualitative research methods were necessary to find out why they were reluctant and to prevent it happening again. This kind of conceptual outcome is a form of knowledge that allow us to criticise, validate and improve our work by informing further processes of inquiry. A new research question was generated “Do work related concerns prevent women from taking part in an RCT trial?”

The attempt to use qualitative research without fully integrating a mixed methods research approach and a philosophical perspective misled the researcher to try an impose a positivist approach onto the qualitative data using methods such as ranking the frequency of keywords or codes.

Time point 4 (T4)

- **Post Viva & Reflection on Experience**
- **Conscious use of MMR**
- **Conscious exploration of Pragmatic Philosophical Framework**
- **Experience leading to knowledge**
- **Rewrite of Thesis as an active process of de-construction and reconstruction**
- **Iterative process of thematic data analysis.**
- **More 'intelligent' approach to study design and/or practice next time.**

The feedback from the viva for version 1 of this thesis, and the further study of mixed methods research (MMR), led to a realisation that the philosophical foundation of Pragmatism which had been unconsciously adopted had much greater implications than I had acknowledged for methodology choices, study design, and the value placed on the outcomes gained. The general characteristics of Pragmatism have been summarised (Johnson and Onwuegbuzie, 2004) and are shown below **Error! Reference source not found.**

(Johnson and Onwuegbuzie, 2004)

Table 1 General Characteristics of Pragmatism

General Characteristics of Pragmatism
The project of pragmatism has been to find a middle ground between philosophical dogmatisms and scepticism and to find a workable solution (sometimes including outright rejection) to many longstanding philosophical dualisms about which agreement has not been historically forthcoming.
Rejects traditional dualisms (e.g. rationalism vs. empiricism, realism vs. anti realism, facts vs. values, free will vs. determinism, Platonic appearance vs. reality, facts vs. values, subjectivism vs. objectivism) and generally prefers more moderate and common sense versions of philosophical dualisms based on how well they work in solving problems.
Recognises the existence and importance of the natural or physical world as well as the emergent social and psychological world that includes language, culture, human institutions, and subjective thoughts.
Places high regard for the reality of and influence of the inner world of human experience in action.
Knowledge is viewed as being both constructed and based on the reality of the world we experience and live in.
Replaces the historically popular epistemic distinction between subject and external object with the naturalistic and process orientated organism-environment transaction.
Endorses fallibilism (current beliefs and research conclusions are rarely, if ever, viewed as perfect, certain, or absolute}.
Justification comes in the form of what Dewey called ‘warranted assertability’
According to Pierce, “reasoning should not form a chain which is no stronger than it’s weakest link, but a cable whose fibres may be ever so slender, provided they are sufficiently numerous and intimately connected” (1868 in Menand, 1997, pp 5-6)
Theories are viewed instrumentally (they become true and they are true to different degrees based on how well they currently work; workability is judged

especially on the criteria of predictability and applicability).
Endorses eclecticism and pluralism (e.g. different, even conflicting, theories and perspectives can be useful; observation, experience, and experiments are all useful ways to gain an understanding of people and the world).
Human inquiry (i.e. what we do in our day-to-day lives as we interact with our environments) is viewed as being analogous to experimental and scientific inquiry. We all try out things to see what works, what solves problems, and what helps us to survive. We obtain warranted evidence that provides us with answers that are ultimately tentative (i.e., inquiry provides the best answers we can currently muster), but in the long run, use of this "scientific" or evolutionary or practical epistemology moves us towards larger Truths.
Endorses a strong and practical empiricism as the path to determine what works.
Views current truth, meaning and knowledge as tentative and as changing over time. What we obtain on a daily basis in research should be viewed as provisional truths.
Capital "T" Truth (i.e. absolute Truth) is what will be the "final opinion" perhaps at the end of history. Lowercase "t" truths (i.e., the instrumental and provisional truths that we obtain and live by in the meantime) are given through experience and experimenting.
Instrumental truths are a matter of degree (i.e., some estimates are more true than others). Instrumental truth is not stagnant and, therefore James (1995: 1907) states that we must "be ready tomorrow to call it falsehood."
Prefers action to philosophizing (pragmatism is, in a sense, an anti-philosophy).
Takes an explicitly value-orientated approach to research that is derived from cultural values; specifically endorses shared values such as democracy, freedom, equality, and progress.
Endorses practical theory (theory that informs effective practice: praxis)
Organisms are constantly adapting to new situations and environments. Our thinking follows a dynamic homeostatic process of belief, doubt, inquiry, modified belief, new doubt, new inquiry…in an infinite loop, where the person or researcher (and research community) constantly tries to improve upon

past understandings in a way that fits and works in the world in which he or she operates. The present is always a new starting point.
Generally rejects reductionism (e.g. reducing culture, thoughts, and beliefs to nothing more than neurobiological processes).
Offers the “pragmatic method” for solving traditional philosophical dualisms as well as for making methodological choices.

Reconciling Dualisms

The dualisms between conventional medicine and complementary medicine are a central theme in this thesis. They permeate the social environment of the study, the choice of clinical subject, the methodology and the philosophical orientation of the project. It is not by coincidence that MMR is suitable for reconciling these different and opposing paradigms (Creswell and Clark, 2007b) and that pragmatism provides a robust philosophical framework for doing so (Shelton, 2013), it is also acknowledged that the treatment of fertility involves both the physical and psychological domains of health (Fields et al., 2013) and therefore is a suitable condition for a mind-body medicine intervention.

The Use Of Extracts From The Data

Quotations from the qualitative data have been used to generate and later to illustrate the themes. The selection of quotations for inclusion followed the rule that they captured the essence of the theme, could be understood in isolation and were representative of the sample. Differing or deviant quotations were explored as part of the thematic analysis (Braun and Clarke, 2006a). Anonymity of the participants has been retained by removing some words and by aggregating the quotes (Bond et al., 2013) so that they cannot be traced back to an internet forum by pasting them into a search engine.

Definitions And Abbreviations

The data from the online forum postings in strand three contain many abbreviations that are derived from the either the terminology around their treatment or from the social conventions of the online community. A glossary of abbreviations used in this thesis is provided here to aid understanding.

Table 2 A list of abbreviations used in this thesis

Abbreviation	Meaning or Definition
AF	Aunty Flo, menstrual period
ART	Assisted Reproductive Technology
BFN	Big Fat Negative (pregnancy test)
CAF	Critical Appraisal Framework
CAM	Complementary and Alternative Medicine
DD	Dear Donor (Egg or Sperm Donor)
DH	Dear Husband
DPO	Days post ovulation
DS	Donor Sperm
EHIQ	Emotional Health In Infertility Questionnaire
EMM	Evolutionary Medical Model
EQ-5D	EQ-5D™ is a standardised instrument for use as a measure of health outcome
ET	Embryo Transfer
FSH	Follicle Stimulating Hormone
GnRH	Gonadotropin Releasing Hormone
GnRHantag	Gonadotropin Releasing Hormone Agonist
GP	General Practitioner
ICSI	Intra-Cytoplasmic Sperm Injection
ICSI	Intra-cytoplasmic Sperm Injection
IM	Integrative Medicine
IUI	Intrauterine Insemination
IUI	Intra-uterine Insemination
IVF	In Vitro Fertilization
LH	Luteinizing Hormone

LP	Luteal-Phase
MM	Mixed Methods
MMR	Mixed Methods Research
NHS	National Health Service
PCOS	Polycystic Ovary Syndrome
PCT	Primary Care Trust
PG	Pregnancy
PNEI	Psycho-Neuro-Endocrine Immunology
PSS	Perceived Stress Score
RCT	Randomised Controlled Trial.
SA	Sperm analysis
SD	Standard Deviation
SPA	Sperm Penetration Assay
TTC	Trying to conceive
USS	Ultrasound Scan

Background

The Social Environment Of This Study

The British Medical Journal (BMJ) provided a lens through which to view the social environment of this study during its conception and design (1993 – 2011). The choice of the BMJ as a portal to view the social and cultural context of the study has to take into account the possibility of bias, and this issue has been raised by the homeopathic community (Fisher, 2010) who would like to see a serious consideration of the evidence for homeopathy, rather than an out of hand dismissal or the mere voicing of opinion (Colquhoun, 2009).

The BMJ has reported, in both articles and letters, the debate over the different controversies around homeopathy: the philosophical basis of healing systems (Buckman and Lewith, 1994), (Reilly, 2001); the provision of homeopathy of the NHS (Fisher and Eden, 1995b), (Kmietowicz, 2010); the need to cast out ‘quacks’ (Fisken, 1996a) and avoid the use of homoeopathy

for life threatening illnesses (Delaunay et al., 2000), (Mashta, 2009); and the popularity of homeopathy (Fisher and Ward, 1994).

Two perspectives emerged from the reading of the BMJ articles firstly the biochemical perspective as a quest for a mechanism of action:
'Is there a verifiable physical mechanism by which the homeopathic remedies themselves affect disease (Buckman and Lewith, 1994)?

And secondly, from a healthcare research perspective, *'do homeopathic remedies make patients **feel** better (Buckman and Lewith, 1994)?*

These two perspectives represent the dual challenge that CAM has faced in order to meet the criteria for evidence based medicine (EBM) and retain its validity as a pluralistic and holistic practice that can be assessed using appropriate methods. These two perspectives are not valued equally in the predominately post-positivist thinking of the medical profession which has focused the debate on ways of providing evidence for a mechanism of action (Kmietowicz, 2010), or on demonstrating effectiveness (Smith, 1995).

The assumption that an RCT was the best model for evaluating the effects of a Ovarium compositum was based on the positivist thinking that was the dominant model in the researcher's social environment (a central London Medical School). Homeopathy was being increasingly subjected to the scrutiny of the medical and scientific community who were calling for a scientific/experimental model of evaluation (Dobson, 2006), (Oh, 1998).

The suitability of this methodology to evaluate homeopathy was also being debated as part of the larger debate around the provision of homeopathy by the NHS (Thompson and Feder, 2005). CAM practitioners, including homeopaths, were concerned about the methodological challenges posed by treatments that were often highly individualised, characterised by a practitioner-patient relationship, that has subtle or long term outcomes and may be concurrent with existing mainstream healthcare:

INTRODUCTION

As homoeopathic prescribing is highly individualized to a person's "constitutional picture" rather than to specific diseases, future research will need to meet this challenge as well as explore a plausible mechanism of action for homoeopathy (Baldwin, 2003)

LITERATURE REVIEW

Chapter 1 Literature Review

Introduction To The Literature Review

This chapter represents a 9-year period of study and covers 9 distinct reviews (see Table 3 The nine distinct reviews in Chapter 1), based on the evolution of the two hypotheses, the methodology, and the philosophical worldview of this thesis (section 1).

The first hypothesis was that a complex homeopathic product called Ovarium compositum could be used to improve the fertility outcomes of women attending an Assisted Reproduction Unit (ARU) at Jersey General Hospital. Section two is concerned with the definitions, prevalence and treatment of female infertility by the medical profession. Section three looks at how homotoxicology (complex homeopathy) is defined and evaluates the three existing trials of homeopathic products used to treat female infertility. Section four reviews the use of Randomised Controlled Trials (RCT) to investigate homeopathy.

The failure to recruit sufficient women to the RCT led to the second area of research and a new hypothesis, that the work related concerns of infertile women prevented them taking part in an RCT trial. To gain a perspective on the reasons for trial failure, section five looks at the concerns of infertile women.

The methodological issues raised by the need to design an additional qualitative strand to the study are covered in section six which reviews thematic analysis, section eight, qualitative research and section nine, mixed methods research. New data had to be sought by using the online infertility forums and section seven examines the issues of ethics and privacy raised by using such data sources.

Table 3 The nine distinct reviews in Chapter 1

Section	Questions	Research Questions	Type of Review
1	Pragmatism	What is Pragmatism? How does it inform this thesis?	Narrative review
2	Infertility	How is infertility defined in published studies, in working practice, what is the estimated prevalence – global and UK? What is the accepted medical treatment for female infertility?	Systematic Qualitative Review with acknowledged limitations.
3	Homotoxicology	What is homotoxicology? Are there any existing trials of homotoxicology to treat infertility?	Systematic Qualitative Review with acknowledged limitations.
		What is the role of CAM in treating infertility?	Narrative Review
4	RCT	What steps can be taken to ensure the model validity of an RCT to measure the efficacy of Ovarium compositum?	Narrative Review
5	Infertile women	What are the concerns of infertile women? Do existing studies offer any insight for trial design?	Narrative Review
6	Thematic analysis	What is thematic analysis and is it an appropriate method of analysis for this project? What does good thematic analysis look like?	Narrative Review
7	Ethics and Internet Data	What are the ethics of using data from internet forums?	Narrative Review
8	Qualitative research	What is qualitative research? How can I make sure my study is credible and valid?	Narrative Review
9	Mixed methods research (MMR)	What is MMR? How do I describe my study and ensure transparency of reporting?	Narrative Review

Reading and 'Writing-up' for both the first and second time was not a passive procedure but a more active set of iterative activities and approaches:

'This set includes de-constructing and re-constructing, disconnecting and re-connecting, as well as shaping and re-shaping.'(Badley, 2009)

Writing up was therefore, not an add-on to the existing research or a simple summarizing of what has been achieved, it was a creative, reflective and critical process, learning and transforming what was known at each stage of the project.

The reading of texts across the disciplines of education and medicine, helped to construct and re-construct the world view to include Pragmatism, which in turn helped meet the aims and purposes of the thesis. Section one looks at Pragmatism and how it can be used to inform our study design, our choice of methodology and the importance of transparency so that methods from different traditions can be integrated in a consistent manner.

Pragmatism became the thread running through the different strands of the study and was the framework for the process of learning new knowledge through action.

Badley describes this process when he takes a Deweyan approach to connecting and re-connecting:

My interpretation of Dewey here is based on the notion that our reading, researching, and writing for academic purposes often forms or 'grows out of' a series of natural chains or threads or connections (Dewey, 1910a), 1-5). When we write reflectively (or re-constructively), we deliberately word and re-word our claims to new knowledge based on a series of connecting ideas and firm reasons (Dewey, 1910a), 6-8)(Badley, 2009)

The Methodology In This Literature Review

The literature review continued throughout the data analysis and writing up process as new and unexpected perspectives were encountered and the use

of theory became more developed (Kelly, 2009). Papers were examined to see if they contained ideas that were useful and meant something for the particular purpose of this thesis. It is not unusual in qualitative research to go backwards and forwards between the literature and the research question during the course of a study with a preliminary literature review being undertaken at the planning stage (Kelly, 2009) and for the bulk of the reading to be done in and around the later stages of data collection and data analysis (Silverman, 2013).

The nine sections of the literature review are summarised in as **Table 3 The nine distinct reviews in Chapter 1** and are a mixture of narrative and systematic qualitative reviews depending upon the research question.

Some papers are considered in more depth because they are popular and well cited e.g. (Pope et al., 2000), other papers are less well cited but very specifically aligned to the ideas or concepts that emerged from the analyses in this thesis e.g. (Shelton, 2013).

Critical Reading

The critical reading process enables us to analyse, collect, evaluate and interpret important ideas that can then be used to synthesize, re-evaluate and re-interpret our new text (Badley, 2009).

The need to include a more critical reading process was highlighted in my first viva. As a response to this need a process a list of questions was developed (using an Open University module studied by the author), this gave a consistent structure to the appraisal of each article included in this chapter when it was rewritten Table 4: Checklist of questions for critical reading of selected articles:

1. What are the underlying philosophical assumptions in this paper?
2. Are these made explicit?
3. What methodology is being used?
4. What methods are being used?
5. What contribution did each of the data collection methods make to the research?
6. Would I have used different data collection methods?
7. Would I have analysed the data differently?
8. What framework is being used to interpret the data?
9. How is language being used? Do we share a common understanding of the terms and phases.
10. Questions: What research questions are being addressed?
11. Setting: What is the sector and setting? (e.g. school, higher education, training, informal learning)
12. Concepts: What theories, concepts and key terms are being used?
13. Findings: What did this research find out?
14. Do I agree with the authors' conclusions?
15. Limitations: What are the limitations of the methods used?
16. Ethics: Are there any ethical issues associated with the research?
17. Implications: What are the implications (if any) for practice, policy or further research?
18. How have subsequent authors built on this research, if at all?
19. Why did I choose to include this paper?

Table 4: Checklist of questions for critical reading of selected articles

The use of mixed methods research and the dualities between CAM and conventional medicine meant that the nine sections cover a broad spectrum of topics. The articles in each of the nine chapters were reviewed using quality assessment tools that varied according to the study design and which methodological feature were being examined.

Some excellent textbooks were used to develop an understanding of Mixed Methods Research (Creswell and Clark, 2007a), qualitative research (Silverman, 2013), the research methods used in healthcare (Bowling, 2011) and clinical research in the field of complementary medicine (Lewith et al., 2010). The textbooks suggested established papers and authors in each field, and helped to ensure consistency of understanding of key concepts and definitions, as well as providing a historical perspective of the field.

A balance was sought between being flexible enough to capture the essence and the use of methodological guidelines and a consistent approach that ensured the validity of the reviews in each section (Sternberg et al., 2011). This will now be explained in more detail for each of the nine sections. It is acknowledged that this balance was not always achieved and that the absence of a fully systematic approach should temper the conclusions reached.

Background - Different Types of Literature Review

At least three types of literature review can be indentified (Green et al.): narrative review, qualitative systematic review and quantitative systematic review. The purpose of a literature review is to objectively report the current knowledge on a topic based on previously published research thus providing the reader with reliable and comprehensive overview.(Green et al.).

Narrative literature reviews

Narrative literature reviews can also be described as three types (Green et al.): editorials, commentaries and overview articles.

The Qualitative Systematic Literature Review

This is a type of literature review that employs detailed, rigorous and explicit methods (Muir Gray, 1997), (Friedland et al., 1998). This means that they can be employed as an evidence based on which to base clinical decisions or for the creation and testing of hypotheses. (Phillips et al., 2001). They are characterised by a detailed search of the literature based upon a focused question or purpose and a step by step methodology is clearly described. Each paper is reviewed in a systematic and consistent manner but these reviews do not include a statistical combination of the results. This is found in quantitative systematic reviews.

The choice of articles for this chapter was also informed by a pragmatist viewpoint of what works and what meets the need? The pitfalls inherent in this approach include the possibility of bias and a lack of credibility and utility in the completed article. As part of the corrections submitted post-viva, this has been addressed by a closer attention to theory, a more transparent reporting of search strategies and a reflective commentary at the end of each of the nine sections.

It was also recognised post-viva that it is especially important to conduct a systematic literature review in this field (CAM) because it works as a mechanism to facilitate interdisciplinary collaboration and a more integrated understanding of health (Karunananthan et al., 2009).

Type of narrative literature reviews	Description	Advantages	Disadvantages
Editorials	Typically written by the editor of a peer reviewed journal or an invited guest	Usually short, selected, narrowly focused review of only a few papers	May be no more than the editor's comments regarding a current issue
Commentaries	Usually written by an expert in the field of the commentary	Draws upon the wisdom of the commentator,intended to provoke scholarly discussion	A biased narrative review and bias can become replicated by citations.
Narrative overview articles, (unsystematic narrative reviews).	Comprehensive narrative syntheses of previously published information.	Provides a useful educational tool with a broad perspective that is readable. Often written by an expert in the field	Can become an opinion orientated argument based upon references.

Table 5 Types of Narrative Literature Reviewed based on Green et al 2006

Literature Review - Section 1 – The Pragmatic World View

Methodology

The articles selected for this chapter were not chosen systematically, they are a record of the reading and thinking process that accompanied the rewriting of the thesis. This section of the literature review is more akin to a narrative review or commentary (Green et al.). Another way to describe this section would be as an extended memo in the tradition of qualitative research, (Charmaz, 2006) in which the writer deconstructs their current understanding, synthesises from new information, abstracts and reconstructs their worldview.

The framework that was developed allowed the author to make sense of the data and the process of rewriting. The utility of this section for other researchers would not be as a systematic review of the literature on Pragmatism but as a practical example of how a philosophical dimension can inform the development of a research project. **The articles selected were read systematically using the critical reading checklist of questions developed by the author**

Table 4: Checklist of questions for critical reading of selected articles.

Research Questions:

What is Pragmatism? How does it inform this thesis?

What is Pragmatism?

When we research something we are looking into the 'truth' of a situation. The 'truth' may take the form of a quantitative truth, for example an accurate measurement or evidence of cause and effect. Another kind of 'truth' would be a qualitative truth such as an empathic understanding of someone else's point of view or discovering the motivation behind their actions.

These two positions will discussed as the two stances of qualitative and quantitative researchers and mixed methodology will be suggested as a third stance that seeks to balance the benefits and drawbacks of each methodology to produce a more complete kind of 'truth'.

Underlying the choice of each methodology is a set of assumptions about the world, knowledge and how we can know things. It is reasonable to assume that as we evolved as a species there has been an evolution in man's thinking about the world and our intellectual tradition has been dominated at different times by theology, empiricism and idealism.

Pragmatism as a school of thought emerged over a century ago, as the first North American original contribution to philosophy, or 'thinking about thinking.' It originated in the writings of three American thinkers: the natural scientist and philosopher Charles Sanders Peirce (1842-1910), the psychologist and philosopher William James (1842-1910) and the philosopher, psychologist and educationalist John Dewey (1859-1952) (Biesta and Burbules, 2003).

They observed the social, cultural and political changes of their time and felt that philosophy should help to solve the real life problems of men rather than the abstract problems of philosophers. They saw an urgent need to balance the scientific and political progress being made with values such as democracy, justice and equality.

For these early pragmatists the central idea was that nothing is ultimately 'True' or 'False'. James believed that truth is 'what works'; Pierce understood it to mean 'something that we will eventually converge upon after a process of inquiry'; and Dewey believed that the truth is what you are 'warranted' in saying is true.

The core of their philosophy lay in their rejection of the Platonic idea of Truth. Philosophers, such as Descartes, have carried this conception forward and is the idea underlying Realism. Realism adheres to a correspondence theory of truth and maintains that there is a reality 'behind' appearances and that true knowledge is knowledge which correspondents to that reality (Cornish and Gillespie, 2009).

After Descartes, philosophy became focused on epistemology, how could a subjective living mind come to know or understand the material world? A division was created between the inner-directed world of observation or self awareness and the outer directed world of observation of the material world, including nature and humans (Tauber, 2009). This is commonly referred to as the mind-body divide where the mind is consigned to the role of a scientific spectator and the human body becomes an impersonal object of scientific study. The Descartian viewpoint therefore set the stage for the application of the scientific method to all of nature and the rise of modern science and technology including medicine (Mehta, 2011).

Pragmatism strongly rejects the correspondence theory of truth. Pragmatists see knowledge not as a mirror of reality, but as a tool for action that also mediates our relationships with the physical and social world (Cornish and Gillespie, 2009).

The pragmatists did not seek to answer the problems created by the mind-body divide, instead they sidestepped them by rejecting the traditional dualisms such as Platonic appearance versus reality. Pragmatists prefer instead to judge knowledge according to its consequences in action. Knowledge is deemed useful if it can help solve problems (Johnson and Onwuegbuzie, 2004).

They were able to do this because they saw humans as being in constant transaction with their environment. They believed that as a result knowledge is a construction, not of the mind, but located in the organism-environment transaction itself (Biesta and Burbules, 2003). For pragmatists it is the practical activity that is the bedrock and the test of knowledge. Knowledge is viewed as being both constructed and based on the reality of the world we experience and live in (Johnson and Onwuegbuzie, 2004).

Pragmatism does not reject the methods and insights of modern science however, they argue that these should be taken into account (Biesta and

Burbules, 2003), while avoiding reductionism, seeking instead 'warranted assertability'.

> *Human inquiry (i.e. what we do in our day-to-day lives as we interact with our environments) is viewed as being analogous to experimental and scientific inquiry. We all try out things to see what works, what solves problems, and what helps us to survive. We obtain warranted evidence that provides us with answers that are ultimately tentative (i.e., inquiry provides the best answers we can currently muster), but in the long run, use of this "scientific" or evolutionary or practical epistemology moves us towards larger Truths (Johnson and Onwuegbuzie, 2004)*

Pragmatists, like scientists, also endorse fallibilism, believing that current beliefs and research conclusions are rarely, if ever, viewed as perfect, certain or absolute. Instead they view the current truth, meaning and knowledge as tentative and changing over time. This iterative process of belief, doubt, inquiry, modified belief, new doubt, new inquiry means that the present is always a new starting point for the researcher who constantly tries to improve upon past understandings in a way that is congruent with the world in which he or she operates (Johnson and Onwuegbuzie, 2004).

All domains of knowledge are recognised and acknowledged as important, the natural or physical world as well as the social and psychological spheres including language, culture and thought. As a result of accepting all these differing domains of knowledge pragmatists endorse eclecticism and pluralism which means that different and even conflicting theories and perspectives can be useful and that observations, experiments and experiences are all useful ways to gain knowledge (Johnson and Onwuegbuzie, 2004).

One of the main critics of Pragmatism was Bertrand Russell, who believed that that it cannot simply be right, that what is useful is true. You may be fooled by your practical experience of the world into believing falsehoods

such as the Earth looks flat. His point was that their position was too simple and that there are independent hard facts out there which we can genuinely discover and call the 'Truth' (Johnson and Onwuegbuzie, 2004).

The pragmatist's answer to this critique was that if we treat the world as if these things do exist we can make things work better because for pragmatists the only sensible yardstick by which to judge a piece of knowledge is whether that knowledge is useful for a given interest (Cornish and Gillespie, 2009).

Johnson and Onwuegbuzie have identified other weaknesses of Pragmatism (Johnson and Onwuegbuzie, 2004) such as the danger that basic research may be neglected in favour of applied research because applied research appears to produce more immediate and practical results. The fact that Pragmatism takes a rather 'moderate and common sense' approach may mean that it promotes incremental change rather than more fundamental, structural, or revolutionary changes in society.

Although perhaps not revolutionary, pragmatism takes an explicitly value-orientated approach to research, that is derived from cultural values; specifically endorsing shared values such as democracy, freedom, equality, and progress which reflect it's birth in the western expansion of the United States. (Johnson and Onwuegbuzie, 2004).

The Pragmatism of John Dewey

John Dewey (1859-1952) was an American philosopher and one of the first pragmatists. He was greatly influenced by the social and cultural changes that he observed taking place at the time and went on to gain an international reputation for his pragmatic approach to philosophy, psychology and liberal politics. His publications in these areas include How We Think (Dewey, 1910b), Reconstruction in Philosophy (Dewey, 1920), Experience and Nature (Dewey, 1958), and Logic: The Theory of Inquiry (Dewey, 1938b).

His most enduring influence is in the field of education (Dewey, 1938a) and it was in this field that his work first came to the attention of the author. The transferability of his ideas the investigation of CAM therapies using MMR is one of the original themes developed in this thesis.

He believed in the unity of theory and practice, not only writing on the subject but for a time participating in a progressive 'laboratory school' for children connected with the University of Chicago (Dewey, 1938a).

The main significance of Dewey's pragmatism for (educational) research is that he deals with questions of knowledge and the acquisition of knowledge within the framework of a philosophy of action. Dewey made it clear that the domain of knowledge and the domain of human action are not separate domains but are intimately connected; that knowledge emerges from action and feeds back into action and that it does not have a separate existence or function.

He attempted to reconcile the gulf between traditional and progressive education by using a robust philosophical framework to promote a more 'intelligent' way of working. At the time his writing was hailed as a guiding beacon for a society that was experiencing rapid social, cultural and economic expansion.

Innovation in schools might be seen as the movement from a traditional model of education towards a progressive model. One of Dewey's contributions was to characterise these two approaches and put forward the idea that progression should not be merely a negative reaction to tradition. He deplored the necessity for pupils taught in a traditional manner to be docile, passive, receptive and obedient (Dewey, 1938a) but did not feel that the opposite extreme was desirable either:

> *Impulses and desires that are not ordered by intelligence are under the control of accidental circumstances… A person whose conduct is controlled in this way has at most only the illusion of freedom.*

> *Actually he is directed by forces over which he has no command. (Dewey, 1938a)*

Dewey acknowledged that teaching in a way that built on the existing experience of the learner, that did not oppress them or impose unnecessary restrictions, required a well thought out philosophy and well planned activities:

> *It is, accordingly, a much more difficult task to work out the kinds of materials, of methods, and of social relationships that are appropriate to the new education than is the case with traditional education (Dewey, 1938a).*

If we draw a parallel between progressive education and CAM then we can explore the ways in which his ideas about education might be applied to the practice and research of CAM. The dualisms between CAM and conventional medicine, like the dualisms between progressive and traditional education, have their foundation in the philosophical differences that divide qualitative and quantitative research methodologies. CAM, like education, is a complex and dynamic system of beliefs and actions that cannot be simply characterised by category or without including the perspectives of the participants.

CAM therapies are sometimes regarded with mistrust by the conventional medical profession because they are not viewed as scientific, for example:

> *It seems to me that we owe it to our patients, as well as to ourselves, to be much more intolerant, aggressive, and demanding in our dealings with fringe medicine, quackery, humbug, and deception of all kinds.*
>
> *Any decent, responsible form of medical practice must be based on logic, sound science, and well conducted research; if it is not then all of the philosophical, social, and political struggles of the*

> *Enlightenment and the sacrifices of our forebears have been in vain and we might as well give up and turn our patients over to the nearest witch doctor.*
> *(Fisken, 1996b)*.

CAM therapists, for their part may regard conventional medicine as too scientific and dehumanising, putting patients in a position where they are 'docile, passive, receptive'. Many of the therapies that make up the spectrum of CAM are based on theories of personal development and individual autonomy, so that they support patients in their journey to become 'whole', 'integrated' and responsible for their own health. This is sometimes seen in terms of a paradigm shift that is currently in progress:

> *The old paradigm was that the human body functions like a machine. The new paradigm focuses on the interconnectedness of body, mind, emotions, social factors, and the environment in determining the status of health.*
> *(Murray and Pizzorno, 1998)*

Dewey's pragmatism rejected such dualisms and sought to use scientific method to create a more intelligent way of working that integrated both scientific method and the way we learn from everyday experiences. He did not reject the scientific method and he was very clear about it's value and importance because *"it's comparative maturity as a form of knowledge exemplifies so conspicuously the necessary place and function of experimentation*" (Biesta and Burbules, 2003)

But his appreciation for the scientific method does not mean that science is the only valid form of knowledge and he rejected the idea that knowledge is the only way in which we can get in touch with reality. This broader definition of knowledge allows the scientific approach to include the rigorous use of both qualitative and quantitative methods to capture what is most characteristic of human life and experience.

One way to understand Dewey's project is to see it as an attempt to undo this mistake so that those dimensions of our being in the world that cannot be traced back to (scientific) knowledge can again be seen as real and rational. (Biesta and Burbules, 2003)

He sought to reconnect scientific thought with an appreciation of to the realm of values, the realm that had been split off or separated by the dualisms of Plato and Descartes. He argued that the domains of action and knowledge were intimately connected and that all knowledge, scientific and non-scientific, is generated by action and is therefore fallible and subject to change.

Like Dewey, researchers using the MMR approach also are attempting to reconcile the gulf between traditional and CAM medicine, by using a robust pragmatic philosophical framework to promote a more 'intelligent' way of working.

If we take forward his idea that progression should not be merely a negative reaction to tradition, we can look for ways to benefit patients by using the best 'evidence' from both the quantitative 'scientific' approach and the new paradigm that recognises the qualitative aspects of health and disease. The articles reviewed next in this section are an exploration of this idea.

A New Look at Medicine and the Mind-Body Problem: Can Dewey's Pragmatism Help Medicine Connect with Its Mission? (Shelton, 2013)

Shelton has a constructivist and pragmatist world view that acknowledges the dualisms of the Cartesian world view and the Faustian pact that medicine has made to trade advances in healthcare and scientific understanding for the humanist holistic approach to patients and their suffering. The multiple perspectives of patients and practitioners are acknowledged as he discusses

the practical implications of the issues for the education of doctors and the practice of medicine.

My perspective in that paper was based on Dewey's pragmatism, which clearly grounds all philosophical problems and issues in the historical process of human culture and society. (Shelton, 2014)

The author describes the changes to the American health care system, and medical education system that have taken place in the 20th and 21st century. He describes how the medical culture of the United States has been shaped by the dominant modern philosophical paradigm and how the cultural and institutional life of modern medicine has its source in the modern Cartesian legacy of mind-body dualism.

His theory is that Dewey, in 1927 was a prophetic voice who made his analysis from a *mature philosophical perspective,* seeing dualism of mind and body as a profound practical problem throughout modern society and especially in the cultural life and activity of scientific medicine.

The central element in this crisis is the disintegrating influence of modern science on everyday life that has changed our understanding of the world to a mechanistic worldview. The result has been a devaluing of the reality of the everyday experiences of men and the noncognitive dimensions of human life (Biesta and Burbules, 2003)

Dewey preferred to see the mind and body as *an integrated whole with nuanced functions and qualities of integrated action.* The narrowly focused scientific perspective, taken alone, not only cuts off mind from the individual human being, it cuts off the environment from behavior by seeing environment as a purely external occasion from which behavior proceeds.

He describes how Dewey also recognized that it is not just the natural environment that is important but also the social environment because it is the social environment that explains how individual humans engage in

speech acts and thinking, the social forms of organized human life of which human consciousness is predicated.

That the rise of medical ethics and humanities in the early 1970's has highlighted the value-laden dimensions of medicine and the physician-practitioner relationship but these are taught and seen as separate from the 'hard language of chemistry and physics'. The values of humanities and ethics are still seen as less important that the value of mastering scientific knowledge. The implication of becoming proficient in evidence-based medicine is that it directs the attention of learners toward the particular disease mechanism and away from the whole person.

Dewey acknowledges that there is an appropriate time for perspectives such as detachment and objectivity but the key point is that any one perspective necessary to care for some needs of the total patient, will not adequately address certain other needs.

Shelton is arguing for a reconnection of medicine with its core mission of caring for the whole person. In line with his pragmatic worldview he is looking for practical ways to nurture this standard of excellence into the practice habits of new physicians by changing both the taught curriculum and the structure of the learning environment.

The use of evidence-based medicine to train doctors is replaced by the concept of becoming the 'virtuous practitioner' as described on page 437. The questions facing the medical education system are 'what kind of practitioners are we striving to educate in a healthcare system driven by market forces and a dominant positivist paradigm? How will these traits be nurtured over a lifetime of learning and practice?'

He quotes the voice of Francis Peabody (1927) who expressed a similar perspective that clinical medicine should care for the total needs of the whole person and we therefore require a certain kind of physician who can deal

with the complex unity of biological, physical, mental, psychological and spiritual factors that makes up the whole person.

'*Diagnosing and treating the disease alone is comparable to the work of a mechanic. But managing the illness of the whole human being is the task of the physician as a clinical artist.'*

'Changing this mindset requires a philosophical perspective that gives equal epistemic standing to all relevant clinical aspects of patient care and unites them into an underlying sense of moral purpose dedicated to provide total care for the patient.'

Shelton provides an insight into the way that the dominant paradigm has become embedded in the provision of healthcare and the education of doctors. He provides an argument with a strong philosophical basis for an emphasis on a more integrated holistic approach to medicine that recognises the needs of society and the individual.

He provides practical suggestions for the way that medicine is taught in order to achieve this including a need to create financial framework for practitioners who wish to train others in a holistic approach. And need to recruit, train and retain 'virtuous' practitioners who can balance private gain and public good in a healthcare system. This concept of 'virtue' is also linked to the Dewey's concept of intelligence, which extends to the crucial importance of self-reflection in medical education, so that physicians are aware of their own attitudes and biases in their encounters with patients.

If this vision is to be achieved then more research into the holistic aspects of health and disease will be needed. This could also be seen as a need for mixed methods research including qualitative research approaches to measure some of these 'virtuous' qualities and their effect on patients.

Shelton recognises the value of both approaches to medicine and healing but acknowledges that no one perspective can provide the whole answer. A

pluralistic philosophy such as Pragmatism provides a framework for reconciling the dualistic views.

The reconciliation of dichotomies or dualities has been a repeating theme through out this literature search, the inherent tension between qualitative and quantitative, progression and tradition, medicine and CAM, the interests of patients and researchers, the scientific standing of doctors and other healthcare providers are all examples of this theme.

It is common to refer to these differences as originating from a different paradigm, and this concept has been used in different ways in the literature (Morgan, 2007). Three essential characteristics of a paradigm can be identified (Harrits, 2011): Firstly it is a set of ontological and epistemological assumptions made about the nature of social reality and the way in which we come to know this reality. Secondly it is a research practice or a specific way of conducting research within a research community. Thirdly, paradigms may have different philosophical assumptions, but this does not imply that they are necessarily incommensurable, having no common measure or fraction.

If they are to be found commensurable then transparency and consistency must be employed in the reporting of the philosophical and methodological choices made. Mesel reflects on this when he says, '*transparency on the philosophical level is important for validity and consistency as well as for attempts to integrate or establish an interface to other research.'(Mesel, 2013)*

Mesel is writing in the context of his role as an Associate Professor of a Department of Religion, Philosophy and History at a Norwegian University Hospital. He is able to argue that the if we make our basic assumptions transparent and available for reflection, then we can start to identify the new positions and formulations which allow the integration of data from different paradigms. He is working from the 'bottom up' starting with the most fundamental category, the philosophical worldview.

It is interesting to compare his perspective with other pragmatist researchers who are working from the other end of the spectrum or ‘top down’. For example, Cornish (Cornish and Gillespie, 2009) who are working in a health psychology context in the field of nursing and midwifery. Their challenge is to be able to promote speedy and positive social action, that addresses the moral, political and social conditions, but they have to make those changes based upon choices between opposing forms of knowledge. They see Pragmatism as an approach that can reconcile the two traditions in health psychology, which can be described at their most basic level, as realism and constructivism.

Although at the time of publication MMR is not a common approach in Scandinavia, and this would explain why Mesel would say that there is a tendency to create dichotomies between qualitative and quantitative methodology within healthcare research.

For example qualitative studies have been recognised as making an important contribution the scientific knowledge of medical sociology and nursing science. Evidence based research within nursing and medicine has concentrated on randomised controlled trials in which quantitative methodology has been the main source of knowledge (Mesel, 2013).

He recognises that clinical practice utilizes both quantitative and qualitative forms of knowledge and that clinical decisions and choices may be influenced by interviews with patients, previous experience as well as data from clinical trials. Cornish rejects the idea of an absolute hierarchy of knowledge with randomised controlled trials at the pinnacle and argues instead that different forms of knowledge are needed for different audiences and purposes.

Knowledge for taking care of oneself (Cornish and Gillespie, 2009)

- Health education has been criticized for taking biomedical accurate information (such as that provided by RCT’s) and assuming that if lay

people are given this information they will think rationally and act accordingly. While an RCT provides service users with useful information it does not help patients make sense of an illness or forge a new identity.

- An illness can change the meaning of a person's life, their relationships, their work and their very self. In creating their health identities people may draw on medical and non-medical knowledge.

- Health researchers can use qualitative methodologies such as grounded theory or discourse analysis to discover which strategies and skills are needed by people to cope with their illnesses. The health researcher could support the construction of knowledge in support groups, survivor groups and service user groups.

- Alternatively action research may help create new strategies or transform service provision to better reflect the needs of others. From a pragmatist point of view the knowledge needs to be useful or actionable from the point of view of the people it is trying to help.

Knowledge for intervention design (Cornish and Gillespie, 2009).

- Health intervention designers face challenges of implementation. They have to work with the complex, real world, everyday practicalities of individuals and communities, where familial, financial, political, cultural and social dimensions are deeply entwined with health behaviours and outcomes.

- Programme success often depends, not only on the evidence base of the intervention but on the skills of ensuring acceptability to service users, commitment from local healthcare workers, and support of managers or powerful stakeholder.

- An RCT may offer some confidence that a chosen method has worked in the past but a new context will produce uncertainties, exceptions, obstacles, and dilemmas that have to be managed.

- Programme designers need generative, adaptive and flexible knowledge to guide them through novel situations. Theories and models can provide such flexible knowledge. Richly detailed case studies can support the development of context-sensitive expertise and skilled decision-making.

Knowledge for cultural critique (Cornish and Gillespie, 2009)

- A pragmatist perspective values research activity, which creates new ways of thinking and acting and thus creating a richer future. The multiple interests that might be served by health research leads us to reject the idea of an absolute hierarchy of evidence although methods might be better than others in relation to particular interests.

- Pragmatism does not determine whose interests should be advanced through research. They suggest three means that health researchers might use to inform their choice of interest to pursue:

1. Tackle problems defined by people's experience
2. Choose problems through public deliberation
3. Critique the choice of interests being served.

Mesel suggests that a focus on justifying the value of a pluralistic approach may be explained by sociological factors such as the power balance between groups of professionals. The professionalism of nurses and their struggle for scientific autonomy and status have led to a need for their qualitative researchers to have strong arguments in favour of the validity of their methods (Mesel, 2013).

He argues that the current philosophical landscape is both complex and nuanced and therefore to avoid falling into twin pitfalls traps of endless debate, or an 'anything goes' form of pragmatic action, that transparent and consistent philosophical declarations should be make on all sides. He agrees with Cornish that a research community that is creative and pluralistic best serves the complex needs of modern healthcare and that mixed methods offer a promising asset in healthcare research.

Limitations To This Narrative Review

The main limitation to this section is that it is not a systematic exploration of Pragmatism, it is a personal exploration of the philosophy that emerged from the process of rewriting and the application of the new world view to the data, methodology, theoretical framework and results of this thesis. The disadvantages of Pragmatism as a worldview are not fully explored and the bias towards the usefulness of pragmatism is recognised as a limitation of this study.

Conclusion

Research Questions:

What is Pragmatism? How does it inform this thesis?

In this section, the methodology chapter and in the introduction I have written about how engaging with pragmatism allowed me to move away from the early assumptions that shaped the early phases of this research project. The general characteristics of pragmatism (Johnson and Onwuegbuzie, 2004) can be used as a framework here to provide practical examples of this change of worldview.

1. Finding a middle ground.

The initial strands were informed by a dominant medical paradigm as the social environment for a study about complementary or alternative medicine.

The parallels between progressive education and complementary medicine, as explored by Dewey (Dewey, 1910a),(Dewey, 1916), as well as in more recent analyses of his work (Shelton, 2013) challenged these assumptions and allowed me to find an intellectually valid space in which to work between these dualisms.

2. Rejects traditional dualisms.

An exploration of the dualisms between a purely scientific position and a holistic approach to healthcare research and knowledge (Cornish and Gillespie, 2009) gave rise to a better understanding of the need for my research to see not just the disease but also the person. The work of Dewey on the reflex arch (Dewey, 1896), the regulatory systems of homotoxicology] (Smit et al., 2010) and the medical model of PNEI are explored in this thesis to describe the connection between mind and body, stress and infertility.

3. Recognises the existence and importance of the natural or physical world as well as the emergent social and psychological world.

By allowing equal value to be placed on the construction of knowledge from qualitative sources as well as the collection of data under controlled conditions, I was able to reconcile the tension of working with the two paradigms (Mesel, 2013).

4. Places high regard for the reality of and influence of the inner world of human experience in action.

The adoption of a pragmatist perspective allowed me to see that it was worth continuing with the project after the failure of the RCT because the understanding of why it failed was useful for future trial designs. If resilience and persistence in the face of difficulty are the hallmarks of a good researcher then pragmatism is surely the researchers best friend and tool for cultivating these traits.

5. Knowledge is viewed as being both constructed and based on the reality of the world we experience and live in.

Pragmatism provided the philosophical framework for adopting the mixed methods research approach and allowed me to include the multiple perspectives of staff, patients and researchers into the trial design, results and analysis. Had this taken place earlier then the outcomes of the RCT trial might have been improved.

6. Organisms are constantly adapting to new situations and environments. Our thinking follows a dynamic homeostatic process of belief, doubt, inquiry, modified belief, new doubt, new inquiry…in an infinite loop, where the person or researcher (and research community) constantly tries to improve upon past understandings in a way that fits and works in the world in which he or she operates. The more intelligent use of theory, and a more intelligent way of working (Dewey, 1910b) contributed to the eventual success of the thesis in my second viva and will inform my future projects: *The present is always a new starting point*.(Johnson and Onwuegbuzie, 2004)

7. Views current truth, meaning and knowledge as tentative and as changing over time. What we obtain on a daily basis in research should be viewed as provisional truths. The need for philosophical transparency in the reporting of the project was highlighted by my reading (Mesel, 2013), (Cornish and Gillespie, 2009) and this focus allowed me to improve my writing of the methodology as well as helping me to clarify my thinking.

Literature Review- Section 2 The Definitions, Prevalence and Treatment of Female Infertility

Research Questions

How is infertility defined in published studies, in working practice, what is the estimated prevalence – global and UK? What is the recommended treatment for female infertility?

Introduction

The site for the planned RCT trial of Ovarium compositum was an assisted reproduction unit (ARU) at Jersey General Hospital and the audience for the trial protocol was a conventional medical audience. The trial design and choice of literature for this phase of the study reflects the need to work within the dominant biomedical paradigm and to have an understanding of the recommended treatments.

Infertility is a major, multifaceted issue worldwide whose prevalence is increasing in both high- and low-income countries (Petraglia et al., 2013) but the specific focus of this search was to find an estimate of global female infertility and working definitions of infertility that could be used in this thesis.

Methodology

The selection of papers can be summarised in four steps as seen in Figure 2.

1. A preliminary search of the literature was performed using MeSH terms "Humans" AND "Infertility/epidemiology" AND "Prevalence" NOT "male infertility on PubMed, resulting in 110 articles. The date of the search was 15th February 2015. The results were filtered for full text articles on human subjects in the last ten years and an additional information source was also included (Fields et al., 2013):

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2. The abstracts for each of these articles were read and sorted into broad themes as detailed below Table 6 The results of the preliminary literature search and Figure 3 Thematic Sorting of Preliminary Search Results

3. The articles that had the best fit to the research question were shortlisted for critical reading and review using the checklist previously described in

Table 4: Checklist of questions for critical reading of selected articles

Selection criteria - These 8 papers (Table 8 Shortlist of 8 papers on the prevalence of infertility) were chosen from the 110 initial candidates to provide an up-to-date estimate of the prevalence of global infertility as well as exploring the definitions of infertility and the types of data used for such estimates. The criteria for including them was that their main focus was on the prevalence of infertility on an international or global dimension, that they were peer reviewed and published in the last 10 years.

4. Three articles were chosen to review in greater detail for this section and the additional information source was included in this analysis(Fields et al., 2013):

1. Fertility (update): summary of NICE guidance (Fields et al., 2013)

2. International estimates of infertility prevalence and treatment-seeking: potential need and demand for infertility medical care (Boivin et al., 2007)

3. National, Regional, and Global Trends in Infertility Prevalence Since 1990: A Systematic Analysis of 277 Health Surveys (Mascarenhas et al., 2012b)

4. Defining infertility – a systematic review of prevalence studies (Gurunath et al., 2011)

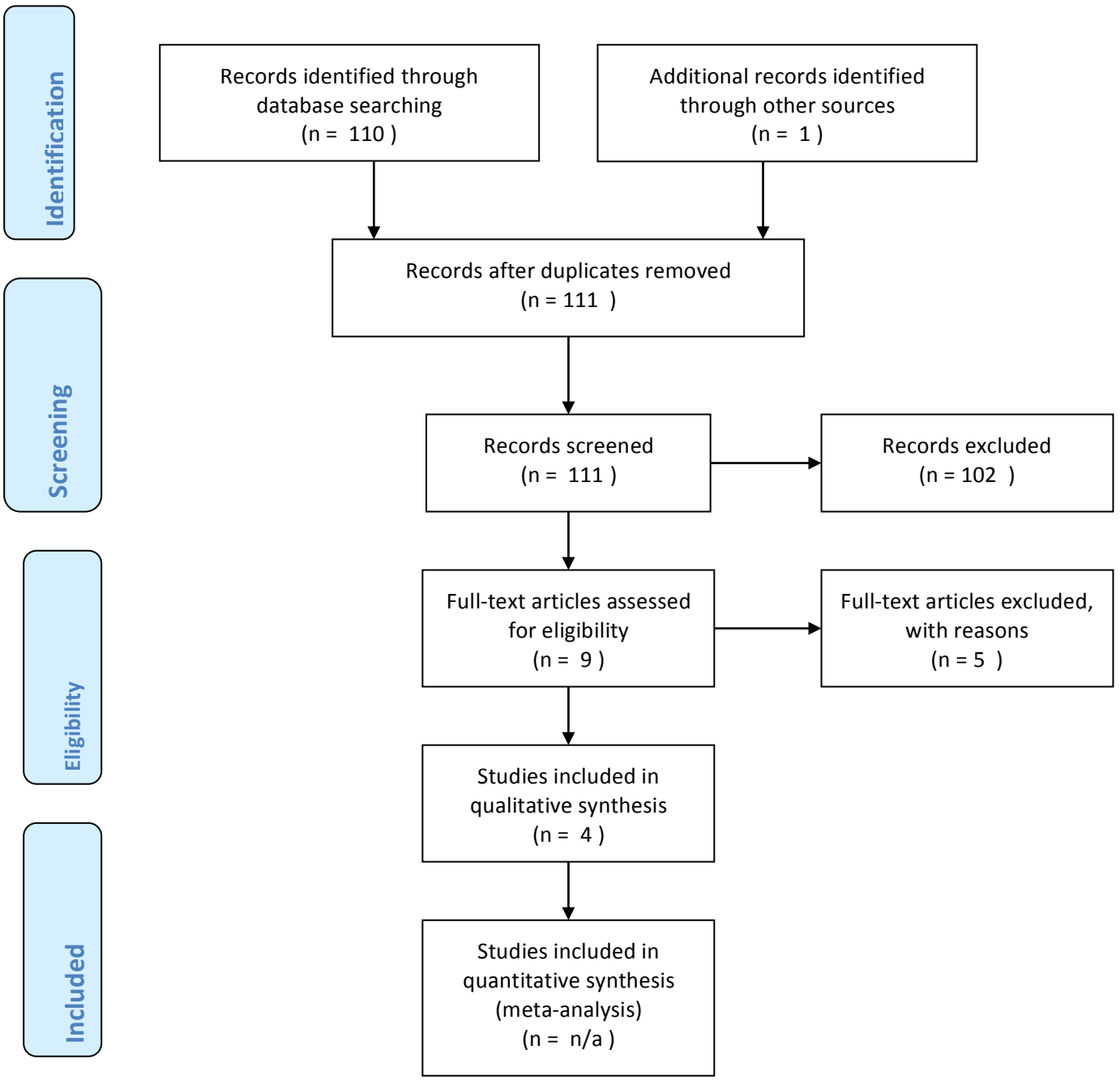
These papers were chosen to provide an up-to-date estimate of the prevalence of global infertility as well as exploring the definitions of infertility and the types of data used for such

estimates. The two systematic reviews were chosen as they represented a more complete and reliable form of evidenced compared to the papers that were excluded. The papers were read critically using the list of questions for as explained in the methodology section of this chapter

Table 4: Checklist of questions for critical reading of selected articles. There was no quantitative synthesis or meta-analysis of the papers.

PRISMA 2009 Flow Diagram

Figure 2 Selection Process for Literature Review on Prevalence and Treatment of Infertility



Results of Literature Searches

Table 6 The results of the preliminary literature search

Name and details of paper found using MeSH search terms **Humans** **Infertility/epidemiology*** **Prevalence** **Not male infertility**	**Reference for bibliography**	**What is the main focus of the paper?**
1: Cedars MI. Introduction: Childhood implications of parental aging. Fertil Steril. 2015 Jun;103(6):1379-80. doi: 10.1016/j.fertnstert.2015.04.011. Epub 2015 Apr 30. PubMed PMID: 25936233.	(Cedars, 2015)	Parental Aging
2: Oron G, Esh-Broder E, Son WY, Holzer H, Tulandi T. Predictive value of maternal serum human chorionic gonadotropin levels in pregnancies achieved by invitro fertilization with single cleavage and single blastocyst embryo transfers. Fertil Steril. 2015 Jun;103(6):1526-31.e1-2. doi: 10.1016/j.fertnstert.2015.02.028. Epub 2015 Apr 22. PubMed PMID: 25910571.	(Oron et al., 2015)	IVF
3: Stern JE, Luke B, Tobias M, Gopal D, Hornstein MD, Diop H. Adverse pregnancy and birth outcomes associated with underlying diagnosis with and without assisted reproductive technology treatment. Fertil Steril. 2015 Jun;103(6):1438-45. doi: 10.1016/j.fertnstert.2015.02.027. Epub 2015 Mar 23. PubMed PMID: 25813277; PubMed Central PMCID: PMC4465778.	(Stern et al., 2015)	ART
4: Reichelt J, Kyvernitakis I, Misselwitz B, Hadji P, Schmidt S, Kalder M. A population based evaluation of the mode of delivery in association with infertility treatment from 1990-2012. Z Geburtshilfe Neonatol. 2015 Feb;219(1):37-44. doi: 10.1055/s-0034-1390414. Epub 2015 Mar 3. PubMed PMID: 25734476.	(Reichelt et al., 2015)	ART
5: Joham AE, Teede HJ, Ranasinha S, Zoungas S, Boyle J. Prevalence of infertility and use of fertility treatment in women with polycystic ovary syndrome: data from a large community-based cohort study. J Womens	(Joham et al., 2015)	Female reproductive pathology

Health (Larchmt). 2015 Apr;24(4):299-307. doi: 10.1089/jwh.2014.5000. Epub 2015 Feb 5. PubMed PMID: 25654626.		
6: Alvarez S. Do some addictions interfere with fertility? Fertil Steril. 2015 Jan;103(1):22-6. doi: 10.1016/j.fertnstert.2014.11.008. Review. PubMed PMID: 25552409.	(Alvarez, 2015)	Environmental factors
7: Cromi A, Serati M, Candeloro I, Uccella S, Scandroglio S, Agosti M, Ghezzi F. Assisted reproductive technology and breastfeeding outcomes: a case-control study. Fertil Steril. 2015 Jan;103(1):89-94. doi: 10.1016/j.fertnstert.2014.10.009. pub 2014 Oct 29. PubMed PMID: 25456795.	(Cromi et al., 2015)	ART
8: Tsai YR, Huang FJ, Lin PY, Kung FT, Lin YJ, Lin YC, Lan KC. Progesterone elevation on the day of human chorionic gonadotropin administration is not the only factor determining outcomes of in vitro fertilization. Fertil Steril. 2015 Jan;103(1):106-11. doi: 10.1016/j.fertnstert.2014.10.019. Epub 2014 Nov 20. PubMed PMID: 25455869.	(Tsai et al., 2015)	Drug interventions
9: Jackson S, Hong C, Wang ET, Alexander C, Gregory KD, Pisarska MD. Pregnancy outcomes in very advanced maternal age pregnancies: the impact of assisted reproductive technology. Fertil Steril. 2015 Jan;103(1):76-80. doi: 10.1016/j.fertnstert.2014.09.037. Epub 2014 Oct 25. PubMed PMID: 25450294.	(Jackson et al., 2015)	ART
10: Akhtar MA, Sur S, Raine-Fenning N, Jayaprakasan K, Thornton J, Quenby S, Marjoribanks J. Heparin for assisted reproduction: summary of a Cochrane review. Fertil Steril. 2015 Jan;103(1):33-4. doi: 10.1016/j.fertnstert.2014.09.005. Epub 2014 Oct 1. Review. PubMed PMID: 25282470.	(Akhtar et al., 2015)	Drug interventions
11: Turan V, Kopuz A, Ozcan A, Kocakaya B, Sahin C, Solmaz U. Sexual dysfunction in infertile Turkish females: prevalence and risk factors. Eur J Obstet Gynecol Reprod Biol. 2014 Nov;182:128-31. doi: 10.1016/j.ejogrb.2014.09.013. Epub 2014 Sep 18. PubMed PMID: 25268781.	(Turan et al., 2014)	Sexual Dysfunction

12: Dhalwani NN, West J, Sultan AA, Ban L, Tata LJ. Women with celiac disease present with fertility problems no more often than women in the general population. Gastroenterology. 2014 Dec;147(6):1267-74.e1; quiz e13-4. doi: 10.1053/j.gastro.2014.08.025. Epub 2014 Aug 23. PubMed PMID: 25157666.	(Dhalwani et al.)	Concurrent pathology
13: Schliep KC, Mumford SL, Hammoud AO, Stanford JB, Kissell KA, Sjaarda LA, Perkins NJ, Ahrens KA, Wactawski-Wende J, Mendola P, Schisterman EF. Luteal phase deficiency in regularly menstruating women: prevalence and overlap in identification based on clinical and biochemical diagnostic criteria. J Clin Endocrinol Metab. 2014 Jun;99(6):E1007-14. doi: 10.1210/jc.2013-3534. Epub 2014 Feb 27. PubMed PMID: 24606080; PubMed Central PMCID: PMC4037737.	(Schliep et al., 2014)	Female reproductive pathology
14: Dinelli L, Courbière B, Achard V, Jouve E, Deveze C, Gnisci A, Grillo JM, Paulmyer-Lacroix O. Prognosis factors of pregnancy after intrauterine insemination with the husband's sperm: conclusions of an analysis of 2,019 cycles. Fertil Steril. 2014 Apr;101(4):994-1000. doi: 10.1016/j.fertnstert.2014.01.009. Epub 2014 Feb 15. PubMed PMID: 24534285.	(Dinelli et al., 2014)	ART
15: Zhang H, Wang S, Zhang S, Wang T, Deng X. Increasing trend of prevalence of infertility in Beijing. Chin Med J (Engl). 2014;127(4):691-5. PubMed PMID: 24534224.	(Zhang et al., 2014)	Specific geographic location and prevalence.
16: Rasheed SM, Amin MM, Abd Ellah AH, Abo Elhassan AM, El Zahry MA, Wahab HA. Reproductive performance after conservative surgical treatment of postpartum hemorrhage. Int J Gynaecol Obstet. 2014 Mar;124(3):248-52. doi: 10.1016/j.ijgo.2013.08.018. Epub 2013 Nov 23. PubMed PMID: 24380610.	(Rasheed et al., 2014)	Surgery (risks and benefits).
17: Kentenich H, Sibold C, Tandler-Schneider A. [In vitro fertilization and intracytoplasmic sperm injection: current medical aspects]. Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz. 2013 Dec;56(12):1653-61. doi: 10.1007/s00103-013-1853-8. Review. German. PubMed PMID:	(Kentenich et al., 2013)	IVF

24337127.		
18: Petraglia F, Serour GI, Chapron C. The changing prevalence of infertility. Int J Gynaecol Obstet. 2013 Dec;123 Suppl 2:S4-8. doi: 10.1016/j.ijgo.2013.09.005. Epub 2013 Sep 7. PubMed PMID: 24112745.	(Petraglia et al., 2013)	Sexually Transmitted Diseases, contraception, incidence of infertility.
19: Malloch L, Rhoton-Vlasak A. An assessment of current clinical attitudes toward letrozole use in reproductive endocrinology practices. Fertil Steril. 2013 Dec;100(6):1740-4. doi: 10.1016/j.fertnstert.2013.08.040. Epub 2013 Oct 7. PubMed PMID: 24112529.	(Malloch and Rhoton-Vlasak, 2013)	Drug interventions
20: Turan V, Bedoschi G, Moy F, Oktay K. Safety and feasibility of performing two consecutive ovarian stimulation cycles with the use of letrozole-gonadotropin protocol for fertility preservation in breast cancer patients. Fertil Steril. 2013 Dec;100(6):1681-5.e1. doi: 10.1016/j.fertnstert.2013.08.030. Epub 2013 Sep 19. PubMed PMID: 24055050; PubMed Central PMCID: PMC3888552.	(Turan et al., 2013)	Fertility and oncology
21: Timberlake KS, Foley KL, Hurst BS, Matthews ML, Usadi RS, Marshburn PB. Association of blood type and patient characteristics with ovarian reserve. Fertil Steril. 2013 Dec;100(6):1735-9. doi: 10.1016/j.fertnstert.2013.08.027. Epub 2013 Sep 19. PubMed PMID: 24055049.	(Timberlake et al., 2013)	ART
22: Xiao J, Chang S, Chen S. The effectiveness of gonadotropin-releasing hormone antagonist in poor ovarian responders undergoing in vitro fertilization: a systematic review and meta-analysis. Fertil Steril. 2013 Dec;100(6):1594-601.e1-9. doi: 10.1016/j.fertnstert.2013.08.024. Epub 2013 Sep 19. Review. PubMed PMID: 24055048.	(Xiao et al., 2013)	Use of hormones in IVF

23: Boots CE, Gustofson RL, Feinberg EC. Does methotrexate administration for ectopic pregnancy after in vitro fertilization impact ovarian reserve or ovarian responsiveness? Fertil Steril. 2013 Dec;100(6):1590-3. doi: 10.1016/j.fertnstert.2013.08.007. Epub 2013 Sep 12. PubMed PMID: 24035728.	(Boots et al., 2013)	Drug interventions
24: Marci R, Marcucci I, Marcucci AA, Pacini N, Salacone P, Sebastianelli A, Caponecchia L, Lo Monte G, Rago R. Hysterosalpingocontrast sonography (HyCoSy): evaluation of the pain perception, side effects and complications. BMC Med Imaging. 2013 Aug 23;13:28. doi: 10.1186/1471-2342-13-28. PubMed PMID: 23968513; PubMed Central PMCID: PMC3765383.	(Marci et al., 2013)	MRI & Imaging
25: du Bois A, Heitz F, Harter P. Fertility-sparing surgery in ovarian cancer: a systematic review. Onkologie. 2013;36(7-8):436-43. doi: 10.1159/000353598. Epub 2013 Jul 8. Review. PubMed PMID: 23921764.	(du Bois et al., 2013)	Fertility and oncology
26: Ziller V, Hadji P, Thielscher C, Ziller M, Kostev K. Prevalence of female subfertility in German gynecological practices. Gynecol Endocrinol. 2013 Aug;29(8):767-70. doi: 10.3109/09513590.2013.798274. Epub 2013 Jun 5. PubMed PMID: 23738676.	(Ziller et al., 2013)	Specific geographic location and prevalence.
27: Moini A, Mohammadi S, Hosseini R, Eslami B, Ahmadi F. Accuracy of 3-dimensional sonography for diagnosis and classification of congenital uterine anomalies. J Ultrasound Med. 2013 Jun;32(6):923-7. doi: 10.7863/ultra.32.6.923. PubMed PMID: 23716512.	(Moini et al., 2013)	MRI & Imaging
28: Song S. Assessing the impact of in utero exposure to famine on fecundity: evidence from the 1959-61 famine in China. Popul Stud (Camb). 2013;67(3):293-308. doi: 10.1080/00324728.2013.774045. Epub 2013 Mar 15. PubMed PMID: 23495746.	(Song, 2013)	Environmental factors
29: Tomassetti C, Meuleman C, Timmerman D, D'Hooghe T. Adenomyosis and subfertility: evidence of association and causation. Semin Reprod Med. 2013 Mar;31(2):101-8. doi: 10.1055/s-0032-1333475. Epub 2013 Feb 27. Review. PubMed PMID: 23446857.	(Tomassetti et al., 2013)	Female reproductive pathology

30: Thoma ME, McLain AC, Louis JF, King RB, Trumble AC, Sundaram R, Buck Louis GM. Prevalence of infertility in the United States as estimated by the current duration approach and a traditional constructed approach. Fertil Steril. 2013 Apr;99(5):1324-1331.e1. doi: 10.1016/j.fertnstert.2012.11.037. Epub 2013 Jan 3. PubMed PMID: 23290741; PubMed Central PMCID: PMC3615032.	(Thoma et al., 2013)	Specific geographic location and prevalence.
31: Mascarenhas MN, Flaxman SR, Boerma T, Vanderpoel S, Stevens GA. National, regional, and global trends in infertility prevalence since 1990: a systematic analysis of 277 health surveys. PLoS Med. 2012;9(12):e1001356. doi: 10.1371/journal.pmed.1001356. Epub 2012 Dec 18. PubMed PMID: 23271957; PubMed Central PMCID: PMC3525527.	(Mascarenhas et al., 2012a)	Systematic review of infertility prevalence
32: Malizia BA, Dodge LE, Penzias AS, Hacker MR. The cumulative probability of liveborn multiples after in vitro fertilization: a cohort study of more than 10,000 women. Fertil Steril. 2013 Feb;99(2):393-9. doi: 10.1016/j.fertnstert.2012.10.018. Epub 2012 Nov 8. PubMed PMID: 23141053.	(Malizia et al., 2013)	IVF (singletons vrs multiple births)
33: Esmaeilzadeh S, Delavar MA, Zeinalzadeh M, Mir MR. Epidemiology of infertility: a population-based study in Babol, Iran. Women Health. 2012;52(8):744-54. doi: 10.1080/03630242.2012.728191. PubMed PMID: 23127216.	(Esmaeilzadeh et al., 2012)	Specific geographic location and prevalence.
34: Butts SF, Ratcliffe S, Dokras A, Seifer DB. Diagnosis and treatment of diminished ovarian reserve in assisted reproductive technology cycles of women up to age 40 years: the role of insurance mandates. Fertil Steril. 2013 Feb;99(2):382-8. doi: 10.1016/j.fertnstert.2012.09.026. Epub 2012 Oct 23. PubMed PMID: 23102859; PubMed Central PMCID: PMC3561490.	(Butts et al., 2013)	Relationship between funding and diagnosis MRI & Imaging
35: Shapiro BS, Daneshmand ST, Restrepo H, Garner FC, Aguirre M, Hudson C. Matched-cohort comparison of single-embryo transfers in fresh and frozen-thawed embryo transfer cycles. Fertil Steril. 2013	(Shapiro et al., 2013)	IVF (singletons vrs multiple births)

Feb;99(2):389-92. doi: 10.1016/j.fertnstert.2012.09.044. Epub 2012 Oct 11. PubMed PMID: 23062733.		
36: Nakashima A, Araki R, Tani H, Ishihara O, Kuwahara A, Irahara M, Yoshimura Y, Kuramoto T, Saito H, Nakaza A, Sakumoto T. Implications of assisted reproductive technologies on term singleton birth weight: an analysis of 25,777 children in the national assisted reproduction registry of Japan. Fertil Steril. 2013 Feb;99(2):450-5. doi: 10.1016/j.fertnstert.2012.09.027. Epub 2012 Oct 9. PubMed PMID: 23058683.	(Nakashima et al., 2013)	IVF (singletons vrs multiple births)
37: Schweiger U, Wischmann T, Strowitzki T. [Mental disorders and female infertility]. Nervenarzt. 2012 Nov;83(11):1442-7. doi: 10.1007/s00115-012-3662-y. Review. German. Erratum in: Nervenarzt. 2013 Mar;84(3):369. PubMed PMID: 23052895.	(Schweiger et al., 2012)	Psychological and Emotional Factors
38: Hagen CP, Vestergaard S, Juul A, Skakkebæk NE, Andersson AM, Main KM, Hjøllund NH, Ernst E, Bonde JP, Anderson RA, Jensen TK. Low concentration of circulating antimüllerian hormone is not predictive of reduced fecundability in young healthy women: a prospective cohort study. Fertil Steril. 2012 Dec;98(6):1602-8.e2. doi: 10.1016/j.fertnstert.2012.08.008. Epub 2012 Sep 6. PubMed PMID: 22959460.	(Hagen et al., 2012)	Hormone levels
39: Practice Committee of the American Society for Reproductive Medicine. Smoking and infertility: a committee opinion. Fertil Steril. 2012 Dec;98(6):1400-6. doi: 10.1016/j.fertnstert.2012.07.1146. Epub 2012 Sep 6. PubMed PMID: 22959451.	(2012)	Environmental Factors
40: Pakpour AH, Yekaninejad MS, Zeidi IM, Burri A. Prevalence and risk factors of the female sexual dysfunction in a sample of infertile Iranian women. Arch Gynecol Obstet. 2012 Dec;286(6):1589-96. doi: 10.1007/s00404-012-2489-x. Epub 2012 Aug 1. PubMed PMID: 22850887.	(Pakpour et al., 2012)	Sexual Dysfunction

41: Artini PG, Uccelli A, Papini F, Simi G, Di Berardino OM, Ruggiero M, Cela V. Infertility and pregnancy loss in euthyroid women with thyroid autoimmunity. Gynecol Endocrinol. 2013 Jan;29(1):36-41. doi: 10.3109/09513590.2012.705391. Epub 2012 Jul 27. Review. PubMed PMID: 22835333.	(Artini et al., 2013)	Concurrent pathology
42: M'Rabet N, Moffat R, Helbling S, Kaech A, Zhang H, de Geyter C. The CC-allele of the PvuII polymorphic variant in intron 1 of the α-estrogen receptor gene is significantly more prevalent among infertile women at risk of premature ovarian aging. Fertil Steril. 2012 Oct;98(4):965-72.e1-5. doi: 10.1016/j.fertnstert.2012.05.048. Epub 2012 Jun 29. PubMed PMID: 22749220.	(M'Rabet et al., 2012)	Genetics and Infertility
43: Haimov-Kochman R, Adler C, Ein-Mor E, Rosenak D, Hurwitz A. Infertility associated with precoital ovulation in observant Jewish couples; prevalence, treatment, efficacy and side effects. Isr Med Assoc J. 2012 Feb;14(2):100-3. PubMed PMID: 22693790.	(Haimov-Kochman et al., 2012)	Environmental Factors
44: Wiesenfeld HC, Hillier SL, Meyn LA, Amortegui AJ, Sweet RL. Subclinical pelvic inflammatory disease and infertility. Obstet Gynecol. 2012 Jul;120(1):37-43. doi: 10.1097/AOG.0b013e31825a6bc9. PubMed PMID: 22678036.	(Wiesenfeld et al., 2012)	Sexually Transmitted Diseases
45: Wan GH, Chung FF. Working conditions associated with ovarian cycle in a medical center nurses: a Taiwan study. Jpn J Nurs Sci. 2012 Jun;9(1):112-8. doi: 10.1111/j.1742-7924.2011.00191.x. Epub 2011 Sep 16. PubMed PMID: 22583945.	(Wan and Chung, 2012)	ART
46: Soares S, Rodrigues T, Barros H. [Infertility prevalence in the city of Porto]. Acta Med Port. 2011 Sep-Oct;24(5):699-706. Epub 2011 Dec 29. Portuguese. PubMed PMID: 22525620.	(Soares et al., 2011)	Specific geographical location
47: Reyes-Muñoz E, Castellanos-Barroso G, Ramírez-Eugenio BY, Ortega-González C, Parra A, Castillo-Mora A, De la Jara-Díaz JF. The risk of gestational diabetes mellitus among Mexican women with a history of infertility and polycystic ovary syndrome. Fertil Steril. 2012 Jun;97(6):1467-71. doi: 10.1016/j.fertnstert.2012.03.023. Epub 2012 Apr 13. PubMed PMID: 22503417.	(Reyes-Munoz et al., 2012)	Female reproductive pathology

48: Maheshwari A, Gurunath S, Fatima F, Bhattacharya S. Adenomyosis and subfertility: a systematic review of prevalence, diagnosis, treatment and fertility outcomes. Hum Reprod Update. 2012 Jul;18(4):374-92. doi: 10.1093/humupd/dms006. Epub 2012 Mar 22. Review. PubMed PMID: 22442261.	(Maheshwari et al., 2012)	Female reproductive pathology
49: Balcerek M, Reinmuth S, Hohmann C, Keil T, Borgmann-Staudt A. Suspected infertility after treatment for leukemia and solid tumors in childhood and adolescence. Dtsch Arztebl Int. 2012 Feb;109(7):126-31. doi: 10.3238/arztebl.2012.0126. Epub 2012 Feb 17. PubMed PMID: 22427790; PubMed Central PMCID: PMC3301974.	(Balcerek et al., 2012)	Fertility and oncology
50: Bushnik T, Cook JL, Yuzpe AA, Tough S, Collins J. Estimating the prevalence of infertility in Canada. Hum Reprod. 2012 Mar;27(3):738-46. doi: 10.1093/humrep/der465. Epub 2012 Jan 17. Erratum in: Hum Reprod. 2013 Apr;28(4):1151. PubMed PMID: 22258658; PubMed Central PMCID: PMC3279129.	(Bushnik et al., 2012)	Specific geographic location and prevalence.
51: Datta SD, Torrone E, Kruszon-Moran D, Berman S, Johnson R, Satterwhite CL, Papp J, Weinstock H. Chlamydia trachomatis trends in the United States among persons 14 to 39 years of age, 1999-2008. Sex Transm Dis. 2012 Feb;39(2):92-6. doi: 10.1097/OLQ.0b013e31823e2ff7. PubMed PMID: 22249296.	(Datta et al., 2012)	Sexually Transmitted Diseases
52: Baraitser P, Alexander S, Sheringham J. Chlamydia trachomatis screening in young women. Curr Opin Obstet Gynecol. 2011 Oct;23(5):315-20. doi: 10.1097/GCO.0b013e32834ac776. Review. PubMed PMID: 21897235.	(Baraitser et al., 2011)	Sexually Transmitted Diseases
53: Keskin U, Coksuer H, Gungor S, Ercan CM, Karasahin KE, Baser I. Differences in prevalence of sexual dysfunction between primary and secondary infertile women. Fertil Steril. 2011 Nov;96(5):1213-7. doi: 10.1016/j.fertnstert.2011.08.007. Epub 2011 Aug 30. PubMed PMID: 21880311.	(Keskin et al., 2011)	Sexual Dysfunction

54: Choi JM, Lebwohl B, Wang J, Lee SK, Murray JA, Sauer MV, Green PH. Increased prevalence of celiac disease in patients with unexplained infertility in the United States. J Reprod Med. 2011 May-Jun;56(5-6):199-203. PubMed PMID: 21682114; PubMed Central PMCID: PMC3122153.	(Choi et al., 2011)	Concurrent pathology
55: Shen L, Wang Q, Huang W, Wang Q, Yuan Q, Huang Y, Lei H. High prevalence of endometrial polyps in endometriosis-associated infertility. Fertil Steril. 2011 Jun 30;95(8):2722-4.e1. doi: 10.1016/j.fertnstert.2011.04.067. Epub 2011 May 14. PubMed PMID: 21575952.	(Shen et al., 2011)	Female reproductive pathology
56: Khoshbaten M, Rostami Nejad M, Farzady L, Sharifi N, Hashemi SH, Rostami K. Fertility disorder associated with celiac disease in males and females: fact or fiction? J Obstet Gynaecol Res. 2011 Oct;37(10):1308-12. doi: 10.1111/j.1447-0756.2010.01518.x. Epub 2011 May 11. PubMed PMID: 21561528.	(Khoshbaten et al., 2011)	Concurrent pathology
57: Gurunath S, Pandian Z, Anderson RA, Bhattacharya S. Defining infertility--a systematic review of prevalence studies. Hum Reprod Update. 2011 Sep-Oct;17(5):575-88. doi: 10.1093/humupd/dmr015. Epub 2011 Apr 14. Review. PubMed PMID: 21493634.	(Gurunath et al., 2011)	Systematic Review of prevalence
58: Cerquaglia C, Verrecchia E, Fonnesu C, Giovinale G, Marinaro A, de Socio G, Manna R. Female reproductive dysfunction in familial Mediterranean fever patients with and without colchicine treatment. Clin Exp Rheumatol. 2010 Jul-Aug;28(4 Suppl 60):S101. Epub 2010 Sep 24. PubMed PMID: 20868586.	(Cerquaglia et al., 2010)	Concurrent pathology
59: Tiboni GM, Verna I, Giampietro F, Leonzio E, Impicciatore GG. Cytogenetic findings and reproductive outcome of infertile couples referred to an assisted reproduction program. Gynecol Endocrinol. 2011 Sep;27(9):669-74. doi: 10.3109/09513590.2010.533799. Epub 2010 Dec 8. PubMed PMID: 21142403.	(Tiboni et al., 2011)	ART

60: Reh A, Chaudhry S, Mendelsohn F, Im S, Rolnitzky L, Amarosa A, Levitz M, Srinivasa S, Krey L, Berkeley AS, Grifo JA, Danoff A. Effect of autoimmune thyroid disease in older euthyroid infertile woman during the first 35 days of an IVF cycle. Fertil Steril. 2011 Mar 1;95(3):1178-81. doi: 10.1016/j.fertnstert.2010.09.053. Epub 2010 Nov 3. PubMed PMID: 21047632; PubMed Central PMCID: PMC3059547.	(Reh et al., 2011)	Concurrent pathology
61: Dhont N, Muvunyi C, Luchters S, Vyankandondera J, De Naeyer L, Temmerman M, van de Wijgert J. HIV infection and sexual behaviour in primary and secondary infertile relationships: a case--control study in Kigali, Rwanda. Sex Transm Infect. 2011 Feb;87(1):28-34. doi: 10.1136/sti.2010.042879. Epub 2010 Sep 18. PubMed PMID: 20852311.	(Dhont et al., 2011)	Sexually Transmitted Diseases
62: Al-Jaroudi D, Hussain TZ. Prevalence of abnormal cervical cytology among subfertile Saudi women. Ann Saudi Med. 2010 Sep-Oct;30(5):397-400. doi: 10.4103/0256-4947.68550. PubMed PMID: 20716829; PubMed Central PMCID: PMC2941254.	(Al-Jaroudi and Hussain, 2010)	Female reproductive pathology
63: Paris K, Aris A. Endometriosis-associated infertility: a decade's trend study of women from the Estrie region of Quebec, Canada. Gynecol Endocrinol. 2010 Nov;26(11):838-42. doi: 10.3109/09513590.2010.487590. PubMed PMID: 20486880.	(Paris and Aris, 2010)	Female reproductive pathology
64: Huddleston HG, Cedars MI, Sohn SH, Giudice LC, Fujimoto VY. Racial and ethnic disparities in reproductive endocrinology and infertility. Am J Obstet Gynecol. 2010 May;202(5):413-9. doi: 10.1016/j.ajog.2009.12.020. Epub 2010 Mar 6. Review. PubMed PMID: 20207341.	(Huddleston et al., 2010)	Genetics and infertility
65: Brown K, Apuzzio J, Weiss G. Maternal obesity and associated reproductive consequences. Womens Health (Lond Engl). 2010 Mar;6(2):197-203. doi: 10.2217/whe.10.9. PubMed PMID: 20187726.	(Brown et al., 2010)	Environmental factors
66: Souter I, Baltagi LM, Toth TL, Petrozza JC. Prevalence of hyperprolactinemia and abnormal magnetic resonance imaging findings in a population with	(Souter et al., 2010)	MRI & Imaging

infertility. Fertil Steril. 2010 Aug;94(3):1159-62. doi: 10.1016/j.fertnstert.2009.12.017. Epub 2010 Feb 8. PubMed PMID: 20116788.		
67: Ilangavan K, Kalu E. High prevalence of endometriosis in infertile women with normal ovulation and normospermic partners. Fertil Steril. 2010 Feb;93(3):e10; author reply e12. doi: 10.1016/j.fertnstert.2009.11.027. Epub 2009 Dec 29. PubMed PMID: 20036358.	(Ilangavan and Kalu, 2010)	Female reproductive pathology
68: Casadei L, Puca F, Privitera L, Zamaro V, Emidi E. Inherited thrombophilia in infertile women: implication in unexplained infertility. Fertil Steril. 2010 Jul;94(2):755-7. doi: 10.1016/j.fertnstert.2009.10.014. Epub 2009 Nov 25. PubMed PMID: 19939360.	(Casadei et al., 2010)	Concurrent pathology
69: Sharma S, Mittal S, Aggarwal P. Management of infertility in low resource countries. BJOG. 2009 Oct;116 Suppl 1:77-83. doi: 10.1111/j.1471-0528.2009.02311.x. Review. PubMed PMID: 19740177.	(Sharma et al., 2009)	Provision and management of infertile patients in developing or low resource countries.
70: Ronda E, García AM, Sánchez-Paya J, Moen BE. Menstrual disorders and subfertility in Spanish hairdressers. Eur J Obstet Gynecol Reprod Biol. 2009 Nov;147(1):61-4. doi: 10.1016/j.ejogrb.2009.07.020. Epub 2009 Aug 26. PubMed PMID: 19713029.	(Ronda et al., 2009)	Environmental Factors
71: Bhattacharya S, Porter M, Amalraj E, Templeton A, Hamilton M, Lee AJ, Kurinczuk JJ. The epidemiology of infertility in the North East of Scotland. Hum Reprod. 2009 Dec;24(12):3096-107. doi: 10.1093/humrep/dep287. Epub 2009 Aug 14. PubMed PMID: 19684046.	(Bhattacharya et al., 2009)	Specific geographic location and prevalence.
72: Dyer SJ. International estimates on infertility prevalence and treatment seeking: potential need and demand for medical care. Hum Reprod. 2009 Sep;24(9):2379-80; author reply 2380-3. doi: 10.1093/humrep/dep219. Epub 2009 Jun 20. PubMed PMID: 19542544.	(Dyer, 2009)	Infertility prevalence

73: Firouznia K, Ghanaati H, Sanaati M, Jalali AH, Shakiba M. Pregnancy after uterine artery embolization for symptomatic fibroids: a series of 15 pregnancies. AJR Am J Roentgenol. 2009 Jun;192(6):1588-92. doi: 10.2214/AJR.07.3904. PubMed PMID: 19457822.	(Firouznia et al., 2009)	Female reproductive pathology
74: Khawaja UB, Khawaja AA, Gowani SA, Shoukat S, Ejaz S, Ali FN, Rizvi J, Nawaz FH. Frequency of endometriosis among infertile women and association of clinical signs and symptoms with the laparoscopic staging of endometriosis. J Pak Med Assoc. 2009 Jan;59(1):30-4. PubMed PMID: 19213374.	(Khawaja et al., 2009)	Female reproductive pathology
75: Joy TR, Hegele RA. Prevalence of reproductive abnormalities among women with familial partial lipodystrophy. Endocr Pract. 2008 Dec;14(9):1126-32. PubMed PMID: 19158052.	(Joy and Hegele, 2008)	Female reproductive pathology
76: Liberty G, Hyman JH, Eldar-Geva T, Latinsky B, Gal M, Margalioth EJ. Ovarian hemorrhage after transvaginal ultrasonographically guided oocyte aspiration: a potentially catastrophic and not so rare complication among lean patients with polycystic ovary syndrome. Fertil Steril. 2010 Feb;93(3):874-9. doi: 10.1016/j.fertnstert.2008.10.028. Epub 2008 Dec 6. PubMed PMID: 19064264.	(Liberty et al., 2010)	MRI & Imaging
77: Noorbala AA, Ramezanzadeh F, Abedinia N, Naghizadeh MM. Psychiatric disorders among infertile and fertile women. Soc Psychiatry Psychiatr Epidemiol. 2009 Jul;44(7):587-91. doi: 10.1007/s00127-008-0467-1. Epub 2008 Nov 20. PubMed PMID: 19023508.	(Noorbala et al., 2009)	Psychological and Emotional Factors
78: Freizinger M, Franko DL, Dacey M, Okun B, Domar AD. The prevalence of eating disorders in infertile women. Fertil Steril. 2010 Jan;93(1):72-8. doi: 10.1016/j.fertnstert.2008.09.055. Epub 2008 Nov 11. PubMed PMID: 19006795.	(Freizinger et al., 2010)	Psychological and Emotional Factors
79: Ombelet W, Cooke I, Dyer S, Serour G, Devroey P. Infertility and the provision of infertility medical services in developing countries. Hum Reprod Update. 2008 Nov-Dec;14(6):605-21. doi: 10.1093/humupd/dmn042. Epub 2008 Sep 26. Review. PubMed PMID: 18820005; PubMed Central	(Ombelet et al., 2008)	Provision and management of infertile patients in developing or low resource countries.

PMCID: PMC2569858.		
80: Kattal N, Cohen J, Barmat LI. Role of coculture in human in vitro fertilization: a meta-analysis. Fertil Steril. 2008 Oct;90(4):1069-76. doi: 10.1016/j.fertnstert.2007.07.1349. Epub 2008 May 19. Review. PubMed PMID: 18490016.	(Kattal et al., 2008)	IVF (co-culture)
81: Slama R, Boutou O, Ducot B, Spira A. Reproductive life events in the population living in the vicinity of a nuclear waste reprocessing plant. J Epidemiol Community Health. 2008 Jun;62(6):513-21. doi: 10.1136/jech.2007.061069. PubMed PMID: 18477750.	(Slama et al., 2008)	Environmental Factors
82: Ozkan S, Murk W, Arici A. Endometriosis and infertility: epidemiology and evidence-based treatments. Ann N Y Acad Sci. 2008 Apr;1127:92-100. doi: 10.1196/annals.1434.007. Review. PubMed PMID: 18443335.	(Ozkan et al., 2008)	Female reproductive pathology
83: Khademi A, Alleyassin A, Amini M, Ghaemi M. Evaluation of sexual dysfunction prevalence in infertile couples. J Sex Med. 2008 Jun;5(6):1402-10. Epub 2007 Dec 14. PubMed PMID: 18086173.	(Khademi et al., 2008)	Sexual Dysfunction
84: Shindel AW, Nelson CJ, Naughton CK, Mulhall JP. Premature ejaculation in infertile couples: prevalence and correlates. J Sex Med. 2008 Feb;5(2):485-91. Epub 2007 Dec 14. PubMed PMID: 18086172.	(Shindel et al., 2008)	Relates to male conditions
85: Hammond CT, Beckjord EB, Arora NK, Bellizzi KM, Jeffery DD, Aziz NM. Non-Hodgkin's lymphoma survivors' fertility and sexual function-related information needs. Fertil Steril. 2008 Oct;90(4):1256-8. Epub 2008 Feb 20. PubMed PMID: 18083170.	(Hammond et al., 2008)	Fertility and oncology
86: Oakley L, Doyle P, Maconochie N. Lifetime prevalence of infertility and infertility treatment in the UK: results from a population-based survey of reproduction. Hum Reprod. 2008 Feb;23(2):447-50. Epub 2007 Nov 22. PubMed PMID: 18033808.	(Oakley et al., 2008)	Specific geographic location and prevalence.

87: Stevenson TL, Lashen H. Empty follicle syndrome: the reality of a controversial syndrome, a systematic review. Fertil Steril. 2008 Sep;90(3):691-8. Epub 2007 Nov 26. Review. PubMed PMID: 18023430.	(Stevenson and Lashen, 2008)	Female reproductive pathology
88: Grunfeld L, Luna M, Mukherjee T, Sandler B, Nagashima Y, Copperman AB. Redefining in vitro fertilization success: should triplets be considered failures? Fertil Steril. 2008 Oct;90(4):1064-8. Epub 2007 Sep 19. PubMed PMID: 17880948.	(Grunfeld et al., 2008)	IVF (singletons vrs multiple births)
89: Albayrak E, Günay O. State and trait anxiety levels of childless women in Kayseri, Turkey. Eur J Contracept Reprod Health Care. 2007 Dec;12(4):385-90. PubMed PMID: 17853171.	(Albayrak and Gunay, 2007)	Psychological and Emotional Factors
90: Ghazizadeh S, Lessan-Pezeshki M, Khatami MR, Mahdavi-Mazdeh M, Abbasi MR, Azmandian J, Razeghi E, Seifi S, Ahmadi F, Maziar S. Infertility among female renal transplant recipients. Saudi J Kidney Dis Transpl. 2007 Sep;18(3):387-90. PubMed PMID: 17679751.	(Ghazizadeh et al., 2007)	Concurrent pathology
91: Jackson JE, Rosen M, McLean T, Moro J, Croughan M, Cedars MI. Prevalence of celiac disease in a cohort of women with unexplained infertility. Fertil Steril. 2008 Apr;89(4):1002-4. Epub 2007 Jul 26. PubMed PMID: 17662282.	(Jackson et al., 2008)	Concurrent pathology
92: Svenstrup HF, Fedder J, Kristoffersen SE, Trolle B, Birkelund S, Christiansen G. Mycoplasma genitalium, Chlamydia trachomatis, and tubal factor infertility--a prospective study. Fertil Steril. 2008 Sep;90(3):513-20. Epub 2007 Jun 4. PubMed PMID: 17548070.	(Svenstrup et al., 2008)	Sexually Transmitted Diseases
93: Kumar D. Prevalence of female infertility and its socio-economic factors in tribal communities of Central India. Rural Remote Health. 2007 Apr-Jun;7(2):456. Epub 2007 May 8. PubMed PMID: 17489647.	(Kumar, 2007)	Specific geographic location and prevalence.
94: Safarinejad MR. Infertility among couples in a population-based study in Iran: prevalence and associated risk factors. Int J Androl. 2008 Jun;31(3):303-14. Epub 2007 May 7. PubMed PMID: 17488339.	(Safarinejad, 2008)	Specific geographic location and prevalence.

95: Boivin J, Bunting L, Collins JA, Nygren KG. International estimates of infertility prevalence and treatment-seeking: potential need and demand for infertility medical care. Hum Reprod. 2007 Jun;22(6):1506-12. Epub 2007 Mar 21. Erratum in: Hum Reprod. 2007 Oct;22(10):2800. PubMed PMID: 17376819.	(Boivin et al., 2007)	Infertility prevalence
96: Svensson AC, Lichtenstein P, Sandin S, Hultman CM. Fertility of first-degree relatives of patients with schizophrenia: a three generation perspective. Schizophr Res. 2007 Mar;91(1-3):238-45. Epub 2007 Jan 31. PubMed PMID: 17275261.	(Svensson et al., 2007)	Psychological and Emotional Factors
97: McGovern PG, Legro RS, Myers ER, Barnhart HX, Carson SA, Diamond MP, Carr BR, Schlaff WD, Coutifaris C, Steinkampf MP, Nestler JE, Gosman G, Leppert PC, Giudice LC; National Institutes for Child Health and Human Development-Reproductive Medicine Network. Utility of screening for other causes of infertility in women with "known" polycystic ovary syndrome. Fertil Steril. 2007 Feb;87(2):442-4. Epub 2006 Dec 4. PubMed PMID: 17141768; PubMed Central PMCID: PMC1813322.	(McGovern et al., 2007)	Female reproductive pathology
98: Clayton HB, Schieve LA, Peterson HB, Jamieson DJ, Reynolds MA, Wright VC. A comparison of heterotopic and intrauterine-only pregnancy outcomes after assisted reproductive technologies in the United States from 1999 to 2002. Fertil Steril. 2007 Feb;87(2):303-9. Epub 2006 Nov 16. PubMed PMID: 17113092.	(Clayton et al., 2007)	IVF (heterotopic pregnancy)
hetero	(Simunic et al., 2007)	Use of hormones in IVF
100: Guo SW, Wang Y. Sources of heterogeneities in estimating the prevalence of endometriosis in infertile and previously fertile women. Fertil Steril. 2006 Dec;86(6):1584-95. Epub 2006 Oct 24. Review. PubMed PMID: 17067588.	(Guo and Wang, 2006)	Female reproductive pathology

101: Werbrouck E, Spiessens C, Meuleman C, D'Hooghe T. No difference in cycle pregnancy rate and in cumulative live-birth rate between women with surgically treated minimal to mild endometriosis and women with unexplained infertility after controlled ovarian hyperstimulation and intrauterine insemination. Fertil Steril. 2006 Sep;86(3):566-71. PubMed PMID: 16952506.	(Werbrouck et al., 2006)	Female reproductive pathology
102: Thornton KL, Goldman MB. Impact of subgroup analysis on estimates of infertility. Fertil Steril. 2006 Sep;86(3):531-3; discussion 534. PubMed PMID: 16952504.	(Thornton and Goldman, 2006)	Infertility prevalence
103: Olive DL, Pritts EA. Estimating infertility: the devil is in the details. Fertil Steril. 2006 Sep;86(3):529-30; discussion 534. PubMed PMID: 16952503.	(Olive and Pritts, 2006)	Infertility prevalence
104: Barnhart KT. The challenge and enjoyment of the interpretation of epidemiologic data. Fertil Steril. 2006 Sep;86(3):527-8; discussion 534. PubMed PMID: 16952502.	(Barnhart, 2006)	Infertility prevalence (methodology)
105: Guzick DS, Swan S. The decline of infertility: apparent or real? Fertil Steril. 2006 Sep;86(3):524-6; discussion 534. PubMed PMID: 16952501.	(Guzick and Swan, 2006)	Infertility prevalence
106: Stephen EH, Chandra A. Declining estimates of infertility in the United States: 1982-2002. Fertil Steril. 2006 Sep;86(3):516-23. PubMed PMID: 16952500.	(Stephen and Chandra, 2006)	Specific geographic location and prevalence.
107: Spandorfer SD, Bongiovanni AM, Fasioulotis S, Rosenwaks Z, Ledger WJ, Witkin SS. Prevalence of cervical human papillomavirus in women undergoing in vitro fertilization and association with outcome. Fertil Steril. 2006 Sep;86(3):765-7. Epub 2006 Jun 16. PubMed PMID: 16782096.	(Spandorfer et al., 2006)	Sexually Transmitted Diseases
108: Somigliana E, Infantino M, Benedetti F, Arnoldi M, Calanna G, Ragni G. The presence of ovarian endometriomas is associated with a reduced responsiveness to gonadotropins. Fertil Steril. 2006 Jul;86(1):192-6. Epub 2006 May 23. PubMed PMID: 16716316.	(Somigliana et al., 2006)	Female reproductive pathology

109: Larsen U, Mlay J, Aboud S, Ballard R, Sam NE, Shao JF, Kapiga SH. Design of a community-based study of sexually transmitted infections/HIV and infertility in an urban area of northern Tanzania. Sex Transm Dis. 2007 Jan;34(1):20-4. PubMed PMID: 16691158.	(Larsen et al., 2007)	Sexually Transmitted Diseases
110: Cousineau TM, Green TC, Corsini EA, Barnard T, Seibring AR, Domar AD. Development and validation of the Infertility Self-Efficacy scale. Fertil Steril. 2006 Jun;85(6):1684-96. Epub 2006 May 4. PubMed PMID: 16677636.	(Cousineau et al., 2006)	Tools and Scales

Table 7 The results of the preliminary literature search

Thematic sorting of preliminary search results

Figure 3 Thematic Sorting of Preliminary Search Results

Two articles were concerned with the provision and management of healthcare provision for infertile patients in developing or low resource countries with low access to assisted reproductive technology (ART) (Sharma et al., 2009) and (Ombelet et al., 2008).

The diagnosis and treatment of infertility were sometimes constructed in the literature as being dependent on the availability or non-availability of ART, one article explored the correlation between state funded treatments and frequency of diagnosis for diminished ovarian reserve:
The presence or absence of state-mandated ART coverage could impact access to care and the mix of patients that pursue and initiate ART cycles in ways that influence these proportions (Butts et al., 2013)

The reproductive technology known as in vitro fertilization (IVF) was the subject of eight articles; two were concerned with the therapeutic use of specific hormones, gonadotropin-releasing hormone (Xiao et al., 2013) and progesterone (Simunic et al., 2007). Four papers were concerned with the implications of singleton or multiple live births in various contexts (Malizia et al., 2013, Shapiro et al., 2013, Nakashima et al., 2013, Grunfeld et al., 2008). Specific outcomes such as heterotopic pregnancy (Clayton et al., 2007)and the role of co-culture were also investigated or subjected to meta-analysis (Kattal et al., 2008).

The risks and benefits of specific surgical treatments (Rasheed et al., 2014) or drug interventions (Malloch and Rhoton-Vlasak, 2013) (Boots et al., 2013) were also the focus of some studies.

Sexually transmitted diseases are major determinant of the prevalence of infertility in most latitudes (Petraglia et al., 2013) and eight papers were found to cover this topic, ranging from HIV infections (Dhont et al., 2011, Larsen et al., 2007) and HPV (Spandorfer et al., 2006) to Chlamydia (Malik et

al., 2006) (Datta et al., 2012, Baraitser et al., 2011, Svenstrup et al., 2008) and Pelvic Inflammatory Disease (Wiesenfeld et al., 2012).

Another reason for the increasing incidence of infertility is the widespread use of contraception, the choice of delaying the first pregnancy until the third decade of life which places women at higher risk for uterine fibroids, endometriosis, polycystic ovary syndrome, and chronic anovulation (Petraglia et al., 2013) and 17 studies reported on aspects of female reproductive pathology. The most commonly reported conditions were adenomyosis and endometriosis.

Adenomyosis occurs when endometrial tissue, which normally lines the uterus, exists within and grows into the muscular wall of the uterus and may be associated with subfertility (Tomassetti et al., 2013). A systematic review (Maheshwari et al., 2012) concluded that further studies are needed to determine the natural history of adenomyosis and implications for fertility and reproductive outcomes, with and without treatment.

MRI imaging has been used to estimate the prevalence of adenomyosis in endometriosis and it's impact on fertility (Kunz et al., 2005) Four other articles were concerned with the use of imaging techniques in ART (Souter et al., 2010, Marci et al., 2013, Moini et al., 2013, Butts et al., 2013, Liberty et al., 2010).

Endometriosis is believed to be associated with female infertility in women with otherwise normal ovulation (Ilangavan and Kalu, 2010), and can cause a reduced responsiveness to the drugs used in IVF (Somigliana et al., 2006). Described as an 'enigmatic' condition (Ozkan et al., 2008) there have been several studies and reviews to try and establish the optimum treatment for affected infertile women (Ozkan et al., 2008).

The need for the surgical treatment of minimal to mild endometriosis was investigated (Werbrouck et al., 2006) who found no difference in IVF cycle pregnancy rates and live births between women affected and women with

unexplained infertility. Endometriosis (ENDO) is believed to have increased during recent years (Paris and Aris, 2010) in women aged 18 -24 who are therefore at a greater risk of infertility. Hysteroscopic polypectomy and removal of endometriotic foci significantly increased the chances of achieving a pregnancy compared with those without polyps (Shen et al., 2011).

The other female reproductive pathologies that have been reported include: fibroids (Firouznia et al., 2009), polycystic ovary syndrome (McGovern et al., 2007), luteal phase deficiency (Schliep et al., 2014), utero-tubal infertility (Audu et al., 2009), empty follicle syndrome (Aktas et al., 2005), (Stevenson and Lashen, 2008) and abnormal cervical cytology (Al-Jaroudi and Hussain, 2010).

Another reason for the increasing prevalence of infertility may be the prolonged exposure to chronic stress and environmental pollutants, which may play a critical role (Petraglia et al., 2013). Published papers in this area include: smoking and infertility (2012), (Neal et al., 2005), the reproductive life events in a population living in the vicinity of a nuclear waste reprocessing plant (Slama et al., 2008) and the effect of chemicals used in a hair dressing salon (Ronda et al., 2009).

The psychological and emotional health of infertile women has been reported in a range of papers covering topics such as alexithymia (Lamas et al., 2006), eating disorders (Freizinger et al., 2010), state and trait anxiety (Albayrak and Gunay, 2007) and schizophrenia (Svensson et al., 2007). Infertile women were found to be at higher risk of developing psychiatric disorders if they were housewives rather than working women (Noorbala et al., 2009). Sexual dysfunction either in women or couples was reported in three papers (Khademi et al., 2008), (Keskin et al., 2011) and (Pakpour et al., 2012).

Although gonadotoxic oncologic treatments allow many patients to survive cancer, it may be at the cost of their fertility. This consideration may justify the development of treatments that preserve fertility (Petraglia et al., 2013),

four papers were identified as dealing with these issues (Turan et al., 2013), (du Bois et al., 2013), (Balcerek et al., 2012, Hammond et al., 2008).

Papers that dealt specifically with the definition of infertility, and estimates of prevalence were examined to see if they could be used to provide a global estimate. Nine papers dealt with a specific geographical area and were excluded (Ziller et al., 2013, Thoma et al., 2013, Esmaeilzadeh et al., 2012, Bushnik et al., 2012, Bhattacharya et al., 2009, Kumar, 2007, Safarinejad, 2008, Stephen and Chandra, 2006, Oakley et al., 2008).

One of these papers found that among married women in the United States, there has been a significant decline in 12-month infertility, which cannot be explained by changes in the composition of the population from 1982-2002 (Stephen and Chandra, 2006) and this apparent reversal in the global trend provoked some methodological debate in response:

Data on trends in fertility and infertility are of significant interest, because they may reflect social, behavioral, biological, or environmental changes. The conclusion that infertility has declined in the United States, based on data from the National Survey of Family Growth, must be interpreted with great caution because of definitional and methodological concerns (Guzick and Swan, 2006)

Self-reported data have serious limitations, particularly when the outcome is constructed from indirect questions. Policy decisions require clearly defined issues, validated tools, careful and comprehensive analysis, and cautious interpretation (Olive and Pritts, 2006)

Conclusions regarding estimates of infertility may reflect study bias based on the definition of infertility used. Careful consideration of how the infertile population is defined, as well its use in subgroup analysis that may not be generalizable to the population of infertile women as a whole, is needed (Thornton and Goldman, 2006).

The idea that how we define infertility affects our ability to detect and report its prevalence was tested in a Moshi town in northern Tanzania (Larsen, 2005) where it was found that the infertility definition made a difference. The researcher concluded that the World Health Organization definition based on 24 months of trying to get pregnant was recommended as the definition that is useful both in clinical practice and research among different disciplines.

The articles that had the best fit to the research question were shortlisted for critical reading and review using the checklist previously described

Table 4: Checklist of questions for critical reading of selected articles

31: Mascarenhas MN, Flaxman SR, Boerma T, Vanderpoel S, Stevens GA. National, regional, and global trends in infertility prevalence since 1990: a systematic analysis of 277 health surveys. PLoS Med. 2012;9(12):e1001356. doi: 10.1371/journal.pmed.1001356. Epub 2012 Dec 18. PubMed PMID: 23271957; PubMed Central PMCID: PMC3525527.	(Mascarenhas et al., 2012a)	Systematic review of infertility prevalence
57: Gurunath S, Pandian Z, Anderson RA, Bhattacharya S. Defining infertility--a systematic review of prevalence studies. Hum Reprod Update. 2011 Sep-Oct;17(5):575-88. doi: 10.1093/humupd/dmr015. Epub 2011 Apr 14. Review. PubMed PMID: 21493634.	(Gurunath et al., 2011)	Systematic Review of prevalence
72: Dyer SJ. International estimates on infertility prevalence and treatment seeking: potential need and demand for medical care. Hum Reprod. 2009 Sep;24(9):2379-80; author reply 2380-3. doi: 10.1093/humrep/dep219. Epub 2009 Jun 20. PubMed PMID: 19542544.	(Dyer, 2009)	Infertility prevalence
95: Boivin J, Bunting L, Collins JA, Nygren KG. International estimates of infertility prevalence and treatment-seeking: potential need and demand for infertility medical care. Hum Reprod. 2007 Jun;22(6):1506-12. Epub 2007 Mar 21. Erratum in: Hum Reprod. 2007 Oct;22(10):2800. PubMed PMID: 17376819.	(Boivin et al., 2007)	Infertility prevalence
102: Thornton KL, Goldman MB. Impact of subgroup analysis on estimates of infertility. Fertil Steril. 2006 Sep;86(3):531-3; discussion 534. PubMed PMID: 16952504.	(Thornton and Goldman, 2006)	Infertility prevalence

103: Olive DL, Pritts EA. Estimating infertility: the devil is in the details. Fertil Steril. 2006 Sep;86(3):529-30; discussion 534. PubMed PMID: 16952503.	(Olive and Pritts, 2006)	Infertility prevalence
104: Barnhart KT. The challenge and enjoyment of the interpretation of epidemiologic data. Fertil Steril. 2006 Sep;86(3):527-8; discussion 534. PubMed PMID: 16952502.	(Barnhart, 2006)	Infertility prevalence (methodology)
105: Guzick DS, Swan S. The decline of infertility: apparent or real? Fertil Steril. 2006 Sep;86(3):524-6; discussion 534. PubMed PMID: 16952501.	(Guzick and Swan, 2006)	Infertility prevalence

Table 8 Shortlist of 8 papers on the prevalence of infertility

Selection criteria - These papers were chosen from the 110 initial candidates to provide an up-to-date estimate of the prevalence of global infertility as well as exploring the definitions of infertility and the types of data used for such estimates. The criteria for including them was that their main focus was on the prevalence of infertility on an international or global dimension, that they were peer reviewed and published in the last 10 years.

Three articles were chosen to review in greater detail for this section and an additional information source was included (Fields et al., 2013):

5. Fertility (update): summary of NICE guidance (Fields et al., 2013)

6. International estimates of infertility prevalence and treatment-seeking: potential need and demand for infertility medical care (Boivin et al., 2007)

7. National, Regional, and Global Trends in Infertility Prevalence Since 1990: A Systematic Analysis of 277 Health Surveys (Mascarenhas et al., 2012b)

8. Defining infertility – a systematic review of prevalence studies (Gurunath et al., 2011)

These papers were chosen to provide an up-to-date estimate of the prevalence of global infertility as well as exploring the definitions of infertility and the types of data used for such estimates. The two systematic reviews were chosen as they represented a more complete and reliable form of evidenced compared to the papers that were excluded. The papers were read critically using the list of questions for as explained in the methodology section of this chapter.

Analysis of Literature Searches

The Definition And Treatment Of Infertility

The first choice of guidelines for the diagnosis and treatment of female infertility were the updated NICE guidelines because these are the guidelines that will be in use at the site of the trial, an assisted reproduction unit at Jersey General Hospital. It is important that the patients, researcher and clinicians at the site share a common understanding of the condition and it's treatment. The guidelines are written from a conventional medical perspective and with a post positivist philosophical framework.

NICE recommendations are based on systematic reviews of the best available evidence and explicit consideration of cost effectiveness. When minimal evidence is available, recommendations are based on the Guideline Development Group's experience and opinion of what constitutes good practice.

These guidelines also recommend that couples should be informed that the effectiveness of complementary therapies for fertility problems has not been properly evaluated and that further research is needed.

The Definition Of Infertility

The way in which we define infertility will influence the way in which data is collected and prevalence is measured. The researcher has to choose between demographic and epidemiological data sources; demographic definitions provide important data on reproductive outcomes in large

populations but may fail to identify couples who need investigation and treatment in order to improve their chances of conception (Gurunath et al., 2011).

Clinical definitions are also useful when determining treatment groups and for the purposes of this study infertile woman who fall into the WHO category 2 and 3 (hypothalamic-pituitary dysfunction and ovarian failure) groups were eligible for study recruitment.

The WHO classifies ovulation disorders into three groups:
Group 1: hypothalamic pituitary failure (hypothalamic amenorrhoea or hypogonadotrophic hypogonadism
Group 2: hypothalamic-pituitary-ovarian dysfunction (predominately polycystic ovary syndrome)
Group 3: ovarian failure.

Both demographic and epidemiological definitions of infertility are important in their own contexts and both types of studies are considered in this section.

Infertility is defined by NICE (Fields et al., 2013) as the period of time people have been trying to conceive without success after which formal investigation is justified and possible treatment implemented. This new definition replaces defining the patient as ‘infertile’ and uses infertility as a unit or status update.

However estimates of prevalence can be affected by our shared understanding of the definitions of terms such as ‘infertility’, ’subfertility’, and ‘sub fecundity’ and how they are used in the data without being clearly defined, as well the terms ‘primary permanent infertility’, ‘unresolved infertility’, ‘childlessness’ and ‘primary unresolved infertility’ (Gurunath et al., 2011)

The main challenge in generating global estimates of infertility are the scarcity of population-based studies and the inconsistent definitions used in the few high-quality studies available (Gurunath et al., 2011).

In order to obtain a clearer understanding of these definitions (Gurunath et al., 2011) has investigated the way that infertility is defined in prevalence studies using a computerised and manual literature search for demographic and epidemiological studies.

The studies selected for review were population-based studies of a random selection of a representative sample, surveyed by postal questionnaires or oral interviews. The 28 epidemiological studies were cross sectional in design. Descriptive cross sectional surveys are based on a representative sample or sub-sample of the population of interest who are questioned at one point in time. The aim is usually to assess the prevalence of disease and associated factors.

The results highlight the fact that the absence of an established definition of infertility results in varying estimates of its prevalence within and between populations. There is considerable heterogeneity in terms of determining exposure and outcomes, the nature of the population sampled and the denominator used to calculate prevalence rates (Gurunath et al., 2011).

While a systematic review of this kind helps us to search for a universal explanation, derived from empirical regularities (Bowling, 2011), it might have also been appropriate to use qualitative research methods to investigate the differences and similarities in global definitions of the concept of infertility.

The Prevalence of Infertility

Estimates of the prevalence of infertility vary slightly between studies, from about one in seven couples in the United Kingdom (HFEA, 2008) to a 9% global prevalence of infertility of 12 months duration (Boivin et al., 2007).

Boivin et al have taken a post-positivist approach to estimating the prevalence of infertility. Population surveys published since 1990 were examined for the prevalence of infertility. A specific Pub Med search yielded

28 studies, which they selected for review. Estimates on population size and variables such as age, marital status and contraception use were made using data from recognised sources.

No statistical modelling was performed but the main findings of this review were that prevalence and demand for infertility treatment were lower than typically cited and remarkably similar between more and less developed countries. The potential need for infertility medical services was approximately 9% based on a sample of 170 000 women. The evidence indicated a 9% prevalence of infertility (of 12 months duration) with 56% of couples seeking medical care (Boivin et al., 2007).

Mascarenhas et al commented on the 12-month duration definition of infertility used by Boivin finding that it was not long enough to compensate for other variables:

We found that a 5-y exposure period is needed to accommodate the time it takes to become pregnant and give birth, and helps prevent unreported temporary separations, periods of postpartum sexual abstinence, or lactation amenorrhea from unduly affecting the infertility measure. Births, rather than pregnancies, are the preferred outcome, as information on live births is collected more often and reported more accurately: neither pregnancies in the first trimester nor voluntary terminations are reliably reported in household surveys.(Mascarenhas et al., 2012b)

Mascarenhas (Mascarenhas et al., 2012b) used an alternative to synthesizing data found in the literature by applying a consistent definition and a statistical model to regularly collected demographic data and reproductive health survey data. One of the stated aims of this project was to use an agreed definition of infertility. They applied consistent definitions of primary infertility (inability to have any live birth) and secondary infertility (inability to have an additional live birth).

The strength of this study is that few comparative analyses of global infertility have been conducted and none have applied a consistent algorithm to demographic and reproductive health survey data both from developing and developed countries, nor used these data to estimate regional and global trends in infertility prevalence.

They estimated the prevalence of primary and secondary infertility trends using household survey data consisting of interviews with the female partner. However there are challenges associated with inferring prevalence from household survey data. Few household surveys ask how long the respondent has tried to get pregnant instead these surveys may collect information on births, couple status, fertility preferences and contraceptive use (Mascarenhas et al., 2012b).

A previous analysis (Mascarenhas et al., 2012a) performed a sensitivity analysis around each of the components (live birth as the outcome and a 5-y exposure period based on union status, use of contraceptives, and desire for a child.), to identify important biases that may arise when information is incomplete .

The scale of this project means that the data collection was appropriate and allowed comparison to be made between different countries. The return rates of the surveys used would allow us to judge how representative they are of the population sampled. They did exclude thirteen studies because at least one response was missing for more than 15% of respondents.

The methodological quality of the study was improved by the use of cross validation to evaluate the predictive validity of their model and a geographical framework was used to evaluate results at global, regional and country level. Some aspects of social and cultural differences were taken into account such as political pressures in China, which may cause underreporting of abortion and contraception.

Limitations of the study include the narrow definition of child-seeking women and data gaps for some countries. This could have been extended, for example, by including women in a same sex union or single women who desired a child.

They found that by using a larger data set and a different algorithm to calculate infertility their estimate of the global number of couples affected by infertility was lower than that of (Boivin et al., 2007) in 2006. They found that in 2010 1.9% of child-seeking women aged 20-44 years old were unable to have a first live birth (primary infertility) and 10.5% of child-seeking women with a prior live birth were unable to have an additional live birth (secondary infertility).

Other findings included:

- The prevalence of primary infertility was higher amongst women aged 20-24 y compared to women aged 25-29y and women aged 30-44y.

- Prevalence of secondary infertility increased sharply with age.

- Both age patterns are less pronounced when calculated as a percentage of all women.

This study was used as a baseline estimate of global infertility rates in a recent paper ‘Fertility drugs, reproductive strategies and cancer risk’ (Tomao et al., 2014):

In the world the number of people with problems of infertility has increased since 1990, resulting in a consistent increase in the use of strategies to improve fertility and reproductive rates. The highest incidence of infertility was found in western countries and in these countries a consistent proportion of the infertile women receive fertility treatments (Mascarenhas et al., 2012b).

Moreover, the clinical use of fertility drugs and other reproductive strategies is expected to increase for the large number of women who postpone pregnancy for economic and social reasons (Mascarenhas et al., 2012b).

The Treatment Of Infertility

There is evidence that more people are having fertility treatment which is increasingly successful (HFEA) and so the NICE guidelines from 2004 have been updated to provide clinicians with a list of recommendations regarding appropriate care (Fields et al., 2013).

NICE recommends that Clinicians should inform people who are concerned about their fertility that:

- Over 80% of couples in the general population will conceive within one year if the women is aged under 40 years and they have regular sexual intercourse without contraception.
- Of those who do not conceive in the first year, about half will do so in the second year (cumulative pregnancy rate over 90%).
- Vaginal sexual intercourse every two to three days optimises the chance of pregnancy.
- Female fertility declines with age.
- That they may find it helpful to contact a fertility support group
- Offer counselling as fertility problems can cause psychological stress.
- Both partners should be informed that:
  Stress in the male and/or female partner can affect the couple's relationship and is likely to reduce libido and frequency of intercourse, in turn contributing to fertility problems (Fields et al., 2013).

Treatment options for women with WHO group 2 annovulatory infertility: clinicians should offer one of the following treatments:

a. Clomiphene citrate for ovulation induction and ovarian stimulation.

b. Metformin
c. A combination of the above

Conclusion

Research Questions

How is infertility defined in published studies, in working practice, what is the estimated prevalence – global and UK? What is the recommended treatment for female infertility?

An examination of the literature shows that both systematic reviews of prevalence studies, and the systematic analysis of demographic data and reproductive health survey data, have been conducted in recent years. The current prevalence of infertility has been calculated at approximately 9% globally or 1 in 7 couples in the UK.

Infertility has been defined in various ways including primary infertility (inability to have any live birth) and secondary infertility (inability to have an additional live birth). For the purposes of this study it is important to know how many couples might be seeking medical help for their infertility and this has been estimated at 56% of couples that have infertility problems. This would create a significant opportunity for the use of Ovarium compositum if it could be shown to improve fertility outcomes for women undergoing fertility treatment.

The age of women seeking to conceive is shown to change their predicted fertility outcomes with the prevalence of primary infertility being higher amongst women aged 20-24 y compared to women aged 25-29y and women aged 30-44y. The prevalence of secondary infertility increases sharply with age and these findings informed the design of the quantitative strand of the thesis (an RCT trial of Ovarian compositum).

The treatment and advice given to couples seeking to conceive have been updated recently by NICE and will form the basis of the treatment for the women who are the focus of this thesis. Treatment options for women with

WHO group 2 annovulatory infertility: clinicians should offer one of the following treatments:

a. Clomiphene citrate for ovulation induction and ovarian stimulation.
b. Metformin
c. A combination of the above

The advice given to couples recognises that infertility can cause psychological stress, and that in turn, stress can have an impact on fertility outcomes. The current advice from NICE to the medical community is that, while counselling or joining a support group may help couples to cope, the value and safety of CAM therapies has not yet been adequately researched.

This thesis seeks to make a contribution to that particular field of knowledge by evaluating the specific effect of a homeopathic preparation prescribed without a homeopathic consultation, as well as questioning the kind of research that is needed to establish the value of CAM therapies in the treatment of infertility.

Limitations To The Overview

It was not possible in the context of this PhD to work with another reviewer or to rate each paper using a scoring system. The initial search was not recorded systematically and the search had to be replicated and recorded in a table format post viva. No attempt was made to search for unpublished work from other sources and so it cannot be claimed that this is a fully systematic qualitative review of the literature on infertility and it's global prevalence. The only database that was searched was the PubMed database.

Literature Review - Section 3 The Treatment Of Infertility Using Homeopathy Or Homotoxicology

Research Questions: What is homotoxicology? Are there any existing trials of homotoxicology to treat infertility? What is the role of CAM in treating homotoxicology?

Methodology

A preliminary search using a search engine, using PubMed and by contacting suppliers of homoeopathic remedies was supported by personal correspondence with the author of a systematic review of randomised controlled trials of homeopathy (Mathie et al., 2013)

Selection of papers for review

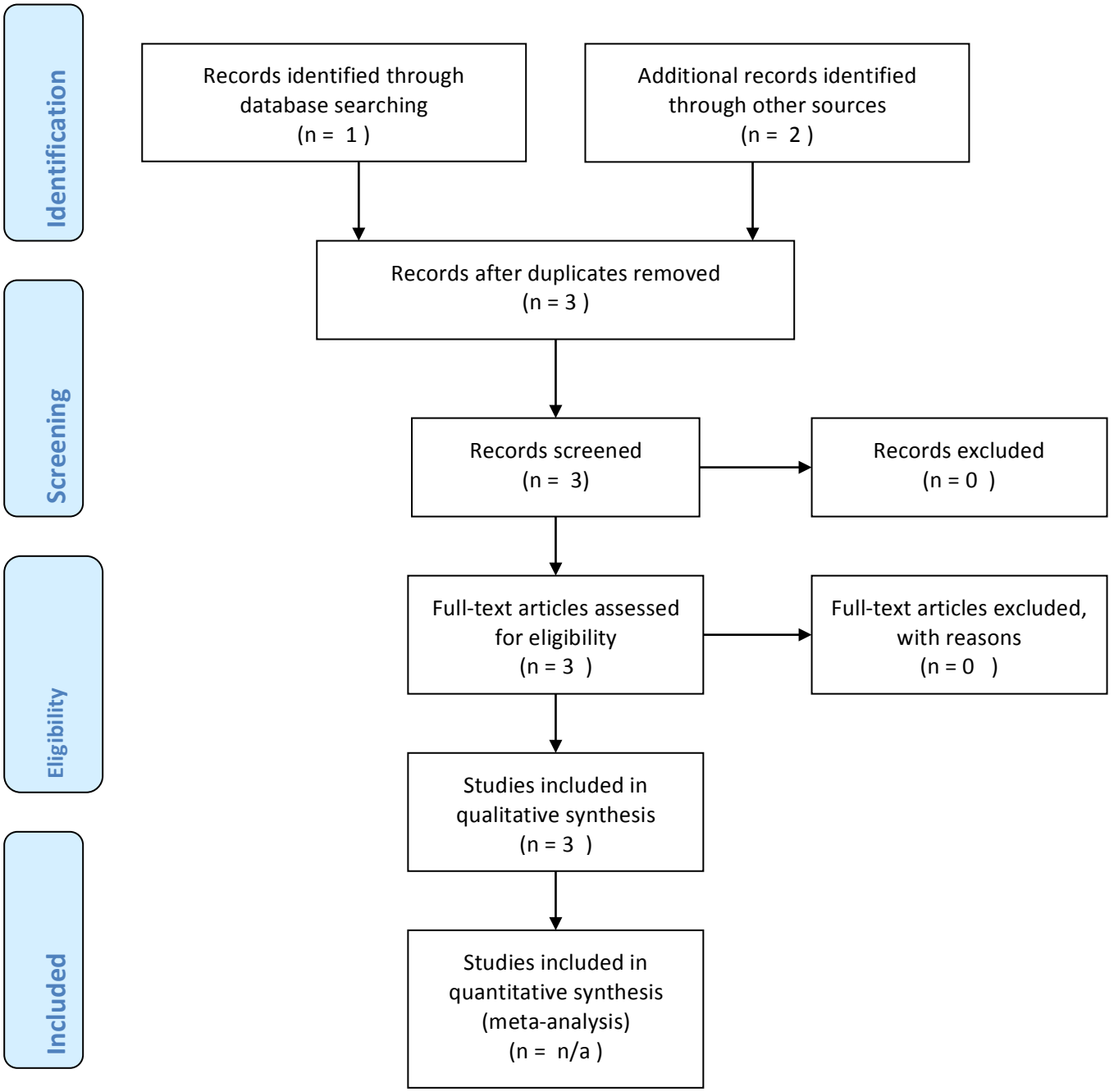
At start of the study the philosophical perspective adopted by the author was a post positivist stance and the only studies considered for review were quantitative in nature and the ideal data being sought was in the form of Randomised Controlled Trials, any qualitative strands to the study design were intended to inform the design of the quantitative phase

Search Strategy

PubMed was searched using the MeSH terms (((homeopathy[MeSH Terms]) AND female infertility[MeSH Terms])) AND homeopathy which yielded one of the papers selected for review, (Bergmann et al., 2000).

Papers were also sourced from the suppliers of homotoxicological products (BioPathica Ltd) and the newsletters from a manufacturer (GUNA srl). The possibility of bias from these sources is acknowledged and this was addressed by using Robert Mathies' systematic list of RCT on homeopathy to check for available papers.

PRISMA 2009 Flow Diagram to show the selection of papers on female infertility and homeopathy



One hallmark of a systematic qualitative review is that *the Authors attempt to obtain all original (primary) research studies published on the topic under study by searching in multiple databases, performing handsearches, and contacting authors of previously published research (Green et al.)* I contacted Robert Maithie via email (7th November 2014), to discuss his systematic search of the RCT literature of homeopathy (Mathie et al., 2013).to make sure that no papers had been missed from my selection and that no translations of papers were available to add to my analysis.

Using this strategy three papers on the use of homotoxicology/homeopathy to treat female infertility could be found and no new studies were available on Pub Med when writing up in February 2015:

1. Homeopathy Versus Conventional Therapy For Female Infertility: Intermediate Report From A Randomised Study.(Gerhard I, 1997)
2. The Homotoxicological Treatment Of Female Functional Infertility: A Clinical Trial.(Lai, 2000)
3. The Efficacy Of The Complex Medication Phyto-Hypophyson L In Female Hormone Related Sterility A Randomized, Placebo-Controlled Clinical Double Blind Study.(Bergmann et al., 2000)

Review of Papers Selected.

Each was evaluated against three frameworks: CONSORT (Hopewell et al., 2008), RedHot (Dean et al., 2007) and the MVHT (Mathie et al., 2012). This ensures that the trial is assessed for validity as a randomised controlled trial that is suitable for homeopathy and that the methodology chosen is a valid model to test the research question for the intervention under investigation.

A table summarising these three evaluations for each study can be found APPENDIX 1. Although the methodological quality of these studies is poor they do provide a perspective on both the available literature on treating

infertility with homoeopathy and the quality of the research being undertaken in that field.

The frameworks being used to evaluate the studies have been developed more recently than the publication date and so this is a retrospective analysis. It is acknowledged that the authors would not have had the benefit of such guiding frameworks and also demonstrates the evolution that has taken, and continues to take place, in the thinking about the appropriate methodology for designing and conducting such trials.

Introduction

The Definition of Homotoxicology

The term homotoxicology is derived from three words: Latin *homo* meaning man or self; “toxic” derived from the Greek *toxikon*, meaning toxin or poison; and “logy” derived from the Green *logos*, meaning study.(Heel, 1986).

The homotoxicological paradigm (Smit A, 2009) is a homeotherapeutic system in which a medical diagnosis is made, followed by an individualized assessment according to the severity of the patient’s disease. This takes into account the response of the patient’s self-regulatory system to exogenous and endogenous stressors. Treatment is given, using predominantly homeopathically prepared medicines, to support the inherent self-regulating ability of the body rather than just treat symptoms, which are seen as an expression of the body’s own defence that should not be suppressed. (Heel, 1986).

Disease and Health are described as a position on a two dimensional scale known as the Disease Evolution Table (DET) (Smit et al., 2010), in which disease is represented as six successive stages along the horizontal axis and the different tissues of the body are shown on the vertical axis according to their embryonic origins.

The six successive stages of disease refer to the relationship between the organism and the presence of ‘toxins’, which cause a reaction. Initially the organism will react with an excretory or inflammatory response and if these strategies fail to restore health the organism will compensate with storage or deposition of the toxins that may lead to a disruption of cellular metabolism or control. (Smit A, 2009)

The Development of Homotoxicology

Dr. Han-Heinrich Reckeweg (1905-1985) was the primary developer of homotoxicology. He started the development in 1948 but it was only in 1952 that the first official article was published (RECKEWEG, 1952) in Germany. This was followed by the definitive work in 1955 (Reckeweg, 1955).

Some of the influences on Reckeweg’s development of homotoxicology are thought to have derived from the teachings of August Bier, a renowned and distinguished surgeon and the director of the Surgical University Clinic in the Ziegelstrasse in Berlin (Vogeler, 1942), where Reckeweg attended several semesters of his medical studies before moving to Bonn, where he received his degree.

Major concepts from Bier and his contemporaries that are incorporated into homotoxicology are the purposefulness of disease (which is seen as a manifestation of the activation of the self-regulation system of the organism), the relationship between the cell and the extracellular matrix (ECM), and the cardinal concept that inflammation is a physiological process rather than a pathological one and a natural response to all stressors (Bier, 1926, Bier, 1930).

Homotoxicology also integrated the work of Cannon and later Hans Selye. Cannon (Cannon, 1916) showed how the biological organism automatically mobilized its physiological and biochemical resources by a built-in "wisdom of the body," to defend itself against real or threatened assault (Mittelmann et al., 1942)

Selye's theory was that various "stressors" (cold, heat, solar radiation, burns, "nervous stimuli") produce a generalized, stereotyped response in the biological organism as it works to "perform certain adaptive functions and then to reestablish normalcy." (Medicine, 2015)

In homotoxicology, disease is seen as the expression of biologically purposeful defence mechanisms against endogenous and exogenous stressors (generally described as homotoxins) or the expression of the organism's effort to compensate for the toxic damage it has sustained (Heel, 1986).

The response to stressors is coordinated by the global autoregulatory system, which is seen as the master system that regulates homeodynamics. Reckeweg depicted this as the Greater Defence System (Heel, 1986).

The six subsections of the Greater Defence System are

1. The reticuloendothelial system
2. The hypothalamus-hypophysis-suprarenal axis
3. The neural reflex system
4. Detoxification by the liver
5. Detoxification of the matrix
6. The mucous membranes

These systems are seen as closely interconnected and may share mediators and receptors. The 'cross talk' between the immune, endocrine, and nervous systems is the basis for the science of psychoneuroimmunology.

In homotoxicology symptoms and signs of illness and disease are thought to be an activation of this system and are therefore supported rather than suppressed. Symptoms may be treated in order to keep the patient comfortable but never just suppressed.

Autoregulatory systems are governed by feedback loops, which can be both positive and negative, they are often characterised by an oscillating pattern that may also include a chronobiological pattern. The goal of treatment with homotoxicology may be to restore and support these autoregulatory patterns

Table 9 Examples of endogenous and exogenous stressors

Exogenous Stressors	Endogenous Stressors
Pollutants	Physiological substances
Metals	Waste products
Agricultural chemicals	Hormones
Plasticizers	Microbial debris
Food Additives	Dental filings and medical implants
Microbial by-products and molds	
Therapeutic and Recreational Drugs	

Source (Heel, 1986)

The Classification of Homotoxicology as a Homeotherapeutic System

The homeotherapeutic schools can be classified according to the manufacturing method of the medication and the method by which it is prescribed. The most important schools include classical homeopathy, clinical homeopathy, combination product homeopathy, isopathy and anthroposophic medicine (Jütte and Riley, 2005).

Homotoxicology has a close connection to clinical homeopathy, combination product homeopathy, and isopathy and the rationale for medications used in homotoxicology follows some of these principles (Heel, 1986).

In **classical homeopathy** medications are chosen by comparing the constellation of symptoms of the diseased individual with the so-called drug picture of the single-ingredient medication. This drug picture is derived from pathogenic trials (and eventually published in a Materia Medica). The detailed picture takes into account the physical, emotional, and mental pictures of the patient. (Heel, 1986).

In **clinical homeopathy** the medication is prescribed according to the pathological picture of the disease, this is also true in homotoxicology, in which a medical diagnosis is made according to the currently accepted guidelines. In addition, the diagnosis will include an assessment of the status of the patient's biological regulatory system and a classification on the Disease Evolution Table (DET) (Heel, 2012).

Reckeweg developed combination medications from homeopathically prepared ingredients selected according to the literature based on the pathogenic trials (therefore based upon the similar principle) and validated by his own observations. He was especially interested in the multi-target approach because he believed that disease was caused by several factors both exogenous and endogenous and therefore needed a multicomponent medication to simultaneously address different targets (Heel, 1986).

Homeopathy versus conventional therapy for female infertility: Intermediate report from a randomized study.

(Gerhard et al., 1997)

The setting for this study was a German University Clinic with approval from the Federal Ministry for Education and Technological research, and was partially funded by the Carl and Veronica Carstens Foundation (http://www.kisswin.de/en/funding/funding-organisations/organisation/0/1/karl-and-veronica-carstens-foundation.html).

Key concepts include the view that infertility may have multiple causes that homeopathy and acupuncture are a holistic mind-body medicine, and that clinical trials are a 'scientific' way of providing evidence of efficacy. The context of the study includes the fact that Assisted Reproduction Technology (ART) is moving forward and developing new techniques.

This paper attempts to take results observed over a three year period in a real life clinical situation, which are acknowledged to be 'alternative and scientifically unrecognised', and tries to replicate them using a quantitative model (randomised two arm study) and a positivist perspective. The conventional medical descriptions of infertility status are used and the homeopathic terms are explained for the non-specialist reader.

The authors understanding of the holistic nature of mind-body medicine is made clear. The nature of infertility as a disease is discussed and the author's opinion is that infertility sometimes has a psychological causation but this mind-body connection is rarely acknowledged and patients are offered medical rather than psychotherapeutic interventions. The rationale for using homeopathy is that by triggering regulatory systems the patient is restored to health on both a somatic and psychic level.

This was designed as quantitative clinical trial model using randomised patients.
When evaluated against the CONSORT criteria, Table 29 Gerhard 1997 evaluated against Consort, the study meets some of the basic criteria but because of the failure to recruit sufficient women the outcomes and adverse events are not reported. The general interpretation of the results has been replaced by a discussion about the problems of recruitment and a proposal for a new study design. The available literature does not provide a trial registration number.

The study was designed as a monocentric, two armed, randomised study. Patients agreeing to take part in the trial were divided into two treatment groups:

1. Single homeopathic remedies prescribed according to repertorisation of their symptoms and the selection of a remedy using the similar principle.
2. Normal hormonal therapy tailored to the individual.

The decision not to use blinding when assigning women to treatment groups is justified by the different treatments used in the conventional treatment arm and the use of individualised remedies in the homeopathy arm.

The criteria for allocating women to homeopathy or conventional treatment is not described but it is clear that women who elected to have homeopathy were allocated to a separate group and treated, as they desired. They were not included in the analysis, as this could have created a placebo effect due to their positive expectations of homeopathy

Using the REDHOT checklist, Table 30 Gerhard et al 1997 evaluated against REDHOT, highlights the issue that the knowledge condition of the patients appeared to present an obstacles to recruitment and that the medication, although listed by trade name, is not described fully.

Although the setting is a clinic with both conventional and alternative practitioners, the details of the experience, accreditation and qualifications of the prescribing practitioners are not made clear. The authors' position as a supporter of the holistic approach to treating infertility is explained and reference made to some of the difficulties that occurred when working with more conventionally trained medical colleagues.

The MVHT analysis, Table 31 Gerhard et al 1997 evaluated against MVHT, confirms that the rationale for the study is appropriate for women with amenorrhoea and sterility through hormonal causes, because there have been historical successes in the clinic. However the case is not so clear for the third group of women with idiopathic sterility and women with simultaneous organic change.

The criteria for inclusion and exclusion were appropriate to control for variables that would affect the outcome of the trial however the recruitment of sufficient numbers of women willing to be randomised was a stumbling block for this study.

The choice of 3,6,9 month testing dates to collect data on hormonal change and ‘questionnaire of sensitivities’ would be appropriate to monitor on-going changes and the patient’s perspective of the experience.

Due to recruitment difficulties the data analysis is not reported in this study, it presents instead a detailed break down of the reasons for recruitment failure. The framework being used to interpret the data is a mathematic (percentages) description of the reasons that women did not recruit. They provided a qualitative answer to what was a quantitative research question: Is it possible to show clinical effectiveness of homeopathic treatment vs. conventional treatment for female infertility using a randomised two-armed clinical trial?

This study found that women might not consent to be randomised to a clinical trial of homeopathy for a variety of clinical, practical and financial reasons. A preliminary qualitative study exploring women’s attitudes towards taking part in a trial might have revealed some of these problems and allowed them to generate a model or theory that would have informed the quantitative research phase. This could have improved on the simple model used to categorise and select women could not accommodate the complexity of their real life situations and choices including the long waiting times for diagnosis and treatment which eroded the number of women willing to be recruited.

The limitations of this study include the very small sample size (due to multiple difficulties recruiting patients) and the lack of subject blinding which would have allowed them to control for placebo.

The treatment regime is not standardised, each patient is being treated using individualised treatment so we are testing the efficacy of an approach not a remedy.

The study is of generally low methodological quality (Dean et al., 2007) because it does not include enough detail about the medications, prescriptions, practitioners, co-interventions, and adverse effects. However the model is valid because it attempts to investigate a condition that has been shown to respond to homeopathic treatment, with sensitive enough outcomes, that are prescribed according to homeopathic principles.

The ethics issues associated with the research centre around including a group that did not receive allopathic treatment which could be viewed as unethical but this is a clinic that women choose to attend because if offers a natural form of medicine. If this study were conducted today they would probably not have randomised to homeopathy vs. allopathic treatment for ethical reasons. Women who have been trying to conceive for a very long time do not want to wait for unnecessary months, as an alternative they could have randomised to placebo or homeopathy in addition to conventional treatment.

The implication for this thesis is that a mixed methods approach might be a better model for researching this kind of field. Infertility is a highly emotive subject and the perspectives of patients need to be taken into account if trial recruitment is to succeed. The findings of this study are particularly relevant to this thesis as it was also found that there are difficulties in recruiting women to this kind of trial in Jersey. The author hoped to avoid these difficulties by conducting a qualitative strand in London and this will explained in more detail later.

It has been cited by 5 other studies two by the same author (Article in German) and two are reviews. One review is a meta analysis of headaches and migraines so is not included here but (Van Wassenhoven, 2005) is of

interest as it summarises the thinking about how best to investigate homoeopathy in 2005.

The Homotoxicological Treatment Of Female Functional Infertility: A Clinical Trial (Lai, 2000). Translated From Italian By Professional Translator.

This article was not published as a peer reviewed article but does appear as a citation in some reviews of homotoxicology (Van Wassenhoven, 2005). Very few papers were available at the time of the original review and this was included as it dealt with homotoxicology and female infertility. The research question being addressed is: How does treatment with homotoxicology compare to allopathic treatment in women with female functional infertility?

The setting appears to be a clinical setting and the results were included in a national convention on homeopathy, homotoxicology and biological medicine in Italy in 2000. The paper has a clear bias towards the superiority of homotoxicology and describes it as a bridge between allopathy and homoeopathy.

Infertility is described using scientific concepts; remedy protocols are described using standard homotoxicology products not individualised remedies. Outcomes recorded are standard medical outcomes. This paper is written from the perspective of a positivist model, but dualistic nature of mind body medicine is accepted and these are made explicit by the author. Key concepts covered by this paper include:

- Homoeopathy as an alternative form of medicine that takes the mind-body connection into account.

- Homotoxicology as a bridge between modern medicine and homoeopathy. Infertility as a disorder that may have different causations.

- Ethical and generational conflicts that arise because of the introduction of new ART approaches and the awaking of public opinion.

- Homotoxicology as a third option between passive acceptance of infertility and the aggressive technology of ART.

Although he uses a quantitative methodology, described as a clinical trial, it is of poor methodological quality. When compared to the criteria on the CONSORT checklist it does not include an explanation about how sample size was determined, the methods used to generate randomisation sequences or a description of the allocation to blinded treatment groups, Table 32 Lai 2000 evaluated against CONSORT.

There is a strong rationale for this study as it sought to build on the clinical experiences described in earlier studies (Lai, 2000) and the success rate at the site clinic. The remedies used are complex formulations from Heel that meet the criteria for inclusion for the Principles domain of the MVHT, Table 34 Lai, 2000 evaluated against MVHT.

The lead author is qualified to prescribe for the condition under investigation but his homeopathic training is not made clear. The outcome measures chosen were suitable to show a clinical effect. There was no long term follow up described but the data was collected over an eight month period which would have been long enough to see some changes of function such as hormone level or endometrial thickness. On the whole this trial does represent a valid model to answer the research question but it is insufficiently reported and cannot therefore be assessed as a high quality clinical trial.

Three subsets of women with different infertility conditions were randomised to homotoxicological or allopathic treatment:

Subset A: women with irregular anovulation suffering from premature luteinisation who were part of the large group entitled Unexplained Infertility. (n=29)

Subset B: women with normal ovulation and presumed minor cervical factor who were part on the group entitled unexplained infertility. (n=34)

Subset C: women suffering from ovulatory disorders associated with Hyperandrogenization (Polycystic Ovary Syndrome). (n=29)

Therapeutic responses were compared in the six resulting groups and the outcomes included: monthly monitoring of ovulation and hormonal status, pregnancy rate, side effects and ovarian volume.

Women were selected on clinical indications so there is no control for practitioner bias, they may have selected women who they thought would do well in the trial.

The type of homeopathy used is evidenced by the description of the treatments and includes the use of mesotherapy at specific acupuncture points, which could confound the results due to the medication. There is no description of which acupuncture points were used or if these were individualised to each patient.

As an alternative to describing this as a clinical trial the authors could have framed it as a series of case studies or observational studies, and included patient questionnaires to gather qualitative data on their perceptions and experiences when taking part in the trial. This data could have then been used to compare the two arms of the trial, inform the design of further investigations or been triangulated with other analyses as part of a mixed methods approach.

However it depends upon the research question being asked, in this case they were assessing the clinical outcomes between two approaches and in order to show a significant difference they would need to collect data from a larger sample and analyse it using a statistical analysis. Some statistical analysis of the data would have allowed stronger associations to be made between the treatment and the outcome. The existing data analysis is quantitative but is observational/descriptive data that cannot therefore be used to make inferences or demonstrate causal relationships.

The authors claim that their results show that patients taking the homotoxicology achieved the same therapeutic response as those patients on allopathic treatment. However this data has limited value due to the poor methodological quality of the trial so the conclusions are not reliable. It is, however, useful as a model of a trial including the homotoxicological approach.

The limitations of this study are highlighted when compared to the REDHOT list of criteria, Table 33 Lai, 2000 evaluated against REDHOT. The author provides very few details about the knowledge condition of the participants and practitioners involved, or the setting and consultation process. There is no information about how the sample size was determined or how randomisation was generated. This means that the study is not reliable or repeatable. The small sample size and poor control of variables makes this study more like a case study or observational study than a clinical trial.

Randomisation of women to a homotoxicology group is not ethical as it withholds treatment from this group. There is no mention of how they have obtained informed consent from the women taking part, no details given about informed consent to be randomised to the different treatment groups and no details about how ethics approval was sought or granted.

Trial design, use of alternative approaches in infertility treatment, ethics of working with women being treated for infertility where their age has a big

impact on their predicted outcomes. This paper was included in review of homeopathy (Van Wassenhoven, 2005).

The efficacy of the complex medication Phyto-Hypophyson L in female, hormone related sterility. A randomized, placebo-controlled clinical double blind study. (Bergmann et al., 2000)

This article is only published in German but there is an English abstract available. The setting of the study was a German University Clinic.

It takes a positivist approach with quantitative clinical trial design and the commonly agreed medical definitions of infertility are used. The data analysis is appropriate for the intention of the trial; the positivist statistical approach would allow the research question to be answered. The research question was: How does Phyto-Hypophyson L compare to placebo when measuring the clinical outcomes of infertile women taking them both over a three month period? Key concepts include Infertility/Sterility as having a functional cause, and that the use of 'alternative' treatment can be measured using quantitative tools.

Randomised double blind placebo controlled study of 67 women with oligomenorrhea and 30 women with amenorrhea received 50 drops of Phyto Hypophyson L or placebo three times a day over 3 months or 3 cycles.

Outcomes measured were spontaneous menstruation, improved concentration of progesterone in the luteal phase, shortening of the cycle, earlier ovulation and pregnancy. Collection of hormonal status data and clinical findings were used to test the difference between remedy and placebo in the subjects.

From the information available the trial quality is compromised because there is no description of randomisation and blinding or the number of participants randomized to each group. The trial registration number is not provided and there is no disclosure of funding sources.

The abstract does not include a rationale for undertaking the study and there is no information about the knowledge condition of the patients regarding homeopathy. The trial medication is name and the dose is described but the whole formula is not discussed in the abstract. The number of practitioners, their qualifications and experience are not given so it is difficult to judge this study according to the REDHOT criteria, Table 36 Bergman 2000 evaluated against REDHOT. The use of placebo is mentioned but there are no details in the abstract regarding its type or manufacture.

The model validity is uncertain, as the abstract does not contain enough information to warrant a 'yes' outcome in all the domains contained in the MVHT model Table 37 Bergman et al 2000 evaluated against MVHT.

The authors could have improved the trial design if they had included a patient well-being questionnaire and conducted interviews to gather qualitative data of how patients felt about being randomised, about taking remedies daily, and exploring their perceptions of themselves as infertile.

There were no significant effects when viewing the whole group; outcomes for women in the oligomenorrhea in the Phyto Hypophyson L group had superior outcomes to the placebo group (82 versus 45% p=0.021).

The verum group showed a significant increase in progesterone during the luteal phase compared to the placebo group and only a very few undesirable drug effects were observed

Details of blinding and randomisation were not reported in abstract, which is a limitation of the study. The original article is only in German, the availability of a full English translation was checked with Robert Mathie at the Faculty of Homeopathy but he only had access to the same translation as myself.

This study is reviewed in Complementary and Alternative Medicine (CAM) in reproductive-age women: a review of randomized controlled trials (Fugh-

Berman and Kronenberg, 2003) as one of only two studies identified that investigate the effectiveness of CAM therapies for female infertility.

It has been noted (Mathie et al., 2012) that some homeopathic trials have been broadly criticized for their lack of acceptable model validity e.g. homeopathic complex medication in female infertility (Bergmann et al., 2000) (Kraft, 2001) and this highlights the need to investigate the third attribute of an RCT, it's model validity.

Papers that explore the use of CAM to treat infertility

Three additional papers were chosen in a non-systematic way, (as part of an iterative cycle of reading and writing) to represent the social context of the use of CAM to treat infertility as a narrative form of review.

Complementary and Alternative Medicine (CAM) in reproductive-age women: a review of randomized controlled trials (Fugh-Berman and Kronenberg, 2003)

Set in the context of an American University and published in Reproductive Toxicology 2003, this paper seeks to review randomised controlled trials of CAM therapies for obstetrical and gynaecologic conditions and presents therapies that are likely to be used by women of reproductive age and pregnant women.

The research question being investigated is 'What are the CAM exposures that can be expected in women of reproductive age?' A positivist methodology was used with a computer search of databases using search term and authors own extensive files. Clinical information was extracted from the articles and summarized in tabular form or in the text. No specific definition of infertility is used.

The main findings were that limited evidence supports the efficacy of some CAM therapies; exposure of women of reproductive age to these therapies can be expected. Most trials are small and definitive efficacy studies are lacking. Mechanisms of action are largely unexplored. Studies are described as ‘intriguing’ and ‘encouraging’.

This study does not meet the PRISMA requirements for a systematic review (Moher et al., 2009) as the methodology is especially weak as there is very little information on the eligibility criteria, the search strategy or the process of selecting studies. Details of the PRISMA criteria for this study can be found in the appendices Table 38 Fugh-Berman and Kronenberg, 2003 evaluated against PRISMA

There is no attempt to assess the trials included in the study for model validity or bias. The findings are therefore limited. It is useful as a list of available studies in this field but does not attempt to review them critically.

They warn that healthcare providers and consumers should be aware that despite the potential usefulness of many CAM therapies, scientific research is limited. They believe that the harmlessness of ‘sub therapeutic’ doses cannot be assumed. CAM therapies are popular with pregnant women and because herbs, vitamins and other natural products have limited patentability and because there is no requirement for testing industry sponsored research will remain limited. Federal, private and other alternative funding sources must bridge this gap. Scientific evaluation of both safety and efficacy of these therapies is important to public health.

It is cited by 95 studies including a study that attempts to evaluate the quality of CAM treatments a few years later:

However, there is still a paucity of well-designed and executed studies [16]. We used the Oxford criteria to evaluate the quality of studies of CAM treatment (Oxford centre for evidence-based medicine 2001). This system places homogeneous systematic reviews of randomized controlled trials

(RCTs) at the highest level, followed by single RCT with narrow confidence intervals, case-control studies, case series, and expert opinions. In this review, we sought to identify systematic reviews, meta-analyses, RCTs and prospective cohort studies ahead of case-series and case reports. (Weiss et al., 2011)

Complementary therapy and obstetrics and gynaecology: a time to integrate (Dooley, 2006)

This study was selected because it is a good example of a Pragmatic worldview, it acknowledges the mind-body divide and recognises the dualisms between conventional and complementary medicine without needing to take a side.

This perspective is made clear in the summary, where he is saying that we need to develop an integrated approach to healthcare. Value is placed on both conventional and alternative medicine.

The paper is probably best described as a position paper, the author runs an integrated health clinic in London, and is a non-systematic review of literature, political and cultural contexts. He offers an opportunity for reconciliation between opposing viewpoints by taking a broader view of the problem and integrating opinions from both mainstream medical and CAM perspectives.

The key concepts covered include: biomedical assumptions, patient choice, complex interventions, holistic integrated approach vs. duality, equality of access to treatments that are funded by individuals, polypharmacy and regulation of CAM.

This paper finds that an integrated approach to infertility may bring some benefits, that there is a need for an integrated approach, he acknowledges that there is a lack of randomized trials but that patient use is high.

He highlights that there is a need to improve patient care and shared communication when working in an integrated way, that there is a funding imbalance when it comes to research in the area of CAM.

The main limitation of this paper is that it is not a systematic review of available data, more of a position paper, but it forms a useful source of information when seeking a context for studies such as this thesis.

This paper represents a clear call to policy makers to consider abandoning traditional dualisms it has been cited by 16 studies including (Erin et al., 2014) a study that uses a qualitative approach to investigate how CAM practitioners might be integrated into the treatment of infertility.

Perspectives of Complementary and Alternative Medicine (CAM) practitioners in the support and treatment of infertility.(Erin et al., 2014)

The objective of this study was to determine the roles of CAM practitioners in the support and treatment of infertility. Ten semi-structured interviews were conducted in Ottawa, Canada in 2011 with CAM practitioners who specialized in naturopathy, acupuncture, traditional Chinese medicine, hypnotherapy and integrated medicine.

They found that CAM practitioners played an active role in both treatment and support of infertility, using a holistic, interdisciplinary and individualized approach. CAM practitioners recognized biological but also environmental and psychosomatic determinants of infertility. Participants were receptive to working with physicians but details of the collaboration were not included.

They concluded that integrated infertility patient care achieved by collaboration with CAM practitioners and incorporation of CAM's holistic,

individualized and interdisciplinary approaches would greatly benefit infertility patients.

For some patients, ART presents significant financial, psychological, moral and ethical challenges, which may lead to discontinuation of treatment [12]. As medicine, in particular ART becomes increasingly technological, patients are choosing complementary and alternative medicine (CAM); perceived as more natural with less side effects.

Conclusion

Research Questions: What is homotoxicology? Are there any existing trials of homotoxicology to treat infertility? What is the role of CAM in treating homotoxicology?

The homotoxicological paradigm (Smit A, 2009) is a homeotherapeutic system in which a medical diagnosis is made, followed by an individualized assessment according to the severity of the patient's disease. This takes into account the response of the patient's self-regulatory system to exogenous and endogenous stressors. Treatment is given, using predominantly homeopathically prepared medicines, to support the inherent self-regulating ability of the body rather than just treat symptoms, which are seen as an expression of the body's own defence that should not be suppressed. (Heel, 1986).

A systematic qualitative review of the existing trials has shown that there is a gap in the literature for a methodologically sound, well-reported trial, to investigate the use of homotoxicology in infertile women. Earlier trials (Lai, 2000), (Bergmann et al., 2000) do seem to indicate that homoeopathic products can provide improved fertility outcomes to women in a clinical setting.

Infertility patients are increasingly using complementary and alternative medicine (CAM) to supplement or replace conventional fertility treatments (Erin et al., 2014) and (Fugh-Berman and Kronenberg, 2003) and therefore more information about their safe use is needed.

The difficulty of reproducing clinical success as a randomised controlled trial has been dubbed the 'efficacy paradox' where the use of quantitative trial designs lead to a situation where internal validity is emphasised at the cost of external validity. It is of little benefit to produce methodologically sound results if they do not reflect the real-world situation (Lewith et al., 2010).

The position paper (Dooley, 2006) captures the context of this thesis, a time where the battle lines between complementary and conventional medicine were being drawn up, and the type of evidence that was being called for by was very much predicated upon quantitative methods. The low methodological quality of the trials that were available also seemed to make it imperative that better RCT trials were needed, whereas by the time this thesis was nearing completion it was clear to the author that good evidence should capture several domains of knowledge including the perspective of the patient and the usefulness of the knowledge to a wider audience or population. A researcher setting out to conduct a similar trial today would have access to alternative designs such as pragmatic trial design rather than automatically choosing an RCT model.

Limitations

At the time that the selected studies were written it was not so common to find mixed methods research designs but if researchers were replicating those studies today it would perhaps seem more obvious that the views and perspectives of the participants needed to be taken into account. In order to improve upon existing studies the trial design for the quantitative phase of this thesis is informed by qualitative data collection and analysis.

LITERATURE REVIEW

Literature Review - Section 4 The Use Of RCT To Investigate Homeopathy/Homotoxicology

Research Question

What steps can be taken to ensure the model validity of an RCT to measure the efficacy of Ovarium compositum?

Introduction

Open-label randomised controlled trials (RCTs), and blinded, placebo controlled RCTs are listed at the top of the hierarchy. They offer the most internal validity and minimization of bias and are considered by many to be the most reliable evidence for evaluation of modern medical interventions. (Lewith et al., 2010)

The choice of a London Medical School for the author's PhD studentship led to the expectation that her study of Ovarium compositum would be quantitative in style. An RCT is the correct method to use when the investigator is aiming to provide unbiased answers to specific hypotheses and theories regarding efficacy and harms of interventions on a well-defined and measured clinical outcome *(Lewith et al., 2010)*.

The control of variables allows the investigator to attribute observed outcomes to the action of the medication. However by controlling the variables the trial situation can become very different from the real life clinical situation. This was not considered to be a problem for Ovarian compositum as it was not going to be prescribed on an individualised basis but as a routine prescription for women undergoing infertility treatment. The trial and the clinical situation would be very similar in structure; if the outcomes of the trial were shown to be beneficial then this would be easily translated into routine clinical use.

Context

The debate around the funding of homeopathy by the NHS provides a practical example of this problem. In 1995 (Smith, 1995) it was recognised that the provision of homoeopathy by the NHS for many years had created a political and cultural acceptance of CAM. However this was increasingly being challenged as by 1997 (Wise, 1997) one London health authority had decided to stop buying homeopathy on 'evidence' based grounds. The vigorous defence of CAM (Fisher and Eden, 1995a) in the medical press has been a catalyst for the development of methodologies for investigating complex and holistic interventions.

Methodology

This section is structured as a narrative overview that reports in a condensed format the contents of each article with a critique of each study. The reasons for writing such an overview is to present an up to date overview which can be used to encourage scholarly discourse and a participatory approach to dynamic knowledge development (Green et al.)

Selection of Papers for Review

Papers were selected from an acknowledged expert in the field, Robert Mathie, PhD who also represents the Faculty of Homeopathy.

Method for appraising model validity of randomized controlled trials of homeopathic treatment: multi-rater concordance study (Mathie et al., 2012)

Model validity refers to the fact that the research must be a fair exemplar of the practice in use and the method chosen to test it must reflect the goals and context of the audience that will use the consequent information.(Lewith et al., 2010)

Throughout this thesis the shift of perspective away from positivist assumptions towards the use of Mixed Methods Research tools has created an awareness of the need to work with transparency, with validated tools and

to demonstrate that the papers chosen have been subjected to critical appraisal. The need for a tool to appraise model validity of randomised controlled trials of homeopathy has been met by the MVHT (Mathie et al., 2012).

Internal validity is the extent to which the design, conduct and analysis of a trial has minimised or avoided bias in its comparison of treatments. This can be adequately measured with existing well-defined criteria such as QUOROM, PRISMA AND CONSORT.

However there are some unique features of homeopathic practice that create the need for a model that is valid for it's investigation so that there is a concordance between the trial study design and "state of the art" practice for the intervention under investigation.

The existing model RedHot (Dean et al., 2007) does not provide the means to define or assess model validity and the high risk of false negative results in the systematic review of the current literature is increased by the absence of a model to use to assess study validity.

The need to create a new model was addressed by an international group of homeopathic practitioners/researchers, who by using an integrative process developed six novel judgement domains. These domains, can be used to assess the model validity of trials of homeopathy with 'fair' to 'almost perfect concordance' and they have been used in this literature review as well as in the review of OVCT-001, the quantitative phase of this thesis.

The domains and their criteria are summarised in the table below which has been adapted from (Mathie et al., 2012).

Table 10 Domains of MVHT

Domain	*Criteria*
Domain 1 (Rationale) Would a significant body of accredited homeopaths support the	

rationale for the intervention used in the study?	
Criteria for a judgment of 'Yes'.	*Both of the following:* *Clinical knowledge and practice inform that, for the condition under investigation, the health of patients may be benefited by homeopathic intervention.* *A substantial number of experienced homeopaths would support the choice of this intervention for this type of patient.*
Criteria for a judgment of 'No'.	*One or both of the following:* *Clinical knowledge and practice do not inform that, for the condition under investigation, the health of patients may be benefited by homeopathic intervention.* *A substantial number of experienced homeopaths would not support the choice of this intervention for this type of patient.*
Criteria for a judgement of 'Unclear'.	*One of the following* *There are likely to be important differences among experienced homeopaths on the rationale for the intervention used.* *Insufficient information to permit judgment of 'yes' or 'no'.*
Domain 2 (Principles) Is the specific intervention used consistent with homeopathic/homotoxicological principles?	
Criteria for a judgement of 'Yes'.	*One or both of the following:* *The intervention used is based on the principle of 'like treats like' or is based on the principle of isopathy.* *Literature sources (material medica, repertory etc.) are available that convincingly justify the specific intervention.*
Criteria for a judgement of 'No'.	*One or both of the following:*

	The intervention used is not based on the principle 'like treats like' or of isopathy *Literature sources do not convincingly justify the specific intervention*
Criteria for a judgment of 'Unclear'.	*Insufficient information to permit judgement of 'yes' or 'no'.*
Domain 3 (Practitioner) Does the study have suitably qualified and experienced homeopathic prescriber input?	
Criteria for a judgement of 'Yes'.	*Either of the following as appropriate:* *Individualised homeopathy: Those who have prescribed the homeopathic medicine(s) are suitably trained and experienced in homeopathy to manage the condition under investigation.* *Non-Individualised homeopathy: There is evidence that experienced homeopathic input (and/or a suitable literature source) has been involved in informing the choice of medicine(s) used commonly for all patients in the study.*
Criteria for a judgement of 'No'.	*Either of the following as appropriate:* *Individualised homeopathy: Those who have prescribed the homeopathic medicine(s) are not suitably trained and experienced in homeopathy to manage the condition under investigation.* *Non-Individualised homeopathy: There is evidence that experienced homeopathic input (and/or a suitable literature source) has not been involved in informing the choice of medicine(s) used commonly*
Criteria for a judgment of 'Unclear'.	*Insufficient information to permit judgement of 'yes' or 'no'.*
Domain 4 (Outcome Measure) Does the main outcome reflect the main effect expected of the intervention used?	
Criteria for a judgement of 'Yes'.	*The main clinical effect expected of the intervention is adequately measured by the main outcome used.*

Criteria for a judgement of 'No'.	*The main clinical effect expected of the intervention is not adequately measured by the main outcome used.*
Criteria for a judgment of 'Unclear'.	*Insufficient information to permit judgement of 'yes' or 'no'.*
Domain 5 (Sensitivity) Is the main outcome capable of detecting change?	
Criteria for a judgement of 'Yes'.	*All of the following:* *The main outcome measure is sensitive to changes of the magnitude expected in the patients under investigation.* *The main outcome measure is capable of determining both improvement and deterioration.* *The main outcome measure shows no evidence of a 'floor effect' and/or 'ceiling effect'.*
Criteria for a judgement of 'No'.	*Any one or more of the following:* *The main outcome measure is not sensitive to changes of the magnitude expected in the patients under investigation.* *The main outcome measure is not capable of determining both improvement and deterioration* *The main outcome measure shows evidence of a 'floor effect' and/or 'ceiling effect'.*
Criteria for a judgment of 'Unclear'.	*Insufficient information to permit judgement of 'yes' or 'no'.*
Domain 6 (Follow up) Is the length of follow-up for the main outcome measure appropriate to detect the intended effect of the intervention?	
Criteria for a judgement of 'Yes'.	*The time-point selected for main follow-up measurement provides sufficient opportunity for a clinical change to be observed.*
Criteria for a judgement of 'No'.	*The time-point selected for main follow-up measurement does not provide sufficient opportunity for a clinical change to be observed.*

Criteria for a judgment of 'Unclear'.	*Insufficient information to permit judgement of 'yes' or 'no'.*

Since 2012 Researches have had the aid of the MVHT to check the model validity of their quantitative studies and although this was not available to the author during the planning stage it has been helpful in reflecting on the trial design:

Domain I (Rationale)

Clinical knowledge and practice inform that, for the condition under investigation, the health of patients may be benefited by homeopathic intervention.

A substantial number of experienced homeopaths would support the choice of this intervention for this type of patient.

The literature review has shown that two studies, although of poor methodological quality, seem to indicate that infertility outcomes can be improved with the use of complex homeopathic prescribing.

Ovarian compositum was considered suitable for the RCT model because the women are part of a clinical group that have been selected due to their well-defined diagnosis. The first qualitative strand was the review of homotoxicology treatment for infertility in the UK, which sought to established support for the choice of intervention for infertile women.

Domain II (Principles).

One or both of the following:

The intervention used is based on the principle of 'like treats like' or is based on the principle of isopathy.

Literature sources (material medica, repertory etc.) are available that convincingly justify the specific intervention.

Homotoxicology uses complex formulations instead of single remedies and is not prescribed on individual indications but instead on clinical indications, each ingredient is selected for its targeted homeopathic action on a tissue, organ or function.

The clinical indications for Ovarium compositum are listed (Heel, 1986) as: "Stimulation of the glandular and defensive functions, as well as those of the connective tissue, in dysmenorrhoea, endometritis, metritis, parametritis, enuresis (in young girls), in the climacteric, hyperemesis, insufficiency of the anterior lobe of the pituitary gland in females, craurosis vulvae, mastodynia, osteomalacia, menorrhagia, as well as in various disturbances of metabolism, including those arising in geriatrics."

Due to its individual homeopathic constituents Ovarian Compositum has an application in the homeopathic treatment of hormonal disturbances, menopausal syndromes and insufficiency of the pituitary gland. The individual ingredients are a mixture of different homoeopathic potencies ranging from D4 – D18.

Domain III (Practitioner)

Either of the following as appropriate:

Individualised homeopathy: Those who have prescribed the homeopathic medicine(s) are suitably trained and experienced in homeopathy to manage the condition under investigation.

Non-Individualised homeopathy: There is evidence that experienced homeopathic input (and/or a suitable literature source) has been involved in informing the choice of medicine(s) used commonly for all patients in the study.

As chief investigator the author, Claire Haresnape, was qualified and insured to prescribe homotoxicological preparations and had also studied classical homoeopathy for five years with a practitioner in North Devon.

The choice of Ovarium compostitum to treat female infertility was supported by the medical expertise of the manufacturer Heel.

Domain IV (Outcome Measure)

The main clinical effect expected of the intervention is adequately measured by the main outcome used.

In the opinion of the author the outcomes chosen will allow sensitive measurement of the differences between individual responses. This was confirmed by the view of the external peer reviewer:

The study uses a number of measures: experimental (endometrial thickness, number of follicles progesterone levels) as well as the Quality of Life measure. These measures seem appropriate and adapted to capture any significant difference between the two groups, as well as offering room for interpretation of the results in terms of possible mechanisms of action.

The inclusion of a blinded placebo group should allow the difference between specific effects due to the remedy and non-specific placebo effects to be detected.

Domain V (Sensitivity)

The main outcome measure is sensitive to changes of the magnitude expected in the patients under investigation.

The main outcome measure is capable of determining both improvement and deterioration.

The main outcome measure shows no evidence of a 'floor effect' and/or 'ceiling effect'.

The outcomes for the quantitative strand of the study are listed below and discussed for their sensitivity and appropriateness:

1. Follicular count and Ovarium volume
2. Follicular stimulating hormone (FSH) levels
3. Estradiol (E2 or 17β-estradiol, also oestradiol) at day 2
4. Progesterone Levels at day 21
5. Pregnancy confirmed with a pregnancy test
6. Live birth

Ovarian volume has been shown to be an important tool in the assessment of ovarian reserve and the prediction of response to ovulation induction (Lass and Brinsden, 1999). The routine use of trans vaginal scans has led to quick, accurate and cost effective assessment of ovarian volume. Poor response to treatment leading to cycle cancellation and failure to retrieve oocytes is associated with smaller ovaries (Lass and Brinsden, 1999), advancing maternal age is also associated with a decrease in ovarian volume and fewer follicles.

The menstrual cycle is a complex combination of synchronized endocrine events involving the release of hormones by the hypothalamus, the anterior pituitary and the ovaries. The measurements of reproductive hormones are an important part of the assessment and management of women undergoing infertility treatment. The measurements are capable of detecting both increases and decreases in hormonal levels.

Follicle Stimulating Hormone (FSH) is measured during the follicular phase (days 2-3) of the menstrual cycle. The normal values are 5-20 mIU/L. FSH values >10 IU/L predict a poor response to ovarian stimulation. FSH values >18IU/L are predictive of poor pregnancy outcomes (Delaney, 2012)

In a study of 1019 infertile but ovulating women, studied during their first IVF cycle of treatment, it was found that serum FSH levels are also a valuable prognostic tool for the assessment of oocyte quality and fecundity (Akande et al., 2002). The number of oocytes retrieved and embryo's available for transfer declined with advancing age and basal serum FSH concentrations.

Estradiol (E2) is a steroid hormone secreted into circulation by granulosa cells of developing ovarian follicles. It is also measured in the follicular phase, days 2-3 of the menstrual cycle. The normal range is 20-400 pg./mL. It is helpful in combination with FSH to establish a baseline ovarian reserve, and has useful prognostic value in the treatment and counseling of patients of advanced reproductive age who are considering ovulation induction and IUI therapy (Buyalos et al., 1997).

Progesterone is a hormone produced mainly in the ovaries by the corpus luteum and it helps to prepare the uterus for the implantation of the fertilized egg. If a fertilized egg implants then the progesterone helps the uterine lining to maintain the pregnancy. Women undergoing fertility treatment usually have their progesterone levels checked about day 21 of a 28-day cycle during the luteal phase. If the progesterone is elevated within a certain range (greater than or equal to 32nmol/L) it means that the woman is ovulating. Low progesterone levels may indicate a failure to ovulate.

The serum progesterone level as been found in some studies to be a better predictor of future live births than levels of any of the other hormones (Murto et al., 2013). One problem with using serum progesterone is that it has a wide range of concentrations during the menstrual cycle (Follicular phase: <3ng/mL, Secretory phase: 5-30ng/mL) so that more than one test is needed. Some researchers now favour the use of serum Anti-Mullerian hormone (AMH) instead of progesterone as it has very little variation during the menstrual cycle (Murto et al., 2013). At the time of designing the quantitative strand of this study AMH testing was not available at Jersey General Hospital although the desirability of using this test was discussed.

The combination of these different hormonal tests allows the collection of data that is sensitive to the individual responses of women to their treatment. Small differences in hormonal status may indicate changes in ovulatory status or be predictive of treatment success or failure.

Outcomes such as pregnancy and live birth may have more significance to the patient or the clinic as part of their success rate and a qualitative study would be an interesting way to further explore the perceptions of women and their clinicians towards the different outcomes that can be measured.

There was no mention found in the literature reviewed of either a floor or ceiling effect when measuring these hormonal levels.

Domain VI (Follow-up)

The time-point selected for main follow-up measurement provides sufficient opportunity for a clinical change to be observed.

The women recruited to the study were expected to attend the clinic for follow-up appointments every 30 days for up to 12 months. This timescale would allow the capture of data, such as hormonal status, on a monthly cycle of treatment and would capture any pregnancies or live births that resulted from treatment. Follow up of live births or pregnancies that occurred after the 12-month treatment period was agreed with the clinic and with Heel.

Randomized controlled trials of homeopathy in humans: characterizing the research journal literature for systematic review (Mathie et al., 2013)

Mathie et al (2013) showed that a placebo controlled RCT can be used as a feasible method for assessing non-individualised homeopathy/ homotoxicology. The context for this paper is the British Homeopathic Association, Faculty of Homeopathy, and the audience is a mixed Medical/ Homeopathy audience.

The research question being investigated is the provision of an up to date and comprehensive systematic review of the entire international RCT literature in homeopathy. This new programme needs to distinguish important attributes that are unique to RCT trials of homeopathy: (a) treatment versus prophylaxis, (b) placebo versus other than placebo (OTP), (c) individualised versus non individualised homeopathy, (d) Peer Reviewed (PR) versus non peer reviewed (NPR) journal sources.

Written from a post positivist perspective this is a uniquely detailed and systematic review of homeopathic randomised controlled trials, searching and categorising trials using electronic databases. The data collection was systematic and made sure that all available published trials were considered for review. Translations were employed to make sure that non-English papers were also considered.

A pragmatist framework was employed to decide about the appropriate categories with which to review RCT trials of homeopathy. Earlier reviews had not considered the need to distinguish between (a) treatment versus prophylaxis, (b) placebo versus other than placebo (OTP), (c) individualised versus non individualised homeopathy, (d) Peer Reviewed (PR) versus non peer reviewed (NPR) journal sources.

This review is of good quality because it is unlikely that important papers have not been included. The conventional clinical trial terminologies are used and the search criteria used different spellings and presentations of homeopathy and homeopath. The categories selected for inclusion and exclusion were suitable to answer the research question. The paper compares well with the criteria for systematic reviews as defined by PRISMA (Moher et al., 2009) and a summary of this can be found in APPENDIX 1 as Table 39 Mathie et al 2013 evaluated against PRISMA.

The findings clarify the RCT literature in homeopathy. The 263 accepted journal papers would be the basis for a forthcoming programme of systematic reviews. The limitation of this review is that it does not include qualitative

studies or MMR, which would capture other important aspects of homeopathy and healthcare provision. 96 studies of placebo controlled, non-individualised homeopathy were identified and included two records for the condition of female infertility: A52 (Bergmann et al., 2000); A74 (Gerhard et al., 1998). The Gerhard paper has not been included in my own literature review because it is not easily available in English. The authors of this study acknowledge that they had access to optimum resources and that the multi-language nature of the literature can be problematic for researchers.

Conclusion

What steps can be taken to ensure the model validity of an RCT to measure the efficacy of Ovarium compositum?

A systematic review of the literature by an expert in the field (Mathie et al., 2013) has shown that there are very few RCT trials of homeopathy versus placebo for female infertility. However 96 studies of placebo controlled, non-individualised homeopathy were identified and so the RCT is shown to be a suitable method for investigating the specific effects of a homeopathic medicine compared to a placebo.

The MVHT (Mathie et al., 2012) provides homeopathic researchers with an appropriate tool to ensure the validity of their own trial designs as well as a way of assessing the validity of published work in this field. It can be used in conjunction with existing tools such as CONSORT to ensure that trial design meets the criteria necessary for a high methodological quality of a good RCT.

Limitations

The choice of papers by an expert in the field of RCT for homeopathy could potentially lead to a bias in the conclusions of this review. However the methods used by Mathie are transparent, rigorous and systematic and his work is therefore considered both credible and reliable as an evidence source.

Literature Review - Section 5 - The Concerns of Infertile Women.

Research Questions

What are the concerns of infertile women? Do existing studies offer any insight for trial design?

Methodology

The narrative literature review for this section was developed and refined as part of an iterative cycle of data collection and review during the fourth qualitative strand of the thesis. Although the papers selected were read critically and systematically using a checklist, this was not a systematic view of the literature, the work of Charmaz on self identity at work was suggested after reading about the methodology of Grounded Theory (Charmaz, 1990).

The work by Brandes on the dropout rates in IVF (Brandes et al., 2009) was first noticed when reading the conference proceedings from ESHRE (The European Society of Human Reproduction and Embryology) 2009.

The paper on the concerns of women undergoing infertility treatment (Finamore et al., 2007) was found using ("employment"[MeSH Terms] OR "employment"[All Fields]) AND ("infertility"[MeSH Terms] OR "infertility"[All Fields]) as a PubMed search (December 2013).

Another research team were recruiting women during the data collection for the fourth strand of this thesis. This was noticed when they also posted a request on same infertility online support group website. Communication was established with Nicola Payne of Middlesex University and some of the insights from their preliminary results are also reviewed in this section. Their full dataset had not been completely analysed at the time of writing this.

Introduction

Themes that were suggested by the staff at the ARU unit at Jersey General Hospital led to a hypothesis that women's concerns about employment and

disclosure were one reason for the failure to recruit sufficient women to the trial of Ovarium compositum. This was surprising as infertile couples are usually considered to be highly motivated to undergo investigation and treatment (Brandes et al., 2009). The literature was therefore searched for reports of the pressures faced by women who both work and seek infertility treatment.

If an employer is not supportive of the frequent absences necessary for treatment then the situation can lead to increased stress level, which in turn could affect fertility. Research suggests that stress, depression, anxiety and other negative psychological feelings result in poorer outcomes for patients undergoing IVF (Demyttenaere et al., 1994, Stoleru et al., 1997, Gallinelli et al., 2001, Boivin and Schmidt, 2005).

In both Jersey and the UK there is a need for men and women to have time off from work to attend appointments at an ARU when couples are undergoing infertility treatment. It has been suggested by the ARU nurse at Jersey General Hospital that women may feel considerable pressure when deciding whether or not to disclose fertility treatment to their employers as few employers have a policy on this and many managers are unsure how to deal with these cases (Hawksworth, 2012).

XpertHR, who offer an online advisory service to HR professionals, summarise the position thus:

‘Fertility treatment is not a "deemed incapacity" for statutory sick pay purposes. However, the treatment can affect people in different ways. An employee may well be ill due to the treatment, for example through depression or stress. If this is the case, it is up to the employer whether or not to accept the incapacity as stated on any medical certificate or form, in order to consider statutory sick pay entitlement.

There is no statutory right for an employee to receive time off, with or without pay, during normal working hours in order to undertake a course of fertility treatment. The maternity pay and rights legislation relates solely to an employee being pregnant and not to the causes of pregnancy.

The Health and Safety Executive recommends that women should be given a reasonable number of paid or unpaid days' absence towards any fertility treatment. Women generally require more treatment for in vitro fertilisation (IVF) than men do for fertility treatment, so they are more likely to incur absences from the workplace to undergo IVF. An employer could be exposed to an indirect discrimination claim if its rules on sickness absence adversely affect a woman undergoing treatment.'

(XpertHR, 2012)

The Legal Position In Jersey

At the time of writing this thesis, working women in Jersey and the UK who are undergoing IVF treatment are not afforded any specific employment protection, and IVF related sickness absences could be taken into account in the same way as other sickness absence for dismissal and disciplinary purposes (Hawksworth).

There have been some developments in European case law in this area (Mayr v. Backerei und Konditorei Gerhard Flockner OHG C-506/06 [2008]) over the past few years but there are still gaps in the law and women are often unsure as to how far they are protected. The current position is that the dismissal of a woman on the grounds of sickness absence due to the later stages of IVF will constitute unlawful sex discrimination.

The Jersey Advisory and Conciliation Service (Patricia Rowan, 2012) offered this advice:

'Without Prejudice

The employment legislation currently does not cover maternity, flexible working etc., nor do we yet have any discrimination legislation - it is hoped that by the end of 2014 this may have changed. Therefore it would only be under individual terms of employment for a business that individuals may be allowed some paid maternity break. It is certainly not uncommon for GP and hospital appointments (for any kind of treatment/illness) to be either taken

outside of working hours and/or the time made up at a later stage. If any employee exceeds the absence levels set by their employer then a capability process can be triggered and therefore jobs can be placed at risk – this applies for absence for any reason.'

The law therefore offers no protection to women in the early stages of infertility treatment such as the women who were being approached for recruitment to this study. Women being treated or evaluated for infertility must have a flexible work schedule and be willing and able to go for frequent office visits, leading to hours and sometimes days missed at work.

One study (Finamore et al., 2007) has explored this situation in more detail. It used a cross sectional questionnaire and then analysed the results using statistical tools.

Social Concerns of Women Undergoing Infertility Treatment (Finamore et al., 2007)

This quantitative study attempts to prove a link between cause and effect, infertility and stress related to needing time off for infertility treatment. It was set in an American University Infertility Treatment Centre and the concepts covered include infertility treatment as a stressful life event and recognition of the mind body connection in the form of PNEI. Their hypothesis is that in certain women, disclosure may lower stress and therefore increase success rate of IVF treatment.

Most women who did disclose did so because they needed a reason to leave work for frequent doctor visits. Among women who did not disclose the main reason for nondisclosure was to protect their privacy. Women who had a high school education were more likely to disclose than those with a college and postgraduate education. African, American/Caribbean American women were least likely to disclose. Those who were out of work more often because of their infertility were more likely to disclose. There was not an association with disclosure and decreasing stress levels.

The method used was a cross sectional questionnaire consisting of 38 questions and including a validated global measure of stress, a four item version of the Perceived Stress Scale (Cohen et al., 1983). Continuous variables such as patient's age, Perceived Stress Scores were analysed using mean and Standard Deviation (SD).

The student's *t* test was used to examine differences in characteristics between women who did and did not disclose their infertility status. Interval data such as gravidity and the number of people disclosed were analysed as proportion of total subjects who responded to the survey. A chi-squared test was applied to compare differences in proportions between women who did and did not disclosure their infertility status and evaluated associations based on odds ration (OR) with an 95% confidence interval (CI). All tests of hypothesis were two tailed, with a type one-error rate set at 5%. Incomplete surveys were not analysed.

The reason for using a cross sectional study is that it may be the only practicable method of studying various problems or where a randomized controlled trial might be unethical, or if the condition to be studied is rare. Cross sectional studies are used to determine prevalence. They are relatively quick and easy but do not permit distinction between cause and effect (Mann, 2003).

Cross-sectional studies are sometimes carried out to investigate associations between risk factors and the outcome of interest but they are limited by the fact that they are carried out at one time point, in this case a 6 month period, and give no indication of the sequence of events and therefore it is impossible to infer causality (Levin, 2006). They are usually used when the purpose of a study is descriptive and there is no hypothesis as such. In this study a hypothesis was being investigated, which was the risk factor of stress in infertility treatment.

They do have the advantage of being relatively inexpensive and take up little time to conduct. Another advantage is that they can be used to assess many outcomes and risk factors in one questionnaire.

The authors acknowledge that there are many confounding factors in their data collection including the fact that the survey was given to women who sought-first time treatment as well as women who were currently undergoing treatment.

The sample frame that was used to select the participants in this study did not represent the population as a whole, so the results cannot be generalized to a larger population. There is a concern that women are more likely to respond to the survey if they have a particular set of characteristics and therefore the responses are biased. Bias will occur when the characteristic is in someway related to the probability of having the outcome (Levin, 2006). In this case the women who are highly stressed may not have wanted to participate in the study or may have only partially completed the questionnaire.

The authors acknowledge that they were not able to determine how many patients refused to participate in the study and they were not able to identify any differences between women who did not and did participate in the study. They did attempt to limit participation bias by collecting in every questionnaire that was given out, however 12% of surveys were incomplete and could not be included in the analysis.

The data collection method does allow the calculation of risk factors but it is a snapshot in time. If a study wanted to look for risk factors in a wider population researchers could have conducted a literature review and possibly looked at data that is available from larger samples. As it stands it has not captured any qualitative aspects of the participants.

The authors acknowledge that there are difficulties controlling for psychological, behavioural and social differences between groups of

participants and perhaps some of these characteristics could have been captured using qualitative methods such as interviews or open-ended questions requiring a written answer. The practical concerns about conducting such as study have to be taken into account and balanced against the possible benefits.

It has generated some useful hypothesis for further study, and these are mentioned in the discussion section of the qualitative strand of the thesis, for example; the fact that women are more likely to disclose to a female supervisor and that women with a higher level of education are less likely to disclose their treatment.

The choice of statistical methods appears to be appropriate for the calculation of the association between the risk factor and the data collected. Demographic data that was collected could also be useful and interesting. For example how did women from different educational or racial backgrounds perceive their infertility, how did disclosure affect their employment status? This author's study seeks to describe some of those perceptions but because it used Internet data, does not distinguish between different ages, races or educational backgrounds.

It is acknowledged that women from different cultures may have different concerns about privacy and infertility. The data from this study did not address those differences, it observed them but did not describe them due to methodological choices.

The perception of stress may also vary between individuals. The Perceived Stress Scale (PSS) (Cohen et al., 1983) attempts to measure stress subjectively, or as perceived by the individual in the context of their cognitively mediated emotional response to an event. It is not a measure of the intensity or frequency of the event itself. This scale therefore is appropriate to capture the individual's response to stress in a situation where different individuals have different resources, support and coping

mechanisms. The scale was developed in America and the setting of the study is also American.

Some of the discussion points are interesting, for example is it possible that women with a higher level of education are in better paid jobs with better working conditions and are therefore able to be more flexible about taking time off work? How does this fit with their desire for promotion compared to their desire for a family? What is meant by privacy, is that to do with shame at being infertile or the desire to appear capable and in control at work?

The limitation of this study is that it is a snapshot in time that can only evaluate the risk factors in a small sample with potential bias towards women who are less stressed. It observes but not describes or explains some of the concerns of the women undergoing treatment.

The findings of this study have implications for the legal status of infertility treatment and the access to time off work, privacy and disclosure. It has been cited 8 times including (Huisman et al., 2009) This multinational, interview-based study was conducted to provide insights into participants' experiences, behavior, attitudes and emotions towards fertility treatments. One study group comprised 185 patients who were undergoing ovarian stimulation for IVF while the other comprised 170 physician and nurse fertility experts. A key study objective was to identify which aspects of ovarian-stimulation treatment contribute to the physical and psychological burden on patients.

It is cited by a second study that reviews the research exploring which psychosocial factors (e.g. personality traits and coping strategies) are associated with the emotional adjustment of IVF patients. The aim is to reveal what is currently known about risk and protective factors for coping with the stress of IVF treatment and where further enquiry would be most beneficial (Rockliff et al., 2014).

There is a commercial interest from pharmaceutical companies and clinics in retaining women for additional cycles of treatment if the first or second IVF cycle fails. This was mentioned in informal discussions with unit staff but has not been systematically investigated in this study. The ethics of such decisions and the potential benefits and harms to patients would make an interesting further area of research.

Disclosure at work and self-identity

Identity, chronic illness and disclosure at work have been investigated by Charmaz (Charmaz, 2010). We can draw valid comparisons between infertility and her analysis of chronic disease because of the long lasting nature of infertility and infertility treatment which can span several years and has a major impact on psychological, emotional and physical health.

Charmaz highlights the need to use insights from research into chronic disease to inform the management of human resources in the international workplace and this is directly relevant to the socioeconomic structure of Jersey which, as an offshore banking community, hosts offices for many multinational corporations:

‘Managers in global organisations may need additional training that focuses on dealing with and facilitating such disclosures, and universities all over the world involved in preparing local and international business graduates need to consider this issue in designing course content.’ (Charmaz, 2010)

Infertility, like chronic disease, may remain invisible in the workplace until people feel forced to reveal their condition or request special accommodations:

‘What is means to disclose illness and disability depends on a person’s health problem, cultural traditions, social values and norms, hierarchical arrangements, and specific policies in a given workplace.’ (Charmaz, 2010).

If visibility does not force disclosure then people see themselves as who they have been, not as who they have become. Workers with a chronic condition may experience daily limitations and restrictions but because they have

devised ways of organizing their life around them they do not feel a need to disclose their condition. Disclosure is often associated with an episode hospitalization and this could be compared with the hospitalization needed for IVF procedures or the aftermath of an unsuccessful implantation.

Charmaz notes that questions about disclosure also involve the relative legitimacy granted to the person's medical condition and as we discussed earlier in this chapter fertility treatment is not a "deemed incapacity" for statutory sick pay purposes. She highlights the fact that legitimacy matters to validate competent work, adult status and social acceptance.

'Experiencing an illness or disability often conflicts with business values that assume constant involvement and productivity, speed, coordinated timing, regular schedules and predictable performance levels.' (Charmaz, 2010)

If as she say; '*Disability does not reside entirely in the individual' but also 'depends on his or her match with a specific job'* then we can see the confusion caused by people switching between two roles: being competent at their job and then becoming unable to maintain that level of competency for a period of time due to the demands of their treatment regime.

It is understandable therefore that the positive or negative feedback from a manager will become an important validation of that person and their self-concept as they fluctuate between these two roles. Face-to-face relationships with shared interactions also shape how employers view people with disabilities (Charmaz, 2010). Employees who spend time face-to-face with their employer are more likely to experience a favourable outcome in negotiations about time needed for treatment.

Infertile men and women also face uncertainty about their probability of becoming parents and may have experienced loss of social and self-worth. In chronic illness this may lead people to struggle with losing their financial independence but in infertility this would not necessarily be the case.

Charmaz provides a model of the dilemmas of disclosure for an employee, which includes choosing between honesty, and privacy where cultural

stigmas associated with may influence that decision, this can be applied directly to infertility because disclosure may result in scrutiny or intrusive questions but also allows the person to explain behaviour that might have looked odd or suspicious.

Work-Life balance & Medically Assisted Reproduction (MAR): MAR users - experiences of workplace support (Payne, 2014)

During the time period that data was being sought on the online infertility forums another research group were also posting a request asking women to come forward and be interviewed about their work-life balance. Nicola Payne was kind enough to correspond with the author and we exchange several emails about our projects. In March 2014 we discussed our progress and she shared her slides for a conference of the European Academy of Occupational Health Psychology. The data analysis is not based on her full data (31 women and 6 men) set but on 15 women with a mean age of 35 (SD =5). They used semi-structured interviews to collect the data, which was then analysed thematically.

The framework for their literature search used role conflict theory (Greenhaus and Beutell, 1985) as this is common approach for research on work-life balance. The aim of their project was to explore the experiences of Medically Assisted Reproduction, (MAR), users of combining work and MAR. They hoped to be able to identify barriers as well as support mechanisms that people used.

The themes that they identified were presented as summary slides and are shown below as a list:

- **MAR-Work conflict**

- Time- and strain-based conflict, which included worrying about the results of treatment and the practical issues around taking time off.

- Work providing a distraction from the anxiety and allowing you to carry on as ‘normal’

- The impact of identity
    - A shift in anchor identity to ‘becoming a parent’ and work being put on the back burner
    - Resentment towards work if it was perceived to be getting in the way.

- **Support for MAR use**

- Manager support
- Most women experienced some degree of support from practical only to also including emotional support
- This enabled women to priories MAR, so supported their anchor identity and reduced conflict

- Shared understanding of the experience helped
- Job flexibility also helped reduce conflict

- The pros and cons of a specific policy
- Policy is needed but few workplaces had a specific policy and where it existed it was limited, so policy or guidance is needed.
- Constraints might include working for a smaller company where the absence has a greater impact on the company.
- There may be mutual benefits to working for a company that has been really good to you and therefore created a loyalty.

(Payne, 2014)

They concluded that MAR users experience a shift in identity to parenthood and so experience a ‘spill over’ conflict. Spillover (is) stress

> experienced in one domain of life, which results in stress in the other domain for the same individual. Spillover is… intra-individual… Thus, spillover is a process by which attitudes and behavior carry over from one role to another (Westman, 2005)

Line manager support and job flexibility can help to reduce this conflict. The existence of a specific policy or guidance is relatively rare but necessary and while there are constraints to providing support this may be mutually beneficial.

These early results have been included in this literature review because they offer a form of triangulation with my own data collection and analysis. They occurred during a similar time frame and with a similar target for recruitment. While they had the advantage of a larger sample they have not had time to perform a full analysis yet.

The other consideration is that they have used a specific framework for grounding the study (role conflict theory) and therefore their codes and assumptions are to some extent shaped by this orientation. Transparency about their choice of theory is strength of the study:

The benefit of greater attention to theory in qualitative research is that it enables a more sophisticated approach to the data so that a range of different questions can be asked of the data set. Theory helps to define what the strategy for analysis should be, including questions about level of analysis, and how to describe the way decisions about analysis have been made.(Kelly, 2009)

If the themes that were found in my own study are similar to the themes identified by Payne (Payne, 2014) then this will help to validate my own analysis, especially if we are starting from different theoretical perspectives and still find some common themes or understandings. It is important to note that her analysis was not available to me during the time that I was coding the data that I collected from the Internet forum.

When And Where Do Sub fertile Couples Discontinue Their Fertility Care? A Longitudinal Cohort Study In A Secondary Care Subfertility Population. (Brandes et al., 2009)

This study was set at The Jeroen Bosch Hospital, which is a large regional secondary care teaching clinic, performing almost all modern fertility treatments. GP's in that region of the Netherlands do not in general perform any basic fertility workup and do not prescribe fertility drugs. They refer couples if despite unprotected intercourse for at last 1 year no on-going pregnancy has occurred. In the Netherlands all treatment cycles are fully reimbursed as well as a maximum of three IVF or ICSI cycles.

Implicit in the study design are the post positivist values of society that acknowledges the emotional and psychological needs of the patient. Best practice is to include a social worker in the care team. This is an observational study that seeks to construct an understanding of a process.

These values and beliefs are explicitly present in the description of the context and the methodology. For example, care is taken that the couples that stopped fertility care at the study site were followed up, so that the study was performed from the patient's perspective and not just the investigators' perspective.

The aim of this study is to analyse at which stage couples from an unselected secondary care subfertility population discontinue fertility care. The reasons for withdrawal and the spontaneous pregnancy rates after discontinuation were secondary outcome measures.

Throughout the reporting the medical understanding of the causes and treatments of infertility are used and the mind-body connection is acknowledged as PNEI. The key concepts being covered are infertility as a medical condition that can be diagnosed and treated. The process that was being observed was divided into six different stages of fertility care:

Stage 1 couples who discontinued treatment before fertility workup was even started (pre-diagnostic testing)
Stage 2 couples who discontinued treatment during diagnostic fertility workup.
Stage 3 couples who discontinued treatment after diagnostic fertility workup but before fertility treatment was started.
Stage 4 couples who discontinued treatment during or after conventional treatment was performed but before IVF or ICSI was started.
Stage 5 couples who discontinued treatment before completing three cycles of IVF or ICSI
Stage 6 couples who discontinued treatment after they underwent at least three cycles of IVF or ICSI.

The methodology being used was quantitative with some qualitative embedded elements. The method was a longitudinal cohort analysis, but it included a qualitative follow up stage, all couples who were missing from follow up were contacted by telephone and a questionnaire of open-ended questions used to investigate their reasons for discontinuation of treatment. Statistical analysis was used to describe the demographic characteristics of the three groups.

About half of the couples stopped before any fertility treatment was started and one-third stopped after at least one IVF cycle. The main reasons for withdrawal were emotional distress and poor prognosis.

The couples who discontinued fertility care were slightly older (33.3 years versus 31.0 years), had a higher basal FSH level (8.6 versus 6.8 UI) and were more frequently secondary subfertile than couples who continued treatment.

Many couples 45.1% had stopped fertility care before starting any form of fertility treatment (Stages 1-3) and 68.7% had discontinued before starting IVF or ICSI.

Before treatment was started couples mainly withdrew because they simply rejected treatment. Couples that discontinued after treatment was started mainly stopped because of emotional distress or because of the doctor's refusal to continue in view of the poor prognosis.

The main reasons were 'emotional distress' 22% and poor prognosis 18.8% and rejection of treatment (17.2%. For 18 couples the reason of discontinuation was not know (5.6%).

Emotional distress was not equally important at all stages in fertility care and reflects the fact that it may be due to a variety of causes, stress because of subfertility, poor prognosis, female age, the chance of treatment that may not result in pregnancy, poor organisational care etc.

This study is transparent and well reported as the numbers of patients that were included or lost at each stage are summarised clearly both in the text and as a flow diagram. Efforts were made to find 243 patients who had been lost to follow up and this was pursued in an ethical manner. 232 couples were found and in total only 44 couples (3.2%) were lost to follow up.

A longitudinal study, like a cross-sectional one, is observational. So, once again, researchers do not interfere with their subjects. However, in a longitudinal study, researchers conduct several observations of the same subjects over a period of time, sometimes lasting many years.

The benefit of a longitudinal study is that researchers are able to detect developments or changes in the characteristics of the target population at both the group and the individual level. The key here is that longitudinal studies extend beyond a single moment in time. As a result, they can establish sequences of events (IWH, 2009).

The open ended questionnaires used to follow up couples who had discontinued treatment asked whether or not an ongoing pregnancy was

achieved in the intervening period and about the reason for discontinuation of treatment. The answers were categorized into 11 groups. If more than one reason was mentioned then the patient was asked to identify the main reason and only the main reason was documented and included in the study. This would lead to a less nuanced analysis but makes it easier to perform a quantitative analysis of the data.

Including a statistical analysis makes the results more credible and less likely to have arisen by chance. The authors could have improved on their analysis if they had documented all of the reasons for drop out not just the 'main one' as that introduces a level of bias into the study, and over simplifies what may be a complex situation. Then the reasons for drop out and discontinuation could have been explored using a thematic analysis to capture the complexity of the situation and how the different elements are interrelated.

The Mind Body connection is acknowledged and the stress of infertility is acknowledged but looking for a simple reason for drop out may not be the most appropriate framework. This framework is best suited to answer question of how many and when but not why. The difference between patients who drop out due to their doctor's recommendation compared to making their own choice to drop out is a valid category to investigate with this method.

A strength of this study is the clear and structured approach to the stages of infertility treatment, which helps to bring the temporal sequence into focus. A greater understand of which stage is most likely to be stressful or to cause drop out is useful and could help future studies select a suitable sample for further investigation.

The setting of the trial in a culture where the cost of treatment is not a variable means that other reasons for drop out can be investigated. The cultural context that recognises the emotional burden of treatment means

that this has appeared as one of the reasons for drop out. It is culturally acceptable for patients to use this as a reason.

The main limitation of this study is that is does not explore the full depth of the reasons for drop out but presents an accurate picture of the frequency and distribution.

Previous studies had mainly focused on dropout rates in IVF/ICSI patients this was the first study in which the focus was on the stage of fertility care at which patients dropped out in an unselected group of fertility patients.

As they found that it is likely that the prognosis of the couples that discontinued fertility care would have been better if they had continued with treatment there are implications for how patients are helped to make well-informed choices about treatment. The authors suggest that counselling should be offered to couples about the difference in chance of conceiving depending on whether they stop or continue treatment. 83 studies have cited this paper so it has had a high impact on subsequent research. More recent studies such as (Boivin et al., 2012) recognise that in order to retain women in treatment cycles the emotional and psychological aspects of infertility treatment need to be recognised and addressed:

Reducing the burden of treatment should lead to improved outcomes, namely better quality of life during treatment and lower discontinuation rates. (Boivin et al., 2012)

Conclusion

Research Questions

What are the concerns of infertile women? Do existing studies offer any insight for trial design?

The social and legal context of infertility treatment means that women may have a variety of concerns ranging from personal emotional distress (Brandes et al., 2009) to concerns about protecting their privacy at work

(Finamore et al., 2007). Although infertility is not legally recognised as a chronic medical condition a comparison can be made with a grounded theory derived model on workplace identity and chronic illness (Charmaz, 2010) because of the tremendous impact that infertility and infertility treatment has on the wellbeing of those afflicted as well as the demanding nature of treatment and the practical implications for time off work.

Borrowing from (Charmaz, 2010) and triangulating with another more recent qualitative analysis (Payne, 2014) confirms that women have difficulty reconciling their two identities as a treatment seeker and as an employee. Limiting their disclose may help to keep these two identities separate, allowing them to function as normally as possible in the workplace but compromising their integrity. Integrity here having the dual meaning of 'wholeness' and 'honesty'. The third longed for status of 'parent' grants a kind of moral legitimacy that would justify time off work or divided priorities for working women and this is further strengthened by the protective legal status accorded to parents who are allowed time off work for parenthood related issues.

The success rate for IVF is greatly influenced by the woman's age (Fields et al., 2013) and therefore age and poor prognosis have been identified as a reason for many couples discontinuing treatment that in fact may have been successful (Brandes et al., 2009). The design of the quantitative strand of this research project needs to take the age of female participants into account when planning the randomisation of patients to placebo and active drug. The concept of supporting the psychological identity of the patient was not taken up when planning the trial, this important facet of the study was left in the hands of the unit staff and was probably a major contributor to the recruitment difficulties experienced in strand 3.

Limitations

The narrative literature review for this section was developed and refined as part of an iterative cycle of data collection and review during the fourth qualitative strand of the thesis. It is therefore not a systematic review of the

literature around the concerns of infertile women. It provides instead some synthesis of ideas from grounded theory, from the research literature and from another research project that was taking place at the same time.

The non systematic nature of this review can also be justified by the literature on qualitative research and grounded theory in which there is a debate about the need for a literature review when creating new theory because of the danger of imposing existing models and interpretations rather than finding new patterns and ideas in the data (Wolcott, 1990), (Silverman, 2013).

The findings in this section should therefore be interpreted within the pragmatic framework as an example of:

'Current truth, meaning and knowledge as tentative and as changing over time. What we obtain on a daily basis in research should be viewed as provisional truths'. (Johnson and Onwuegbuzie, 2004)

These provisional truths should therefore not be used as an evidence base for making clinical decisions, that is the role of the RCT, but can be seen as a source of specific and local knowledge regarding trial design for this specific group of women.

Literature Review - Section 6 - Thematic Analysis

Research Questions: What is thematic analysis and is it an appropriate method of analysis for this project? What does good thematic analysis look like?

Methodology

This **section is a brief narrative review of the most popular and well known paper on Thematic Analysis, it was read critically using a check list of questions, as previously described**

Table 4: Checklist of questions for critical reading of selected articles. An example of thematic analysis of a CAM therapy was chosen as part of an iterative cycle of reading and writing regarding the methodology of this thesis.

Using Thematic Analysis in psychology.

The good practice of thematic analysis (TA) as a qualitative research method has been defined by Braun and Clarke in 2006 (Braun and Clarke, 2006a) and their article has been widely cited. A citation check in November 2014 showed that this article had been cited 10509 times.

Their paper was written from their perspective as psychologists interested in qualitative research in the field of same sex and heterosexual relationships. Their starting point was that, at that time, TA was both poorly demarcated and widely used, because of its ubiquitous use by researchers in so many other research traditions. They argued that people who claimed that they were using rigorous theories such as grounded theory or comparative analysis were often using thematic analysis because they did not go further than a surface level analysis of the data and did not create new theory.

Their aim was to argue convincingly that TA should be regarded as a method in its own right, and to provide an article that could be used to reference TA as both a research and a teaching tool.

This text adds to the existing body of knowledge by locating TA in the research literature and tradition and by providing clear guidelines for conducting TA as well as criteria for evaluating the quality of studies using TA. Braun and Clarke, by providing us with a standard protocol, have opened up the opportunity for the qualitative results of different trials to be compared or combined in a larger analysis.

The advantages of this relatively simple, flexible method are explained and can be used by researchers to justify their choice of TA as a tool:

- Flexibility.
- Relatively easy and quick method to learn, and do.
- Accessible to researchers with little or no experience of qualitative work.
- Results are generally accessible to educated general public.
- Useful method for working within participatory research paradigm, with participants as collaborators.
- Can usefully summarise similarities and differences across the data set.
- Can generate unanticipated insights.
- Allows for social as well as psychological interpretation of data.
- Can be useful for producing qualitative analyses suited to informing policy development.

Adapted from Table 3: Advantages of Thematic Analysis (Braun and Clarke, 2006a)

TA is described as a foundational method for qualitative research that provides an opportunity to develop core skills that will be useful in conducting other forms of research. TA had previously been regarded as a tool to use within different methods (Boyatzis, 1998) because the creation of themes of meanings is a generic skill across qualitative analysis (Holloway and Todres, 2003).

This plurality of use is the key to understanding TA; it is not automatically linked to any pre-existing theoretical framework and so can be used to do different things within different frameworks. The flexibility of TA is it's characteristic feature:

'Thematic analysis can be an essentialist or realist method, which reports experiences, meanings and the reality of participants, or it can be a constructionist method, which examines the ways in which events, realities, meanings, experiences and so on are the effects of a range of discourses operating within society (Braun and Clarke, 2006a)'.

The key to whether it is being used to unpick reality or reflect reality is the theoretical position of the researcher. This text describes how TA differs from other approaches such as Grounded Theory (GT) and Discourse Analysis (DA). Both of these require a detailed theoretical and technical knowledge where as TA offers a more accessible form of analysis to the relatively inexperienced researcher.

The paper provides clear guidelines for such a researcher by explaining the need for transparency of theoretical framework and assumptions about knowledge. The actual method for conducting the TA is broken down into six stages that are easy to understand and reproduce. The key terms are well defined and in particular the discussion around what constitutes a 'theme' is helpful.

The distinction is made between inductive and theoretical themes, and at another level between semantic or latent themes and allows the researcher to describe their analysis, locating it, for example, within constructionist or realist paradigm.

The text provides help with the practical application of TA by listing both the potential pitfalls and characteristics of good TA.

The first of these potential pitfalls is a failure to actually analyse the data at all:

'Thematic analysis is not just a collection of extracts strung together with little or no analytic narrative. Nor is it a selection of extracts with analytic comment that simply or primarily paraphrases their content." (Braun and Clarke, 2006a)

The second pitfall to is the use of data collection questions to form the themes that are reported and in such a case no analytic work has been done to identify themes across the entire data set, or make sense of the patterning of responses.

The third pitfall is a weak or unconvincing analysis where the themes do not appear to work. The fourth is a mismatch between the data and the analytic claims that are made about it.

In the field of qualitative analysis criteria for conducting good research do exist and this paper shows how the issues raised in many general qualitative research assessment criteria can be more or less applied to thematic forms of analysis.

"As thematic analysis is a flexible method, you will also be clear and explicit about what you are doing, and what you say you are doing needs to match up with what you actually do. In this sense, the theory and the method need to be applied rigorously, and "rigour lies in devising a systematic method whose assumptions are congruent with the way one conceptualises the subject matter" (Reicher and Taylor, 2005)549"
(Braun and Clarke, 2006a)

Their 15-point checklist of Criteria for Good Thematic Analysis is helpful for the novice researcher also helps to characterise Thematic Analysis compared to other methods:

Table 11 Checklist of criteria for good thematic analysis

Process	No.	Criteria
Transcription		The data have been transcribed to an appropriate level of detail, and the transcripts have been checked against the tapes for 'accuracy'.
Coding	2	Each data item has been given equal attention in the coding process
	3	Themes have not been generated from a few vivid examples (an anecdotal approach), but instead the coding process has been thorough, inclusive and comprehensive.
	4	All relevant extracts for all each theme have been collated
	5	Themes have been checked against each other and back to the original data set.
	6	Themes are internally coherent, consistent, and distinctive
Analysis	7	Data have been analysed – interpreted, made sense of – rather than just paraphrased or described.
	8	Analysis and data match each other – the extracts illustrate the analytic claims.
	9	Analysis tells a convincing and well-organised story about the data and topic.
	10	A good balance between analytic narrative and illustrative extracts is provided.
Overall	11	Enough time has been allocated to complete all phases of the analysis adequately, without rushing a phase or giving it a once over lightly.
Written Report	12	The assumptions about, and specific approach to, thematic analysis are clearly explicated.
	13	There is a good fit between what you claim to do, and what you show you have done – i.e. described method and reported analysis are consistent.

	14	The language and concepts used in the report are consistent with the epistemological position of the analysis.
	15	The reporter is positioned as *active* in the research process; themes do not just 'emerge'.

Adapted from Table 2: 15 point checklist of Criteria for Good Thematic Analysis (Braun and Clarke, 2006a)

"*We do not subscribe to a naïve realist view of qualitative research where the researcher can simply 'give voice' see (Fine, 1992) to their participants. As (Fine, 1992) argues, even a 'giving voice' approach "involves carving out unacknowledged pieces of narrative evidence that we select, edit and deploy to border our arguments. However neither do we think there is one ideal theoretical framework for conducting qualitative research, or indeed one ideal method? What is important is that the theoretical framework and methods match what the researcher wants to know, and that they acknowledge these decisions, and recognise them as decisions."*

In essence their position is that they believe in the plurality of different realities and perspectives and therefore the validity of using a plurality of methods needed to investigate them. They do not mention Mixed Methods Research perhaps because it would have been at an early stage of development in 2006. This article would have been written and published in the time between the first publications that developed the procedures and those that advocated and expanded the use of MMR.

Greene et al had identified a classification system of types of mixed methods designs (Greene et al., 1989), and (Tashakkori and Teddlie, 1998) had provided a comprehensive treatment of many aspects of MMR. In 2007 papers that focused on the multiple ways of seeing, hearing and making sense of the social world (Greene, 2007) were published and (Creswell and Clark, 2007a) were advocating and engaged in disseminating technical expertise in this field.

The method used in this paper reflects the subject matter; the key themes that identify Thematic Analysis are picked out and narrated in a convincing manner that provides encouragement as well as guidance. It is not an unbiased, objective opinion but it does provide an overview of the benefits as well as the disadvantages of using TA.

It does not depart from general good practice for conducting qualitative research and this simplicity reflects the relatively simple analytical tool that is TA. There are quotes and examples from published work in the field of sexuality and these are effective in supporting the argument and also provide examples of the kind of work that could be analysed using TA.

There is still room to debate the role of TA as a tool utilised in a skilful way rather than a distinct methodology in it's own right but the paper does provide a clear explanation of how to use that tool and what good practice would look like.

The writing style is clear and accessible for the novice researchers who might be interested in using this form of analysis and the text is well organised into logical sections and steps.

An Example Of Thematic Analysis

The Effect Of Acupuncture On Psychosocial Outcomes For Women Experiencing Infertility: A Pilot Randomized Controlled Trial. (Smith et al., 2011)

This is a mixed method randomised controlled trial, comparing acupuncture with a wait list control set at the Centre For Complementary Medicine Research, the University Of Western Sydney, Sydney, Australia. Thirty-two (32) women aged 20–45 years, with a diagnosis of infertility, or a history of unsuccessfully trying to conceive for 12 months or more, were recruited to the study using local papers, online forums and a press release.

The underlying concept being investigated was that stress has an impact on fertility through the HPA axis, and that acupuncture can reduced stress and increase well being because Traditional Chinese Medicine is a holistic treatment.

The language of the paper includes some technical acupuncture terms that need some specialist knowledge to understand their significance. The psychological interventions are described using conventional medical terms. The mind body connection is described in terms of PNEI, the statistical analysis is described using the conventional statistical language and the trial design uses the usual language of clinical trials. This paper is therefore useful to all medically trained readers but some explanation of acupuncture would also be helpful.

The authors examine the hypothesis that acupuncture compared to a wait-list control would demonstrate improvements in infertility self-efficacy, and reductions in anxiety and infertility-related stress and women's experiences of acupuncture are also reported.

A mixed method approach is being used to triangulate data from qualitative and quantitative sources. This approach acknowledges that a plurality of methods are necessary to capture the infertility related stress.

The subjects were randomised to acupuncture or wait list, those subjects in the treatment group received six sessions of acupuncture over eight weeks. Randomisation to treatment or wait list attempts to measure the impact of having acupuncture treatment against not having acupuncture treatment while on the wait list for treatment.

Both quantitative and qualitative data were collected. The quantitative data were collected as outcome measures of three questionnaires: The Fertility Problem Inventory (FPI) (Newton et al., 1999), the Infertility Self-Efficacy

Scale (ISE) (Cousineau et al., 2006) and the State-Trait Anxiety Inventory (STAI) (Spielberger et al., 1970).

Use of validated questionnaires to measure infertility-related stress. The FPI - Scores are summated into five domains: social concern, sexual concern, relationship concern, rejection of childfree lifestyle, and need for parenthood. ISE has been specifically validated with infertility patients and is a self-report questionnaire consisting of 16 items that probe into the respondents' perceptions about their ability to deal with various aspects of fertility treatment. The results were analysed using statistical methods to ascertain their significance of results and to explore any causal relationships.

The qualitative data were 10 in-depth interviews with women who completed the 8 weeks of acupuncture. The Interview data were digitally recorded, transcribed and then subjected to a process of coding and thematic analysis following established protocols for thematic analysis (Braun and Clarke, 2006a)

The 10 interviews with women were intended to find out how they felt about acupuncture. The interviews explored the women's experiences of infertility, its psychological impact, and the perceived impact of acupuncture on cognitive control. Women were first asked an open-ended question about their fertility treatment and how it affects them, with prompt questions including reasons for joining the trial, previous experience of fertility treatment, and expectations of treatment.

They were then asked about their sessions with the acupuncturist, including what happened, how they felt, whether it made them feel differently, and whether their feelings about it changed over time. Finally, women were asked about the effects of acupuncture, including problems and difficulties and feelings for the future.

The findings were based upon a sample of 16 who women were allocated to the acupuncture treatment group and 14 to the wait-list control. They found

that more research is needed to evaluate the preliminary results, which suggest that acupuncture, may be a useful intervention to assist with the reduction of infertility-related stress.

The data also show promising trends in relation to improve self-efficacy and reduced anxiety. At the end of the 8-week intervention, women in the acupuncture group reported significant changes on two domains on the FPI, less social concern defined as sensitivity to comments, reminders of infertility, feelings of social isolation, and alienation from family or peers.

The in-depth interviews highlighted a changed perception for women with regard to coping, feeling less anxious, feeling physically calm, relaxed and overall having achieved a greater sense of well-being. Women's responses are organised under three themes: "expectations of acupuncture: invoking change," "positive experiences of acupuncture," and "changes achieved after acupuncture."

The usefulness of this study could have been increased if they had also interviewed 10 women from the other group, the wait group, and carried out a thematic analysis of the two groups to compare their experiences.

Control groups are usually associated with quantitative research methods where in classic experimental design where patients are randomly assigned to two or more differently treated groups (experimental and control) (Bowling, 2011)

The comparison of two groups, with similar naturalistic settings (Lloyd-Jones, 2008), could be seen as a pragmatist version of a control group in qualitative research and this would have allowed them to see how their experiences differed from the treatment group, and in turn that would have made a greater contribution to the research question that was inquiring into the effect of the acupuncture on infertility related stress compared to no acupuncture.

Discussion

The thematic analysis has resulted in themes that are credible and the authors acknowledge the limitations of the study, which are a small sample size, the lack of participant blinding, and the short follow up time. Some strengths of the thematic analysis can be identified using the criteria from Braun and Clarke:

- Interview data were digitally recorded and transcribed verbatim by a professional transcribe. Transcripts of the interviews were de-identified and checked for transcription accuracy.

- Three researchers read the transcripts independently and subjected the data to a process of coding and thematic analysis, based on notions of consistency, commonality, and the function and effects of specific themes, following established protocols.

- To begin with the data were subject to open coding involving a close reading of each transcript to identify first order concepts. Axial coding was employed to develop categories. In the final stages of selective coding a core category was developed which essentially linked all of the concepts and categories.

- They report that the research was largely inductive, where the concepts and categories came from the data, rather than being deductive or informed by existing preconceptions about acupuncture and fertility.

It is not clear from reading the paper if the qualitative themes were informed by the results of the quantitative surveys, the combining of results could have occurred at an early analytical stage in the study or later in the reporting stage, and a good study should make this clear.

The structure and quality of mixed methods research designs is explored in more detail in a later section. But before moving away from the experiences

of infertile women some time is taken to look into the ethics of using data that is mined from their personal postings on infertility Internet forums.

Conclusion

Research Questions: What is thematic analysis and is it an appropriate method of analysis for this project? What does good thematic analysis look like?

This account of thematic analysis by acknowledged experts in the field (Braun and Clarke, 2006a) helped me to improve on my first submission of my thesis which had mistakenly claimed to included grounded theory as an analytical tool. The clear guidelines offered by Braun and Clarke gave me a step by step method to follow as I re-analysed my data from strand one and strand four, looking for the themes in the data. My clearer understanding of what thematic analysis looks like was also reflected in a clear declaration of my methodology and methods in the second submission of the thesis.

The use of thematic analysis is especially suited to researchers in the early stages of their career and can be used as a stepping stone to achieve a deeper, more abstracted level of analysis leading in time to a full blown grounded theory. It is my intention to continue along this path after successful submission of my corrections by working on an article regarding my findings in conjunction with another, experienced researcher Dr Carol Rivas.

The example of thematic analysis (Smith et al., 2011) as applied to the field of CAM and female infertility was included to show that the method is appropriate for my research questions, can provide useful results and can be reported in a transparent manner. The criteria for good thematic analysis as reported by Braun and Clarke were used to check the credibility of the example as well as my own work in strands one and four.

Limitations To This Section

This was not a systematic qualitative review of all the literature available on Thematic Analysis and cannot therefore be interpreted as an unbiased account of the advantages and disadvantages of using this method.

Literature Review - Section 7 - The Ethics of using Internet Data Sources

Methodology

The articles chosen for this narrative review were selected by an internet search of articles on PubMed using the search terms ((ethics[MeSH Terms]) AND internet[MeSH Terms]) AND data and filtered for articles published in the last 5 years. The results were not systematically selected for review but the abstracts of the articles were read before choosing the most relevant and up to date paper for critical reading (Bond et al., 2013)

Memos were kept to record this process and they are included in the APPENDIX 12 memos written during thematic analysis of strand 4. Memo writing is a technique from the qualitative research method known as Grounded Theory (Charmaz, 2006) in which informal analytic notes that chart, record and detail the analytic phases of the project.

The characteristics of pragmatism include the idea that our thinking follows a *dynamic homeostatic process of belief, doubt, inquiry, modified belief, new doubt, new inquiry…in an infinite loop, where the person or researcher (and research community) constantly tries to improve upon past understandings in a way that fits and works in the world in which he or she operates. (Johnson and Onwuegbuzie, 2004)*. This dynamic model seem particularly appropriate for the study of a new and constantly changing field of knowledge such as the growth of the internet, the increasing use of patient forum's and the explosion of data available to researchers from this source.

Any systematic review would quickly be out of date, for example A PubMed seach on 30th December 2015 using the MeSH terms ("internet/ethics"[MeSH Terms]) AND patient data privacy [MeSH Terms] returned 55 search results

published within the last 5 years, 5 of which have been published since this thesis was submitted for re-examination.

It is anticipated that is section of the thesis will be developed as an article intended for publication and that a thorough and up to date qualitative literature review will be undertaken at that time.

The narrative review undertaken here is sufficient as an introduction to the field but is not intended to be complete or definitive.

Introduction

Research question: What are the ethics of using data from internet forums?

When the recruitment to trial OVCT-001 failed, the author was faced with a dilemma, the lack of quantitative data made it impossible to write a thesis and yet the time and energy already invested made abandoning the project altogether an unappealing prospect. There was also the new research question to be answered, 'Why did recruitment fail?'

In an ideal situation the women who had been approached for recruitment phase would have been sampled for a qualitative study to find an answer to this question. It was not possible to gain the support of the ARU staff to carry out this strand of the study so the pragmatist solution was to turn to the data that was available which found online via the Internet infertility forums.

This data could be viewed as existing in the public domain and yet it to some extent 'belongs' to the person posting it, a person who may not even be identifiable in order to seek informed consent. The blurring of the traditional boundaries between data, subject and researcher has created new questions some of which are explored in this section.

The author also sought the opinion of the forum administrators, and her supervisors who had experience in this field, and these are documented in the methodology section as Strand Four (2012 -2015).

The Conceptual And Practical Ethical Dilemmas Of Using Health Discussion Board Posts As Research Data.

(Bond et al., 2013)

The use of the Internet in modern society is introduced as the context for this study and the introduction charts the evolution of an ethical framework in response to technological change. The online discussion boards of people living with the long-term medical condition, diabetes, are the focus of the study.

The blurring of the boundary between private and public information is a consequence of the rapid expansion of posting in a forum and the views and perspectives of the people posting have not been adequately explored.

The scale of personal posting was not anticipated in the early days of this debate and some published research provide principles but not specific ethical guidelines for researchers who wish to use such data.

To date the views of those people posting health information online in relation to how they anticipate the information they post being used has not featured significantly in the debate and so this study seeks to bring their voices into the knowledge base by examining the views of people living with diabetes who share health information online. Four active diabetes forums were identified by the PI and chosen as platforms to recruit participants into the study.

A qualitative approach was employed using online semi structured asynchronous email interviews conducted with the users of an online diabetes discussion boards. Both the primary investigator and the project researcher had experience in online interviewing techniques. The target number of 24 participants was set prior to recruitment with the ability to

increase this should the need arise. Drawing on previous experience it was correctly anticipated that saturation of data would be reached by this stage.

The Ethics Committee of the School of Health and Social Care, Bournemouth University granted ethical approval for this study. Forum Moderators and administrators were approached prior to posting on the forum in order to gain their approval for posting for research purposes.

Data collection commenced in April 2012 and concluded in May 2012.
Four active diabetes forums were identified and participants were eligible for the study if they were active as a member on at least one of the forums identified. CSB and OHA posted in each of the forums on different threads within the forum in order to give the recruitment posts more publicity.

The recruitment posts described the study and provided contact details for the investigators. Individuals interested in participating were invited to contact them by email for more information. Once interested individuals had made contact with the research team they were sent a brief overview of the study along with an information sheet. Following this, if the participants were happy to participate they were sent the first interview questions by email and the interview was started.

The data from participants were collected using asynchronous semi structured interviews. The semi structured nature of these interviews meant that similarly themed information was collected from the participants, while the fact that the interviews were asynchronous enables participants to respond to questions in their own time (but within the time constraints of the research programme).

Participants were sent several emails during the course of the interview with each email containing 1-2 questions. The questions aimed to ascertain whether participants felt it was acceptable for researchers to use information on health discussion boards, what permission should be sought prior to using this information, and whether the length of time since the post was made

influenced the need to obtain permission. Once the participants had answered all of the questions, they were thanked for their contributions and their participation in the study was over.

Following the requests for recruitment posted on the discussion boards, 33 individuals expressed an interest in participating and were contacted by the research team. 30 participants consented and responded to at least one question in the interview sequence, while four participants who did not complete the interview questions did not respond to further follow-up prompts. The remaining 26 participants completed all of the semi structured interview questions and their answers were included for analysis.

All of the interviews were completed in less than 10 days. Of the 26 completed interviews 12 participants were identified as being male and 9 as female and there were 6 participants who it was not possible to identify.

A qualitative approach using interpretative description methodology (Thorne et al., 1997) was used to assess the interview transcript and quotations were extracted and anonymised to support each theme.

It is our view that nursing's uniqueness has gradually shifted the priorities within our research enterprise to the point that we can begin to build methods that are grounded in our own epistemological foundations, adhere to the systematic reasoning of our own discipline, and yield legitimate knowledge for our practice.

We put forward interpretive description as one of many possible "generic" nursing approaches.
(Thorne et al., 1997)

Because they address the dialectic between individual cases and common patterns, nursing studies can also capitalize on this strategy. Interpretive description in nursing requires that nurse researchers come to know individual cases intimately, abstract relevant common themes from within these individual cases, and produce a species of knowledge that will itself be

applied back to individual cases. In order to do this effectively, they must engage in both the ethereal abstractions of theorizing and the earthbound concrete realities of the practice context in order to produce sound and usable knowledge.(Thorne et al., 1997)

Interpretative Description has its roots in qualitative approaches used by nurse researchers and therefore has strong connections to practical situations. It is recommended that immersion in the data is interleaved with exposure to the field (Thorne et al., 1997) but there is no evidence that these researchers have experience of working with this field of chronic illness. They do not explain why Diabetes was chosen as the context for this study.

An inductive approach was adopted; allowing the themes to emerge from the data rather then testing previously identified themes on the data.
The analysis of the rigor of this study was based on Guba and Lincoln's principles of credibility, confirmability and dependability (Lincoln, 1989).

Four forums were selected in order to ensure that any particular character or interest on a board would not have undue influence on the findings.
The rigor was achieved through prolonged engagement with sufficient depth of data, peer debriefing and analysis of material, linking assertions, findings, and interpretations with the data and third party auditing of the data collection and analysis process. The process is set out as a flow chart making the study transparent and suitable for replication.

Two investigators read each transcript several times independently and loosely attributed themes to the data with no consultation occurring between the assessors at this stage. Discussion was then undertaken to compare the themes identified and to resolve any areas of disagreement with theme allocation. Quotations were extracted to support themes and each participant was assigned a number when using the supporting quotations. Following this process and the identification of themes their findings were sent out to the other members of the research team in order to verify the themes.

In view of the lack of consensus on some issues among the study participants someone not previously involved in the analysis who reviewed the themes and the conclusions to ensure consistency carried out a final check.

Four main themes were identified

1. The views of people living with diabetes are needed.
2. Posts made are in the public domain
3. Permission (two subthemes)
4. Use of citations

1. The views of people living with diabetes are needed.

There was general support for researchers using information posted on discussion boards as this was seen as a way of giving a 'voice' to such people.

The use of such data was seen to be altruistic and not for commercial gain.

2. Posts made are in the public domain

There was a general acceptance by the participants in this study that once information is posted on a forum it is available to the public and this could be accessed and used for research purposes. Some people felt that it could be used unreservedly and some people felt it should be restricted.

3. Permission (two subthemes)

Respondents were asked if they thought researchers need permission to use information in their posts and the responses were grouped into two subthemes: Those who felt that their information was in the public domain and therefore available to be used did not feel there was any need for permission to be sought. Those who acknowledged the public nature of the forum but expressed reservations felt that some sort of permission should be sought from the person who posted the information.

Site administrators also failed to come to a consensus about their role in giving permission.

4. Use of citations

There was no correlation between the date that the post was made and the need to obtain permission.

Aggregated data was not considered as needing permission however direct quotes were seen as needing some sort of citation. Aggregating quotes also helps to protect user anonymity. Some quotes are included to show the links to empirical data and the comparison with concepts from mass media studies help to offer insights.

The use of thoughtfully constructed aggregated quotes is discussed as a way of providing richly textured and comprehensive data sets and to give depth to the participants meaning. This contributes to the debate about ethics and methodology but they acknowledge that the findings may not be transferrable to other domains outside discussion board-type communications.

Conclusion

What are the ethics of using data from internet forums?

The findings of this study were helpful when dealing with the ethical dilemma of how to approach the use of data in strand four of this thesis. The idea that the views of people living with a condition can be heard and acknowledged needs to be balanced with their desire for privacy. The choice of an internet forum as a form of expression creates an expectation of anonymity combined with identify as part of a group. These results triangulate with and agree well with the findings of my own thematic analysis in the results chapter.

The use of aggregated quotes; the seeking of permission from forum administrators and the feedback of results to the forum can all be incorporated into my own research design and methodology.

Limitations

It is acknowledged that this existing narrative review is not systematic and therefore the conclusions need to be interpreted with caution as bias cannot be excluded.

Literature Review - Section 8 – Qualitative Research

Research question: What is qualitative research? How can I make sure my study is credible and valid?

Introduction

The move towards a mixed methods research design meant that a greater emphasis was placed on the qualitative strand of the study, particularly the fourth strand, which explores the concerns of infertile women:

The use of qualitative techniques to explore this aspect of the study was consistent with the development of the pragmatist worldview:

Pragmatism recognises the existence and importance of the natural or physical world as well as the emergent social and psychological world that includes language, culture, human institutions, and subjective thoughts. (Johnson and Onwuegbuzie, 2004)

In order to make sure that this part of the study was written to the required standards of credibility and rigor a framework for evaluating qualitative research was sought in the literature.

Methodology

This is not a systematic qualitative review but a narrative review that reflects the iterative cycle of reading, thinking and rewriting that accompanied the development of the pragmatist world view. Many of the ideas were clarified during the reading of (Silverman, 2013) and (Creswell and Clark, 2007b).

Memos were kept to record this process and they are included in the APPENDIX 12 memos written during thematic analysis of strand 4. Memo

writing is a technique from the qualitative research method known as Grounded Theory (Charmaz, 2006) in which informal analytic notes that chart, record and detail the analytic phases of the project. Memo writing is a pivotal intermediate step between data collection and writing drafts of papers (Charmaz, 2006). Memos catch your thoughts, allow you to make comparisons and connections leading to new directions for you to explore.

The characteristics of qualitative research are covered in more detail in the next section as part of the narrative review of mixed methods research.

The paper selected for critical reading (Pope et al., 2000) was widely cited (3772 times on 31/12/15) and was published in the BMJ. It was therefore seen as reliable and credible as a source of information to researchers from a quantitative tradition who might need a road map of this unfamiliar territory.

The paper on standards for reporting qualitative research (O'Brien et al., 2014b) was chosen as an up to date source that had been systematically prepared and peer reviewed.

The authors identified guidelines, reporting standards, and critical appraisal criteria for qualitative research by searching PubMed, Web of Science, and Google through July 2013; reviewing the reference lists of retrieved sources; and contacting experts. Specifically, two authors reviewed a sample of sources to generate an initial set of items that were potentially important in reporting qualitative research. Through an iterative process of reviewing sources, modifying the set of items, and coding all sources for items, the authors prepared a near-final list of items and descriptions and sent this list to five external reviewers for feedback. The final items and descriptions included in the reporting standards reflect this feedback.
(O'Brien et al., 2014b)

Discussion

A basic framework for describing qualitative research was provided by (Pope et al., 2000) who noted that

- Qualitative research produces large amounts of textual data in the form of transcripts and observational field notes.

- The systematic and rigorous preparation and analysis of these data is time consuming and labour intensive.

- Data analysis often takes place alongside data collection to allow questions to be refined and new avenues of inquiry to develop.

- Textual data are typically explored inductively using content analysis to generate categories and explanations; software packages can help with analysis but should not be viewed as short cuts to rigorous and systematic analysis.

- High quality analysis of qualitative data depends on the vision, skill and integrity of the researcher and should not be left to the novice.

Not all qualitative researchers accept that they need to establish the credibility of their research results by using measures of reliability (Pope et al., 2000) but as qualitative research has become increasingly common and valued in the medical and medical education literature (O'Brien et al., 2014a) there is widespread agreement about the need for clear and complete reporting.

The Standards for Reporting Qualitative Research (SRQR) (O'Brien et al., 2014a) is an instrument consisting of 21 items. It has the aim of improving the transparency of all aspects of qualitative research by providing clear standards for reporting such work. It has the strength of being grounded in a systematic review of previously reported literature and by the diversity of experience and perspectives of its authors.

Experts in three countries have also critically reviewed it. It was therefore chosen as a suitable framework for reviewing some of the qualitative studies referenced in this thesis and for self-evaluation of the methodology section of this thesis. A table detailing the 21 items is included here and in the appendix as Table 40 Standards for Reporting Qualitative Research.

	Topic	Item
1	Title	Concise description of the nature and topic of the study identifying the study as qualitative or quantitative or indicating the approach or data collection method is recommended.
2	Abstract	Summary of key elements of the study using the abstract format of the intended publication; typically includes background, purpose, methods, results and conclusions.
	Introduction	
3	Problem formulation	Description and significance of the problem/phenomenon studied; review of relevant theory and empirical work; problem state
4	Purpose or Research Question	Purpose of the study and specific objectives or questions
	Methods	
5	Qualitative approach and research paradigm	Qualitative approach (e.g. ethnography, grounded theory, narrative research) and guiding theory if appropriate; identifying the research paradigm (e.g. post positivist, constructivist/interpretivist) is also recommended; rationale that briefly discusses the justification for choosing that approach; the assumptions and limitations implicit in that choice and how those choices influence study conclusions and transferability.
6	Researcher characteristics and reflexivity	Researchers' characteristics that may influence the research, including personal attributes, qualifications/experience, relationships with participants, assumptions, and/or presuppositions; potential or actual interaction between researchers characteristics and the research question, approach, methods, results, and/or transferability.
7	Context	Setting/Site and salient contextual factors, rationale.
8	Sampling strategy	How and why research participants, documents and events were selected, criteria for deciding when no further sampling was necessary (sampling saturation), rationale.
9	Ethical issues pertaining to	Documentation of approval by an appropriate ethics review board and participant consent, or explanation for

	human subjects	lack thereof; other confidentiality and data security issues.
10	Data collection methods	Types of data collected; details of data collection procedures including start and stop dates of data collection and analysis, iterative process, triangulation of sources/methods, and modification of procedures in response to evolving study findings, rationale.
11	Data collection instruments and technologies	Description of instruments (e.g. interview guides, questionnaires) and devices (e.g. audio recorders used for data collection; if/how the instruments changed over the course of the study.
12	Units of study	Number and relevant characteristics of participants, documents or events included in the study, level of participation (could be recorded in results).
13	Data processing	Methods for processing data prior to and during analysis, including transcription, data entry, data management and security, verification of data integrity, data coding, and anonymization/deidentification of excerpts
14	Data analysis	Process by which inferences, themes, etc. were identified and developed including the researchers involved in data analysis, usually references to a specific paradigm or approach, rationale.
15	Techniques to enhance trustworthiness	Techniques to enhance trustworthiness and credibility of data analysis 9e.g member checking, audit trail, triangulation), rationale.
	Results/Findings	
16	Synthesis and interpretation	Main findings (e.g. interpretations, inferences, and themes); might include development of a theory or model, or integration with prior research or theory.
17	Links to empirical data	Evidence (e.g. quotes, field notes, text excerpts, photographs) to substantiate analytic findings.
	Discussion	
18	Integration with prior work, implications, transferability, and contributions to the field	Short summary of main findings; explanation of how findings and conclusions connect to, support, elaborate on, or challenge conclusions of earlier scholarship; discussion of scope of application/generalizability; identification of unique contribution(s) to scholarship in a discipline or field.
19	Limitations	Trustworthiness and limitations of findings
20	Conflicts of interests	Potential source of influence or perceived influence on study conduct and conclusions, how these were managed
21	Funding	Sources of funding and other support; role of funders in data collection, interpretation and reporting.

Table 12 21 Standards for reporting qualitative research (O'Brien et al., 2014a)

Summary

Research questions: What is qualitative research? How can I make sure my study is credible and valid?

Qualitative research springs from a research paradigm which values evidence from a wider variety of sources than quantitative research. The adoption of a pragmatist worldview brings an opportunity to use both qualitative and quantitative data and this is discussed in greater detail in the next section.

Quantitative purists articulate assumptions that are consistent with what is called a positivist philosophy. That is they believe that social observations should be treated as entities in much the same way that physical scientists treat physical phenomenon. Further, they contend that the observer is separate from the entities that are subject to observation. They maintain that social science inquiry should be objective. That is time- and context-free generalizations are desirable and possible, and real causes of social science outcomes can be determined reliably and validly.

According to this school of thought. Researchers should eliminate their biases, remain emotionally detached and uninvolved with the objects of study, and test or empirically justify their stated hypotheses.

These researchers have traditionally called for rhetorical neutrality, involving a formal writing style using the impersonal passive voice and technical terminology, in which establishing and describing social laws is the major focus (Tashakkori and Teddlie, 1998)

Qualitative researchers, also called constructivists and interpretivists (Johnson and Onwuegbuzie, 2004) they reject positivism and argue for the superiority of constructivism, idealism, humanism, hermeneutics and, sometimes, postmodernism (Lincoln, 1989)

These purists contend that multiple-constructed realities abound, that time- and context-free generalizations are neither desirable nor possible, that research is value-bound, that it is impossible to differentiate fully cause and effect, that logic flows from specific to general (e.g. explanations are generated inductively from the data), and that knower and known cannot be separated because the subjective knower is the only source of reality (Guba, 1990).

Qualitative purists are also characterized by a dislike of a detached and passive style of writing, preferring, instead, detailed, rich, and thick (empathetic) description written directly and somewhat informally (Johnson and Onwuegbuzie, 2004).

Conclusion

The guidelines described by (O'Brien et al., 2014a) ensure that qualitative research can be clearly and transparently reported, to satisfy the need for credibility and rigour without compromising the unique and characteristic qualities of qualitative research. This is necessary in this project as the intended audience for my findings includes lay people, medical staff and academic mentors, examiners and supervisors. By making sure that I adhere to these guidelines the utility of my findings will be ensured in line with my pragmatic worldview.

Pragmatism endorses practical theory (theory that informs effective practice: praxis (Johnson and Onwuegbuzie, 2004)

My findings could be used for example to help students writing a PhD thesis, medical staff planning a clinical trial design, CAM practitioners planning a pragmatic clinical trial, a support group for infertile women or anyone interested in how pragmatism can be applied to the research process.

Limitations

This is a narrative review, not a systematic qualitative review and therefore the conclusions should remain provisional. The iterative use of theory, memo's, data collection and return to theory are partially documented in the appendix **APPENDIX 12 memos written during thematic analysis of strand 4**

Literature Review Section 9 - Mixed Methods Research

Research question: What is MMR? How do I describe my study and ensure transparency of reporting?

Methodology

This is not a systematic qualitative review but a narrative review that reflects the iterative cycle of reading, thinking and rewriting that accompanied the development of the pragmatist world view. Many of the ideas were developed during the reading of (Creswell and Clark, 2007b). Memos were kept to record this process and they are included in the APPENDIX 12 memos written during thematic analysis of strand 4. The paper by (Bishop and Holmes, 2013) was sourced during this process as being closely aligned with the focus of this thesis as well as being systematic and up to date.

Introduction

This section aims to define mixed methods research, to locate it in the literature as a 'third paradigm', and to explore the ways in which the critical appraisal of such a methodology can be conducted. The section ends with insights into the relationship between using mixed methods research and a pragmatist philosophical worldview.

Mixed Methods Researchers may plan to include both qualitative and quantitative methods within their design or the design may evolve as their study progresses. Creswell and Clark (Creswell and Clark, 2007a) characterise this situation as a continuum with 'fixed design' at one end and 'emergent design' at the other.

This thesis is a four strand structure that started as a 'fixed' design but evolved to become an 'emergent' design (Creswell and Clark, 2007a). The use of both qualitative and quantitative methods was planned at the start of

the research process but the failure of the quantitative trial to recruit sufficient patients led to an additional qualitative analysis as the fourth strand.

The typology adopted in this thesis is a variation of a Mixed Methods Sequential Design (Morse and Niehaus, 2009) because the phases are sequential. However we will also be comparing this study to the concept of a Multiphase Design

The factors that decided the choice of study design included the intended audience, the problem to be addressed and the questions to be answered. The intended audience for this thesis has been one of the factors that contributed to the choice of study design. The intended audience consisted of both health practitioners, clinical investigators, academics and trial participants and each audience required a certain kind of information (Lewith et al., 2010).

Health practitioners such as the staff at the Assisted Reproduction Unit (study site) wanted to know if Ovarium compositum was safe to use with women who may become pregnant, if it is a cost effective treatment and if it could improve the outcomes of their patients. Some of this kind of evidence is to be found in the safety data and case studies for Ovarium compositum.

The nurses at the unit will want to know if the treatment is complex or difficult to administer or likely to cause their patients additional stress. This can be researched using the quality of life (QoL) questionnaires. The additional workload imposed upon staff as a result of hosting the trial also had to be taken into account. Working from a pragmatist perspective means that the trial design must work in practice and not just appear to answer the research questions with an appropriate design.

The clinical investigators and academic supervisors will want to know how much improvement can be demonstrated in the trial group who received the Ovarium compositum compared to another group who received placebo which necessitates a quantitative strand of evidence in the form of the RCT.

The flexibility of this approach is consistent with the underlying philosophical framework of this thesis, pragmatism, which allows the researcher to select 'what works' as the best method to answer the research question. In this case the research question itself also evolved to include an additional question about the reasons for poor trial recruitment.

Discussion: The Paradigm Wars

(Johnson and Onwuegbuzie, 2004)

For more than a century, the advocates of quantitative and qualitative research paradigms have engaged in ardent dispute. From these debates, purists have emerged on both sides.

Both sets of purists view their paradigm as the ideal for research and, implicitly if not explicitly, advocate the incompatibility thesis (Howe, 1988) which posits that qualitative and quantitative research paradigms, including their associated methods, cannot and should not be mixed. (Johnson and Onwuegbuzie, 2004)

Table to show the simplified comparison of typical characteristics of quantitative and qualitative approaches to research adapted from (Bishop and Holmes, 2013).

Table 13 Typical characteristics of quantitative and qualitative paradigms

Characteristic	Quantitative approaches	Qualitative approaches
Ontology (the nature of being)	Realist	Relativist
Epistemology (theory of knowledge)	Knowledge limited only by technologies of knowing	Knowledge is embedded in value and culture (including the research process).
Aims/intended outcomes	Universal Laws	Locally situated and contextualised understandings
Relationships between	Distant, objective	Close, subjective

researcher and participants		
Scope	General, nomothetic	Specific, idiographic
Nature of information	Causal, mechanistic explanation and prediction	Meaning, understanding
Relationship between theory and data	Hypothetico-deductive-data confirms/falsifies theory	Inductive, theory emerges from data

Johnson and Onwuegbuzie (Johnson and Onwuegbuzie, 2004) presented mixed methods research as the third research paradigm which has the goal, not of replacing either of the other approaches, but rather to draw from the strengths and minimize the weaknesses of both in single research studies and across studies. *"If you visualize a continuum with qualitative research anchored at one pole and quantitative research anchored at the other, mixed methods research covers the large set of points in the middle area."*

Bishop (Bishop and Holmes, 2013) highlights the way that we can see MMR from as both a philosophical perspective (as a methodology) as well as (from a technical perspective) a method:

"As a methodology, it involves philosophical assumptions that guide the direction of the collection analysis of data and the mixture of qualitative and quantitative approaches in the many phases of the research process. As a method it focuses on collecting, analysing, and mixing both quantitative and qualitative data in a single study or series of studies."(Creswell and Clark, 2007a)

The term methodological eclecticism means MMR practitioners select and creatively integrate the most appropriate techniques from a wide variety of qualitative, quantitative and mixed strategies in order to thoroughly

investigate the phenomenon of interest (Teddlie and Tashakkori, 2010, Denzin and Lincoln, 2011). The researcher is seen as a connoisseur of methods who knowledgeably and often intuitively selects the best techniques available to answer research questions that may evolve as a study unfolds (Teddlie and Tashakkori, 2012).

Methodological eclecticism stems from rejection of *the incompatibility of methods thesis,* which stated that it is inappropriate to mix qualitative and quantitative methods due to fundamental philosophical or epistemological differences between the paradigms underlying those methods. This is replaced by the *compatibility thesis* which distinguishes MMR from other fields of research (Teddlie and Tashakkori, 2012).

Teddlie and Tashakkori (Teddlie and Tashakkori, 2012) consider that there are at least three issues related to the core characteristic of integrating qualitative and quantitative research: Firstly there are concerns that researchers can adequately develop the diverse skill set's required. Secondly that existing MMR research features relatively unimaginative combinations of quantitative and qualitative methods. Thirdly is the need to engage in philosophical discussion with supporters of the incompatibility thesis.

In answer to the first and third concerns, the researcher found that in order to complete this thesis it was necessary to take extra time to develop the qualitative research skills necessary, the real key to integrating the different strands of the investigation was the discovery that a strong pragmatic philosophical foundation gave the whole project relevance, structure and meaning.

In answer to the second point the need to adapt the initial design to include a final qualitative strand led to a new typology that falls somewhere between a small scale multiphase design and an exploratory sequential design and this will be explored in more detail later.

Descriptions of MMR

The methodology employed in this thesis follows a sequential mixed methods research (MMR) design and it is helpful to employ the agreed MMR notation for the purposes of describing and analysing it.

Table To Show The Summary Of Notations Used To Describe Mixed Methods Designs adapted from (Creswell and Clark, 2007a)

Table 14 Notations used to describe MMR

Notation	Example Application	What the notation indicates	Key Citations
Shorthand: Quan, Qual	Quan strand	Quantitative methods	Morse (1991, 2003)
Upper case letters: QUAN, QUAL	QUAL priority	The qualitative methods are prioritized in the design	Morse (1991, 2003)
Lowercase letters: quan, qual	qual supplement	The qualitative methods have a lesser priority in the design	Morse (1991, 2003)
Plus sign: +	QUAN + QUAL	The QUAN and QUAL methods occur concurrently	Morse (1991, 2003)
Arrow: ➔	QUAN ➔	The methods occur in sequence of QUAN followed by qual	Morse (1991, 2003)
Parentheses: ( )	QUAN (qual)	A method is embedded within a larger design or procedure or mixed within a theoretical or program objective framework	Plano Clark (2005)
Double arrows ➔	QUAL➔QUAN	The methods are implemented in a recursive process (QUAL➔QUANèQUALèQUAN	Nastasi et al (2007)

		etc.	
Bracket [ ]	QUAL➔QUANT➔[QUAN +qual]	Mixed methods is used within a single study or project within a series of studies	Morse & Niehaus (2009)
Equal sign:=	QUAN èqual = explain results	The purpose for mixing methods	Morse & Niehaus (2009)

Mixed Methods research is the type of research in which a researcher combines elements of qualitative or quantitative research techniques for the purpose of breadth and depth of understanding and corroboration. (Creswell and Clark, 2007a)

In mixed methods the researcher (Creswell and Clark, 2007a):

- Collects and analyses persuasively and rigorously both qualitative and quantitative data based on research questions.
- Mixes or integrates the two forms of data by combining them sequentially or embedding them one within the other
- Gives priority to one or to both forms of data
- Uses these procedures in a single study or in multiple phases of a program of study
- Frames these procedures within philosophical worldviews and theoretical lenses and
- Combines the procedures into specific research designs that direct the plan for conducting the study.

There are times when qualitative research may be best, because the researcher aims to explore a problem, honour the voices of participants, map the complexity of a situation and convey multiple perspectives of participants. (Creswell and Clark, 2007a)

At other times quantitative research may be best because the researcher aims to understand the relationship between variables or determine if one group performs better on an outcome than another group (Creswell and Clark, 2007a).

We know that qualitative data provides a detailed understanding of a problem while quantitative data provides a more general understanding of a problem. Both approaches have their limitations and each provides a different perspective. The limitations of one method can be offset by the advantages of the other.

Table to show the Contemporary "Core" Characteristics of Mixed Methods Research. (Teddlie and Tashakkori, 2012)

Table 15 Core characteristics of MMR

Characteristic Number	Description of Characteristic
1	Methodological eclecticism
2	Paradigm pluralism
3	Iterative cyclical approach to research
4	Set of basic "signature" research designs and analytical processes
5	Focus on the research question (or research problem) in determining the methods employed within any given study
6	Emphasis on continua rather than a set of dichotomies
7	Emphasis on diversity at all levels of the research enterprise
8	Tendency towards balance and compromise that is implicit within the "third methodological community"
9	Reliance on visual representations (e.g., figures, diagrams) and a common notational system

This dynamic approach to study design is characteristic of the evolving field of MMR where there are on-going debates about the typology and

classification of designs and approaches. Some researcher are even concerned that the field is moving towards a convergence that will stifle the expression of diverse perspectives and reduce MMR to a set of techniques and procedures (Leech, 2010) but the common characteristics of MMR such as eclecticism, diversity and pluralism make this unlikely (Teddlie and Tashakkori, 2012).

Discussion: The Critical Appraisal of Mixed Methods Studies

How can we ensure that the mixed methods research studies are of sufficiently high quality to be included in the evidence base for their field? If the criteria demanded by qualitative and quantitative researchers are based upon different understandings of 'knowledge' and 'knowing', how can such trials meet their understandings of 'good evidence'?

Quality criteria differ for qualitative and quantitative methods because they have different underlying assumptions and aims. Studies using different methods are therefore typically subject to quality appraisal using different tools. These tools cannot easily be adapted to assess mixed methods studies and so new tools have been developed for systematic reviews which include both qualitative and quantitative studies per se (Bishop and Holmes, 2013).

One research group (Heyvaert et al., 2013) has recently appraised the existing critical appraisal frameworks (CAF's) and their paper is reviewed below. They found 13 unique CAFs that had been developed to evaluate the methodological quality of primary MMR articles published between 2004-2009 (Heyvaert et al., 2013). Their paper provides an overview of the available Critical Appraisal Frameworks (CAFs) developed to evaluate the methodological quality of primary MMR articles. They also compare and critically evaluate the quality criteria proposed in these frameworks.

The Critical Appraisal of Mixed Methods Studies (Heyvaert et al., 2013)

Because a mixed methods study is more than just the sum of the individual qualitative and quantitative strands of the study the combined application of qualitative and quantitative critical appraisal criteria is most likely not

sufficient to evaluate the methodological quality of a primary MMR article. (Heyvaert et al., 2013)

The setting for this study is an Educational Science Research Group, at a University in Belgium. The research question of this paper is 'Can we construct a CAF that provides clear guidelines on how to critically evaluate mixed methods research so that they primary MMR studies can be included in systematic reviews without compromising review quality?'

The authors take pragmatism as their mixed methods philosophical stance, advocating the integration of quantitative and qualitative methods within a single study from a question-driven philosophy. They argue that the construction of a critical appraisal framework instrument should include the fact that it is easy, quick and clear in it's use.

This implies that one should apply the best-suited combination of methods and modes of analysis to answer the posed research question(s). Emphasising processes of abduction, intersubjectivity, and transferability (Morgan, 2007), pragmatism offers the researcher alternatives to the dichotomous choice between (post) positivism and constructivism, driven by the question of utility.

As well as searching academic databases the search was extended by focusing on grey literature databases and dissertations and theses databases. In addition they conducted a hand search of 10 journals with a tradition of providing information on MMR methodology. They searched backwards by searching the reference lists of all identified relevant articles and forwards by searching three citation databases. Authors of retrieved relevant studies and MMR experts were contacted regarding any additional published or unpublished work. There were no restrictions on the language of published work and search strings were combined using Boolean logic.

It is unlikely that important relevant studies were missed as by searching published and unpublished work across a wide variety of sources they

included data that characterised MMR. The first author conducted the search for articles. An agreement check was conducted with a second and third author were necessary. The inter-rater agreement was 99.93%

Only publications reporting on CAFs developed to evaluate the methodological quality of primary MMR articles were included. Studies that used the same CAF were excluded. 1,4200 articles were involved in the check and from this the 13 unique CAF's for evaluating the methodological quality of primary MMR articles were chosen and their content categorised using a constant comparative method.

In the opinion of the investigators they included the criteria that are necessary to investigate MMR. Some are generic for the critical evaluation of primary research studies (post positivist assumptions) and some are specific to MMR.

Using a constant comparative method they generated 13 headings that group similar criteria of the retrieved frameworks:

1. Criteria for the qualitative part of the study
2. Criteria for the quantitative part of the study
3. Criteria for mixing and integration of methods
4. Rationale for mixing methods stated
5. Theoretical framework
6. Research aims and questions
7. Design
8. Sampling and data collection
9. Data analysis
10. Interpretation, conclusions, inferences and implications
11. Context
12. Impact of investigator
13. Transparency

They found that there were large differences between the numbers of domains included in the respective frameworks. For all of the CAFs the procedures domain was most extensively described

Their analysis of the retrieved CAF's was an inductive one, generating headings that group similar criteria of the retrieved frameworks by applying a constant comparative method. Having done so they then discuss the idea that their framework could be used to carry out a deductive analysis.

- Standard protocols turned out to be lacking and the substantial differences between the construction of the 13 frameworks and the included quality criteria can be observed.

- The two criteria *appropriateness of mixing qualitative and quantitative research components* and *providing a rationale for conducting MMR* should be included in each CAF for evaluating MMR articles.

- It is not sufficient to merely apply critical appraisal instruments for the separate qualitative and quantitative strands, the strands should be appropriately mixed in order to answer the posed research question and the overall study should be coherent and insightful.

There are three possibilities when constructing a CAF:

1. It may not be possible or desirable to construct a Universal CAF due to the diversity of published studies.

2. A set of general criteria that should minimally be addressed in each primary MMR study could be provided but each secondary researcher could add criteria to this set based on the type of the study and their philosophical orientation.

3. The secondary researcher can pick and choose criteria, from a larger pool, to compose a set of criteria and account for this choice based on the type of study and their philosophical orientation.

This field is novel and still being developed and this paper makes a contribution to that field especially as they acknowledge that their identified criteria can be used to continue the dialogue on potential and necessary elements to be included in a future check list.

The main limitation of the study was the cut off point for data collection as December 31st 2009 and many of the frameworks mentioned are being or have been updated for example Pluye et al, whose 2009 framework was used in this paper and who have since gone on to produce the MMAT (Pace et al., 2012).

Mixed Methods in CAM Research: A Systematic Review of Studies Published in 2012 (Bishop and Holmes, 2013).

This recent paper discusses the importance of viewing mixed methods from a philosophical perspective, in order to address the tensions inherent in mixing qualitative and quantitative methods, but the authors do not make their own perspective clear. It helps to describe the prevalence of MMR for CAM in recent years.

A quantitative methodology is used and the method is a systematic review with the aim of describing the major mixed methods designs and their use in CAM research; to identify the strengths and limitations of mixed methods studies published in the CAM journals and to suggest strategies for improving the design, conduct and reporting of future MM CAM research.

It is unlikely that important papers were missed although the selection procedure was only systematic for the year of publication (2012) selected and focused on (then) current mixed methods research. All the studies

published in the top 10 integrative and complementary medicine journals were screened.

Journals were selected according to impact factor assuming that they are the most widely read and have the most influence on the literature. Full texts as well as titles and abstracts were searched using a definition of MMR that was a quite minimal. Although only one researcher collected the articles, 10% were checked by a second researcher to ensure they were suitable for inclusion

Ten of the 95 articles reported on studies using a single method but described how this related to another study, which used a different method. In nine of these cases it was possible to locate and include the article reporting the related study.

Studies were also screened for inclusion based on the criteria set out in the screening questions of the quality appraisal tool The Mixed Method Appraisal Tool (MMAT) (Pace et al., 2012). This means that the selected studies were appraised using a framework that was also used to select them. It is also interesting that the researcher selected this tool although it does not included a domain about the philosophical orientation of the study which was an important part of the research question and one of the findings of the study.

The MMAT results suggest that some mixed methods elements were of good quality and the quantitative components were generally of a higher quality than the qualitative components. In the majority of studies the mixed methods design was relevant to the research questions and the qualitative and quantitative components were integrated at some stage to address the research question. Often this integration occurred at the interpretation stage but sometimes it occurred during data analysis.

- Only 5% of studies acknowledged or reflected on the limitations of their mixed methods design and none of the studies acknowledged or

addressed the philosophical tensions involved in a mixed methods research project.

- Quantitative studies dominated the top 10 CAM journals in 2012 (84%) of all published papers.

- 4% of papers reported mixed methods studies while just 1% reported purely qualitative methods alone. The remaining 11% of papers did not report primary research findings.

- Of the mixed methods studies the most common study design for qualitative components was ethnography (65%). Qualitative studies also used phenomenological methods (24%), qualitative description (6%), grounded theory (2.5%) and qualitative case study (2.5%).

- The most common study design for quantitative components was an incidence or prevalence study (72.5%) following by RCT (12.5%), cross-sectional analytical study (6%), case report (4%), cohort study (2.5%) and case series (2.5%)

The MMAT distinguishes between four major mixed methods designs: sequential exploratory, sequential explanatory, triangulation and embedded. These designs have been described in detail by (Creswell and Clark, 2007a).

The insights from this review lead us into the next section which explores the way in which a pragmatist philosophical perspective can help to reconcile the use of quantitative and qualitative methods within a single study.

In future CAM researchers might consider pragmatism as a way of addressing the philosophical challenges of mixed methods research…. in essence a pragmatic perspective involves judging a piece of research on the extent to which it achieves its stated external goals. Applying pragmatism, a qualitative component might be judged on the extent to which the findings

enable an intervention to be delivered in a way that respects and engages patients; a quantitative component might be judged on the extent to which it provides persuasive evidence that leads to policy makes funding an intervention. (Bishop and Holmes, 2013)

Summary

What is MMR? How do I describe my study and ensure transparency of reporting?

The application of complementary medicine to a conventional medical fertility unit presents challenges regarding *the incompatibility of methods thesis,* which stated that it is inappropriate to mix qualitative and quantitative methods due to fundamental philosophical or epistemological differences between the paradigms underlying those methods.

Mixed Methods Research based upon a Pragmatist world view offers a way to reconcile these dualisms based upon the *compatibility thesis* (Teddlie and Tashakkori, 2012). *Mixed Methods research is the type of research in which a researcher combines elements of qualitative or quantitative research techniques for the purpose of breadth and depth of understanding and corroboration*. (Creswell and Clark, 2007a)

Bishop (Bishop and Holmes, 2013) highlights the way that we can see MMR from as both a philosophical perspective (as a methodology) as well as (from a technical perspective) a method.

In mixed methods the researcher (Creswell and Clark, 2007a):

- Collects and analyses persuasively and rigorously both qualitative and quantitative data based on research questions.
- Mixes or integrates the two forms of data by combining them sequentially or embedding them one within the other
- Gives priority to one or to both forms of data

- Uses these procedures in a single study or in multiple phases of a program of study
- Frames these procedures within philosophical worldviews and theoretical lenses and
- Combines the procedures into specific research designs that direct the plan for conducting the study.

The reporting of such studies must include the different quality criteria for quantitative and qualitative studies as well as addressing the philosophical tensions. Other concerns that need to be addressed have been identified as, the skills needed by the researcher and the tension between the creative and imaginative use of MMR, compared to the desire to unify and characterise this emerging field (Teddlie and Tashakkori, 2012)

Guidelines for designing and reporting MMR have been suggested in a systematic study (Heyvaert et al., 2013) and they include 13 headings that group similar criteria of the retrieved frameworks:

1. Criteria for the qualitative part of the study
2. Criteria for the quantitative part of the study
3. Criteria for mixing and integration of methods
4. Rationale for mixing methods stated
5. Theoretical framework
6. Research aims and questions
7. Design
8. Sampling and data collection
9. Data analysis
10. Interpretation, conclusions, inferences and implications
11. Context
12. Impact of investigator
13. Transparency

A study (Bishop and Holmes, 2013) that focused on studies in the field of CAM used a quality appraisal tool The Mixed Method Appraisal Tool (MMAT) (Pace et al., 2012). Attention to the criteria used in both these tools should be sufficient to ensure the quality and transparency of the MMR in this thesis.

Conclusion

Although MMR is a relatively recent and quickly evolving 'third paradigm' of methods and methodology there are already some systematic studies of the field and thoughtful discussions of the philosophical debate available to guide the researcher engaged in this field. The study of CAM is especially compatible with MMR due to the wide range of outcomes being measured that can include both quantitative and qualitative domains of knowledge.

Limitations

This section is not a systematic review of the literature on mixed methods research and the conclusions reached must be viewed as both tentative and provisional.

Reflections on The Limitations of the Literature Review Chapter

This literature review has evolved over time to become nine discrete sections each one dealing with an aspect of the thesis. It is a mixture of narrative reviews and systematic qualitative reviews as summarised in **Table 3 The nine distinct reviews in Chapter 1**.

It is also a record or narrative of the development of the methodology and philosophical foundation of the thesis and this will be further explored in Chapter 2.

There is therefore a tension throughout Chapter 1 between the need for a systematic approach to the literature on each topic and the exploratory nature of the way the thesis was written in an iterative cycle of reading, writing, feedback, response to feedback as writing and this has explained as a model in Figure 1 Model to show the development of the researcher world view.

Most of the nine sections were not written as systematic qualitative reviews and this deficiency as been acknowledged and to some extent addressed (post viva) by a closer attention to theory, a more transparent reporting of search strategies and a reflective commentary at the end of each of the nine sections.

It was also recognised post-viva that it is especially important to conduct a systematic literature review in this field (CAM) because it works as a mechanism to facilitate interdisciplinary collaboration and a more integrated understanding of health (Karunananthan et al., 2009).

The benefits of conducting a more systematic literature review would have included a more systematic analysis leading to the generation of credible theoretical insights from this thesis. These theoretical insights would be of greater use in the design of clinical trials for CAM therapies if they have been generated systematically and that is a primary goal for this field of research.

However this thesis has made different contribution in that it has explored the methodological issues around the trial design and philosophical worldview in great detail and used the literature reviewed to stimulate theoretical sensitivity, to stimulate questions, to direct theoretical sampling (Silverman, 2013) in order to develop a thematic analysis that differs from the existing literature.

On balance the need to incorporate a more systematic approach has been acknowledged and will be an important aspect of any published work derived from this thesis and it will continue to be combined with the close attention to theory and philosophy that I have already begun to develop.

Chapter 2 - Methodology

Introduction

The quality of work is dependent upon consistent reflection on the dynamics between research question, philosophical assumptions and methodology (Mesel, 2013).

This section aims to describe the methodology used in this thesis and explain the reasons for choosing it. It will then be evaluated using the appropriate frameworks and discussed against suitable criteria for both 'rigour and relevance' (Lewith et al., 2010).

The pragmatic worldview that became the central theme of this thesis has been made explicit, and has four broad features: it is concerned with the consequences of actions; it is problem centred, it is pluralistic in its approach to methodology and it is orientated towards "what works" and practice (Creswell and Clark, 2007a).

The choice of a mixed methods approach and the use of Thematic Analysis (TA) (Braun and Clarke, 2006a) were guided by this pragmatic world view. However, in an iterative process of reflection and rewriting, the recognition of the pragmatic worldview also occurred while researching the theoretical foundations of mixed methods research and the use of TA as a method.

Researchers who wish to employ mixed methods in this way need to employ a philosophical strategy to clarify their inclusion of data from two different paradigms and this section describes the development of that strategy for this thesis.

Teddlie and Tashakkori (Teddlie and Tashakkori, 2012) recognise the connections between epistemological and ontological assumptions as one of

the main challenges for mixed methodologies and advocate what they call paradigm pluralism:

'This implies that mixed methods does not define ownership of a certain methodology to a certain paradigm, and second, opens up for multiple frameworks or philosophical paradigms even within the same study.'
(Mesel, 2013)

This pluralistic approach seemed especially appropriate for this thesis because it sought to integrate a complementary medical approach with a traditional medical approach and represented a meeting point of two paradigms.

Pragmatism As The Guiding Principle For The Study

Pragmatism does not mean 'try anything that works' it should be a philosophically informed approach to research. But research seldom begins with a set of philosophical assumptions, and rather usually with a defined problem and a set of questions that attempt to provide answers for the problem at hand (Morgan, 2007). These research questions determine the method that is chosen to answer these questions.

Underlying this process, however, is a set of (acknowledged or unacknowledged) philosophical assumptions that indirectly define how the research object is viewed, what research questions are asked and what methods are chosen. Mesel believes that acknowledging this bottom-up perspective allows for better communication between potentially incommensurate positions by adopting a pragmatic approach that is closer to everyday research (Mesel, 2013).

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Explicit philosophical reflection is especially important if this bottom up pragmatic approach is explicitly adopted in order to ensure transparency and internal consistency.

Mixed Methods Research And The Reasons For Choosing MMR For This Thesis.

It is necessary to be explicit about the reasons for choosing to use mixed methods and the framework chosen here is that of Bryman (Bryman, 2006b) because it offers a more detailed list of researchers' reasons than the earlier model developed by Greene et al (Greene et al., 1989). The Bryman typology here is adapted from a table from (Creswell and Clark, 2007a) page 62-63.

The choice of a framework to evaluate the use of MMR was also guided by this author's philosophical stance. Researchers (Greene and Hall, 2010) have identified five stances on mixing paradigms whilst mixing methods: purist, complementary strengths, dialectic, aparadigmatic, and pragmatism as an alternative paradigm. The stance adopted in this thesis is pragmatism.

Therefore the chosen frameworks of Creswell and Clarke (Creswell and Clark, 2007a) are used in this study as they are pragmatic frameworks with a strong orientation towards philosophical assumptions (Heyvaert et al., 2013). Their list is therefore likely to include an emphasis on 'what works', 'what is feasible', 'what is the most appropriate tool' and to be driven by the research question.

Triangulation

Triangulation for greater validity refers to the traditional view that quantitative and qualitative research might be combined to triangulate findings in order than they may be mutually corroborated.

Fielding and Fielding (Fielding and Fielding, 1986) suggest that the use of triangulation should operate according to ground rules:

1. Always begin from a theoretical perspective or model
2. Choose methods and data that will give you an account of structure and meaning from within that perspective.

For the current study the chosen methods, if full data sets were available, would have provided insights into both the clinical efficacy as well as the patient's experience of quality of life during the trial. Safety data from the trial could have been added to the existing portfolio held by the manufacturer and the cost of treating infertile women with Ovarium compositum as an additional therapy could be estimated.

It was necessary to establish the external context of the trial, i.e. how do homotoxicologists treat infertility? How do patients feel about taking part in a trial where they might receive a placebo? How do clinic staff feel about hosting such a trial? Qualitative phases early in the protocol design helped to move the project forward. Some of the problems that were encountered during recruitment were predicted in the early qualitative phases and perhaps should have alerted the researcher to the need to establish a better line of communication with the clinic staff in Jersey.

In the final analysis the triangulation attempted to explore a different question, why is it difficult to recruit women who are undergoing infertility treatment to a clinical trial?

Offset

Offset refers to the suggestion that the research methods associated with both quantitative and qualitative research have their own strengths and weaknesses so that combining them allows the researcher to offset their weaknesses to draw on the strengths of both.

In this study the final qualitative strand, (the investigation into the work related concerns of women undergoing infertility treatment), seeks to offset the weaknesses in the thesis caused by lack of the planned quantitative data. The strength of the first and second qualitative strands is that they can help us to understand the perceptions of patients and practitioners towards infertility and it's treatment using homoeopathy or homotoxicology.

The methods used in the quantitative strand have the weakness of being unable to identify the reasons for recruitment difficulty, that information has to be sought using qualitative methods.

The strength of the quantitative strand is that an RCT model can be used to measure the difference between the effect of the placebo and active medication on the fertility outcomes of trial participants.

Completeness

Completeness refers to the notion that the researcher can bring together a more comprehensive account of the area of inquiry in which he or she is interested if both quantitative and qualitative research methods are employed. The pragmatic worldview would be that both forms of knowledge are generated through the transactions of all participants with their natural and social environment. To understand that knowledge we need to be able to use language and concepts that would be understood by all the participants. As Cornish would say:

Lay people and scientists alike construct knowledge in the context of action: knowledge guides action and action feeds back into knowledge construction. (Cornish and Gillespie, 2009)

Process

Quantitative research provides an account of structures in social life but qualitative research provides a sense of process. In this study the researcher used qualitative research to explore the patient's perspective on their infertility treatment and how it might reveal a conflict with their identity as both a treatment seeker and an employee. An understanding of the process of taking part in infertility treatment is sought in the data from the online support forums. The process of treating infertility with CAM therapists was explored using a practitioner questionnaire and the process of taking part in a randomised placebo controlled trial was explored using a patient questionnaire and by talking to clinic staff at The Bridge Centre.

Different Research Question

This refers to the argument that quantitative and qualitative researches can each answer different research questions. In this study the questions that were approached with a quantitative method were related to the clinical efficacy of the trial medication: 'What is the effect of Ovarium compositum as an additional treatment on fertility outcomes in infertile women undergoing treatment?'

The questions that were asked from a qualitative perspective included: 'how do homotoxicologists treat infertility? Will women agree to be randomised?' Why is it difficult to recruit women to a trial when they are already undergoing infertility treatment? How do women experience balancing work with infertility treatment?'

Explanation

Explanation refers to when one line of research is used to help explain findings generated by the other. In this case qualitative research were used to seek an explanation for the poor recruitment to the quantitative phases of the design.

Unexpected Results

Surprising results generated by one can be understood by employing the other. In this case it is widely assumed that infertile women are highly motivated to seek treatment (Brandes et al., 2009) and therefore it was surprising that women were not more willing to participate in the trial of Ovarium compositum. The ideal qualitative follow up would have been targeted at those same women but as this was not possible then the internet forums provided some data on the experiences of women in a similar situation.

Instrument Development

This refers to contexts in which qualitative research is employed to develop questionnaire and scale items – for example, so that better wording or more comprehensive closed answers can be generated. The results of my

thematic analysis could be used in the future for these purposes. Also the use of the non-validated EHIQ would have provided useful data to its authors.

Sampling

This refers to situations in which one approach is used to facilitate the sampling of respondents or cases. The sample of participants for the quantitative strand was dictated by the infertility unit and did not depend upon the results of the early qualitative strands.

Credibility

Refers to suggestions that employing both approaches enhances the integrity of findings. The planned trial design would have provided results or an enhanced understanding that would have been of interest to both medical and CAM practitioners. The chosen methodology would have given the thesis credibility both as a clinical trial and as a sensitive exploration of the participants' perspectives.

The actual thesis sought to regain credibility (as a thesis) by using qualitative research to explore the reasons for poor recruitment.

Illustration

Refers to the use of qualitative data to illustrate quantitative findings, often referred to as "putting meat on the bones" of "dry" quantitative findings. In this thesis the 'dry bones' were really the 'non-findings' and qualitative analysis was needed to make those non-findings useful or any conclusions, drawn from the poor recruitment, credible.

Utility Or Improving The Usefulness Of Findings

The suggestion that combining the two approaches will be more useful to practitioners and others. It is of little use to say that women are reluctant to participate in trials about infertility unless we can explain why.

Diversity Of Views

Firstly this means to combine the researchers' and participants' perspectives, and secondly, to reveal meanings amongst research participants through qualitative research. This thesis sought to explore the diversity of views in three different contexts: firstly amongst practitioners using homotoxicology to treat infertility; secondly the views of patients and staff at a London Infertility Unit about treating infertility with CAM or mainstream medicine and about being randomised to a trial; thirdly the diversity of views of women about their infertility experience were sought in the internet forum.

Enhancement Or Building Upon Quantitative And Qualitative Findings

The enhancement of findings from one methodology by findings from another methodology is the unifying theme in the choice of a MMR.

Description Of The Structure Of MMR Used In This Thesis

Introduction

This section aims to further describe the chosen methodology and locate it in the field of Mixed Methods Research (MMR).

This project has four strands, a strand is a component of a study that encompasses the basic process of conducting quantitative or qualitative research: posing a question, collecting data, analysing data, and interpreting results based on that data (Teddlie and Tashakkori, 2009).

The four distinct strands that can be identified in this thesis are shown below:

Strand	Methodology	Method
1st	Qualitative	A questionnaire of practitioners
2nd	Qualitative	A questionnaire of patients, a discussion group and questionnaire of nurses
3rd	QUANTITATIVE (qualitative embedded)	An RCT trial and quality of life questionnaire of patients
4th	QUALITATIVE	A thematic analysis of data from an internet forum

Table 16 The study design

It is important that each strand has clear research objectives or a research question and these are found in each strand and are summarised below:

1. A practitioner survey to investigate the choice of medication to use in a randomised controlled trial of homotoxicology to treat female infertility
2. To investigate practitioner perceptions of the cause and treatment of infertility.
3. To explore the role of the CAM practitioner in treating infertility

Strand 2 there are two qualitative research objectives:

1. Will it be possible to recruit women to a double blind randomised placebo controlled trial of a homoeopathic product and
2. What will be the likely attitudes of the staff of the clinic towards such a trial?

Strand 3 - this is framed as a qualitative objective (1 with prior knowledge of the outcome) but it could also be framed as a quantitative research question (2):

1. Is it possible to show that Ovarium compositum can improve the fertility outcomes of women undergoing infertility treatment at the Assisted Reproduction Unit of Jersey General Hospital?
2. What is the specific effect of Ovarium compositum on the fertility outcomes of women attending an ARU at Jersey General Hospital?

Strand 4 there is a clear qualitative research objective:

1. The purpose of this study was to further investigate the reasons for recruitment failure that were suggested by the nursing staff at the trial site.

The first qualitative strand was the review of homotoxicology treatment for infertility in the UK and the aim was to check the model validity of the quantitative strand. As a preliminary stage to the design of the trial protocol it was deemed necessary to establish the choice of trial medication and method for treating female infertility by seeking a consensus of opinion from homotoxicologists working in the UK. These were identified and approached via the annual conference of the Society of Homotoxicology, the database of a supplier and the British Register of Complementary Therapists. A questionnaire was sent to 60 homotoxicologists and the return rate was 33%. Thematic Analysis (TA) was used to analyse the responses.

The second qualitative strand was a feasibility study with patients and staff at The Bridge Centre, a private infertility clinic in London. Gerhard et al (Gerhard I, 1997) attempted to design and implement a monocentric, two armed, randomised study at the University Hospital of Obstetrics and Gynaecology, Heidelberg The trial proved impossible to implement for a number of reasons including the fact that only 14% of patients agreed to be randomised instead of the anticipated 60-70%.

Potential obstacles to success were discussed with the discussion group who then completed a survey of nine open questions. Their responses were analysed thematically create a qualitative evaluation of the data and their

concerns and insights used to generate a patient questionnaire. 127 patient questionnaires were distributed at the registration desk over a 9-month period. The results of this survey were used to support the decision to pilot a trial at Jersey General Hospital.

The third strand, quantitative with an embedded qualitative aspect, was originally conceived as the main focus of the study and consisted of a RCT of the use of Ovarium Compositum as an adjunct treatment for infertile women in an assisted reproduction unit. The study was sponsored by Clinical Pharmacology, Barts and The London, Queen Mary's School of Medicine and Dentistry, Charterhouse Square, London and funded by Biologische Heilmittel Heel GmbH Dr. Reckeweg-Straße 2-4 76532 Baden-Baden, Germany.

The primary objective was to assess whether the administration of Ovarium Compositum as an adjunct therapy could make a significant difference to fertility outcomes in infertile women seeking medical intervention. The second objective was to measure quality of life in women undergoing treatment for infertility and using Ovarium compositum. The study was designed as a one centre, double blind placebo randomised controlled trial located at the Department of Obstetrics and Gynaecology, Jersey General Hospital, Gloucester Street, St Helier, Jersey, JE1 3QS, and the study period was intended to be twelve months.

The fourth strand was a qualitative investigation into the work-related concerns faced by women seeking infertility treatment in the British Isles to investigate themes suggested by the staff at the site of the RCT phase. This stage was theory driven and the choice of data and the method of collection were informed by the need to investigate a particular theory or hypothesis. The data was approached with a particular research question in mind and the source of the data, the online forum, was a pragmatic choice driven by what was available and accessible in a realistic timeframe. It was not possible to work with the study site team to collect qualitative data for this stage in spite of several attempts to do so.

Mixed Methods Designs have been categorised and described (Creswell and Clark, 2007a) into six main designs as depending on four key decisions, (1) The level of interaction between the strands, (2) the relative priority of the strands, (3) the timing of the strands and (4) the procedures for mixing the strands.

In this thesis the qualitative and quantitative strands are very interactive and the results of one strand feeds directly into the design of the next. At the start of the study priority was given to the importance of the quantitative data and the role of the qualitative data was to support the collection of quantitative data. These priorities changed as the trial progressed and became explanatory and exploratory in nature.

The timing was sequential rather than concurrent because each strand was a distinct phase in the research study. Mixing of the quantitative and qualitative data occurred at the level of design as well as during the final conclusions to each strand and the end of the whole project.

This study could be characterised as a variant of two sequential designs, the exploratory sequential design followed by the explanatory sequential design, (Creswell and Clark, 2007a).

The first two strands begins with and prioritizes the collection and analysis of qualitative data and building from those results the researcher conducts a second quantitative phase (strand three), however because of the failure of trial recruitment the study was not complete and began an explanatory sequential design where the quantitative data (or lack thereof) was the starting point for a qualitative phase to explain the quantitative findings.

This is congruent with the pragmatist world view of the researcher where:
Organisms are constantly adapting to new situations and environments. Our thinking follows a dynamic homeostatic process of belief, doubt, inquiry, modified belief, new doubt, new inquiry…in an infinite loop, where the person

or researcher (and research community) constantly tries to improve upon past understandings in a way that fits and works in the world in which he or she operates. The present is always a new starting point.(Johnson and Onwuegbuzie, 2004)

The study does not meet the definition of a multiphase design (Creswell and Clark, 2007a) because the purpose of those designs is to implement multiple phases to address a wider objective such as large-scale program development and education. Although strongly informed by a philosophical worldview this thesis did not employ a transformational design as it was not collecting and analysing data within a transformative theoretical framework, for example feminism, that guided the methods and decisions. It might be better described as a **pragmatic design** that views human inquiry as being analogous to experimental and scientific inquiry:

We all try out things to see what works, what solves problems, and what helps us to survive. We obtain warranted evidence that provides us with answers that are ultimately tentative (i.e., inquiry provides the best answers we can currently muster), but in the long run, use of this "scientific" or evolutionary or practical epistemology moves us towards larger Truths (Johnson and Onwuegbuzie, 2004).

The Methods Used In Each Strand.

Methodology for Strand One (2006)

Introduction

The first qualitative strand was the review of homotoxicology treatment for infertility in the UK. As a preliminary stage to the design of the trial protocol it was important to establish the choice of trial medication and method for treating female infertility by seeking a consensus of opinion from homotoxicologists working in the UK. This approach is also suggested in the MVHT (Mathie et al., 2012) in order to ensure that the trial has external validity and that it is representative of the way the patients would be treated in a homeopathic clinic.

The sample practitioners were identified and approached via the annual conference of the Society of Homotoxicology and the British Register of Complementary Therapists. At the time that this study was being designed homotoxicologists were self-regulating in the UK and the registration body was the British Register of Complementary Therapists. UK practitioners using homotoxicology to treat infertility, registered Homotoxicologists and practitioners attending an annual symposium were asked to complete a questionnaire. The questionnaire is included in the appendix Figure 4 Questionnaire for practitioners from strand 1

The primary aim of this questionnaire was to find out how Homotoxicologists currently practicing in the UK would treat infertility. The results were used to inform the trial design of a pilot study of Ovarium compositum. The secondary aim of this study was to explore the role of Thematic Analysis as a research tool to understand which practices, beliefs and concepts the CAM approach shares with the mainstream medical treatment of infertility and where it diverges.

Problem formulation

METHODOLOGY

There are multiple approaches to using homoeopathy and homotoxicology to treat infertility and each CAM therapist may also utilise more than one therapy or approach. In order to design a trial with both internal and external validity it was necessary to understand three things: How homotoxicology might be used to treat infertility in practice? What is the role of the CAM practitioner in the treatment of infertility? Is there a specific treatment that can be given without a consultation and in the absence of an individualised prescription?

Purpose or Research Question

1. A practitioner survey to investigate the choice of medication to use in a randomised controlled trial of homotoxicology to treat female infertility
2. To investigate practitioner perceptions of the cause and treatment of infertility.
3. To explore the role of the CAM practitioner in treating infertility

Methods

A paper questionnaire with both open and closed questions (see Figure 4 Questionnaire for practitioners from strand 1.)

Data collection methods

The questionnaire was designed to firstly establish practitioner opinions regarding a specific case study and then to investigate their approach towards treating infertility in general. The case study used was characteristic of the patient group that will be enrolled in the pilot study.

The second version of the questionnaire was created when it became apparent that the sponsor might be Heel and therefore the Heel products needed to be included in the protocol.

The questionnaire was composed of four questions:

- Question one asked for tick options to five protocols for a case study of female infertility, participants were allowed to select more than one option.

- Question two asked them to recommend a protocol for treating female infertility with homotoxicology.
- Question three asked them to recommend a protocol for treating male infertility with homotoxicology.
- Question four was an open question asking if they had any other recommendations.

Data collection instruments and technologies

The case study was based upon a real life example of a successfully treated case of female infertility in the researcher's own practice. The choices of the five protocols for the case study were based upon the researcher's personal experience of treating female infertility and therefore introduced some treatment bias into the questionnaire. The protocols chosen had to include possible trial medications from a list of three manufacturers, Heel, Nelsons and Guna. This bias was balanced by allowing an open response to questions two, three and four.

Qualitative approach and research paradigm

The results of questions 2-4 of the practitioner questionnaire were analysed using a qualitative approach, content thematic analysis (Braun and Clarke, 2006a). This approach was chosen in order to organise the data into themes that can be used to describe the plurality of approaches used by individual therapists to treat infertility and to explore their understanding of the causes of the condition. The results are discussed in more detail in the results chapter (see The Results Of The Practitioner Questionnaire).

This sample of therapists has a spectrum of diagnostic skills ranging from the conventional medical approach to alternative systems of healing such as acupuncture (for sampling see below). They will therefore have their own individual belief systems regarding the nature of health, disease and healing. Qualitative analysis of their responses should reveal some these embedded concepts and beliefs.

Sampling strategy

The survey was posted to the 10 registered Homotoxicologists in the UK. They were selected from a register supplied by the Institute for Complementary Medicine Register or BRCP (British Register of Complementary Practitioners). This is the only recognized UK registration body for Homotoxicology.

An additional 50 copies were distributed via the mailing list of one of the homotoxicology suppliers to target therapists using the products. The mailing list consisted of CAM practitioners supplied by the UK sole distributors of products from Germany and Italy. The details of the mailing list were not supplied to the researcher but the questionnaires were sent to the distributor to include with a monthly statement posted to practitioners.

Delegates at the annual conference of the Society of Homotoxicology (UK) were encouraged to return their copies during a verbal presentation explaining the purpose of the study and how their responses would be used.

A letter did not accompany the forms but at the top it stated:

RESEARCH PROJECT; Homoeopathy and Infertility. Supervised by Prof Atholl Johnston, Clinical Pharmacology, Barts and The London, Queen Mary's School of Medicine and Dentistry.

The return of the form was used as implied consent to include their responses in the study.

Researcher characteristics and reflexivity

The researcher is a qualified homotoxicologist who was acquainted with many of the therapists who were participants in the study. The protocols being discussed had also been included in some of the training sessions that she had delivered, in her role as a practitioner/teacher, to some of them. The benefit of this closeness is that the researcher had a good understanding of the treatments that were suggested by the respondents and there was no

need to seek clarification of the technical terms used. The disadvantage is that the researcher cannot free herself of her 'theoretical and epistemological commitments' to the context of the data (Braun and Clarke, 2006a) . There is also the possibility that knowing me influenced the participants and this could have biased the results. However as many of them were experienced CAM practitioners their responses would reflect their experience rather than a desire to support the study by selecting a potential sponsor from the options offered.

Context

Homotoxicology was relatively new to the UK at the time and some of the therapists were attending the conference to find out more about the use of homotoxicology in the UK, some of them were already registered homeopaths and homotoxicologists using CAM therapies in the UK

Ethical issues pertaining to human subjects

Participants in the questionnaire were not asked to reveal any of the details of their patients' identity. No patients would be identifiable as a result of the questionnaire.

Data analysis

The results of question 1 were counted to give a numerical count of the popularity of 5 different protocols. The results of the questions 2-4 of the practitioner questionnaire were analysed by sorting the responses using a qualitative approach, content thematic analysis, according to the protocols suggested by (Braun and Clarke, 2006a). The data were read to familiarise the researcher with the content and then the responses were printed out as individual slips that could be treated as codes. The slips were then organised into themes in an iterative process of reading and sorting until coherent themes emerged. The data was revisited and the themes explored and refined as part of the rewriting period in January 2013.

Copy of Questionnaire

Question One:

METHODOLOGY

Please would you read the following summary of an infertility case and indicate which of the suggested protocols would, in your opinion, be appropriate. You may tick more than one option.

Case Details:

Sex: Female, Date of Birth 13th April 1962, Age at first consultation 42 years old

Marital Status: Married (happily)

Appearance: Dark haired, athletic build.

Family history: Not available as patient was adopted. She has undertaken psycho-emotional therapy regarding her adoption and is actively tracing her birth mother.

Presenting condition: Failure to respond to Gonadotrophins injections for IVF treatment. An earlier IVF treatment had resulted in a successful pregnancy but the pregnancy was terminated following tests for Down's syndrome.

General Health is good, no menstrual difficulties, few acute infections, and infrequent headaches. No financial anxieties. Regular exercise (horse riding), but some pain from muscles, diagnosed as lactic acid build-up.

Vaccination: Hepatitis; Yellow fever, Typhoid. Malaria treatment. 1998

Other Health Choices: Hypnosis and Herbal treatment for high mercury levels.

Figure 4 Questionnaire for practitioners from strand 1

Please tick the options that in your opinion are appropriate, you may chose more than one:

QUESTIONNAIRE VERSION ONE

Option number	Description of Treatment	Tick
1	Treatment of the vaccinations using potentised vaccines, Silica and Thuja.	
2	Treatment of the hormone balance using potentised hormones (GUNA): FSH D6 20 drops three times a day from the 1st to the 3rd day of the menstrual cycle. Beta Estradiol D6 20 drops three times a day from the 4th to the 14th day of the menstrual cycle. Luteinizing Hormone D6 20 drops three times a day from the 4th to the 15th day of the menstrual cycle. Progesterone D6 20 drops three times a day from the 14th to the 24th day of the menstrual cycle.	
3	Use of the indicated remedies: Nat Mur 6 and Sepia 6 daily for two weeks.	

4	Treatment of Miasmatic ‘Psoric’ tendency with Psorinum nosode and drainages.	
5	Treatment of Pituitary-Ovarian feedback mechanism using complex remedy ‘G3’ (GUNA): Composition: Ovarium D8/D12/D30, Corpus Luteum D8/D12/D30, Pulsatilla D6/D8/D30, Kali Carb 6CH/30CH.	

QUESTIONNAIRE VERSION TWO

Please tick the options that in your opinion are appropriate, you may chose more than one:

Option 1:

Remedy	Manufactured by	Dosage	Frequency
Syzygium Compositum	-Heel Biologische Heilmittel Heel GmbH www.heel.com	10 drops	3 times daily
Galium-heel®	-Heel Biologische Heilmittel Heel GmbH www.heel.com	10 drops	3 times daily
Gynäcoheel®	-Heel Biologische Heilmittel Heel GmbH www.heel.com	10 drops	3 times daily

Option 2: Treatment Of The Declining Hormone Levels Using Potentised Hormones (GUNA):

Remedy	Manufactured by	Dosage	Frequency
FSH D6	GUNA srl www.guna.it	20 drops	3 times daily from the 1st to the 3rd day of the menstrual cycle

B-estradiol D6	GUNA srl www.guna.it	20 drops	3 times daily from the 4th to the 14th day of the menstrual cycle
LH D6	GUNA srl www.guna.it	20 drops	3 times daily from the 4th to the 15th day of the menstrual cycle.
Progesterone D6	GUNA srl www.guna.it	20 drops	3 times daily from the 14th to the 24th day of the menstrual cycle.

Option 3: Constitutional Treatment and Correction of Miasmatic Tendency Using Classical Homeopathy

Option 4: Treatment Of Pituitary-Ovarian Feedback Mechanism Using Complex Remedy 'G3' (GUNA): Composition: Ovarium D8/D12/D30, Corpus Luteum D8/D12/D30, Pulsatilla D6/D8/D30, Kali Carb 6CH/30CH.

Remedy	Manufactured by	Dosage	Frequency
G3	GUNA srl www.guna.it	Begin with 5 drops twice a day, and then increase by 1 drop daily up to 10 drops three times a day.	Daily

Question Two

What would you use in your practice as a well indicated homoeopathic/ homotoxicological protocol for treating female infertility due to declining hormone levels?

Question Three

What would you use in your practice as a well indicated homoeopathic/homotoxicological protocol for treating male infertility due to low sperm count?

Question Four

Are there any other lifestyle choices or changes that you would recommend to a patient seeking advice regarding infertility?

Methodology for Strand Two (2006-2007)

The second strand was a qualitative study with patients and staff at The Bridge Centre, a private infertility clinic in London. Patient and public involvement (PPI) was a political and grassroots initiative at the time that this study was being designed (Mockford et al., 2012), and under New Labour there was a greater emphasis on public and user participation in public services (Newman, 2001) which stressed the importance of citizenship as well as consumerism, responsibilities as well as rights.

The idea of including the pluralistic perspectives of patients, nurses, researcher, practitioner in study design meets this need for research to be more responsive to the service users as well as endorsing Pragmatist shared values such as democracy, freedom, equality, and progress.

Background: Gerhard et al (Gerhard I, 1997) attempted to design and implement a monocentric, two armed, randomised study of single homeopathic remedies (prescribed according to repertorisation of their symptoms and the selection of a remedy using the similar principle) at the University Hospital of Obstetrics and Gynaecology, Heidelberg The trial proved impossible to implement for a number of reasons including the fact that only 14% of patients agreed to be randomised instead of the anticipated 60-70%.

The first aim of this PhD project was to design and implement a double blind randomised trial of Ovarian Compositum in conjunction with an infertility clinic in Jersey. Before embarking on a trial it was important to try to make sure that sufficient numbers of women would agree to take part. Understanding their motivation for agreeing to take part in such a trial would help with the recruitment programme.

Objectives:

1. To find out if women undergoing infertility treatment would consent to be randomised to a double blind placebo controlled trial and what might be their motivation for taking part.

2. To investigate the attitude of women receiving infertility treatment towards homeopathy/homotoxicology

3. To investigate the attitudes of clinic nursing staff towards the idea of a trial of a homeopathic product.

Research Question:

Will it be possible to recruit women to a double blind randomised placebo controlled trial of a homoeopathic product and what will be the likely attitudes of the staff of the clinic towards such a trial?

Method: Interviews and questionnaires were used to investigate the attitudes of staff and patients at the clinic.

Ethics

Ethics approval for the patient questionnaire was granted by the Chair of the ethics committee at The Bridge Centre based on the understanding that an information sheet about homotoxicology accompanied the questionnaire.

The Staff Interviews and Questionnaires

A group interview was conducted with five nurses who then completed a survey of nine open questions. Their responses were organised using MaxQDA and then analysed thematically to create a qualitative evaluation of the data. It is acknowledged that a sample of five nurses is not enough to produce sufficient data to achieve saturation of themes but for practical reasons this was the maximum number available. A copy of the questionnaire is available in appendix.

The Patient Questionnaire

This patient survey took place at the Bridge Centre, London. 127 Questionnaires and patient information sheets were distributed to the registration desk over a 9-month period and were completed by women who were waiting for their treatment. They were able to post them back to the Matron of the clinic in a postage paid envelope or hand them into reception. A copy of the questionnaire and patient information sheet is available in appendix see Questionnaire for nurses at The Bridge Centre, Questionnaire for Patients at The Bridge Centre, and Patient Information Sheet included with questionnaires.

Development of the Patient Questionnaire

The patient questionnaire (Table 24 Table of results for patient questionnaire) was developed by Claire Tyson (as chief investigator of the trial), and was designed to investigate possible obstacles to running the trial such as previous treatment with homoeopathy, bias against homeopathy, willingness to take a placebo, willingness to take their medication at home, willingness to give up caffeine and peppermint, willingness to take part in a trial that might bring benefit to others in the future rather than immediate personal benefit.

There were nine closed questions that were intended to yield a simple yes or no answer that could be counted rather than rich information for thematic analysis. Questions 3, 4, and 9 were designed to investigate the pitfalls encountered in earlier studies of homeopathy for infertility (Gerhard I, 1997) in which women declined to be randomised to a placebo group or expressed a preference for homeopathy.

If the questions could be been chosen after conducting the qualitative fourth strand of this thesis then the concerns of working women could have been explored and the results used to plan the recruitment to the quantitative strand three.

The questionnaire was not used with the patients in Jersey but the results of the questionnaire in London were used to assess the feasibility of recruiting women to the trial at the Jersey Site.

An attempt was made to research the social context of public attitudes to homeopathy in Jersey by contacting Jersey Citizens Advice Bureau and seeking the contact details for homeopaths registered on the island (https://cab.org.je/index.php?option=com_content&view=article&id=535:homeopathy-1033&catid=59&Itemid=56).

Two homeopaths were identified and contact and one of them, Dr Guy Wildy communicated via email regarding attitudes towards homeopathy in Jersey (Wilding, 2012):

Q1. How long have you worked as a doctor in Jersey?
A1: Twenty Eight Years

Q2. Have you seen changes in public perceptions and attitudes towards Complementary and Alternative Medicine (CAM) during that time?
A2: No change they have always been interested.

Q3. Have you heard of Homotoxicology?
A3: No

Q4. Have you helped with recruitment to any clinical trials in Jersey and if so what were your experiences?
A4: No.

Q5. In your experience how often do women seeking infertility treatment disclose their treatment to their employers?
A5: I do not know.

Q6. What is the prevailing public opinion towards clinical trials in Jersey?
A6: The prevailing public opinion is indifference.

Q7. What differences do you notice between patient populations in Jersey and the mainland UK regarding attitudes towards (i) CAM and (ii) clinical trial participation.
A7: I do not know what these trials are.

Q8. Do you have any insights into obstacles that might prevent patients enrolling in a clinical trial in Jersey?
A8: No obstacles unique to Jersey.

Discussion

The answers to the questions posed via email seem to indicate that there is no hostility towards homeopathy although it is acknowledged that Dr Wildy's experiences may be biased towards patients who seek him out because they are supporters of homeopathy. The answers generated in London were therefore assumed to be relevant to the situation that might be expected in Jersey. The major limitations of this questionnaire are the assumption that patients in Jersey and London will exhibit similar preferences for treatment and that the questions only explore practical aspects of implementing a trial of a homeopathic product and do not investigate the possible social and psychological obstacles to recruitment.

Researcher characteristics and reflexivity

As a researcher with a homeopathic background the researcher felt that her study might not be viewed as suitable for a clinic that uses assisted reproduction technology. The dualisms which separate conventional from complementary medicine might have made it very difficult to build a working relationship with the clinic staff. It was important to find out if they felt strongly about the use of homeopathy and if they had experience of their patients using it. A negative attitude from clinic staff would create a bias in the study if they were consciously or unconsciously discouraging their patients from taking part.

Sampling strategy

London was chosen for the site of this strand of the study as it was not possible to access the clinic in Jersey for regular meetings due to time and budget constraints. There was also an intention of expanding the study to include a London site if possible and this qualitative study was seen as a way of building a working relationship with the clinic.

The sampling for this strand was pragmatist, the Matron at the Bridge Centre invited the nursing staff to attend the group interview and those who were willing and available took part. The sampling for the patient questionnaires was a self-selected sample and therefore might be biased towards women who are interested in taking part in such a study.

There is no data available on how many women chose not to take a copy of the questionnaire and no distinction was made between women who were starting treatment or women who had already received treatment and all replies were anonymous. No data was collected on their age or which type of treatment they were undergoing.

Data processing

The data from the nurses' questionnaires were transcribed by the researcher into word documents and then organised into codes using MaxQDA.

The data from the nurses' interviews were transcribed as notes and used to supplement the creation of themes from the questionnaire data.

The data from the patient questionnaires were counted manually and recorded on a word document in table form.

Data analysis

Thematic analysis was used to analyse the nurses' responses into themes according to protocols established for that approach as before (Braun and Clarke, 2006a).

The nurse questionnaire was deliberately open-ended so as to investigate their individual attitudes and understandings about their role, about homoeopathy and about their patient's use of CAM. It was hoped that new or surprising responses would be captured in this way and that the data would be rich and qualitative.

The patient questionnaire was more structured and included mostly closed questions because it was important to obtain the answers to some very specific questions that made the trial feasible. The use of a pragmatist framework means that the trial design is based upon an understanding of what is going to work in practice as well as acknowledging that the problems to be solved need an empirical solution acceptable to the scientific audience of nurses and other medical staff.

Techniques to enhance trustworthiness

No other researchers were approached to analyse the data and so it is recognised that the interpretation is subjective and that the context is the researchers' own experience of meeting the nurses and working with infertile patients using homotoxicology.

The use of both group interviews and questionnaires with the nurses helps to make sure that the analysis is trustworthy and that themes found in the questionnaire are also reflected in the narrative of the meeting.

By today's definitions this approach was an example of 'participation' where people take part in a research study by completing a questionnaire or participating in a focus group as part of a research study. This does not meet the criteria for 'involvement', where members of the public are actively involved in research projects and in research organisations as joint grant holders or co-applicants on a research project. Involvement may include identifying research priorities, commenting and developing patient information leaflets or other research materials. (INVOLVE, 2015).

Methodology for Strand Three (2007 – 2012)

Title: A Pilot Study Of Ovarium Compositum In Infertile Women.

Introduction

The third strand, quantitative with an embedded qualitative aspect, was originally conceived as the main focus of the study and consisted of a RCT of the use of Ovarium Compositum as an adjunct treatment for infertile women in an assisted reproduction unit. The small sample size and experimental nature of the trial design led to this being designated as a pilot study. A copy of the protocol is included in the appendix (see Protocol No.: OVCT-001)

A Pilot study is sometimes confused with a feasibility study and recently efforts are being made to provide clearer definitions and guidelines for the reporting of preliminary studies (London, 2015)

An early report of the findings of the research group cited above states that the analysis of pilot studies should be mainly descriptive, outlining well-defined aims and objectives that highlight methodological rigor and scientific validity and most importantly, the lessons learned that could be useful in designing the main study (Dolgin, 2013)

A review of the literature (Whitehead et al., 2014) found that the distinguishing features of a pilot study from a feasibility study are as follows:

- Stricter study methodology (e.g., a justification of the sample size)
- An intention for further work
- Smaller version of the main study (e.g., use of a control group and randomisation)
- A focus on trial processes

Whitehead believes that researchers should not use the title ‘pilot’ for a trial, which evaluates a treatment effect. It was acknowledged by the trial

reviewers that the study was underpowered to demonstrate such an effect and that it's intention but it was to test the feasibility of randomisation, and the use of RCT to test a homeopathic intervention. On balance it would be best described as a pilot study because it included a randomised control group and feasibility studies do not include this.

Abstract Women who experience infertility may seek help using complementary and alternative medicine (CAM). There is a need for further research to provide an evidence base for the safety, efficacy and cost effectiveness of CAM. Ovarium compositum is a preparation of homeopathic ingredients purporting to treat female infertility. It is prescribed in the UK by registered Homotoxicologists and other clinicians. The aim of this pilot study is to evaluate the effectiveness of Ovarium compositum vs. placebo in a randomised trial of 90 women attending an infertility clinic for ovarian stimulation and assisted reproduction. The outcomes to be evaluated are both quantitative (response to ovulation drugs, length of time to pregnancy) and qualitative (quality of life).

The study sponsor: Clinical Pharmacology, Barts and The London, Queen Mary's School of Medicine and Dentistry, Charterhouse Square, London, EC1M 6BQ, UK, Tel: +44 (20) 7882 3404, Fax: +44 (20) 7882 3408

Funding: Heel GmbH

***Objectives*:** The primary objective is to assess whether the administration of Ovarium Compositum as an adjunct therapy can make a significant difference to fertility outcomes in infertile women seeking medical intervention. The second objective is to measure quality of life in women undergoing treatment for infertility and using Ovarium compositum.

Study Design: One centre, double blind placebo randomised controlled exploratory/pilot trial and two QoL questionnaires

METHODOLOGY

Study Location: Department of Obstetrics and Gynaecology, Jersey General Hospital, Gloucester Street, St Helier, Jersey, JE1 3QS, Telephone 01534 622 660

Study Period: 12 Months

Pharmaceutical Agents: Subjects will be randomised to Ovarium Compositum vs. Placebo. Both supplied as white tablets with identical appearance for composition see Table 19 Treatment Formulations Table for active drug and Table 20 Formulation of Placebo.

Route of Administration: Oral Tablet, one tablet three times a day to be dissolved in the mouth

***Duration of administration*:** Daily, on-going until positive pregnancy test or trial ends

Study Duration: Expected to take 12 months

***Sample Size*:** 45 active plus 45 placebo N=90

Non-participating women at clinic to be consented for access to data for comparison

Research Question

Is it possible to show that Ovarium compositum can improve the fertility outcomes of women undergoing infertility treatment at the Assisted Reproduction Unit of Jersey General Hospital?

Methods

A quantitative method using a randomised, double blind, placebo controlled trial design in order to measure the specific effect of Ovarium compostitum compared to a placebo. A comparison group composed of women who did not agree to take part in the trial (i.e. a usual care arm) was planned. If they would consent to have their data included in the trial it would also then be

possible to compare them to the outcomes in the placebo arm and generate a measure of the placebo effect.

One of the characteristics of Pragmatism is that it places high regard for the reality of and influence of the inner world of human experience in action (Johnson and Onwuegbuzie, 2004). This aspect can be captured using Quality of Life data (QoL) is also of interest and will be collected using a validated questionnaire the EQ-5D (Rabin and Charro, 2001) and an unvalidated questionnaire, that is specific to infertility, the Emotional Health in Infertility Questionnaire (EHIQ) (Farmer, 2007).

A full trial protocol is included in the appendix Protocol No.: OVCT-001and the two QoL tools are considered in more detail in Qualitative Data Collection in Strand Three, see Qualitative Data Collection in Strand Three.

Researcher characteristics and reflexivity

The researcher is not based in Jersey and is not medically qualified to treat infertility. She has experience of working with infertile women using homotoxicology and homeopathy as a CAM modality and has trained in clinical trial design. As a science graduate she is familiar with the medical concepts involved and the language used.

The researcher has adopted a Pragmatic worldview in which Pragmatism endorses a strong and practical empiricism as the path to determine what works. (Johnson and Onwuegbuzie, 2004). Therefore this strand of the trial design is intended to produce data that can be triangulated with the theory generated in the qualitative strands (one, two, and four).

As a practitioner in CAM she is familiar with the concept of placebo and the possible effects generated by an individualised consultation and prescription. The trial is designed to control for these effects by not including a consultation with the researcher.

Context

The site for the trial is the Assisted Reproductive Unit at Jersey General Hospital. Jersey is the largest of the Channel Islands and sits in the English Channel, closer to France than to England. It covers 45.5 square miles and has a population of 98,000 (Jersey, 2012). Jersey, Guernsey and the Isle of Man are part of the British Isles. England, Scotland and Wales make up Great Britain, while the United Kingdom includes Great Britain and Northern Island. Jersey is a British Crown Dependency. Jersey is self-governing and has its own financial and legal systems and its own court of law. Jersey was chosen as the site of the RCT trial because the researcher had supported the treatment of a patient whose treatment had initially been unsuccessful in producing a live birth. After homotoxicology treatment and a successful live birth the lead consultant at the clinic had expressed an interest in finding out more about homotoxicology and it's potential to help other patients.

Ethics

The researcher encountered a variety of difficulties in obtaining ethics approval due to Jersey's unique legal and constitutional position. Clarification of the necessary route of application took some 28 months. It was established that only local ethics approval is required for clinical trials taking place in the Channel Islands and that there is no need for MHRA approval in the form of Clinical Trials Authorisation (CTA) because Jersey falls outside the existing legal and regulatory framework (Haresnape, 2013a).

The initial inquiry to the Medicines and Healthcare products Regulatory Agency confirmed that:

'*UK clinical trial legislation does not apply in the Channel Islands. The Channel Islands and the Isle of Man are self-governing dependencies of the British Crown, that is, Her Majesty Queen Elizabeth II is their Head of State but they are not part of the UK. They are subject to European Unity Directives so far as trade is concerned but the inhabitants are not citizens of the EU…. For your clinical trial in sites in Jersey you will need local ethical approval and may require local regulatory approval but you do not require MHRA approval of a CTA*.' (Ward, 2008)

The response from Jersey General Hospital was positive but that they would prefer an opinion from an ethics committee in London first followed by a local application to Jersey. Their pharmacy department pointed out that it was more than 10 years since they undertook any clinical trials involving investigational medical products (IMPs) and that they had their own 'very out-dated' regulations under the Medicines (Jersey) Law 1995 and having an opinion from a mainland committee would give them additional confidence. (McCabe, 2009).

The National Research Ethics Service (NRES) Queries Line were then approached to provide guidance in this dilemma and their response was as follows:

'*Jersey is not part of the UK and the favourable opinion from the UK REC would not formally confer ethical approval for the study in Jersey. Nor would the REC undertake any site-specific assessment of the Jersey research site as this is outside its remit. It is entirely a matter for the island authorities to determine what process is required to include a site in Jersey.' (Line, 2009).*

The status of homoeopathic and homotoxicological medicines was also an issue at this point. On 18th March Professor Johnston, PhD supervisor, queried the position of homeopathic and homotoxicological remedies in the European Union (EU) Directive with the MHRA (Johnston, 2008). Dr Malcolm Barratt-Johnson, Medical Assessor at the Clinical Trials Unit and to the Licensing Division at the MHRA, confirmed that homoeopathic products lie within the scope of a clinical trials authorization (CTA) because they have the ability or potential to treat individuals. According to European Legislation (Article 1, paragraph 2 of Directive 65/65 EEC) a preparation constitutes medicinal product where*:*

'The substance or combination of substances either prevent or treat disease in human beings or are administered to human beings with a view to making a medical diagnosis or to restore, correct or modify physiological functions in humans.'.(EEC, 1965)

On the basis that this was an IMP an application was made to the Guy's Research Ethics Committee for the October 2009 meeting (application reference 09/H0804/93). A response was received confirming that: '*the study cannot be reviewed by an NHS REC, as it is a CTIMP happening outside of the UK. We are therefore unable to give a legally valid opinion on the application and it has been withdrawn with immediate effect.' (Hill, 2009).*

Professor Johnston queried this decision with the local research ethics committee (LREC) who in turn escalated it to one of the NRES regional managers for guidance. Maria Robinson, SRES Manager, South West gave the following response:

'*This is an interesting scenario, Although outside the UK and technically outside our remit for ethical review, this study being a CTIMP falls under the EU regs and therefore must be reviewed by a UKECA recognized REC and receive authorization form the MHRA. This being the case, we would need to review this project.' (Robinson, 2009)*

In December 2009 David Neal, Deputy Director (policy), National Research Ethics Service, was asked for his opinion. He agreed that this was an unprecedented situation and apologized that it had not been clarified sooner. His email of 10th December 2010 is shown below:

'*I explained that we had sought advice from the Department of Health about whether a mainland REC could review the trial on a voluntary basis. We have now been advised as a matter of policy that it should not do so.*

The background is as follows:

The European Clinical Trials Directive applies to the Crown Dependencies, which for purposes of European law are considered to be part of the UK Member State, although not part of the UK in domestic law. The States of Jersey were therefore required to transpose the Directive into States law by 1 May 2004; they have not so far done so. The Medicines for Human Use (Clinical Trials) Regulations 2004 do not apply to Jersey, and under present arrangements the United Kingdom Ethics Committee Authority is not able to recognise ethics committees to review trials taking place in Jersey, though

we understand that the Crown Dependencies have been offered the option of UKECA recognition for their ethics committees.
In these circumstances, it is not considered appropriate for a mainland REC to review and give an opinion or otherwise advises on a trial taking place solely in Jersey. Responsibility for the trial lies with the authorities in Jersey. If it were proposed to start the trial at a mainland site, an application could then be reviewed by a UKECA recognised REC and an opinion given in relation to that site.'(Neale, 2010)

This clarification of the situation allowed the project to proceed with a local application to Jersey in September 2009 (Johnston, 2009). Written confirmation that the committee were *'minded to grant a favourable ethical opinion subject to receipt of an amended patient information leaflet'* was received on 24th March 2010 in a personal email to the researcher (McCabe, March 2010).

Sampling strategy

Female patients were recruited via the infertility clinic consultant who was in charge of their conventional treatment. There were two categories of women that were of interest to this trial: firstly those that respond very poorly to standard ovulation induction agents and secondly those annovulatory women who are being given ovulation induction agents.

Women presenting at the clinic, because they had been referred by their GP for infertility treatment, were offered the opportunity to take part in the trial during their consultation and the lead clinician sent out a letter of invitation to those who expressed an interest (see appendix Figure 17 Letter of Invitation to Trial Participants).

Those women who fulfilled the selection criteria were consented and then allocated a protocol on a randomised basis. The clinician allocating them to a trial protocol was blinded to treatment but not to their age. Chronological age is an important predictor of outcome and so each treatment group was to

be stratified for chronological age. A copy of the consent form is included in the appendix as Figure 14 Consent forms for participants in pilot study. It was planned to consent women who did not wish to take part so that their data could be used as a comparison with the placebo group. Although the consent form was printed and supplied to the clinic (see Figure 15 Consent forms for non participants in pilot study) no women were consented in this way. A patient information sheet accompanied the consent form and this is also included in the appendix, see Figure 16 Patient Information Sheets for Pilot Study.

Previous use of homeopathic remedies was not considered to be an exclusion factor. However a washout period of one month would be necessary if they were taking any homeopathic remedies.

Data collection methods

Quantitative data collection was designed to take place during their clinic appointments and was captured by their consultant using a Case Report Form (CRF) see appendix Figure 18 Case report form for pilot study. The CRF had three carbon copies, one for the patient file, one for the trial master file and one for the researcher.

Data collection instruments and technologies

The clinic staff received some basic training on the CRF during a site visit but they were not involved in the design of the CRF and this has been identified as a limitation of the study. The consultant used a case report form (CRF) to manually capture the outcome data on:

1. Follicular count and Ovarium volume
2. Follicular stimulating hormone (FSH) levels
3. Estradiol (E2 or 17β-estradiol, also oestradiol) at day 2
4. Progesterone Levels at day 21
5. Pregnancy confirmed with a pregnancy test

6. Live birth

For an initial screening visit additional information was requested on the CRF that included:

1. A check on inclusion and exclusion criteria
2. Demographic data (age, height, weight, BMI)
3. Smoking and Alcohol consumption
4. Medication
5. Previous medical history
6. Physical Examination and vital signs (repeated on each visit)
7. Ovarian Function Investigations

Units of study

Inclusion Criteria

In order to be eligible to enter the study, volunteers must meet the following criteria:

1. Female
2. Age stratified in active and placebo groups (see Table).
3. Diagnosed with poor response to ovulation induction or annovulatory (WHO Group2)
4. Absence of other significant endocrine dysfunction including diabetes
5. Absence of other known causes of infertility

Exclusion Criteria

Taking medication for other medical conditions that may affect ovulation

1. Pregnancy
2. Tubal infertility or any other cause of infertility
3. Previous pregnancy
4. BMI <20kg/m2 and >35kg/m2
5. Concomitant use of other CAM therapies
6. Use of peppermint, caffeine, nicotine, recreational drugs or alcohol

	Treatment Given	Plus
Group one N=15	Clomid	Placebo
Group two N=15	Clomid	Ovarium Compositum
Group three N=15	FSH	Placebo
Group four N=15	FSH	Ovarium Compositum
Group five N =15	IVF	Placebo
Group six N=15	IVF	Ovarium Compositum

Table 17 Table to Show The Proposed Treatment Groups

Recruitment

Recruitment was started in November 2011 and stopped in July 2012, during that time 4 patients were enrolled and 4 more identified as appropriate and sent a recruitment invitation letter by the unit. Further details are discussed in the results section (Chapter 3 Results for Strands 1, 2 & 3).

When the difficulties regarding recruitment became apparent in Jersey the literature was searched for existing studies that might offer some insights. There are relatively few papers published regarding research conducted in the Channel Islands. A pubmed search using the MeSH terms "Channel Islands/epidemiology"[MeSH Terms] AND "humans"[MeSH Terms] returns 12 studies published between 2012 and 1992 .Table 43 Table to show a Pub Med Search for Published Studies in the Channel Islands

One of the authors, Dr Ellison, was contacted by email to investigate the possible obstacles to conducting a clinical trial in Jersey (Ellison, 201) as he had conducted an epidemiological study of the Jersey population. His opinion was that we should not encounter any particular problems in clinical trial recruitment and that it would be worth making contact with Professor Ian Fentiman who ran the Breast Cancer Study on the neighbouring Channel Island of Guernsey.

Professor Fentimen was able to offer the following insights:

Our work involved volunteers on Guernsey which does have a different health system from Jersey. There were 5 studies in all and I was involved with the 3rd study and its sequels. The study aim was to identify risk factors for breast cancer in a normal population. In the 3rd study 5104 women aged >35 years recruited between 1977 and 1985. We involved the surgeons who were part of the general practices at the time and paid a fee for each patient that the surgeons examined. We were involved in multiple articles in the Guernsey Evening Press and local radio and television. Additionally we

employed a local coordinator who was able to network widely and help with recruitment.(Fentimen, 2012)

Discussion

The suggestions made by Professor Fentimen were discussed with the clinic staff in Jersey but for various reasons they were not implemented as ways of supporting our own recruitment drive. One of the major limitations of this thesis was the lack of planning to support the recruitment drive and the difficulty of supporting a trial at site that is relatively difficult to visit on a regular basis.

Randomisation and Allocation

The patients were to be randomised, to treatment, using a randomisation sequence designed by Heel, in blocks of four. They were to be stratified according to chronological age and treatment group. The randomisation sequence was designed by Heel (manufacturer) who provided sealed envelopes for the codes they had generated. A template was provided for the generation of labels so that clinic staff in Jersey could label patient files. Copies of the label templates are included in the appendix Figure 19 Medication labels for pilot study

The consulting physician who randomised the patient to the next number in the appropriate age controlled allocation of the study drug and treatment group, the allocation code was passed to pharmacy that held the medication labelled with the allocation codes. The allocation codes are included in the appendix see Figure 20 Randomisation Codes for Pilot Study.

The sealed envelope was added to the patient's file of notes and a sticker was attached to the front of the file to identify them as a trial participant and included their allocation code. In the event of an adverse event the envelope could be opened and the code broken. Patients, researchers, doctors and pharmacy were all blinded as to the allocation of patients to the active drug or placebo.

Unit staff and site pharmacy recorded the randomisation of the allocation code on a word document provided by the investigator (see appendix Figure 20 Randomisation Codes for Pilot Study).

Medication	Clomid Vs. Placebo	Clomid Vs. Placebo	Clomid Vs. Placebo	FSH Vs. Placebo	FSH Vs. Placebo	FSH Vs. Placebo	IVF Vs. Placebo	IVF Vs. Placebo	IVF Vs. Placebo
Years of age on date of trial entry	<30	30-35	>35	<30	30-35	>35	<30	30-35	>35

Table 18 Table to show Age Stratification Bands

Study Procedures

Schedule of Visits.

Visit One:

- The Volunteers will report to the Study Centre at a pre-agreed time.
- The active agent will be randomly distributed and 100 tablets dispensed to the Subject by the responsible administering Clinician with full instructions on frequency and timing of dosages.
- Dose frequency and timing: one tablet dissolved in the mouth three times a day, at least 15 minutes before or after meals. Dose to be taken at 9am, 12 noon and 9pm.
- Subjects will at all times continue with their conventional infertility treatment as prescribed by the Consultant.

Visits 2 - 12

- On completion of this dose for 30 days Subjects are expected to attend an evaluation session and if they still fulfil the criteria of the trial the dose can be repeated.
- A further 100 tablets will be dispensed.
- Volunteers will be evaluated in this way every 30 days.
- Unused tablets to be returned to the Principal Investigator in a sealed bag, labelled with Subjects name and date of birth for counting.
- Subjects will be instructed to discontinue trial drug after an ART intervention and wait until a pregnancy test is performed.
- The maximum length of trial is 12 months.
- Patients will be discharged when the trial ends (12 months) or on a positive pregnancy test.

Parameters for evaluation

Demography, Medical History

Includes initials, date of birth, BMI, race, height and weight. A full medical and surgical history will also be evaluated including previous pregnancies or treatments for infertility, to be recorded on the Case Report Form (CRF).

EHIQ (Emotional Health in Infertility Questionnaire) and the EQ-5D

Subjects will be asked to complete a QoL questionnaire for infertile women The EHIQ and the validated questionnaire The EQ-5D, copies are included in the appendix as Figure 11 The Oxford Fertility Questionnaire EHIQ and Figure 13 The EQ-5D.

Vital Signs

Vital signs, including body temperature, sitting radial pulse and blood pressure will be performed at the screening visit.

Clinical Tests Associated With The Trial and Fertility Treatment

Baseline ultrasound scans every month to assess ovarian follicles, monthly blood tests including FSH, E2 at day 2 and Progesterone level at day 21.

Adverse Events

Subjects will be monitored for adverse events throughout the study. Adverse events may be spontaneously reported by the subject, observed by the study personnel or elicited by the study personnel, who should ask subjects the following non-leading question: 'How do you feel?' or 'How have you been feeling since I last asked you?' The same questions will be used throughout the study.

There is a form for reporting SAE included in the CRF see Figure 18 Case report form for pilot study

Serious Adverse Events will be reported to the Sponsor, the COREC recognised Research Ethics Committee and the MHRA. If a Grade 3 r 4 toxicity (based on the Common Toxicity Criteria (CTCv3.0)) or other serious adverse events occurs, no further dosing of the subjects will occur until the cause of the event and its relationship to the study drug has been clarified. Continuation of the trial will be contingent upon approval by the Sponsor. There is a database for ADRs at Heel's Safety Department (only one ADR listed for Ovarium Compositum).

Qualitative Data Collection in Strand Three

Qualitative data were captured on two questionnaires that the patients were asked to complete at each appointment and return to the clinician on their next visit.

Infertility is known to cause emotional distress (Finamore et al., 2007) and the hormonal treatment regimes can also be difficult for women to manage, therefor it is important to include a measurement of their quality of life.

Infertility and subsequent treatment are acknowledged to have potentially detrimental effects on emotional health. Qualitative studies suggest that infertility can be a devastating experience, especially for women, but empirical findings have tended to be less conclusive. (Weil et al., 2007)

Including a QoL measurement broadens the outcomes to include a consideration of the impact of the condition and it's treatment on the person's emotional, physical and social functioning and life style.

It addresses the question of whether the treatment leads to a life worth living, and it provides a subjective, patient-led baseline against which the effects of interventions can be evaluated (Bowling, 2011).

In order to measure changes the tool chosen must be valid for the purpose, reliable, precise, responsive to change and sensitive enough to capture changes (Bowling, 2011). Disease specific tools will have a narrower focus and can pick up small but clinically relevant changes. In order to capture a broad picture of health status, and a narrower focus on the specific impact of infertility and its treatment, two different questionnaires were chosen for this study.

The two forms that were used were the EQ-5D (Mark Oppe, 2007) and the EHIQ (Farmer, 2007). A description of the two tools and the reasons for choosing them are discussed in more here.

The EQ-5D

A copy of the EQ-5D is included in the appendix see Figure 13 The EQ-5DThe EQ-5D was chosen because it is relatively simple to print and complete and provides a standardized measure of health status appraisal. It is applicable to a wide range of health conditions and treatments, it provides a simple descriptive profile and a single index value for health status that can be used in the clinical and economic evaluation of health care as well as in population health surveys*. (Mark Oppe, 2007)*

One advantage of using the EQ-5D is that it is designed for self-completion by respondents and the instructions needed to complete it are included in the questionnaires, it was therefore suitable for trial subjects to take away with them as the clinician did not have time to complete the survey with the patients.

It is designed to measure current health on five domains mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension has 3 levels: no problems, some problems, severe problems. This decision results in a 1-digit number expressing the level selected for that dimension. The digits for 5 dimensions can be combined in a 5-digit number describing the respondent's health state *(Mark Oppe, 2007).*

Some disadvantages have been reported by researchers such as a lack of sensitivity at the ceiling level, being insensitive to health changes that are important to patients, and some inconsistencies in the wording which may increase response error (Bowling, 2011). However the EQ-5D has been found to be superior to the other preference-based measures of health related quality of life (Brazier et al., 1999) and the possible lack of sensitivity is addressed in this study by using a second infertility-specific questionnaire.

The EHIQ

A copy of the EHIQ is included in the appendix see Figure 11 The Oxford Fertility Questionnaire EHIQ. The Emotional Health In Infertility Questionnaire was a designed by a nurse researcher, Gail Farmer (Farmer, 2007), as part of her Masters Degree and was reported in 2007 as oral presentation at the ESHRE Lyon conference (Weil et al., 2007).

The existing generic instruments tend to focus on psychological states and psychopathy rather than the emotional strain associated with infertility in otherwise healthy individuals. The EHIQ was created in response to a perceived need for the construction and validation of a new infertility-specific measure of emotional health.

It was designed following a process of qualitative research and statistical validation. Twenty-three, largely unstructured interviews were undertaken with males and females separately at different stages of infertility investigation and treatment. Qualitative analysis revealed three major themes: the effects on self, on relationships and on life plans. This analysis, combined with a literature review, formed the basis of the 64 items that made up the developmental version of the questionnaire.

The questionnaire was then piloted with a large sample (n = 204 women and n = 187 of their male partners) undergoing treatment for infertility at the Oxford Fertility Unit, with response rates for those who received questionnaires of 79% and 70% respectively.

A 40 item version of the questionnaire was developed in which nine domains accounting for 65% of the variance were identified: personal strain; partner relationship strain; sexuality; social support; confidence in treatment; guilt and blame; financial strain; need for privacy and couple concordance.

The EHIQ was chosen for this thesis because it has been rigorously developed to quantify emotional health in infertility, measuring emotional strain in healthy individuals, rather than psychopathology. It has the potential to be a useful tool in studying issues such as the emotional effects of infertility, the effectiveness of interventions to reduce emotional distress in this population and the influence of emotional health on treatment perseverance and treatment outcome.

The Study Drug in Strand 3

Ovarium Compositum

Ovarium compositum is manufactured in Germany according to Good Manufacturing Standards (Certificate included in appendix see Figure 12 Certificate of Good Manufacturing Standards for Ovarium compositum). Ovarium compositum is on the market in 20 different countries with an import licence, a registration or with a marketing authorization (Russia, Poland, Latvia). Figures of sales show approximately 700.000 - 900.000 Ampoules per year (2008).

Labelling for the trial medication (both placebo and active drug) was designed and supplied by Heel with the randomisation codes included and these are shown in the appendix see Figure 19 Medication labels for pilot study.

Clinical indications are listed (Heel, 1986) as : *"Stimulation of the glandular and defensive functions, as well as those of the connective tissue, in dysmenorrhoea, endometritis, metritis, parametritis, enuresis (in young girls), in the climacteric, hyperemesis, insufficiency of the anterior lobe of the pituitary gland in females, craurosis vulvae, mastodynia, osteomalacia, menorrhagia, as well as in various disturbances of metabolism, including those arising in geriatrics."*

Due to its individual homeopathic constituents, see Table 19 Treatment Formulations Table for active drug, Ovarian Compositum has an application in the homeopathic treatment of hormonal disturbances, menopausal syndromes and Insufficiency of the pituitary gland.

METHODOLOGY

The preparation is formulated as follows:

Name	Potency	Amount (mg)
Ovarium suis	D8	1
Placenta suis	D10	1
Uterus suis	D10	1
Salpinx suis	D10	1
Cypripedium	D6	1
Lilium tigrinum	D4	1
Pulsatilla	D18	1
Aquilegia vulgaris	D4	1
Sepia	D10	1
Lachesis	D10	1
Apisnum	D8	1
Kreosotum	D8	1
Bovista	D6	1

Name	Potency	Amount (mg)
Ipecacuanha	D6	1
Mercurius solubilis Hahnemanni	D10	1
Hydrastis	D4	1
Acidum cis-aconiticum	D10	1
Magnesium phosphoricum	D10	1
Carrier		
Lactose-Monohydrat		297
Magnesium stearate		1.5mg

Table 19 Treatment Formulations Table for active drug

Table 20 Formulation of Placebo

Carrier		
Lactose-Monohydrat		297
Magnesium stearate		1.5mg

Homeopathic Medicinal Products

Modern definitions of homeopathic remedies tend to focus on what remedies are rather than how they are used (Kayne, 2006). The definition given in both the EU Directive for Medicinal Products (1992) and UK Statutory Instrument (SI 1995/308) is as follows (Kayne, 2006):

Homeopathic medicinal product means a medicinal product (which may contain a number of principles) prepared from products, substances or compositions called homeopathic stocks in accordance with a homeopathic manufacturing procedure described by the European Pharmacopoeia or, in the absence thereof, by any pharmacopoeia used officially in an (EU) member state.

The UK Medicines and Healthcare Products Regulation Authority (MHRA) and other European regulatory bodies use the term *stocks* for the starting solutions, usually mother tinctures, from which homeopathic potencies are prepared.

In 1988 The German Health Ministry took the initiative to establish standards for the manufacture of homeopathic medicines and this led to the production of a European Pharmacopoeia in 2002.

About 65% of all remedies are prepared from extracts of plant materials, and because of this homeopathy is often confused with herbalism by many people. The difference lies in the manner of producing the two types of medicine. Herbal products are generally the result of an aqueous or alcoholic extraction alone, whereas in homoeopathy an additional dilution process is involved. Either the whole plant may be used or only the leaves, stems, flowers or roots as specified in the pharmacopoeia monographs. The species of plants, the parts taken, the time of collection and the extraction

procedures may well differ according to the particular pharmacopoeia being consulted (Kayne, 2006).

Animal and insect material must be obtained from healthy specimens. Biological materials from healthy animal or vegetable secretions or from bacterial cultures are made into remedies known as sarcodes. If the remedy is derived from diseased tissue then the finished remedy is known as a nosode.

‘Suis organ preparations (sarcodes) are homeopathic attenuations of wholesome organs or tissues obtained from healthy animals, in this case pigs.’ (Heel)

Suis organs are said to act like ‘organ specific nosodes’ to create a stimulative treatment where damage has occurred to the organs and tissues in question. These medications are claimed to be ‘particularly successful in treatment of degenerative damage as well as functional insufficiency of the organs.’(Heel, 1986) The Suis organ preparations are said to ‘guide’ other active homeopathic substances in their presence to the corresponding targeted organ, thereby intensifying their efficacy.

Preparation of remedies

Extraction

Mother tinctures are the liquid preparations resulting from the extraction of suitable source material with alcohol/water mixtures, which form the starting point for the production of most homeopathic remedies. Comminution followed by standard percolation, maceration and squeezing techniques are used on fresh plants and succulents while dried specimens are subjected to percolation with alcohol.(Kayne, 2006)

The resulting solutions are strained and can contain one part drug to three parts mother tincture, when the final tincture represents one tenth of the concentration of the original drug it is in effect a 1x dilution (Kayne, 2006).

With insoluble chemicals such as Aurum (gold), Plumbum (lead) or Sulphur the solid material must be triturated and serially diluted with lactose powder using a pestle and mortar in a precise and documented manner (Kayne, 2006).

Potentization

Most mother tinctures are subjected to a two stage process involving dilution and succession (Kayne, 2006), this process is known as potentization. The Hahnemannian method offers two scales of dilution, centesimal and decimal (Kayne, 2006). The remedies that make up Ovarium Compositum are in the decimal scales of dilution. In modern pharmaceutical practice it is common to use a triple distilled alcohol and water system, the strength of which varies from 20 – 60%, in the preparation of homeopathic dilutions (Kayne, 2006). The solution resulting from a mixture of the two liquids is subjected to the vigorous shaking with impact known as succession.

After the initial processes, successive serial dilutions follow, using fresh glass vials at each stage, until the solution reaches 6x for example. The process involves adding one drop to nine drops of diluent. A number designates the potencies with the letter 'x' following it. Thus 6x represents a 1 in 10 dilution carried out serially six times, each with a burst of succession.

In large-scale manufacture homeopathic granules are medicated and then compressed to form the tablets in a process similar to allopathic manufacture.

Dilution	Concentration	Decimal Potency
1:10	10^{-1}	1x or D1
1:100	10^{-2}	2x or D2
1:1 000	10^{-3}	3x or D3
1:10 000	10^{-4}	4x or D4
1:100 000	10^{-5}	5x or D5
1:1 000 000	10^{-6}	6x or D6
$1:10^{30}$	10^{-30}	30x or D30

Table 21 Decimal potencies (Kayne, 2006)

Homeopathic Indications for the Individual Constituents of Ovarium Compositum

For a full description of each ingredient please refer to the appendix (APPENDIX 6 The Study Drug) a summary is included below as Table 22 The ingredients of Ovarium compositum

Table 22 The ingredients of Ovarium compositum

Ingredient	**Examples of Homeopathic Indications (Heel, 1997)**
Ovarium suis (ovary) D8	Disturbances of the ovarian function.
Placenta suis (placenta) D10	Dysmenorrhea and peripheral circulatory disturbances.
Uterus suis (uterus) D10	Dysmenorrhea.
Salpinx suis (fallopian tube) D10	Dysmenorrhea and sterility through inflammatory diseases of the salpinx uteri.
Cypripedium calceolus var. pubescens D6	Conditions of nervous irritation, insomnia with restlessness and twitching of the body.
Lilium tigrinum D4	Uterus descensus, dysmenorrhea, nervous cardiac disturbances with anxiety, fluor albus. Menses early, scanty, dark, clotted, offensive; flow only when moving about…Pain in ovaries.
Pulsatilla pratensis D18	Migrating disorders (worse before menses), delayed menses, dysmenorrhea, remedy for affectations of the mucosa, venous stasis. Amenorrhea, irregular menses.
Aquilegia vulgaris (columbine) D4	Disturbances of the menses, climacteric disorders
Sepia officinalis (cuttlefish) D10	Climacteric disorders, nervous exhaustion, depression, chronic inflammation of the uterus and adnexa. Tendency to abortion from 5th to 7th month, sterility, dull heavy pains in ovaries, prolapse, pelvic

	organs relaxed with bearing down sensation, menses too late, too scanty or early and profuse.
Lachesis mutus (bushmaster) D10	Climacteric disorders (hot flushes), dysmenorrhea, left ovary very painful and swollen, ovarian tumors, menses irregular.
Apisinum (bee venom) D8	Oedema, ovarian cysts, dysmenorrhea, ovarialgia, metrorrhagia. Severe ovarian pains, Amenorrhea of puberty, abortion (miscarriage) during early months, pain and enlargement in right ovary during menses. Uterine hemorrhage during pregnancy.
Kreosotum (beech tar creosote) D8	Catarrh of the mucosa with acrid secretions, e.g. fluor albus, pruritus vulvae, menorrhagia (excessive bleeding at the regular period), metrorrhagia (bleeding from the womb otherwise than at the proper period. It is usually due to a uterine lesion). Hyperemesis (vomiting in pregnancy).
Bovista D6	Menorrhagia, dysmenorrhea, venous hemorrhages, swelling of the ovaries, depressed before menses, chronic ovaritis.
Ipecacuanha D6	Uterine haemorrhages, in gushes. Hyperemesis, menses too early and too profuse, cutting pain in uterus from left to right, prolapse of uterus worse during menses, threatened abortion (miscarriage).
Mercurius solubilis Hahnemanni D10	Suppuration, acute and chronic inflammation of the lymphatic system, chronic affections of the connective tissue.
Hydrastis canadensis D4	Remedy for affections of the mucosa; thick ropy, yellowish white secretions, menorrhagia, viscid, metrorrhagia, myomatous hemorrhages.
Acidum cis-aconiticum D10	Active factor of the citric acid cycle and of redox systems.
Magnesium phosphoricum D10	Anti spasmodic remedy, Dysmenorrhea, tendency towards cramps, neuralgia.

Safety & Tolerability

Global evaluation of toxicity

The manufacturer (Heel) commissioned an expert report on Ovarium Compositum, this report (see Figure 10 The Expert Report on Ovarium Compositum) which concluded that '*The current scientific fundamentals and the clinical experiences did not reveal serious signs to suspect the containing amount of all homeopathic dilutions for causing toxicological risks.*'

The following statements are quoted from the report, which is shown in full in the appendix as Figure 10 The Expert Report on Ovarium Compositum:

Reproductive Function

Results from direct studies of reproductive or teratogenic toxicity as well as fetotoxic side effects influencing fertility are not available. Researching the literature produced no hint for such risks

Embryo-Foetal and Peri-Postnatal Toxicity

Results from direct studies of embryo toxic/ fetotoxic or peril-, postnatal toxicity are not available. Researching the literature produced no suggestion of such risks.

Mutagenic Potential

Results from direct studies of mutagenic toxicity are not available. Researching the literature produced no hint for such risks.

Carcinogenic Potential

Results from direct studies of carcinogenicity are not available. Researching the literature produced no hint for such risks.

Immunotoxicity

No indications show that the effects of single components of Ovarium Compositum injection are sensitising or will provoke allergic reactions by the parenteral application. Possible risks or adverse drug reactions of parts or components of the plants have not been observed regarding the pharmacovigilance of the compounds of Ovarium Compositum or similar composed drugs.

Interactions

There are no hints that the effects of single components of the incorporated homeopathic dilutions and substances may be enhanced or inhibited by incorporated drugs or substances which interfere with their characteristic pharmacodynamic or toxicological effects. Potential risks or interactive effects associated with the combined administration of the incorporated homeopathic dilutions have not been substantiated in drug surveillance studies and pharmacovigilance on the use of the incorporated drugs in human.

Pharmacovigilance

Observing pharmacovigilance data, which have been determined by a dispensing of a formula with the same composition, can also show the drug safety of Ovarium Compositum tablet. The components showed identical finishing dilutions. Consequently the dispensing carried the same risk potential.

Within the framework of the supervision of drug safety no adverse event was reported since 1998 (745.510 ampoules delivered only in Germany), globally seen. This result is striking for the good safety profile of Ovarium Compositum. This result of the pharmacovigilance points out that adverse drug reactions after parenteral application of the homeopathic dilution in Ovarium Compositum tablet are a rarity and that this preparation cannot be related to an increased risk especially concerning the gastro-intestinal, cardiovascular or central-neurogenic body organ system or the skin.

Conclusions

The scientific findings material and the clinical experiences do not reveal any indications concerning toxicological risks caused by components of the homeopathic drug Ovarium Compositum if the speciality is applied according to a recommended dosage of the manufacturer. Components of an immunotoxicological potential are included with a very small concentration. Consequently, a corresponding risk during treatment does not need to be taken into account.

Discussion

The Investigators were targeted to enrol up to ninety (90) female volunteers who met the trial inclusion criteria and they were to be randomised into six treatment groups. The usual blood tests and clinical evaluations were to be made by the fertility clinic. In order to measure the placebo effect as well as the specific effects of Ovarium compositum women who are not taking part in the trial were to be asked to consent to allow their data to be used as a comparison group. In order to make sure there is no placebo effect from a consultation with a prescribing homotoxicologist the trial design did not include such a consultation for any of the trial groups.

The trial protocol was reviewed internally by WHRI Table 42 WHRI internal review of trial from strand 3 and externally by Dr Alexander Tournier, who found that, as there were no know toxicology issues, the choice of medication was suitable for the condition under investigation Table 41 External peer review of the protocol for strand 3. Both reviews noted the small sample size that was not sufficiently powered for statistical analysis but accepted the fact that this was a pilot study designed to test for feasibility of study design.

Details of the protocol were sent to Neil MacLachlan at Jersey General Hospital in order to ask for his feedback and input. The Protocol was also reviewed by Heel in 200 and Dr Robbert Van Haselen (Haselen, 2007) emailed me in September 2007 to say that Heel had had internal discussions and that they like the protocol and were happy in principle to support the

study. He made some useful suggestions about trial structure and duration and also acknowledged that this was primarily a hypothesis generating-pilot trial and therefore it was acceptable to have a variety of outcome measurements.

The emotional strain of infertility treatment may affect the decision to continue or discontinue treatment (Brandes et al., 2009). If homeopathy could be shown to reduce the strain associated with treatment and retain women for more cycles of IVF then this would be a desirable outcome for the clinic. Quality of life measurements both specific and general therefore formed a part of this phase of the study.

Pragmatism recognises the existence and importance of the natural or physical world as well as the emergent social and psychological world that includes language, culture, human institutions, and subjective thoughts (Johnson and Onwuegbuzie, 2004), by combining a randomised controlled trial with quality of life data both perspectives are acknowledged and the results triangulated so that they may be mutually corroborated.

Methodology for Strand Four (2012 -2015)

Title An Investigation Into The Work-Related Concerns Faced By Women Seeking Infertility Treatment In The British Isles

Introduction

This was a qualitative investigation into the work-related concerns faced by women seeking infertility treatment in the British Isles.

Objectives- The purpose of this study was to further investigate the reasons for recruitment failure that were suggested by the nursing staff at the trial site.

Background – The failure to recruit sufficient women to the planned clinical trial was investigated using a qualitative analysis of online infertility forum postings.

Context

The time constraints of the PhD study meant that there was not time to obtain ethical approval for further investigations at Jersey General Hospital and it was also apparent that unit staff would not welcome further involvement in the study. As a solution to this dilemma it was decided to use the information available on Internet forums for infertility treatment seekers.

Method – Stage 1: A semi-structured questionnaire was posted on the research section of two popular infertility Internet forums inviting participants to respond (see Figure 5 Details of posting on forum). The responses were organised using MaxQDA and then analysed using a deductive thematic analysis to use to construct initial codes. Quotations were extracted, aggregated and anonymised to illustrate and support each theme; the data segments are included in the appendix (APPENDIX 11 Qualitative Data From Strand 4)

Stage 2: The second stage of analysis was to use naturalistic data in the form of the online postings of 213 forum users from the ‘My Story’ section of

one of the forums. This data was examined on a line-by-line basis (theoretical thematic analysis) for the codes that were generated in stage 1. The data is included in the appendix (APPENDIX 11 Qualitative Data From Strand 4).

Researcher characteristics and reflexivity

The reading of the online stories was emotionally disturbing as so many of them expressed feelings of grief and loss. The researcher was able to reflect on these during one to one mentoring sessions with Dr Sue Davies who had been a mentor for a number of years. This avoided an unnecessary bias towards the themes of emotional distress and helped to develop an understanding of the participants' perspective. The researcher also kept a research diary in which to record her responses to the data, and record the process of conducting this strand.

Sampling strategy

Stage 1: The initial postings were open for anyone to reply to, male and female responses were equally welcome and it did not matter if their treatment was current or historical. The only inclusion criterion was that they were or had been undergoing infertility treatment.

Stage 2: The principal use of the 'My Story' (MS) section of the forum is to record the experiences of women during their infertility treatment and the sample is a good indication of the range of concerns that they have. At the time of posting no specific forums for Jersey so the answers received are not specific to Jersey but come from a larger sample of Internet users from the British Isles

Ethical issues pertaining to human subjects

The issue of using Internet forums as a form of data source also raises methodological and ethical questions, which are examined in more detail here.

Stage 1: After seeking permission from site administrators a semi structured research question was posted on the research section of two popular infertility forum websites.

Stage 2: The second stage of analysis was to use naturalistic data in the form of the online postings of 213 forum users from the 'My Story' section of one of the forums. Permission was obtained from the site administrators before data was used.

This data could be viewed as existing in the public domain and yet it to some extent 'belongs' to the person posting it, a person who may not even be identifiable in order to seek informed consent.

The author also sought the opinion of the forum administrators, and her supervisors who had experience in this field. The consensus of their opinion was that the posts were public and could be used without permission as long as individuals who were posted were not approached outside of the forum (Johnston, 2013).

Data collection methods

Stage 1: a semi structured research question was posted on the research section of two popular infertility forum websites and participants were invited to respond by email.

Stage 2: A manual search of the My Story Section of the Infertility Network UK forum. 250 individual stories posted in the 'MS' section of the forum of INUK (Forum) were examined and 213 stories were found to be of use, the other 37 were found to be missing or duplicated and were not included in the analysis.

Data collection instruments and technologies

The Internet was searched using an Apple Mac PC and MacBook Air. The two sites used were selected on the basis that a Google Search would locate

the most commonly used sites. The sites were selected by typing in 'Infertility forum UK' and this resulted in the choice of Fertility Friends and Infertility Network UK. Both site were contacted by email to request permission to post a thread on the 'Research Questions' section of the forum. When approval was received the following posts were made:

Details of postings

Figure 5 Details of posting on forum

Fertility Friends (Friends, 2012)

Hi, I am interested in finding out about couples or individuals who have chosen or felt forced to reveal their fertility status and treatment at work. How much legitimacy is granted to your condition and have you had to choose between being open and privacy? Are you worried about risking loss of promotion? Where does your experience fall on the continuum between acceptance and ostracism? You can email me on c.harenape@qmul.ac.uk Thanks and best wishes.

Infertility Network UK. (UK)

I am currently writing up my PhD research project looking at supporting infertility treatment using CAM therapies. The pilot study I was running in Jersey had trouble recruiting enough women to take part and the reason given was the stress of telling employers about treatment and needing time off to attend appointments. I would like to collect more data on this topic and therefore would like to hear the experiences and stories of women who have or have not disclosed their treatment at work.

Units of study

Stage 1: Seven forum users emailed a direct response with information about their personal experiences.

Stage 2: 213 postings from the My Story section of the Infertility UK forum.

Data processing

Stage 1: responses, which were received as emails were transcribed into a word document and organised using MaxQDA. Then the coded sections or quotes were printed out and cut into slips so that they could be manually sorted into themes.

Stage 2: data was extracted from the forum posting using a cut and paste into a word document and then organised using Max QDA.

Data analysis

Stage 1: The seven responses were read through several times in order to familiarise the researcher with their content. Notes were made of patterns and meanings that could lead to codes. The initial codes reflected ideas that seemed to be important to the respondents. Using MaxQDA allowed the data to be coded in a way that it can be retrieved and manipulated to explore different themes

The initial quotes, once coded, were printed out and cut into slips so that they could be manually sorted into meaningful groups. The researcher worked from a constructionist perspective seeking to understand the socio-cultural contexts and structural conditions that generate the observed themes. Eight themes were constructed and these are discussed in the results section (

Chapter 4 Results).

Stage 2: The second stage of analysis was to use naturalistic data in the form of the online postings of 213 forum users from the ‘My Story’ section of one of the forums.

After familiarisation with the data by repeated reading of the postings the data was examined on a line by line basis (deductive thematic analysis) for the codes that were generated in stage 1 (Braun and Clarke, 2006a). This theoretical or ‘top-down’ approach to coding was driven by the researchers theoretical interest in the themes that were generated in the smaller sample.

The rules used to guide the coding were that each code can only be used once in each paragraph and that only the initial posting on the forum was used not any posts added or comments made at a later date.

The frequency and proximity of codes and keywords were examined (using MaxQDA) as part of the development of the themes. This increasingly used ‘concordance’ approach was suggested by Carol Rivas and has been used by (Seale et al., 2006) to analyse qualitative interview data and forum postings of men and women with cancer. The analysis did yield some useful insights but in the end was supplementary to the development of the themes and the model that was generated.

Stage 3: Writing up the themes was an integral part of the analysis and there was an iterative process of reading and writing as patterns of meaning and areas of interest were studied. The early engagement with the literature had suggested ‘emotional distress’ as a theme but some reading was left until later to avoid narrowing the researchers field of view.

A mind map of themes was generated (Figure 21 Mind map from early coding memo) and this model was discussed with two other researchers who helped to refine the themes by contributing their own perspective, for

example Dr Carol Rivas suggested the idea that a crisis of identity lay at the heart of the themes around disclosure.

The smaller sample (stage 1) was analysed again by comparing it with the Charmaz model of ‘’Forms of Telling” and the results of this analysis used to generate the ‘Relative Risk vs. Benefit’ model see Figure 7 Thematic Map.

This model was shared with forum users via the Research Section of the Infertility Network UK forum for their feedback but no responses were received.

Techniques to enhance trustworthiness

The coding and themes were checked with two other researchers (CR and NP) and a bias towards the negative experiences of working and undergoing treatment in my forum postings was noted and discussed. The bias was kept in mind when performing the analysis so that it did not unconsciously affect the coding of data. The data set was reread after the themes had been decided upon to check that the data worked in relation to the themes. If there had been more time to code the 213 stories in a ‘bottom-up’ inductive analysis then new themes might also have emerged but nothing occurred on the rereading that challenged the validity of the suggested model. The model generated by this researcher was shared with another researcher who was working on a similar project at the same time (Payne, 2014) and this process of triangulation appeared to confirm the credibility of the themes.

Conclusions Regarding The Methodology

Many lessons were learned during the evolution of this study and on several conceptual levels. The deeper understanding of the underlying philosophical framework grew from an analysis of the mixed methods research approach to the methodology. There were however several points that were specific to the methodology and these are listed below. Attention to these points will allow any future projects to yield interesting, credible and authentic results.

METHODOLOGY

The main lessons regarding the methodology from Strand One were:

1. That the two versions of the questionnaires for the practitioners should have been analysed separately. The earlier version could have been treated as a pilot in order to refine the questions. The reason for the change of questionnaire was the change in potential study sponsor and therefore remedy choice but they should not have been combined in the analysis stage.

2. The initial analysis claimed to use Grounded Theory but this misunderstanding of the depth of analysis needed to meet that claim was corrected after the first viva. During rewriting it was realised that what I had actually used was thematic analysis and a section on this method was added to the literature review.

3. The methodology chosen was appropriate to answer the research questions but it was not systematic enough in the way it was applied to the situation.

The main lessons regarding the methodology in strand 2 were:

1. Results generated at a clinic in London are not necessarily applicable to a clinic in Jersey. It is always important to take the social and cultural context into account, the methodology should have been changed to sample the population of infertile women seeking treatment in Jersey and I might have done this through my existing private patient network.

2. Patient questionnaires that are returned on a voluntary basis are susceptible to bias as only those patients interested are likely to take part and return them.

3. The methodology did generate some useful results and greater attention could have been paid to these when designing the methodology for Strand 3.

METHODOLOGY

The main lessons regarding the methodology in Strand 3 were:

1. It would have been helpful, prior to study design, to carry out research regarding the social and legal implications of choosing Jersey as the study site. A lot of time was spent trying to establish the requirement for mainland ethics and this delayed the time available for recruitment before the study drug expired.

2. Greater participation from the study site unit staff in the design of the Case Report Form would have resulted in a methodology that was easier to implement and therefore more ownership, goodwill, and support for recruitment.

3. The trial design was appropriate for the research question and had the necessary level of model validity for investigating a homeopathic substance.

The main lessons regarding the methodology in Strand 4 were:

1. From the new perspective of a pragmatist worldview this strand could have been carried out as strand one and informed the design of the rest of the study. This would still have been a mixed methods study but greater priority could have been given to the role of qualitative data, sourced from the patient forums, in an early exploratory phase of the study.

2. The initial methods (ranking of responses and keyword frequency) used to analyse the qualitative patient data were not appropriate to answer the research question. The rewritten thesis used thematic analysis to explore the attitudes of women towards disclosing their treatment and this led to useful insights that could have been used to plan the methodology in Strand 3.

3. The questions posted on the forum had a bias towards the difficulties experienced by women and it is recognised that biased questions can lead to results that are less credible and therefore less useful in trial design.

4. The small sample size of the direct responses to the question posted on the forum (n=7), is acknowledged as a limitation, but the close attention to theory, adherence to the guidelines for good thematic analysis and cross referencing with other researchers/sources of data helps to improve the credibility of the conclusions drawn using this method.

RESULTS

Chapter 3 Results for Strands 1, 2 & 3

Introduction

The purpose of this section is to present the main findings from each of the four strands of the study and to expand upon the synthesis of findings into themes where appropriate. The findings from strand four are further developed into a model of risk and benefit of disclosure.

The four distinct strands that can be identified in this mixed methods research design are:
qual ➔ qual ➔QUAN(qual) ➔QUAL

The first qualitative strand was the review of homotoxicology treatment for infertility in the UK and the aim was to check the model validity of the quantitative strand. A questionnaire was sent to 60 homotoxicologists and the return rate was 33%. Thematic Analysis (TA) was used to analyse the responses.

The second qualitative strand was a feasibility study with patients and staff at The Bridge Centre, a private infertility clinic in London. Potential obstacles to success were discussed with the discussion group who then completed a survey of nine open questions. Their responses were analysed thematically create a qualitative evaluation of the data and their concerns and insights used to generate a patient questionnaire. 127 patient questionnaires were distributed at the registration desk over a 9-month period.

The third strand was a quantitative design with an embedded qualitative aspect. The quantitative element was a RCT of the use of Ovarium Compositum as an adjunct treatment for infertile women in an assisted reproduction unit.

The fourth strand was a qualitative investigation into the work-related concerns faced by women seeking infertility treatment in the British Isles to investigate themes suggested by the staff at the site of the RCT phase. Data from forum users were analysed thematically (Braun and Clarke, 2006a) and used to create of model of risk and benefits around disclosure of treatment in the work place.

Results from Strand one

The Results Of The Practitioner Questionnaire

Units of study

60 copies in total were distributed and 20 replies were received (33%).
Of the two versions sent out the break down was as follows:
Version One: Replies received 13
Version Two: Replies received 7

Negative responses (not qualified or have chosen not to complete questionnaire) received from 4 practitioners. One participant was excluded as she worked for the manufacturer of one of the products being considered for trial. The results therefore included the responses from 16 participants.

The returning therapists are characterised in the table below:

Question one asked the respondents to choose one or more options for the treatment of female infertility

Table 23 Practitioner response to question 1

	1:V1	**1: V2**	**2: V1 & V 2**	**3: V1**	**4: V1**	**3: V2**	**5:V1 and 4: V2**	**n**
Practitioner								
1	Ticked	-	-	-	-			**1**
2	Ticked	-	-	-	Ticked		Ticked	**3**
3	Ticked	-	Ticked	Ticked	Ticked			**4**
4	-	-	Ticked	-	-		Ticked	**2**
5	-	-	-	Ticked	-			**1**
6	-	-	Ticked	-	Ticked			**2**
7	Ticked	-	-	-	Ticked		Ticked	**3**
8	-	-	-	-	-			
9	-	-	Ticked	-	Ticked		Ticked	**3**
10	-	-	Ticked	-	-		Ticked	**2**
11	-	Ticked	Ticked	-	-	Ticked		**3**
12	-	Ticked	-	-	-	-		**1**
13	Ticked	Ticked	-	-	Ticked	-	Ticked	**4**
14	-	-	-	-	-	-	-	
15		Ticked	-			Ticked	Ticked	**3**
16	-	-	-	-	-	-	-	
Total	**5**	**4**	**6**	**2**	**6**	**2**	**7**	

Discussion of results for question 1

The most popular protocol for treating the case study given was the correction of the miasmatic tendency. This is a homeopathic concept relating to constitutional treatment. The Psoric miasm can be defined as a constitutional tendency to 'hypo functioning' or lack of reaction. The Heel Remedy Psorinoheel contains nosodes for the psoric, tubercular and sycotic miasm and could therefore be used to treat a wide variety of patients in a double blind trial setting.

The second most popular option, the choice of 7 therapists, was the use of the remedy G3, this is a combination remedy produced by Guna in Milan. It is formulated to stimulate the ovarian-pituitary feedback mechanism. It contains 2 classical homoeopathic remedies (Pulsatilla and Kali Carbonicum) and two suis organ preparations (Ovarium and Corpus Luteum). It is indicated in cases of ovarian hypofunction and functional dysregulation. Again this remedy does not need to be individualised as the underlying physiological mechanisms are common to all women and therefore the remedy could be used in a double blind trial.

The use of potentised doses (D6) of the hormones, LH, FSH, Progesterone and Beta-estradiol was the third most popular choice, receiving 6 ticks. These remedies are universally applicable to all women and could be used in a double blind trial but the protocol is more complicated with different drops being taken on different days of the month. This may mean that they are unsuitable for use in a trial where the patient is responsible for taking their remedies daily at home.

5 therapists supported the view that a vaccination detox was justified, 4 supported the option of supporting pancreatic function and detoxification using Syzygium compositum and Galium heel. The least popular option was the use of the classical homoeopathy and this was congruent with the qualifications of the sampled practitioners and their forms of practice.

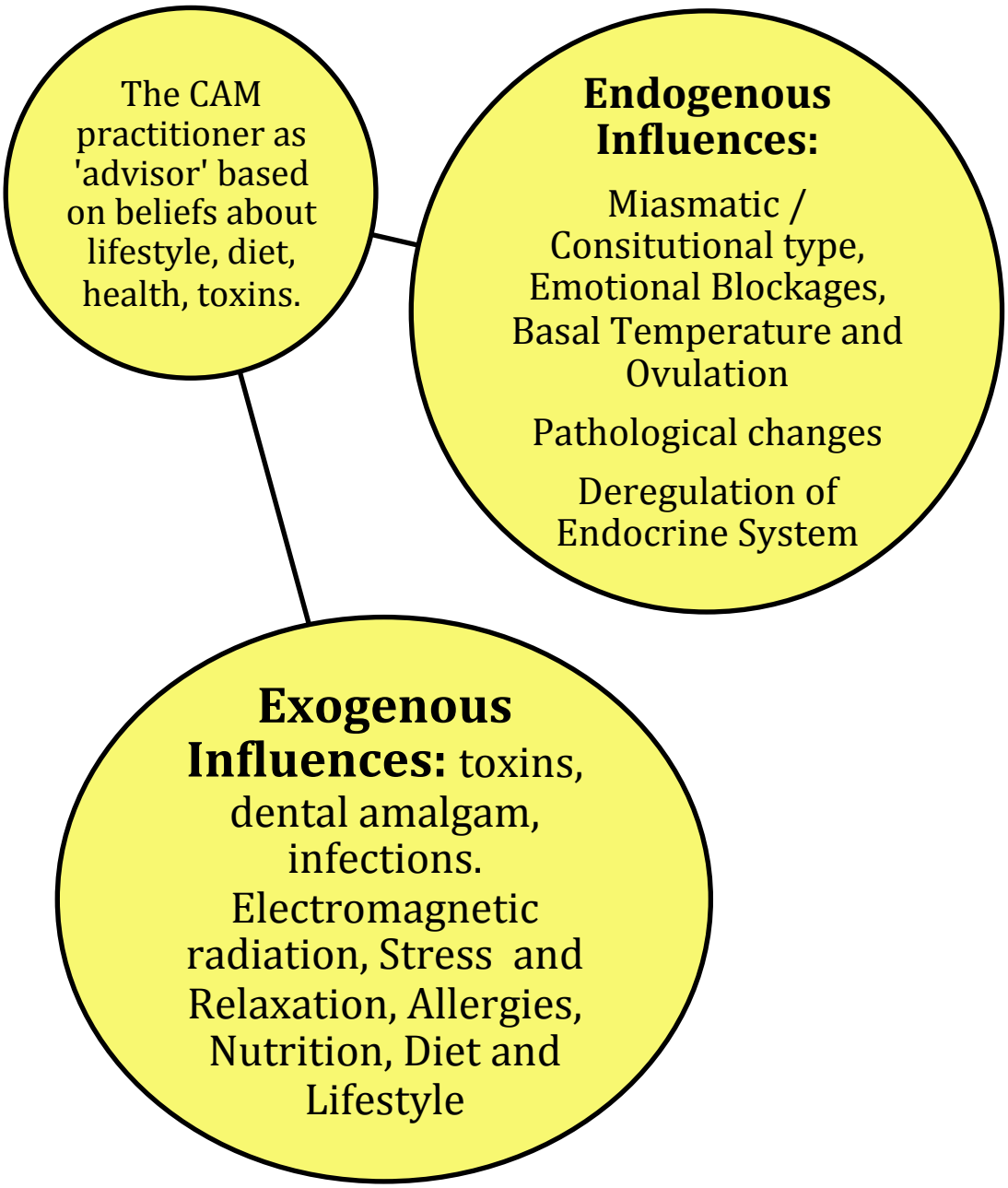
Homotoxicology is characterised by the use of more than one homoeopathic remedy at a time, which is why it is sometimes called ‘complex homoeopathy’. 5 therapists were happy to tick three options from the list to be given together. 2 therapists ticked four of the available options and 3 therapists were happy to give just one and two of the choices on offer.

3 therapies was the mean average as well as the mode or most frequently chosen. In a real life therapeutic setting this would be feasible but from a clinical trial point of view it may be better to test one remedy at a time in order to ascertain the specific effect of that one remedy.

The main weakness is the confusion between the two versions of the questionnaire, the results are not analysed separately. The decision to include a second version of the questionnaire was due to the fact that the funding for trial medication changed half way through the process and so some of the Heel products were included in the questions. After the questionnaire had been completed and negotiations with Heel were taking place it was clear that the remedy that they would like to trial was the Ovarium compositum tablet formula, this is analogous to the Guna G3 formulation and works on the same principles.

The decision was made that as G3 was the second most popular choice the equivalent remedy from Heel, Ovarium compositum, would be an appropriate medication for trial. As a tablet formulation it had the advantage of being easy to randomise to placebo in a tablet form and easy to patients to self-administer.

Figure 6 Cluster Diagram showing the emerging themes from analysis of the results



Thematic Analysis of Questions 2,3,4

The iterative sorting of the slips led to three main themes being identified:

- **The role of the practitioner in patient choice and self-care**
- **The role of endogenous influences**
- **The role of exogenous influences**

These themes are represented in Figure 6 Cluster Diagram showing the emerging themes from analysis of the results, the data that was collected is included in table form in the appendix: see Table 45 Summary of Practitioner Responses to Question Two; Table 46 Summary of Practitioner Responses to Question Three; Table 47 Analysis of Practitioner Responses to Question Four.

The Role Of The Practitioner

The practitioners emerged as ‘advisors’ and their advice was based on their beliefs about the causes of infertility:

I would seek to find out what is causing the infertility..

The focus on treating various kinds of ‘toxicity’ is not surprising when the sample is targeted at homotoxicologists. Toxins causing infertility fell into two groups, exogenous and endogenous, and the advice given spanned the ‘whole’ range of mental, emotional, ‘energetic’ (e.g. vitalism), and physical domains of health and disease.

Dietary advice was given to avoid processed foods, wheat (an allergen for some people), sugar and dairy products and some quotes indicated that this treatment would be individualised. An organic diet, high in vegetables and complex carbohydrates was recommended and as well as supplementation of deficiencies:

Eat only high quality protein, fish, beef and lamb…eat only fresh food…organic food if possible…avoid white meats…avoid dairy products…minimise wheat and sugar and dairy dependent on further case taking….a diet high in vegetables and complex carbohydrates…Male supplements: anti-oxidants…vitamin C, ginseng, zinc, flaxseed oil, Females: evening primrose oil, copper, zinc, vitamin B complex, fish oils…maca supplement..

Both male and female cases were recommended to avoid nicotine, caffeine, alcohol and recreational drugs.

No alcohol, no smoking, no drugs..reduce/eliminate intoxicants, cigarettes, alcohol or recreational drugs….avoid caffeine.

The avoidance of plastics, microwaves, chemicals, and mobile phones were all recommended as well as the reduction of extreme lifestyles, exercise and exhaustive journeys.

Eliminate mercury fillings...remove all toiletries…plus what is individually indicated…avoid all chemicals…avoid plastics and microwaves...particular emphasis on mobile telephone usage (if in trouser pocket can microwave sperm.)…reduce extreme lifestyles…do not fly long haul…de stress cortisone cycle.. blood sugar and adrenaline levels…

Male patients were encouraged to avoid overheating in general and overheating the testicles in particular by wearing loose fitting underwear.

Abandon Y fronts in favour of boxer shorts to cool the testicles…

The emotional strain of infertility was recognised by practitioners who gave advice about counselling and stress reduction techniques.

The emotional freedom technique may release deep emotions…the strain that couples go through with IVF is often marriage breaking so to give

counselling or advise external counsellor to see this through…reduce stress….teach a meditation/visualisation technique to improve positive thinking and results…yoga…and relaxation classes…energy and personal development work.

The giving of advice in this way implies that by making these lifestyle changes the infertility will be 'treated'. One limitation of the methodology of this strand is that the questionnaire does not capture the context of how the benefits of giving up and the chances of success would be explained to the patient. This kind of data might have been captured using practitioner interview or by observing some consultations.

Some homotoxicologists also recommended other concomitant treatment with therapies such as flower essences, reflexology or Chinese herbal medicine.

Homotoxicologists who are also holistic dentists recommended the removal of crowns on the front teeth because they believe that the front teeth are positioned on certain meridians (Chinese medicine) that are influential in fertility outcomes.

Some practitioners recognised the limitations of their knowledge or qualifications to treat:

I would refer patient as I only treat dental problems.. not qualified to answer..I would pass this one, it would all depend on the patient..

The accuracy and authority of the advice was sometimes based upon a diagnostic tool such as Electro acupuncture (EAV) or Vega testing, typically recorded by the practitioner as 'checking' or 'testing':

I would correct any imbalances apparent with vega testing.. the environment of the couple needs to be scrutinized with EAV…check miasms… test for mumps nosode..this would include checking for genetic inherited toxins,

viruses, bacteria (e.g.Chlamydia), amoeba and parasites.. check for NSU, check endocrine system for MMR and Scarlet Fever..I have no specific protocol under homotoxicology however I work with EAV.. using BFD..

Another use of technology was *general assessment using a biofeedback machine for current health status*

Endogenous Influences

The Deregulated Endocrine System

Practitioners believed that infertility in both male and female cases was often being caused by a deregulated endocrine system, particularly the sub-optimal functioning of ovaries or testes, although other glands were mentioned. Pathologies that can lead to infertility were also suggested as causes:

Test for thyroxine and testosterone levels…Check out hyperthyroidism…strengthen liver and pancreas…I would check her thyroxine/thyroid level function...Nutri-Thyroid extract

Endometriosis...undiagnosed ovarian cysts…

The predominant therapy chosen to treat male infertility was the use of the Suis Organ remedies to stimulate the glandular function of the male gonads. Suis Organ remedies are homoeopathic attenuations of wholesome organs or tissues obtained from healthy animals, in this case pigs. The pig is selected because of the similarity between pig and human tissues.

Homotoxicologists believe that the remedies act like an organ specific nosode and are believed to have stimulating properties in accordance with the homoeopathic similar principle, rather than being prescribed on individual symptom pictures.

K2M…Testis compositum, ductus suis, coenzyme compositum, Testis suis… Roy Martina Endocrinotox 2 (General Male Regulation) and 7 (Male Gonad Endocrine Type)…

Where practitioners suggested that female infertility is due to a deregulated endocrine system, basal temperature checking would allow patients to self-diagnose and the suggested treatment included combinations of classical homeopathic remedies, suis organs and potentised hormones:

Thalamus comp..Ovarian compositum…K2F…Hormeel.. Potentised Hormones such as Beta-Estradiol, Progesterone D6 (luteal phase deficit), LH (D6-D30), FSH (D6-D30) ….Sepia D6..Gynacoheel..single low potencies of hormones..G3..Ovarian suis..overall stimulation of pituitary-adrenal axis using R29 Dr Reckeweg products..

Ovarian compositum was a popular choice and was not prescribed on individual symptom pictures but on the clinical indications of infertility due to ovarian deficiency.

Exogenous Influences

Many practitioners believed that environmental toxins were a cause of infertility. Some practitioners address these issues using Homotoxicology as a treatment. The theme of exogenous toxins included past and present infections, as well as hereditary weaknesses, which were all seen as barriers to fertility, that could be treated with nosode therapy. Some, as evidenced in the third extract below, demonstrated a holistic approach:

Would look for endotoxins and exotoxins…High mercury levels..reduce external toxins through skin and air and from food..we also need to look for exotoxins, lead pipes etc..radiation…I find problems with fungus and mycotoxins in people's houses..occupational hazards..jobs, hobbies, activities of both partners, geopathic stress, environmental pollution especially electro smog, phone masts,(G3), EMF's etc…Water and quality of water, cosmetics, shampoos, household… endocrine disruptors etc…xenoestrogens, plastics etc…

Check miasms...test for mumps nosode...past infections particularly mumps..treat with Psorinoheel..check and treat miasms… brucella, past infections, viruses, bacteria (e.g. Chlamydia), amoeba and parasites..check for NSU, check endocrine system for MMR and Scarlet Fever

The herbal treatment for high mercury levels are a concern here, due to mercury there may be some candida present

One approach to the treatment of emotional blocks and stress, as an exogenous cause of disturbance to fertility, was the use of flower remedies to remove emotional 'blocks'.

Discussion

The sample of practitioners was drawn from the database of UK registered homotoxicologists as well as other users of homotoxicology. The themes that developed from the responses were influenced by an understanding of infertility as seen through the framework of homotoxicology theory. The homotoxicological paradigm (Smit A, 2009) is a homeotherapeutic system in which a medical diagnosis is made, followed by an individualized assessment according to the severity of the patient's disease. This takes into account the response of the patient's self-regulatory system to exogenous and endogenous stressors.

The results show that the practitioners perceive infertility to have both exogenous causes such as stress and toxins as well as endogenous causes such as reproductive pathology or hormonal imbalance. The holistic view that fertility is an expression of health and infertility is a disturbance of health is found in the theoretical framework of homotoxicology where treatment is given, to support the inherent self-regulating ability of the body rather than just treat symptoms, which are seen as an expression of the body's own defence that should not be suppressed. (Heel, 1986).

The coding was also performed by myself, a qualified homotoxicologist and so the choice of codes may have been influenced by that same framework. The reliability of the coding could perhaps have been improved, if another researcher from outside the homotoxicology community had checked it, but that might have been at the cost of losing the detailed understanding of the concepts from the emic perspective.

One of the aims of this strand was to investigate how homotoxicology might be used to treat infertility in practice and the analysis shows that homotoxicology may be used alone, or in conjunction with other therapies, to support the detoxification of the patient (e.g. Heel detox kit, gallium heel) for exogenous toxins and to support the endogenous factors such as regulation of the endocrine system (e.g. Testis compositum, Ovarian compositum).

What is the role of the CAM practitioner in the treatment of infertility? The CAM practitioner takes a holistic view of the health of the infertile patient, as shown in one of the extracts above in particular, and may advise a range of strategies to support their health and fertility including diet, nutritional supplementation, stress reduction, detoxification of endogenous and exogenous toxins, and stimulation of the endocrine system. Treatments may be individualised by taking case histories or by using diagnostic techniques and technologies such as electro-acupuncture (EAV), Vega testing or Bio-Functional diagnosis (BFD).

Is there a specific treatment that can be given without a consultation and in the absence of an individualised prescription? The use of complex homotoxicological preparations such as Ovarium compositum (females) and Testis compositum (males) are prescribed on clinical indications rather than individual case histories and would be suitable for use in a randomised controlled trial where the sample of patients are being recruited by the clinic for a specific clinical indication.

The results of strand one and the successful negotiation of a funding contract with Heel led to the selection of Ovarium compositum as the trial medication for the third strand of the study.

Results from Strand 2 - The Bridge Centre

Themes From The Staff Questionnaire And Discussion Group

Units of study

Five nursing staff attended the interview and completed the questionnaire. 127 questionnaires were distributed at the reception desk and 24 completed forms were returned for analysis. Copies of the questionnaires are included in the appendix see Questionnaire for nurses at The Bridge Centre

Theory

Nursing theory is a pluralistic discipline and the four central concepts of person, environment, health and nursing are interpreted in different ways according to the theoretical position of the nurse (Masters, 2014). Some theories are more holistic than others, for example the Jean Watson philosophy and science of caring model (Watson, 1979) emphasizes the integration of mind, body and spirit and is open to the mysterious and unknown dimensions of life, death and suffering (Watson, 1979).

Based on humanistic nursing theories such as Callista Roy's (Roy et al., 2009) adaptation model, nursing may include the concept of caring for the holistic man (person), who is on a daily position along a health-illness continuum. This can be compared to the perspective of the doctor, whose focus is on **disease** and whose goal is to move the patient along the continuum from 'illness' to 'health' (Simoni, 1981)

Some nursing theory models, for example (Watson, 1979), have a focus on the principle of 'caritas' which means to love or cherish and again this can be compared to the principle of 'virtue' that has been proposed as the guiding principle for a medical training, that has internal norms and values, as well as

a technical body of knowledge (Shelton, 2013). The 'virtuous doctor' and the 'caring nurse' would make an interesting area of research, particularly if undertaken from a feminist perspective or using a transformative theoretical lens.

There is also a philosophical debate around 'virtue', as either an Aristotelian absolute that exists 'out there' to be attained or as Dewey argues, a position that is gained by acting reflecting on experience within specific contexts:

Aristotle assumed the embodiment of certain virtues in the polis, such as courage, prudence, temperance, and bravery, but in a pluralistic democratic and postmodern age, our virtues are not given. If they exist at all, they will be determined by conscious agreement and dedication on the basis of insight into an understanding of the conditions of life and those actions most compatible with life and flourishing, or what Dewey called "intelligence." (Shelton, 2013)

Themes

The data used to generate the themes is included in the appendix see Coded Data from Staff Questionnaire and Discussion Group

Nurses As A Bridge for patients between CAM and IVF.

A core theme generated by the eight codes used was the idea that the nurses represented a bridge between the CAM therapies and the conventional medical perspective. They could see the potential benefits to patients of using homeopathy and this positive attitude was tempered by their professionalism and caution. They were well informed about the practical issues of running a trial at the clinic and could anticipate the likely reactions of the staff and patients towards such an idea.

Some nurses had experience of homeopathy and CAM that gave them confidence as shown in the extract below:

As a midwife I've cared for many women using remedies so I've gained some knowledge… Personal use to treat Hay fever… Echinacea with colds, rescue remedy with stress, gingko balboa for memory…

Caring For The Patient

By putting the needs of the patient first nurses could see that homeopathy might provide benefits in the form of stress reduction, placebo effect or increased well being. The homeopathy could be seen as 'more natural' by women who are having invasive assisted reproduction techniques. Caring for women undergoing IVF also involves nurses supporting women who are emotionally distressed by treatment failure, if their nursing education has prepared them to care for the whole person including mental and emotional health they may see homeopathy as offering support on a more holistic level:

I think believing in the remedies will make someone to use them with a hope of success and belief = success…More pregnancies…More relaxed patients… Not a quick cure but something that can help/ease illness… General wellbeing, find treatment less stressful, patients able to move on with life re deciding not to continue with treatment… For certain patients with problems like overweight which may affect their chances of having children I think they will benefit from the project…Relaxes the body and minds as well as relieves their stresses therefore promote health… I would probably say try anything (safe) once if it will help you get pregnant or have another positive effect on your health…. It is their choice, if it is beneficial then let them try…

There was also a perceived benefit as a unique selling point for the clinic:

Potentially it could be of great benefit to clinic if we can sell the clinic as having an option of IVF or IVF plus homeopathy…

Boundaries Of Professional Role

A conflict arose when trying to balance holistic needs of the patient with their role as 'technical assistants' to the doctor's performing the assisted reproduction.

They did not feel that the doctors would agree with them, or share their interest, and they recognised that patients may also have concerns about taking part in a randomised trial with an unknown drug and the possibility of being randomised to placebo:

Lack of knowledge on Doctors behalf, unwilling to believe, patients not wanting to go on a placebo, patients not wanting to delay treatment… Asking women if they are willing to delay treatment with a 50% chance they will be on a placebo…

Patients not wanting to try the homeopathy…patients getting angry or upset because trial hasn't worked or no benefits…. Professional (concerns), patients, drugs not known so tend to stop…

The Need For A Theoretical Perspective

To balance these concerns the nurses needed to feel that they were well informed about the trial drug and it's possible side effects so that they could explain the risks and benefits to the patients or support them in making a decision:

Need more information…Fine with more training re homeopathy…To explain the mechanism to clients…Knowledge, actually understanding everything I'm telling patients before I talk with them… It's a very good idea but not enough training to impart knowledge... Ethical dilemmas – consider!!!

They were happy to take part in the trial because they felt that hosting the trial they were helping to provide an evidence base for something that might support their patients:

I'm interested but sometimes sceptic, I like the idea of research and proof and if scientific research can justify then fantastic…Fine with more training re homeopathy… positive...Happy (to take part)…

They identified practical difficulties in hosting a trial, such as the appointment times that would need to be extended, and the need to get a large sample size to create a credible result:

Talk 30 mins to one hour, probably best to organise further talk…Not long enough, 5-8 minutes approx….More (time needed)…Not enough with nurses talks up to one hour….OK just hope we can recruit enough women to get results

Discussion of Results

The nurses at the clinic provided a perspective that appeared to bridge the dualistic choice between the dismissal of homeopathy by some medical practitioners and the personal choice to use homeopathy made by some patients

They were open to the idea and potential benefits and could also see practical challenges to implementing a trial. Their support would be necessary to run such a trial and would need to be fostered by the researcher. They would like to receive more training and information so that they could advise patients and colleagues and this would need to be planned into the trial schedules. They recognised that their patients often suffer emotional distress and disappointment at treatment failure and for that reason may not wish to take part in a trial where they could be randomised to placebo. The other issue raised was that it would not be ethical to delay any conventional treatment as women's fertility outcomes decline with age.

The sample of nurses in the discussion group were not asked about their training or theoretical orientation and that would have provided a conceptual level to the analysis if it had been included. There has been some debate in the nursing profession about the need for reflection on theory and the

cultivation of metaparadigms in order to raise the professional standing of nurses (Lee and Fawcett, 2013) and to avoid ‘burn out’ in the work place. A future research project springing from this study could aim to find out more about the influence of nursing theory on the acceptance or rejection of CAM.

The Patient Questionnaire from The Bridge Centre

Table 24 Table of results for patient questionnaire

Question	*Yes*	*No*
Question One. Have you ever tried Homotoxicology as a therapy?	*3*	*21*
Question Two. Have you tried Homotoxicology as part of your treatment for infertility?	*1*	*23*
Question Three. Would you consider trying Homotoxicology in the future as part of your treatment for Infertility?	*22*	*2*
Question Four. Would you be prepared to take part in a clinical trial where you may receive a placebo or no medication instead of the active remedy?	*15*	*9*
Question Five. Would you be willing to take your medication daily at home, as drops or tablets?	23	1
Question Six. Would you be willing to give up peppermint and coffee?	24	0
Question Seven What would be your motivation to take part in a clinical trial of homotoxicology		
(i) To increase my chances of ovulating?	20	1
(ii) To help other couples in the future?	22	1
(iii) To increase knowledge about homeopathy?	20	2
(iv) Decided to stop trying with IVF/ART	7	7
Question Eight Would you be happy to pay for homotoxicology in the future if this was shown to be an effective therapy?	20	2
Question Nine Would you be prepared to take homotoxicology remedies at the same time as your conventional medication?	21	3

Discussion of results from the patient questionnaire

The patient group that was surveyed is a vulnerable group undergoing stressful psychological and physical experiences and therefore sensitivity was required when asking for their cooperation. Postal questionnaire response rates are declining in the general population and strategies on how to increase them were employed, including the use of a prepaid return envelope and a university return address. The response rate to this questionnaire (19%) was average for its type and the patient group concerned (Roberts PJ, 2002).

A high level of altruism was displayed by respondents 91% of whom were motivated by the desire to take part in a trial that would help other infertile couples in the future, 85% were motivated by the point that a trial of this kind would increase our knowledge about homotoxicology and homeopathy.

It is likely that the respondents who chose to respond will have a positive bias towards the subject matter, but as future patient choice would be an important factor in integrating CAM this survey can be viewed as a positive indicator of potential patient demand. Nevertheless, homotoxicology represents a novel intervention to the respondents, as 88% had not tried this therapy before. A high level of interest (92%) was shown in trying homotoxicology in the future. A large majority, 83%, would be willing to pay for treatment if homotoxicology was shown to be effective. The use of homotoxicology is apparently not viewed as an alternative by these patients; only 2% indicated that they would consider homotoxicology because they were considering stopping IVF/ART.

The feasibility of setting up a double blind trial is enhanced by the fact that 62% would be prepared to take part in a trial where they may receive a placebo. A high level of participant compliance is indicated by the fact that 95% would be prepared to take their medication at home and to 100% would be happy to give up peppermint and coffee.

Limitations

It was not possible to record the number of patients who did not take a questionnaire from reception and therefore the sample of respondents is biased towards patients that have some interest in taking part or finding out more about the trial.

Summary

In conclusion it appeared that a randomised controlled double blind trial was a feasible option and that there would be a high level of participant compliance and motivation. The focus group provided some valuable insights about trial recruitment and implementation, for example the amount of time nurses will have to discuss the trial with potential subjects, the need for specialist training in the background information about homotoxicology and the ethical dilemma of asking women to consider taking part in a trial when they are already undergoing stressful treatment.

The results of this survey were presented at the William Harvey Research Institute Open Day in 2007 and a copy of the abstract and poster are included in the appendix Figure 22 Poster.

Results from Strand 3 - A Double Blind, Randomised Controlled Trial of Ovarian Compositum in Infertile Women

THE RECRUITMENT TO STUDY OVCT-001

Introduction

Recruitment was started in November 2011 and stopped in July 2012, during that time 4 patients were enrolled and 4 more identified as appropriate and sent a recruitment invitation letter by the unit. They are summarised in Table 25 Summary of recruitment below.

Of the 3 patients that were consented 1 withdrew after initial screening as she became pregnant before she started the trial medication. 1 patient completed 6 months of treatment, 1 patient withdrew after 1 month due to compliance issues and 1 patient withdrew after 2 months also with compliance issues.

Randomisation number	Age band (years)	Treatment Group	Trial medication group	Outcome
1201	30-35	Clomid	Ovarium compositum	Treatment stopped after 2 months
1202	30-35	Clomid	Ovarium compositum	Treatment stopped after 1 months
1204	30-35	Clomid	Placebo	Withdrawn from trial due to pregnancy before taking trial medication
1301	>35	Clomid	Placebo	Completed 6 months of treatment

Table 25 Summary of recruitment

Delays To Recruitment Caused By Damage To Trial Medication

During December 2011 another event delayed recruitment to the trial, the Pharmacy in Jersey alerted the researcher to the fact that the trial medication was compromised. There were a number of broken containers and containers with broken seals. A list of the damaged tablet containers is shown in the appendix see APPENDIX 9 Damage To Trial Medication

The recruitment process was suspended pending further investigation and in early February 2012 Ms C Haresnape (Researcher and CI), Prof Atholl Johnston (PhD supervisor) and Dr Istvan Zatik (Funder- Heel GmBh) flew to Jersey for a site visit. It was ascertained that the trial medication had not been examined on arrival at pharmacy and so it may well have been damaged during transportation. Some pots were opened with broken seals and there were no security seals on the boxes of pots. The outer boxes were sealed and unopened as so it was decided that the packaging of the tablets was at fault and had not been strong enough for the transportation process by air.

Sufficient medication was available for the recruitment targets and so it was deemed appropriate to continue with the trial. The damaged pots were removed for secure destruction by pharmacy. The incident created a further two-month delay to recruitment.

Timeline of recruitment.

The final feedback during a site visit in September 2012 was that with hindsight the set up and design of the project should have been a joint consultation with nursing staff as this project had created a strain on the department.

This strain had become evident from the email correspondence during November 2011 when the full time nurse in the Assisted Reproduction Unit (ARU) found that the time taken to book screening appointments was putting pressure on her existing workload (Thomas, 2011). She described the service as ‘small but overstretched’ and suggested that the lead consultant

had not fully appreciated the impact that running a trial would have on the unit.

A site visit was arranged for 1st February 2012 to discuss recruitment and other issues. The unit staff suggested that the extra appointments required for USS and blood tests were a reason for low recruitment and retention of patients to the trial. The doctors suggested that we started recruiting from the pool of patients who had already started their Clomid or FSH treatment.

The nurse had reported problems with compliance and in order to try and boost retention a change to the protocol was proposed which allowed patients to take their medication three times a day, morning, afternoon and evening but not at a specific time. These changes were made and the ethics committee informed.

The ARU nurse provided further emailed feedback in February 2012 (Thomas, 2012) making the following points:

There had been no further requests from patients to join the trial.

Patients feel it is too big a commitment as they have to attend the unit during their working day and treatment may persist for several months or even years.

In March 2012 there was again little to report and the message from the unit was that subjects ‘don’t like the extra hassle’ (MacLachlan, 2012a) but there was the intention of continuing to try and recruit further patients.

The need to increase recruitment was becoming increasingly urgent as the expiry date of the trial medication had to be taken into account. Any patient who did enrol must be guaranteed a 12-month supply of medication and this meant that recruitment must stop in July 2012.

With this in mind the ethics of a campaign of publicity was discussed with Heel to include meetings with the local media, meetings with local GP’s, meetings with local patient support groups. These ideas were put forward to the Jersey unit but the response (MacLachlan, 2012c) was that the local

fertility group is new and very much aimed at IVF; the local GP's do not prescribe Clomid so their patients do not meet the inclusion criteria for the trial; and that although approaching the local press was seen as a good idea the main problem still appears to be the need to attend additional appointments.

Towards the end of March 2012 a telephone conference with the ARU nurse highlighted the following points:

- If she had been consulted earlier in this process she would have predicted the difficulties in recruitment due to her experience and knowledge of the patients.

- She could have helped design the documentation by using existing file formats and templates.

- Patients are stressed by extra appointments because Jersey is such a small island and it is difficult to maintain privacy around their treatment.

In April 2012 a telephone conference with Dr Istvan Zatik from Heel GmbH confirmed that we would not be able to boost recruitment by looking to move this trial to another UK site, as Heel senior management would not support that move. No further trial medication was to be authorised and a meeting was arranged with Dr Alta Smit of Heel GmbH in London for early May 2012 to discuss these points.

In June 2012 we discussed closing down the trial via email and the response from the unit (MacLachlan, 2012b) was that despite their genuine wish for the trial to succeed a number of unforeseen circumstances had created obstacles to success. This included a perception by patients that taking part in the trial might slow down their transition through the conventional treatment modalities and also created extra visits, blood tests and intrusive scans.

A formal letter of trial closure was sent to all stakeholders in July 2012 and a final site visit was made in September 2012 to meet, collect the paperwork and discuss the outcome.

Discussion points arising from recruitment

The clinical staff at the unit identified the following themes: compliance, frequent blood testing and USS, high expectations, coincidental issues.

Compliance.

2 out of the 4 patients stopped taking medications because of difficulty taking the tablets 3 times daily at a fixed time. It was also noted that they felt that the taking of the trial medication acted as a perpetual reminder that they were infertile and this created emotional distress

Frequent blood testing and USS (Ultrasound Scan).

In addition to monthly blood tests for FSH, E2 at day 2 and Progesterone at day 21, patients needed to have baseline USS every month and this was not normal practice for Clomid patients. This added extra appointments to their schedule, which were difficult for patients who were working to accommodate.

High Expectations

The feedback from the clinic was that patients had elevated expectations of the success of their treatment because they were taking daily medication and having more frequent blood tests and USS.

Coincidental Issues

During the autumn/winter of 2011 and spring 2012 the clinic experienced a higher pregnancy success rate and this made the recruitment of new trial subjects more difficult.

The Recruitment process - Reflection and feedback from clinic staff.

A clinic with a higher input of a more homogenous patient group would make recruitment easier and they suggested that future trials should focus on one subgroup with a specific definition of infertility.

Some patients were biased against trying CAM, as they were worried it might slow down their progress through their conventional treatment. Patients are conscious of the timescale of their fertility treatment, as age is a predictor of success.

There are a high percentage of Portuguese girls in the local population and they are expected to bring a friend or translator, this made it more difficult to make the additional appointments needed for trial participation.

The fertility clinic feeds into a mainland IVF unit and they had expressed some doubts about patients being involved in a CAM treatment and this was based on some evidence about Chinese herbs.

It would be preferable to have a research Doctor based on site as the lead investigator.

Summary

Over a period of nine months (November 2011 – July 2012) unit staff identified suitable patients who attended the ARU. Four patients agreed to take part and three of them were consented. Of the 3 patients that were consented 1 withdrew after initial screening as she became pregnant before she started the trial medication. 1 patient completed 6 months of treatment, 1 patient withdrew after 1 month due to compliance issues and 1 patient withdrew after 2 months after compliance issues.

Recruitment and retention rates were low due to a combination of reported circumstances:

- A higher than expected pregnancy rate at the clinic left fewer eligible subjects.

- The difficulty of attending additional appointments for working women who are wary of disclosing their treatment to colleagues, family or friends
- The burden of extra work on the ARU staff who did not feel any 'ownership' for this trial, as they had not been involved in the planning stages.
- Patient perceptions of the impact of taking part in a trial on their treatment progression or outcomes
- The subjects that were recruited to the trial OVCT-001 are summarised as follows:

Randomisation number	Age band (years)	Treatment Group	Trial medication group	Outcome
1201	30-35	Clomid	Ovarium compositum	Treatment stopped after 2 months
1202	30-35	Clomid	Ovarium compositum	Treatment stopped after 1 months
1204	30-35	Clomid	Placebo	Withdrawn from trial due to pregnancy before taking trial medication
1301	>35	Clomid	Placebo	Completed 6 months of treatment

Table 26 Summary of Recruitment to study OVCT-001

The data for the four subjects who were consented to the study was collected from Jersey General Hospital and is included in the appendix as APPENDIX 10 Data collected from Jersey General Hospital participants in pilot study.

The data is described but cannot be subjected to statistical analysis as the sample was too small and only one subject attended more than two appointments.

This study failed to meet its recruitment targets for the reasons given above and this generated a new hypothesis for further investigation into the work related concerns of women seeking infertility treatment, this is investigated in strand four of the thesis.

Chapter 4 Results for Strand 4

Results for Strand 4 - A Qualitative Analysis Of The Work Related Concerns Of Infertile Women

Theory

Writing up the themes was an integral part of the analysis and there was an iterative process of reading and writing as patterns of meaning and areas of interest were studied. The early engagement with the literature had suggested 'emotional distress' as a theme so emotions but some reading was left until later to avoid narrowing the researchers field of view.

Scientists who study the relationship between emotional health and physical health (psychosomatic medicine), have seen several theoretical shifts in the last 30 years (Medicine, 2015). Scientists have moved away from simple behavioural models based on theories of stimulus and response in lower organisms (Skinner, 2011) towards a concept of an integrated complex and dynamic system of two way communication between mind and body (Hiramoto et al., 1997)

The early model that was based upon psychoanalysis has been replaced with concepts that mostly derive from the work of early twentieth century Harvard physiologist Walter B. Cannon. Cannon's model was that of the biological organism that automatically mobilized its physiological and biochemical resources to defend itself against real or threatened assault using it's own innate 'wisdom' (Cannon, 1916). The presence of negative emotions such as fear or rage would cause the organism to prepare for fight or flight by shutting down energy-storing functions and activating energy-releasing ones. Cannon also defined the word homeostasis in 1932, deriving it from the Greek words *homios* (the same) *and stasis* (stance or posture). Homeostasis thus means to stay in the same condition or position (Smit A, 2009) and this concept will be explored in more detail later in this thesis.

These ideas were further developed by Wolff (Wolff, 1953) and then Hans Selye who emerged as a leading proponent of stress based theories (Selye, 1973). Selye's theories were based upon the idea that "stressors" such as cold, heat, solar radiation, burns and 'nervous stimuli' produced a generalised response it the biological organism as an adaptive response. The stress response was divided into three stages and included both the nervous system and endocrine system as part of a cascade of neuro-hormonal messenger molecules from the hypothalamus to the adrenal glands. The three stages were known as the 'alarm', 'adaptation' and exhaustion phase.

Selye's work was influential in a wide range of medical and other health related fields including the development of Homotoxicology. Homotoxicology theory includes the concept of the role of the Hypothalamus-Hypophysis-Suprarenal cortex in the Greater Defence System (Smit A, 2009) (INSERT CROSS REFERENCE to literature review)

The discovery that the nervous system and the immune system were able to share a common language of neuropeptides and neurotransmitters was popularised in the 1990's (Pert, 1997) and more recently the interactions between psychological processes and the nervous, immune and endocrine systems of the body are being studied as a new branch of medicine called Psycho-neuro-endocrine-immunology (PNEI), sometimes referred to as just PNI (psychoneuroimmunology).

Psychoneuroimmunology refers to the study of the interactions between the behavioural, neural, neuroendocrine, and immunological process of adaption Although relationships between the brain and the immune system have been suggested for many years, research has now provided mechanisms for how these systems may interact (Weigent et al., 2011).

The widely held belief is that it represents a bi directional system. The nervous system not only influences immune function but the immune system modifies the nervous system. (Weigent et al., 2011)

Collectively these relationships provide the foundation for behaviourally induced alterations of immune function and for immunologically based changes in behaviour. (Weigent et al., 2011)

By 1894 Pragmatism had also challenged the dualism that viewed mind and body as separate. Dewey, Tufts, Mead and Angell were forming the basis of the so-called "Chicago group" of psychology.

They had a practical emphasis on action and application. In Dewey's article "The Reflex Arc Concept in Psychology" (Dewey, 1896) he reasoned against the traditional stimulus-response understanding of the reflex arc in favour of a "circular" account in which what serves as "stimulus" and what as "response" depends on how one considers the situation, and defends the unitary nature of the sensory motor circuit

He developed the idea that there is a coordination by which the stimulation is enriched by the results of previous experiences. The response is modulated by sensorial experience**.** This article has become a classic in the history of modern psychology and is often identified as the beginning of the functionalist approach in psychology (Titchener, 1898).

Dewey characterized the organism-environment transaction as a process of continuous readjustment, not simply as an external stimulus and then an organism’s response. Through selection and assimilation the organism establishes a dynamic coordination with its environment. The increase of the range of coordination is one of the central development processes, leading to a new state of intelligence (Biesta and Burbules, 2003).

The idea that environmental and emotional experiences, in conjunction with genetic and epigenetic factors, can modify inflammation pathways, brain structure and emotional responses is one that the advances in neuroimaging and neurochemistry are being used to explore in diverse fields such placebo effects (Benedetti et al., 2011), posttraumatic stress disorder (Pace and

Heim, 2011), wound healing (Gouin and Kiecolt-Glaser, 2011) and cancer (Lissoni, 2012).

The effects of prenatal maternal stress has been shown to cause immune disorders in offspring, psychological stress acts as a programming determinant by setting functional parameters to abnormal levels, thus inducing postnatal maladaptation (Veru et al., 2014).

Stress promotes inflammation, impairs antibody responses to vaccination, slows wound healing, and suppresses cell-mediated immune function, Thus, stress-induced immune deregulation during pregnancy has unique implications for both maternal and fetal health, particularly preterm birth. The application of psychoneuroimmunology research models to the perinatal period is being used to elucidate the biological pathways by which stress may affect adverse pregnancy outcomes, maternal health, and fetal development (Christian, 2012).

Higher levels of stress as measured by salivary alpha-amylase are associated with a longer time-to-pregnancy (TTP) and an increased risk of infertility (Lynch et al., 2014). It is thought that stress significantly reduced the probability of conception each day during the fertile window, possibly exerting its effect through the sympathetic medullar pathway (Louis et al., 2011).

The mechanisms are thought to include centrally controlled GnRH pulse inhibition (Ferin, 1999) (Li et al., 2010) as well as autonomic nervous system activation leading to alterations in ovarian and uterine function (Schenker et al., 1992) (Rockliff et al., 2014).

The impact of emotional stress upon fertility has been investigated (Cousineau and Domar, 2007) who found that the inability to conceive children is experienced as a stressful situation by individuals and couples all around the world. *The consequences of infertility are manifold and can include societal repercussions and personal suffering. Evidence is emerging*

of an association between stress of fertility treatment and patient drop- out and pregnancy rates. (Cousineau and Domar, 2007)

Psychological interventions, especially those emphasizing stress management and coping-skills training, have been shown to have beneficial effects for infertility patients. Further research is needed to understand the association between distress and fertility outcome, as well as effective psychosocial interventions (Cousineau and Domar, 2007).

Their findings have been updated by a more recent systematic review of psychosocial factors associated with emotional adjustment in in vitro fertilization patients (Rockliff et al., 2014) who found that social support as a coping strategy and perceiving one's social circle as supportive were positivity associated with reduced emotional stress. Neuroticism and escapist coping strategies were found to be associated with increased distress by numerous studies (Rockliff et al., 2014).

They acknowledge that:
There is also a paucity of research using positive emotional outcome measures (e.g. well-being, positive affect, happiness or life satisfaction) to quantify psychological adjustment (Rockliff et al., 2014).

The distinction between mind and body is not maintained if PNEI is used as a framework for viewing the connection between stress and infertility, they are acknowledge to be an integrated system, working together in an adaptive manner to overcome disturbances to health.

There does however remain the question of what to measure and how to measure it. If a quantitative perspective is taken of the phenomenon then a quantitative answer will be produced, the same phenomenon studied using a qualitative technique will produced and the dualism is still present in the results and interpretation of the results.

It is argued in this thesis that Mixed Methods research would allow both perspectives to be integrated and allow a fuller understanding of the phenomenon.

Summary

The field of PNEI offered an opportunity to research the role of emotional stress in female infertility using a scientific post positivist perspective, a homotoxicological perspective and a pragmatist philosophical perspective. All three models view the organism as dynamic, adaptive and in constant transaction with their internal and external environment. These perspectives will be used as a theoretical framework for the explanation of the themes in this chapter.

Results for Strand 4

Units of study

Stage 1: Seven forum users emailed a direct response with information about their personal experiences.

Stage 2: 213 postings from the My Story section of the Infertility UK forum. The data used to generate the themes is included in the appendix see APPENDIX 11 Qualitative Data From Strand 4

A mind map of themes was generated (Figure 21 Mind map from early coding memo) and this model was discussed with two other researchers. This discussion led to refinement of the themes; for example the concept of a crisis of identity as lying at the heart of the themes around disclosure resulted from this discussion of the data.

After this talk it was clear that Charmaz' work on disability disclosure had parallels with my own work. This shift in underpinning theory to better fit the theoretical framework to the data is common in thematic analyses (Kelly, 2010) and is recognised in the CASP checklist for quality of qualitative analysis. (http://media.wix.com/ugd/dded87_29c5b002d99342f788c6ac670e49f274.pdf)

The smaller sample (stage 1) was then analysed again by comparing it with the Charmaz model of ''Forms of Telling" as the theoretical underpinning, and the results of this analysis used to generate the 'Relative Risk vs. Benefit' model Figure 7 Thematic Map.

Charmaz - Disclosure At Work And Self-Identity

Identity, chronic illness and disclosure at work have been investigated by Charmaz (Charmaz, 2010). We can draw valid comparisons between infertility and her analysis of chronic disease because of the long lasting nature of infertility and infertility treatment which can span several years and has a major impact on psychological, emotional and physical health.

Charmaz highlights the need to use insights from research into chronic disease to inform the management of human resources in the international workplace and this is directly relevant to the socioeconomic structure of Jersey which, as an offshore banking community, hosts offices for many multinational corporations:

‘Managers in global organisations may need additional training that focuses on dealing with and facilitating such disclosures, and universities all over the world involved in preparing local and international business graduates need to consider this issue in designing course content.’ (Charmaz, 2010)

Infertility, like chronic disease, may remain invisible in the workplace until people feel forced to reveal their condition or request special accommodations:

‘What is means to disclose illness and disability depends on a person’s health problem, cultural traditions, social values and norms, hierarchical arrangements, and specific policies in a given workplace.’ (Charmaz, 2010).

If visibility does not force disclosure then people see themselves as who they have been, not as who they have become. Workers with a chronic condition may experience daily limitations and restrictions but because they have devised ways of organizing their life around them they do not feel a need to disclose their condition. Disclosure is often associated with an episode hospitalization and this could be compared with the hospitalization needed for IVF procedures or the aftermath of an unsuccessful implantation.

Charmaz notes that questions about disclosure also involve the relative legitimacy granted to the person’s medical condition and as we discussed earlier in this chapter fertility treatment is not a "deemed incapacity" for statutory sick pay purposes. She highlights the fact that legitimacy matters to validate competent work, adult status and social acceptance.

‘Experiencing an illness or disability often conflicts with business values that assume constant involvement and productivity, speed, coordinated timing, regular schedules and predictable performance levels.’ (Charmaz, 2010)

If as she say; '*Disability does not reside entirely in the individual' but also 'depends on his or her match with a specific job'* then we can see the confusion caused by people switching between two roles: being competent at their job and then becoming unable to maintain that level of competency for a period of time due to the demands of their treatment regime.

It is understandable therefore that the positive or negative feedback from a manager will become an important validation of that person and their self-concept as they fluctuate between these two roles. Face-to-face relationships with shared interactions also shape how employers view people with disabilities (Charmaz, 2010). Employees who spend time face-to-face with their employer are more likely to experience a favourable outcome in negotiations about time needed for treatment.

Infertile men and women also face uncertainty about their probability of becoming parents and may have experienced loss of social and self-worth. In chronic illness this may lead people to struggle with losing their financial independence but in infertility this would not necessarily be the case.

Charmaz provides a model of the dilemmas of disclosure for an employee, which includes choosing between honesty, and privacy where cultural stigmas associated with may influence that decision, this can be applied directly to infertility because disclosure may result in scrutiny or intrusive questions but also allows the person to explain behaviour that might have looked odd or suspicious.

Disclosure may be staged or spontaneous depending upon the felt emotional intensity, difficulty in telling, emotional and informational control, amount and kind of planning and intended audience effect (Charmaz, 2006).

Models From HIV Theory

Additional models for disclosure are provided by the studies that have looked at HIV status disclosure in men (Derlega and Chaikin, 1977) and women (Serovich et al., 2008), (Serovich, 2001).

The findings suggested that women may evaluate the rewards and costs of disclosure to family and friends before it occurs but the study design did not allow data to be collected on how this processing occurs, how rewards and costs are weighed, who is involved. (Serovich et al., 2008).

The disease progression model has been used in HIV theory to explain disclosure that occurs as the disease becomes more visible or requires hospitalisation (Crandall and Coleman, 1992). The parallel could be drawn with women who need to ask for time off work in order to attend the infertility treatment appointments or whose treatment side effects are making them unwell.

Consequence theory has also been used to explain the decision to disclose HIV status (Serovich, 2001) . The consequence theory of HIV disclosure suggests that disease progression influences disclosure through individuals' perception of the consequences anticipated as a result of disclosure. This may include the consequences of disclosing to sexual partners, children and friends and the anticipated positive or negative outcomes of disclosure.

Thematic Analysis

The analysis of the two samples gives an indication of the concerns faced by working women undergoing infertility treatment. The response to the direct request for information was a small one, about 0.18%, considering the size of the forums (described 4000 members by the administrator) on which the request was posted and may indicate that employment concerns are of low importance compared to other challenges faced when trying to conceive. It must also be noted that my request may only have been seen by a small percentage of forum users. The themes identified in the first, smaller sample are described in detail here with additional quotes from the forum users. The themes are developed into an analytical interpretation of the relative risks and benefits of disclosure at work, to friends and family and on the forum.

Themes

Two main themes were identified, firstly the conflicting identities of the respondent as both an employee and an infertile treatment seeker, and secondly, the emotional distress caused by infertility and infertility treatment. Linking these was a further theme about the legitimacy of their condition.

Consideration of the subthemes within these led to development of a higher order thematic map as shown below in Figure 7 Thematic Map:

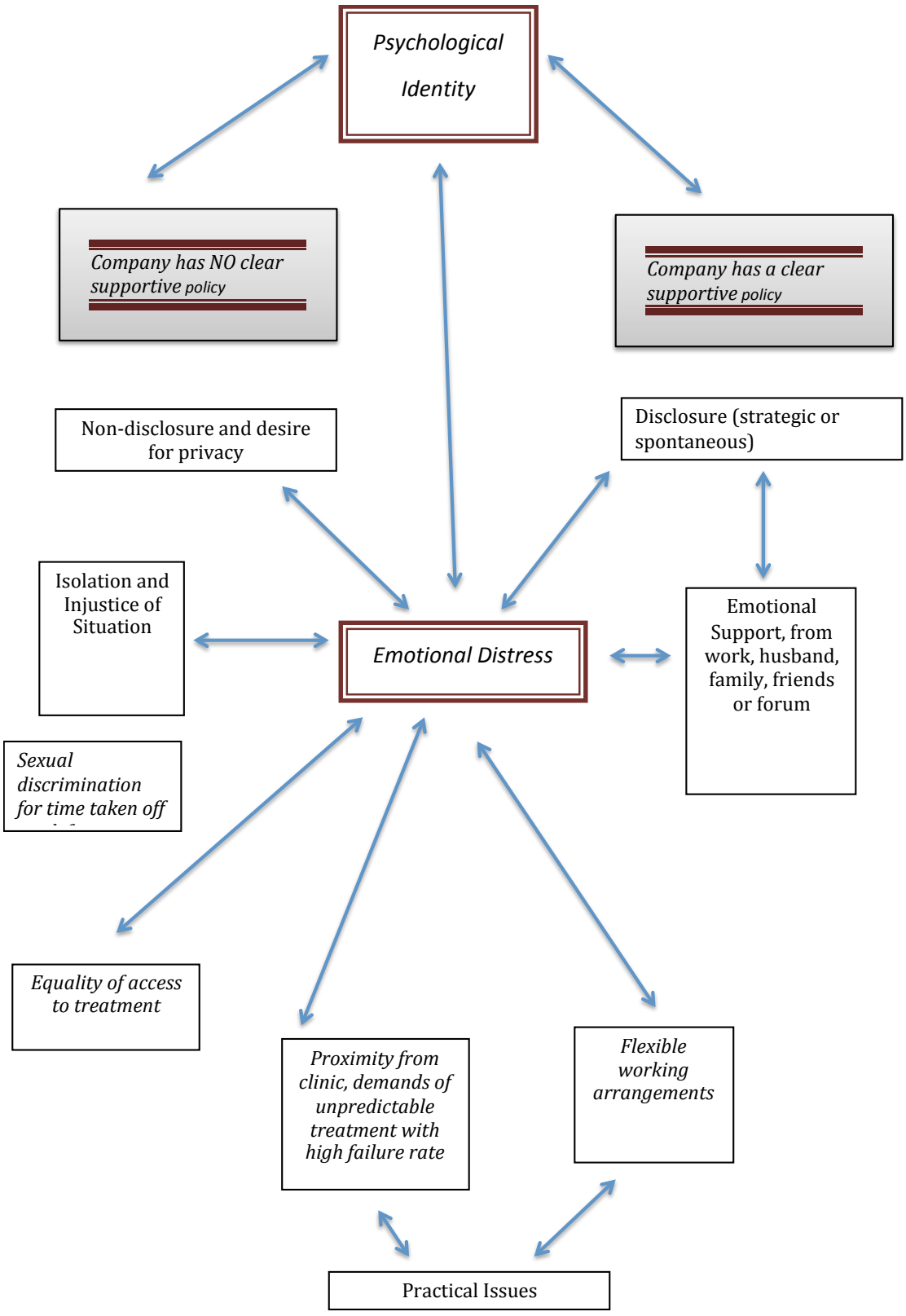


Figure 7 Thematic Map

Theme One - The Psychological Identity Of The Respondent As An Employee Or A Treatment Seeker

Psychological Identity

This theme concerns the inherent tension between the desire for parenthood, the requirements of the treatment and the requirements of the work place. Women may have difficulty reconciling their identity as an infertile treatment seeker with their identity as an employee. They have to balance the practical and psychological aspects of their situation and often in the context of a workplace where there is no clear policy for their managers to follow.

I feel very conflicted a lot of the time as in June last year I started a new job which is basically my dream job working for a great charity, and don't want to be messing them around - or to give it up - but at the same time I know that having a child would be the most important thing in my life, much more important than any job..

To top it off I've been offered a promotion at work but don't want to accept it if im going to start IVF this year…

Identity as Infertile

Different Degrees Of Infertility

Women were able to find hope in their situation when things went wrong if they had progressed towards fertility by falling pregnant.

Even though i am devastated I take solace in the fact that i got pregnant again...and started to go to the clinic counsellor which was a great help… I did not want to have IVF again and be so upset again..It was an awful time, but slowly we picked ourselves up and everyone said at least you know you can get PG….Even though i am devastated I take solace in the fact that i got pregnant again…

The parents demonstrated a strong attachment to their babies, even at a very early stage of the pregnancy, describing them as babies or girls, rather than embryo's or zygotes. This strong sense of personhood means that they have to bear the associated loss when things go wrong at an early stage of the pregnancy or when a baby is stillborn:

Our little girl was a frozen embryo, created in the late summer of 2006, and so had already overcome being frozen and defrosted. We at least have the consolation that we were able to "meet" her when she was only 3 cells old … he next day was our scan and the clinic agreed to go ahead even though they were reluctant as they feared what I already knew deep down - it was over. No picture of a heartbeat and a bean like being on the screen - nothing. I have never felt emotional pain like it. DH didn't know what to do, it was unbearable.

Women were able to use the forum to share their grief at the loss of a child whist protecting their privacy and avoiding the negative reactions of work or family:

She was conceived on our third attempt after many years of striving to become parents so her loss was particularly difficult to bear….Our little girl was born asleep on 25th June and we miss her so very much. She was born at 36+6 at 6.45pm and just looked so perfect and beautiful. ..We had lost our darling baby

Secondary Infertility

The isolation and emotional distress of women who suffer from secondary infertility, who having had one child are unable to conceive a second one, was slightly different as they receive less sympathy and support from friends, family and health professionals and feel guilty complaining when they already have one child. They are not able to identify themselves as fertile or infertile:

…Grieving for the child I couldn't have, sorrow for my son not having a sibling (I am very close to my sibling), pain at my incomplete family and feeling totally isolated dangling somewhere between the worlds of the fertile and infertile…I just didn't belong or fit in anywhere and feeling totally isolated dangling somewhere between the worlds of the fertile and infertile. I just didn't belong or fit in anywhere. After 2 solid years of trying every cycle we went to our GP who referred us on to a fertility clinic. It was not a very pleasant experience, the first time i turned up to the clinic the consultant came out into the waiting room and shouted loudly at me that i could not be seen at this clinic as 'I already had one kid, what more did i want?' It was awful, left totally humiliated

Company Has A Clear Supportive Policy

If a company has no clear policy regarding infertility, treatment decisions are often left to the judgment of individual managers and the implementation of rules often links to the amount of empathy between manager and employee. Managers have the opportunity to make a decision at their individual decision rather than upholding a company policy, which takes the decision away from them. This has the effect of blurring the boundary between personal and professional domains of decision making for both the employee and the employer:

Also not sure how much time to take off from work (very stressful workplace!!) What do you think is acceptable? Does anyone know how long after planning how long before treatment starts roughly. How much time will I need off work? I am a teacher and it obviously has a big impact on the children I teach when I am continually out at appointments? …as I am the first and only woman I know they haven't had to work out maternity leave before, let alone whether they have a policy for people going through IVF treatment.

There are several problems with this approach. For example, it was totally dependent on the particular relationship and amount of empathy between

manager and employee. In the first extract below for example, the empathy was lacking, whereas in the second example below there was empathy:

When i 1st started my journey I was an assistant manager in a well know retail store. My store manager and area manager, at first, were quite sympathetic. This soon changed when i needed to go for daily bloods and scans Her attitude changed towards my treatment but then from then on i thought, stuff it, they don't care about me, Im just a number and instead of having the odd day off after embryo transfer etc, i had more time off to suit my needs and not of that of the business! Work is incredibly hard at the moment, my (female) manager does not really understand and my job is extremely stressful….I know I'm teetering on the edge of depression - I suffered from it in June 2006 following severe bullying by a senior manager at work (I left the organisation as a result but now have my own business). I feel helpless, scared and so desperately sad

Any hospital appointments that followed I emailed her about to let her know, and she was happy for me to attend…I was honest about my appointments, if they were in the middle of the day I took holiday so as not to be a complete pain, if they were early or late I worked around them….– I was allowed time off for egg collection and embryo transfer…He said he appreciated my being open and that I could just let the manager know when my appointments were, that was fine…She was fine about it, chatty, agreed the time I needed.. he was really pleased… The situation really hit me last October 4 days before my Nieces 1st birthday and I turned to our senior leader who was brilliant and really made a tough week as easy as it was going to be.

The gender of the manager was in some cases was perceived to affect their empathy for the employee, although not all female managers were shown to be sympathetic to requests for time off. For one subject it was less embarrassing to discuss the reasons for treatment with a female manager.

.Luckily it was a female manager who dealt with it.. .Work is incredibly hard at the moment, my (female) manager does not really understand and my job is extremely stressful…

The requirements of a business might include commercial and operational factors such as the business plans for the company and the need to cover busy shifts, as explained in the first example below. The demanding nature of infertility treatment, it's unpredictability and high failure rate mean that it can be difficult to plan time off in advance and this can create additional tension between the needs of the company and the needs of the treatment seeker. Again this is something that guidelines might have helped to clarify, at least reducing the stress on the part of the treatment seeker,

'*I was very upset in front of the nurses as I knew that it would be frowned upon as Saturdays are our busiest day and my area manager was visiting too'…I was made aware that this was very inconvenient to the business and sometimes I was made to still let the cleaners in the store at 7 am and wait until another manager arrived to relieve me from my duties…She was very annoyed and her words were " I am very sympathetic regarding your needs but I have a business to run and you're wanting to leave on a Saturday afternoon?!*

But then the stress levels seem to rise Which clinic? How long to get appointment? How much time off work? (as i work as a f/t nanny difficult to get time off!) etc.....I'm sure you have all faced the same choices!

Where a company has a clear policy regarding infertility treatment, which guides the decisions of managers, and employees then the employees feel supported and there is an increase in goodwill, openness and a willingness to be flexible in return:

Yes, I got the job on merit, I had no problems whatsoever with having time off; working for a large organisation, with a terrific foundation on offering staff a good work / life balance – I was allowed time off for egg collection and embryo transfer
We have it written in our t&c that females having Ivf are allowed an extra 5 days leave in a rolling 12 mths, so if you had 1 cycle every year you can claim the extra 5 days leave, men and civil partners are allowed 2 days in a rolling 12 mths.

I have requested my 5 days together as I am going abroad and have taken a weeks leave before and a weeks leave after.

Women were able to view the dilemma from both sides:
So just hoping things will work out and I won't need too much time off for treatment. I think they would be fine about it - and my line manager has young children of his own so should understand - but I wouldn't be pleased if I was them so why should they be?

Practical Issues

Proximity of treatment centre to work

Another factor is the proximity of the clinic to the workplace, which will dictate how long employees need to take off to attend appointments, and may affect their choice to disclose or not disclose their treatment. The choice of clinic takes several factors in to account such as proximity, funding and success rates:

As we chose a clinic some distance from our home, this led to quite a lot of time off
Luckily my clinic was only 20 minutes from the office and my scans and blood tests were always first thing I had a good number of blood tests over the next few months. I was a nursery manager and at that point I worked in a nursery on a hospital site so didn't really need to say much as it was easy to fit in…This made me feel anxious as I had to then travel 8 miles to the

hospital, get parked up and be there before 9. Whilst in the waiting area I was constantly aware of the time as they needed me back asap. Sometimes 2 hours would pass waiting from bloods and then onto scans, depending on how many patients were in that day.

The waiting lists for NHS funded IVF was outside of our timescales so we chose to go privately, made easy by the fact that the Clinic was about 20 minutes down the road…We have found a lovely clinic nearby with…Anyway fast forward a few months and we have been really lucky we have found a clinic 30 mins from home with excellent results and no NHS waiting list…as the travelling alone would be a minimum of 2 hours each time.

Flexible working arrangements

Subjects often showed a willingness to be flexible about time taken off for treatment, for example using their annual leave, which often forms the basis of a mutual trust in this process.

They let me book the Monday as annual leave for the IUI, and then we waited…
I was honest about my appointments, if they were in the middle of the day I took holiday so as not to be a complete pain, if they were early or late I worked around them… I was able to take a combination of flexi and holiday as I felt necessary

This also means that time off work that should be for rest and relaxation is being used for stressful treatment with a high failure rate.

Thanks to Easter I have not had to take too much time off work but have been back a week now…April 07 - 1st IVF - this was our private one. Got 11 eggs, 8 fertilised. 2 embies transferred 2 days later on 14th November - a 4 cell b & a 3 cell b. Took the 2ww off & did all I could to optimise chances..Again I didn't work during 2ww & I did all I did last time & a few

extra things such as acupuncture, a hypnotherapy cd, paraben free shower gel etc, no nail polish etc.

Sexual Discrimination For Time Taken Off

Taking sick leave can also avoid the need for disclosure unless they work for a company that demands evidence of medical treatment. For some patients company policy does not recognise infertility treatment as a valid reason for authorised leave and so employees who take time off sick might be threatened with disciplinary procedures as a result of time off. Women also used annual leave as a way of avoiding disclosure of treatment

Have now been to Cyprus twice without anyone at work having any idea of the reasons behind our trip – just a last minute holiday…We have decided though that as we have holiday in April we are going to try and tie everything in with that.
..They have provisionally booked me in for EC and ET for week beginning feb 13th and We have both booked off that week..3th August embryo put back, again not a nice experience but copable, like an extended smear test...2 weeks of pessaries, 1 week at work the other one on leave at M-I-L caravan to relax.

Taking sick leave for stress and anxiety caused by infertility or by infertility treatment can also avoid the need for disclosure unless they work for a company that demands evidence of medical treatment.

Shortly after this 2nd failed go I took some leave ill as I was suffering from anxiety/stress…I had depression and anxiety and had been signed of work prior to our IUI commencing, the miscarriage from our IVF just compounded that..It was the hardest thing i have ever done. Dr'ing was horrible, i suffered badly emotionally and didnt make it very long into treatment before needing to be signed off work….At this point very depressed . Hit rock bottom. Sure we would not have children! ..Signed off work for 2 weeks.. We finally saw the Cons again whilst I was on sick leave to talk through the treatment

options and she told us we could start as soon as possible as there was in fact DS available and no waiting list

Disclosure And Non-Disclosure

The conflict between their identity as a treatment seeker or as an employee can make it difficult for women to know when and how much to disclose to their family as there are risks and benefits to both positions. The benefits can include increased support when treatment fails and flexible working arrangements:

We finally told our families and very close friends what was going on. We'd wanted to keep it private but actually telling others was helpful - especially my family. I eventually also told work too when I requested to go part time which helped enormously... Went back to work today, which was hard, but everyone has been very sympathetic. A colleague at work, has a sister who has gone through IVF too which helps a bit, ….I was intending on working right up to EC but I really struggled with the side effects, mainly the hot sweats, very emotional and tiredness like i've never felt before. I decided to take leave from work until after ET – my manager was wonderful, so supportive!

For some patients, company policy does not recognise infertility treatment as a valid reason for authorised leave, and so employees who take time off sick might be anxious about being threatened with disciplinary procedures as a result of time off.

I can't get time off work until July so expect to start down regging June ish time.
I went to my GP last Monday and she signed me off for a week - i do not feel ready to go back to work yet but cannot get appointment at docs till Tuesday.... so what do i do re work and will docs renew sick note over phone?

Additional emotional distress may be caused by the financial losses associated with the cost of treatment or loss of earnings/promotion due to time off for treatment.

Know I am wasting my time but can't help hoping for a miracle. Just can't stop crying so desperate for me and DH to have a baby. Don't know where to go from here. We said we wouldn't keep throwing money at this but I just can't accept we won't have children…

I had to take a day off one day because I was so upset after a terrible appointment with a gynaecologist and having to explain why was awful, so I have that stress plus the stress of not getting paid for any time off I take for appointments.
proof to show work, that's also about 4 hours of wages a month I am missing out on, which doesn't sound like much but really it's the principle and I don't exactly get paid very much anyway

My 1st failed ivf attempt i was that upset that my partner rang in work for me to say that i wouldn't be in work the following day. I was hysterical during the conversation wouldn't be in work the following day. I was hysterical during the conversation and my manager could hear me in the background but because the company policy is to ring in yourself I didn't get paid… We couldn't afford the amount being asked privately and didn't yet qualify under the NHS criteria of 3 yeas ttc, (we were 2.5 yrs) so we looked into the private system to see if we could in any way afford it possibly with some help from family. Things really grim now because we are out of money and my hormones are utterly messed up and periods haven't returned. Need to be scanned for cysts. Feel in quite a low place now as time is ticking, my DD is getting older and money is very low

Theme Two - Emotional Distress

This theme explores the emotional and psychological suffering associated with treatment, treatment failure and the feelings of loss and grief as expressed by the individuals. This code was applied to text whenever the emotion was described directly or whenever emotive language was used. The code was not applied to text that merely described treatment without any emotional value being assigned to the experience. Spelling mistakes made by the forum posters have not been corrected and a list of infertility acronyms is included below to help with understanding the extracts:

AF	Aunty Flo, menstrual period
BNF	Big Fat Negative (pregnancy test)
DD	Dear Donar (Egg or Sperm Donar)
DH	Dear Husband
DPO	Days post ovulation
DS	Donar Sperm
ET	Embryo Transfer
GP	General Practitioner
ICSI	Intra-cytoplamic Sperm Injection
IUI	Intra-uterine Insemination
IVF	In Vitro Fertilization
LP	Luteal-Phase
NHS	National Health Service
PCT	Primary Care Trust
PG	Pregnancy
SA	Sperm analysis
SPA	Sperm Penetration Assay
TTC	Trying to conceive

Source: http://www.resolve.org/support/Managing-Infertility-Stress/infertility-acronyms.html

Subtheme Devastation and Injustice

Women frequently described the discovery of their own or their partner's infertility as 'devastating' and often questioned the reason for it happening to them:

I couldnt understand why this was happening to me.. to my shock was told I had a probable endometrioma on my ovary and most likely had endometriosis and would need a Laparoscopy….Unfortunately, I had a BFN in June and was utterly devastated…We were devastated. We didn't realise how much we wanted the baby until we lost it. If that makes sense! I was so shocked and yet again devastated and hurt -..the cycle was abandoned and I was devastated…As you can imagine I was devastated, I couldn't get my head round why this was happening, I've never been a bad person or hurt anyone why was this happening to us! This is the worst experience of my life. Every month is a bereavement. The unexplained element is bewildering and not understanding why drives me demented. The prospect of facing a future without ever experiencing pregnancy and having children of my own, is horrific…I have been in a state of panic and shock for most of the last 3 years… I have deep, deep feelings of failure, anger and incredulousness at our situation…The disappointment, injustice, lack of understanding I feel is overwhelming…. Of course I can't help feeling a little resentment, why do other people have a baby at the drop of a hat I ask?

Their sense of injustice might also include distress as a result of having to disclose their treatment or condition at work or anger at the way they have been treated at work.

Whilst typing it up i was sobbing as i felt humiliated and in disbelieve that i had to do it…She did her floor walk with the store manager looked at me and ignored me…I felt hurt and anxious…This made me feel angry and i spoke to the store manager about it saying that i felt sick and really upset.. I know I'm teetering on the edge of depression - I suffered from it in June 2006 following severe bullying by a senior manager at work (I left the organisation as a

result but now have my own business)…I feel helpless, scared and so desperately sad.

Women also perceived injustice when they compared the way they were treated with the needs of other groups such as parents of children who have childcare issues, men and civil partners.

..men and civil partners are allowed 2 days in a rolling 12 mths.. The worst thing is that people with children are allowed time off for 'dependant care', I know more than a few people who abuse this and take days off pretending that they can't get child care and they're not disciplined for it but when I had to take a day off because I was so distressed it went through as 'sickness' and I was given a verbal warning which stays on my file for a year… but I had disciplinary action as a result of being off that day..

Subtheme Access To Treatment

Not all women experience equality of access to infertility treatments and this was another source of perceived injustice, and having to fight for treatment increased their sense of emotional distress:

We were told that there was no DS on the NHS, we were told to go to the USA, we were told that the wait here would be 5 years...I have had to fight and got my MP behind me, harassed my poor GP to death and it went to the exceptional case panel. I have just found out that they have approved it and I get what I am entitled too. Whoopie doo! I should be grateful for that! I am SO angry. We were devastated and with my mum's help we complained to the GP and PCT and after 8 months of letters, phone calls, crying and appointments, we were transferred to another clinic….

Subtheme Treatment Failure

Women and their partners often felt immense grief at the failure of their treatment. The nature of infertility treatment is that success or failure can be encountered at every stage from ovulation, sperm production, fertilization, implantation, pregnancy test, scans to successful delivery of a live birth. These are all significant milestones which are either successfully passed or

mark a failure along the way. The use of language such as ‘cheated’ and ‘robbed’ implies that women felt that a successful outcome was due to them and is somehow being withheld. This sense of entitlement was also found in the extracts of data relating to husbands. The status of ‘wife’ is assumed to include the status of ‘mother’ as in the saying ‘wife and mother’ and when this does not come to fruition women experience a tremendous and devastating sense of loss.

Every month the cycle of negative test sticks is quite wearing …had 7th cycle using donor eggs, but donor pulled out. World then fell well and truly apart but found that leap of faith to try using donor eggs just once more…Felt like the end of the world…At this point i went on to the sales floor and cried my heart out…as I just couldn’t cope with the thought of someone else having what I longed for and as his wife should be entitled to.

i started to bleed even before the blood results came so we knew, yet our heart broke when we got the phone call with the negative result.. I was given the option of waiting or having an injection called methotrexate to end it. I chose the injection I could not wait. The next day it happened. I broke my heart, I wanted to hide away and I did, the trouble with losing something so wanted and precious if it changed you forever, I wasn’t sure I would ever get over this but I did with time and understanding

I couldn't believe I could feel so sad and empty. I couldn't believe that me, someone with nothing wrong with them, a youngish age and of good health, could get a BFN. I feel cheated and robbed and all the other horrible horrible feelings are that all of us here deal with on a daily basis.

Women were aware that age is an important predictor of success in infertility treatment and the loss of available treatment time due to misdiagnosis, failed treatment, life events or choices were an additional source of emotional distress:

I've recently been unsuccessful at ICSI (2nd attempt) and miscarried after a short time recently - 1 day before my 39th birthday so hugely disappointed and really struggled this time round - I feel a mid-life crisis coming on!

The women characterised their infertility journey using numbers such as time, age and quantities as units with which to describe themselves and to measure success, failure or progress of their infertility treatment:

We started trying to conceive in 2004 and fell pregnant after about 6 months but sadly miscarried at 7 weeks…. The GP told me that most couples will conceive within the first 6- 8 months of ttc, and the majority by a year… Anyway, things have been awful since then. Made extra 3 embryoes with first round of IVF. Had frozen cycle a couple of months ago. 2 died and 1 was 'barely there' on day of ET so no surprises we ended up with a BFN.

I am a 44 yr old woman with endo/cysts and a blocked fallopian tube. I had my son with a known donor at 40 using IVF at a London clinic (2nd attempt).. Me almost 38, DH almost 44..we have unexplained secondary infertility.. 6 miscarriages later, and unable to conceive since our last miscarriage in 2006, a failed IVF and recently a failed ICSI..

The biological differences between men and women also lead to emotional distress caused by women's sense of time urgency.

If I'm honest DH isn't as worried as me. He's younger and in less of a rush, he's more patient, he can't hear his clock ticking, he's more worried about money, he's got an exciting new job which he's really enjoying and if I'm honest he was quite dismissive and it seemed that he was relieved at the start of the year when we didn't get lucky

Subtheme Grief And Loss At Her Infertility

The women who had lost a baby or whose treatment had failed experienced a range of emotions that could also lead them to dislike themselves for

becoming jealous or ‘cold’ as in the first extract. The natural stages of grieving for someone who has not yet been born were all experienced and described as anger, grief, self pity, jealousy and ultimately exhaustion and depression at their failure as in the second extract:

I work in a hospital environment and and have to deal with seeing people who are pregnant and with children all the time, I have created a professional and cold shell I put up to allow me to function but inside I am screaming, tears come late at night after my husband sleeps and when I am alone - pathetic I know, I'm doing it again now. I used to like me and I am a good person I hope, most of the time -I am a caring person, now all I see is a stressed and tired woman looking back at me at odds with the world wondering when did all this take over me and when will I ever be able to not wake to the thoughts I do and drift off to sleep without a tear stained pillow.

It's like I am grieving for the child that hasn't been born.. I’ve got to the point where I have moments when I really struggle and feel utterly consumed with sadness at the thought of no baby..I know I have a lot to be grateful for, and I am, but I also have this void, this huge emptiness that hits me like a kick in the stomach when I least expect.. This news made me feel inadequate, a failure and less of a women. The sense of failure that I can’t do something that to me is part of being a woman – being able to have children, when some people find it so, so easy.

Finding something physical wrong may mean that an explanation of infertility is provided and with it the hope of a solution:

Part of me really wanted them to find something physical so we could pin point it and fix it! Had a cry after the procedures from all the pent up anxiety, frustration and much relief that my body is in working order…So went for the scan with DH in tow, & the sonographer asked me if I knew I had ovarian cysts. Cue a bit of crying, followed by rational 'at least we know & can deal with it'.

Emotional Support - Relationship with Partner/Dear Husband (DH)

Some husbands and wives were being able to share their grief work and by working to support each other survive the stress of infertility:

Thankfully my husband was there with me and we grieved together… I sobbed and howled, my husband and I were inconsolable, our hearts were broken. Seeing my husband cry was also extremely distressing. It took a few weeks to get back to any sense of normality,..

After that appointment we decided just to stop everything for two months, to concentrate on each other again, go on holiday in the sunshine, see our friends and find some joy in our lives again... We've managed to get our marriage back on track and despite the ongoing pain of infertility, are stronger than ever

A more unusual situation occurred when the husband would like to wife to continue with treatment in spite of her own feelings about it:

My husband and I were in shock and disbelief at first, I just felt numb - he was clearly devastated and angry. 4 months on my husband wanted me to try IVF again. 6 weeks ago I told him that there is no way that I can do this again for the moment - if it did not work then this would just destroy me. I don't know when we will do it again now, but have said that if we do it again then that really is the last time I can go through this god awful process!

Women who felt that their husbands had not supported them emotionally blamed this on a variety of reasons, their own anger and grief, their own sense of isolation, his family background and their obsession with the need to get pregnant:

BFN followed and I lost the plot, was on a plane the next day to see my parents in Spain and to give my DH a breather from the mad woman... DH isn't coping too well. He is doing the caveman bit and retreating. So I thought this would be a good way for me to get off my chest, stuff I know I want to say to DH, but cant at the moment.. Successful transfer then spotting 2 days before pregnancy test, which was, negative result. My husband and I were devastated..

I am all alone away from my friends and family and honestly don't know how to get through the next few days. My husband is the silent type who says he just wants to move on... When I suggest getting a second opinion (preferably in a language we can understand and in a country with few legal restrictions) he says I must not get scary and obsessed.

Everything spiralled down, with me pushing Matt away at times, it was easier to grieve alone, or so I thought... After the SA results dh and i seriously grew apart. I was a like a demon possessed, desperately searching the web for info and stories of ivf and reading every book going. He on the other hand refused to discuss any of it, completely shut me out of everything and stuck his head in the sand (plus he didn't want me to talk to anyone either, got very upset if i mentioned wanting to speak to any family or friends and all but forbid me to even speak to my mum!!). Eventually the strain became too much and we split.

Over the year things have moved on, I've regularly broken down - tears most month, the odd hissy fit for no reason and a couple of good heart to hearts. I'm still hurt that he never seems upset. Does that make me weird? It's not that I was to see him upset but I want to see that he cares. He's being more supportive as time goes on and I'm sure it's just a mars venus thing. Sometimes it seems he just saying the right thing but doesn't really feel it but then his family are dryer than mine emotionally.

Subtheme It's Ok For Him

Women who have married a man who already has children and then finds that they cannot have children together are often in a difficult situation, as some PCT's will not fund their treatment. The resentment that this inequality brings may be added to the feeling that partners with their own children do not understand the depth of suffering experienced by the infertile partner:

My partner had 2 children to a previous relation ship which made things more difficult for me to cope with, and at times i thought that he didn't even understand, as after all he had 2 children, so how could he?

Picking up my partner's three children and seeing the mother of his children, only added insult to injury. They do not know about what we are going through so there have been lots of excuses and brave faces, something I could have done without. My partner has been brilliant and very supportive but dare I say, this is very different for him: he has three children and he is a man so I believe his understanding is limited. No one can understand this unless you have been through it yourself.

I was living in ignorance, thinking that I might just need some tablets and now I am sterile! My DH is trying to understand but he has and always will have 2 lovely children. What about me? I have to heal for 3 months now before I begin the "real" journey but feel like I have been through the mill already!!!

It's His Fault

Women who found out that their infertility as a couple was caused by a male factor were often shocked to discover their husband was not able to produce healthy sperm. Their desire was to have a biological child with their partner and alternatives such as sperm donation had to be come to terms with so that their treatment could proceed. Men also experienced the news as a tremendous assault on their masculinity:

DH is azoospermic (absolutely zilch). He dealt with it as only men can - very badly. He was turning 40 as well, and all that turned into a mid-life crisis of sorts. Pleased to report he's on the up, just as I lose my optimism and stamp my feet about the injustice of it all!..After DH going to pieces initially I think he was expecting the negative result but I was, and still am, completely floored. My best friend has just had her second child and the fact I will never have DH's baby makes me feel sick. I am finding it very, very hard to accept…we had bad news that unexpectedly my DH's sperm count and motility had drastically reduced so they couldn't go ahead with IUI - we were totally devastated and couldn't understand it and neither could the clinic because he was fine a month before. It felt like the world was falling apart…I still feel very , very sad that I will never have my husbands biological children, I will never look at them and think they have his nose / eyes / build etc. I still feel that I don't want another man's baby and feel guilty that my fertility (as far as we know) is fine, and cannot imagine how he feel..

Specialist asked husband to do sp.test - to our shock it came back low - 8ml. Advised to do a secondary swim up test. Returned to the hospital in Nov for results, devastated to find DH result was even worse at 5ml…Married in 1997and started ttc in 1999, after about 9 months we went to the doctors and had all the initial blood tests and sperm samples were sent away but to be honest we didn't really think anything of it, therefore it came as a massive shock when dh sperm sample came back as no sperm in them, my blood tests were all ok…

The use of donor sperm was one of the easier things to come to term with for me…

I had to break the news to my DH when he got home from work and he was devastated. We then waited two weeks to see a consultant to explain things ….As I'm sure most of you will understand we were devasted and my DH feels awful - he even told me I should leave him and find myself a 'real man'. Felt so bad and no matter how hard I tried I couldn't make him feel better. Scary to think of the journey ahead but I want children with my DH not

anyone else... My husband has did not really speak about our news and I suppose I had to let him come to terms with it in his own way as it's male factor infertility, all my tests came back normal.

Subtheme Isolation

The sense of isolation caused by infertility may affect relationships with family, partner, friends or colleagues. Some times this is because women have not disclosed their treatment and sometimes because they feel that no one can understand how they are feeling.

I am SO unbelievably happy for her but man was it difficult the first few months of her starting to show. It was just so hard. I just wanted to hide. With time I am getting better about it but it still is just so difficult. She is my best friend and we depend on each other so much as our families are far away but our friendship is so strained right now.

Where we live, most of our friends now have children or are expecting, which has left us feeling quite isolated - we sometimes joke about the fact that we need to find new friends. Of course we still spend time with our friends, but their life styles have changed and they cannot do the same things as they used to…

I think the hardest part for me is that three of my four closest friends are all pregnant and all became pregnant in the first month of trying. I feel alienated from them as babies and pregnancy is all the talk about with each other. Sadly I feel I am avoiding situations when we are all together. I know it has affected my friendships with them. It not their fault they are pretty sensitive but they can never understand the frustrations having month after month of disappointment as then didn't even have one. .. Perhaps I am being mean?

I get very low and because so few people around me are aware of the problem, I often feel misunderstood…what I'm struggling with the most is how distant I now feel from a lot of my friends who were once in the same boat as me but now seem to have got on with their lives with their new

families and we just don't see so much of them or it can be a little strained - I guess they don't know what to say, others are just plain silent.

I can't stand the loneliness anymore. I was initially reluctant to tell anyone because I had this idea in my head that I would get pregnant and it would be this amazing surprise to everyone

The pain of infertility is so entrenched, all consuming and inexplicable, it will never ever leave me. Unless you have been there, it is really totally impossible to understand. I cannot begin to pretend to understand the depth of pain of total childlessness, but I have a fair idea of how I felt dealing with our infertility. I wouldn't wish it on my worst enemy. Its unfair, cruel and heart-breaking and nobody should have to suffer it, least of all alone.. Knowing no one who has gone through the same thing I have found this a very lonely time.

The experience of being infertile while others are starting families makes it difficult to maintain existing friendships because the fertile women take on a new identity and wish to celebrate their new status as mothers. The happy new mothers or their families are perceived as insensitive and lacking in support, this may be made worse when grandparents are seen to be helping fertile siblings or friends with their children, so the lucky mothers who get the baby and the support of their families:

But feel that all other family members are really negative and would rather not know what is going on. No support- I get really frustrated by this.... and makes me feel worse... especially as my parents are so supportive of my sister and her 3 children…

In an ideal world we would be open with those closest to us but people struggle with understanding how we feel and find it awkward knowing what to say. Listening to comments like "you'll be ok in the end" or "relax and stay positive" don't help but can understand why people say them

But my husband's family have found our situation hard. They have (not consciously) made it much harder, especially this year since the birth of their first grandchild. The comments that have been made, the pressure that's put on us to attend big family get together and the lack of understanding even though we've tried to explain is proving really hard to deal with and causing us a lot of distress

One of the struggles that infertile women have is to face the fact that fertility very visible and is celebrated in our society and that they are constantly faced with reminders of their own inability to conceive:

I cannot stand pregnant women, especially the ones who are oblivious to the fact that someone around them may not be as lucky as them and who think everyone should fawn all over them and make a fuss of them (a so called friend who knew what I was going through thrust her positive pregnancy test under my nose a week to show me her success after I had my first failed IVF such was her lack of empathy and self absorption). I've had some pregnant friends who have been lovely and worked hard to not rub my face in it but I really have difficulty being around them. When I cry, the grief comes from so deep down in my very depths and I just howl with sorrow

I´m surrounded (it feels like) by pregnant people and I can´t relate to them anymore and more importantly feel incredibly isolated, as my usual sources of help and support are pregnant and how uncomfortable for all involved to pour your heart out about being childless to someone heavily pregnant!!!! Or

Im sick of the pregnant people, sick of new mums with babys forcing theirs on me and the pitying smile of "it will be you soon dont stress it will happen!" Im sick of the announcements and the " i wanted to let you know im pregnant and i dont want to upset you because you cant have one!" Ive had enough of it all, i hate being the only wife alone. They all group together for mum and baby stuff and im left out on the side lines forgotten about because i dont fit into their group!

Friends around me didn't understand and I felt lost and left out the loop or club. every announcement that was made by friends made my isolation worse.

Infertile women may also find it very difficult to cope with close relations becoming pregnant or finding out that someone has had an abortion because that is seen as deliberately throwing away the one thing that they truly desire, and as another injustice to add to the situation:

I'm also having to cope with a difficult family situation. My younger (29) sister got accidently pregnant last year and chose to have an abortion. She and my mother debated not telling me, but did. So I had to bury all my own feelings to support her including listening to her complain about her pregnancy symptoms before the procedure. Didn't she realise that I'm desperate to feel like that? Life is so unfair. That little life was flushed away. My sister is incapable of offering support to me so I'm feeling angry at her (for this more than the abortion). We've now fallen-out and I don't have the emotional energy to sort it out.

then my younger, unmarried, unattached sister announced her pg and it felt like a knife in the heart...I cried and cried and think I lost the plot for a while. No-one understands as all my family and freinds have kids and if anyone else says "at least there is IVF", I think I wil hit them! Lol.. I have to put a smile on my face and pretend that I am ok to everyone around me cos I think they will get sick of hearing me moaning! It would be great to hear back from anyone as I feel so very alone right now

Subtheme Getting Help

There were two main ways that people sought help for their emotional distress, formal counselling and the use of the forum to share their feelings and read about others. The counselling as a support therapy was often seen as helpful in coming to terms with their situation and find strength for

further treatment. The use of a professional counselling service allows the benefits of disclosure with out the risks associated with disclosing to friends, family or work colleagues.

.I had counselling throughout the first cycle and through our loss, every week. Our counsellor was fantastic…From speaking to the fertility counsellor I realised my feelings were normal and as a result I haven't beat myself up about whether I'm being irrational…In time counselling helped me to see things differently. On reading some of the stories, I decided I was strong enough to look to the future and I booked a counciling session for us and an appointment with the hospital nurses to discuss the next steps as I wanted to again donate my eggs…

The forum was used as a place to tell their story and draw inspiration from the strength or successes of other women and men going through the same processes. It was widely reported that they knew that the other posters would understand their situation and feelings. The isolation that women felt in their life outside the forum could be assuaged by contact with other women in the same situation, they created a new identity as a forum user by becoming part of a group or community and described themselves as 'us':

Went through IVF in 2007 in Oxford and conceived by beautiful, amazing DD first go. Feel very guilty writing that but hopefully it gives people hope. Dreams can come true.

I'm fairly new on here and joined in the hope that some of you are in similar situations with male infertility. I feel very alone, but know that I'm not alone - just don't know anyone who is in the same situation. …Has anybody out there, had a similar situation? I really feel like I need to talk about this, but like most people on here none of my family or friends understand. New to INUK so thought I provide some background to my story and hope to speak to individuals who understand the pain I am going through… I joined IFUK to remind myself that I'm not alone, and I'm encouraged by the stories on here.

It is great to know that I am not alone in this desperate situation but sad that there are so many of us out there…This is the first time I have written anything about what I'm feeling in relation to our 'unexplained' infertility. ..This is my story. I would really like to hear back from anyone who is in a similar position as I don't feel there is anyone I know who truly understands how I feel. I found out this week that our second attempt at IVF didn't work…I'm looking forward to hearing from you lovely ladies, and knowing that I've got this forum as an outlet.. I'm so glad I've finally joined this site. I dipped in and out for so long, but got to the point where I really needed someone who properly understood. Friends and family support, but it's not the same.

Well, I picked up a card for INUK 2 1/2wks ago at the hospital having ET, I desperately hoped I'd never have the need to find out what it was all about, but here I am so that says alot…It's just nice to have somewhere to put my thoughts and feelings. It just helps me to write about it…but would love to hear from anyone with words of encouragement to keep my spirits up and to hear your own experiences of IVF.. Hopefully, like anyone who may read this, one day the longed for result will happen and this constant ache and emptiness will go away.

The act of writing their story was seen as a way of acknowledging that their situation was real:

I will update this piece by piece as there is just too much to put down in one go. I think I am trying to prolong putting it all down as once it is written down then it becomes real, our story, something I wouldn't wish on my worst enemy... but the loneliness was just too much to bear. So we have gradually starting telling people. And this is my next step in reaching out, writing this… this the first time I have ever really sat down and tried to tell anyone about all of this....sorry if I go on, just don't have anyone I can discuss this with and to find this network has opened my eyes so much, hopefully you won't judge me. Up until now I felt like the loneliest person in the world!

The forum was seen as a safe outlet for disclosing their infertility status where they could share their feelings without hurting the feelings of other people in their everyday life and where they could be sure of support:

Feel very alone with all the worry as my partner gets upset when I get tearful about it all, so I try to keep as much of the black mood to myself as possible. Most of my friends have kids and say they feel guilty if I tell them how sad I get...so - quite isolated and blue. that's why i'm here… I felt something like this may help if I had a focus each month where I could talk to others in the same situation and we could swap thoughts. I had felt so alone before this.

Sorry to be moaner thanks for listening it's helped just to put this to paper so to speak. Better go and put my face on again and pretend everything is OK... am getting to be quite the expert…I've been in tears reading some of your experiences - thank you all so much for sharing as it must have been really difficult… I really just need to be in touch with people who understand and can make me feel less lonely…The support and stories on here give me hope that miracles can happen. Just so empty at min and finding it had to carry on.. We havent told anybody about our if so when we found this website it was a godsend and provides the needed support although to date we havent come across anyone in the exactly the same position.

Subtheme Out Of My Control

Successful professional men or women who are used to feeling in control of their destiny may also struggle to come to terms with the loss of control associated with infertility and infertility treatment leaving them with a need to create new *strategies for finding success or coping with failure:*

I had always worked hard with determination and commitment in everything I had done in my life...but this..this was different. It didn't matter what i did I could not influence the outcome
l. I would need IVF!! I was devastated, I had been lead to believe I would just need some pills?..After a long wait of 25 months, one beautiful wedding and

both brothers having 6 children between them and me feeling a complete failure

I am 30 in August and DH will be 39, like all of the ladies on this wonderful site I dread every birthday and every Christmas as for me it marks yet another year of ttc and for me it makes me feel a failure. I was a successful carrer girl and controlled all aspects of my life and this is the one thing I can't control or buy!..

And now I feel like I am totally failing and there is absolutely nothing I can do to improve the situation – I can't study harder, I can't work longer hours, I can't be a better daughter or wife. Usually I know the answer to things and know what I have to do to improve the situation. But not about this. I've always been known as the 'rational' friend, the person to turn to in need, the person who can work through things logically.

I am a successful professional and I have always held the belief that if you want something badly enough you will get it with determination and grit. Whilst that may be true of career goals, it doesn't seem to be true of fertility. I am used to being in control and calling the shots. This infertility experience has left me feeling hopelessly lost and despondent.

The cost to patients of being infertile and undergoing infertility treatment may be financial, emotional or psychological

It's not so much the cost of all this treatment but the cost to me emotionally, and in time off work….Cycles appeared to return to normal then april to june cycle 7 weeks - think this is due to huge stress and unhappiness at work..

Despite the difficulty in reconciling their identities as treatment seekers or employees women viewed the opportunity to conceive and have a family as so important that they were prepared to try and balance the demands of both roles:

In 2009 we started our treatment. It hasn't been that bad but the emotional journey is quite hard. I spend so much time trying to convince myself that we should just accept that we don't have to have children and we can get a dog or travel again but the desire for a family has become so great now that I can't see how I will accept just being the two of us.

Hoping that it is going to be that week as will be difficult to rearrange the time off. Plus found out recently that I am moving to a new department in work first week in March around time of end of the 2 week wait (assuming the dates don't change). Not the best timing! Will have to get to know new staff, new boss, different way of working! Not ideal but hopefully will be ok.

Am just playing the waiting game now- was hoping to start asap while I am on summer holidays (I'm a teacher). If period arrives this week, embryo collection and transfer would be in the first week of the new term. Not very convenient!

Work wise, I am in the middle of an intensive three year training course where TTC isn't the best idea, but at the same time having a family means so much to us that we want all the precious time on our side that we can get

In October, it was announced that my office was going to close, this really hit me as I moved to this office so that I could have mat leave, return to work part time, and be close to home, that made me really sad,
Work is crazily manic and I worry about my ability to balance the relaxed zen that I need to get through the next few weeks with my need to perform and not let the side down in work.

There were some indications that when one identity failed (ie failure to conceive) the alternative identity as an employee provided a solace or a distraction:

I came off the pill at the same time that I left a busy stressful job in London and began working for myself at home. So we were trying but not trying too hard whilst I worked on getting the business off the ground… I am staying busy, went straight back to work after the results on monday and havent stopped, think thats the best way for me…

When I was having treatment I didn't tell anyone at work although I was tempted on several occasions. I'm really glad I didn't. It was hard getting over the disappointment privately so dealing with other people too wouldn't have suited me. It also meant at work I could temporarily forget about it.

My one good luck story in 3 years has been my new job, which I started 2 weeks after 1st IVF failure. So now, at least, DH and myself are both finally settled in jobs that we love, so some stability at long last.

Conceptual Model The Risks and Benefits of Disclosure and Non-Disclosure

The infertility 'journey' may involve multiple appointments and consultations as the subject is passed from his/her GP to a specialist clinic. There will be appointments for ultrasound scans, internal examinations, sperm analysis and blood tests before a treatment regime is decided. In many primary care trusts there are waiting lists for treatment.

Infertility treatment is demanding and often unpredictable by nature because each stage is controlled by the patient's responses to the earlier treatment. The response to ovulation drugs, the number of sperm or eggs retrieved, the number of fertilized eggs, the number of viable embryos, fluctuating hormone levels are just some examples of the dependent variables that might influence timing of the next step. This means that women cannot simply plan a schedule of treatment and hand this to their manager with a request for time off.

Now I'm going to need time off twice a month for ultrasounds and blood tests and it will be extra stressful because these appointments will be made over the phone…They said that i may need to go back that day for my treatment… This was really frustrating as it is not an exact science and all depends on your body clock…

Ironically women are often told that stress with decrease their chances of conception and that they need to stay as calm as possible

Prior to my second cycle I was told that I needed to stay as stress-free as possible and ideally reduce my hours of work.

Women had to make a decision about whether to share or withhold information about treatment with their friends, family colleagues or managers. The decision to disclose or not disclose was seen as central theme in this

analysis because it connected the idea of an identity crisis (am I a treatment seeker or an employee?) with the risks (emotional distress) and benefits (practical and/or emotional support) of telling work, friends, family or forum members about their status (see Table 27 The Risk Benefit Model of Disclosure).

The decision to tell work was sometimes prompted by a need to arrange time off and gain benefits such as flexible working hours meaning that women took a high risk for high reward approach:

I eventually also told work too when I requested to go part time which helped enormously…Going to speak to my Fed rep at work tomorrow and advise her of what we are doing so I can get some guarantees of support from my bosses.. I have to say though that our employers have been fantastic. My boss even looked at the INUK site and fact sheets and has been great at telling me to take as much time as I need, not to rush back to work etc. I couldn't have asked for more, so we have to count our blessings on that front. They have been incredibly understanding..

One of the risks that women took was that disclosure at work might compromise their identity as an employee with a loss of status, income or promotion:

The day after our diagnosis I started the biggest job of my career in a new company. I don't tend to do things by halves .. To top it off Ive been offered a promotion at work but don't want to accept it if im going to start IVF this year.

The confidentiality gained by not disclosing their treatment status may be violated because company policy demands evidence of medical appointments:

I had to take a day off one day because I was so upset after a terrible appointment with a gynaecologist and having to explain why was awful.. I had

no choice but to tell work because I work in a call centre and can't just come in and leave when I like, i have to show proof and they have to photocopy everything and time off has to be approved depending on the staffing

The lack of a clear legal framework to guide managers can mean that there is an inequality in the way that subjects were treated in different companies. Some were disciplined for taking time off, some decided not to disclose and some were supported emotionally and practically by their managers:

Work is incredibly hard at the moment, my (female) manager does not really understand and my job is extremely stressful… and hurt i rang the union who gave me some really good advise and they told me what she was doing was more of sexual discrimination rather than victimisation. .. but I had disciplinary action as a result of being off that day.

Compared to:

My company have been fantastic and haven't even asked to see any evidence of treatment… possible but that I was taking a drug (clomid) that impacts on your hormones and I would need a blood test at day 21. They were fine with this and I think appreciated that I could have completely kept this to myself, both the owner and the manager have two young children…

A decision not to disclose treatment at work was sometimes the result of a desire to protect privacy in an emotionally sensitive situation:

When I was having treatment I didn't tell anyone at work although I was tempted on several occasions. I'm really glad I didn't. It was hard getting over the disappointment privately so dealing with other people too wouldn't have suited me. It also meant at work I could temporarily forget about it… I haven't told work anything yet - I think I may have to but very reluctant - especially as its such a small team, there are about 10 employees… I am not telling work either, my job is quite pressured and I couldn't stand the speculation. They already suspect I am pregnant as I put on weight post wedding. The irony of

it isn't lost on me!! …So the next step is basically doing it! We have to keep things very quiet here at work, for many reasons, so getting the time/dates to do it is proving a bit of a nightmare.. .

Maintaining their identity as an employee sometimes meant that infertility distress had to be hidden away behind a professional façade:

I work in a hospital environment and have to deal with seeing people who are pregnant and with children all the time, I have created a professional and cold shell I put up to allow me to function but inside I am screaming, tears come late at night after my husband sleeps and when I am alone - pathetic I know, I'm doing it again now.

Confronting this conflict led to some women realising that they had to adopt a different position or identity:

I also went on a motivational course with work in January and had to face up to some things and be honest with myself that family is more important than work for me. I think I was going for promotions as some sort of displacement for how I really feel!

The intimate nature of infertility treatment and the social stigma attached to being infertile mean that subjects may wish to keep their treatment a secret.

We have decided not to tell anyone about our situation and over time a lot of people have stopped asking us questions. … it took me about 5 weeks to pluck up the courage to show a manager my letter from assisted conception with my first appointment on it because I was so embarrassed, my boyfriend also works in here so that makes me feel even more embarrassed - I really wish that managers in here didn't know so much about my personal life.

In addition to this the high failure rate and the emotional vulnerability that this engenders may mean that subjects want to protect themselves by not sharing what is happening. Women who decided not to tell their friends and

family sometimes were motivated by the shame that either partner felt about their infertility:

I have chosen not to tell many people because I do not think people understand unless they have had to deal with IF themselves. DH struggles to talk about it although he does talk more since the IVF. But I do not think men have the same need to talk as we do and of course Male Factor IF does have a big impact on the male ego.

Not telling friends and family provided privacy but it also has the effect of isolating women from potential sources of support or understanding, a low risk but low reward approach:

He on the other hand refused to discuss any of it, completely shut me out of everything and stuck his head in the sand (plus he didnt want me to talk to anyone either, got very upset if i mentioned wanting to speak to any family or friends and all but forbid me to even speak to my mum!!). Eventually the strain became too much and we split. I am in my Mid thirties….Can anyone help me in my isolation , i have had to carry out all past procedures in secret apart from a few close friends and family members

The benefits of disclosing their infertility status to friends and family were that it created an additional source of support, but at the risk of losing privacy or status, this could be seen as a high risk but high reward strategy:

We finally told our families and very close friends what was going on. We'd wanted to keep it private but actually telling others was helpful - especially my family… I've told a few close friends but not a wide circle of people that we're ttc. In a way the more people you tell the more pressure you put on yourself. After all the end of your story to conceive might (sadly) be a bit of a way off. Telling my friends was hard (silly pride) but having one of two people you can really open up to aside from your partner I think is a real comfort…

There is also the risk that family or friends will not provide the expected support:

I told my mum who is quite ill herself and she was naturally very upset but instead of the support I thought I'd get she said "if you're trying again please don't tell me until you've had the all clear ad it's too upsetting for me"!!!

The benefits of using the forum as a means of disclosure were that privacy was protected by using an online identity but they were guaraneeted a sympathetic and receptive audience as a source of support and so this was seen as a low risk, high reward strategy:

We haven't told friends or family, we are quite private and want to do this our way. This site really is an outlet for me to share and understand others experiences, even more so for us… We havent told anybody about our if so when we found this website it was a godsend and provides the needed support although to date we havent come across anyone in the exactly the same position….We've had three cycles in all now, ending in BFNs, but we've really kept everything to ourselves since that first time, which I don't think is healthy - hence finally, so very late in the day, joining in the forums, although I have been reading your posts and thoughts and feelings. I can't say how much they have helped me through some dark times

STRATEGY	RISKS	BENEFITS
TELLING F & F	Being misunderstood Emotional pain to self and others Disappointment at treatment failure Loss of privacy	Receiving support and understanding
NOT TELLING F & F	Not receiving support and understanding Creates a sense of isolation	Protects privacy
TELLING WORK	Loss of earnings Disapproval from manager Career prospects damaged Discrimination Being misunderstood Loss of privacy	Support and understanding Flexibility for time to attend treatment
NOT TELLING WORK	Disciplinary action and Loss of earnings for time off Not receiving support and understanding	Maintain privacy and professional role
TELLING VIA FORUM	Negative experiences reported by others might be overwhelming.	Support and understanding with privacy due to anonymity

Table 27 The Risk Benefit Model of Disclosure

Triangulation of data

Source One

The forum administrator from IFNUK had previously collected some data on the concerns of working women and these were shared as amalgamated extracts with the researcher:

TELLING YOUR EMPLOYER EXAMPLES

1. *I've chosen not to tell my work about my IVF journey- I felt too vulnerable. My firm has suffered badly with the recession in the last few years, and still makes regular redundancies. I feel that them knowing that I am trying to get pregnant will put me in line for the next redundancy*

2. *I work as an Accountant and have a great career with my current employer. I am in the Top 20% of my current band, which means promotion within the next 12 months from Management to Senior Management. If I had discussed with my Manager, I would be discriminated against with regard to next job moves and promotion.*

3. *The CFO of the business is basically 'leader of the boys club' and has made particularly unprofessional remarks about women in Finance who go on maternity leave. Whereas I have the added stress of trying to be discreet and take time off sick, my husband has the full support of his male boss and everyone in his office. When really it is I, who need the stress taking away so that I have less to worry about whilst waiting for results.*

4. *I told my employer that I was going to be doing IVF, but in my case, I only told my immediate manager (a man) who was very understanding, having had a very close friend go through IVF treatment and so was aware of the stress and trauma that*

could arise.. However, I believe that a lot of the trust and support he gave me had been earned through the years, as I was very good at my job, hugely reliable, and dedicated to still meeting deadlines and responsibilities even throughout IVF treatment. This meant that I could take some time off etc without questions being raised, and also so I could avoid some foreign travel which I would have normally done very frequently. He treated me very fairly and it was my own choice to book some days off as annual leave rather than using sick days, although in hindsight I should probably have used sick days. My manager didn't ask too many questions – but asked just enough to make sure I was OK.

5. *I wanted to pass this on as I think there's a big difference in telling the 'company' you work for – as opposed to just telling your manager. Unfortunately, not everyone will have such an understanding person as a manager!*

WHAT TO TELL YOUR EMPLOYER EXAMPLES

6. *I'm the first person at my company to go through ivf although I know a few colleagues have had time off for miscarriages. There are no policies at all in place and it's quite obvious my boss and manager (both mums) haven't a clue about what ivf entails and how much of a strain it is not only physically but emotionally. This round they have kindly agreed I can take time off for stimming and collection and transfer as unpaid and then I'm taking holiday for my 2ww. However, they cannot understand why I do not want other members of staff knowing what I'm going through and give me the impression I'm being awkward and a bit precious by saying it all must remain confidential. They also do not understand why I'm finding it all so hard emotionally. This then adds to my stress as I'm worrying about my job as well as the ivf. .*

7. *My husband works for a very large global finance and business advice company with offices in London but also across the world. He spoke to his HR dept about accompanying me to appts and collection/transfer who said "the company does not support IVF"! I guess it just shows even big well known companies just are not up to date with fertility treatment and how to manage the situation. It's also a company which entitles employees to up to six months paid sick leave a year, so if my husband was going through depression etc he would get the time off with full pay.*

8. *My company does not have an IVF policy and like many other companies decisions are made by line managers about how IVF is dealt with. I didn't tell my boss until I felt like I had to. I increasingly needed to take time off for appointments, often at short notice, and due to it being an NHS cycle I was often waiting for 1-2 hours before I was actually seen so it didn't seem like an option not to tell her. She had started to worry that I was looking for another job!*

MANAGING TIME OFF EXAMPLES

9. *I opted to tell my boss before my 1st cycle, and gave suggestions about how I could best manage things. I manage a team of people, and was keen to ensure I was as stress free as possible. I also confided in a friend at work which was invaluable as a sounding board when needed. if your boss knows, then it may be possible to keep your diary more open and flexible during this time and maybe you could work from home around appointments on the days you have to go to the clinic*

10. *I had a chat with my boss and she told me that she doesn't want to set a precedent of people working from home, but she will give me a few days of compassionate leave and I can take*

the rest as holiday - so I don't need to go into the office and juggle/rush backwards and forwards from meetings during this time (which was my biggest worry

11. *The further into this process I get, the more that I really feel that the law has to change to give women going through IVF more support. It's just ridiculous in this day and age that we have to go through all this worry of trying to negotiate days off and having to juggle sick leave and holiday. For most other serious health conditions - and IF is a serious health condition - there would be no question about taking time off for treatment*

12. *I was lucky and my boss was fine about time off. This may be because I'd already worked at the company for 6 years when I started treatment and had had no other sickness and always worked hard. My boss's attitude may have been different if I often took time off or wasn't fully commited to my work.*

13. *Prior to my second cycle I was told that I needed to stay as stress-free as possible and ideally reduce my hours of work. This is not practical in my job but I spoke to my boss and suggested that I work from home a couple of days a week which she agreed to. Reducing my hours would only have stressed me out as I'd have the same work to do in less time!*

The extracts are included, despite the lack of knowledge about the sampling, because they form a useful comparison with this analysis but were not used to create the codes or themes in this analysis as there was no indication of the method used to obtain them. Permission was granted by the forum administrator to include them in the thesis.

Extract 1 relates to the decision not to disclose treatment because their identity as an employee will suffer, they will be at risk of losing their job because their company is making people redundant. This is despite the fact

that her company would not be allowed to discriminate against her during IVF treatment without laying themselves open to sexual discrimination charges.

Extract 2 is also an illustration of someone who has chosen not to disclose their status but for the reason that they are doing well in their career and want to be considered for promotion. They are illustrating the basic conflict between identity as a treatment seeker and identity as an employee as being mutually incompatible. Both examples of disclosure are perceived as being high risk decisions because the identity as an employee is uppermost.

Extracts 3 and 11 are examples of the injustice felt by women who face sexism at work and are distressed by the fact that they need emotional support more than ever during treatment. They are forced to conceal their status as a treatment seeker by being 'discrete' and taking sick leave. Women would like to be able to reconcile their identities as being both employees and treatment seekers by seeing them as belong to different domains, one is about their health and the other one is about their work.

Extract 4 shows the benefits of disclosure at work if there is a supportive manager or company policy leading to a mutual negotiation of flexible time off and empathy. **Extract 12** implies that this employer goodwill has to be 'earned' by being a good employee rather than having a legal right to sick leave or pay.

Extract 5 is an example of how the personal relationship with the manager can lead to a 'partial' disclosure to the 'person' rather than the company. This illustrates the empathy theme and also shows that not all female managers are more empathetic than male managers.

Extract 6 describes the emotional stress caused by lack of empathy from managers even when they have agreed to be flexible. There are no company policies in place so protect the privacy of the treatment seeker.

Extract 7 highlights the way that infertility and infertility treatment are not recognised by some companies as a legitimate reason for men and/or women to take time off work. This lack of recognition of their condition means that the legitimacy of their identity as a treatment seeker (as a health issue) is also being challenged at work, this is why the identity as a treatment seeker conflicts with their identity as an employee as they are contained within the same domain of 'work'.

Extract 8 shows how the decision not to disclose is sometimes pragmatic because of the demands of treatments and the need for flexible working arrangements and the fact that the company has not clear policy.

Extracts 9 & 13 provide a positive picture of the benefits of disclosure at work and to a friend in order to receive support and flexibility in return. The identity as a treatment seeker and as an employee are integrated and the tone of the extract is positive.

Extract 10 illustrates the theme that time off has to be taken from holiday time or as compassionate leave because the company has no clear policy and doesn't want to set a precedent, again denying the legitimacy of the 'treatment seeker' role.

Triangulation Source Two

Another source of data that could be used to check the credibility of this analysis was the work being conducted at Middlesex University by Nicola Payne (Payne, 2014) During the time period that data was being sought on the online infertility forums another research group were also posting a request asking women to come forward and be interviewed about their work-life balance.

Nicola Payne was kind enough to correspond with me and we exchange several emails about our projects. In March 2014 we discussed our progress and she shared her slides for a conference of the European Academy of Occupational Health Psychology. The data analysis is not based on her full data (31 women and 6 men) set but on 15 women with a mean age of 35 (SD =5). They used semi-structured interviews to collect the data, which was then analysed thematically.

The framework for their literature search used role conflict theory (Greenhaus and Beutell, 1985) as this is common approach for research on work-life balance. The aim of their project was to explore the experiences of Medically Assisted Reproduction, (MAR), users of combining work and MAR. They hoped to be able to identify barriers as well as support mechanisms that people used.

The themes that they identified were presented as summary slides and are shown below as a list:

MAR-Work conflict

1. Time- and strain-based conflict, which included worrying about the results of treatment and the practical issues around taking time off.

2. Work providing a distraction from the anxiety and allowing you to carry on as ‘normal’

3. The impact of identity
4. A shift in anchor identity to ‘becoming a parent’ and work being put on the back burner
5. Resentment towards work if it was perceived to be getting in the way.

Support for MAR use

6. Manager support
7. Most women experienced some degree of support from practical only to also including emotional support
8. This enabled women to priories MAR, so supported their anchor identity and reduced conflict
9. Shared understanding of the experience helped
10. Job flexibility also helped reduce conflict

The pros and cons of a specific policy

11. Policy is needed but few workplaces had a specific policy and where it existed it was limited, so policy or guidance is needed.
12. Constraints might include working for a smaller company where the absence has a greater impact on the company.
13. There may be mutual benefits to working for a company that has been really good to you and therefore created a loyalty.

(Payne, 2014)

They concluded that MAR users experience a shift in identity to parenthood and so experience a ‘spillover’ conflict. Line manager support and job flexibility can help to reduce this conflict. The existence of a specific policy or guidance is relatively rare but necessary and while there are constraints to providing support this may be mutually beneficial.

My own analysis also showed time and strain based conflict (1) which centred around the impact of the conflict of identity (3) as either a

treatment seeker or an employee. Payne identified the desire for parenthood as an issue of identity rather than 'treatment seeking' because she has focused on the outcome of treatment (4). My own analysis did not bring out the theme of work providing a distraction from anxiety (2) as strongly as hers and I have used 'injustice' rather than 'resentment' to describe the conflict of roles (5). The role of supportive managers (6) was also found in my analysis with the same theme that support might be emotional or practical (7) depending on company policy and the levels of empathy. I did not find that most women experienced some degree of support (7) or that women were able to reduce their stress by prioritising their treatments (8).

My study did find that shared understanding of the experience (9) particularly through social support including the forum helped women cope and that job flexibility (10) was an advantage that could be gained by disclosure.

The idea that a specific policy and guidance about how to implement it (11) would create a more equalble access to treatment for all women was certainly reflected in my analysis as well as the idea that smaller companies may have difficult accompodating employees who need time off for treatment (12). The final point that a mutually beneficial relationship can be achieved was also found in my analysis (13).

Conclusion.

There was a high level of agreement between the themes found by (Payne, 2014) and by myself suggesting that these themes are credible and authentic. The main differences were that most of her women had experience some degree of support and the reason for that difference may lie in the sampling techniques used especially in the biased form of my posting on the forum and the use of naturalistic data.

RESULTS

In the final chapter of this thesis I attempt to draw together the philosophical worldview, the choice of methodology, the theoretical framework and the results of the four strands, before this discussion I present a brief summary of the main findings of this thesis below:

Conclusion And An Overview Of The Main Findings

Strand 1 The Practitioner Survey

- Homotoxicology practitioners perceive infertility to have both exogenous causes such as stress and toxins as well as endogenous causes such as reproductive pathology or hormonal imbalance.

- Unlike classical homeopathy the use of complex homotoxicological preparations such as Ovarium compositum are prescribed on clinical indications rather than individual case histories and would be suitable for use in a randomised controlled trial where the sample of patients are being recruited by the clinic for a specific clinical indication.

Strand 2 The Discussion Group and Questionnaire Survey of Staff at The Bridge Centre

- The nurses at the clinic provided a perspective that appeared to bridge the dismissal of homeopathy by some medical practitioners and the personal choice to use homeopathy made by some patients

- They were open to the idea and potential benefits and could also see practical challenges to implementing a trial.

- Their support would be necessary to run such a trial and would need to be fostered by the researcher.

- They would like to receive more training and information so that they could advise patients and colleagues and this would need to be planned into the trial schedules.
- They recognised that their patients often suffer emotional distress and disappointment at treatment failure and for that reason may not wish to take part in a trial where they could be randomised to placebo.

- The other issue raised was that it would not be ethical to delay any conventional treatment as women's fertility outcomes decline with age.

Strand 2 The Questionnaire Survey of Patients at The Bridge Centre

- The response rate to this questionnaire was 19% but it was not possible to record the number of patients who did not choose to take a questionnaire from reception.
- 91% of respondents were motivated by the desire to take part in a trial that would help other infertile couples in the future
- 85% were motivated to increase our knowledge about homotoxicology and homeopathy.
- 88% had not tried this therapy before.
- A high level of interest (92%) was shown in trying homotoxicology in the future.
- 83%, would be willing to pay for treatment if homotoxicology was shown to be effective.
- 2% indicated that they would consider homotoxicology because they were considering stopping IVF/ART.
- 62% would be prepared to take part in a trial where they may receive a placebo.
- 95% would be prepared to take their medication at home.
- 100% would be happy to give up peppermint and coffee.

Strand 3 A Randomised Controlled Trial of Ovarian Compositum versus placebo at Jersey General Hospital

RESULTS

Over a period of nine months (November 2011 – July 2012) unit staff identified suitable patients who attended the ARU. Four patients agreed to take part and three of them were consented. Of the 3 patients that were consented 1 withdrew after initial screening as she became pregnant before she started the trial medication. 1 patient completed 6 months of treatment, 1 patient withdrew after 1 month due to compliance issues and 1 patient withdrew after 2 months after compliance issues.

Recruitment and retention rates were low due to a combination of reported circumstances:

- A higher than expected pregnancy rate at the clinic left fewer eligible subjects.
- The difficulty of attending additional appointments for working women who are wary of disclosing their treatment to colleagues, family or friends
- The burden of extra work on the ARU staff who did not feel any ‘ownership’ for this trial as they had not been involved in the planning stages.
- Patient perceptions of the impact of taking part in a trial on their treatment progression or outcomes

Strand 4 A Qualitative Analysis Of The Concerns Of Infertile Women

A thematic analysis (Braun and Clarke, 2006a) and an iterative cycle of reading, writing and reflecting, led to the development of two themes found in the experiences of infertile women undergoing treatment: firstly the conflicting identities of the respondent as both an employee and an infertile treatment seeker, and secondly, the emotional distress caused by infertility and infertility treatment. Linking these was a further theme about the legitimacy of their condition that was dependent upon the existence or absence of a clear company policy on infertility treatment. Consideration of the subthemes within these led to development of a higher order thematic map as shown in Figure 7 Thematic Map.

The themes were further developed on a conceptual level into a theory of 'telling others: **Risk Vs. Benefit** identity model' where disclosure of infertility treatment status to their work, friends, family or forum could be made on the basis of anticipated gains (support, flexibility, empathy) compared to potential losses (job security, friendships, emotional rejection/lack of empathy, loss of privacy), all of which had an effect on identity, see Figure 8 Risk vrs Benefit Theory of Disclosure.

The development of these themes was aided by the literature on identity conflict in chronic disease (Charmaz, 2010, Charmaz, 2006, Charmaz, 1983) and disclosure theories from the field of HIV research (Serovich, 2001), (Serovich et al., 2008, Rouleau et al., 2012).

The literature on stress and infertility was also revisited in order to include findings from the field of psycho-neuro-endocrine-immunology being used to elucidate the biological pathways by which stress may affect adverse pregnancy outcomes, maternal health, and fetal development (Christian, 2012).

	RISKS	BENEFITS
TELLING F & F	Being misunderstood Emotional pain to self and others Disappointment at treatment failure Loss of privacy	Receiving support and understanding
NOT TELLING F & F	Not receiving support and understanding Creates a sense of isolation	Protects privacy
TELLING WORK	Loss of earnings Disapproval from manager Career prospects damaged Discrimination Being misunderstood Loss of privacy	Support and understanding Flexibility for time to attend treatment
NOT TELLING WORK	Disciplinary action and Loss of earnings for time off Not receiving support and understanding	Maintain privacy and professional role
TELLING VIA FORUM	Negative experiences reported by others might be overwhelming.	Support and understanding with privacy due to anonymity

Figure 8 Risk vrs Benefit Theory of Disclosure

RESULTS

Chapter 5 Discussion and Conclusions.

Integration with prior work, implications, transferability, and contributions to the field

The aim of this final chapter is to review the philosophical and theoretical frameworks, methodology, and results of this thesis and comment on how they integrate with prior work; to explore their implications and transferability; and to reflect on how I have contributed to the field of study which is finding appropriate trial designs for the effects of homotoxicology to treat female infertility. There were two main research objectives for this thesis:

Research Question 1 (Strand 1,2,3)

> **Does Ovarium compositum improve the fertility outcomes of women undergoing infertility treatment at the Assisted Reproduction Unit of Jersey General Hospital?**

Research Question 2 (Strand 4)

> **What are the reasons for recruitment failure to a trial of Ovarium compositum (strand 3) to improve the fertility outcomes of women undergoing infertility treatment at the Assisted Reproduction Unit of Jersey General Hospital?**

The rest of the chapter is structured around these with reference to the earlier chapters in this thesis as summarised in the preceding section.

Research Question 1

Does Ovarium compositum improve the fertility outcomes of women undergoing infertility treatment at the Assisted Reproduction Unit of Jersey General Hospital?

A review of the literature showed that there was a knowledge gap about safety of CAM therapies (Fields et al., 2013) and for a methodologically sound, well-reported trial, to investigate the use of homotoxicology in infertile women. The use of both systematic and non systematic qualitative narrative reviews is discussed in the literature review chapter and it is acknowledged that a systematic review is a higher level of evidence for making clinical decisions but that a non systematic review may provide a stimulus for philosophical and scholarly discourse, hypothesis generation or for an iterative cycle of rewriting and reading.

'Methodologically sound' refers to the need for any trial of homoeopathy or homotoxicology to demonstrate model validity (Mathie et al., 2012) and to address the so-called 'efficacy paradox' where the use of quantitative trial designs lead to a situation where internal validity is emphasised to the detriment of external validity. This problem was encountered in existing studies of homotoxicology in infertility where successful clinical experiences were not easily translated into either clinical trial design or results (Gerhard I, 1997, Bergmann et al., 2000, Lai, 2000).

My study design was a development on these studies; I included blinding, randomisation and rigorous allocation to randomisation procedures. No existing treatment was withheld from women, unlike the Lai study in which homotoxicology was an **alternative** to conventional treatment, something that has ethical issues.

However my study, like Gerhard's, also failed to recruit sufficient women and although I carried out a qualitative analysis in Strand 4 this might instead have been undertaken as a preliminary to recruitment and might have improved the outcome.

A systematic review (Mathie et al., 2013) has identified 96 studies of placebo controlled, non-individualised homeopathy including two records for the condition of female infertility: A52 (Bergmann et al., 2000); A74 (Gerhard et al., 1998). These existing trials had methodological shortcomings as well as being poorly reported. However it is shown that a randomised placebo controlled trial would be the most effective method for establishing the specific effect of Ovarium compositum compared to both placebo and non-participation.

There is also a 'paucity' of research using positive emotional outcome measures (e.g. well-being, positive affect, happiness or life satisfaction) for women undergoing fertility treatment (Rockliff et al., 2014) and so the measurement of the quality of life of women taking part in the trial was intended to go some way to rectifying this, by using both a validated (Mark Oppe, 2007) but generic and non-validated (but specific) (Farmer, 2007) QoL instrument.

This study was intended to test the feasibility of measuring a specific effect in a homeopathic/homotoxicological product as well as the feasibility of recruiting women to such a trial. The negative results from the trial should not be interpreted, as a failure of homotoxicology and the trial design itself ought to have been sufficient to measure a specific remedy effect if recruitment targets had been achieved.

This study did demonstrate that the nature of homotoxicology as a complex formulation means that it can be prescribed on clinical indications rather than a single remedy prescribed on an individualised symptom picture. Homotoxicology can therefore be administered to a homogenous group of

patients with similar clinical indications and compared to a placebo and future trials could be planned using a similar protocol to strand 3. The limitations of this attempt were acknowledged, particularly the lack of homogeneity in the women attending the ARU and the lack of communication with site staff when planning and implementing the trial.

The finding that it is not feasible to plan a trial where recruitment is left to clinical staff was an important one and would need to be addressed if this pilot study was to be used as the blueprint for a full-scale clinical trial. This conclusion is based on the survey findings showing doctors tending to a bias to conventional medicine and nurse perspectives bridging doctor and patient views and with nurses needing ownership in a study. Thus a clinician as study champion might be helpful, as in any clinical trial, but in a homotoxicology trial is unlikely to be sufficient.

The difficulties in recruitment led to several hypotheses by site staff about the emotional stresses faced by women attending their unit, the importance of investigating these further led to a deeper understanding of the importance of attending to the data from the earlier, qualitative aspects of the project.

The qualitative results from strand 1 were used to design the quantitative trial design by helping select the medication used as well as the RCT trial design. The qualitative results from strand 2 were used to inform the feasibility of the RCT trial but the results would have been even more valuable if more attention should have been paid to some of the concerns expressed by the nurses at The Bridge Centre about hosting a trial from an ARU unit.

They had identified practical difficulties, such as the appointment times that would need to be extended, and the need to get a large sample size to create a credible result.

These ideas were explored in more detail during the fourth strand of the study and during the writing and rewriting of the thesis.

Research Question 2

What are the reasons for recruitment failure to a trial of Ovarium compositum (strand 3) to improve the fertility outcomes of women undergoing infertility treatment at the Assisted Reproduction Unit of Jersey General Hospital?

The nurses who cared for women undergoing treatment in both London and Jersey reported this patient group to be vulnerable to stress and a review of the literature also highlighted that the prognosis of the couples who discontinued fertility care because of emotional distress would have been better if they had continued with treatment (Brandes et al., 2009).

More recent studies such as (Boivin et al., 2012) recognise that in order to retain women in treatment cycles the emotional and psychological aspects of infertility treatment need to be recognised and addressed:

Reducing the burden of treatment should lead to improved outcomes, namely better quality of life during treatment and lower discontinuation rates. (Boivin et al., 2012)

The relationship between stress and infertility was seen to be implicit in the earlier papers reviewed (Brandes et al., 2009, Finamore et al., 2007) and more recent papers have been able to connect this implied relationship to more explicit findings from the emerging field of PNEI (Christian, 2012).

This thesis seeks to understand the mind-body connection that is central to both homotoxicology and pragmatism and apply it to the context of stress and infertility, this synthesis of concepts represents one of the unique contributions made to the field and will explored in more detail below.

From the results of this qualitative analysis it is possible that women attending the ARU unit in Jersey were experiencing difficulty in disclosing their treatment status at work in order to attend appointments and that taking part in the trial might be a distressing reminder of their condition. It was clear

from the thematic analysis that infertile working women experience a conflict between their psychological identities as both treatment seekers and employees.

My theory explores this conflict in more detail and examines the relative risks and benefits of disclosing to different audiences. The risks of disclosing at work are exacerbated by the lack of a legal status for treatment seekers and the dependence upon the empathy or goodwill of the employer to support the treatment seeker.

It is concluded that women could be spared some of this additional distress if there was a clear policy for companies to follow regarding women seeking treatment for infertility and a legal framework that offered protection and guidance for all parties.

Anonymous disclosure via a forum can help women forge an identity as a treatment seeker and express their emotional distress, but does not necessarily resolve the identity conflict at work. Empathy and support from employers, colleagues, friends, family and fellow forum posters are highly valued by infertile women and help to combat the emotional distress and sense of isolation caused by their situation. The ownership of data posted on public forums by patients is debated and is an intended area for my further research and publication.

Reflections On The Methodology

Mixed Methods studies are not the most common form of CAM publication, some authors reporting that they make up only 4% of papers (Bishop and Holmes, 2013), this thesis was an exploration of the use of MMR. It is important to ensure that it met the criteria for mixed methods research so that this thesis can make a solid contribution to the literature around the use of MMR in CAM (Pace et al., 2012). Its fit to the criteria is now discussed.

At the start of the study design the use of mixed methods was both planned (as in strand 1 and 2 as well as the embedded aspect of strand 3) and unplanned (as in strand 4). The emergent nature of the design was shaped by the results of strand three as well as the increasingly pragmatist worldview of the researcher whose thinking followed:

…A dynamic homeostatic process of belief, doubt, inquiry, modified belief, new doubt, new inquiry…in an infinite loop, where the person or researcher (and research community) constantly tries to improve upon past understandings in a way that fits and works in the world in which he or she operates. The present is always a new starting point. (Johnson and Onwuegbuzie, 2004)

When trial recruitment failed (strand 3) there was the option to abandon the study altogether, but perhaps because the researcher has a background as a homotoxicological practitioner, there remained an interest in how the experiences of the infertile women had influenced their choices about trial participation. This moved the research question from a quantitative approach to a qualitative approach based upon *the existence and importance of the natural or physical world as well as the emergent social and psychological world that includes language, culture, human institutions, and subjective thoughts (Johnson and Onwuegbuzie, 2004).*

DISCUSSION

The MMR approach was used to plan the quantitative strand (3) and to address the research question: **What are the reasons for recruitment failure to a trial of Ovarium compositum (strand 3) to improve the fertility outcomes of women undergoing infertility treatment at the Assisted Reproduction Unit of Jersey General Hospital?**

Including the perspective of practitioners, nursing staff and patients was intended to make the study design more feasible and effective in answering the research objectives.

An example of this would be strand 1, where the therapists who participated were using homotoxicology to treat patients for infertility; the questionnaire was designed to capture two kinds of data, firstly on the specific kind of infertility case that would be the focus of the trial (a patient attending an ARU for IVF due to failure to ovulate).

Secondly, the questionnaire also asked about general attitudes and approaches to infertility treatment in order to explore the perceptions, knowledge and experiences of the prescribers. This was important to inform the trial design for the quantitative phase, especially the exclusion factors and the use of a placebo and the intention to have a non-participating control group in normal care.

The data collection needs to be suitable to address the research objectives or questions; model validity requires that the follow-up period is long enough for the outcome to occur. In strand 1 and strand 2 sufficient time was allowed to collect in the questionnaires, in Strand 3 recruitment attempts took place over 8 months and was stopped so that any patient who did enrol was guaranteed was 12 month supply of medication. In strand 4 the time needed to complete the qualitative analysis was provided by the thesis rewrite period.

The qualitative data from the small sample of direct responses that were used in strand 4 were not the ideal choice but a pragmatic choice. It would have improved the study if there had been a larger sample of responses to

the invitation to share their experiences of working and undergoing infertility treatment so that saturation of themes could have been achieved. The small sample has been triangulated with other data, from the forum administrator and from another similar concurrent study (Payne, 2014) in order to check for missing themes and to compensate for this small sample size.

The data from the forum users was also a pragmatic choice but it did allow the researcher to seek for the themes in a larger sample of naturalistic data and to explore how themes might be interrelated. If there had been a forum just for infertile women in Jersey then that would have been helpful when forming a conclusion about the uniqueness of findings at the clinic. Pragmatism takes a naturalistic view of man and therefore naturalistic data is an appropriate choice.

Thematic analysis (TA) was a good choice for this study because it is relatively simple for a new researcher to use and the process of using it has been well described (Braun and Clarke, 2006b). The flexibility of TA allowed me to apply it to different data sets from strands 1,2 and 4 and develop my understanding of how to seek for themes in the data at an increasingly conceptual depth.

I was able to use it to categorise social data as well as data obtained from my questionnaires and discussion groups. This plurality of use is possible because it is not automatically linked to any pre-existing theoretical framework and so can be used to do different things within different frameworks. The flexibility of TA also means that as a researcher I had to be explicit about my methods, theoretical framework and philosophical worldview.

The randomisation of the patients in the quantitative strand (3) was clearly described. The patients were to be randomised, to treatment, using a randomisation sequence designed by Heel, in blocks of four. They were to be stratified according to chronological age and treatment group. The randomisation sequence was designed by Heel (manufacturer) who provided

sealed envelopes for the codes they had generated. A template was provided for the generation of labels so that clinic staff in Jersey could label patient files. The randomisation allocation was captured by the unit staff and site pharmacy on a word document provided by the investigator.

The methodology section also clearly describes how the consulting physician who allocated the patient to the next number in the approach age and treatment group controlled allocation of the study drug. The allocation code was passed to pharmacy that held the medication labelled with the allocation codes. The sealed envelope was added to the patient's file of notes and a sticker was attached to the front of the file to identify them as a trial participant and included their allocation code. In the event of an adverse event the envelope could be opened and the code broken. Patients, researchers, doctors and pharmacy were all blinded as to the allocation of patients to active drug or placebo.

The selected outcomes and associated measurements in the quantitative strand were appropriate to capture both small and large changes in the patient group, for example blood tests of hormonal levels are a sensitive measure of small changes compared to pregnancy tests. The trial design was checked against the criteria for the MVHT method (Mathie et al., 2012) to make sure that there was a concordance between the trial study design and "state of the art" practice for the intervention under investigation.

Philosophical Worldview

The integration of both the qualitative (1 & 2) and quantitative strands (3) was made possible by the philosophical worldview. Pragmatism which is a pluralistic philosophy provides a framework for reconciling the dualistic views originating from quantitative and qualitative research traditions (Mesel, 2013). This thesis values the knowledge that can be gained from conducting both quantitative and qualitative methods in order to gain a wider, more complete perspective on the research question.

The need to report philosophical orientation when writing up a mixed methods study was highlighted by (Bishop and Holmes, 2013) who reviewed articles from the field of CAM and found that only 5% of studies acknowledged or reflected on the limitations of their mixed methods design. None of the studies they reviewed acknowledged or addressed the philosophical tensions involved in a mixed methods research project. This study seeks to make a contribution to the field by reporting with transparency both the pragmatic philosophical framework and the process through which it was developed.

The lack of quantitative data meant that there was not a problem with divergence of results from qualitative and quantitative sources, but if a complete data set had been collected it would have answered the quantitative research question: What is the specific effect of Ovarian compositum on the fertility outcomes of women attending an ARU at Jersey General Hospital?

The decision to then further investigate the work related concerns of women attending treatment would have been seen as an extension to the study rather than an integral part of the initial design. The actual study design was a pragmatist response to the problems and challenges encountered along the way and in turn led to an understanding of the pragmatist foundations for MMR.

DISCUSSION

Practicalities (in the collection of data) led to a deeper understanding of philosophy. A deeper understanding of the philosophy led in turn to a more informed approach to methodology. The adoption of pragmatism meant that this researcher's journey from post positivist to pragmatist worldview was informed by a philosophical worldview, that the decisions made were purposeful and it bought a sense of cohesion to the project as a whole.

Pragmatism replaces the need to view the mind and body as separate by viewing human beings in naturalistic way as biological organisms in constant transaction with their environment.

One of the ideas expressed at the start of this thesis was that it was an exploration of the reconciliation of dualisms that exist between conventional medicine and complementary medicine and that these originate from the Cartesian legacy of mind-body dualism (Shelton, 2013).

Pragmatism views man as a biological organism in constant transaction with its environment. This is in direct contrast with the narrowly focused scientific perspective which cuts off mind from the individual human being and cuts off the environment from behavior by seeing environment as a purely external occasion from which behavior proceeds (Shelton, 2013).

The role of pragmatism as a philosophical framework for uniting dualisms has been described in the literature review (Shelton, 2013, Mehta, 2011), and the link to mixed methods research designs is described by several authors (Bishop and Holmes, 2013, Creswell and Clark, 2007b). My own analysis seeks to build on this existing knowledge by describing some of the similarities between the scientific model of PNEI and the CAM model of homotoxicology and their links with pragmatism as a philosophical worldview.

So if we take Pragmatism as a starting point, this leads to a view of mankind as the organism, which as long as it is alive is always in constant dynamic transaction with the environment, (Dewey, 1896).

DISCUSSION

For Dewey the biological theory of stimulus and response was dualistic as it assumed a gap between the organism and it's external environment. The stimulus that caused a response was external to the organism. He replaced this dualistic notion with a dynamic model of **continuous** readjustment where the selection and assimilation of information leads to a dynamic coordination with the environment (Dewey, 1896). The stimulus can only be said to have been found at the moment that the (adequate) response has been found, it is not a prior condition of stimulus leading to a response. (Biesta and Burbules, 2003).

Dewey postulated two possible states: firstly where the connection between stimulus and response has already been made (an accomplished adaptation) and secondly where the connection has not yet been made and the organism is searching for a stimulus (Dewey, 1896, Biesta and Burbules, 2003). This earlier open phase in which there is a tension, need or conflict resolves into a later closed phase described as an integrated interaction of organism and environment.

Dewey linked this idea of the construction of a stimulus through experimental action to the acquisition of knowledge and habit. This was not seen as the acquisition of information about the world 'out there' but learning in the sense of the acquisition of a complex set of predispositions to act. Knowledge is seen as becoming gradually more useful and intelligent through experience, without the need to attribute reality to an independent entity, essence or external reality. (Biesta and Burbules, 2003). The adoption of this model would naturally lead to a constructionist perspective of knowledge and learning theory.

Homotoxicology also views man as both and open and closed system that is constantly influenced by the surrounding environment. Interactions between the inner and outer environments trigger correcting processes (autoregulation) in order to maintain the homeostatic balance necessary for life (Smit A, 2009). Cannon defined the word homeostasis in 1932, deriving it from the Greek words *homoios* (the same) *and stais* (stance or posture).

Homeostasis thus means to stay in the same condition or position (Smit A, 2009) but today the understanding would be that this is a dynamic equilibrium or steady state.

This steady state is achieved by the workings of the Greater Defence System, a model postulated by Reckeweg (Reckeweg, 1984) made up of six subsystems working together to eliminate toxins from the body and restore tissue damage. Detoxification and drainage as well as immunomodulation are the main treatment pillars in homotoxicology.

The six systems all merge into each other and have a synergist effect, working actively together to defend the body and maintain homeostasis. As can be seen from the table below the components of the Greater Defence System are consistent with the immune regulation system as seen in modern medicine.

The positivist perspective can be found in pyscho-neuro-endocrine-immunology (PNEI), a multidisciplinary medical approach. PNEI describes this active maintenance of internal homeostasis and health by the interactions of the neurological, endocrine and immune systems under genetic, epigenetic and psychological influences.

Homotoxicology would describe these genetic and epigenetic influences as a concept called Miasm. The role of stress as describe by Selye (Selye, 1936) in health and disease is another central concept shared by both homotoxicology (Smit A, 2009) and PNEI (Campagne, 2006) theoretical frameworks.

Table 28 Comparison of the Greater Defence System with PNEI

	Component of the Greater Defence System (Smit A, 2009)	**Component of PNEI systems**
1.	The reticuloendothelial system	Cells of the immune system

		(macrophages, monocytes, dendritic cells, lymphatic system)(Steinman and Cohn, 1973), (Sallusto and Lanzavecchia, 2002)
2.	The hypothalamus-hypophysis-suprarenal axis	The hypothalamus-hypophysis-suprarenal axis(Campagne, 2006)
3.	The neural reflex system	Neural reflex regulation (Vasquez et al., 1997)
4.	Detoxification by the liver	Physiological functions and local immunity (Knolle and Gerken, 2000)
5.	Detoxification of the matrix	Structural, transport and immune functions of the extracellular matrix (Bonnans et al., 2014)
6.	The mucous membranes	Immune functions and stress (Papadopoulos et al., 2014)

The concept of an ‘intelligent’ system that is reacting continuously to respond to it’s external environment and create a homeostatic internal reality is found in pragmatism, homotoxicology and the medical field of PNEI as well some of the nursing theories explored in strand 3 (Masters, 2014). By taking this pragmatist viewpoint the basic dualism between quantitative and qualitative approaches to research is reconciled, the theoretical framework of homotoxicology offers a way to reconcile the mind body connection because of it’s similarity with PNEI.

There does however remain the question of what to measure and how to measure it. If a quantitative perspective is taken of the phenomenon then a quantitative answer will be produced, the same phenomenon studied using a qualitative technique will produce a qualitative answer and the so dualism is still present in the results and interpretation of the results. It is argued in this thesis that mixed methods research would allow both perspectives to be integrated and allow a more complete, credible and nuanced understanding of the phenomenon.

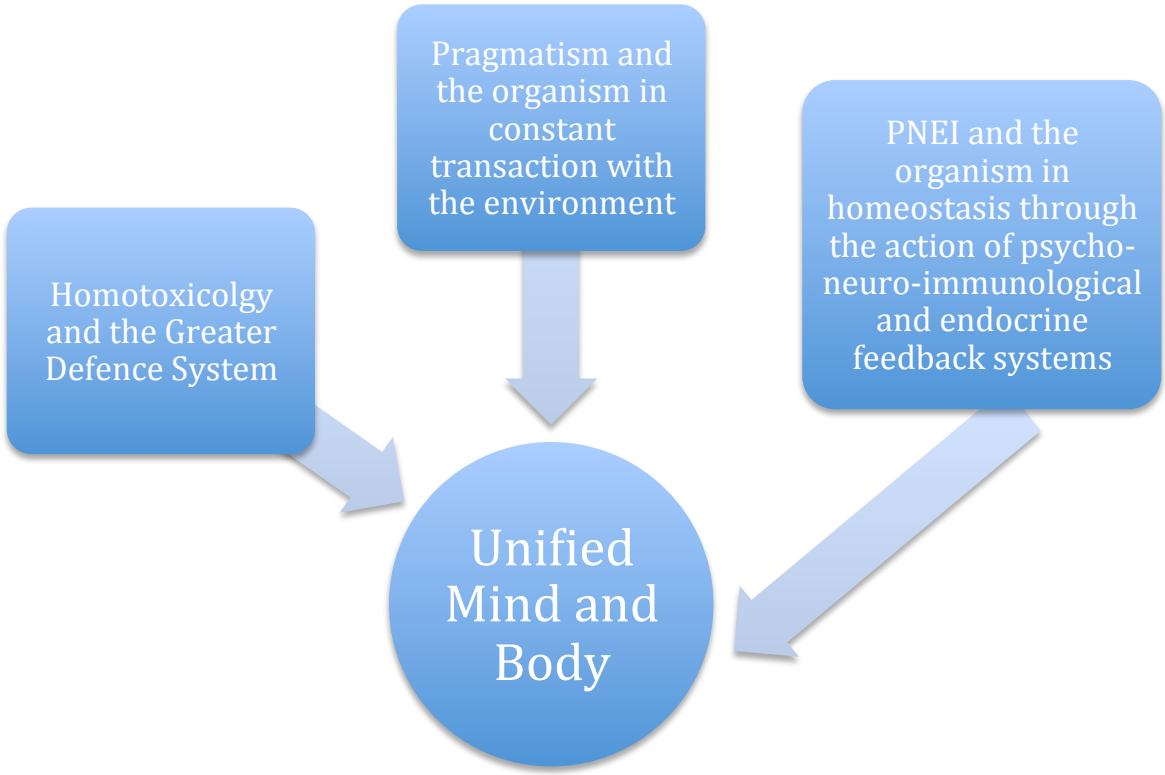


Figure 9 The similarities between homotoxicology, pragmatism and PNEI

Limitations

An important lesson was that a systematic approach to the literature can ensure the credibility and utility of the results and conclusions based upon the results. It was also recognised post-viva that it is especially important to conduct a systematic literature review in this field (CAM) because it works as a mechanism to facilitate interdisciplinary collaboration and a more integrated understanding of health (Karunananthan et al., 2009).

Strand One

In the early strands of the study there was the possibility that my familiarity with the homotoxicology community and my known associations and friendship with the suppliers and producers of products may well have biased the responses of the participants in Strand 1. It is difficult to say where goodwill begins and where it turns into bias. It is hoped that participants were motivated to respond to the questionnaire but as professionals were responding with an unbiased view of the subject. The possibility of this bias is reported as part of the methodology so that it can be taken into account.

It is acknowledged that the two versions of the questionnaires for the practitioners should have been analysed separately. The earlier version could have been treated as a pilot in order to refine the questions. The reason for the change of questionnaire was the change in potential study sponsor and therefore remedy choice but they should not have been combined in the analysis stage.

The initial analysis claimed to use Grounded Theory but this misunderstanding of the depth of analysis needed to meet that claim was corrected after the first viva. During rewriting it was realised that what I had actually used was thematic analysis and a section on this method was added to the literature review.

DISCUSSION

The methodology chosen was appropriate to answer the research questions but it was not systematic enough in the way it was applied to the situation.

Strand 2

In strand 2, the researcher had direct contact with the nurses and matron at The Bridge Centre but no contact with the patients. This was reflected in the thematic analysis where the nursing staff were seen as a 'bridge' (no pun intended) between the public and the therapies or treatments on offer. The nurses were under no obligation to support the study by attending the discussion group but were motivated by their own interest in the subject. It is noted in the methodology section that this was therefore a self-selected sample that might be biased towards an acceptance of the homotoxicology and in turn may pass on that bias to their patients.

Results generated at a clinic in London are not necessarily applicable to a clinic in Jersey. It is always important to take the social and cultural context into account, the methodology should have been changed to sample the population of infertile women seeking treatment in Jersey and I might have done this through my existing private patient network.

Patient questionnaires that are returned on a voluntary basis are susceptible to bias as only those patients interested are likely to take part and return them. The methodology did generate some useful results and greater attention could have been paid to these when designing the methodology for Strand 3.

Strand 3.

Strand 3 (quantitative) did not have a complete data outcome and the major limitation of this research study was the lack of quantitative outcome data as only 4 out the anticipated 90 participants were enrolled (0.04%)

Another limitation was the sampling strategy of the quantitative phase. The women attending the ARU were a heterogeneous population in terms of their

infertility reasons, ages and treatments. The trial design was designed to accommodate this but the feedback at the end of the trial was that it a clinic with a higher input of a more homogenous patient group would make recruitment easier and they suggested that future trials should focus on one subgroup with a specific definition of infertility. The difficulty is that the clinic would not generate sufficient numbers of women to create a large sample of one subgroup so an alternative site or sites would have to be considered.

It would have been helpful, prior to study design, to carry out research regarding the social and legal implications of choosing Jersey as the study site. A lot of time was spent trying to establish the requirement for mainland ethics and this delayed the time available for recruitment before the study drug expired.

Greater participation from the study site unit staff in the design of the Case Report Form would have resulted in a methodology that was easier to implement and therefore more ownership, goodwill, and support for recruitment.

However the trial design was appropriate for the research question and had the necessary level of model validity for investigating a homeopathic substance.

Strand 4

From the new perspective of a pragmatist worldview this strand could have been carried out as strand one and informed the design of the rest of the study. This would still have been a mixed methods study but greater priority could have been given to the role of qualitative data, sourced from the patient forums, in an early exploratory phase of the study.

In strand 4 a posting was made on the infertility forum and it was noted that this was biased towards the problematic nature of working and having infertility treatment, this influenced the responses and the themes emerging

from those responses. The bias was noted by a supervisor and made explicit in the methodology reporting. The bias was somewhat balanced by the use of naturalistic data from the My Story section for the analysis but the themes had already been largely identified from the smaller sample.

One of the major lessons from this thesis is biased questions can lead to results that are less credible and therefore less useful in trial design. The increased attention to theory helped to balance this tendency in the early stages of the project.

The small sample size of the direct responses to the question posted on the forum (n=7), is acknowledged as a limitation, but the close attention to theory, adherence to the guidelines for good thematic analysis and cross referencing with other researchers/sources of data helps to improve the credibility of the conclusions drawn using this method.

The initial methods (ranking of responses and keyword frequency) used to analyse the qualitative patient data were not appropriate to answer the research question. The rewritten thesis used thematic analysis to explore the attitudes of women towards disclosing their treatment and this led to useful insights that could have been used to plan the methodology in Strand 3.

The choice of a forum for the data for strand four made it necessary to explore the ethics of using data that has been posted by private individuals,

as well as recognising that those postings were written for a particular reason and for a particular audience. It did have the advantage of offering the researcher an 'insider' perspective on the process of undergoing infertility treatment.

If it had been possible to interview the women from Jersey who had taken part in the study or decided not to take part in the study that would have created a closer fit between strands three and four. One form of data that is reported but perhaps not analysed sufficiently is the feedback from the unit staff in Jersey. It was necessary to make a decision to either investigate the reported reasons for patients not wishing to take part or to investigate the possibility that the difficulties faced by the unit staff were largely responsible for poor recruitment. At the time it was deemed more appropriate to take their reported reasons for trial failure at face value:

Conclusion

If we conclude with the idea that this thesis is led by pragmatist thinking then the knowledge gained should be useful for creating more intelligent activity and should seek to make a contribution in line with democratic values.

The perceived injustices and emotional distress of women undertaking infertility treatment such as the inequality of treatment at work, access to treatment and high failure rates have all been explored using thematic analysis as a qualitative methodology in Strand 4. These insights could have been used at the start of the research project to plan a better pilot study with a successful recruitment rate.

A positive outcome of this study would be to use the results and the lessons learned to try and improve the **benefits** to women of disclosing their treatment status compared to the risks. For example women taking part in the trial could be encouraged to create an identity as a community of trial participants with their own forum.

This would allow their anonymity could be preserved but it would give them an opportunity to increase their sense of identity as a treatment seeker and receive support and encouragement without losing privacy or dignity. Belonging to a community of treatment seekers would help to validate their identity and legitimise their status particularly if their infertility is not recognised at work as a legitimate reason for time off.

As well as supporting the psychological identity of the women they are seeking to recruit researchers interested in working with infertile women could offer a flexible appointment system to help women avoid the conflict between their roles as employees and treatment seekers.

A major lesson learned from this trial would be to include the ARU staff at an early stage not as ‘participants’ taking part in a research study by completing a questionnaire or participating in a focus group but with true ‘involvement’ (INVOLVE, 2015). If they had been actively involved as co-applicants on the research project and their role included identifying research priorities, commenting and developing patient information leaflets or other research materials there might have been a different outcome from the recruitment process. From the researchers pragmatist point of view it is also true to say that if the ARU staff had been consulted at an earlier stage the whole project might have been deemed too arduous for them to host and therefore been abandoned before it began.

A final point would be that this thesis has demonstrated both in practice and through an exploration of theory, that a pragmatist philosophical worldview can help to bring conceptual meaning to a difficult process of change, structure to an evolving and dynamic study and can allow the researcher to reconcile the use of data from both quantitative and qualitative paradigms within a constructionist framework.

The use of mixed methods research with a ‘pragmatic’ design exploring both qualitative and quantitative data, was found to be suitable to inform the design of a valid clinical trial model to establish the specific effects of

Ovarium compositum and investigate the problems encountered during recruitment. This pragmatic approach needs to be balanced with a systematic approach to both data and literature in my future work.

The use of a pragmatic worldview ensured that the focus was kept on seeking practical solutions to these challenges. The final test of value of these finding will be if they can inform future trials that seek to work with infertile women. Perhaps it is appropriate to let John Dewey have the last word, he was writing about education but the concepts can equally apply to medicine without losing their meaning:

To suppose that scientific findings decide the value of educational undertakings is to reverse the real case. Actual activities in educating test work of scientific results. They may be scientific in some other field, but not in education until they serve educational purposes, and whether they really serve or not can be found out only in practice. (Dewey, 1929)

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Conflicts of interests

The researcher has used products supplied by Heel GmbH in her private practice, attending their training workshops, and provided freelance training/education and consultancy services to BioPathica Ltd, Ashford Kent.

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VOLUME TWO - THE APPENDICES

William Harvey Research Institute

PhD

The Challenges of Designing and Implementing a Pilot Study of Ovarium Compositum in Infertile Women

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25th March 2015

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APPENDICES

Contents

APPENDIX 1 The Literature Review

Appendix 1 Evaluation Frameworks Used In The Literature Review

Homeopathy versus conventional therapy for female infertility: Intermediate report from a randomized study.

(Gerhard et al., 1997)

Evaluation against CONSORT

(Hopewell et al., 2008)

The original article being published in German the review has been based upon the CONSORT guidelines (Hopewell et al., 2008) for assessing abstracts of randomised trials. An English translation was provided by a non-specialist in the field and checked against an English translation provided by Robert Mathie (Mathie et al., 2013) to ensure accuracy and consistency.

Table 29 Gerhard 1997 evaluated against Consort

Item	Description	Reported on line number
Title	Identification of the study as randomized	2
Authors *	Contact details for the corresponding author	In German abstract
Trial design	Description of the trial design (e.g. parallel, cluster, non-inferiority)	3
Methods		
Participants	Eligibility criteria for participants and the settings where the data were collected	4
Interventions	Interventions intended for each group	3-4
Objective	Specific objective or hypothesis	3
Outcome	Clearly defined primary outcome for this report	4
Randomization	How participants were allocated to interventions	
Blinding (masking)	Whether or not participants, care givers, and those assessing the outcomes were blinded to group assignment	5
Results		
Numbers randomized	Number of participants randomized to each group	6
Recruitment	Trial status	10-11
Numbers analysed	Number of participants analysed in each group	7
Outcome	For the primary outcome, a result for each group and the estimated effect size and its precision	
Harms	Important adverse events or side effects	
Conclusions	General interpretation of the results	
Trial registration	Registration number and name of trial register	
Funding	Source of funding	11, 9

Homeopathy versus conventional therapy for female infertility: Intermediate report from a randomized study.

(Gerhard et al., 1997)

Evaluation against REDHOT

Table 30 Gerhard et al 1997 evaluated against REDHOT

Checklist for Reporting Data on Homeopathic Treatments (REDHOT) (Dean et al., 2007)			
Item	Treatment (CONSORT item number)	Description	*Reported on page number*
1	Rationale (2)	Type of homeopathy Individualized (aka classical, constitutional)	4 of translation
2	Participants (3)	Knowledge Condition Baseline health definition in provings	10
3	Medications (4)	Manufacture Manufacturer, pharmacopoeia (or process), references. Potency and scale Dilution Method Nomenclature Individualised: list or frequency table Formula: Constituents, trade name Dosage	

		Dose, timing, form	
4	Consultations (4)	Setting Clinical history detail Duration, frequency Number needed to agree prescription Group process or expert consultation Confidence in prescriptions	Setting 4-5 Clinical History 6,8 Frequency of consultations p9
5	Practitioners (4)	Number in Study Experience, accreditation, qualifications Current schools or styles of homeopathy	9
6	Co-interventions (4)	Included Rationale, intended effect, references Duration, frequency Excluded Stopping of mainstream interventions Antidotes	
7	Control interventions (4)	Active Rationale, references Placebo Manufacturing process	Placebo p5

8	Adverse events (19)	Aggravations	

Homeopathy versus conventional therapy for female infertility: Intermediate report from a randomized study.

(Gerhard et al., 1997)

Evaluation against the MVHT

(Mathie et al., 2012)

Table 31 Gerhard et al 1997 evaluated against MVHT

Table: Verdicts for domains 1-6, indicating rating for 'Yes', 'No' and 'Unclear' (Mathie et al., 2012)			
Paper (Gerhard I, 1997)			
	Yes	Uncertain	No
1 Rationale	*Clinical knowledge and practice inform that, for the condition under investigation, the health of patients may be benefited by homeopathic intervention.* **Author quotes figures from his clinic showing good results with women with amenorrhoea and sterility through hormonal causes.**	*A substantial number of experienced homeopaths would support the choice of this intervention for this type of patient.* **The patients are divided into three subgroups and it is not clear if homeopathy is suitable for all three groups/pathologies**	
2 Principles	One or both of the following: *The intervention used is based on the principle of 'like treats like' or is based on the principle of isopathy.* *Literature sources (material medica, repertory etc.) are available that convincingly justify the specific intervention.* **Patients were given individually prescribed homeopathic remedies** **They received single homeopathic remedies according to**		

Table: Verdicts for domains 1-6, indicating rating for 'Yes', 'No' and 'Unclear' (Mathie et al., 2012)			
Paper (Gerhard I, 1997)			
	Yes	Uncertain	No
	repertorisation with regard to the Similar principle.		
3 Practitioner	Individualised homeopathy: Those who have prescribed the homeopathic medicine(s) are suitably trained and experienced in homeopathy to manage the condition under investigation **Authors worked as doctors using Integrated Medicine at a University Clinic in Germany**		
4 Outcome Measures	*The main clinical effect expected of the intervention is adequately measured by the main outcome used.* **Hormone levels and patient attitudes would be a good indicator of clinical effect as functional change precedes structural change.**		
5 Sensitivity	All of the following: *The main outcome measure is sensitive to changes of the magnitude expected in the patients under investigation.* **Yes. Patients treated for hormonal disturbance with classical homeopathy would expect to see some changes in mood or symptoms after 3 months of treatment** *The main outcome measure is capable of determining both improvement and*	*The main outcome measure shows no evidence of a 'floor effect' and/or 'ceiling effect'*	

Table: Verdicts for domains 1-6, indicating rating for 'Yes', 'No' and 'Unclear' (Mathie et al., 2012)			
Paper (Gerhard I, 1997)			
	Yes	Uncertain	No
	deterioration. **Yes – Hormone levels can go up or down.**		
6 Follow up	*The time-point selected for main follow-up measurement provides sufficient opportunity for a clinical change to be observed.* **Yes the 3,6,9 month time periods would have been sufficient to see clinical change. It was acknowledged in the study that some patients took longer to recruit and treat because they required detoxification treatment first.**		

The Homotoxicological Treatment Of Female Functional Infertility: A Clinical Trial (Lai, 2000). Translated From Italian By Professional Translator.

Evaluated against CONSORT (Schulz et al., 2010)

Table 32 Lai 2000 evaluated against CONSORT

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	1-2
	2b	Specific objectives or hypotheses	
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	3
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	
Participants	4a	Eligibility criteria for participants	2-3
	4b	Settings and locations where the data were collected	3
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	3
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	3-7

	6b	Any changes to trial outcomes after the trial commenced, with reasons	
Sample size	7a	How sample size was determined	
	7b	When applicable, explanation of any interim analyses and stopping guidelines	
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	
	11b	If relevant, description of the similarity of interventions	
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	
	13b	For each group, losses and exclusions after randomisation, together with reasons	
Recruitment	14a	Dates defining the periods of recruitment and	

		follow-up	
	14b	Why the trial ended or was stopped	
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	3-7
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	8
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	7-9
Generalizability	21	Generalizability (external validity, applicability) of the trial findings	
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	
Other information			
Registration	23	Registration number and name of trial registry	
Protocol	24	Where the full trial protocol can be accessed, if available	

Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	

The Homotoxicological Treatment Of Female Functional Infertility: A Clinical Trial (Lai, 2000). Translated From Italian By Professional Translator.

Evaluated against RedHot

Table 33 Lai, 2000 evaluated against REDHOT

Checklist for Reporting Data on Homeopathic Treatments (REDHOT) (Dean et al., 2007)			
Item	Treatment (CONSORT item number)	Description	*Reported on page number*
1	Rationale (2)	Type of homeopathy Individualized (aka classical, constitutional) Formula (aka clinical = single constituent or complex = multi constituent) Isopathy Evidence base Sources, references	3
2	Participants (3)	Knowledge Condition Baseline health definition in provings	
3	Medications (4)	Manufacture Manufacturer, pharmacopoeia (or process), references. Potency and scale Dilution Method Nomenclature Individualised: list or frequency table	

		Formula: Constituents, trade name Dosage Dose, timing, form	3,5 trade name only, dose and timing
4	Consultations (4)	Setting Clinical history detail Duration, frequency Number needed to agree prescription Group process or expert consultation Confidence in prescriptions	Setting assumed as clinic p3
5	Practitioners (4)	Number in Study	
		Experience, accreditation, qualifications Current schools or styles of homeopathy	
6	Co-interventions (4)	Included Rationale, intended effect, references Duration, frequency Excluded Stopping of mainstream interventions Antidotes	3-5, 6 (diet)
7	Control interventions (4)	Active Rationale, references Placebo	3-5

		Manufacturing process	
8	Adverse events (19)	Aggravations	8

The Homotoxicological Treatment Of Female Functional Infertility: A Clinical Trial (Lai, 2000). Translated From Italian By Professional Translator.

Evaluated against the MVHT

Table 34 Lai, 2000 evaluated against MVHT

Table: Verdicts for domains 1-6, indicating rating for 'Yes', 'No' and 'Unclear' (Mathie et al., 2012)			
Paper (Lai, 2000)			
	Yes	Uncertain	No
1 Rationale	*Clinical knowledge and practice inform that, for the condition under investigation, the health of patients may be benefited by homeopathic intervention.* **References the Lai Study (Lai, 2000)**	*A substantial number of experienced homeopaths would support the choice of this intervention for this type of patient.* **Does not make clear the clinical success experienced previously at the same clinic that led to this trial.**	
2 Principles	*One or both of the following:* *The intervention used is based on the principle of 'like treats like' or is based on the principle of isopathy.* *Literature sources (material medica, repertory etc.) are available that convincingly justify the specific intervention* **Remedies used were Heel remedies that are formulated using homeopathic and isopathic principles and the prescription of**		

	these remedies for these conditions is found in the literature published by Heel (Heel, 1986)		
3 Practitioner	*Non-Individualised homeopathy: There is evidence that experienced homeopathic input (and/or a suitable literature source) has been involved in informing the choice of medicine(s) used commonly for all patients in the study.*	**Author is listed as Specialist in Obstetrics and Gynaecology, Managing Doctor at the Centre for the Study and Treatment of the Menopause. National Secretary for the Italian College of Biological Obstetricians and Gynaecologists**	
4 Outcome Measures	*The main clinical effect expected of the intervention is adequately measured by the main outcome used.* **Yes each sub group was assessed using a variety of outcomes that indicate changes to the clinical picture such as ovulation rate, progesterone levels, and endometrial thickness.**		
5 Sensitivity	*All of the following: The main outcome measure is sensitive to changes of the magnitude expected in the patients under investigation.* **yes** *The main outcome measure is capable of determining both improvement and*	*The main outcome measure shows no evidence of a 'floor effect' and/or 'ceiling effect'.*	

	deterioration. **yes**		
6 Follow up		*The time-point selected for main follow-up measurement provides sufficient opportunity for a clinical change to be observed.* *It is not clear how long individual patients were treated for. It is suggested that the trial* ***recruited (assessed)*** *women between June 1998 and January 1999. Subset B was assessed for 8 monthly cycles. And Subset C underwent allopathic treatment that was subdivided into two 4-month cycles.* *~The results tables seem to indicate that data was collected for 8 months* *HTX group remedies were prescribe twice weekly so sufficient time would be needed to complete the task*	

The efficacy of the complex medication Phyto-Hypophyson L in female, hormone related sterility. A randomized, placebo-controlled clinical double blind study. (Bergmann et al., 2000)

The original article being published in German only the review has been based upon the CONSORT guidelines (Hopewell et al., 2008) for assessing abstracts of randomised trials.

Table 35 Bergman et al 2000 evaluated against CONSORT

Item	Description	Reported on line number
Title	Identification of the study as randomized	1
Authors *	Contact details for the corresponding author	Names only
Trial design	Description of the trial design (e.g. parallel, cluster, non-inferiority)	2
Methods		
Participants	Eligibility criteria for participants and the settings where the data were collected	8
Interventions	Interventions intended for each group	9
Objective	Specific objective or hypothesis	8
Outcome	Clearly defined primary outcome for this report	10-11
Randomization	How participants were allocated to interventions	
Blinding (masking)	Whether or not participants, care givers, and those assessing the outcomes were blinded to group assignment	
Results		
Numbers randomized	Number of participants randomized to each group	
Recruitment	Trial status	
Numbers analysed	Number of participants analysed in each group	
Outcome	For the primary outcome, a result for each group and the estimated effect size and its precision	
Harms	Important adverse events or side effects	16-17
Conclusions	General interpretation of the results	10-16
Trial registration	Registration number and name of trial register	

Funding	Source of funding

The efficacy of the complex medication Phyto-Hypophyson L in female, hormone related sterility. A randomized, placebo-controlled clinical double blind study. (Bergmann et al., 2000)

Table 36 Bergman 2000 evaluated against REDHOT

Checklist for Reporting Data on Homeopathic Treatments (REDHOT) (Dean et al., 2007)			
Item	Treatment (CONSORT item number)	Description	*Reported on page number*
1	Rationale (2)	Type of homeopathy Individualized (aka classical, constitutional) Formula (aka clinical = single constituent or complex = multi constituent) Isopathy Evidence base Sources, references	Abstract
2	Participants (3)	Knowledge Condition Baseline health definition in provings	
3	Medications (4)	Manufacture Manufacturer, pharmacopoeia (or process), references. Potency and scale Dilution Method Nomenclature	Manufacturer is named in abstract

		Individualised: list or frequency table Formula: Constituents, trade name Dosage Dose, timing, form	One constituent is named Dose is shown in abstract
4	Consultations (4)	Setting Clinical history detail Duration, frequency Number needed to agree prescription Group process or expert consultation Confidence in prescriptions	Clinical classification in abstract
5	Practitioners (4)	Number in Study	
		Experience, accreditation, qualifications Current schools or styles of homeopathy	
6	Co-interventions (4)	Included Rationale, intended effect, references Duration, frequency Excluded Stopping of mainstream interventions Antidotes	

7	Control interventions (4)	Active Rationale, references Placebo Manufacturing process	Placebo is not explained
8	Adverse events (19)	Aggravations	Mentioned but not described in abstract

The efficacy of the complex medication Phyto-Hypophyson L in female, hormone related sterility. A randomized, placebo-controlled clinical double blind study. (Bergmann et al., 2000)

Evaluated against MVHT

Table 37 Bergman et al 2000 evaluated against MVHT

Table: Verdicts for domains 1-6, indicating rating for 'Yes', 'No' and 'Unclear' (Mathie et al., 2012)			
Paper			
	Yes	Uncertain	No
1 Rationale	.	*Both of the following:* *Clinical knowledge and practice inform that, for the condition under investigation, the health of patients may be benefited by homeopathic intervention.* *A substantial number of experienced homeopaths would support the choice of this intervention for this type of patient* **No discussed in abstract but context of trial is a clinical setting**	
2 Principles	*One or both of the following:* *The intervention used is based on the principle of*	*One or both of the following:* *The intervention used is based on the principle of*	

	'like treats like' or is based on the principle of isopathy. *Literature sources (material medica, repertory etc.) are available that convincingly justify the specific intervention*	*'like treats like' or is based on the principle of isopathy.* *Literature sources (material medica, repertory etc.) are available that convincingly justify the specific intervention*	
3 Practitioner			
4 Outcome Measures			
5 Sensitivity			
6 Follow up			

Complementary and Alternative Medicine (CAM) in reproductive-age women: a review of randomized controlled trials (Fugh-Berman and Kronenberg, 2003) evaluated using PRISMA.

Table 38 Fugh-Berman and Kronenberg, 2003 evaluated against PRISMA

Section/topic	#	Checklist item	Reported on page #
TITLE: Complementary and Alternative Medicine (CAM) in reproductive-age women: a review of randomized controlled trials			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	Review
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	137
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	137-138
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	137
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify	

		additional studies) in the search and date last searched.	
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	

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Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating, which were pre-specified.	
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for	

		exclusions at each stage, ideally with a flow diagram.	
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: **www.prisma-statement.org**.

Randomized controlled trials of homeopathy in humans: characterizing the research journal literature for systematic review (Mathie et al., 2013)

Evaluated using PRISMA

Table 39 Mathie et al 2013 evaluated against PRISMA

Section/topic	#	Checklist item	Reported on page #
TITLE- Randomized controlled trials of homeopathy in humans: characterizing the research journal literature for systematic review (Mathie et al., 2013)			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	3
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4-6
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as	5-6

		criteria for eligibility, giving rationale.	
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	4
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5-6
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	5 & In a report to follow (p4)
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	4-5-6
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	Categories
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	n/a
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	n/a
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	7
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	8-20
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	23
Limitations	25	Discuss limitations at study and outcome level (e.g., risk	23

		of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	23-24
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	24

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

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Table to show the Standards for Reporting Qualitative Research (SRQR)

(O'Brien et al., 2014a)

Table 40 Standards for Reporting Qualitative Research

	Topic	Item
1	Title	Concise description of the nature and topic of the study identifying the study as qualitative or quantitative or indicating the approach or data collection method is recommended.
2	Abstract	Summary of key elements of the study using the abstract format of the intended publication; typically includes background, purpose, methods, results and conclusions.
	Introduction	
3	Problem formulation	Description and significance of the problem/phenomenon studied; review of relevant theory and empirical work; problem state
4	Purpose or Research Question	Purpose of the study and specific objectives or questions
	Methods	
5	Qualitative approach and research paradigm	Qualitative approach (e.g. ethnography, grounded theory, narrative research) and guiding theory if appropriate; identifying the research paradigm (e.g. post positivist, constructivist/interpretivist) is also recommended; rationale that briefly discusses the justification for choosing that approach; the assumptions and limitations implicit in that choice and how those choices influence study conclusions and transferability.
6	Researcher characteristics and reflexivity	Researchers' characteristics that may influence the research, including personal attributes, qualifications/experience, relationships with participants, assumptions, and/or presuppositions; potential or actual

		interaction between researchers characteristics and the research question, approach, methods, results, and/or transferability.
7	Context	Setting/Site and salient contextual factors, rationale.
8	Sampling strategy	How and why research participants, documents and events were selected, criteria for deciding when no further sampling was necessary (sampling saturation), rationale.
9	Ethical issues pertaining to human subjects	Documentation of approval by an appropriate ethics review board and participant consent, or explanation for lack thereof; other confidentiality and data security issues.
10	Data collection methods	Types of data collected; details of data collection procedures including start and stop dates of data collection and analysis, iterative process, triangulation of sources/methods, and modification of procedures in response to evolving study findings, rationale.
11	Data collection instruments and technologies	Description of instruments (e.g. interview guides, questionnaires) and devices (e.g. audio recorders used for data collection; if/how the instruments changed over the course of the study.
12	Units of study	Number and relevant characteristics of participants, documents or events included in the study, level of participation (could be recorded in results).
13	Data processing	Methods for processing data prior to and during analysis, including transcription, data entry, data management and security,

		verification of data integrity, data coding, and anonymization/deidentification of excerpts
14	Data analysis	Process by which inferences, themes, etc. were identified and developed including the researchers involved in data analysis, usually references to a specific paradigm or approach, rationale.
15	Techniques to enhance trustworthiness	Techniques to enhance trustworthiness and credibility of data analysis 9e.g member checking, audit trail, triangulation), rationale.
	Results/Findings	
16	Synthesis and interpretation	Main findings (e.g. interpretations, inferences, and themes); might include development of a theory or model, or integration with prior research or theory.
17	Links to empirical data	Evidence (e.g. quotes, field notes, text excerpts, photographs) to substantiate analytic findings.
	Discussion	
18	Integration with prior work, implications, transferability, and contributions to the field	Short summary of main findings; explanation of how findings and conclusions connect to, support, elaborate on, or challenge conclusions of earlier scholarship; discussion of scope of application/generalizability; identification of unique contribution(s) to scholarship in a discipline or field.
19	Limitations	Trustworthiness and limitations of findings
20	Conflicts of interests	Potential source of influence or perceived influence on study conduct and conclusions, how these were managed
21	Funding	Sources of funding and other support; role of funders in data collection, interpretation and

		reporting.

Table 41 External peer review of the protocol for strand 3

Review of the protocol:

A PILOT STUDY OF OVARIUM COMPOSITUM IN INFERTILE WOMEN.

By Claire Haresnape

Reviewer: Dr Alexander Tournier, PhD Research Fellow Cancer Research UK and practitioner specialised in Homeopathy, practicing in Covent Garden and Southfields.

30 October 2008

The appropriateness of the study design in relation to the objectives of the study, the statistical methodology, and the potential for reaching sound conclusions with the smallest number of research participants necessary. Feasibility and Deliverability.

The protocol as it stands appears appropriate in terms of the objectives of the study, namely to measure the effectiveness of Ovarium Co. as an adjunct to conventional treatment in dealing with female infertility.

The study uses a number of measures: experimental (endometrial thickness, nber of follicles progesterone levels) as well as the Quality of Life measure. These measures seem appropriate and adapted to capture any significant difference between the two groups, as well as offering room for interpretation of the results in terms of possible mechanisms of action.

The number of participants seems to be adapted. A small concern is that the study might not have enough statistical power to resolve between the different arms: Clomid + Ov. Co. vs Clomid + Placebo (similarly for the FSH and IVF groups). This is not a serious limitation of the design as this is not the main question of the study. The results of the study should nevertheless offer interesting insights in terms of these three conventional treatment groups. Overall, N=90 is a reasonable number for this type of study and is likely to provide adequate statistical power for the aims of the trials.

A 3rd arm of the study is mentioned several times as ‘a group that has been consented to allow access to their data’. Comparisons with this 3rd group could yield interesting results in terms of the effect of placebo, also it is quite a cost effective way of doing so. The present protocol gives little indication as

to how this 3rd group is going to be populated so as to guarantee that the populations of the three groups will indeed be comparable. As small note about this would resolve the issue. It is unclear from the present text whether this 3rd group is actually part of the design, this should be clarified one way or the other.

The justification of predictable risks and inconveniences weighed against the anticipated benefits for the research participants, other present and future patients, and the concerned communities.

There being no known toxicity associated with Ovarium Co., I see no risk in the participation in this trial.

The intervention being an adjunct to conventional treatment I see no inconvenience for the participants.

The study should yield interesting and useful results for future patients.

Assessment for broad ethical concerns, which may result in harm to the participants.

The participants will follow their conventional treatment all through the trial and therefore will not miss out on validated conventional treatment.

The safety of the participants is appropriately taken care of in this design.

Value for Money: e.g. not addressing the most important question, leading to low impact or otherwise poor value for users of research; unrealistic targets for recruitment of clinical centres and participants, leading to a likelihood of cost over-runs. Identification of funding processes and administration.

The most important question is well defined and the tools chosen adapted to answering it. The results will be useful to both researchers and patients.

Recruitment criteria appear realistic and the location appropriate for this trial.

Impact to Service: Affordability of extra clinical interventions/processes/visits, which are not covered in the funding, cost breakdown. Impact on service capacity including affiliated services such as pharmacy, pathology, imaging, etc.

Acceptable.

Small note:

Important typo on page 24, ‘succussion’ has been replaced by ‘succession’, it seems MS Word does it automatically.

Table 42 WHRI internal review of trial from strand 3

WHRI RESEARCH GOVERNANCE COMPLIANCE CERTIFICATE

Queen Mary, University of London

1. Project Title **A pilot study of ovarium compositum in infertile women**			
2. Project Start Date	1st November 2008	**Expected Project End Date**	1st May 2010

3. Details of Contact Person(s)

Lead Investigator	**Co-Investigators** (list all)

Surname(s) and Title Ms Haresnape	1. Name and Address Professor Atholl Johnston Clinical Pharmacology Barts and the London Charterhouse Square EC1M 6BQ
First Name Claire	
Address Petrona Foords Lane Vines Cross TN21 9ER	2. Name and Address Dr. Art Tucker The Ernest Cooke Vascular & Microvascular Unit St. Barts, EC1A 7BE
Telephone no.: 07720060116 Fax no.: E-mail address: c.haresnape@qmul.ac.uk	3. Name and Address

4. Detail of Referees **Comments and Review** It is encouraging to see a proper randomised placebo controlled trial for complementary

therapies as there is a dearth of robust studies in the literature upon which the clinical and scientific community can judge the effectiveness of such treatments. The protocol is well planned although I cannot judge whether adequate recruitment levels can be achieved as the study will not take place within Barts and the London NHS Trust. My major concern is that there are no statistical power calculations to estimate whether the recruitment numbers are adequate to resolve the effects of OC. I acknowledge improvements in study design over that of Gerard et al but am unconvinced that 90 patients will be adequate.

5. Date of Certification 6th August 2008

_____

Signature of Research Governance Lead

APPENDIX 2 Copy of questionnaires sent to therapists in Strand One.

Letter of Invitation and Questionnaire sent to Therapists Taking Part in Practitioner Survey

Please return to Claire Dadswell

Registered Homoeopath

Email: Claire@clairedadswell.co.uk

Fax: 01435 867518 Telephone 0772 006 0116

RESEARCH PROJECT; Homoeopathy and Infertility. Supervised by Prof Atholl Johnston, Clinical Pharmacology, Barts and The London, Queen Mary's School of Medicine and Dentistry.

Question One:

Please would you read the following summary of an infertility case and indicate which of the suggested protocols would, in your opinion, be appropriate. You may tick more than one option.

Case Details:

Sex: Female, **Date of Birth** 13th April 1962, Age at first consultation 42 years old

Marital Status: Married (happily)

Appearance: Dark haired, athletic build.

Family history: Not available as patient was adopted. She has undertaken psycho-emotional therapy regarding her adoption and is actively tracing her birth mother.

Presenting condition: Failure to respond to Gonadotrophin injections for IVF treatment. An earlier IVF treatment had resulted in a successful pregnancy but the pregnancy was terminated following tests for Downs Syndrome.

General Health is good, no menstrual difficulties, few acute infections, and infrequent headaches. No financial anxieties. Regular exercise (horse riding), but some pain from muscles, diagnosed as lactic acid build-up.

Vaccination: Hepatitis; Yellow fever, Typhoid. Malaria treatment. 1998

Other Health Choices: Hypnosis and Herbal treatment for high mercury levels.

Please tick the options that in your opinion are appropriate, you may chose more than one:

- **Option 1:** Treatment of the vaccinations using potentised vaccines, Silica and Thuja.

- **Option 2:** Treatment of the hormone balance using potentised hormones (GUNA):
    - FSH D6 20 drops three times a day from the 1st to the 3rd day of the menstrual cycle.
    - Beta Estradiol D6 20 drops three times a day from the 4th to the 14th day of the menstrual cycle.
    - Luteinizing Hormone D6 20 drops three times a day from the 4th to the 15th day of the menstrual cycle.
    - Progesterone D6 20 drops three times a day from the 14th to the 24th day of the menstrual cycle.

- **Option 3:** Use of the indicated remedies: Nat Mur 6 and Sepia 6 daily for two weeks.

- **Option 4**: Treatment of Miasmatic 'Psoric' tendency with Psorinum nosode and drainages.

- **Option 5**: Treatment of Pituitary-Ovarian feedback mechanism using complex remedy 'G3' (GUNA): Composition: Ovarium D8/D12/D30, Corpus Luteum D8/D12/D30, Pulsatilla D6/D8/D30, Kali Carb 6CH/30CH.

Question Two

What would you use in your practice as a well indicated homoeopathic/ homotoxicological protocol for treating female infertility due to declining hormone levels?

Question Three

What would you use in your practice as a well indicated homoeopathic/homotoxicological protocol for treating male infertility due to low sperm count?

Question Four

Are there any other lifestyle choices or changes that you would recommend to a patient seeking advice regarding infertility?

APPENDIX 3 Strand 2 The Study At The Bridge Centre

Table 43 Table to show a Pub Med Search for Published Studies in the Channel Islands

	URL	Description	Details	ShortDetails	Resource	Type	Identifiers	Db	Entrez UID	Properties
Cardiovascular disease in a cohort exposed to the 1940-45 Channel Islands occupation.	/pubmed/18764932	Head RF, Gilthorpe MS, Byrom A, Ellison GT.	BMC Public Health. 2008 Sep 2;8:303. doi: 10.1186/1471-2458-8-303.	BMC Public Health. 2008	PubMed	citation	PMID:18764932 | PMCID:PMC2543024	pubmed	18764932	create date:2008/09/04 | first author:Head RF
The impact of the Occupation of Guernsey 1940-1945 on breast cancer	/pubmed/17504356	Fentiman IS, Allen DS, Ellison GT.	Int J Clin Pract. 2007 Jun;61(6):937-43.	Int J Clin Pract. 2007	PubMed	citation	PMID:17504356	pubmed	17504356	create date:2007/05/17 | first author:Fentiman IS

risk factors and incidence.										
Growth of Jersey schoolchildren during the 1940-1945 German occupation: comparison with schoolchildren on mainland Britain.	/pubmed/16715836	Ellison GT, Kelly M.	Hum Biol. 2005 Dec;77(6): 761-72.	Hum Biol. 2005	PubMed	citation	PMID:16715836	pubmed	16715836	create date:2006/05/24 | first author:Ellison GT

District nurses' involvement and attitudes to mental health problems: a three-area cross-sectional study.	/pubmed/16102149	Haddad M, Plummer S, Taverner A, Gray R, Lee S, Payne F, Knight D.	J Clin Nurs. 2005 Sep;14(8): 976-85.	J Clin Nurs. 2005	PubMed	citation	PMID:16102149	pubmed	16102149	create date:2005/08/17 | first author:Haddad M
The dental caries experience of 14-year-old children in	/pubmed/15074872	Pitts NB, Boyles J, Nugent ZJ, Thomas N, Pine CM.	Community Dent Health. 2004 Mar;21(1): 45-57.	Community Dent Health. 2004	PubMed	citation	PMID:15074872	pubmed	15074872	create date:2004/04/13 | first author:Pitts NB

England and Wales. Surveys co-ordinated by the British Association for the Study of Community Dentistry in 2002/2003.										
The incidence of childhood leukaemia around the La Hague nuclear waste	/pubmed/11413175	Guizard AV, Boutou O, Pottier D, Troussard X, Pheby D, Launoy G, Slama R, Spira A; ARKM.	J Epidemiol Community Health. 2001 Jul;55(7):469-74.	J Epidemiol Community Health. 2001	PubMed	citation	PMID:11413175 | PMCID:PMC1731936	pubmed	11413175	create date:2001/06/20 | first author:Guizard AV

reprocessing plant (France): a survey for the years 1978-1998.		Registre des cancers de La Manche.								
The effect of HFE mutations on serum ferritin and transferrin saturation in the Jersey population.	/pubmed/9609537	Merryweather-Clarke AT, Worwood M, Parkinson L, Mattock C, Pointon JJ, Shearman JD, Robson KJ.	Br J Haematol. 1998 May;101(2):369-73.	Br J Haematol. 1998	PubMed	citation	PMID:9609537	pubmed	9609537	create date:1998/06/03 | first author:Merryweather-Clarke AT

Tackling the tobacco challenge: achieving 'healthy public policy' in tobacco control in Guernsey.	/pubmed/8987340	Jeffs D, Hodgkinson A.	J R Soc Health. 1996 Dec;116(6):367-75.	J R Soc Health. 1996	PubMed	citation	PMID:8987340	pubmed	8987340	create date:1996/12/01 | first author:Jeffs D
The association of height, weight, menstrual and reproductive events with breast cancer: results	/pubmed/8347782	De Stavola BL, Wang DY, Allen DS, Giaconi J, Fentiman IS, Reed MJ, Bulbrook RD, Hayward JL.	Cancer Causes Control. 1993 Jul;4(4):331-40.	Cancer Causes Control. 1993	PubMed	citation	PMID:8347782	pubmed	8347782	create date:1993/07/01 | first author:De Stavola BL

from two prospective studies on the island of Guernsey (United Kingdom).										
Snoring, asthma and sleep disturbance in Britain: a community-based survey.	/pubmed/8491303	Fitzpatrick MF, Martin K, Fossey E, Shapiro CM, Elton RA, Douglas NJ.	Eur Respir J. 1993 Apr;6(4):531-5.	Eur Respir J. 1993	PubMed	citation	PMID:8491303	pubmed	8491303	create date:1993/04/01 | first author:Fitzpatrick MF
Hazards of commercial fishing.	/pubmed/8397749	Grainger CR.	World Health Forum. 1993;14(3):313-5.	World Health Forum. 1993	PubMed	citation	PMID:8397749	pubmed	8397749	create date:1993/01/01 | first author:Grainger CR

Some mortality data for Grimsby lumpers" and fishermen."	/pubmed/1345598	Grainger CR.	Bull Inst Marit Trop Med Gdynia. 1992;43(1-4):51-5.	Bull Inst Marit Trop Med Gdynia. 1992	PubMed	citation	PMID:1345598	pubmed	1345598	create date:1992/01/01 | first author:Grainger CR

Strand Two The Study at The Bridge Centre

Data collection instruments and technologies

Questionnaire for nurses at The Bridge Centre

1. What are your experiences of Homeopathy?
2. What are your expectations of Homeopathy?
3. How do you feel about clients who have tried alternative and complementary medicine?
4. How much time do you get with clients to go over consent forms and dispense medicine?
5. How do you feel about being asked to do this study?
6. What is the most difficult part of your role?
7. What is the most rewarding aspect of your role?
8. What problems can you foresee with the proposed project?
9. What benefits to the patients and the clinic can you foresee with the proposed project?

Questionnaire for Patients at The Bridge Centre

Barts and The London
Queen Mary's School of Medicine and Dentistry

Would you like to do something to help research into the potential benefits of Homotoxicology for infertile women?

The Bridge Centre is assisting research into the use of complex homoeopathy (Homotoxicology – see Page 4). If you would like to help then please complete this questionnaire and return it in the S.A.E. to:

Ms Pauline Wright, Matron
The Bridge Centre
One St Thomas Street
London Bridge
London
SE1 9RY

Your answers will be analysed to find out if it is feasible to plan a trial of Homotoxicology. The aim of the trial to see if the use of Homotoxicology remedies can increase the number and quality of eggs produced during ovulation induction. If complex homoeopathy is shown to have an effect then this may mean that older women, or women who have failed to respond to the ovulation induction drugs, have a higher chance of ovulating using Assisted Reproduction.

Please only answer those questions that you are happy and comfortable to answer. You are not under any obligation to complete this questionnaire, it is entirely voluntary.

This project is supervised by a senior academic at a leading London medical school.

Question One.
Have you ever tried Homotoxicology as a therapy?

yes *no*

Question Two.
Have you tried Homotoxicology as part of your treatment for infertility? *yes* *no*

Question Three.
Would you consider trying Homotoxicology in the future as part of your treatment for Infertility? *yes* *no*

Question Four.
Would you be prepared to take part in a clinical trial where you may receive a placebo or no medication instead of the active remedy?

yes *no*

Question Five.
Would you be willing to take your medication daily at home, as drops or tablets? *yes* *no*

Question Six.
Would you be willing to give up
peppermint and coffee? *yes*
no

Question Seven.
What would be your motivation to take
part in a clinical trial of Homotoxicology?
(You may tick more than one answer).

(i) *To increase my chances of ovulating* *yes*
no
(ii) *To help other couples in the future* *yes*
no
(iii) *To increase knowledge about homoeopathy* *yes*
no
(iv) *Deciding to stop trying with IVF/ART* *yes*
no
(v) *Other reasons. (Please specify them below if you wish).* *yes*
no

……
……
……
……..

Question Eight.

Would you be happy to pay for homotoxicology
Treatment in the future, if this was shown to be an effective therapy?

yes *no.*

Question Nine.
Would you be prepared to take homotoxicology remedies
at the same time as your conventional medication?

yes

no.

Thank you for taking the time to complete this survey. You do not need to supply your name and address but for research purposes it would be helpful to know your date of birth:

D.O.B ____/____/_____(dd/mm/yyyy). 12

Patient Information Sheet included with questionnaires

What is Homotoxicology?

- A German Doctor called Hans-Heinrich Reckeweg established Homotoxicology 50 years ago.

- Sometimes it is called Anti-Homotoxic Therapy or Complex Homoeopathy.

- It is similar to Homoeopathy but not the same.

- **Homoeopathy** makes use of single remedies carefully chosen to match the symptoms of the individual person.

- **Homotoxicology** makes use of combinations of remedies chosen to match the nature and severity of the disease that the person is suffering from.

- As well as using the traditional remedies made from plants, animals and minerals, Homotoxicology uses preparations made from very diluted hormones and other chemicals found naturally in the human body.

- By giving remedies made from very diluted hormones Homotoxicology aims to bring about a regulation of hormone levels in the body.

- There are other kinds of preparations made from very dilute amounts of cells and tissues of healthy pigs. These are believed to stimulate and regenerate the body's systems that regulate our health.

Conclusion

Homotoxicology makes use of remedies derived from natural sources to bring about a return to a health. It aims to correct the control systems of the body, which sometimes become disturbed. It works by gently stimulating these control systems.

Appendix 4 The Protocol for The Pilot Study Strand 3. dix

APPENDIX 4 Protocol for Pilot Study from Strand 3

PRIVATE & CONFIDENTIAL

A PILOT STUDY OF OVARIUM COMPOSITUM IN INFERTILE WOMEN.

Protocol No.: OVCT-001

Version 5.3

4th February 2012

SPONSOR:

William Harvey Research Institute
Barts and the London School of Medicine & Dentistry
Queen Mary University of London
London
EC1M 6BQ

AMENDMENTS:

1.

4.11.10 Sponsor changed from Seahorse Scientific Services to

William Harvey Research Institute
Barts and the London School of Medicine & Dentistry
Queen Mary University of London
London
EC1M 6BQ

22.01.11

1. Exclusion Factors changed to remove previous pregnancy and other CAM therapies
2. Quality of Life Questionnaires to be completed on stimulation phase of the cycle
3. Follicular tracking charts to be photocopied and attached to CRF
4. Primary outcome changed to ovulatory response and secondary outcome changed to length of time to pregnancy

04.02.12

1. Amendment to Patient Information Sheet to inform patients that they can take the medication +\- one hour either side of stated time and that if they miss a dose then they continue with the next dose.

A PILOT STUDY OF OVARIUM COMPOSITUM IN INFERTILE WOMEN.

Claire Haresnape

Abstract

Persistent treatment failure may encourage women to seek out help using complementary and alternative medicine (CAM). There is a need for further research to provide an evidence base for the safety, efficacy and cost effectiveness of CAM. Ovarium compositum is a preparation of homeopathic ingredients purporting to treat female infertility. It is prescribed in the UK by registered Homotoxicologists and other clinicians. The aim of this pilot study is to evaluate the effectiveness of Ovarium compositum vrs placebo in a randomised trial of 90 women attending an infertility clinic for ovarian stimulation and assisted reproduction. The outcomes to be evaluated are both quantitative (response to ovulation drugs, length of time to pregnancy) and qualitative (quality of life).

APPENDICES

1. Synopsis

Study Title **A pilot study of the use of Ovarium Compositum as an adjunct treatment for infertile women in an assisted reproduction unit.**

Sponsor

William Harvey Research Institute
Barts and the London School of Medicine & Dentistry
Queen Mary University of London
London
EC1M 6BQ

Funder: **Heel GmB**

OBJECTIVES:

The primary objective is to assess whether the administration of Ovarium Compositum as an adjunct therapy can make a significant difference to fertility outcomes in infertile women seeking medical intervention.

The second objective is to measure quality of life in women undergoing treatment for infertility and using Ovarium compositum.

Study Design: One centre, double blind placebo randomised controlled trial

Study Location: Department of Obstetrics and Gynaecology
Jersey General Hospital
Gloucester Street, St Helier
Jersey, JE1 3QS
Telephone 01534 622 660

Study Period: 12 Months

Pharmaceutical Agents: Subjects will be randomised to one of the following agents

Ovarium Compositum vrs Placebo

Route of Administration: Oral Tablet, one tablet three times a day to be dissolved in the mouth

Duration of administration: Daily, ongoing until positive pregnancy test or trial ends

Study Duration: Expected to take 12 months

Sample Size: 45 active plus 45 placebo N=90

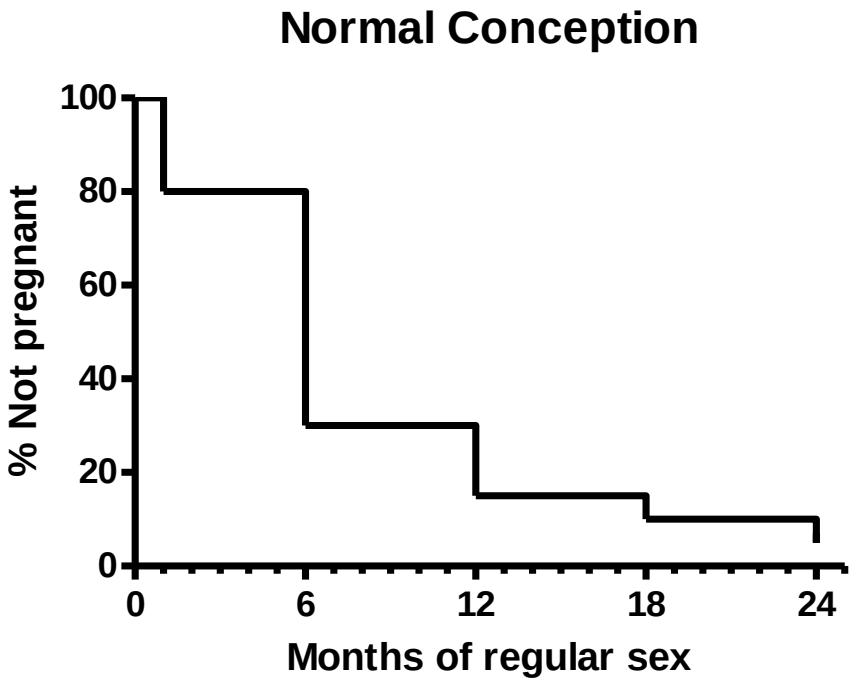
Non participating women at clinic to be consented for access to data for comparison.

2. Introduction

2.1 BACKGROUND

It has been estimated that at some time in their reproductive lives at least a quarter of couples experience a period of infertility (inability to conceive) lasting over 1 year. Some of these couples continue to be unable to conceive, leading to at least 1 in 6 couples seeing an infertility specialist at a hospital In the clinic setting ovulation induction problems are some of the commonest problem encountered. **Anovulation** is the failure to ovulate (expel a mature oocyte) owing to dysfunction of the ovary or suppression by drug treatment. Anovulation is a common cause of female infertility. Most often, women who do not ovulate also do not menstruate (amenorrhea).

Table One



If a woman is not ovulating by herself then ovulation induction may be required. The most common causes of failure to ovulate are stress, weight fluctuations and Polycystic Ovarian Syndrome (P.C.O.S.). Other causes may include disorders of the pituitary gland, thyroid gland and raised prolactin

levels. In some cases failure of ovulation is due to the ovarian failure. This may occur following treatment for cancer or may be the start of the menopause - premature ovarian failure[i].

Many couples may therefore require some form of medical treatment to induce ovulation and assist with conception. Ovulation induction aims to achieve repeated unifollicular ovulation in the correction of anovulatory infertility. Therapies to induce ovulation first involve the use of the anti-oestrogen clomiphene citrate.

If ovulation is not occurring, then drugs may be administered with the onset of menstruation to stimulate egg production. If tablets are not effective then more powerful fertility injections may be necessary to stimulate egg production in the ovaries. Ovulation is induced using one of two main drug regimens:

Clomiphene or Clomid tablets increase the production of follicle stimulating hormone (FSH) by the pituitary gland, thereby stimulating follicles and hence egg growth. This tablet is normally given in a starting dose of 50 mgs (1 tablet) taken from the 2nd to the 6th day of the period. If the periods are very infrequent then it may be necessary to induce a period by giving a different type o tablet called Nor-ethisterone.

Gonadotrophins: these are given by injection. Their active ingredient is follicle stimulating hormone. Examples are: Menopur, Ronal F and Puregon. These injections are given on a daily basis and start at a dose of 75 i.u. each day.

The response to any drugs given is monitored by ultrasound scans. When follicles have reached an appropriate size intercourse is advised, or an injection of hCG is given to facilitate the timing of intercourse or IUI. Individual responses to treatment can be unpredictable and if, during the monitoring, the response is insufficient or too strong, the cycle may have to be cancelled and restarted as appropriate. If the response to the drugs is satisfactory, treatment usually continues for 6 cycles; treatment cycles can be carried out consecutively without a break.

Potential side effects are mainly related to the drugs. Multiple pregnancies are a risk of ovulation induction treatments. Twins can result in up to 10% of cases with clomiphene treatment, and 20% with gonadotrophins. Triplets

may also occur in around 1% of cases. With careful monitoring the risk of multiple pregnancies is reduced but not eliminated. Gonadotrophophin releasing hormone antagonists (GnRHantag) are increasingly used in In-vitro fertilisation/Intra Cytoplasmic Sperm Injection (IVF/ICSI) treatment cycles. With their use, however, there are concerns of reduced pregnancy rates.[ii]

A study from ESHRE LYON 2007 [iii] concludes that natural ICSI cycles with minimal stimulation in poor responder patients represents a cheap and easy approach which offer significantly higher implantation rates compared to conventionally stimulated cycles. The use of Ovarium compositum may potentially represent a form of minimal stimulation and an alternative to the administration of high levels of gonadotrophins.

2.2 NICE GUIDELINES FOR THE TREATMENT OF INFERTILE WOMEN.

NICE Guidelines for the treatment of infertility suggest that a couple should seek help after 2 years of unprotected sexual intercourse. However where the women are aged 35 or more then assessment and referral to a specialist team should take place earlier.

Women with WHO group II ovulation disorder (hypothalamic-pituitary dysfunction) should be offered treatment with comifene citrate as a first line of treatment for up to 12 months because it is likely to induce ovulation (1.6.1.1)

Women with WHO group II ovulation disorders who do not ovulate with clomiphene citrate can be offered treatment with Gonadotrophins such as FSH. (1.6.4.1).

One of the key priorities of the NICE guidelines is that after 3 years of infertility couples should be offered 3 cycles of IVF. For pituitary down regulation as part of IVF treatment using gonadotrophins releasing hormone agonist in addition to gonadotrophins stimulation facilitates cycle control and results in higher pregnancy rates than the use of gonadotrophins alone (1.6.7.1)

The effectiveness of complementary therapies for fertility problems has not been properly evaluated and further research is needed so that such interventions can be integrated. The use of homotoxicology is not currently part of the conventional approach to treating infertility as insufficient data exists as to both the efficacy and cost effectiveness. However, according to a spokesperson for Clarence House commenting on the Smallwood Report, past research indicates that as many as 16 million people in the UK have used complementary treatments and so there is a clear need for reliable information on this subject).

M Dooley[iv] has reviewed the background to complementary and alternative medicine and the evidence for its introduction into mainstream obstetrics and gynaecology. He discusses the difficult of obtaining good evidence and concludes that the need to develop an integrated approach to healthcare is particularly relevant and important in obstetrics and gynaecology. With this integration in mind he emphasises the need to encourage clinical research in this area.

In my unpublished study[v] of UK practitioners using homotoxicology to treat infertility, registered Homotoxicologists and practitioners attending the annual symposium were asked to complete a questionnaire.. The primary aim of this questionnaire was to find out how Homotoxicologist currently practising in the UK would treat infertility. The need to obtain a consensus of opinion was highlighted by Professor Edzard Ernst, Director of Complementary Medicine, Peninsula Medical School, Universities of Exeter & Plymouth, who kindly advised the author in a personal interview.

The Questionnaire was designed to firstly establish their opinions regarding a specific case study and then to investigate their approach towards treating infertility in general. The specific case study in question one was characteristic of the patient group that will be enrolled in the pilot study. 60 questionnaires were distributed and a total of 20 questionnaires were returned. Four had chosen not to participate and of the remaining 16 practitioners, five had a medical/dentistry qualification. For 6 of the therapists Homotoxicology is a core skill, they have a recognised qualification in Homotoxicology and able to register as Homotoxicologists with the British Register of Complementary Practitioners.

The results showed that in cases of female infertility the professional clinicians and registered practitioners are willing to recommend preparations such as Ovarium compositum, purporting to stimulate the Ovarium-Pituitary feedback mechanism. The therapeutic indications for Ovarium compositum are listed in the BioTherapeutic Index as:

'*Stimulation of the glandular and defensive functions, as well of those of the connective tissue, in dysmenorrhoea, endometritis, metritis, parametritis, enuresis (in young girls), in the climacteric, hyperemesis, insufficiency of the anterior lobe of the pituitary gland in females, craurosis vulvae, mastodynia, osteomalacia, menorrhagia, as well as in various disturbances of metabolism, including those arising in geriatrics. (Page 379).*

The therapeutic use is listed according to the homeopathic drug proving. Approximately 2000 units have been prescribed in the UK over the last 3 years. European Sales are in the region of 150,000 in the same time period. Each unit represents a box of 10 ampoules which is a five week course.[1]

2.3 RATIONALE

In the context of assisted reproductive technology, effective strategies to overcome the impact of ovarian aging and diminished ovarian reserve on pregnancy remain elusive. This study aims to investigate the impact of Ovarium compositum on the success rates of ART in a group of women who attend an assisted reproduction unit. The effectiveness of complementary therapies for fertility problems has not been properly evaluated and further research is needed so that such interventions can be integrated if they prove to be cost effective and safe.

Infertile women will frequently seek out a holistic approach to overcoming their infertility. Infertility Clinics sometimes offer access to advice on integrating acupuncture, nutrition, psychological and emotional health, but there is little or no available information about interventions using homotoxicology. The NICE guidelines list one study of homeopathic treatment in their table of evidence[vi] Gerhard et al (1999) recruited 77 women. 43 were offered individualised homeopathic treatment (sepia,

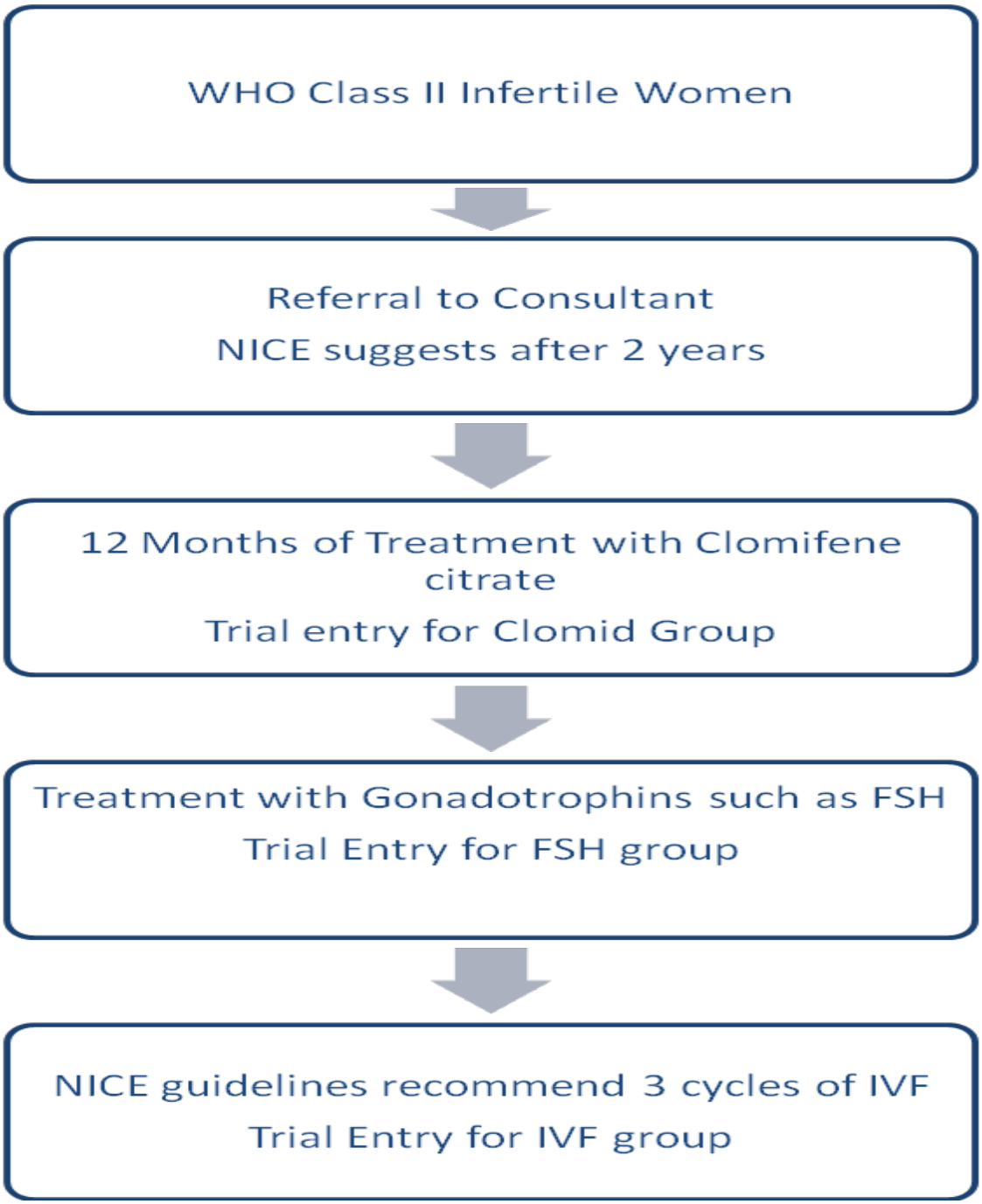
[1] Sales figures quoted by Mr Roger Wilson, UK agent, BioPathica Ltd.

pulsatilla, thuja phosphorous etc) and 34 were offered conventional treatment (IVF, Clomifene-hCG, and FSH). The outcomes that were measured were live birth rate and pregnancy rate. The results were not considered statistically significant and the dropout rate was 34%. The editors of the report comment on the fact that the patients were allowed to change groups and that the method of randomisation, allocation, concealment and blinding were unclear.

My pilot study seeks to improve upon this trial design in several important ways: firstly the use of a combination homeopathic preparation means that treatment does not have to be individualised. All patients will receive Ovarium compositum or Placebo as well as their conventional treatment. Secondly, Patients will not be able to change groups. Thirdly the methodology of blinding, randomisation and allocation will be made explicit in the study design documentation. Fourthly we are looking at several additional outcomes that may be more sensitive indicators of change such as the response to doses of ovulation induction drugs in all groups and Quality of Life (QOL) in both groups.

Table Two

Progression of Infertility Treatment according to NICE guidelines.



A recent paper [vii] suggests that persistent treatment failure encourages women to seek out complementary therapies. Qualitative studies suggest that infertility can be a devastating experience especially for women. This pilot study offers an opportunity to collect data on the quality of life for women undergoing treatment.

Making the positive changes suggested by these therapists may generate a clinically significant placebo effect through reducing stress. The measurement of the Quality of Life of trial participants may yield data on this area. Comparison of data between blinded participant groups and none participating, consented patients at the same clinic may allow quantitative data to be collected on the placebo effect

The new infertility-specific tool being developed at University of Oxford is called the EHIQ (Emotional Health in Infertility Questionnaire) [viii] this measures emotional strain in healthy individuals, rather than psychopathy. (See Appendix 4). It is a potentially useful tool in studying the emotional effects of infertility and the effectiveness of interventions to reduce emotional distress in this population and the influence of emotional health on treatment perseverance and treatment outcomes.

The Questionnaire [ix] has nine domains:

1. Personal Strain
2. Partner relationship strain
3. Sexuality
4. Social support
5. Confidence in treatment
6. Guilt and blame
7. Financial strain
8. Need for privacy
9. Couple concordance (where appropriate).

As this is a new tool that has not been fully validated the EQ5D will be used as well (Appendix 6).

There are two categories of women that are of interest to this trial: firstly those that respond very poorly to standard ovulation induction agents and secondly those anovulatory women who are being given ovulation induction agents Chronological age is an important predictor of outcome and so each group will be stratified for chronological age. Women presenting at the clinic will be offered the opportunity to take part in the trial. Those who fulfil the selection criteria will be consented and then allocated a protocol on a randomised basis. The principal investigator will assign them, blinded to everything except their age.

3. Objectives

1. To measure the response to doses of ovulation induction drugs in all groups:
    - 1.1 Measuring endometrial thickness at ovulation/mid cycle
    - 1.2 Measure the number of follicles
2. Progesterone level on day 21 mid luteal phase (>35 means you have ovulated) 1. To measure the length of time to pregnancy in all groups
3. To measure the Quality of Life (QOL) in both groups using the EHIQ and EQ5D (See Appendix 4)

4. Subjects

Female patients will be recruited via the infertility clinic consultant. Previous use of homeopathic remedies is not considered to be an exclusion factor. However a washout period of one month will be necessary if they are taking any homeopathic remedies.

Volunteers will be provided with a full explanation of the nature, purpose and requirements of the study including Information Sheets and Informed Consent Forms. The trial design will need to include an active group, a

control group and a group that has been consented to allow access to their data. This means that we could compare outcomes in a group that was not experiencing a placebo response to those taking both the placebo and the active trial medication.

The Investigators will enrol up to ninety (90) female volunteers into the study who will be randomised into six treatment groups.

Table Three Proposed Treatment Groups

	Given	Plus
Group one N=15	Clomid	Placebo
Group two N=15	Clomid	Ovarium Compositum
Group three N=15	FSH	Placebo
Group four N=15	FSH	Ovarium Compositum
Group five N =15	IVF	Placebo
Group six N=15	IVF	Ovarium Compositum

The specific inclusion and exclusion criteria are indicated below:

4.1 INCLUSION CRITERIA

In order to be eligible to enter the study, volunteers must meet the following criteria:

1. Female
2. Age stratified in active and placebo groups (see Table Four).
3. Diagnosed with poor response to ovulation induction or anovulatory(WHO Group2)

4. Absence of other significant endocrine dysfunction including diabetes

4.2 EXCLUSION CRITERIA

1. Taking medication for other medical conditions that may affect ovulation

2. Pregnancy

3. BMI <20kg/m^2 and >35kg/$m^{2\,x}$

4. Use of peppermint, caffeine, nicotine, recreational drugs or alcohol

Table Four: Age Stratification Bands

Medication	Clomid Vrs Placebo	Clomid Vrs Placebo	Clomid Vrs Placebo	FSH Vrs Placebo	FSH Vrs Placebo	FSH Vrs Placebo	IVF Vrs Placebo	IVF Vrs Placebo	IVF Vrs Placebo
Years of age on date of trial entry	<30	30-35	>35	<30	30-35	>35	<30	30-35	>35

5. Study Methodology

Up to ninety (90) subjects are planned to be enrolled.

5.1 DESIGN

One-centre, randomised, double blind trial in female volunteers who meet the inclusion criteria.

Allocation to treatment will be controlled by the principal investigator and the fertility consultant at study site. The usual blood tests and clinical evaluations will be made by the fertility clinic and no additional or specific tests are required for this study.

5.2 SCREENING EVALUATION

Prospective subjects will attend the study site for their routine screening visit. They will have the nature of the study, the procedures and the risks fully explained.

Before any screening procedures occur they must sign an Informed Consent Form in which they acknowledge that they are willing to be assessed for enrolment in the study; that they agree to providing personal particulars to the investigators and recognise that these may be available to non-medical investigators and may be sighted by the Sponsor; that they agree to having the biochemistry; haematology, and urinary tests conducted.

During the screening evaluation the following procedures will be conducted and recorded for all volunteers:

- Informed Consent
- Evaluation of compliance with inclusion and exclusion criteria
- Access to Demography and Medical History
- No additional Laboratory Tests except as required for their infertility treatment
- Assessment of any concurrent medications

Volunteers who satisfy all of the inclusion and exclusion criteria, who sign the Informed Consent Form for Study Participation and who agree to the conditions of the study, will be eligible to enter the study.

5.2.1 The Randomisation and Allocation Procedure.

The patients will be randomised, in blocks of four. They will be stratified according to chronological age and treatment group.(see Table Four).

5.3 STUDY PROCEDURES

5.3.1 Treatment Procedures

Prior to the study, the Investigator shall review all Volunteers' check-in details, consent documents and indicate whether each volunteer has been accepted into the study.

Schedule of Visits.

Visit One:

- The Volunteers will report to the Study Centre at a pre-agreed time.
- The active agent will be randomly distributed and 100 tablets dispensed to the Subject by the responsible administering Clinician with full instructions on frequency and timing of dosages.
- Dose frequency and timing: one tablet dissolved in the mouth three times a day, at least 15 minutes before or after meals. Dose to be taken at 9am, 12 noon and 9pm, plus or minus one hour.
- If a dose is missed then subjects will take the next dose as normal
- Subjects will at all times continue with their conventional infertility treatment as prescribed by the Consultant.

Visits 2 - 12

- On completion of this dose for 30 days Subjects are expected to attend an evaluation session and if they still fulfil the criteria of the trial the dose can be repeated.
- A further 100 tablets will be dispensed.

- Volunteers will be evaluated in this way every 30 days.
- Unused tablets to be returned to the Principal Investigator in a sealed bag, labelled with Subjects name and date of birth for counting.
- Subjects will be instructed to discontinue trial drug after an ART intervention and wait until a pregnancy test is performed.
- The maximum length of trial is 12 months, however most patients will be prescribed their fertility treatment for a 6 month period. For example failure to ovulate is treated with Clomid for 6 months, FSH stimulation would follow for 6 months and then IVF would be started.
- The patients in the trial group for Clomid, for example, would discontinue their trial medication when they discontinue their Clomid treatment. They would not automatically be assigned to the next trial group.
- Patients will be discharged when the trial ends (12 months) or on a positive pregnancy test.

5.4 RESTRICTIONS:

5.4.1 Dietary

Subjects will be free to consume normal meals at all times.

Peppermint and coffee are to be excluded from the diet but the use of mint flavoured toothpaste is allowed.

No food or drink to be consumed or teeth cleaned within 15 minutes of dose of study drug.

5.4.2 Smoking

Smoking and tobacco consumption are exclusion criteria due to the harmful effects in pregnancy.

5.4.3 Concurrent Medication

Subjects who meet the inclusion criteria will not be asked to abstain from prescribed medications.

The Subject must inform Study Personnel if any additional medication is required. If drug therapy or medication is required during the study, a decision to continue or discontinue the subject will be made by the principal Investigator based on the time the medication was administered and its pharmacology and pharmacokinetics. All details of concomitant medications will be recorded in the Subject's Diary and Case Report Form (CRF).

5.5 PARAMETERS FOR EVALUATION

5. 5.1 Demography, Medical History

Includes initials, date of birth, BMI, race, height and weight. A full medical and surgical history will also be evaluated including previous pregnancies or treatments for infertility.

5.5.2 EHIQ (Emotional Health in Infertility Questionnaire)

Subjects will be asked to complete an EHIQ (See Appendix 4)

5.5.3 Vital Signs

Vital signs, including body temperature, sitting radial pulse and blood pressure will be performed at the screening visit.

5.5.4 Adverse Events

Subjects will be monitored for adverse events throughout the study. Adverse events may be spontaneously reported by the subject, observed by the study personnel or elicited by the study personnel, who should ask subjects the following non-leading question: ‘How do you feel?’ or ‘How have you been feeling since I last asked you?’ The same questions will be used throughout the study.

Serious Adverse Events will be reported to the Sponsor, the COREC recognised Research Ethics Committee and the MHRA. If a Grade 3 r 4 toxicity (based on the Common Toxicity Criteria (CTCv3.0)) or other serious adverse events occurs, no further dosing of the subjects will occur until the cause of the event and its relationship to the study drug has been clarified. Continuation of the trial will be contingent upon approval by the Sponsor. There is a database for ADRs at Heel’s Safety Departement (only one ADR listet for Ovarium Comp)

5.6 STUDY DRUGS

Ovarium compositum is manufactured in Germany according to Good Manufacturing Standards and the certificate is attached (Appendix 5) Ovarium compositum is on the market in 20 different countries. It is on the market with an import licence,with a registration or with a marketing authorization (Russia, Poland, Latvia). Figures of sales show 700.000 - 900.000 Ampoules per year

In the countries where the product is on the market you find as indication on the leaflet: "Stimulation of the glandular and defensive functions, as well as those of the connective tissue, in dysmenorrhoea, endometritis, metritis, parametritis, enuresis (in young girls), in the climacteric, hyperemesis, insufficiency of the anterior lobe of the pituitary gland in females, craurosis vulvae, mastodynia, osteomalacia, menorrhagia, as well as in various disturbances of metabolism, including those arising in geriatrics."

Due to its individual homeopathic constituents Ovarian Compositum has an application in the homeopathic treatment of hormonal disturbances, menopausal syndromes and Insufficiency of the pituitary gland.

APPENDICES

5.6.1 Treatment Formulations Table Five

The preparation is formulated as follows:

Ovarium suis		**D8**	**1mg**
Placenta suis		**D10**	**1mg**
Uterus suis	**D10**	**1mg**	
Salpinx suis	**D10**	**1mg**	
Cypripedium		**D6**	**1mg**
Lilium tigrinum	**D4**	**1mg**	
Pulsatilla	**D18**	**1mg**	
Aquilegia vulgaris	**D4**	**1mg**	
Sepia	**D10**	**1mg**	
Lachesis	**D10**	**1mg**	
Apisnum	**D8**	**1mg**	
Kreosotum	**D8**	**1mg**	
Bovista	**D6**	**1mg**	
Ipecacuanha		**D6**	**1mg**
Mercurius solubilis Hahnemanni		**D10**	**1mg**
Hydrastis	**D4**	**1mg**	
Acidum cis-aconiticum	**D10**	**1mg**	
Magnesium phosphoricum		**D10**	**1mg**

Carrier	
Lactose-Monohydrat	**297mg**
Magnesium stearate	**1.5mg**

5.6.2 Homeopathic Medicinal Products

Modern definitions of homeopathic remedies tend to focus on what remedies are rather than how they are used.[xi] The definition given in both the EU Directive for Medicinal Products (1992) and UK Statutory Instrument (SI 1995/308) is as follows:[xii]

Homeopathic medicinal product means a medicinal product (which may contain a number of principles) prepared from products, substances or compositions called homeopathic stocks in accordance with a homeopathic manufacturing procedure described by the European Pharmacopoeia or, in the absence thereof, by any pharmacopoeia used officially in an (EU) member state.

The UK Medicines and Healthcare Products Regulation Authority (MHRA) and other European regulatory bodies use the term *stocks* for the starting solutions, usually mother tinctures, from which homeopathic potencies are prepared.

In 1988 The German Health Ministry took the initiative to establish standards for the manufacture of homeopathic medicines and this led to the production of a European Pharmacopoeia in 2002.

About 65% of all remedies are prepared from extracts of plant materials, and because of this homeopathy is often confused with herbalism by many people. The difference lies in the manner of producing the two types of medicine. Herbal products are generally the result of an aqueous or alcoholic extraction alone, whereas in homoeopathy an additional dilution process is involved. Either the whole plant may be used or only the leaves, stems, flowers or roots as specified in the pharmacopoeia monographs. The species of plants, the parts taken, the time of collection and the extraction procedures may well differ according to the particular pharmacopoeia being consulted.[xiii]

Animal and insect material must be obtained from healthy specimens. Biological materials from healthy animal or vegetable secretions or from bacterial cultures are made into remedies known as sarcodes. If the remedy is derived from diseased tissue then the finished remedy is known as a nosode.

'Suis organ preparations (sarcodes) are homeopathic attenuations of wholesome organs or tissues obtained from healthy animals, in this case pigs.' [xiv]

Suis organs are said to act like 'organ specific nosodes' to create a stimulative treatment where damage has occurred to the organs and tissues in question. These medications are claimed to be 'particularly successful in treatment of degenerative damage as well as functional insufficiency of the organs.' [xv] The Suis organ preparations are said to 'guide' other active homeopathic substances in their presence to the corresponding targeted organ, thereby intensifying their efficacy.

5.6.3 Preparation of remedies:

5.6.3.1 Extraction

Mother tinctures are the liquid preparations resulting from the extraction of suitable source material with alcohol/water mixtures which form the starting point for the production of most homeopathic remedies. Comminution followed by standard percolation, maceration and squeezing techniques are used on fresh plants and succulents while dried specimens are subjected to percolation with alcohol.

The resulting solutions are strained and can contain one part drug to three parts mother tincture, when the final tincture represents one tenth of the concentration of the original drug it is in effect a 1x dilution.

With insoluble chemicals such as Aurum (gold), Plumbum (lead) or Sulphur the solid material must be triturated and serially diluted with lactose powder using a pestle and mortar in a precise and documented manner.[xvi]

5.6.3.2 Potentisation

Most mother tinctures are subjected to a two stage process involving dilution and succussion, this process is known as potentisation. The Hahnemanian method offers two scales of dilution, centesimal and decimal. The remedies that make up Ovarium Compositum are in the decimal scales of dilution. In modern pharmaceutical practice it is common to use a triple distilled alcohol and water system, the strength of which varies from 20 – 60%, in the preparation of homeopathic dilutions. The solution resulting from a mixture of the two liquids is subjected to the vigorous shaking with impact known as succussion.

After the initial processes, successive serial dilutions follow, using fresh glass vials at each stage, until the solution reaches 6x for example. The process involves adding one drop to nine drops of dilutent. The potencies are designated by a number with the letter ‘x’ following it. Thus 6x represents a 1 in 10 dilution carried out serially six times, each with a burst of succussion.

In large scale manufacture homeopathic granules are medicated and then compressed to form the tablets in a process similar to allopathic manufacture.

Table Six: Decimal potencies

Dilution	Concentration	Decimal Potency
1:10	10^{-1}	1x or D1
1:100	10^{-2}	2x or D2
1:1000	10^{-3}	3x or D3
1:10 000	10^{-4}	4x or D4
1:100 000	10^{-5}	5x or D5
1: 1000 000	10^{-6}	6x or D6
1: 10^{30}	10^{-30}	30x or D30

5.6.4 Homeopathic Indications for the Individual Constituents

Ovarium suis (ovary)

The Biotherpeutic Index entry for Ovarium Compositum includes Ovarium suis with the following symptoms: *Disturbances of the ovarian function e.g. dysmenorrhoea, metrorrhagia, climacteric disorders.*

These indications are also found in the homeopathic literature [xvii] : 'Disturbances of the ovarian function, dysmenorrhoea, amenorrhoea, climacteric with manifestations of ovarian endocrine deficiency; hypermenorrhhoea, metrorrhagia, female sterility, climacteric neurosis with depression, nymphomania, delusional ideas of jealousy, kraurosis vulvae, mastodynia, and osteomalacia'.

Placenta Suis (entire placenta)

The Biotherpeutic Index entry for Ovarium Compositum includes Placenta Suis with the following symptoms: *Dysmenorrhoea, peripheral circulatory disturbances.*

The attenuations of this sarcode are prepared using the whole placenta from the uterus of a healthy female pig (sus scrofa domesticus) with young.[xviii]

Indications[xix] for use: Peripheral circulatory disorders, cutis marmorata, decubiutus, pernios, Buerger's disease, ulcus cruris, rhagades, eczema, infolding of skin, sclerodermia, dysbasia intermittens, dysmenorrhoea, sural spasms, muscular rheumatism.

A proving of this substance was conducted in the fall of 1994 by Dr David Riley. Congruent Symptoms with Dr Reckeweg:

- Disorders of the peripheral circulation
- Prostration
- Rheumatism
- Cramps of the calf muscles

Uterus Suis (uterus)

The Biotherpeutic Index entry for Ovarium Compositum includes Uterus Suis with the following symptoms: *Dysmenorrhoea.*

The attenuations of this sarcode are prepared from the womb removed from healthy pigs (Sus scrofa domesticus).[xx]

The main indications are:

Uterine prolapsed. Uterine fibroids. Dysmenorrhoea. Pre-cancerous state of the uterus. Cervical erosion. Female sterility. Other degenerative diseases of the uterus.

Salpinx Uteri Suis (Fallopian Tube)

The Biotherpeutic Index entry for Ovarium Compositum includes Salpinx Suis with the following symptoms: *Dysmenorrhoea, sterility through inflammatory diseases of the salpinx uteri*

The attenuations of this sarcode are prepared from the Fallopian tube removed from healthy pigs (Sus scrofa domesticus).
The main indications are:
Female sterility resulting from inflammatory disease of the Fallopian tube, (consequences of gonorrhoea, etc). Disorders of ovulation, Dysmenorrhoea. Menopausal problems.[xxi]

Cypripedium Pubescens - Lady's Slipper

The Biotherpeutic Index entry for Ovarium Compositum includes Cypripedium with the following symptoms: *Conditions of nervous irritability, insomnia with restlessness and twitching of the body.*

The mother tincture is prepared from the fresh rootstock, gathered in autumn, of the plant Cypripedium calceolus, var. Pubescens (Willd.) Corell., a native of North America. N.O. Orchidaceae.

The main indications for the homeopathic dilution are: Abuse of Coffee. States of nervous irritation. It's listing as an ingredient of Ovarium Compositum states: Conditions of nervous irritation, insomnia with restlessness and twitching of the body.[xxii]

Cypripedium is said to be particularly effective in nervous women, whose nerves are affected by illness or by abuse of tea or coffee. (Impregnation phases according to the Disease Evolution Table see Appendix 2). However it is also recommended in consequences of mental over-exertion, night watching and exhaustion of the nervous system in influenza.
The German Monograph-Preparation Commission for the Homeopathic Field of Therapy has, under the Preparation Monograph for Cypripedium calceolus var. Pubescens, published the following indication in the German Bundesanzeiger (German Federal Gazette): Insomnia

Clarke[xxiii] has the following information: Cypripedium has great repute as a 'nervine' among eclectics, and in domestic practice. For the female sphere it is indicated for Amenorrhoea, with hysterics, Great nervous debility and despondency, Irritability of vagina; hysterical symptoms, sleeplessness and agitation.

Lilium tigrinum (Tiger Lily)

The Biotherpeutic Index entry for Ovarium Compositum includes Lilium tigrinum with the following symptoms: *Uterus descensus, dysmenorrhoea, and nervous cardiac disturbances with anxiety, fluor albus.*

The mother tincture is prepared from the fresh aerial parts in flower of Lilium lancifolium Thunb., a native of China and Japan and often cultivated for decorative purposes. N.O. Liliaceae.

The main indications are[xxiv]: Palpitations, squeezed sensation (similar to Cactus). Leucorrhoea. Dysmenorrhoea. Uterine prolapsed. Left sided ophoritis. Bearing down sensation. Burning and heat in the palms of the hands and soles of the feet. Pulsations throughout the body. The German Monograph-Preparation Commission for the Homeopathic Field of Therapy has, under the Preparation Monograph for Lilium lancifolium, published the following indications in the German Federal Gazette) for lilium tigrinum: complaints associated with prolapsed of the uterus during menopause; inflammations and painful conditions of the female reproductive organs; nervous cardio circulatory complaints; irritable emotional discord or upset.

Pulsatilla – Wind Flower/Meadow Anemone

The Biotherpeutic Index entry for Ovarium Compositum includes Pulsatilla with the following symptoms: *Migrating Disorders (worse before menses),*

delayed menses, dysmenorrhoea, remedy for affections of the mucosa, venous statis.

The Mother Tincture is prepared from the whole fresh plant, gathered while in flower, of Pulsatilla pratensis Miller, which occurs in the mountains of Europe and Russia. N.O. Ranunculaceae.[xxv]

The tincture prepared from the Wind Flower, Pulsatilla Pratensis, contains protoanemonin (an antibiotic substance), tannin, resin and saponin, and shows typical therapeutic indications, which cover both psychic and somatic symptoms.

Hans-Heinrich Reckeweg lists the following typical symptoms and indications:

1. Aggravation in a warm room and in hot weather, amelioration in fresh air and waling about gently.

2. Pulsatilla is usually indicated for female patients who are full of complaints. Inflammations and disorders of the female reproductive organs, vaginitis accompanied by purulent discharge.

3. Disorders experienced during pregnancy and nursing.

4. Consequences of suppressed gonorrhoea, or of suppressed leucorrhoea with orchitis or oophoritis.

5. Concomitant catarrh of the bladder, cystitis.

Aquilegia vulgaris (columbine)

The Biotherpeutic Index entry for Ovarium Compositum includes Aqilegia with the following symptoms: *Disturbances of the menses, climacteric disorders.*

The mother tincture is prepared from the whole fresh plant in bloom. Aquilegia vulgaris L. N.O. Ranunculaceae. [xxvi] Menstrual disturbances, functional amenorrhoea, menopausal problems, depression during the menses.

Sepia (cuttlefish)

The Biotherpeutic Index entry for Ovarium Compositum includes Sepia with the following symptoms: *Climacteric disorders, nervous exhaustion, depression, chronic inflammation of the uterus and adnexa.*

The attenuations are prepared from the dried secretion of the ink gland of the cuttlefish, Sepia officinalis L., which inhabits the Mediterranean, the North Sea and the Atlantic Ocean. N.O.Sepiidae.[xxvii] Menopausal complaints with hot flushes, emotional depression and irritability (alternating). Tearfulness, hypersensitivity and indifference (to business and family). General weakness, every movement causing outbreaks of sweating. Feeling of faintness. Yellowish-green leucorrhoea, offensive and excoriating in cervical erosion, menses mostly late and scanty, menopause.

Lachesis (bushmaster)

The Biotherpeutic Index entry for Ovarium Compositum includes Lachesis with the following symptoms: *Climacteric disorders (hot flushes) dysmenorrhoea.*

The attenuations are prepared from the careful dried venom of the snake, Lachesis mutus L., which occurs in Central and South America. N.O. Crotalidae.[xxviii] The homoeopath Dr. Constantine Hering investigated venom of Lachesis muta in 1892 in South America combining the known toxicology with a homeopathic proving. It is used by homoeopaths as an ovarian remedy indicated for endometritis worse on the left side, menopause, ovarian dysfunction and especially hot flushes.

Apisnum (bee venom)

The Biotherpeutic Index entry for Ovarium Compositum includes Apisnum with the following symptoms: *Oedema, Ovarian cysts, dysmenorrhoea, ovarialgia, and metrorrhagia.*

The mother tincture is prepared from the whole honey bee, Apis mellifica L. N.O. Apidae.[xxix]

Apis is indicated for right sided adnexitis and other kinds of right-sided inflammatory illnesses, inflammations and disorders with collection of fluid in tissues and cavities of the body.

Kreosotum (beech tar creosote)

The Biotherpeutic Index entry for Ovarium Compositum includes Kreosotum with the following symptoms*: Catarrh of the mucosa with acrid secretions, pruritus vulvae, menorrhagia, metrorrhagia, hyperemesis.*

The attenuations are prepared from Cresosote, a mixture of Guaiacol, Cresol and Cresolene obtained by distillation of beechwood tar.[xxx] Creosote was formerly used allopathically as an anti-tubercular, antiseptic and styptic and especially in dyspepsia. In dentistry creosote was used to serve as an additive to arsenic paste for the devitalisation of dental pulp. Homoeopaths employ the homeopathic dilution of Kreosotum to treat widely varying mucosal conditions with offensive, acrid, excoriating discharges, carcinoma of the uterus, general haemorrhagic tendency and inflammations of the urinary and reproductive organs.

Bovista (Warted Puff-ball)

The Biotherpeutic Index entry for Ovarium Compositum includes Bovista with the following symptoms: *Menorrhagia, dysmenorrhoea, venous haemorrhages*.

The attenuations are prepared from the dried ripe fungus Calvatia gigantean without its peridia, which grows in Central Europe in pastures and dry meadows everywhere. N.O. Lycoperdaceae.[xxxi]

Employed homeopathically to treat Menorrhagia, menses come too early, uterine bleeding.

Ipecacuanha (ipecacuanha)

The Biotherpeutic Index entry for Ovarium Compositum includes Ipecacuanha with the following symptoms: *Uterine haemorrhages, hyperemesis*

The mother tincture is prepared from the dried underground parts of Cephaelis ipecacuanha (Brot.) A. Rich., a plant growing in Brazil, India and Malaysia. N.O. Rubiaceae[xxxii]

It is used to treat bright red gushing haemorrhages, menorrhagia and metrorrhagia.

Mercurius solubilis Hahnemanni (mixture containing essentially mercuroamidonitrate)

The Biotherpeutic Index entry for Ovarium Compositum includes Mercurius with the following symptoms: *suppurations, acute and chronic affections of the connective tissue.*

The attenuations are prepared from mixture consisting essentially of mercury (II)-amidonitrate and metallic mercury [xxxiii] it is used for the following indications: mucosal inflammations of the respiratory passages, the gastrointestinal tract, and the urinary and reproductive organs; skin diseases; inflammations of the tonsils, lymph glands, liver, and kidneys; inflammations of other glandular organs.

Hydrastis Canadensis (golden seal)

The Biotherpeutic Index entry for Ovarium Compositum includes Hydrastis with the following symptoms: *remedy for affectations of the mucosa; thick, ropy, yellowish-white secretions, menorrhagia, viscid, metrorrhagia, myomatous haemorrhages.*

The mother tincture is prepared from the dried rootstock, with roots attached, of the plant, Hydrastis Canadensis L., which occurs in shady mountain forests of Atlantic North America. N.O. Ranunculaceae. [xxxiv] The preparation contains three alkaloids: hydrastine, berberine and meconin, apart from phytosterin, volatile oil and resins. It is used by homoeopaths in diseases of the uterus with vaginal discharge.

Acidum cis-aconiticum (aconitic acid)

The Biotherpeutic Index entry for Ovarium Compositum includes Acidum cis –acniticum with the following symptoms: *active factor of the citric acid cycle and of redox systems.*

The attenuations are prepared from cis-aconitic acid, $COOHCHC(COOH)CH_2COOH$.

M.W: 174.2[xxxv]

As with all catalysts of the citric acid cycle, aconitic acid too shows and affinity for internal respiration. The drug picture of cis-Aconiticum Acidum

was composed in September 1996 by David Riley, M.D., Santa Fe (New Mexico), USA and includes: Pain at menses improving, sensation as if menses would come on.

Magnesium phosphoricum (magnesium phosphate)

The Biotherpeutic Index entry for Ovarium Compositum includes Magnesium phosphoricum with the following symptoms: *dysmenorrhoea, tendency to cramps and neuralgia.*

The attenuations are prepared from Magnesium hydrogen phosphate trihydrate. $M_gHPO_4.3H_2O$, MW:174.3[xxxvi] The triturations and liquid potencies prepared from magnesium phosphate are according to Heinigke, 'one of our most important pain remedies..',.

Magnesium phosphoricum is also an important remedy in dysmenorrhoea and when the menses arrive too early, especially when there is swelling and sensitivity of the vagina and so called ovarian neuralgia.

5.7 SAFETY & TOLERABILITY

5.7.1 Global evaluation of toxicity

The manufacturer (Heel) commissioned an expert report on Ovarium Compositum, this report concluded that 'The current scientific fundamentals and the clinical experiences did not reveal serious signs to suspect the containing amount of all homeopathic dilutions for causing toxicological risks.'[xxxvii] The following data is from that report, (Appendix 3).

5.7.2 Reproductive Function

Results from direct studies of reproductive or teratogenic toxicity as well as fetotoxic side effects influencing fertility are not available. Researching the literature produced no hint for such risks

5.7.3 Embryo-Foetal and Peri-Postnatal Toxicity

6. Results from direct studies of embryo toxic/ fetotoxic or peril-, postnatal toxicity are not available. Researching the literature produced no suggestion of such risks.

5.7.4 Mutagenic Potential

Results from direct studies of mutagenic toxicity are not available. Researching the literature produced no hint for such risks.

5.7.5 Carcinogenic Potential

Results from direct studies of carcinogenicity are not available. Researching the literature produced no hint for such risks.

5.7.6 Immunotoxicity

No indications show that the effects of single components of Ovarium Compositum injection are sensitising or will provoke allergic reactions by the parenteral application. Possible risks or adverse drug reactions of parts or components of the plants have not been observed regarding the pharmacovigilance of the compounds of Ovarium Compositum or similar composed drugs.

5.7.7 Interactions

There are no hints that the effects of single components of the incorporated homeopathic dilutions and substances may be enhanced or inhibited by incorporated drugs or substances which interfere with their characteristic pharmacodynamic or toxicologic effects. Potential risks or interactive effects associated with the combined administration of the incorporated homeopathic dilutions have not been substantiated in drug surveillance studies and pharmacovigilance on the use of the incorporated drugs in human.

5.7.8 Pharmacovigilance

The drug safety of **Ovarium Compositum** tablet can also be shown by observing pharmacovigilance data, which have been determined by a dispensing of a formula with the same composition. The components showed identical finishing dilutions. Consequently the dispensing carried the same risk potential.

Within the framework of the supervision of drug safety no adverse event was reported since 1998 (745.510 ampoules delivered only in Germany), globally seen. This result is striking for the good safety profile of **Ovarium Compositum**. This result of the pharmacovigilance points out that adverse drug reactions after parenteral application of the homeopathic dilution in **Ovarium Compositum** tablet are a rarity and that this preparation cannot be related to an increased risk especially concerning the gastro-intestinal, cardiovascular or central-neurogenic body organ system or the skin.

5.7.9 Conclusions

The scientific findings material and the clinical experiences do not reveal any indications concerning toxicological risks caused by components of the homeopathic drug **Ovarium Compositum** if the speciality is applied according to a recommended dosage of the manufacturer.

Components of an immunotoxicological potential are included with a very small concentration. Consequently, a corresponding risk during treatment does not need to be taken into account.

5.8. ADVERSE EVENTS

During a clinical study, onset of Adverse Events may occur. An AE is defined as any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and that does not necessarily have a causal relationship with this treatment (where 'treatment' includes also all investigational agents such as comparative agents and placebo). An adverse event can therefore be any unfavourable and unintended sign (including abnormal laboratory finding, see Section 5.7.2), symptom, or disease.

All adverse events encountered during the clinical study are to be reported on the Adverse Event Forms contained in the Case Report Form (CRF). For each adverse event which occurs during the clinical study the Principal Investigator will give a judgment on its severity and make a causality assessment of the treatment using one of the four given definitions: certainly related, probably related, possibly related and definitely unrelated. Moreover, the Principal Investigator will indicate the action to be taken for the adverse event that has occurred and its outcome. In the case of an adverse event, the trained medical personnel will act with appropriate diagnostic and therapeutic measures until the subject has recovered. Adverse events will be classified as 'serious' and 'non serious'. All this information will be recorded for each adverse event on the Adverse Event Form of the CRF. Detailed information on the compilation of the Adverse Event Form is available in Appendix 1.

5.8.1 Serious Adverse Events

A Serious Adverse Event is defined as any untoward medical occurrence that at any dose: results in death; is life-threatening; requires inpatient hospitalisation or prolongation of existing hospitalisation; results in persistent or significant disability/incapacity; is a congenital anomaly/birth defect or any other event which is considered clinically/medically significant. As Grade 3 or 4 toxicities (based on the Common Toxicity Criteria (CTC v3.0) are considered clinically/medically significant, they will be classified as serious adverse events.

Serious adverse events will be reported to the Principal Investigator and the Sponsor (see Section 8) within 24 hours. The 24 hours emergency contact numbers are listed on page iii of this protocol.

Serious adverse events will also be reported to:

Barts & The London School of Medicine and Dentistry, Joint Research Office. Central Office for Research Ethics Committees (COREC) approved Research Ethics Committee (the responsibility of the investigator) as soon as possible, but in any case within 72 hours.

All available information will be provided, referring to the Serious Adverse Event paragraph of the Reporting Adverse Events document (Appendix 1). The Investigator will complete the Serious Adverse Event Form by carefully following the relevant instructions (Appendix 1) and will fax it within 24 hours to the Sponsor.

The Investigator, and others responsible for subject care, should institute any supplementary investigations of serious adverse events based on their clinical judgment of the likely causative factors. This may include seeking further opinion from a specialist in the field of the adverse event. The Sponsor may also request extra tests. If a subject dies, any post-mortem findings (including histopathology) if available, will be provided to the Sponsor. No medical help, diagnosis, or advice, should be withheld from the subject due to an inability to contact the Sponsor.

If a serious adverse event (including a Grade 3 or 4 toxicity), occurs, no further dosing of the subjects will occur until the cause of the event and its relationship to the study drug has been clarified. Continuation of the trial will be contingent upon approval from an independent safety review Committee.

5.8.2 Non Serious Adverse Events

A non-serious adverse event is one, which does not meet any of the criteria listed in the Section 5.7.1.1 defining serious adverse events, which is otherwise judged by the Investigators as significant.

If a non-serious adverse event occurs, the Investigator will fill in one Adverse Event Form for each adverse event describing its complete evolution to the outcome. Therefore the assessment of severity, frequency and causality will be given at the event outcome. The completed Adverse Event Form will be sent to the Sponsor.

During a clinical study, an adverse event previously reported as a non-serious event may change becoming, upon the Investigator's clinical judgment, a serious adverse event (i.e. dramatic worsening with hospitalisation etc.). At this moment, the Investigator will follow directions for reporting a serious adverse event.

5.9 WITHDRAWALS AND DROP-OUTS

During the study, treatment may be discontinued for many reasons such as the occurrence of a disease, an adverse event that could interfere with the subject's evaluation, or simply upon the subject's request to discontinue for any reason. Intercurrent medical events that do not interfere with either continued administration of study drug or scheduled testing, and that are judged by the Investigator to not have an effect on the outcome measures will not disqualify a subject from continuing in the study. If a subject is withdrawn from the study because of an adverse event, treatment discontinuation must be explained on the Adverse Event Form of the CRF, and this subject will be followed-up to the satisfaction of the Principal Investigator, and a withdrawal visit scheduled where possible.

Subjects will be advised that they are free to withdraw from the study at any time for any reason or, if necessary, the Investigator may withdraw a subject from the study to protect the subject's health. The Investigator may withdraw a subject from the study if it is considered that the scientific, and therefore, ethical standards of the study are compromised. Subjects may also be withdrawn for not complying with study procedures. The reasons for withdrawal will be fully recorded on the CRF. Subjects who withdraw or are withdrawn from the study for any reason other than toxicity will be replaced to ensure sixty (60) subjects. Subjects who are withdrawn because of serious adverse events (including a Grade 3 or 4 toxicity (based on the Common Toxicity Criteria (CTC) version 3.0) will not be replaced. The Ethics Committee will be notified in writing of any study withdrawals that may occur as a result of toxicity.

6. Case Report Form (CRF)

6.1 PRESENTATION OF THE CRF

The CRF to be used for the study consists of pages that contain within the header or footer the Protocol number, subject initials, subject number and other relevant information. It is composed of an introductory section for the selection and inclusion of subjects in the study and a section for the treatment period. Contained within the treatment period section are the forms for registration of possible adverse events and for any suspension of the study.

6.2 HOW TO USE THE CRF

All CRFs will be completed using a ball-point pen with black ink. All unused CRFs for drop-outs must be retained.

All requested information must be entered on the CRFs. If an item is not available or is not applicable, this fact should be indicated; there should be no blank spaces. Corrections should be made by striking through the incorrect entry with a single line and by entering the correct information adjacent to it. The correction must be initialled and dated by an Investigator or a designated qualified individual. Each set of completed CRFs must be reviewed, signed and dated by an Investigator. The completed original CRFs are to be returned to the Sponsor as soon as is practicable after completion and review. A photocopy of each completed CRF is to be retained by the Investigator.

7. Data Management

All data management procedures will be detailed and referred to as the Data Management Plan. All data will be entered and checked by a second person.

The database will be designed and built by research team using Microsoft Excel. Appropriate Case Report Forms (CRFs) will be prepared for the collection of the data requested by the Protocol. All response variables will be entered into the database by the data management personnel.

8. Monitoring & Quality Assurance

The conduct of the study will be monitored by the Investigators, and if required by a representative of the sponsor in accordance with the GCP Guidelines. The investigator will co-operate fully with any study monitors and auditors.

The organisation, monitoring, and quality assurance of the present clinical study is the responsibility of the Sponsor.

In order to ensure the accuracy of data, direct access to source documents by the representatives of both the Sponsor is mandatory. Anonymity of the subject will be maintained at all times.

9. *Study Completion or Discontinuation*

Upon completion of the study, the following activities, when applicable, must be conducted by the Investigator Investigators, as appropriate:

- Return of all study data to William Harvey Research Institute.
- Data clarifications and/or resolutions.
- Accounting, reconciliation, and final disposition of used and unused study drugs.
- Unused investigational product will be returned destroyed in line with local policy.
- Review of site study records for completeness.

In addition, Barts & The London School of Medicine and Dentistry and the Principal Investigator reserve the right to temporarily suspend or prematurely discontinue this study for any reason. If such action is taken, Barts & The London School of Medicine and Dentistry will discuss this with the Investigator (including the reasons for taking such action) at that time. If the study is terminated for safety reasons, Barts & The London School of Medicine and Dentistry will promptly inform the regulatory authorities of the suspension or termination of the study and the reason(s) for the action. The Investigator must inform the Ethics Committee promptly and provide the reason for the suspension or termination. After such a decision, the investigator must call in all participating subjects within a reasonable time period. At this visit all Medical Files and Case Report Forms must be completed as far as possible.

If the study is prematurely discontinued, all study data must be returned to William Harvey Research Institute. In addition, the site must conduct final disposition of all unused study drugs in accordance with Barts & The London School of Medicine and Dentistry procedures for the study.

10. *Investigator Responsibility*

Except where the Principal Investigator's signature is specifically required, it is understood that the term 'Investigator' as used in this Protocol and on the CRFs refers to the Principal Investigator or a designated member of the staff that the Principal Investigator designates to

perform specified duties of the Protocol. The Principal Investigator is ultimately responsible for the conduct of all aspects of the study.

11. *Study Report*

The Final Report shall include the data from the Clinical Summary prepared by the statistical data. The Final Report will be reviewed and signed by the Investigator(s).

12. *Administrative Procedures*

12.1 ETHICAL CONSIDERATIONS

The study will be conducted in accordance with the principles of the Declaration of Helsinki (Recommendations guiding Medical Doctors in Biomedical Research Involving Human Subjects).

12.2 ETHICAL REVIEW COMMITTEE

The Protocol, Consent Forms and Subject Information Sheet will be submitted to a Central Office for Research Ethics Committees (COREC) approved Research Ethics Committee before volunteers are recruited and subjects are enrolled. The Investigators will receive all the documentation needed for submitting the present Protocol to the Ethics Committee. No study activities will be initiated until the written approval of that Committee is received. A copy of the respective approval letters will be transmitted to the Sponsor before starting the study. The composition of the Ethics Committee will also be provided to the Sponsor. If approval is suspended or terminated by the Ethics Committee, the Investigator will notify the Sponsor immediately.

It is the responsibility of the Investigator to report study progress to the Ethics Committee as required or at intervals not greater than one year.

The Investigator will be responsible for reporting any serious adverse events to the Ethics Committee as soon as possible and in any event within 72 hours.

12.3 REGULATORY AUTHORITIES

The Clinical Trial Authorisation (CTA) requirements of the Medicines and Healthcare Products Regulatory Authority (MHRA) will be met before commencement of the study.

The Principal Investigator will report all serious adverse events to the Sponsor. The Sponsor will be responsible for reporting all serious adverse events to the MHRA and other appropriate agencies. The MHRA only requires notification of serious adverse events which are unexpected and deemed to be related to the study medication. Fatal or life-threatening unexpected adverse events will be notified to the Sponsor and MHRA as soon as possible but no later than 7 calendar days after first knowledge by the Sponsor that a case qualifies, followed by as complete a report as possible within 8 additional calendar days. Serious, unexpected adverse events that are not fatal or life threatening shall be filed as soon as possible but no later than 15 calendar days. Serious adverse events that are unrelated to the study medication shall be included in the end of study report.

12.4 INFORMED CONSENT

Before enrolment into the study, subjects will be fully informed of the nature of the study, the properties and side effects of the study drug, and all relevant aspects of study procedures. Subject information is provided predominantly by the medical investigator during recruitment. Each prospective candidate will be provided with the Privacy Information and the Information for Volunteers Sheet and Informed Consent Forms. At the pre-study screening evaluation visit, volunteers will be required to sign an Informed Consent Form. Consent Forms shall be signed and dated by the appropriate parties. A notation that written informed consent has been obtained will be made on the subject's CRF. Completed Consent Forms will be retained by the Investigator and a copy of this will be provided by the Investigator to the subject. The Informed Consent Form is included as part of the submission to the Ethics Committee.

12.5 SUBJECT DATA PROTECTION

Subjects will be informed that their data are held on file, that these data may be viewed by Sponsor on behalf of the sponsor and by external auditors on behalf of either the sponsor or regulatory agencies. They will similarly be informed that this data and a report of the study will be submitted to the Sponsor and may also be submitted to government agencies and perhaps for publication, but that they will only be identified in such reports by their study identification number, initials and perhaps their gender and age. The investigators undertake to hold all personal information in confidence

Investigator(s).

12.6 EMERGENCY CONTACT WITH INVESTIGATORS

Suitable arrangements will be made for subjects to contact the Investigators in the event of an emergency. All subjects will be provided with a telephone number with details of whom to contact in the case of an emergency.

12.7 NOTIFICATION OF PRIMARY CARE PHYSICIAN

With the consent of the volunteer, it is the Investigator's responsibility to notify the primary care physician (if applicable) of the subject's participation in the study by sending a letter stating the nature of the study, the treatment, expected benefits, the most common adverse drug events observed in previous studies and concomitant drugs to be avoided. A copy shall be retained by the study site for verification by the Sponsor. The primary care physician may contact the Investigator for any further information regarding the subject's participation in the study.

12.8 INVESTIGATOR INDEMNIFICATION

Indemnity will be provided by Queen Mary, University of London and the Barts & The London NHS Trust.

The study Sponsor will ensure sufficient insurance is available to enable it to indemnify and hold the investigator(s) and relevant staff as well as any hospital, institution, ethics committee or the like, harmless from any claims for damages for unexpected injuries, including death, that may be caused by the study drug but only to the extent that the claim is not caused by the fault or negligence of the subjects or investigator(s).

12.9 FINANCIAL ASPECTS

The conduct of the study is subject to financial support from

Biologische Heilmitte Heel GmbH

Dr Reckeweg-Str.2-4

76532 Baden-Baden

Deutschland

12.10 INFORMATION DISCLOSURE AND INVENTIONS

12.10.1 Ownership

All data and records provided by the William Harvey Research Institute or generated during the study (other than a subject's medical records) and all inventions discovered in the course of conducting the study are the property of the William Harvey Research Institute. If a written contract for the conduct of the study, which includes ownership provisions inconsistent with this statement is executed, that contract's ownership provisions shall apply rather than this statement.

12.10.2 Confidentiality

The Investigator and other study site personnel will keep confidential any information provided by the William Harvey Research Institute (including this protocol) related to this study and all data and records generated in the course of conducting the study, and will not use the information, data, or records for any purpose other than conducting the study. These restrictions do not apply to: information which becomes publicly available through no fault of the investigator or study site personnel; information which it is necessary to disclose in confidence to an Ethics Committee solely for the evaluation of the study; information which it is necessary to disclose in order to provide appropriate medical care to a study subject, or study results which may be published as described in Section (x) If a written contract for the conduct of the study, which includes confidentiality provisions inconsistent with this statement, is executed then that contract's confidentiality provisions shall apply rather than this statement.

12.10.3 Publication

Prior to submitting for publication, presenting, using for instructional purposes or otherwise disclosing the results of the study, the Investigator requires written permission from the William Harvey Research Institute. Following permission for publication, presenting, using for instructional purposes or otherwise disclosing the results of the study, the Investigator shall allow a period of at least sixty (60) days (or, for abstracts, at least fifteen (15) working days) to review the proposed publication or disclosure prior to its submission for publication or other disclosure. The William Harvey Research Institute must approve final copies of publications, presentations, and uses for instructional purposes or otherwise disclosing the results of the study prior to submission. Publications or disclosures of study results shall not include other, confidential information of the William Harvey Research Institute. If the proposed publication/disclosure risks the William Harvey Research Institute's ability to patent any invention related to the study, the publication or disclosure will be modified or delayed, at the William Harvey Research Institute's option, to allow the William Harvey Research's to seek patent protection of the invention. If a written contract for the conduct of the study which

includes publication provisions inconsistent with this statement is executed, that contract's publication provisions shall apply rather than this statement.

12.11 PROTOCOL AMENDMENTS

Neither the Investigator nor the William Harvey Research Institute will modify the Protocol without first obtaining the concurrence of the other in writing. Protocol modifications that impact on subject safety or the validity of the study will be approved by the Ethics Committee. No changes (amendments) to the Protocol may be implemented without prior approval from the Sponsor and the appropriate Ethics Committee. If a Protocol amendment requires changes in an informed consent form, the revised informed consent form prepared by the Investigator must be approved by the Ethics Committee.

Once the final Protocol has been issued and signed by the Investigator and the authorized signatories, it shall not be informally altered. Protocol amendments are alterations to a legal document and have the same legal status. Therefore they must pass through appropriate steps before being implemented. In general, any important change which theoretically increases risk to subjects constitutes an amendment. Minor changes of a purely administrative nature need documentation and advice to the committee, but may be implemented without prior approval.

It is the responsibility of the Investigator to submit the amendment to the Ethics Committee for their approval; written approval should be obtained and a copy provided to the Sponsor. The Sponsor is responsible for determining whether or not the local regulatory authority must be notified of the Protocol change. Completed and signed Protocol amendments will be circulated to all those who were on the circulation list for the original Protocol.

The original signed copy of amendments will be kept in the Study File with the original Protocol. It should be noted that where an amendment to the Protocol substantially alters the study design or the potential risks to the subjects, each subject's consent to continue participation should be obtained.

12.12 PROTOCOL COMPLIANCE

The instructions and procedures specified in this Protocol require diligent attention to their execution. Should there be questions or consideration of deviation from the Protocol, clarification will be sought from the Principal Investigator and Sponsor. Any subject treated in a manner that deviates from the Protocol, or who is admitted into the study but is not

qualified according to the Protocol as amended by the William Harvey Research Institute and the Investigator, may be ineligible for analysis and thereby compromise the study.

Only when an emergency occurs that requires a departure from the Protocol for an individual will there be such a departure. The nature and reasons for the Protocol violation shall be recorded in the CRF.

The Investigator and designees will comply with all applicable federal, state and local laws.

12.13 ARCHIVES: RETENTION OF STUDY RECORDS

All source documents, CRFs and trial documentation will be kept by the Investigator for at least 15 years after the study completion.

Glossary of Terms

FSH	Follicle Stimulating Hormone
LH	Luteinizing Hormone
IUI	Interuterine insemination
PCOS	Polycystic Ovary Syndrome
ICSI	Intra-cytoplasmic sperm injection
IVF	Invitro fertilisation
GnRH	Gonadotrophin releasing hormone
GnRHantag	Gonadotrophin releasing hormone agonist
CAM	Complementary and Alternative Medicine
EHIQ	Emotional health in infertility questionnaire

Appendices for Protocol

Appendix 1: Reporting Adverse Events

Appendix 2: The Disease Evolution Table

Appendix 3: Expert Report on Ovarium Compositum

Appendix 4: Oxford Fertility Questionnaire

Appendix 5: Certificate of Good Manufacturing Standards

Appendix 6: The EQ-5D

Appendix 7 Protocol Amendments

Appendix 1

Reporting Adverse Events

All Serious Adverse Events will be reported in accordance with the local policies of the Sponsor organisation.

DEFINITIONS

ADVERSE EVENT/ADVERSE DRUG REACTION

An adverse event (AE) is defined as any untoward medical occurrence in a patient or clinical investigational subject administered a pharmaceutical product and that does not necessarily have a causal relationship with this treatment (where 'treatment' includes also all investigational agents such as comparative agents and placebo). An AE can therefore be any unfavourable and unintended sign (including abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product.

In the case of an investigational medicinal product, worsening of the pathology under study must be considered an AE only if unexpected in terms of timing or severity; in such a case, the AE form will be filled as usual. If on the contrary, the worsening is considered an expected episode of the natural history of the disorder, it will be reported as a treatment failure.

Worsening of a concurrent or pre-existing disorder will be reported as an AE.

All noxious and unintended responses to a medicinal product related to any dose should be considered an Adverse Drug Reaction (ADR). The phrase 'responses to a medicinal product' means that a causal relationship between a medicinal product and an AE is at least a reasonable possibility, i.e. the relationship cannot be ruled out.

UNEXPECTED ADVERSE DRUG REACTION

An unexpected adverse reaction is one for which the nature of its severity is not consistent with the applicable product information (e.g. Investigator's Brochure for an unapproved investigational medicinal product). Therefore, this definition involves events previously unobserved or undocumented, i.e. expected/unexpected from the perspective of previous observations, not only on the basis of what might be anticipated from the pharmacological properties of a medicinal product.

SERIOUS ADVERSE EVENTS

A Serious Adverse Event (SAE) is defined as any untoward medical occurrence that at any dose: results in death; is life-threatening; requires inpatient hospitalisation or prolongation of existing hospitalisation; results in persistent or significant disability/incapacity; is a congenital anomaly/birth defect or any other event which is considered clinically/medically significant. As a Grade 3 or 4 toxicity (based on the Common Toxicity Criteria (CTCv3.0) is considered clinically/medically significant, they will be classified as serious adverse events.

The term 'life-threatening' refers to an event in which the patient is at real risk of death at the time of the event, it does not refer to an event, which hypothetically might have caused death if it were more severe.

Medical and scientific judgment should be exercised in deciding whether other situations, such as important medical events that may not be immediately life-threatening or result in death or hospitalisation, but may jeopardise the patient or may require intervention to prevent one of the other outcomes listed in the definition above should also usually be considered serious. Examples of such events are intensive treatment in an emergency room or at home for allergic bronchospasm, blood dyscrasias, or convulsions

that do not result in hospitalisation, or development of drug dependency or drug abuse.

INSTRUCTIONS FOR COMPLETING THE ADVERSE EVENTS FORM

The Adverse Events Form must be fully reviewed by the Principal Investigator.

For each AE the following information must be entered in the AE Form by the Principal Investigator or his/her designated nominee (including nursing staff): subject initials; subject number; treatment at the time of event; description of the event; source; onset; frequency; severity; action taken; outcome; duration; resolution or death and duration.

DESCRIPTION

Record a clear and concise description of the AE.

SOURCE

Record from whom the AE has been reported.

ONSET OF THE AE

Record both the time and date of the onset of the AE. Time shall be recorded in 24 hour time, and date in DD/MMM/YY format.

FREQUENCY

Record the frequency of the AE as either a single episode, intermittent or continuous.

SEVERITY

In order to indicate the severity of the event, the following guidelines should be followed:

Mild: if well tolerated by the patient; patient is capable of carrying out everyday activities without any reduction in posology, or interruption or discontinuation of the study drug, or necessity of specific treatment of the event.

Moderate: if poorly tolerated by the patient; patient has difficulty in carrying out day-to-day activities; it may be necessary to reduce the posology of the

study drug, or to interrupt or discontinue its administration, or to initiate specific treatment for the event.

Severe: if it is impossible for the patient to carry out everyday activities, imposes discontinuation of the study drug and the implementation of specific therapy for the event. The term 'severe' refers to the intensity of the event, not to its seriousness.

ACTION TAKEN

Any action taken in response to the AE shall be documented (none, study drug dose adjusted, study drug interrupted, study drug discontinued, concomitant medication administered, other). Any changes to the study treatment should be recorded in the 'Additional Comments' section, in which all dates, times and doses shall be reported. All entries in the 'Additional Comments' section shall be initialled and dated.

OUTCOME OF THE EVENT

Document whether the AE has been resolved, unresolved, or resulted in death.

RESOLUTION OR DEATH

Record both the time and date of the resolution of the AE or death. Time shall be recorded in 24 hour time, and date in DD/MMM/YY format. In the case of death a specific form must be completed

a. If death is the outcome of an AE, it must be clearly defined and exhaustively described.
b. If death is not related to an already-known event, the Investigator must report the supposed or ascertained cause(s).
c. If autopsy has been carried out, the findings must be reported.
d. If the test drug was administered at the time of death, this must be recorded or the precise time prior to death when treatment with study drug ended.

e. The Investigator must make a judgment as to the relationship between death and the test drug (certainly, probably, possibly, definitely unrelated).

DURATION

The duration of the AE shall be recorded in days, hours, minutes and seconds. In the case of an intermittent AE, the mean duration of each episode should be reported.

REVIEW OF THE EVENT

The Principal Investigator *may* complete the interim review, if required, and *must* conduct a final review of the AE.

If possible, the Principal Investigator should indicate the AE as a diagnosis rather than a description. The Principal Investigator shall also include the affected body system in the final review section, and complete the sections: 'Event Expectation' and 'Relationship to Study Treatment'.

EVENT EXPECTATION

An unexpected AE, is one for which the nature of its severity is not consistent with the applicable product information (e.g., Investigator's Brochure or Product Information sheet), and includes AEs that have not been previously documented or observed.

RELATIONSHIP TO STUDY TREATMENT

The correlation between the AE observed and the drug administered before onset is to be annotated according to the following evaluations:

Certainly Related:

a) the event is observed within a reasonable time period after administration of the drug;
b) the event occurs with a clinical presentation already known for the drug under study;
c) suspension of the drug is followed by resolution or improvement in the event (positive dechallenge);
d) After renewed administration of the drug, signs and symptoms previously observed reappear (positive rechallenge).

Probably Related:

a) the event is observed within a reasonable time period after administration of the drug;
b) the event occurs with a clinical presentation already known for the drug under study;
c) suspension of the drug is followed by resolution or improvement in the event (positive dechallenge);
d) The event cannot be satisfactorily explained by the clinical condition of the patient, by concomitant drug treatment, or by any other factor.

Possibly Related:

a) the event is observed within a reasonable time period after administration of the drug;
b) the event occurs with a clinical presentation already known for the drug under study;
c) The event can be satisfactorily explained by the clinical condition of the patient, by concomitant drug treatment, or by any other factor.

Definitely Unrelated:

a) An event can be considered definitely unrelated to the drug when none of the above referenced criteria is satisfied.

Appendix 2 for Protocol

Disease Evolution Table

The Six Phase Table of homotoxicosis, first developed by Reckeweg and later expanded to include more detail (Disease Evolution Table) is a coordinate system showing the relationship between the degree of 'clogging' of the intercellular matrix and possible health consequences. The Table's six columns show increasing toxin loads (on the vertical axis) in relationship to the disturbance they cause in the different organs (on the horizontal axis). Progression of the patient's illness (progressive vicariation) is tracked from left to right, improvement (regressive vicariation) from right to left. [xxxviii]

To better understand the rationale and methods for Homotoxicology it is helpful to define what toxins are: Any agent (physical, chemical, microbial, etc.) that adversely modifies or damages a balanced biological system is considered a 'toxin'.[xxxix] Toxins may originate from within or without the body. Examples of exogenous toxins are recreational drugs, cosmetics, food additives, gaseous pollutants, metals, agricultural chemicals, plasticizers and PBBE's. Examples of endogenous toxins include accumulations of adrenalin and histamine.

Modern medicine is successful in diagnosing and treating acute intoxications as medical emergencies for heavy metal poisoning, drug poisoning etc. However subclinical states of chronic intoxications are not recognised.

Subclinical states of intoxication are of great importance to biological medicine, as well as recognition of the variation in individual's susceptibility to specific toxins.

'The clinical manifestations of biological effects of toxins depend upon the physical and chemical properties of the toxin itself, but also on the duration and route of exposure, it's mechanism of action, and obviously on the individual susceptibility..'[xl]

According to the theory of Homotoxicology the body deals with homotoxins essentially in six different ways. The six phases are assigned to three groups of two (the humoral, the matrix and the cellular phases), which are divided halfway through the matrix phase by the regulation/compensation division. Once this division is crossed, it indicates that the toxins or their effects are evolving from extracellular to intracellular.

The humoral phases include the excretion and the inflammation phases. They are characterised by repeated attempts by the body to achieve elimination. The intracellular structures remain intact; although we see that numerous cells may be lost in the

inflammation process but will later be replaced by intact, healthy cells. There is a spontaneous trend towards improvement.

The matrix phases include the deposition and impregnation phases. The diseases in these phases occur at the basic substance level (Ground Regulation System or Extra Cellular Matrix).
It is in these phases that the step from extra cellular to intra cellular homotoxin presence or effect occurs. The properly regulated extra cellular matrix is seen as fundamental in the promotion of health and the protection against an evolution into chronic disease.

The cellular phases consist of the degeneration and neoplasm phases or dedifferentiation phases. They are on the other side of the biological division. This means that intoxication has taken place not only between the cells but also inside the cells. Cellular functions are progressively inhibited up to the point of destruction.

The Disease Evolution Table (DET) allows us to form a conceptual model for understanding the severity of a disease (level of intoxication) and the body's reaction to this intoxication.

	HUMORAL PHASES		MATRIX PHASES		CELLULAR PHASES	
Organ system	**Excretion Phases**	**Inflammation Phases**	**Deposition Phases**	**Impregnation Phases**	**Degeneration Phases**	**Dedifferentiation Phases**
Skin	Episodes of sweating	Acne	Naevi	Allergy	Scleroderma	Melanoma
Nervous system	Difficulty concentrating	Meningitis	Cerebrosclerosis	Migraine	Alzheimer's disease	Gliosarcoma
Sensory System	Tears, otorrhea	Conjunctivitis, otitis media	Chalazion, cholesteatoma	Iridocyclitis, tinnitus	Macular degeneration, anosmia	Amaurosis, malignant tumor
Locomotor System	Joint pains	Epicondylitis	Exostosis	Chronic rheumatoid arthritis	Spondylosis	Sarcoma, chondroma
Respiratory Tract	Cough, expectoration	Bronchitis, acute	Silicosis, smoker's lung	Chronic (obstructive) bronchitis	Bronchiectasia, emphysema	Bronchial carcinoma
Cardiovascular System	Functional heart complaint	Endocarditis, pericarditis, myocarditis	Coronary heart disease	Heart failure	Myocardial infarction	Endothelioma
Gastrointestinal System	Heartburn	Gastroenteritis, gastritis	Hyperplastic gastritis	Chronic gastritis, malabsorption	Atrophic gastritis, liver cirrhosis	Stomach cancer, colon cancer
Urogenital System	Polyuria	Urinary tract infection	Bladder stones, kidney stones	Chronic urinary tract infection	Renal atrophy	Cancer
Blood	Reticulocytosis	Leucocytosis, suppuration	Polycythaemia, thrombocytosis	Aggregation disturbance	Anemia, thrombocytopenia	Leukemia
Lymph System	Lymphedema	Lymphangitis, tonsillitis, lymphadenitis	Lymph-node swelling	Insufficiency of the lymph system	Fibrosis	Lymphoma, Hodgkin-/non-Hodgkin-lymphoma
Metabolism	Electrolyte shift	Lipid metabolism disturbance	Gout, obesity	Metabolic syndrome	Diabetes mellitus	Slow reactions

Hormone System	Globus sensation	Thyroiditis	Goitre, adenoma	Hyperthyroidism, glucose intolerance	Menopausal symptoms	Thyroid cancer
Immune System	Susceptibility to infection	Weak immune system, acute infection	Weak reactions	Autoimmune disease, immunodeficiency, chronic infections	AIDS	Slow reactions
	Alteration*	**Reaction***	**Fixation***	**Chronic Forms***	**Deficits***	**Decoupling***
Psyche	Functional psychological disturbance, «nervousness»	Reactive depressive syndromes, hyperkinetic syndrome	Psychosomatic manifestation, neuroses, phobias, neurotic depression	Endogenous depression, psychosis, anxiety neurosis, organic psychosyndrome	Schizophrenic defective states, mental deficiency	Mania, catatonia

Biological **Division**

Note: The six-phase table is a field matrix reflecting medical experience based on careful observation and empirical learning. It is a phase-by-phase arrangement of disorders with no direct relationship between them. No causal pathogenetic link between disorders can be inferred. The structure of the table makes it suitable for developing a prediction system giving a better assessment of the possibilities for a vicariation effect.

APPENDICES

Appendix 2 Copy Of Questionnaires Sent To The Therapists

Appendix 3 for Protocol

Expert Report on Ovarium Compositum

HEEL GmbH

Part I C2 – Expert Report to Part III

According to Notice to Applicants (NTA)

- Toxicological and Pharmacological Documentation

Ovarium Compositum Injection

Bulk-No.: 8527

Figure 10 The Expert Report on Ovarium Compositum

Part III – Toxicological and Pharmacological Documentation

1 INTRODUCTION

The presented homeopathic combination remedy Ovarium Compositum injection is composed of the following components:

One ampoule (2.2 ml) **Ovarium Compositum** contains:

Aquilegia vulgaris	D 4	22 µl
Hydrastis canadensis	D 4	22 µl
Lilium tigrinum	D 4	22 µl
Bovista	D 6	22 µl
Cypripedium calceolus var. pubescens	D 6	22 µl
Ipecacuanha	D 6	22 µl
Apisinum	D 8	22 µl
Kreosotum	D 8	22 µl
Ovarium suis	D 8	22 µl
Acidum cis-aconitum	D 10	22 µl
Lachesis mutus	D 10	22 µl
Magnesium phosphoricum	D 10	22 µl
Mercurius solubilis Hahnemanni	D 10	22 µl
Placenta suis	D 10	22 µl
Salpinx suis	D 10	22 µl
Sepia officinalis	D 10	22 µl
Uterus suis	D 10	22 µl
Hypophysis suis	D 13	22 µl

Pulsatilla pratensis	D 18	22 µl

The scientific findings material on all the active agents has been evaluated and an expert opinion delivered on it by Committee D appointed by the Federal Health Office and published in Monographs in the Bundesanzeiger [Federal Gazette].

The present Expert Opinion was drawn up to provide information in accordance with the EU Commission's 'Notice to Applicants' on possible toxicological risks of the drug being assessed.

Information on the pharmacodynamics (Part III F under the NTA) and pharmacokinetics (Part III G under the NTA) of the homeopathic dilutions is quoted and discussed in connection with possible toxicological data. Instead of drawing up my own view of pharmacodynamic and pharmacokinetic findings in the Expert Opinion assessment of the homeopathic drug based on the particularities of the treatment orientation, I have referred to Part I C 3 – Expert Opinion on Part IV – Clinical Documentation.

Each component entailing a risk has been appraised with regard to its toxicological potential. In this appraisal the classification has followed that of the Notice to Applicants; the identification letters are each found in the title of the chapter. It is of further interest to answer the question of whether the dose and duration of treatment admit a safety margin between the dose administered and the possible risks; if on the basis of the bibliography there were no restrictions on the duration of treatment with the dose used, a time limitation on treatment was not deemed necessary.

2 TOXICOLOGY

The assessment follows standard practice and knowledge applied to allopathic drugs with the same constituents. The homeopathic dosage is comparable in part to the usual recommendations in drug therapy. In addition to the medical and toxicological profile of the substance already known, research was also carried out in a few special databases of the chemical or cosmetic industry or other health organisations.

7. In general, on the one hand the toxicological risks have been specified by means of precisely defined limits, e.g. the minimum workplace concentrations [MAC] or short-term use limits [SEL] of the WHO, the Food Additives Organisation [FAO] and the International Agency for Cancer Research [IACR]; on the other hand the quantities required for homeopathic treatment have been evaluated. The therapeutic requirements and the tolerable levels for chronic exposure have been proportioned in order to determine the therapeutic applicability of the substances.

It is seldom that the question of the exact concentration in drugs can be answered for homeopathic finished products, unless they contain highly active components. That is why in principle no content assays of the main constituents were carried out by the pharmaceutical manufacturer on the end products or mother tinctures. Since the HAB likewise requires no values for the content assay of each individual substance, the quantitative determination of individual constituents were worked out by own calculations.

The constituents or main components are well documented by type and quantity in the pharmacopoeia, which means that the characteristic content can be determined by DAB 10 or EUAB, for example.

One way of acquiring a notion of the content of the substance in plant components when there are no exact control data extant for the mother tincture, is to calculate the corresponding quantities back using the Manufacturing Specifications in the HAB.

Hahnemann in his day regarded the system of potentisation as a safety factor to minimise the risk of homeopathic drugs. Nowadays data from

experiments on animals during toxicological studies sometimes help to establish guide values for human application, and to decide whether administering a mother tincture or the subsequent attenuations of a plant or animal drug poses a toxicological risk or the toxicological effects can be disregarded. With many components of homeopathic tinctures and dilutions however this knowledge is very fragmentary and incomplete.

If the homeopathic dilution is above the toxicological limit and no interaction with other constituents has to be considered for the assessment, the safety of the drug is discussed in the SURVEYS in the Appendix.

The manufacturer itself conducted no toxicological studies with the preparation submitted. The comments below were drawn up on the basis of extant documentation, supported by a pool of bibliography constantly updated by half-yearly research.

2.1 TOXICITY (III A)

Given the low toxicity or low concentrations of the constituents, in the evaluation of **Bovista (D6), Cypripedium calceolus var. pubescens (D6), Apisinum (D8), Kreosotum (D8), Acidum cis-aconitum (D10), Lachesis mutus (D10), Magnesium phosphoricum (D10), Mercurius solubilis (D10), Sepia officinalis (D10), Pulsatilla pratensis (D18)** and of all **Suis extract** dilutions in an end concentration between D10 and D15 (s. Chapter 2.1.1) no toxicological aspects that would have to be taken into account in the **Ovarium Compositum** ampoules speciality come into consideration for the risk/benefit ratio (s. following table).

Homeopathic dilution	**Concentration**	**End concentration**
Bovista	D 6	D 8
Cypripedium calceolus var. pubescens	D 6	D 8
Apisinum	D 8	D 10
Kreosotum	D 8	D 10
Ovarium suis	D 8	D 10
Acidum cis-aconitum	D 10	D 12
Lachesis mutus	D 10	D 12
Magnesium phosphoricum	D 10	D 12

Mercurius solubilis Hahnemanni	D 10	D 12
Placenta suis	D 10	D 12
Salpinx suis	D 10	D 12
Sepia officinalis	D 10	D 12
Uterus suis	D 10	D 12
Hypophysis suis	D 13	D 15
Pulsatilla pratensis	D 18	D 20

For a more detailed study of the relevant toxicological data, refer to the SURVEYS in the Appendix compiled from the bibliography.

On the other hand, the constituents of the officinal plants used **Aquilegia vulgaris; Hydrastis canadensis, Lilium tigrinum** and **Ipecacuanha** require closer inspection at least in special risk discussions. The aforementioned drugs are so well documented in pharmacopoeia and botanical lexicons that the pharmacodynamic/toxicological effects can be derived at least approximately from known data.

2.1.1 Extracts of suis organs

Extracts of suis organs are homeopathic preparations from parts of the body of a pig. The manufacturing process is conducted in a way that the infectious nature and an immunotoxicological risk (Hypophysis, Ovarium, Placenta, Salpinx, and Uterus suis) seem to be completely suppressed. In suis xenoprotein sensitised guinea pigs test dilutions >$1O^5$ of the glycerol extract gave no positive challenge reactions in the skin sensitisation test (Dermal Sensitisation called Maximisation Test according to Magnusson and Kligman) and according to the conducted quality control [OECD Guideline No. 406, Stahl 1991]. Taking into account an additional security margin of a 3 log dilution regarding eventual species differences between guinea pigs and man, the suis organ extracts should have no immunogenic xenoprotein risk potential for humans at $\geq$D8. All preparations to the method described in the official homeopathic pharmacopoeia resulted also in a virus inactivation.

The composition Ovarium Compositum injection (2.2 ml) contains an amount of 22 mg of Ovarium suis (D8). Due to the pharmaceutical formulation the quantitative amount i.e. homeopathic potency decreases from the resulted

extract to its final concentration within the composition of the remedy (corresponding with ≥D10). According to the manufacturing process the toxicology of xenoproteins can be regarded as negligible. This evaluation complies also with the assessment of the immunotoxicological risks of Hypophysis, Placenta, Salpinx, and Uterus suis in which attenuations of different parts of the body are incorporated. To characterise their toxicological profiles the surveys can be found in Appendix 5.1.

No toxic effects have been described in the literature. The common toxicology of the incorporated dilution can be evaluated as very slight. The low doses of the composition provide evidence that preparation risks are absent or negligible.

2.1.2 Aquilegia vulgaris

8.

Besides different fatty acids some cyanogenic glycosides of the trigloquinine-type were found as components in the fresh subterranean and above ground organs of **Aquilegia vulgaris,** a plant which is native in the moderate areas of Europe, Africa, and North America [Hager-ROM 2002]; more exact data are not found in the literature. The only existing pharmacodynamic data of acylated and non-acylated derivatives of 3-mono-glucosides and 3,5-diglucosides of delphinidine, pelargonidine and cyanidine, the anthocyanidines extracted of the flowers describe chemotaxonomic measurements. Extracts of the roots shall be applied as stone-dissolving drugs and diuretic by Paracelsus; in the Middle Ages Aquilegia was praised as medicinal plant against icterus as well as against liver and spleen disorders [Madaus]. Scientific articles describing appropriate experiences cannot be found.

The extract of the fresh above ground organs of Aquilegia vulgaris was neither analysed pharmacologically nor toxicologically. Observations from the European popular medicine led to the assumption that it has internal

therapeutic effects in scurvy and icterus, and due to its tranquilizing qualities is able to improve excitation [HagerRom 2002].

The available literature and all information gathered from diverse data systems about the basis material applied, which is used to produce the *Aquilegia vulgaris* dilution D4 and an end concentration of D6 do not give any proof of a toxic potential [Teuscher/Lindequist 1994, von Mühlendahl et al., 1995, Hager-ROM 2002].

To produce Ovarium Compositum ampoules *Aquilegia vulgaris* is used in a dilution D4 that corresponds to a finishing dilution D=6. Due to the available data, a toxicological valuation of the employed proportion of the glucosides of delphinidine, pelargonidine and cyanidine and some others contained in the available finished preparation is not possible regarding quantitative standard measures. The available literature and all information gathered from diverse data systems about the basis material applied do not give any proof of a toxic potential [Teuscher/Lindequist 1994, von Mühlendahl et al., 1995]. The low end concentration of the possibly pharmacodynamic-working alkaloids reveals that, during a therapeutical application of Ovarium Compositum ampoules, a risk of an unexpected toxic event caused by the named components is not expectable.

2.1.3 Alkaloids of Lilium tigrinum

Some species of the plant family Liliaceae are toxic and contain steroid saponins which can lead to disorders of the liver and to photosensibilization e.g. by Narthecine or Colchicine with typical zyto-toxic qualities. Others were found to be derivatives of the cardenolids and bufadienolids with cardiotoxic effects. Besides the immuno-toxic acting tulipalins and allylsulfides as Allicin, cardenolids and buffadienolids shall be found in Lilium tigrinum [Frohne]. Obviously, there is a strong relationship to the effects of other liliaceae species like Allium sativa and Allium cepae.

Whether there are intolerance reactions after the oral application of high doses of Lilium tigrinum is not known. Reports of intoxications cannot be found in the literature.

There are no previous reports validating the pharmacological and toxicological effects of this herbal remedy. Neither Teuscher/Lindequist nor Mühlendahl mentioned intoxications with parts or extracts of *Lilium tigrinum* during the last decade [Teuscher/Mühlendahl]. To produce Ovarium Compositum injection *Lilium tigrinum* is used in a dilution D4 that corresponds to the finishing dilution D6. Due to the available data, a toxicological valuation of the employed quality and proportion of the drug components contained in the available finished preparation is not possible regarding quantitative standard measures. Though, the low end concentration reveals that, during a therapeutical application of Ovarium Compositum injection, a risk of an unexpected toxic event caused by *Lilium tigrinum* is not expectable.

2.1.4 Benzylisoquinoline-alkaloids from Hydrastis canadensis

The benzyl isoquinoline derivatives of benzophenanthridin-, protoberberin-, rhoeadin- and protopin type as well as the phthalidisoquinoline-type **Chelidonine, Chelerythrine, Sanguinarine, Berberine, Coptisin, Sanguinarine** and **Protopin** as well as **Hydrastine** belong to a group of alkaloids that are – orally applied - known for their spasmolytic effects on the smooth muscles of the gastro-intestinal system and the biliary tract as well as for their centrally sedative effects besides their stimulating effects on heart rate and blood pressure (see toxicological profile of Hydrastis canadensis in the Appendix). Hydrastine can lead to anaesthesia and mydriasis and in higher doses extracts of hydrastis canadensis tend to lead to convulsions. In rabbits the mean convulsive dose shall be 100 times higher than after the intravenous application dose of 0,2 mg/kg bw (+)-Bicucullin-hydrochlorid [Hager 1992], that is approx. 20 mg/kg bw. In neurological research (+)-Bicucullin-hydrochlorid represents the most used kompetitive antagonist of the inhibiting neurotransmitter γ-aminobutyric acid (GABA) of the A-receptor and shows within a group of 45 phthalidisoquinoline alkaloids in rats on

synaptic membrane of the brain the strongest inhibiting effect on the receptor.

In the past intoxications after using or consuming parts of Sanguinaria canadensis or Chelidonium majus were reported though, but cannot be confirmed in the current literature. Occasional complaints of the gastro-intestinal system after internal application were only reported once [Roth/Daunderer 1987, Schilcher 1997, Teuscher 1994]. Due to the increasing activity of microsomal enzymes in hepatocytes of rats suspects of a toxic risk were focussed on sanguinarine. Whether this can be transferred to the area of human medicine and especially on hdrastine cannot be determined precisely enough due to the experimental character of the previous literature as there are no reliable data to this [Dalvi 1981, Dalvi 1985].

The alkaloids coptisin, chelerythrine and sanguinarine proved to be highly toxic combinations in examinations on the comparative determination of the cytotoxicity of the different Schöllkraut-alkaloids in primary cultures of hepatocytes of rats. Gebhardt and Gaunitz could show that the median of EC_{50}-values for the cytotoxicity amounted to approximately 5 mg/ml in 34 Schöllkraut extracts and preparations. The EC_{50}-values of garlic preparations or rather artichoke extracts in comparison to this do not show a value lower than 50 mg/ml or rather 10 mg/ml [Gebhardt/Gaunitz 1999]. The resulting toxicity though strongly depends on the choice of the plant parts, the extraction procedure and similar parameters. The results confirm Dalvi's works, who used doses in his damage model though that meet a limiting value 250 times as high. What becomes quite clearly discernible on the other hand is that a dose of 0.2 mg/kg/day over a period of 56 days could not be able to cause visible damages [Ulrichová et al., 1996].

In what way hydrastine will be involved in these results and whether they can be transferred to humans, remains difficult to assess. With this background the following model is calculated by Gebhardt and Gaunitz assuming the most inconvenient conditions [Gebhardt/Gaunitz, 1999]:

Taking the average liver weight of 2 kg as a basis an alkaloid amount of 8 µg/ml coptisin, usually occurring as main alkaloid of Schöllkraut extracts, could be able to exert an acute cytotoxic effect, which could thus have an effect on some few cells already. This again would correspond to an average alkaloid amount of 8 mg daily. Therefore a total amount of 2.5 mg alkaloids per day should be acceptable as maximal daily dose.

Due to the structural differences of the alkaloids of the phthalidisoquinoline-type as hydrastine and the alkaloids of the benzophenantridin-, protoberberin- and protopin-type as sanguinarine there may be concluded that the above mentioned toxic effects on the hepatocytes cannot be shown by phthalidisoquinolines because no cases are reported of therapeutically often used drugs as noscapine which belongs to the same group of alkaloids.

The question is whether these results have an impact to the application of Hydrastis canadensis which does not contain the components sanguinarine, chelerythrine or coptisin (see toxicological profile of Hydrastis canadensis in the appendix). According to the D monograph an oral application of Hydrastis canadensis is possible from the dilution D4. Hydrastis canadensis is added to the dilutions potentised as D4 to manufacture Ovarium Compositum injection corresponding arithmetically to an end dilution D=6. The mother tincture of Hydrastis canadensis contains at least 0.27 % alkaloids and 0.50 % at most, calculated as berberine [$C_{20}H_{19}NO_5$]. That means that the average alkaloid content of one ampoule is 110 ng, calculated as berberine. This low amount indicates that the final drug does not show any toxicological risk regarding the berberine concentration.

2.1.5 Isoquinoline alkaloids from Cephaelis ipecacuanha

The derivatives of isoquinoline **emetine** and **cephaeline** of **cephaelis ipecacuanha** are part of a group of alkaloids, whose oral application was appreciated by the natives of South America in the 17th century due its

antibiotic effect in dysenteric diseases. Nowadays the drug is primarily used to extract emetine, which is used as an expectorant as well as to fight amoebiasis evoked by Entamoeba histolytica. The method, which was originally employed in the states and advised to administer a syrup of ipecac as an emetic agent in poisoning of children, is also quite customary in Europe [Teuscher/Lindequist 1994].

The dried subterranean organs of cephaelis ipecacuanha contain 1,8-3,5 % alkaloids, where approximately 40-80 % of emetine and 25-55 % of cephaelin are involved as main alkaloids. Furthermore, the secondary alkaloids psychotrine, emetamine, ipecoside and proto-emetine can be found, too [Teuscher/Lindequist 1994].

Intoxications with cephaelis ipecacuanha can occur as severe vomiting, diarrhoea, tachycardia, cardiac dysrhythmia, hypotension, leucocytosis as well as dysfunction of the respiratory activity [Andersen et al. 1997, Saincher et al. 1997]. The symptoms possibly last for weeks (see toxicological profile of cephaelis ipecacuanha in the appendix). In the past intoxications after the administration of herbal parts were reported but the applications were of a mere medical nature [Saincher et al. 1997, Mühlendahl 1994]. Severe intoxications in infants after the intake of 100 mg alkaloids were observed [Rechling et al. 1984]. There is a report about a lethal outcome of an intoxication after the intake of 200 mg in a 4-year old child [Adler 1980].

The acute toxicity of emetine was determined in animal experiments with 12.1 mg/kg injected intraperitoneally in rats and 32 mg/kg injected subcutaneously in mice. The oral administration of 30 mg/kg body weight is considered to be the lethal dosage for children [Teuscher/Lindequist 1994, Hager 1998].

According to the preparation monography an oral application of cephaelis ipecacuanha is possible from D2 for globules and D4 for other oral and the parenteral administration forms. The composition of **Ovarium Compositum** injectable solution contains 22 mg of cephaelis ipecacuanha dilution D6 in

2.2 ml, which corresponds arithmetically to a final dilution of approximately D8.

The mother tincture of cephaelis ipecacuanha contains maximal 0.18 % alkaloids, i. e. 1.0 ml D4 correspond to an approximate proportion of 0.18 µg alkaloids; 22 mg cephaelis ipecacuanha D6 do therefore contain approximately 0.396 ng alkaloids meaning that the average content of one ampoule, calculated as emetine, relates to approximately 396 pg. Within the proposed dosage for **Ovarium Compositum** injectable solution the weekly dose for adults corresponds up to three times one ampoule, which would be equivalent to an alkaloid proportion of approximately 1.188 ng per week, calculated as emetine (see toxicological profile). This low amount indicates that the ready-to-use remedy does not carry any toxicological risk regarding the concentration calculated as emetine.

2.1.6 Global evaluation of toxicity

By means of presented documentation and with respect to the application form all homeopathic dilutions of the composition Ovarium Compositum injection are recommended by the commission D at the German Health Authority (Farm, former BGA). The current scientific fundamentals and the clinical experiences did not reveal serious signs to suspect the containing amount of all homeopathic dilutions for causing toxicological risks.

2.2 REPRODUCTIVE FUNCTION (III B)

Results from direct studies of reproductive or teratogenic toxicity as well as fetotoxic side effects influencing fertility are not available. Researching the literature produced no hint for such risks

2.3 EMBRYO-FOETAL AND PERI-POSTNATAL TOXICITY (III C)

9. Results from direct studies of embryo toxic/ fetotoxic or peri-, postnatal toxicity are not available. Researching the literature produced no suggestion of such risks.

2.4 MUTAGENIC POTENTIAL (III D)

Results from direct studies of mutagenic toxicity are not available. Researching the literature produced no hint for such risks.

2.5 CANCEROGENIC POTENTIAL (III E)

Results from direct studies of carcinogenicity are not available. Researching the literature produced no hint for such risks.

2.6 IMMUNOTOXICITY (III Q)

No indications show that the effects of single components of Ovarium Compositum injection are sensitising or will provoke allergic reactions by the parenteral application. Possible risks or adverse drug reactions of parts or components of the plants have not been observed regarding the pharmacovigilance of the compounds of Ovarium Compositum or similar composed drugs.

2.7 INTERACTIONS (III H)

There are no hints that the effects of single components of the incorporated homeopathic dilutions and substances may be enhanced or inhibited by incorporated drugs or substances which interfere with their characteristic pharmacodynamic or toxicologic effects. Potential risks or interactive effects associated with the combined administration of the incorporated homeopathic

dilutions have not been substantiated in drug surveillance studies and pharmacovigilance on the use of the incorporated drugs in human.

3 OTHER INFORMATION

3.1 Pharmacovigilance

The drug safety of **Ovarium Compositum** injectable solution can also be shown by observing pharmacovigilance data, which have been determined by a dispensing of a formula with the same composition. The components showed identical finishing dilutions. Consequently the dispensing carried the same risk potential.

Within the framework of the supervision of drug safety no adverse event was reported since 1998 (745.510 ampoules delivered only in Germany), globally seen. This result is striking for the good safety profile of **Ovarium Compositum** injectable solution. This result of the pharmacovigilance points out that adverse drug reactions after parenteral application of the homeopathic dilution in **Ovarium Compositum** injectable solution are a rarity and that this preparation cannot be related to an increased risk especially concerning the gastro-intestinal, cardiovascular or central-neurogenic body organ system or the skin.

4 CONCLUSIONS

The scientific findings material and the clinical experiences do not reveal any indications concerning toxicological risks caused by components of the homeopathic drug **Ovarium Compositum** injectable solution if the speciality is applied according to a recommended dosage of the manufacturer.

Components of an immunotoxicological potential are included with a very small concentration. Consequently, a corresponding risk during treatment does not need to be taken into account.

It is recommendable to grant the application for registration of **Ovarium Compositum** injectable solution.

Bergisch Gladbach, 12.12.2003

Wolfgang Strösser, MD, PhD

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APPENDICES

Appendix 2 Copy Of Questionnaires Sent To The Therapists

Figure 11 The Oxford Fertility Questionnaire EHIQ

Oxford Fertility Unit **University of Oxford**

Emotional health and infertility questionnaire

Please answer each of the questions indicating the response that applies best to how you have felt over the past four weeks. Do not spend too much time considering your answer; your immediate response is likely to be more accurate.

These questions ask about your overall health.

In general would you say your health has been:	Excellent ..... 1 Very good ..... 2 Good 3
Please circle one number only	Fair ..... 4 Poor 5
How much have you been bothered by emotional problems such as feeling anxious, depressed, irritable or	Not at all ..... 1 Slightly ..... 2 Moderately ..... 3 Quite a lot ..... 4 Extremely 5

down-hearted and sad?

Please circle one number only

These questions ask you how you have felt about your fertility problem over the <u>past four weeks</u>.
Frequently we have used the term "our fertility problem". This relates to your problem in trying to conceive as a couple, regardless of what that problem is.

How true are each of the following statements for you? Please tick the box that best applies.

	Definitely true	Mostly true	Not sure	Mostly untrue	Definitely untrue
I feel that information given by staff is sometimes inadequate.	☐	☐	☐	☐	☐
2. I feel upset when people make insensitive comments about childless couples.	☐	☐	☐	☐	☐
3. I get upset when family and/or friends talk about their children..	☐	☐	☐	☐	☐

4. I may have to stop treatment sooner than I would like because of the financial cost.	☐	☐	☐	☐	☐
5. My life is on hold because of fertility treatment.	☐	☐	☐	☐	☐
6. I find it hard to share my feelings about infertility with my family and/or friends.	☐	☐	☐	☐	☐
7. I feel my partner blames me for our fertility problem.	☐	☐	☐	☐	☐
8. I find it hard to cope with our fertility problem.	☐	☐	☐	☐	☐
9. Trying to maintain privacy during treatment is stressful.	☐	☐	☐	☐	☐
10. At times I feel we are not getting the best treatment.	☐	☐	☐	☐	☐
11. I resent having to put other aspects of my life on hold because of infertility.	☐	☐	☐	☐	☐
12. I find it hard to help my partner cope with our fertility problem.	☐	☐	☐	☐	☐
13. I avoid seeing family and/or friends who have children.	☐	☐	☐	☐	☐

14. Infertility strains my relationship with my partner. ☐ ☐ ☐ ☐ ☐

15. I feel that decisions about treatment are out of my control. ☐ ☐ ☐ ☐ ☐

16. I feel pressured to have sex at the 'right time' even when I don't feel like it. ☐ ☐ ☐ ☐ ☐

17. Infertility has taken over my life. ☐ ☐ ☐ ☐ ☐

18. I feel unsupported by family and/or friends. ☐ ☐ ☐ ☐ ☐

Definitely true	**Mostly true**	**Not sure**	**Mostly untrue**	**Definitely untrue**

19. I feel that sex is more about conceiving than expressing our love for each other. ☐ ☐ ☐ ☐ ☐

20. Fertility treatment makes me feel like a 'thing' rather than a person. ☐ ☐ ☐ ☐ ☐

21. I find it difficult to talk to my partner about our fertility problem without one of us getting upset or angry. ☐ ☐ ☐ ☐ ☐

22. I find it painful when family ☐

members and/or friends become pregnant.	☐	☐	☐	☐	☐
23. I will feel incomplete as a person if I cannot have my own child.	☐	☐	☐	☐	☐
24. Sometimes I think that infertility could lead to us separating.	☐	☐	☐	☐	☐
25. Infertility makes me feel I have lost control of my life.	☐	☐	☐	☐	☐
26. I disagree with my partner about how much money to spend on treatment.	☐	☐	☐	☐	☐
27. I avoid places where there might be pregnant women or children.	☐	☐	☐	☐	☐
28. I feel my partner is obsessed with trying to have children.	☐	☐	☐	☐	☐
29. Sex is less enjoyable now that I know about our fertility problem.	☐	☐	☐	☐	☐
30. I blame myself for our fertility problem.	☐	☐	☐	☐	☐
31. I feel my partner is not as committed to having children as I am.	☐	☐	☐	☐	☐

32. I find it hard to agree with my partner whether to tell family and/or friends about our fertility problem. ☐ ☐ ☐ ☐ ☐

33. I am exhausted by the emotional roller coaster of infertility. ☐ ☐ ☐ ☐ ☐

Definitely true	**Mostly true**	**Not sure**	**Mostly untrue**	**Definitely untrue**

34. I find trying to balance fertility treatment with my other commitments stressful. ☐ ☐ ☐ ☐ ☐

35. I feel less sexually attractive since discovering our fertility problem. ☐ ☐ ☐ ☐ ☐

36. I feel angry that I may not be able to have a / another child. ☐ ☐ ☐ ☐ ☐

37. Each birthday without a / another child is more upsetting. ☐ ☐ ☐ ☐ ☐

38. I feel guilty that my past actions may have affected my fertility. ☐ ☐ ☐ ☐ ☐

39. Having a fertility problem makes me feel inadequate. ☐ ☐ ☐ ☐ ☐

40. Finding the money for treatment is a constant worry. ☐ ☐ ☐ ☐ ☐

If you would like to add anything further please do so here.

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Thank you for your help.

Appendix 5 for Protocol

Certificate of Good Manufacturing Standards

Figure 12 Certificate of Good Manufacturing Standards for Ovarium compositum

REGIERUNGSPRÄSIDIUM TÜBINGEN
LEITSTELLE ARZNEIMITTELÜBERWACHUNG BADEN-WÜRTTEMBERG

HERSTELLUNGSERLAUBNIS

Der Firma

Biologische Heilmittel Heel GmbH, Baden-Baden

wird gemäß § 13 Abs. 1 des Gesetzes über den Verkehr mit Arzneimitteln (Arzneimittelgesetz - AMG) in der geltenden Fassung die Erlaubnis erteilt zur Herstellung von

Humanarzneimitteln und Tierarzneimitteln

in der Betriebsstätte

Biologische Heilmittel Heel GmbH,
Dr.-Reckeweg-Straße 2 - 4, Baden-Baden
gemäß der vorliegenden Lagepläne vom 18.02.2004

Die Erlaubnis erstreckt sich ausschließlich auf die in

- Anlage 1 aufgeführten Herstellungstätigkeiten, Arzneimittel und Darreichungsformen
- Anlage 2 aufgeführten mit der teilweisen Prüfung der Arzneimittel beauftragten Betriebe

Im Rahmen einer Abnahmebesichtigung nach § 64 AMG in der geltenden Fassung wurde festgestellt, dass der Hersteller in der Lage ist zu gewährleisten, dass die Herstellung und Prüfung der genannten Arzneimittel nach dem Stand von Wissenschaft und Technik, insbesondere dem EU-GMP-Leitfaden, vorgenommen wird. Der Inhaber der Erlaubnis ist verpflichtet, die GMP-Konformität bei der Herstellung und Prüfung fortlaufend zu gewährleisten.

Anschrift: Regierungspräsidium Tübingen . Konrad-Adenauer-Straße 20 . 72072 Tübingen
Telefonzentrale (0 70 71) 7 57-0
Telefax (0 70 71) 7 57-31 90
Besucherparkplatz
Überweisungen an die Landesoberkasse Baden-Württemberg:
Baden-Württembergische Bank Karlsruhe
(BLZ 660 200 20) Konto-Nr. 4 002 015 800
Sprechzeiten:
Mo.-Do. 09:00 - 11:30 Uhr
14:00 - 15:30 Uhr
Fr 09:00 - 11:30 Uhr
Telefonische Voranmeldung empfohlen

Az.: 24d/5483.0-1.3/ Heel GmbH

Karlsruhe, den 17.06.2005
Regierungspräsidium Tübingen
Leitstelle Arzneimittelüberwachung Baden-Württemberg
Dienstsitz Karlsruhe

Dr. Koglin
Oberpharmazierat

REGIERUNGSPRÄSIDIUM TÜBINGEN

Anlagen:

Anlage 1: Herstellungstätigkeiten, Arzneimittel und Darreichungsformen, Herstellungsumfang

Anlage 2: Beauftragte Betriebe für die Prüfung gemäß § 14 Abs. 4 AMG

Anlage 1 zur Herstellungserlaubnis
für Biologische Heilmittel Heel GmbH, Baden-Baden
vom 17.06.2005:

Herstellungstätigkeiten:
Arzneimittel und Darreichungsformen, Herstellungsumfang

Sterile Arzneimittel

Flüssige Darreichungsformen (kleinvolumige Arzneimittel zur parenteralen Anwendung)
- endsterilisiert

Nicht-sterile Arzneimittel

Flüssige Darreichungsformen

Halbfeste Darreichungsformen

Feste Darreichungsformen
- Pulver
- Granulate
- Tabletten
- Streukügelchen
- Suppositorien

Abpacken, Kennzeichnen

Flüssige Darreichungsformen
(Augenarzneimittel und weitere sterile Arzneimittel)

Weitere

Tees
homöopathische Urtinkturen, flüssige Verdünnungen und Verreibungen
Arzneimittel für klinische Prüfungen

Az.: 24d/5483.0-1.3/ Heel GmbH

Karlsruhe, den 17.06.2005
Regierungspräsidium Tübingen
Leitstelle Arzneimittelüberwachung Baden-Württemberg
Dienstsitz Karlsruhe

Dr. Koglin
Oberpharmazierat

REGIERUNGSPRÄSIDIUM TÜBINGEN

**Anlage 2 zur Herstellungserlaubnis
für Biologische Heilmittel Heel GmbH, Baden-Baden
vom 17.06.2005:**

Beauftragte Betriebe für die Prüfung gemäß § 14 Abs. 4 AMG

beauftragter Betrieb (Name, Anschrift)	**Art der Prüfung**
BioChem Labor für biol. und chem. Analytik GmbH Daimlerstraße 5b 76185 Karlsruhe	LAL-Endotoxin-Test nach Ph.Eur. 2.6.14
PhytoLab GmbH und Co. KG Dutendorfer Straße 5 - 7 91487 Vestenbergsgreuth	Untersuchungen auf Pesticid-Rückstände nach Ph.Eur. 2.8.13 (GC, UV-VIS) Prüfung auf mikrobielle Reinheit nach Ph.Eur. 2.6.12 und 2.6.13 Untersuchung auf Schwermetallrückstände nach Ph.Eur. 2.2.23 HPLC, ICP-MS, HPLC-MS, GC-MS
Berghof Analytik + Umweltengineering GmbH und Co. KG Ob dem Himmelreich 9 72074 Tübingen	Untersuchungen auf Pesticid-Rückstände nach Ph.Eur. 2.8.13 (GC, UV-VIS) HPLC Untersuchung auf Schwermetallrückstände nach Ph.Eur.2.2.23 Untersuchung auf Ethylenoxid nach Ph.Eur. 2.4.25
Labor L + S AG Mangelsfeld 4 97708 Bad Bocklet	Prüfung auf mikrobielle Reinheit nach Ph.Eur. 2.6.12 und 2.6.13 Prüfung auf Sterilität nach Ph.Eur. 2.6.1
Analytisches Institut Bostel GmbH & Co.KG Florianstraße 13 70188 Stuttgart	Untersuchungen auf Pesticid-Rückstände nach Ph.Eur 2.8.13 (GC, UV-VIS)
Labor für Rückstands- und Spurenanalytik der Sebastian-Kneipp-Forschung der Kneipp-Werke Leonhard-Oberhäußer-Straße 1 86825 Bad Wörishofen	HPLC Untersuchung auf Schwermetallrückstände nach Ph.Eur. 2.2.23 Untersuchungen auf Pesticid-Rückstände nach Ph.Eur. 2.8.13 (GC, UV-VIS)

Az.: 24d/5483.0-1.3/ Heel GmbH

Karlsruhe, den 17.06.2005
Regierungspräsidium Tübingen
Leitstelle Arzneimittelüberwachung Baden-Württemberg
Dienstsitz Karlsruhe

Dr. Koglin
Oberpharmazierat

REGIERUNGSPRÄSIDIUM TÜBINGEN

REGIERUNGSPRÄSIDIUM TÜBINGEN
LEITSTELLE ARZNEIMITTELÜBERWACHUNG BADEN-WÜRTTEMBERG

MANUFACTURING AUTHORISATION

According to Sect. 13 of the German Drug Law (Arzneimittelgesetz - AMG), the company

Biologische Heilmittel Heel GmbH, Baden-Baden

is granted the permission for manufacturing of

medicinal products for human use and veterinary use

at the premises

Biologische Heilmittel Heel GmbH,
Dr. Reckeweg-Straße 2 - 4, 76532 Baden-Baden
according to the site plans dated 18-02-2004.

This authorisation applies to

- production activities, medicinal products and dosage forms as referred to in annex 1
- laboratories contracted for partial testing of medicinal products as referred to in annex 2

As confirmed by an inspection according to Sect. 64 of the German Drug Law the manufacturer is capable to ensure that production and quality control of the medicinal products as covered by this authorisation are carried out in substantial compliance with state-of-the-art science and technology especially in compliance with the EU guide to Good Manufacturing Practices (GMP). The manufacturing authorisation holder must ensure continuous compliance of production and quality control with applicable guidelines.

reference number - 24d-5483.0-1.3/Heel GmbH
Karlsruhe, den 17-06-2005

Dr. Koglin
Oberpharmazierat

Annex:
Annex 1: production activities, medicinal products, dosage forms, scope of authorisation
Annex 2: contract laboratories for quality control according to Sect. 14 Para. 4 AMG

Anschrift: Regierungspräsidium Tübingen . Konrad-Adenauer-Straße 20 . 72072 Tübingen
Telefonzentrale (0 70 71) 7 57-0
Telefax (0 70 71) 7 57-31 90
Besucherparkplatz
Überweisungen an die Landesoberkasse Baden-Württemberg:
Baden-Württembergische Bank Karlsruhe
(BLZ 660 200 20) Konto-Nr. 4 002 015 800
Sprechzeiten:
Mo.-Do. 09:00 - 11:30 Uhr
14:00 - 15:30 Uhr
Fr. 09:00 - 11:30 Uhr
Telefonische Voranmeldung empfohlen

Manufacturing authorisation - Annex 1
for Biologische Heilmittel Heel GmbH, Baden-Baden
dated: 17-06-2005

production activities:
medicinal products and dosage forms, scope of manufacturing

sterile products

liquid dosage forms (small volume parenterals)
- terminally sterilised

non-sterile products

liquid dosage forms

semi-solid dosage forms

solid dosage forms

- powders
- granules
- tablets
- globuli (homoeopathic pellets)
- suppositories

packaging, labelling

liquid dosage forms
(ophthalmologic and other sterile medicinal products)

other

teas
homeopathic mother tinctures, liquid dilutions and triturations
investigational medicinal products

reference number - 24d-5483.0-1.3/Heel GmbH
Karlsruhe, den 17-06-2005

Dr. Koglin
Oberpharmazierat

Manufacturing authorisation - Annex 2
for Biologische Heilmittel Heel GmbH, Baden-Baden
dated 17-06-2005

contract laboratories for quality control according to Sect. 14 Para. 4 AMG

contract accepting site (name, address)	**type of testing**
BioChem Labor für biol. und chem. Analytik GmbH Daimlerstraße 5b 76185 Karlsruhe	LAL-endotoxin-Test pursuant to Ph.Eur. 2.6.14
PhytoLab GmbH und Co. KG Dutendorfer Straße 5 - 7 91487 Vestenbergsgreuth	Testing for pesticide residues pursuant to Ph.Eur. 2.8.13 (GC. UV-VIS) Test for microbial purity pursuant to Ph.Eur. 2.6.12 and 2.6.13 Test for heavy metal residues pursuant to Ph. Eur. 2.2.23 HPLC- ICP-MS, HPLC-MS, GC-MS
Berghof Analytik + Umweltengineering GmbH und Co. KG Ob dem Himmelreich 9 72074 Tübingen	Testing for pesticide residues pursuant to Ph.Eur. 2.8.13 (GC, UV-VIS) HPLC Test for heavy metal residues pursuant to Ph.Eur. 2.2.23 Test for ethylene oxide pursuant to Ph.Eur. 2.4.25
Labor L + S AG Mangelsfeld 4 97708 Bad Bocklet	Test for microbial purity pursuant to Ph.Eur. 2.6.12 and 2.6.13 Test for sterility pursuant to Ph.Eur. 2.6.1
Analytisches Institut Bostel Florianstraße 13 70188 Stuttgart	Testing for pesticide residues pursuant to Ph.Eur. 2.8.13 (GC, UV-VIS)
Labor für Rückstands und Spurenanalytik der Sebastian-Kneipp-Forschung der Kneipp-Werke Leonhard-Oberhäußler-Straße 1 86825 Bad Wörishofen	HPLC Test for heavy metal residues pursuant to Ph.Eur. 2.2.23 Testing for pesticide residues pursuant to Ph.Eur. 2.8.13 (GC, UV-VIS)

reference number - 24d-5483.0-1.3/Heel GmbH
Karlsruhe, den 17-06-2005

Dr. Koglin
Oberpharmazierat

Figure 13 The EQ-5D

Appendix 6 for Protocol The EQ-5D

EQ-5D Health Questionnaire

(English version for the UK)

(validated for use in Eire)

By placing a tick in one box in each group below, please indicate which statements best describe your own health state today.

Mobility

I have no problems in walking about ❑

I have some problems in walking about ❑

I am confined to bed ❑

Self-Care

I have no problems with self-care ❑

I have some problems washing or dressing myself ❑

I am unable to wash or dress myself ❑

Usual Activities (*e.g. work, study, housework, family or leisure activities)*

I have no problems with performing my usual activities ❑

I have some problems with performing my usual activities ❑

I am unable to perform my usual activities ❑

Pain/Discomfort

I have no pain or discomfort ❑

I have moderate pain or discomfort ❑

I have extreme pain or discomfort ❑

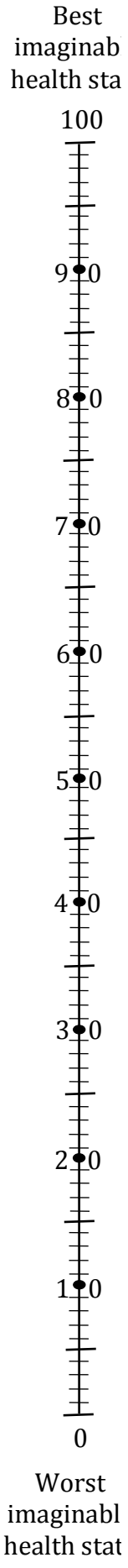
Anxiety/Depression

I am not anxious or depressed ❑

I am moderately anxious or depressed ❑

I am extremely anxious or depressed ❑

To help people say how good or bad a health state is, we have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked 100 and the worst state you can imagine is marked 0.



We would like you to indicate on this scale how good or bad your own health is today, in your opinion. Please do this by drawing a line from the box below to whichever point on the scale indicates how good or bad your health state is today.

Your own health state today

APPENDICES

Appendix 7 Protocol Amendments

Protocol No OVCT-001

Number of Protocol amendments issued:

( ) 1 Version 4 – 1st September 2008

APPENDICES

APPENDIX 5 Documentation from Pilot Study

Figure 14 Consent forms for participants in pilot study

Consent Forms for Participants in OVCT-001

Title of research proposal: A pilot study of Ovarium compositum in infertile women (OVCT-001)

Name of Researchers: Mr Neil MacLachlan, Ms Claire Haresnape, Prof Atholl Johnston and Dr Arthur T. Tucker

Name of Patient / Volunteer (Block Capitals)**:**

Address:

STUDY CONSENT FORM

(Initial boxes to agree with statement)

1. I confirm that I have read and understand the information sheet dated 23rd, July 2009, version 4, for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐
2. I confirm that I have decided NOT to actively participate in this study of *Ovarium compositum*. ☐
3. I give permission for details of my routine treatment to be used in the observational part of this study. ☐
4. I understand that relevant sections of any of my medical records generated during my routine and planned treatment for infertility may be looked at by responsible individuals from Queen Mary University of London Medical School. I ☐

give permission for these individuals to have access to my records.

_____ _____

_____

Name of Patient Date

Signature

_____ _____

_____

Name of Person taking consent Date Signature

(if different from researcher)

_____ _____

_____

Researcher

Figure 15 Consent forms for non participants in pilot study

Consent Forms for Non-Participants in OVCT-001

Title of research proposal: A pilot study of Ovarium compositum in infertile women (OVCT-001)

Name of Researchers: Mr Neil MacLachlan, Ms Claire Haresnape, Prof Atholl Johnston and Dr Arthur T. Tucker

Name of Patient / Volunteer (Block Capitals)**:**

Address:

STUDY CONSENT FORM

(Initial boxes to agree with statement)

5. I confirm that I have read and understand the information sheet dated 23rd, July 2009, version 4, for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐
6. I confirm that I have decided NOT to actively participate in this study of *Ovarium compositum*. ☐
7. I give permission for details of my routine treatment to be used in the observational part of this study. ☐
8. I understand that relevant sections of any of my medical records generated during my routine and planned treatment for infertility may be looked at by responsible individuals from Queen Mary University of London Medical School. I give permission for these individuals to have access to my records. ☐

_____ _____

_____

Name of Patient Date

Signature

_____ _____

_____

Name of Person taking consent Date Signature

(if different from researcher)

_____ _____

_____

Researcher

Figure 16 Patient Information Sheets for Pilot Study

Patient Information Sheet for OVCT-001

Study Number: OVCT-001

Study title: A Pilot study of Ovarium compositum in Infertile Women

Sponsor: Clinical Pharmacology, Barts and The London, Queen Mary's School of Medicine and Dentistry, Charterhouse Square, London, EC1M 6BQ, UK , Tel: +44 (20) 7882 3404, Fax: +44 (20) 7882 3408

Part 1

Invitation

You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully. Talk to others about the study if you wish.

Part 1 tells you the purpose of this study and what will happen to you if you take part.

Part 2 gives you more detailed information about the design of the study.

Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Seahorse Scientific Services is the sponsor of this research.

What is the purpose of the study?

The purpose of this study is to find out if Ovarium compositum is more effective than placebo in supporting the treatment of women for female infertility, caused by the failure to ovulate. This is to be taken in addition to your normal treatment, not as an alternative. We would also like to measure your quality of life (QoL) during your infertility treatment to find out how it affects your sense of wellbeing. We propose to use two questionnaires to do this. Because this is a double blind trial you may receive either Ovarium compositum or a placebo. Placebo means a dummy drug that has no active ingredients.

Ovarium compositum is a homoeopathic product that is prescribed by holistic therapists working with female infertility. Infertile women will frequently seek out a holistic approach in support of their medical treatment to overcoming

their infertility and more information about the effectiveness of CAM (complementary and alternative medicine) would be helpful.

This drug is routinely prescribed by Homotoxicologists in the United Kingdom and Europe for female infertility and will be taken exactly as normally prescribed.

Why have I been chosen?

You are being asked to take part in this study because you are a woman seeking treatment for infertility due to problems with ovulation.

Do I have to take part?

No. It is up to you to decide whether or not to take part. If you do, you will be given this information sheet to keep and be asked to sign a consent form. You are still free to withdraw at any time and do not have to give a reason.

Before you can begin the study

You are welcome to read the full study protocol, as well as this Information Sheet. This gives many details about Ovarium compositum (the study preparation) and the study. The recruiting investigator will tell you about the study and any adverse events (reactions) that could potentially occur. You will be told exactly what the study entails and what will be required of you. You are encouraged to ask the Investigators conducting the recruitment interview, questions until you are satisfied that you fully understand the nature of the study and what will be required of you.

What will happen to me if I take part?

If you agree to take part and to sign a Consent for Study Screening Form, you will be invited to a selection session.

Screening Visit

This will occur no more than 28 days before the first administration of study medication.

You will be examined by your infertility consultant who will assess your suitability for this study based upon the normal procedures for your conventional treatment.

With your permission we may contact your General Practitioner to advise them of your potential participation in this study. If during the health screening tests any abnormal results are found, you will be immediately referred for clinical review as appropriate.

Visit 2

Once accepted onto the study, we will ask you to come to the Department of Obstetrics and Gynaecology, Jersey General Hospital, Gloucester Street, St Helier, Jersey, JE1 3QS.

At this time you will undergo a check-in procedure and sign Consent for Study Participation Form.

One of the study Doctors will give you thirty (30) days of the preparation (active or placebo) that you were recruited for and instructions for the timing of each dose. You will be asked to complete two questionnaires that are designed to measure your quality of life (QoL).

Visits 3 to 13

Thirty days later you will be asked to attend for the third visit if you are happy to continue with the study you will be given a further 100 tablets and asked to complete the two questionnaires again. This procedure will be repeated every 30 days until you chose to leave the study or become pregnant or the study ends (after 12 months)

Expenses and payments:

There is no payment for taking part in this study. The indirect benefits of taking part may include a sense of satisfaction at taking part in a study that may help other couples in the future.

What do I have to do?

If you choose to take part in this study you must not be taking part in any other study. You must also not have taken part in any other study within the last four months.

In addition to your planned infertility treatment, you will need to come to the clinics at the times requested and remain there for the duration of time required for each visit; this will be about half an hour.

From the screening to the end of the study, you should not take any other homoeopathic medicines or take part in acupuncture treatments. You should also abstain from drinking coffee and eating peppermints during this whole study period as some people believe that these can antidote homoeopathic medicines. You must inform your research doctor of all other medications you are taking including over the counter medications. You should not take any medications without first consulting the research team.

If you experience any changes in your health whether or not you feel that this is related to your study medication then you must inform your research doctor, we will tell you how to do this.

What are the possible benefits of taking part?

The indirect benefits of taking part in this study include the knowledge that you are making a contribution to our knowledge about complementary medicine which may help other infertile couples in the future. It has not yet been proved that taking supplements of this kind can increase fertility rates but it may be that there is some direct benefit to taking the active preparation.

What happens when the research study stops?

You will continue with your conventional fertility treatments

What if there is a problem?

Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed. The detailed information on this is given in Part 2.

If you have a complaint please contact the following in the first instance: Claire Haresnape or Dr Arthur Tucker.

If you feel any discomfort or distress during the investigations, you must say so and we will stop the test medicine immediately at any time.

Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed. A contact number for complaints will be given.

Will my taking part in the study be kept confidential?

Yes. All the information about your participation in this study will be kept confidential.

Contact Details:

If you require any further information please contact:

Ms Claire Haresnape
Research Student
Barts and the London
Clinical Pharmacology
Charterhouse Square
London, EC1M 6BQ

Telephone and Fax 01435 813 101
Mobile/Cell phone 07720 060 116

Or:

Dr Arthur Tucker
The Ernest Cooke Vascular & Microvascular Unit,
4th Floor Dominion House,
St. Bartholomew's Hospital,
West Smithfield.
London, EC1A 7BE.
Telephone: 020 7601 8498
This completes Part 1 of the Information Sheet.
If the information in Part 1 has interested you and you are considering participation, please continue to read the additional information in Part 2 before making any decision.

Part 2

What if relevant new information becomes available?

Sometimes during the course of a research project, new information becomes available about the treatment/drug that is being studied. If this happens, your research doctor will tell you about it and discuss whether you want to or should continue in the study. If you decide not to carry on, your research doctor will make arrangements for your care to continue. If you decide to continue in the study you will be asked to sign an updated consent form.

Also, on receiving new information your research doctor might consider it to be in your best interests to withdraw you from the study. He/she will explain the reasons and arrange for your care to continue. If the study is stopped for any other reason, you will be told why and your continuing care will be arranged.

What will happen if I don't want to carry on with the study?

If you withdraw from the study we will need to use the data collected up to your withdrawal.

If your participation in the study is discontinued after you have received the study drug you will be asked to undergo a final examination for your own safety. If the reason for ending the study is, for example, an adverse event or a side-effect of the drug, you will be asked to give information on these in order to protect the other patients taking part in this clinical study.

What if there is a problem?

We would not expect you to suffer any harm or injury because of your participation in this study. If you are harmed by taking part in this study, there is no special compensation arrangement. If you are harmed due to someone's negligence, then you may have grounds for legal action but you may have to pay your legal costs. Regardless of this, if you wish to complain or have any concerns about any aspect of the way you have been approached or treated during the course of this study, the normal National Health Service complaints mechanisms should be available to you. These arrangements do not affect your right to pursue a claim through legal action.

Complaints

If you have a concern about any aspect of this study, you should ask to speak with the Research Team who will do their best to answer your questions (Claire Haresnape mobile telephone 0772 006 0116 or landline 01435 813 101; Dr Arthur Tucker, telephone 020 7601 8498).

If you remain unhappy and wish to complain formally you can do this by contacting: The Complaints Officer, c/o The Chief Operating Officer for Seahorse Scientific Services, 'Nonsuch' House, 21, Rhodesia Road, Leytonstone, London, E11 4DF, UK. (:020 8257 8412

Will my taking part in this study be kept confidential?

All the information obtained about you in the course of the study is confidential and will be kept in a secure locked room. The investigators performing the study and a study Monitor will have access to the data collected in this study. They may also be looked at by representatives of regulatory authorities and by authorised people from Seahorse Scientific Services to check that the study is being carried out correctly. All will have a duty of confidentiality to you as a research participant and nothing that could reveal your identity will be disclosed outside the research site.

Involvement of the General Practitioner/Family doctor (GP)

With your permission we may contact your General Practitioner to advise them of your potential participation in this study.

What will happen to the results of the research study?

The results of this study may be published or presented at meetings. You will not be identified in any report / publication or presentation.

Who is organising and funding the research?

This research is being sponsored by Seahorse Scientific Services funded by an unrestricted educational grant from Heel GmbH.

Who has reviewed the study?

This study has been given a favourable ethical opinion for conduct in the XXXXXX Research Ethics Committee reference

Before you sign this consent form please ask any questions you have about the study.

Thank you for taking the time to read this information sheet.

APPENDICES

Figure 17 Letter of Invitation to Trial Participants

Letter of Invitation to Trial Participants

On Jersey General Hospital letterhead

Dear

I would like to invite you to participate in a clinical trial that is taking place at the Jersey General Hospital. The purpose of this study is to find out if Ovarium compositum is more effective than placebo in supporting the treatment of women for female infertility, caused by the failure to ovulate.

This is to be taken in addition to your normal treatment, not as an alternative. We would also like to measure your quality of life (QoL) during your infertility treatment to find out how it affects your sense of wellbeing. We propose to use two questionnaires to do this. Because this is a double blind trial you may receive either Ovarium compositum or a placebo. Placebo means a dummy drug that has no active ingredients.

Ovarium compositum is a homoeopathic product that is prescribed by holistic therapists working with female infertility. Infertile women will frequently seek out a holistic approach in support of their medical treatment to overcoming their infertility and more information about the effectiveness of CAM (complementary and alternative medicine) would be helpful.

This drug is routinely prescribed by Homotoxicologists in the United Kingdom and Europe for female infertility and will be taken exactly as normally prescribed.

If you would like to find out more about the trial then please read the enclosed Patient Information Sheet.

Yours sincerely,

Mr Neil MacLachlan FRCOG
Consultant Gynaecologist and Obstetrician

Figure 18 Case report form for pilot study

Case Report Form For OVCT-001 Data Collection

Available as a pdf document, working draft shown on next page.

Study Code:	OVCT-001	Randomisation no:		Subject initials:	

CASE REPORT FORM

STUDY TITLE

A Pilot Study of Ovarium Compositum in Infertile Women

Study reference number **OVCT-001**

CLINICAL TRIAL SITE/UNIT: **Jersey General Hospital**

PRINCIPAL INVESTIGATOR: **Claire Haresnape**

Subject Initials: | | |

Subject Randomisation Number: | | |

I am confident that the information supplied in this case record form is complete and accurate data. I confirm that the study was conducted in accordance with the protocol and any protocol amendments and that written informed consent was obtained prior to the study.

Investigator's Signature: .....

Print Name:

Date of signature: | | | | | | | | | |

d d m m m y y y y

1

CASE REPORT FORM

STUDY TITLE

A Pilot Study of Ovarium Compositum in Infertile Women

Study reference number **OVCT-001**

CLINICAL TRIAL SITE/UNIT: **Jersey General Hospital**

PRINCIPAL INVESTIGATOR: **Claire Haresnape**

Subject Initials: | | | |

Subject Randomisation Number: | | | |

I am confident that the information supplied in this case record form is complete and accurate data. I confirm that the study was conducted in accordance with the protocol and any protocol amendments and that written informed consent was obtained prior to the study.

Investigator's Signature: ----------

Date of signature:

D	d	m	m	m	y	y	y	y

Inclusion Criteria		Yes	No*
1	Is the subject a healthy female aged between 18 and 60 years?	☐	☐
2	Has the subject willingly given written informed consent?	☐	☐
3	Has the subject been diagnosed with poor response to ovulation induction or is anovulatory?	☐	☐
4	Has the subject an absence of other significant endocrine dysfunction including diabetes?	☐	☐
5	Has the subject an absence of other known causes of infertility?	☐	☐

*If any inclusion criteria are ticked no then the patient is not eligible for the study.

Exclusion Criteria		Yes*	No
1	Is the subject taking medication , for any other condition, that may affect ovulation?	☐	☐
2	Is the subject pregnant?	☐	☐
3	Has the subject been diagnosed with tubal infertility?	☐	☐
4	Has the subject had a previous pregnancy?	☐	☐
5	Has the subject a BM1 <20kg/m^2 or >35kg/m^2 ?	☐	☐
6	Does the subject have concomitant use of any other complementary or alternative therapies?	☐	☐
7	Does the subject ingest strong peppermint or caffeine?	☐	☐
8		☐	☐

9 ☐ ☐

* If any exclusion criteria are ticked yes then the patient is not eligible for the study.

INFORMED CONSENT

Please note: written informed consent must be given before any study specific procedures take place or any current therapy is discontinued for the purposes of participation in this study.

Has the subject freely given written informed consent? Yes ☐ No ☐

VISIT 1 (SCREENING)

Date:

_____

DD MMM YYYY

DEMOGRAPHIC DATA

Age (yrs): ☐☐ Sex: Female ☐ Male ☐

Height (m): ☐ • ☐☐

Weight (Kg): ☐☐ • ☐

Body Mass Index (BMI = Wt (kg)/H^2 (M): [ ][ ] • [ ]

SMOKING HABITS

Does the subject smoke or use tobacco products? *Yes [ ] No [ ]

***** How many cigarettes per day? [ ][ ]

Other, specify ----------

ALCOHOL CONSUMPTION

Does the subject consume alcohol? Yes [ ] No [ ]

If yes, how many units per week? [ ][ ]

MEDICATIONS TAKEN

Is the subject currently or previously taking any medication including OTC, vitamins and/or supplements? Yes [ ] No [ ]

*Record **all** medication on Concomitant Medications page

VISIT 1 (SCREENING)

PREVIOUS MEDICAL HISTORY

Is there any relevant medical history in the following systems?

Code	System	*Yes	No
1	Cardiovascular		
2	Respiratory		
3	Hepato-biliary		
4	Gastro-intestinal		
5	Genito-urinary		
6	Endocrine		

Code	System	*Yes	No
9	Neoplasia		
10	Neurological		
11	Psychological		
12	Immunological		
13	Dermatological		
14	Allergies		

7	Haematological				15	Eyes, ear, nose, throat		
8	Musculo-skeletal				00	Other		

*If ***YES*** for any of the above, enter the code for each condition in the boxes below, give further details (including dates) and state if the condition is currently or potentially active. If giving details of surgery please specify the underlying cause. Use a separate line for each condition.

		Currently Active?	
Code	**Details (including dates)**	**Yes**	**No**

VISIT 1 (SCREENING)

PHYSICAL EXAMINATION (to be carried out by medical staff only)

Code	System	*Abnormal	Normal
1	General Appearance		
2	Heart		
3	Lungs		
4	Abdomen		
5	Extremities		

* If ***ABNORMAL*** enter the code for each condition in the boxes below and give brief details. Please use a separate line for each condition.

Code	Details

VITAL SIGNS

Pulse rate ☐☐☐ Bpm

Blood pressure (seated) ☐☐☐ / ☐☐☐ mmHg

ECG

Is the ECG: Normal ☐ Abnormal ☐ **

**Description _____

Retain signed and dated trace in the plastic sleeve at back of CRF

VISIT 1 (SCREENING)

LABORATORY ANALYSIS		**Initials**
Blood for haematology and biochemistry	Taken by	

✓	**Repeat Sample Required?**	**Date Taken (dd mmm yyyy)**
	Haematology	
	Clinical Chemistry	

Please insert a copy of all results in the plastic sleeve at the back of the CRF.

Are all final results:	Normal		Abnormal NCS		**Abnormal CS	
**Description:	**Ovarian Function Investigations**					
Endometrial thickness at ovulation/midcycle						
Ovarian volume of both ovaries	*Left*			*Right*		
Antral follicle count day 3-5 at beginning of	*Left*			*Right*		
Progesterone level on day 21 mid-luteal phase.						

Does any result contradict study entry?	*Yes		No		

Initials:	

*If YES, subject must not continue. Please complete off study page.

APPENDICES

VISIT 1 (SCREENING)

End of Visit Checklist: to be completed by Investigator

		Yes	No
1	Does the subject satisfy the inclusion and exclusion criteria to date?	☐	☐
2	Have all screening procedures been completed?	☐	☐
3	Has the concomitant medication page been completed?	☐	☐
4	Is the subject willing to proceed?	☐	☐

Investigator

	Yes	No
Is the subject to continue?	☐	☐
Has medication been collected from Pharmacy?	☐	☐
Have the dosing instructions been explained to the patient?	☐	☐

Signature: ---------- Date: ☐☐☐☐☐☐☐☐

d d m m m y y y y

If '**Yes**' please:

Complete details of next visit and any other needed instructions on the instruction card.

Give the subject the instruction card

VISIT 2 (WEEK 1)

Date:_____

DD MMM YYYY

PHYSICAL EXAMINATION (to be carried out by medical staff only)			
Code	**System**	***Abnormal**	**Normal**
1	General Appearance		
2	Heart		
3	Lungs		
4	Abdomen		
5	Extremities		
*** If any changes from baseline, complete adverse event page.**			

VITAL SIGNS

Pulse rate ☐☐☐ Bpm

Blood pressure (seated) ☐☐☐ / ☐☐☐ mmHg

LABORATORY ANALYSIS **Initials**

Blood for haematology and biochemistry Taken by ☐

✓	**Repeat Sample Required?**	**Date Taken (dd mmm yyyy)**
☐	Haematology	☐☐☐☐☐☐☐☐☐☐☐
☐	Clinical Chemistry	☐☐☐☐☐☐☐☐☐☐☐

Please insert a copy of all results in the plastic sleeve at the back of the CRF.

Are all final results:	Normal		Abnormal NCS		**Abnormal CS		
**Description							
Does any result contradict continuation in the study?			*Yes		No		

*If YES, subject must not continue. Please complete off study page.

Are all final results:	Normal		Abnormal NCS		**Abnormal CS		
**Description:	**Ovarian Function Investigations**						
Endometrial thickness at ovulation/midcycle							
Ovarian volume of both ovaries	*Left*			*Right*			
Antral follicle count day 3-5 at beginning of	*Left*			*Right*			
Progesterone level on day 21 mid-luteal phase.							
Does any result contradict study entry?		*Yes			No		
Initials:							

*If YES, subject must not continue. Please complete off study page.

VISIT 3 (WEEK ?)

Date:_____

DD MMM YYYY

PHYSICAL EXAMINATION (to be carried out by medical staff only)			
Code	**System**	***Abnormal**	**Normal**
1	General Appearance		
2	Heart		
3	Lungs		
4	Abdomen		
5	Extremities		
*** If any changes from baseline, complete adverse event page.**			

VITAL SIGNS

Pulse rate ☐☐☐ Bpm

Blood pressure (seated) ☐☐☐ / ☐☐☐ mmHg

LABORATORY ANALYSIS **Initials**

Blood for haematology and biochemistry Taken by ☐

✓	**Repeat Sample Required?**	**Date Taken (dd mmm yyyy)**
☐	Haematology	☐☐ ☐☐☐ ☐☐☐☐
☐	Clinical Chemistry	☐☐ ☐☐☐ ☐☐☐☐

Please insert a copy of all results in the plastic sleeve at the back of the CRF.

Are all final results:	Normal		Abnormal NCS		**Abnormal CS	
**Description						
Does any result contradict continuation in the study?			*Yes		No	

*If YES, subject must not continue. Please complete off study page.

Are all final results:	Normal		Abnormal NCS		**Abnormal CS	
**Description:	**Ovarian Function Investigations**					
Endometrial thickness at ovulation/midcycle						
Ovarian volume of both ovaries	*Left*		*Right*			
Antral follicle count day 3-5 at beginning of	*Left*		*Right*			
Progesterone level on day 21 mid-luteal phase.						
Does any result contradict study entry?		*Yes		No		
Initials:						

*If YES, subject must not continue. Please complete off study page.

VISIT 4 (WEEK ?)

Date:_____

DD MMM YYYY

PHYSICAL EXAMINATION (to be carried out by medical staff only)

Code	System	*Abnormal	Normal
1	General Appearance		
2	Heart		
3	Lungs		
4	Abdomen		
5	Extremities		

*** If any changes from baseline, complete adverse event page.**

VITAL SIGNS

Pulse rate ☐☐☐ Bpm

Blood pressure (seated) ☐☐☐ / ☐☐☐ mmHg

LABORATORY ANALYSIS **Initials**

Blood for haematology and biochemistry Taken by ☐

✓	Repeat Sample Required?	Date Taken (dd mmm yyyy)
	Haematology	☐☐ ☐☐☐ ☐☐☐☐
	Clinical Chemistry	☐☐ ☐☐☐ ☐☐☐☐

Please insert a copy of all results in the plastic sleeve at the back of the CRF.

Are all final results:	Normal		Abnormal NCS		**Abnormal CS		
**Description							
Does any result contradict continuation in the study?			*Yes		No		

*If YES, subject must not continue. Please complete off study page.

Are all final results:	Normal		Abnormal NCS		**Abnormal CS		
**Description:	**Ovarian Function Investigations**						
Endometrial thickness at ovulation/midcycle							
Ovarian volume of both ovaries	*Left*			*Right*			
Antral follicle count day 3-5 at beginning of	*Left*			*Right*			
Progesterone level on day 21 mid-luteal phase.							
Does any result contradict study entry?		*Yes			No		
Initials:							

*If YES, subject must not continue. Please complete off study page.

VISIT 5 (WEEK ?)

Date:_____

DD MMM YYYY

PHYSICAL EXAMINATION (to be carried out by medical staff only)

Code	System	*Abnormal	Normal
1	General Appearance		
2	Heart		
3	Lungs		
4	Abdomen		
5	Extremities		

*** If any changes from baseline, complete adverse event page.**

VITAL SIGNS

Pulse rate ☐☐☐ Bpm

Blood pressure (seated) ☐☐☐ / ☐☐☐ mmHg

LABORATORY ANALYSIS **Initials**

Blood for U+Es Taken by

✓	Repeat Sample Required?	Date Taken (dd mmm yyyy)
	Clinical Chemistry	

Please insert a copy of all results in the plastic sleeve at the back of the CRF.

Are all final results:	Normal		Abnormal NCS		**Abnormal CS	
**Description						
Has renal function remained stable?		Yes		*No		

*If No, record on adverse event page.

Are all final results:	Normal		Abnormal NCS		**Abnormal CS	
**Description:	**Ovarian Function Investigations**					
Endometrial thickness at ovulation/midcycle						
Ovarian volume of both ovaries	*Left*		*Right*			
Antral follicle count day 3-5 at beginning of	*Left*		*Right*			
Progesterone level on day 21 mid-luteal phase.						

Does <u>any</u> result contradict study entry?	*Yes		No	

Initials:	

*If YES, subject must not continue. Please complete off study page.

CONCOMITANT MEDICATIONS

Medication	Total Daily Dose	Units	Reason	Start Date (MM/DD/YYYY)	Stop Date (MM/DD/YYYY)	Continuing
				__ __/__ __/__ __ __ __	__ __/__ __/__ __ __ __	☐
				__ __/__ __/__ __ __ __	__ __/__ __/__ __ __ __	☐
				__ __/__ __/__ __ __ __	__ __/__ __/__ __ __ __	☐
				__ __/__ __/__ __ __ __	__ __/__ __/__ __ __ __	☐
				__ __/__ __/__ __ __ __	__ __/__ __/__ __ __ __	☐
				__ __/__ __/__ __ __ __	__ __/__ __/__ __ __ __	☐
				__ __/__ __/__ __ __ __	__ __/__ __/__ __ __ __	☐
				__ __/__ __/__ __ __ __	__ __/__ __/__ __ __ __	☐
				__ __/__ __/__ __ __ __	__ __/__ __/__ __ __ __	☐

Adverse Events

Has the patient experienced any Adverse Events since signing the Informed Consent? ☐ Yes, specify below ☐

AE no.	Adverse Event (diagnosis (if known) or signs/symptoms)	Start Date dd/mmm/yyyy and Time (24 hour clock)	Stop Date dd/mmm/yyyy and Time (24 hour clock)	Outcome 1=Recovered 2=Recovered with sequelae 3=Continuing 4=Patient Died 5=Change in AE 6=unknown	Severity 1=Mild 2=Moderate 3=Severe	Plausible relationship to Study Drug	Action taken with Study Drug 1=None 2=Dose Reduction Temporarily 3=Dose Reduced 4=Discontinued Temporarily 5=Discontinued	Withdrawn due to AE?	Serious AE (SAE)?
		/ / :	/ / :			☐ Yes ☐ No		☐ Yes ☐ No	☐ Yes ☐ No
		/ / :	/ / :			☐ Yes ☐ No		☐ Yes ☐ No	☐ Yes ☐ No
		/ / :	/ / :			☐ Yes ☐ No		☐ Yes ☐ No	☐ Yes ☐ No

OFF STUDY FORM

Date Off Study: __ __ / __ __ / __ __ __ __

(MM/DD/YYYY)

Date Last Study Medication Taken: __ __ / __ __ / __ __ __ __

(MM/DD/YYYY)

Reason Off Study (Please mark only the primary reason. Reasons **than Completed Study** require explanation next response)

☐ Completed study

☐ AE/SAE **(complete AE CRF & SAE form, if ap**

_____

☐ Lost to fol

_____

_____

☐ Non-compliant part

_____

_____

☐ Concomitant med

_____

_____

☐ Medical contraind

_____

_____

☐ Withdraw c

_____

_____

☐ Death **(complete SAE**

_____

☐

_____

_____

APPENDICES

Figure 19 Medication labels for pilot study

Medication Labels for OVCT-001 – Single Dose

Subject No.: 1101 - 1120

Department of Obstetrics and Gynaecology, Jersey General Hospital, Gloucester Street, St Helier, Jersey, JE1 3QS, Phone: 01534 622 660

Study-Code: OVCT-001 Clomid treatment, age < 30 yrs
Subject-No.: 00

EudraCT-No.: 2008-005858-20

100 tablets for oral use

Directions for use: 1 tablet, 3 times daily; 15 min before

Subject No.: 1201 - 1220

Department of Obstetrics and Gynaecology, Jersey General Hospital, Gloucester Street, St Helier, Jersey, JE1 3QS, Phone: 01534 622 660

Study-Code: OVCT-001 Clomid treatment, age 30 -35 yrs
Subject-No.: 00

EudraCT-No.:2008-005858-20

100 tablets for oral use

Directions for use: 1 tablet, 3 times daily; 15 min before

Subject No.: 1301 - 1320

Department of Obstetrics and Gynaecology, Jersey General Hospital, Gloucester Street, St Helier, Jersey, JE1 3QS, Phone: 01534 622 660

Study-Code: OVCT-001 Clomid treatment, age > 35 yrs
Subject-No.: 00

EudraCT-No.:2008-005858-20

100 tablets for oral use

Directions for use: 1 tablet, 3 times daily; 15 min before or after meals; at 9 am, 12 noon and 9 pm

Subject No.: 2101 - 2120

Department of Obstetrics and Gynaecology, Jersey General Hospital, Gloucester Street, St Helier, Jersey, JE1 3QS, Phone: 01534 622 660

Study-Code: OVCT-001 FSH treatment, age < 30 yrs
Subject-No.: 00

EudraCT-No.: 2008-005858-20

100 tablets for oral use

Directions for use: 1 tablet, 3 times daily; 15 min before or after meals; at 9 am, 12 noon and 9 pm

Subject No.: 2201 – 2220

Department of Obstetrics and Gynaecology, Jersey General Hospital, Gloucester Street, St Helier, Jersey, JE1 3QS, Phone: 01534 622 660

Study-Code: OVCT-001 FSH treatment, age 30 -35 yrs
Subject-No.: 00

EudraCT-No.: 2008-005858-20

100 tablets for oral use

Directions for use: 1 tablet, 3 times daily; 15 min before

Subject No.: 2301 - 2320

Department of Obstetrics and Gynaecology, Jersey General Hospital, Gloucester Street, St Helier, Jersey, JE1 3QS, Phone: 01534 622 660

Study-Code: OVCT-001 FSH treatment, age > 35 yrs
Subject-No.: 00

EudraCT-No.: 2008-005858-20

100 tablets for oral use

Directions for use: 1 tablet, 3 times daily; 15 min before or after meals; at 9 am, 12 noon and 9 pm

Subject No.: 3101 - 3120

Department of Obstetrics and Gynaecology, Jersey General Hospital, Gloucester Street, St Helier, Jersey, JE1 3QS, Phone: 01534 622 660

Study-Code: OVCT-001 IVF treatment, age < 30 yrs
Subject-No.: 00

EudraCT-No.: 2008-005858-20

100 tablets for oral use

Directions for use: 1 tablet, 3 times daily; 15 min before or after meals; at 9 am, 12 noon and 9 pm

Subject No.: 3201 - 3220

Department of Obstetrics and Gynaecology, Jersey General Hospital, Gloucester Street, St Helier, Jersey, JE1 3QS, Phone: 01534 622 660

Study-Code: OVCT-001 IVF treatment, age 30 -35 yrs
Subject-No.: 00

EudraCT-No.: 2008-005858-20

100 tablets for oral use

Directions for use: 1 tablet, 3 times daily; 15 min before or after meals; at 9 am, 12 noon and 9 pm

APPENDICES

Subject No.: 3301 - 3320

Department of Obstetrics and Gynaecology, Jersey General Hospital, Gloucester Street, St Helier, Jersey, JE1 3QS, Phone: 01534 622 660

Study-Code: OVCT-001 IVF treatment, age > 35 yrs
Subject-No.: 00

EudraCT-No.: 2008-005858-20

100 tablets for oral use

Directions for use: 1 tablet, 3 times daily; 15 min before or after meals; at 9 am, 12 noon and 9 pm

Medication Labels for OVCT-001 – Patient Package

Subject No.: 1101 - 1120

Department of Obstetrics and Gynaecology, Jersey General Hospital, Gloucester Street, St Helier, Jersey, JE1 3QS, Phone: 01534 622 660

Study-Code: OVCT-001 Clomid treatment, age < 30 yrs
Subject-No.: 00

EudraCT-No.: 2008-005858-20

12 x 100 tablets for oral use

Directions for use: 1 tablet, 3 times daily; 15 min before

Subject No.: 1201 - 1220

Department of Obstetrics and Gynaecology, Jersey General Hospital, Gloucester Street, St Helier, Jersey, JE1 3QS, Phone: 01534 622 660

Study-Code: OVCT-001 Clomid treatment, age 30 -35 yrs
Subject-No.: 00

EudraCT-No.:2008-005858-20

12 x 100 tablets for oral use

Directions for use: 1 tablet, 3 times daily; 15 min before

Subject No.: 1301 - 1320

Department of Obstetrics and Gynaecology, Jersey General Hospital, Gloucester Street, St Helier, Jersey, JE1 3QS, Phone: 01534 622 660

Study-Code: OVCT-001 Clomid treatment, age > 35 yrs
Subject-No.: 00

EudraCT-No.:2008-005858-20

12 x 100 tablets for oral use

Directions for use: 1 tablet, 3 times daily; 15 min before or after meals; at 9 am, 12 noon and 9 pm

Subject No.: 2101 - 2120

Department of Obstetrics and Gynaecology, Jersey General Hospital, Gloucester Street, St Helier, Jersey, JE1 3QS, Phone: 01534 622 660

Study-Code: OVCT-001 FSH treatment, age < 30 yrs
Subject-No.: 00

EudraCT-No.: 2008-005858-20

12 x 100 tablets for oral use

Directions for use: 1 tablet, 3 times daily; 15 min before or after meals; at 9 am, 12 noon and 9 pm

Subject No.: 2201 - 2220

Department of Obstetrics and Gynaecology, Jersey General Hospital, Gloucester Street, St Helier, Jersey, JE1 3QS, Phone: 01534 622 660

Study-Code: OVCT-001 FSH treatment, age 30 -35 yrs
Subject-No.: 00

EudraCT-No.: 2008-005858-20

12 x 100 tablets for oral use

Directions for use: 1 tablet, 3 times daily; 15 min before

Subject No.: 2301 - 2320

Department of Obstetrics and Gynaecology, Jersey General Hospital, Gloucester Street, St Helier, Jersey, JE1 3QS, Phone: 01534 622 660

Study-Code: OVCT-001 FSH treatment, age > 35 yrs
Subject-No.: 00

EudraCT-No.: 2008-005858-20

12 x 100 tablets for oral use

Directions for use: 1 tablet, 3 times daily; 15 min before or after meals; at 9 am, 12 noon and 9 pm

Subject No.: 3101 - 3120

Department of Obstetrics and Gynaecology, Jersey General Hospital, Gloucester Street, St Helier, Jersey, JE1 3QS, Phone: 01534 622 660

Study-Code: OVCT-001 IVF treatment, age < 30 yrs
Subject-No.: 00

EudraCT-No.: 2008-005858-20

12 x 100 tablets for oral use

Directions for use: 1 tablet, 3 times daily; 15 min before or after meals; at 9 am, 12 noon and 9 pm

Subject No.: 3201 - 3220

Department of Obstetrics and Gynaecology, Jersey General Hospital, Gloucester Street, St Helier, Jersey, JE1 3QS, Phone: 01534 622 660

Study-Code: OVCT-001 IVF treatment, age 30 -35 yrs
Subject-No.: 00

EudraCT-No.: 2008-005858-20

12 x 100 tablets for oral use

Directions for use: 1 tablet, 3 times daily; 15 min before or after meals; at 9 am, 12 noon and 9 pm

Subject No.: 3301 - 3320

Department of Obstetrics and Gynaecology, Jersey General Hospital, Gloucester Street, St Helier, Jersey, JE1 3QS, Phone: 01534 622 660

Study-Code: OVCT-001 IVF treatment, age > 35 yrs
Subject-No.: 00

EudraCT-No.: 2008-005858-20

12 x 100 tablets for oral use

Directions for use: 1 tablet, 3 times daily; 15 min before or after meals; at 9 am, 12 noon and 9 pm

Labeling For Trial Medication

Department of Obstetrics and Gynaecology, Jersey General Hospital, Gloucester Street, St Helier, Jersey, JE1 3QS
Phone: 01534 622 660

Study-Code: Subject-No.: 00

EudraCT-No.:?

100 tablets for oral use

Directions for use: 3 times daily; 15 min before or after meals; at 9 am, 12 noon and 9 pm

Template for Labels with The Randomisation Codes for OVCT-001

OVCT-001 Subject Randomisation 3301	OVCT-001 Subject Randomisation 3301	OVCT-001 Subject Randomisation 3301
OVCT-001 Subject Randomisation 3301	OVCT-001 Subject Randomisation 3301	OVCT-001 Subject Randomisation 3301
OVCT-001 Subject Randomisation 3301	OVCT-001 Subject Randomisation 3301	OVCT-001 Subject Randomisation 3301
OVCT-001 Subject Randomisation 3301	OVCT-001 Subject Randomisation 3301	OVCT-001 Subject Randomisation 3301
OVCT-001 Subject Randomisation 3301	OVCT-001 Subject Randomisation 3301	OVCT-001 Subject Randomisation 3301

OVCT-001 Subject 3301	**Randomisation**	
OVCT-001 Subject 3301	**Randomisation**	
OVCT-001 Subject 3301	**Randomisation**	
OVCT-001 Subject 3301	**Randomisation**	
OVCT-001 Subject 3301	**Randomisation**	
OVCT-001 Subject 3301	**Randomisation**	

Figure 20 Randomisation Codes for Pilot Study

The Randomisation Codes As Generated By Heel And For Use On Site.

Randomisation Lists for Trial OVCT-001

Clomid age < 30		**Clomid age 30-35**		**Clomid age >35**	
Medication number	Patient number	**Medication number**	Patient number	**Medication number**	Patient number
1101		**1201**		**1301**	
1102		**1202**		**1302**	
1103		**1203**		**1303**	
1104		**1204**		**1304**	
1105		**1205**		**1305**	
1106		**1206**		**1306**	
1107		**1207**		**1307**	
1108		**1208**		**1308**	
1109		**1209**		**1309**	
1110		**1210**		**1310**	
1111		**1211**		**1311**	

1112		**1212**		**1312**	
1113		**1213**		**1313**	
1114		**1214**		**1314**	
1115		**1215**		**1315**	
1116		**1216**		**1316**	
1117		**1217**		**1317**	
1118		**1218**		**1318**	
1119		**1219**		**1319**	
1120		**1220**		**1320**	

FSH age < 30		**FSH age 30-35**		**FSH age >35**	
Medication number	Patient number	**Medication number**	Patient number	**Medication number**	Patient number
2101		**2201**		**2301**	
2102		**2202**		**2302**	
2103		**2203**		**2303**	
2104		**2204**		**2304**	

2105		2205		2305	
2106		2206		2306	
2107		2207		2307	
2108		2208		2308	
2109		2209		2309	
2110		2210		2310	
2111		2211		2311	
2112		2212		2312	
2113		2213		2313	
2114		2214		2314	
2115		2215		2315	
2116		2216		2316	
2117		2217		2317	
2118		2218		2318	
2119		2219		2319	
2120		2220		2320	

IVF age < 30		IVF age 30-35		IVF age >35	
Medication number	Patient number	**Medication number**	Patient number	**Medication number**	Patient number
3101		**3201**		**3301**	
3102		**3202**		**3302**	
3103		**3203**		**3303**	
3104		**3204**		**3304**	
3105		**3205**		**3305**	
3106		**3206**		**3306**	
3107		**3207**		**3307**	
3108		**3208**		**3308**	
3109		**3209**		**3309**	
3110		**3210**		**3310**	
3111		**3211**		**3311**	
3112		**3212**		**3312**	
3113		**3213**		**3313**	
3114		**3214**		**3314**	
3115		**3215**		**3315**	

3116		**3216**		**3316**	
3117		**3217**		**3317**	
3118		**3218**		**3318**	
3119		**3219**		**3319**	
3120		**3220**		**3320**	

APPENDIX 6 The Study Drug

Homeopathic Indications for the Individual Constituents of Ovarium Compositum

Ovarium suis (ovary)

The Biotherpeutic Index (Heel, 1986) entry for Ovarium Compositum includes Ovarium suis with the following symptoms: *Disturbances of the ovarian function e.g. dysmenorrhoea, metrorrhagia, climacteric disorders.*

These indications are also found in the homeopathic literature (Heel): 'Disturbances of the ovarian function, dysmenorrhoea, amenorrhoea, climacteric with manifestations of ovarian endocrine deficiency; hypermenorrhhoea, metrorrhagia, female sterility, climacteric neurosis with depression, nymphomania, delusional ideas of jealousy, kraurosis vulvae, mastodynia, and osteomalacia'.

Placenta Suis (entire placenta)

The Biotherapeutic Index (Heel, 1986) entry for Ovarium Compositum includes Placenta Suis with the following symptoms: Dysmenorrhoea, peripheral circulatory disturbances. The attenuations of this sarcode are prepared using the whole placenta from the uterus of a healthy female pig (sus scrofa domesticus) with young.(Reckeweg, 2002). Indications for use: Peripheral circulatory disorders, cutis marmorata, decubiutus, pernios, Buerger's disease, ulcus cruris, rhagades, eczema, infolding of skin, sclerodermia, dysbasia intermittens, dysmenorrhoea, sural spasms, muscular rheumatism (Heel).

A proving of this substance was conducted in the fall of 1994 by Dr David Riley (Reckeweg, 2002). Congruent Symptoms with Dr Reckeweg: disorders of the peripheral circulation, prostration, rheumatism, and cramps of the calf muscles.

Uterus Suis (uterus)

The Biotherapeutic Index entry for Ovarium Compositum includes Uterus Suis with the following symptoms: *Dysmenorrhoea.*

The attenuations of this sarcode are prepared from the womb removed from healthy pigs (Sus scrofa domesticus) (Reckeweg, 2002). The main indications are: Uterine prolapsed, uterine fibroids, Dysmenorrhoea, Pre-cancerous state of the uterus, cervical erosion. Female sterility. Other degenerative diseases of the uterus

Salpinx Uteri Suis (Fallopian Tube)

The Biotherapeutic Index entry (Heel, 1986) for Ovarium Compositum includes Salpinx Suis with the following symptoms: *Dysmenorrhoea, sterility through inflammatory diseases of the salpinx uteri.*

The attenuations of this sarcode are prepared from the Fallopian tube removed from healthy pigs (Sus scrofa domesticus). The main indications are:

Female sterility resulting from inflammatory disease of the fallopian tube, (consequences of gonorrhoea, etc.), disorders of ovulation, dysmenorrhea, menopausal problems (Reckeweg, 2002).

Cypripedium Pubescens – (Lady's Slipper)

The Biotherapeutic Index entry (Heel, 1986) for Ovarium Compositum includes Cypripedium with the following symptoms: *Conditions of nervous irritability, insomnia with restlessness and twitching of the body.*

The mother tincture is prepared from the fresh rootstock, gathered in autumn, of the plant Cypripedium calceolus, var. Pubescens (Wild.) Corell., a native of North America. N.O. Orchidaceae. The main indications for the homeopathic dilution are: abuse of coffee, states of nervous irritation. Its listing as an ingredient of Ovarium Compositum states: conditions of nervous irritation, insomnia with restlessness and twitching of the body (Heel, 1986). Cypripedium is said to be particularly effective in nervous women, whose nerves are affected by illness or by abuse of tea or coffee. (Impregnation phases according to the Disease Evolution Table (Heel, 2012). However it is

also recommended in consequences of mental over-exertion, night watching and exhaustion of the nervous system in influenza.

The German Monograph-Preparation Commission for the Homeopathic Field of Therapy has, under the Preparation Monograph for Cypripedium calceolus var. Pubescens, published the following indication in the German Bundesanzeiger (German Federal Gazette): Insomnia

Clarke (Clarke)has the following information: Cypripedium has great repute as a ‘nervine’ among eclectics, and in domestic practice. For the female sphere it is indicated for Amenorrhoea, with hysterics, Great nervous debility and despondency, Irritability of vagina; hysterical symptoms, sleeplessness and agitation.

Lilium tigrinum (Tiger Lily)

The Biotherapeutic Index entry (Heel, 1986) for Ovarium Compositum includes Lilium tigrinum with the following symptoms: Uterus descensus, dysmenorrhoea, and nervous cardiac disturbances with anxiety, fluor albus.
The mother tincture is prepared from the fresh aerial parts in flower of Lilium lancifolium Thunb, a native of China and Japan and often cultivated for decorative purposes. N.O. Liliaceae.

The main indications (Reckeweg, 2002) are: palpitations, squeezed sensation (similar to cactus), leucorrhoea. Dysmenorrhea, uterine prolapsed, left sided ophoritis, bearing down sensation, burning and heat in the palms of the hands and soles of the feet, pulsations throughout the body.

The German Monograph-Preparation Commission for the Homeopathic Field of Therapy has, under the Preparation Monograph for Lilium lancifolium, published the following indications in the German Federal Gazette) for lilium tigrinum: complaints associated with prolapsed of the uterus during menopause; inflammations and painful conditions of the female reproductive

organs; nervous cardio circulatory complaints; irritable emotional discord or upset.

Pulsatilla – Wind Flower/Meadow Anemone

The Biotherapeutic Index entry (Heel, 1986) for Ovarium Compositum includes Pulsatilla with the following symptoms: migrating Disorders (worse before menses), delayed menses, dysmenorrhoea, remedy for affections of the mucosa, venous stasis.

The Mother Tincture is prepared from the whole fresh plant, gathered while in flower, of Pulsatilla pratensis Miller, which occurs in the mountains of Europe and Russia. N.O. Ranunculaceae.(Reckeweg, 2002). The tincture contains protoanemonin (an antibiotic substance), tannin, resin and saponin, and shows typical therapeutic indications, which cover both psychic and somatic symptoms.
Hans-Heinrich Reckeweg lists the following typical symptoms and indications: aggravation in a warm room and in hot weather, amelioration in fresh air and walking about gently.

Pulsatilla is usually indicated for female patients who are full of complaints. Inflammations and disorders of the female reproductive organs, vaginitis accompanied by purulent discharge. Disorders experienced during pregnancy and nursing; consequences of suppressed gonorrhoea, or of suppressed leucorrhoea with orchitis or oophoritis; concomitant catarrh of the bladder, cystitis.

Aquilegia vulgaris (columbine)

The Biotherapeutic Index entry (Heel, 1986) for Ovarium Compositum includes Aquilegia with the following symptoms: *Disturbances of the menses, climacteric disorders.*
The mother tincture is prepared from the whole fresh plant in bloom. Aquilegia vulgaris L. N.O. Ranunculaceae.(Reckeweg, 2002) Menstrual disturbances, functional amenorrhoea, menopausal problems, depression during the menses.

Sepia (cuttlefish)

The Biotherapeutic Index entry (Heel, 1986)for Ovarium Compositum includes Sepia with the following symptoms: Climacteric disorders, nervous exhaustion, depression, chronic inflammation of the uterus and adnexa.

The attenuations are prepared from the dried secretion of the ink gland of the cuttlefish, Sepia officinalis L., which inhabits the Mediterranean, the North Sea and the Atlantic Ocean. N.O.Sepiidae. (Reckeweg, 2002)

Menopausal complaints with hot flushes, emotional depression and irritability (alternating). Tearfulness, hypersensitivity and indifference (to business and family), general weakness, every movement causing outbreaks of sweating, feeling of faintness, yellowish-green leucorrhoea, offensive and excoriating in cervical erosion, menses mostly late and scanty, menopause.

Lachesis (bushmaster)

The Biotherapeutic Index entry (Heel, 1986) for Ovarium Compositum includes Lachesis with the following symptoms: *Climacteric disorders (hot flushes) dysmenorrhoea.*

The attenuations are prepared from the careful dried venom of the snake, Lachesis mutus L., which occurs in Central and South America. N.O. Crotalidae.(Reckeweg, 2002) The homoeopath Dr. Constantine Hering investigated venom of Lachesis muta in 1892 in South America combining the known toxicology with a homeopathic proving. It is used by homoeopaths as an ovarian remedy indicated for endometritis worse on the left side, menopause, ovarian dysfunction and especially hot flushes.

Apisnum (bee venom)

The Biotherapeutic Index entry (Heel, 1986)for Ovarium Compositum includes Apisnum with the following symptoms: *Oedema, Ovarian cysts, dysmenorrhoea, ovarialgia, and metrorrhagia.* The mother tincture is

prepared from the whole honey bee, Apis mellifica L. N.O. Apidae (Reckeweg, 2002).

Apis is indicated for right-sided adnexitis and other kinds of right-sided inflammatory illnesses, inflammations and disorders with collection of fluid in tissues and cavities of the body.

Kreosotum (beech tar creosote)

The Biotherapeutic Index entry (Heel, 1986) for Ovarium Compositum includes Kreosotum with the following symptoms: Catarrh of the mucosa with acrid secretions, pruritus vulvae, menorrhagia, metrorrhagia, hyperemesis.

The attenuations are prepared from Creosote, a mixture of Guaiacol, Cresol and Cresolene obtained by distillation of beech wood tar(Reckeweg, 2002). Creosote was formerly used allopathically as an anti-tubercular, antiseptic and styptic and especially in dyspepsia. In dentistry creosote was used to serve as an additive to arsenic paste for the devitalisation of dental pulp. Homoeopaths employ the homeopathic dilution of Kreosotum to treat widely varying mucosal conditions with offensive, acrid, excoriating discharges, carcinoma of the uterus, general haemorrhagic tendency and inflammations of the urinary and reproductive organs.

Bovista (Warted Puff-ball)

The Biotherapeutic Index entry (Heel, 1986) for Ovarium Compositum includes Bovista with the following symptoms: *Menorrhagia, dysmenorrhoea, venous haemorrhages*.

The attenuations are prepared from the dried ripe fungus Calvatia gigantean without its peridia, which grows in Central Europe in pastures and dry meadows everywhere. N.O. Lycoperdaceae (Reckeweg, 2002). It is employed homeopathically to treat Menorrhagia, menses come too early, uterine bleeding.

Ipecacuanha

The Biotherapeutic Index entry (Heel, 1986) for Ovarium Compositum includes Ipecacuanha with the following symptoms: *Uterine haemorrhages, hyperemesis.*

The mother tincture is prepared from the dried underground parts of Cephaelis ipecacuanha (Brot.) A. Rich., a plant growing in Brazil, India and Malaysia. N.O. Rubiaceae (Reckeweg, 2002). It is used to treat bright red gushing haemorrhages, menorrhagia and metrorrhagia.

Mercurius solubilis Hahnemanni (mixture containing essentially mercuroamidonitrate)

The Biotherapeutic Index entry (Heel, 1986) for Ovarium Compositum includes Mercurius with the following symptoms: *suppurations, acute and chronic affections of the connective tissue.*

The attenuations are prepared from mixture consisting essentially of mercury (II)-amidonitrate and metallic mercury (Reckeweg, 2002)it is used for the following indications: mucosal inflammations of the respiratory passages, the gastrointestinal tract, and the urinary and reproductive organs; skin diseases; inflammations of the tonsils, lymph glands, liver, and kidneys; inflammations of other glandular organs.

Hydrastis Canadensis (golden seal)

The Biotherapeutic Index entry (Heel, 1986) for Ovarium Compositum includes Hydrastis with the following symptoms: remedy for affectations of the mucosa; thick, ropy, yellowish-white secretions, menorrhagia, viscid, metrorrhagia, myomatous haemorrhages.

The mother tincture is prepared from the dried rootstock, with roots attached, of the plant, Hydrastis Canadensis L., which occurs in shady mountain forests of Atlantic North America. N.O. Ranunculaceae. (Reckeweg, 2002). The preparation contains three alkaloids: hydrastine, berberine and meconin, apart from phytosterin, volatile oil and resins. It is used by homoeopaths in diseases of the uterus with vaginal discharge.

Acidum cis-aconiticum (aconitic acid)

The Biotherapeutic Index entry (Heel, 1986) for Ovarium Compositum includes Acidum cis –acniticum with the following symptoms: *active factor of the citric acid cycle and of redox systems.*

The attenuations are prepared from cis-aconitic acid, $COOHCHC(COOH)CH_2COOH$. M.W: 174.2(Reckeweg, 2002) As with all catalysts of the citric acid cycle, aconitic acid too shows and affinity for internal respiration. The drug picture of cis-Aconiticum Acidum was composed in September 1996 by David Riley, M.D., Santa Fe (New Mexico), USA and includes: Pain at menses improving, sensation as if menses would come on.

Magnesium phosphoricum (magnesium phosphate)

The Biotheraeutic Index entry (Heel, 1986) for Ovarium Compositum includes Magnesium phosphoricum with the following symptoms: *dysmenorrhoea, tendency to cramps and neuralgia.*

The attenuations are prepared from Magnesium hydrogen phosphate trihydrate. $M_gHPO_4.3H_2O$, MW: 174.3 (Reckeweg, 2002). The trituration and liquid potencies prepared from magnesium phosphate are according to Heinigke, ‘one of our most important pain remedies.’

Magnesium phosphoricum is also an important remedy in dysmenorrhoea and when the menses arrive too early, especially when there is swelling and sensitivity of the vagina and so called ovarian neuralgia.

APPENDICES

APPENDIX 7 Qualitative Data

Table 44 Coded data segments from direct forum participants who responded to my posting

CODED DATA FROM DIRECT RESPONDENTS FROM THE FORUM FOR MANUAL SORTING INTO THEMES

Doc	Code	Segment
TH	Identity as a treatment seeker or employee\proximity of clinic to work	P I had a good number of blood tests over the next few months. I was a nursery manager and at that point I worked in a nursery on a hospital site so didn't really need to say much as it was easy to fit in
TH	Identity as a treatment seeker or employee\gender of boss	She was fine about it, chatty, agreed the time I needed
TH	Identity as a treatment seeker or employee\flexibility	Any hospital appointments that followed I emailed her about to let her know, and she was happy for me to attend.
TH	Identity as a treatment seeker or	I was honest about my appointments, if they were in the middle of the day I took holiday so as not to be a complete pain, if they were early or late I worked

Doc	Code	Segment
	employee\flexibility	around them.
TH	Identity as a treatment seeker or employee\flexibility	He said he appreciated my being open and that I could just let the manager know when my appointments were, that was fine.
TH	Identity as a treatment seeker or employee\flexibility	The manager and director happily accommodated my appointments
TH	Identity as a treatment seeker or employee\Using annual leave for treatment time	They let me book the Monday as annual leave for the IUI, and then we waited.
TH	Identity as a treatment seeker or employee	(and even though that day he was telling us about how the business was developing and how our roles could grow and change within it) he made it very clear that even though it put a spanner in the works from a professional point of view, on a personal level he was really pleased.

Doc	Code	Segment
TC	Identity as a treatment seeker or employee\company has clear policy on IVF	We have it written in our t&c that females having Ivf are allowed an extra 5 days leave in a rolling 12 mths, so if you had 1 cycle every year you can claim the extra 5 days leave, men and civil partners are allowed 2 days in a rolling 12 mths.
TC	Identity as a treatment seeker or employee\Using annual leave for treatment time	I have requested my 5 days together as I am going abroad and have taken a weeks leave before and a weeks leave after.
SW	Identity as a treatment seeker or employee\flexibility	Yes, I got the job on merit, I had no problems whatsoever with having time off; working for a large organisation, with a terrific foundation on offering staff a good work / life balance – I was allowed time off for egg collection and embryo transfer…
SW	Identity as a treatment seeker or employee\company has clear policy on IVF	– I was allowed time off for egg collection and embryo transfer…
SW	Identity as a	I was able to take a combination of flexi and holiday

Doc	Code	Segment
	treatment seeker or employee\Using annual leave for treatment time	as I felt necessary.
SOC	Identity as a treatment seeker or employee\gender of boss	luckily it was a female manager who dealt with it
ND	Identity as a treatment seeker or employee\proximity of clinic to work	As we chose a clinic some distance from our home, this led to quite a lot of time off
RBI	Identity as a treatment seeker or employee\proximity of clinic to work	Luckily my clinic was only 20 minutes from the office and my scans and blood tests were always first thing
RBI	Identity as a treatment seeker or employee\Using	have now been to Cyprus twice without anyone at work having any idea of the reasons behind our trip – just a last minute holiday.

Doc	Code	Segment
	annual leave for treatment time	
AJ	Identity as a treatment seeker or employee	When i 1st started my journey I was an assistant manager in a well know retail store. My store manager and area manager, at first, were quite sympathetic. This soon changed when i needed to go for daily bloods and scans. I was made aware that this was very inconvenient to the business and sometimes I was made to still let the cleaners in the store at 7 am and wait until another manager arrived to relieve me from my duties.
AJ	Identity as a treatment seeker or employee\proximity of clinic to work	This made me feel anxious as I had to then travel 8 miles to the hospital, get parked up and be there before 9. Whilst in the waiting area I was constantly aware of the time as they needed me back asap. Sometimes 2 hours would pass waiting from bloods and then onto scans, depending on how many patients were in that day. O
AJ	Identity as a treatment seeker or employee	I was very upset in front of the nurses as I knew that it would be frowned upon as saturdays are our busiest day and my area manager was visiting too.
AJ	Identity as a treatment seeker or	She was very annoyed and her words were "Andrea. I am very sympathetic regarding your needs but I have a

Doc	Code	Segment
	employee	business to run and your wanting to leave on a Saturday afternoon?!
AJ	Identity as a treatment seeker or employee	attitude changed towards my treatment but then from then on i thought, stuff it, they don't care about me, Im just a number and instead of having the odd day off after embyo transfer etc, i had more time off to suit my needs and not of that of the business!

Doc	Code	Retrieved Segment
TH	Emotional distress	and to be honest I was not much fun, sometimes I'd come back to work on a high because I'd had good news, sometimes in pieces because it was not the news I'd hoped for.
TH	Emotional distress	I was absolutely broken to find out that there was only one follicle that had grown large enough and on that basis we needed to cancel my cycle. The centre suggested to give that follicle a chance and not waste the whole cycle, we could convert it to IUI. We decided to do that, and I went back to work in pieces
TH	Emotional distress\b	They offered to send me home but I stayed and finished

Doc	Code	Retrieved Segment
	eing worthy	the day
SOC	Emotional distress	I had to take a day off one day because I was so upset after a terrible appointment with a gynaecologist and having to explain why was awful,
SOC	Emotional distress\financial loss	so I have that stress plus the stress of not getting paid for any time off I take for appointments.
SOC	Emotional distress\financial loss	proof to show work, that's also about 4 hours of wages a month I am missing out on, which doesn't sound like much but really it's the principle and I don't exactly get paid very much anyway
AJ	Emotional distress	I have been trying assisted conception now for four years. 3 failed iuis, 7 ivf with 2 pregnancies which sadly ended in miscarraige. my words that could only describe this process is its like being on an emotional roller coaster. Very stressful at times and I felt like a was the only person that understood what I was going through.
AJ	Emotional distress\feeling isolated	My partner had 2 children to a previous relation ship which made things more difficult for me to cope with, and at times i thought that he didn't even understand,as after all he had 2 children,so how could

Doc	Code	Retrieved Segment
		he?
AJ	Emotional distress\counselling	In time counselling helped me to see things differently
AJ	Emotional distress\being worthy	On my return i felt that guilty that i often missed my break or lunch break as i felt i and to make the time back.
AJ	Emotional distress	At this point i went on to the sales floor and cried my heart ou
AJ	Emotional distress	She did her floor walk with the store manager looked at me and ignored me.
AJ	Emotional distress	I felt hurt and anxious.
AJ	Emotional distress	Whilst typing it up i was sobbing as i felt humiliated and in disbelieve that i had to do it
AJ	Emotional distress	My 1st failed ivf attempt i was that upset that my partner rang in work for me to say that i wouldn't be in work the following day. I was hysterical during the conversation

Doc	Code	Retrieved Segment
AJ	Emotional distress\financial loss	wouldn't be in work the following day. I was hysterical during the conversation and my manager could hear me in the background but because the company policy is to ring in yourself I didn't get paid.
AJ	Emotional distress	This made me feel angry and i spoke to the store manager about it saying that i felt sick and really upset
AJ	Emotional distress\putting you first	attitude changed towards my treatment but then from then on i thought, stuff it, they don't care about me,Im just a number and instead of having the odd day off after embyo transfer etc, i had more time off to suit my needs and not of that of the business!

Doc	Code	Segment
TH	Trust and Support from Manager	She was fine about it, chatty, agreed the time I needed, and knowing my tendancy to push myself a bit hard sometimes came and did a 'welfare check' on my first day back at work.
TH	Trust and Support from Manager\empathy from boss	both the owner and the manager have two young children and understood that much as I wanted this to happen, didn't mean it ever would and did not impair my ability to do my job in the meantime.

Doc	Code	Segment
TH	Trust and Support from Manager\empathy from boss	We got the green light to go, and my manager was almost as excited as we were, possibly more because she didn't have the fear to deal with that came with it.
TH	Trust and Support from Manager\empathy from boss	My drugs were delivered to work, she signed for them and we both squeaked with excitement, like we had just signed for a baby in a box.
TH	Trust and Support from Manager\empathy from boss	we all jumped up and down about the result. Even the director
TH	Trust and Support from Manager	d I have done this with the goodwill, support, compassion and empathy of my employer.
SW	Trust and Support from Manager\empathy from boss	I have fabulous understanding bosses
SW	Trust and Support from Manager	work for a forward thinking organisation –
ND	Trust and	tive secondary school and we have an assistant

Doc	Code	Segment
	Support from Manager\empathy from boss	head who is responsible for staff welfare. When I told her about our IVF she was incredibly supportive and told me that I could take whatever time I needed and not to worry if appointments were sometimes at the last minute as that was the "nature of the beast".
RBI	Trust and Support from Manager\lack of empathy	I am a branch manager and have had to tell my MD on a couple of occasions about employees being pregnant. HER (the MD's) response has always been very negative – what it will cost the company for cover, training requirements when employees' return to work etc. She did at one point tell me she hated pregnant women! (She does have children of her own.)
RBI	Trust and Support from Manager\lack of empathy	I do not know what the response from my MD would be if I told her I was having fertility treatment.
AJ	Trust and Support from Manager\lack of empathy	This was done on a rota basis and made me feel upset as to why the store manager couldn't get the others to do it to help me out
AJ	Trust and Support from Manager\feelin	The 1st time i felt let down and resentful

Doc	Code	Segment
	g let down	
AJ	Trust and Support from Manager\empathy from boss	The nurses were very sympathetic and apperently hear about these work related stories all of the time.
AJ	Trust and Support from Manager\lack of empathy	After that she was quite horrible about my treatment
AJ	Trust and Support from Manager\lack of empathy	that rules could be bent and that she should have had more empathy.
AJ	Trust and Support from Manager\empathy from boss	but I wonder to myself if he is more empathetic as he himself has friends who have had ivf treatment so he understands how difficult it can be.

Doc	Code	Retrieved Segment
TH	Being open	but I was open with my deputy manager as he and I worked very closely together and I'm not great at hiding things.

TH	Being open	My first real discussion with my line manager (Regional Operations Manager) about this was when I recieved an appointment for a laparoscopy and dye test. My letter came just before my annual appraisal, so once we had agreed our business targets etc, we discussed on a personal level that we had been trying for a year and a half for 'number 2' at that point and that this is where I was at with investigating our infertility
TH	Being open	I explained we had been trying for a second child for some time, that at this point we didn't think it would be possible but that I was taking a drug (clomid) that impacts on your hormones and I would need a blood test at day 21. They were fine with this and I think appreciated that I could have completely kept this to myself
TH	Being open	I was honest about my appointments, if they were in the middle of the day I took holiday so as not to be a complete pain, if they were early or late I worked around them.
TH	Being open	I had spoken to the owner/ director about the fact that we were waiting to find out if we could have IVF when we had been making an off site visit to another setting, and we had a lengthy car journey because I had an opportunity to instigate this when there was a good couple of hours available. I said I was speaking to him about this because there would be periods of time that it would be time consuming and I really

Doc	Code	Retrieved Segment
TH	Being open	but I was open with my deputy manager as he and I worked very closely together and I'm not great at hiding things.
TH	Being open	My first real discussion with my line manager (Regional Operations Manager) about this was when I recieved an appointment for a laparoscopy and dye test. My letter came just before my annual appraisal, so once we had agreed our business targets etc, we discussed on a personal level that we had been trying for a year and a half for 'number 2' at that point and that this is where I was at with investigating our infertility
TH	Being open	I explained we had been trying for a second child for some time, that at this point we didn't think it would be possible but that I was taking a drug (clomid) that impacts on your hormones and I would need a blood test at day 21. They were fine with this and I think appreciated that I could have completely kept this to myself
		needed his goodwill to be able to do it without compromising my position
TH	Being open	but safe in the knowledge that I have no big secret
SW	Being open	I had a job interview in October 2009, one of the questions that I was asked was “would you consider

Doc	Code	Retrieved Segment
TH	Being open	but I was open with my deputy manager as he and I worked very closely together and I'm not great at hiding things.
TH	Being open	My first real discussion with my line manager (Regional Operations Manager) about this was when I recieved an appointment for a laparoscopy and dye test. My letter came just before my annual appraisal, so once we had agreed our business targets etc, we discussed on a personal level that we had been trying for a year and a half for 'number 2' at that point and that this is where I was at with investigating our infertility
TH	Being open	I explained we had been trying for a second child for some time, that at this point we didn't think it would be possible but that I was taking a drug (clomid) that impacts on your hormones and I would need a blood test at day 21. They were fine with this and I think appreciated that I could have completely kept this to myself
		job-share?" to which I responded that I was specifically looking at a full-time role at the time, but wouldn't rule out the possibility of being a job sharer in the future. I was asked to elaborate further! I advised the interview panel that I was hoping to undergo fertility treatment in the future, and if successful, I would like to take up a part-time role to spend as much time as possible at home.

Doc	Code	Retrieved Segment
TH	Being open	but I was open with my deputy manager as he and I worked very closely together and I'm not great at hiding things.
TH	Being open	My first real discussion with my line manager (Regional Operations Manager) about this was when I recieved an appointment for a laparoscopy and dye test. My letter came just before my annual appraisal, so once we had agreed our business targets etc, we discussed on a personal level that we had been trying for a year and a half for 'number 2' at that point and that this is where I was at with investigating our infertility
TH	Being open	I explained we had been trying for a second child for some time, that at this point we didn't think it would be possible but that I was taking a drug (clomid) that impacts on your hormones and I would need a blood test at day 21. They were fine with this and I think appreciated that I could have completely kept this to myself
SW	Being open	I wasn’t expecting to be handed the job on a plate, but I would have felt guilty if I had been offered the job, then handing my employers a schedule of treatment to arrange the time off. But by the same token, I wanted to be upfront and honest
RBI	Being open\non	When I discovered I would need IVF treatment, I made

Doc	Code	Retrieved Segment
TH	Being open	but I was open with my deputy manager as he and I worked very closely together and I'm not great at hiding things.
TH	Being open	My first real discussion with my line manager (Regional Operations Manager) about this was when I recieved an appointment for a laparoscopy and dye test. My letter came just before my annual appraisal, so once we had agreed our business targets etc, we discussed on a personal level that we had been trying for a year and a half for 'number 2' at that point and that this is where I was at with investigating our infertility
TH	Being open	I explained we had been trying for a second child for some time, that at this point we didn't think it would be possible but that I was taking a drug (clomid) that impacts on your hormones and I would need a blood test at day 21. They were fine with this and I think appreciated that I could have completely kept this to myself
	disclosure	the decision not to tell
RBI	Being open	I told one employee who would be covering for me while I attended appointments.
RBI	Being open\non	I will admit I did come up with some ridiculous ‘white lies’ to tell to other members of staff.

Doc	Code	Retrieved Segment
TH	Being open	but I was open with my deputy manager as he and I worked very closely together and I'm not great at hiding things.
TH	Being open	My first real discussion with my line manager (Regional Operations Manager) about this was when I recieved an appointment for a laparoscopy and dye test. My letter came just before my annual appraisal, so once we had agreed our business targets etc, we discussed on a personal level that we had been trying for a year and a half for 'number 2' at that point and that this is where I was at with investigating our infertility
TH	Being open	I explained we had been trying for a second child for some time, that at this point we didn't think it would be possible but that I was taking a drug (clomid) that impacts on your hormones and I would need a blood test at day 21. They were fine with this and I think appreciated that I could have completely kept this to myself
	disclosure	
RBI	Being open\non disclosure	When my IVF didn’t work and I was told I would require donor eggs I decided I didn’t want anyone in my employment to know a
AJ	Being open	When I arrived at work that morning I had a quiet word with the area manager and explained that depending

Doc	Code	Retrieved Segment
TH	Being open	but I was open with my deputy manager as he and I worked very closely together and I'm not great at hiding things.
TH	Being open	My first real discussion with my line manager (Regional Operations Manager) about this was when I recieved an appointment for a laparoscopy and dye test. My letter came just before my annual appraisal, so once we had agreed our business targets etc, we discussed on a personal level that we had been trying for a year and a half for 'number 2' at that point and that this is where I was at with investigating our infertility
TH	Being open	I explained we had been trying for a second child for some time, that at this point we didn't think it would be possible but that I was taking a drug (clomid) that impacts on your hormones and I would need a blood test at day 21. They were fine with this and I think appreciated that I could have completely kept this to myself
		on my blood results that afternoon I may need to go infer treatment.

Doc	Code	Segment

TC	The legal position\sexual discrimination	men and civil partners are allowed 2 days in a rolling 12 mths.
SW	The legal position\sexual discrimination	maybe I would have kept quiet if I was employed by a smaller company – certainly in previous jobs I was told quite candidly that they would no longer employ ladies of ‘child bearing age’
SOC	The legal position\disciplinary action at work	but I had disciplinary action as a result of being off that day
SOC	The legal position\disciplinary action at work	The worst thing is that people with children are allowed time off for 'dependant care', I know more than a few people who abuse this and take days off pretending that they can't get child care and they're not disciplined for it but when I had to take a day off because I was so distressed it went through as 'sickness' and I was given a verbal warning which stays on my file for a year.
AJ	The legal position\sexual discrimination	and hurt i rang the union who gave me some really good advise and they told me what she was doing was more of sexual discrimination rather than victimisation.

AJ	The legal position	After getting advise i sort of knew where i stood, although there are no laws in place for ivf and just pregnancy laws, the advise given made me feel better.

Doc	Code	Segment
TH	The demands of treatment	Possible but that I was taking a drug (clomid) that impacts on your hormones and I would need a blood test at day 21.
SW	The demands of treatment	as the travelling alone would be a minimum of 2 hours each time.
SOC	The demands of treatment	Now I'm going to need time off twice a month for ultrasounds and blood tests and it will be extra stressful because these appointments will be made over the phone
AJ	The demands of treatment	They said that I may need to go back that day for my treatment.
AJ	The demands of treatment	This was really frustrating as it is not an exact science and all depends on your body clock

Document	Code	Segment
TC	Confidentiality	My company have been fantastic and haven't even asked to see any evidence of treatment.
SOC	Confidentiality	I had no choice but to tell work because I work in a call centre and can't just come in and leave when I like, i have to show proof and they have to photocopy everything and time off has to be approved depending on the staffing.
SOC	Confidentiality	it took me about 5 weeks to pluck up the courage to show a manager my letter from assisted conception with my first appointment on it because I was so embarrassed, my boyfriend also works in here so that makes me feel even more embarrassed - I really wish that managers in here didn't know so much about my personal life.
AJ	Confidentiality	Whislt typing it up i was sobbing as i felt humiliated and in disbelieve that i had to do it

Document	Code	Segment

Doc	Code	Segment
TH	The demands of treatment	Possible but that I was taking a drug (clomid) that impacts on your hormones and I would need a blood test at day 21.
SW	The demands of treatment	as the travelling alone would be a minimum of 2 hours each time.
SOC	The demands of treatment	Now I'm going to need time off twice a month for ultrasounds and blood tests and it will be extra stressful because these appointments will be made over the phone
AJ	The demands of treatment	They said that I may need to go back that day for my treatment.
AJ	The demands of treatment	This was really frustrating as it is not an exact science and all depends on your body clock

Documen t	Code	Segment
RBI	career prospects	I do not know what the response from my MD would be if I told her I was having fertility treatment. It is so expensive though I cannot take the risk of letting on and then losing my

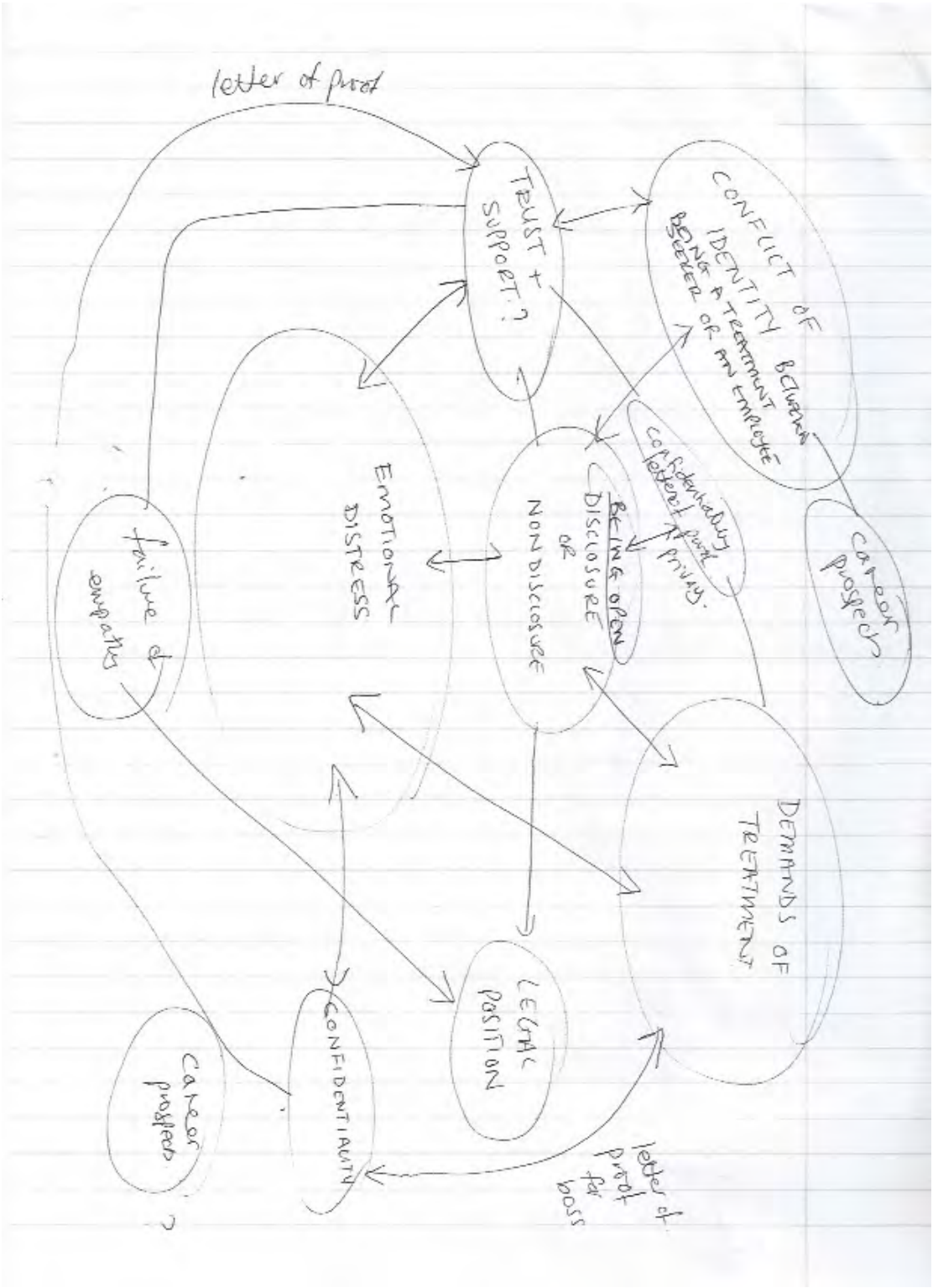
Doc	Code	Segment
TH	The demands of treatment	Possible but that I was taking a drug (clomid) that impacts on your hormones and I would need a blood test at day 21.
SW	The demands of treatment	as the travelling alone would be a minimum of 2 hours each time.
SOC	The demands of treatment	Now I'm going to need time off twice a month for ultrasounds and blood tests and it will be extra stressful because these appointments will be made over the phone
AJ	The demands of treatment	They said that I may need to go back that day for my treatment.
AJ	The demands of treatment	This was really frustrating as it is not an exact science and all depends on your body clock

Documen t	Code	Segment
		job because of it – through work life just being made generally difficult, so forced out.

APPENDICES

Figure 21 Mind map from early coding memo

MIND MAP OF INTIAL CODES AND THEMES



APPENDIX 8 – Results and Data

Results from Strand 1

Summary of results for Question Two

What would you use in your practice as a well indicated homoeopathic/ homotoxicological protocol for treating female infertility due to declining hormone levels?

A table showing the practitioner responses to question two is shown in appendix three.

Table 45 Summary of Practitioner Responses to Question Two

(A) Homotoxicology	(B) Other Measures	(C) Methodology
Mercury Removal (1)	Chinese Herbal Medicine (1)	Need to individualise the treatment (1)
Nosode Therapy (4)	Basal Temperature chart (1)	Need to identify causative agent (1)
Regulation of	Flower Essence	

Endocrine System (9)	Remedies (1)	
Detoxification (3)	Check for Ovarian Cysts (1)	Use of machine based diagnosis (4)
Organ Support (2)	Referral to another practitioner (2)	
Ovarian Stimulation (3)	Mineral and Nutritional supplementation (2)	
Miasmatic Treatment (1) **Total statements 23**	Holistic Dentistry (1) **Total statements 9**	**Total statements 6**

Question Three

What would you use in your practice as a well indicated homoeopathic/homotoxicological protocol for treating male infertility due to low sperm count?

A table showing the practitioner responses is shown in appendix five and the subsequent coding in appendix six.

Table 46 Summary of Practitioner Responses to Question Three

(A) Homotoxicology	(B) Other Measures	(C) Methodology
Detoxification (5)	Identification of environmental factors such as mobile phone radiation and toxic exposure (3)	Vega testing (1)
Miasmatic Treatment (2)	Reflexology (1)	
Mumps nosode (2)	Chinese Herbal Medicine (1)	
Testis compositum (6)	Classical homoeopathy (1) Nutrition and Diet (8)	
K2M (2) Thalamus compositum (1)	Other lifestyle choices (1)	

Therefore suis organ therapy = 10 Total number of statements 18	Total number of statements = 15	Total number of statements = 1

Question Four

Are there any other lifestyle choices or changes that you would recommend to a patient seeking advice regarding infertility?

The practitioner responses are shown in appendix 7 and the coded data in appendix 8.

Table 47 Analysis of Practitioner Responses to Question Four

Suggestions	Sub-group	Number of statements
Identify Causative agents	Allergies	1
	Hyperthyroidism	1
Subtotal		2
Environmental factors	Tested via machine based testing such as EAV	1
	Avoid 'chemicals'	3
	Exposure to pollution	1
	Exposure to EMF/microwaves	2
	Exposure to chemicals found in household products	2
	Water Quality	1
	Endocrine disruptors such as plastics	2
	Fungus and mycotoxins	1

Suggestions	**Sub-group**	**Number of statements**
Subtotal		13
Diet and Lifestyle		
Diet		6
Nutritional Supplementation		6
Avoidance of caffeine, alcohol and nicotine		7
Subtotal		19
Other holistic therapies	Reflexology	1
	Flower essences	1
Subtotal		2
Detoxification	Dental amalgam	2
	Environmental factors	1
Subtotal		3
Stress reduction	Yoga /exercise	3
	Psycho-dynamic work	7
Subtotal		10
Total number of		49

Suggestions	Sub-group	Number of statements
statements		

Results from Strand 2

Coded Data from Staff Questionnaire and Discussion Group

Table 48 Coded Data from Staff Questionnaire at The Bridge Centre

CODE USED	RETRIEVED SEGMENT OF QUOTE
Concerns about randomisation to placebo	OK just hope we can recruit enough women to get results Q5, 6 Asking women if they are willing to delay treatment with a 50% chance they will be on a placebo Q6, 6 Lack of knowledge on Doctors behalf, unwilling to believe, patients not wanting to go on a placebo, patients not wanting to delay treatment Q8, 3 Patients not wanting to try the homeopathy, patients getting angry or upset because trial hasn't worked or no benefits Q8, 4 Consent from women and compliance Q8, 6
Scepticism	I'm interested but sometimes sceptic, I like the idea of research and proof if scientific research can justify then Q3, 6 Lack of knowledge on Doctors behalf, unwilling to believe, patients not wanting to go on a placebo, patients not wanting to delay treatment Q8, 3

CODE USED	RETRIEVED SEGMENT OF QUOTE
Not enough time	Talk 30 mins to one hour, probably best to organise further talk Q4, 3 Not long enough, 5-8 minutes approx. Q4, 4 More Q4, 5 Not enough with nurses talks up to one hour Q4, 6
Request for more information or training	Need more information Q2, 3 Fine with more training re homeopathy Q5, 3 To explain the mechanism to clients Q6, 7 Knowledge, actually understanding everything I'm telling patients before I talk with them Q6, 4
Belief in benefit	African background way back, I think believing in rx will make someone to use them with a hope of success and belief = success Q1, 6 Not a quick cure but something that can help/ease illness Q2, 6 General wellbeing, find treatment less stressful, patients able to move on with life re deciding not to continue with treatment

CODE USED	RETRIEVED SEGMENT OF QUOTE
	Q9, 3 More pregnancies More relaxed patients Q9, 4-5 For certain patients with problems like overweight which success in their treatment Q9, 6 Potentially it could be of great benefit to clinic if we can sell the clinic as having an option of IVF or IVF plus homeopathy Q9, 7
No comment or no entry	None Q1, 9 No experience Q1, 5 Q1, 2 Q2, 2 blank Q3, 7 blank Q4, 7 Q4, 2

CODE USED	RETRIEVED SEGMENT OF QUOTE
	Q5, 2
Caution due to unknown interactions	Professional, patients, drugs not known so tend to stop Q1, 4
Some previous knowledge or experience	Echinacea with colds, rescue remedy with stress, gingko balboa for memory, I've never seen a homeopath but as a midwife I've cared for many women using remedies so I've gained some knowledge Q1, 8 Personal Hay fever Q1, 3
Seen as more natural	To be an alternative if applicable for conventional medicine and to be more of a natural medicine Q2, 4
Let them try	I don't know of any but if I did I would probably say try anything (safe) once if it will help you get pregnant or have another postitive effect on your health. Q3, 4 It is their choice, if it is beneficial then let them try Q3, 5
Cautious but positive	It's a very good idea but not enough to impart knowledge Q3, 3 I'm interested but sometimes sceptic, I like the idea of research and proof if scientific research can justify then fantastic Q3, 6

CODE USED	RETRIEVED SEGMENT OF QUOTE
	Not bad but I just don't know how the patients will respond to it Q5, 4
Willing to take part	Fine with more training re homeopathy Q5, 3 postive Q5, 5 Happy Q5, 7
Unwilling to take part	
Ethical issues	Ethical dilemmas – consider!!! Q8, 5

Table 49 Bridge Centre discussion group responses to questionnaire

	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9
Respondents									
1	Personal Hay fever Professional, patients, drugs not known so tend to stop	Need more information	It's a very good idea but not enough to impart knowledge	Talk 30 mins to one hour, probably best to organise further talk	Fine with more training re homeopathy	blank	Dealing with patients	Lack of knowledge on Doctors behalf, unwilling to believe, patients not wanting to go on a placebo, patients not wanting to	General wellbeing, find treatment less stressful, patients able to move on with life re deciding not to continue with treat

	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9
Respondents									
								delay treatment	ment
2	No experience	To be an alternative if applicable for conventional medicine and to be more of a natural medicine	I don't know of any but if I did I would probably say try anything (safe) once if it will help	Not long enough, 5-8 minutes approx.	Not bad but I just don't know how the patients will respond to it	Knowledge, actually understanding everything I'm telling patients before I talk with them	Seeing patients pleased with what I have explained to them and happy with their treatment. And	Patients not wanting to try the homeopathy, patients getting angry or upset because trial hasn't worked or	More pregnancies More relaxed patients

	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9
Respondents									
			you get pregnant or have another positive effect on your health.				(obviously) seeing the women get pregnant	no benefits	
3	African background way back, I think believing in rx will make	50% chance of success	It is their choice, if it is beneficial then let them	More	Positive	To take site/ decision for patients	When having positive results then "child" at	Ethical dilemmas – consider!!!	For certain patients with problems like over weigh

	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9
Respondents									
	some one to use them with a hope of success and belief = success		try				the end or completed family		t which may affect their chances of having childr en I think they will benefit from the project. Relaxes the body and mind

	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9
Respondents									
									s as well as relieves their stresses therefore promote health thus success in their treatment
4	Echinacea with colds, rescue	Not a quick cure but something	I'm interested but sometim	Not enough with nurses	OK just hope we can recrui	Asking women if they are willing	Getting feedback from wom	Consent from women and compl	Potentially it could be of great

	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9
Respondents									
	remedy with stress, gingko balboa for memory, I've never seen a homeopath but as a midwife I've cared for many women using	that can help/ ease illness	es sceptic, I like the idea of research and proof if scientific research can justify then fantastic	talks up to one hour	t enough women to get results	to delay treatment with a 50% chance they will be on a placebo	en who you have cared for and who m have got pregnant	iance	benefit to clinic if we can sell the clinic as having an option of IVF or IVF plus homeopathy

	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9
Respondents									
	remedies so I've gained some knowledge								
5	None	It is effective for Infertile women	Blank	Blank	Happy	To explain the mechanism to clients	Blank	Blank	Blank

Codes used to organise the data from the Nurse's at The Bridge Centre

CODE USED	RETRIEVED SEGMENT OF QUOTE
Concerns about randomisation to placebo	OK just hope we can recruit enough women to get results Q5, 6 Asking women if they are willing to delay treatment with a 50% chance they will be on a placebo Q6, 6 Lack of knowledge on Doctors behalf, unwilling to believe, patients not wanting to go on a placebo, patients not wanting to delay treatment Q8, 3 Patients not wanting to try the homeopathy, patients getting angry or upset because trial hasn't worked or no benefits Q8, 4 Consent from women and compliance Q8, 6
Scepticism	I'm interested but sometimes sceptic, I like the idea of research and proof if scientific research can justify then Q3, 6 Lack of knowledge on Doctors behalf, unwilling to believe, patients not wanting to go on a placebo, patients not wanting to delay treatment Q8, 3
Not enough time	Talk 30 mins to one hour, probably best to organise further talk Q4, 3 Not long enough, 5-8 minutes approx. Q4, 4 More

CODE USED	RETRIEVED SEGMENT OF QUOTE
	Q4, 5 Not enough with nurses talks up to one hour Q4, 6
Request for more information or training	Need more information Q2, 3 Fine with more training re homeopathy Q5, 3 To explain the mechanism to clients Q6, 7 Knowledge, actually understanding everything I'm telling patients before I talk with them Q6, 4
Belief in benefit	African background way back, I think believing in rx will make someone to use them with a hope of success and belief = success Q1, 6 Not a quick cure but something that can help/ease illness Q2, 6 General wellbeing, find treatment less stressful, patients able to move on with life re deciding not to continue with treatment Q9, 3 More pregnancies More relaxed patients Q9, 4-5 For certain patients with problems like overweight which success in their treatment

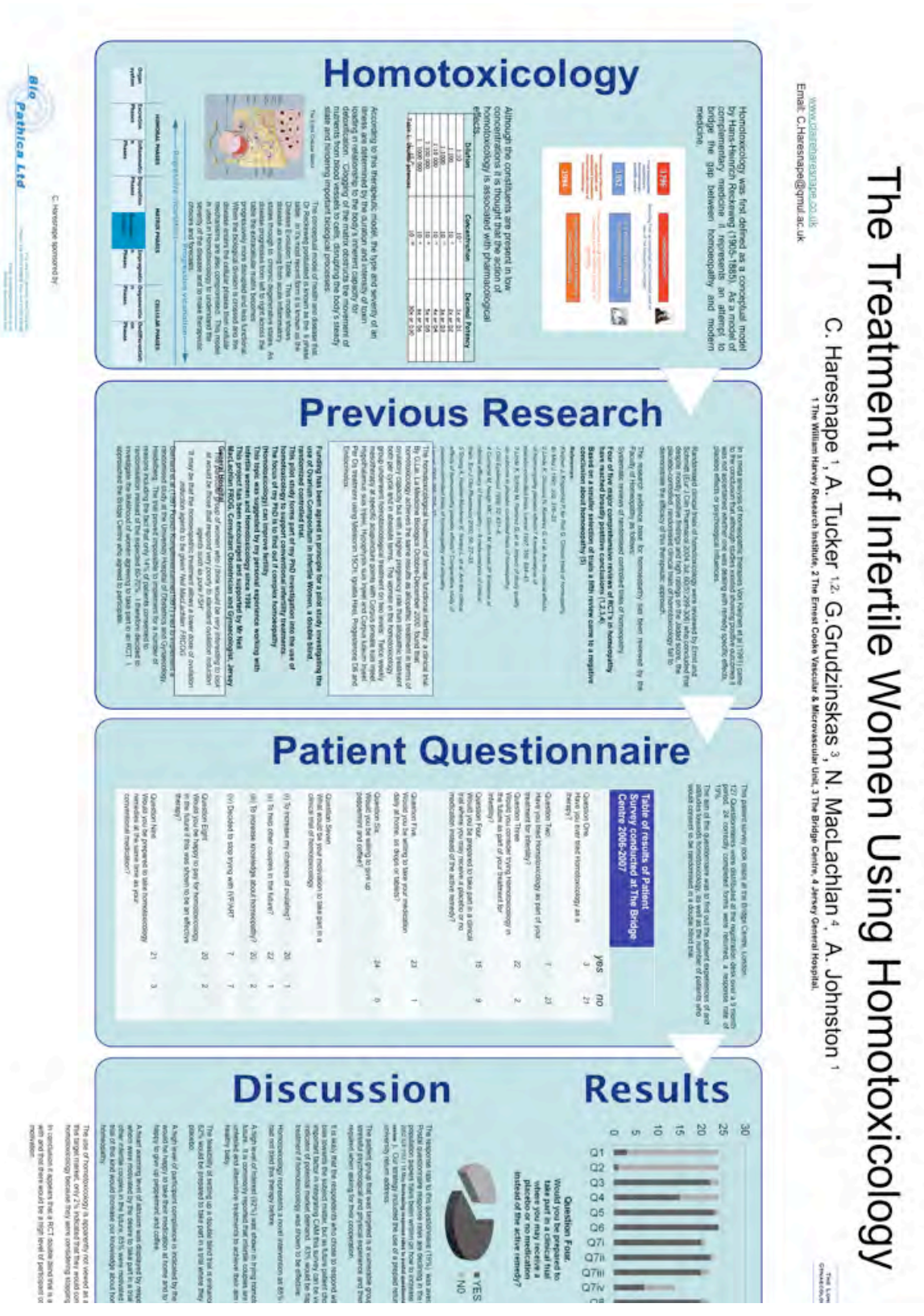
CODE USED	RETRIEVED SEGMENT OF QUOTE
	Q9, 6 Potentially it could be of great benefit to clinic if we can sell the clinic as having an option of IVF or IVF plus homeopathy Q9, 7
No comment or no entry	None Q1, 9 No experience Q1, 5 Q1, 2 Q2, 2 blank Q3, 7 blank Q4, 7 Q4, 2 Q5, 2
Caution due to unknown interactions	Professional, patients, drugs not known so tend to stop Q1, 4
Some previous knowledge or experience	Echinacea with colds, rescue remedy with stress, gingko

CODE USED	RETRIEVED SEGMENT OF QUOTE
	balboa for memory, I've never seen a homeopath but as a midwife I've cared for many women using remedies so I've gained some knowledge Q1, 8 Personal Hay fever Q1, 3
Seen as more natural	To be an alternative if applicable for conventional medicine and to be more of a natural medicine Q2, 4
Let them try	I don't know of any but if I did I would probably say try anything (safe) once if it will help you get pregnant or have another postitive effect on your health. Q3, 4 It is their choice, if it is beneficial then let them try Q3, 5
Cautious but positive	It's a very good idea but not enough to impart knowledge Q3, 3 I'm interested but sometimes sceptic, I like the idea of research and proof if scientific research can justify then fantastic Q3, 6 Not bad but I just don't know how the patients will respond to it Q5, 4

CODE USED	RETRIEVED SEGMENT OF QUOTE
Willing to take part	Fine with more training re homeopathy Q5, 3 postive Q5, 5 Happy Q5, 7
Unwilling to take part	
Ethical issues	Ethical dilemmas – consider!!! Q8, 5

Figure 22 Poster

Poster that was accepted for display at the William Harvey Day 16th October 2007



Barts and The London
Queen Mary's School of Medicine and Dentistry

William Harvey Day
Tuesday 16 October 2007

Abstract Form

Presenter:	Claire Haresnape
Institute/Organisation	William Harvey Research Institute
Contact Address	Clinical Pharmacology
Telephone	0772 006 0116
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Title: **The Treatment of Infertile Women using Homotoxicology**

Abstract: Homotoxicology is the European form of complex homoeopathy and was first defined as a model of complementary medicine by Hans-Heinrich Reckeweg (1905-1985).

In a meta analysis of homoeopathic therapies Von Kleijnen et al (1991) reached the conclusion that although studies existed showing positive outcomes it was not ascertained whether one was dealing with remedy specific effects, placebo effects or psychological influences.

Gerhard et al published a paper in 1997 (Forsch Komplementarmed 1997; 262-269) summarising their attempts to design and implement a monocentric, two armed, randomised study at the University Hospital of Obstetrics and Gynaecology, Heidelberg The trial proved impossible to implement for a number of reasons including the fact that only 14% of patients agreed to be randomised instead of the anticipated 60-70%.

It is aim of my PhD project to design and implement a double blind randomised trial of Ovarian Compositum in conjunction with infertility clinics in Jersey and London.

Before embarking on a trial it is important to make sure that sufficient numbers of women would agree to take part. I have worked with The Bridge Centre, London to design and distribute a questionnaire to their patients.

127 Questionnaires were distributed at the registration desk over a 9-month period and the return rate was 19%. Of the patients who completed and returned a questionnaire 87% had not previously tried homotoxicology as a therapy. 91% indicated that they would be willing to try homotoxicology, as part of their treatment for infertility and 62% were willing to take part in a trial where they may

APPENDIX 9 Damage To Trial Medication

Damage to Trial Medication

Upon inspection it was found that the following containers were broken open and the tablets were found in the bottom of the white boxes (some tablets were also found in the outer brown boxes):

Subject 1202: Containers 6 & 10

Subject 1320: Container 8

Subject 2116: Container 10

Subject 3216: Container 10

Subject 1305: Container 6

Subject 1316: Containers 4 & 6

Subject 1313: Container 6

Subject 1207: Container 6

Subject 2219: Container 6

Subject 2218: Container 11

The following containers had broken seals:

Subject 3215: Container 7

Subject 2205: Container 8

Subject 3216: Container 8

Subject 2304: Container 2

Subject 2220: Container 1

Subject 3308: Container 4

Subject 3209: Container 4

Subject 2113: Containers 6 & 7

Subject 3316: Container 2

Subject 2117: Container 4

Subject 1320: Container 10

Subject 1207: Containers 4 & 8

Subject 1202: Container 8

Subject 2101: Container 4

Subject 3208: Containe

Subject 1316: Container 9

Subject 1203: Containers 6 & 9

Subject 1216: Container 6

Subject 1313: Container 3 & 4

APPENDICES

APPENDIX 10 Data collected from Jersey General Hospital participants in pilot study

The Data Collected From The Jersey General Hospital For Trial OVCT-001

The quantitative data regarding clinical outcomes was collected via a specially designed case report form (CRF) and comprised of the following variables per cycle/visit:

- Age
- BMI
- Endometrial thickness (mm)
- Ovarium volume (cm^3) for left and right ovaries
- Antral follicle count for left and right ovaries
- Progesterone level on day 21 (nmol/L)
- Prescribed Treatment
- Dose of prescribed treatment
- FSH level day 3-5 (iu/L)
- Estradiol level (pmol/L)
- HCG Mediation
- HCG medication dose

- Pregnancy test

:

COUNTRY	TRIAL MEDICATION	VISIT	AGE (YRS)	BMI	ENDOMETRIA L THICKNESS (mm)	LEFT OVARIUM VOLUME (CM3)	RIGHT OVARIUM VOLUME (CM3)	LEFT ANTRAL FOLLICLE COUNT	RIGHT ANTRAL FOLLICLE COUNT	PROGESTERONE LEVEL ON DAY 21 (nmol/L)	PRESCRIBED TREATMENT	DOSE OF PRESCRIBED TREATMENT (mg)	FSH LEVEL DAY 3-5 (iu/L)	ESTRADIOL LEVEL (pmol/L)	AGE ON DAY ONE OF STIMULATION	STIMULATION DRUG	HCG MEDICATION	HCG MEDICATION DOSE	PREGNANCY TEST
		1 = SCREENING, 2 = CYCLE 1, 3 = CYCLE 2, 4 = CYCLE 3, 5 = CYCLE 4, 6 =CYCLE 5, 7 = CYCLE 6																	
JERSEY	PLACEBO	1	42	24		7.8	5.9	3	4	-	CLOMID	50	-	-	-	-	-	-	-
JERSEY	PLACEBO	2	42	24	10.6	7.8	5.9	3	4	32.8	-	-	6.5	-	42		PREGNYL	10,000	NEGATIVE
JERSEY	PLACEBO	3	42		8.2					50.6							PREGNYL	10,000	NEGATIVE
JERSEY	PLACEBO	4			11.3	9.9	5.7	8	5	46.8			5.7	151	42		PREGNYL	10,000	NEGATIVE
JERSEY	PLACEBO	5			11.5	7.6	6.9	4	4	102			5.4	180			OVITRELLE	6500	
JERSEY	PLACEBO	6			9.1	6.2	6.2	2	3								OVITRELLE	6500	NEGATIVE
JERSEY	PLACEBO	7			11.6	14	4	6	2				5.6	131			OVITRELLE	6500	NEGATIVE
JERSEY	OVARIUM COMPOSITUM	1	34	34	9.4	5.6	4	7	5	41.3	CLOMID	50	7.2						
JERSEY	OVARIUM COMPOSITUM	2	34		6.4	5.6	4	7	5	25.8			7.2		34		PREGNYL	10,000	NEGATIVE
JERSEY	OVARIUM COMPOSITUM	1	31	19		3.8	8.9	6	8	25.2	CLOMID								
JERSEY	OVARIUM COMPOSITUM	2			7.1	2.7	6.1	7	7	61	CLOMID				31		PREGNYL	5000	NEGATIVE

Figure 23 Snapshot of The Information From The Case Report Forms (CRF)

DOMAINS OF THE EHIQ SCORED SEPERATELY 1-40

VARIABLE ID		COUNTRY	CYCLE	GENERAL HEALTH	EMOTIONAL PROBLEMS	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
VARIABLE DESCRIPTION	PATIENT ID NUMBER			Excellent= 1, Very Good=2, Good=3, Fair=4, Poor =5, missing data = 9	Not at all=1, Slightly=2, Moderately=3, Quite a lot=4, Extremely=5, missing data = 9	Definitely True = 1, Mostly True = 2, Not sure = 3, Mostly Untrue=4, Definitely Untrue =5, missing data = 9	Definitely True = 1, Mostly True = 2, Not sure = 3, Mostly Untrue=4, Definitely Untrue =5missing data = 9	Definitely True = 1, Mostly True = 2, Not sure = 3, Mostly Untrue=4, Definitely Untrue =5missing data = 9	Definitely True = 1, Mostly True = 2, Not sure = 3, Mostly Untrue=4, Definitely Untrue =5missing data = 9	Definitely True = 1, Mostly True = 2, Not sure = 3, Mostly Untrue=4, Definitely Untrue =5, missing data = 9	Definitely True = 1, Mostly True = 2, Not sure = 3, Mostly Untrue=4, Definitely Untrue =5, missing data = 9	Definitely True = 1, Mostly True = 2, Not sure = 3, Mostly Untrue=4, Definitely Untrue =5, missing data = 9	Definitely True = 1, Mostly True = 2, Not sure = 3, Mostly Untrue=4, Definitely Untrue =5, missing data = 9	Definitely True = 1, Mostly True = 2, Not sure = 3, Mostly Untrue=4, Definitely Untrue =5, missing data = 9	Definitely True = 1, Mostly True = 2, Not sure = 3, Mostly Untrue=4, Definitely Untrue =5, missing data = 9	Definitely True = 1, Mostly True = 2, Not sure = 3, Mostly Untrue=4, Definitely Untrue =5, missing data = 9	Definitely True = 1, Mostly True = 2, Not sure = 3, Mostly Untrue=4, Definitely Untrue =5, missing data = 9	Definitely True = 1, Mostly True = 2, Not sure = 3, Mostly Untrue=4, Definitely Untrue =5, missing data = 9	Definitely True = 1, Mostly True = 2, Not sure = 3, Mostly Untrue=4, Definitely Untrue =5, missing data = 9	Definitely True = 1, Mostly True = 2, Not sure = 3, Mostly Untrue=4, Definitely Untrue =5, missing data = 9	Definitely True = 1, Mostly True = 2, Not sure = 3, Mostly Untrue=4, Definitely Untrue =5, missing data = 9	Definitely True = 1, Mostly True = 2, Not sure = 3, Mostly Untrue=4, Definitely Untrue =5, missing data = 9	Definitely True = 1, Mostly True = 2, Not sure = 3, Mostly Untrue=4, Definitely Untrue =5, missing data = 9	Definitely True = 1, Mostly True = 2, Not sure = 3, Mostly Untrue=4, Definitely Untrue =5, missing data = 9	Definitely True = 1, Mostly True = 2, Not sure = 3, Mostly Untrue=4, Definitely Untrue =5, missing data = 9
	1301	JERSEY	1	3	3	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
	1301	JERSEY	2	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9
	1301	JERSEY	3	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9
	1301	JERSEY	4	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9
	1301	JERSEY	5	9	9	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
	1301	JERSEY	6	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9
	1201	JERSEY	1	1	1	4	3	4	5	5	4	5	4	3	4	5	4	5	5	5	2	5	5	2	3
	1202	JERSEY	1	3	4	4	2	4	4	4	2	5	3	2	5	4	5	4	3	2	4	3	4	4	2

PATIENT ID	CYCLE	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	sum of domains
		Definitely True = 1, Mostly True = 2, Not sure = 3, Mostly Untrue=4, Definitely Untrue =5, missing data = 9	Definitely True = 1, Mostly True = 2, Not sure = 3, Mostly Untrue=4, Definitely Untrue =5, missing data = 9	Definitely True = 1, Mostly True = 2, Not sure = 3, Mostly Untrue=4, Definitely Untrue =5, missing data = 9	Definitely True = 1, Mostly True = 2, Not sure = 3, Mostly Untrue=4, Definitely Untrue =5, missing data = 9	Definitely True = 1, Mostly True = 2, Not sure = 3, Mostly Untrue=4, Definitely Untrue =5, missing data = 9	Definitely True = 1, Mostly True = 2, Not sure = 3, Mostly Untrue=4, Definitely Untrue =5, missing data = 9	Definitely True = 1, Mostly True = 2, Not sure = 3, Mostly Untrue=4, Definitely Untrue =5, missing data = 9	Definitely True = 1, Mostly True = 2, Not sure = 3, Mostly Untrue=4, Definitely Untrue =5, missing data = 9	Definitely True = 1, Mostly True = 2, Not sure = 3, Mostly Untrue=4, Definitely Untrue =5, missing data = 9	Definitely True = 1, Mostly True = 2, Not sure = 3, Mostly Untrue=4, Definitely Untrue =5, missing data = 9	Definitely True = 1, Mostly True = 2, Not sure = 3, Mostly Untrue=4, Definitely Untrue =5, missing data = 9	Definitely True = 1, Mostly True = 2, Not sure = 3, Mostly Untrue=4, Definitely Untrue =5, missing data = 9	Definitely True = 1, Mostly True = 2, Not sure = 3, Mostly Untrue=4, Definitely Untrue =5, missing data = 9	Definitely True = 1, Mostly True = 2, Not sure = 3, Mostly Untrue=4, Definitely Untrue =5, missing data = 9	Definitely True = 1, Mostly True = 2, Not sure = 3, Mostly Untrue=4, Definitely Untrue =5, missing data = 9	Definitely True = 1, Mostly True = 2, Not sure = 3, Mostly Untrue=4, Definitely Untrue =5, missing data = 9	Definitely True = 1, Mostly True = 2, Not sure = 3, Mostly Untrue=4, Definitely Untrue =5,missing data = 9	Definitely True = 1, Mostly True = 2, Not sure = 3, Mostly Untrue=4, Definitely Untrue =5, missing data = 9	Definitely True = 1, Mostly True = 2, Not sure = 3, Mostly Untrue=4, Definitely Untrue =5, missing data = 9	Definitely True = 1, Mostly True = 2, Not sure = 3, Mostly Untrue=4, Definitely Untrue =5, missing data = 9	
1301	1	5	4	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	199
1301	2	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	
1301	3	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	
1301	4	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	
1301	5	5	4	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	199
1301	6	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	
1201	1	5	5	2	5	4	3	5	5	4	3	5	2	4	2	3	1	5	5	5	5	160
1202	1	4	2	2	5	2	5	4	4	4	2	4	4	1	2	4	2	2	4	2	3	132

Figure 24 Snapshot of data from the EHIQ

The two domains that are of particular interest to this study are:

9. Trying to maintain privacy during treatment is stressful.

34. I find trying to balance fertility treatment with my other commitments stressful.

VARIABLE	ID	COUNTRY	CYCLE	GENERAL HEALTH	EMOTIONAL PROBLEMS	9	34	sum of domains
VARIABLE DESCRIPTION	PATIENT ID NUMBER			Excellent= 1, Very Good=2, Good=3, Fair=4, Poor =5, missing data = 9	Not at all=1, Slightly=2, Moderately=3, Quite a lot=4, Extremely=5, missing data = 9	Definitely True = 1, Mostly True = 2, Not sure = 3, Mostly Untrue=4, Definitely Untrue =5, missing data = 9	Definitely True = 1, Mostly True = 2, Not sure = 3, Mostly Untrue=4, Definitely Untrue =5, missing data = 9	
	1301	JERSEY	1	3	3	5	5	10
	1301	JERSEY	2	9	9	9	9	
	1301	JERSEY	3	9	9	9	9	
	1301	JERSEY	4	9	9	9	9	
	1301	JERSEY	5	9	9	5	5	10
	1301	JERSEY	6	9	9	9	9	
	1201	JERSEY	1	1	1	3	2	5
	1202	JERSEY	1	3	4	2	2	4

Figure 25 Table to show the results for domains 9 and 34 of the EHIQ

Analysis

Subject 1301 showed the highest possible score for cycles one and five showing that it was definitely untrue that they had problems with maintaining privacy and with balancing other commitments with their treatment.

Subject 1201 scored 3 for question 9 and 2 for question 34 indicating that they were not sure if they found trying to maintain privacy during treatment stressful and that it was mostly true that they found find trying to balance fertility treatment with their other commitments stressful.

Subject 1202 scored 2 for question 9 and 2 for question 34 indicating that it was mostly true that they found trying to maintain privacy during treatment stressful and that it was mostly true that they found find trying to balance fertility treatment with their other commitments stressful.

Summary

Due to the small sample size it is unclear if there is a general trend for the two questions that relate to privacy and balancing commitments. There is not enough evidence to prove or disprove the hypothesis suggested by the ARU

nurse that women were reluctant to attend appointments due to the stress caused by forced disclosure of their treatment at work.

VARIABLE N	ID	COUNTRY	CYCLE	MOBILITY	SELFCARE	ACTIVITY	PAIN	ANXIETY	STATE	EQ_VAS
VARIABLE DESCRIPTION	patient ID number	1=no problems,2 = some problems, 3=extreme problems, 9=missing value		1=no problems, 2 = some problems, 3=extreme problems, 9=missing value	1=no problems, 2 = some problems, 3=extreme problems, 9=missing value	1=no problems, 2 = some problems, 3=extreme problems, 9=missing value	1=no problems, 2 = some problems, 3=extreme problems, 9=missing value	1=no problems, 2 = some problems, 3=extreme problems, 9=missing value		999=missing value
Data Row	1301	JERSEY	1	1	1	1	1	2	11112	70
	1301	JERSEY	2	1	1	1	1	2	11112	65
	1301	JERSEY	3	1	1	1	1	1	11111	86
	1301	JERSEY	4	1	1	1	1	1	11111	79
	1301	JERSEY	5	1	1	1	1	2	11112	86
	1301	JERSEY	6	1	1	1	1	1	11111	85
	1201	JERSEY	1	1	1	1	1	1	11111	95
	1202	JERSEY	1	1	1	1	1	1	11111	78

Figure 26 Snapshot to show the results of the EQ-5D

The Results Per Subject

Subject 1201

Randomisation number	Age band (years)	Treatment Group	Trial medication group	Outcome
1201	30-35	Clomid	Ovarium compositum	Treatment stopped after 2 months

Table 50 Subject 1202

Summary of CRF for subject 1201

The differences that were observed between cycle one and cycle two were that the endometrial thickness diminished by 3mm, the progesterone level on day 21 declined by 15.5 nm/l and there was no change in follicle count or ovarian volume.

The EHIQ for subject 1201

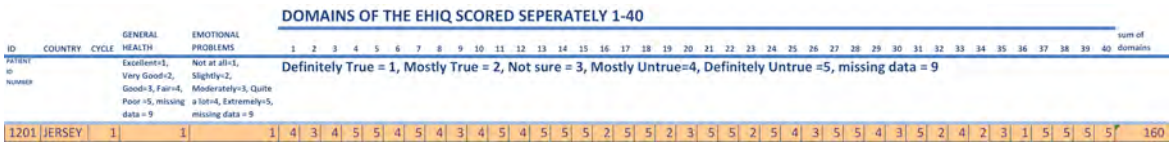


Figure 27 Snapshot of EHIQ for subject 1201

The baseline measurement for Emotional Health in Infertility was a total score of 160. They rated themselves as being in excellent health with no emotional problems at that time. No further measurements were taken for this subject.

This respondent scored 3 for question 9 and 2 for question 34 indicating that they were not sure if they found trying to maintain privacy during treatment stressful and that it was mostly true that they found find trying to balance fertility treatment with their other commitments stressful.

The EQ-5D for subject 1201

Subject 1201 rated themselves as 11111 which indicates no problems with mobility, self-care, activity, pain and anxiety. On the VAS she rated herself as 95/100 indicating that they see themselves in an almost optimal health state.

Subject 1202

1202	30-35	Clomid	Ovarium compositum	Treatment stopped after 1 months

Figure 28 Subject 1202

Summary of CRF for subject 1202

Subject 1202 shows a decrease of 1.1cm^3 in left Ovarium volume and a decrease in right Ovarium volume of 2.8 cm^3 between visit one and visit two. The follicle count increased by one follicle on both the left and the right ovaries between visit one and visit two. The progesterone level increased by 35.8 nmol/l between visit one and visit two.

VARIABLE NAME	ID	COUNTRY	TRIAL MEDICATION	VISIT	AGE (YRS)	BMI	ENDOMETRIAL THICKNESS (mm)	LEFT OVARIUM VOLUME (CM3)	RIGHT OVARIUM VOLUME (CM3)	LEFT ANTRAL FOLLICLE COUNT	RIGHT ANTRAL FOLLICLE COUNT	PROGESTERONE LEVEL ON DAY 21 (nmol/L)	DOSE OF PRESCRIBED TREATMENT	PRESCRIBED TREATMENT	AGE ON DAY ONE OF STIMULATION	ESTRADIOL LEVEL (pmol/L)	FSH LEVEL DAY 3-5 (iu/L)	STIMULATION DRUG	HCG MEDICATION	HCG MEDICATION DOSE	PREGNANCY TEST	
VARIABLE DESCRIPTION	patient ID number			1 = SCREENING, 2 = CYCLE 1, 3 = CYCLE 2, 4 = CYCLE 3, 5 = CYCLE 4, 6 =CYCLE 5, 7 = CYCLE 6																		
	1202	JERSEY	OVARIUM COMPOSITUM	1	31	19		3.8	8.9	6	8	25.2	CLOMID									
	1202	JERSEY	OVARIUM COMPOSITUM	2			7.1	2.7	6.1	7	7	61	CLOMID					31		PREGNYL	5000	NEGATIVE
OBSERVED CHANGE								1.1	2.8	1	1	35.8										

Figure 29 Snapshot of The EHIQ for subject 1202

The baseline measurement for Emotional Health in Infertility was a total score of 160. They rated themselves as being in good health with quite a lot of emotional problems at that time. No further measurements were taken for this subject.

Subject 1202 scored 2 for question 9 and 2 for question 34 indicating that it was mostly true that they found trying to maintain privacy during treatment

stressful and that it was mostly true that they found find trying to balance fertility treatment with their other commitments stressful.

The EQ-5D for subject 1202

The subject rated herself as 11111 which indicates no problems with mobility, self-care, activity, pain and anxiety. On the VAS she rated herself as 78/100 indicating that she perceived herself to be in a good health state

Subject 1301

1301	>35	Clomid	Placebo	Completed 6 months of treatment

Table 51 Subject 1301

Summary of CRF for subject 1301

There were seven visits for subject 1301 which makes it possible to represent the collected data in a graphic form:

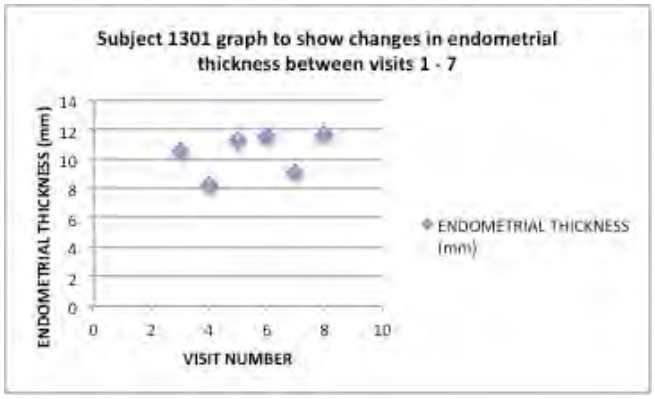


Figure 30 Graph to show the changes in endometrial thickness for subject 1301

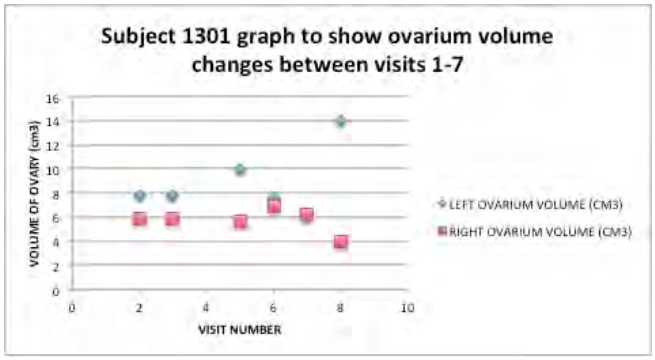


Figure 31 Graph to show the changes in ovarium volume in subject 1301

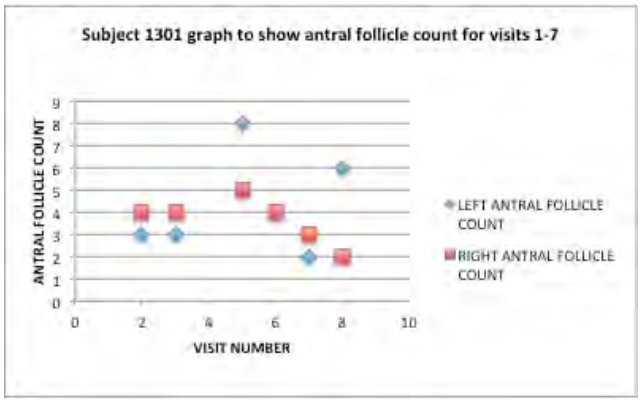


Figure 32 graph to show antral volume count for subject 1301

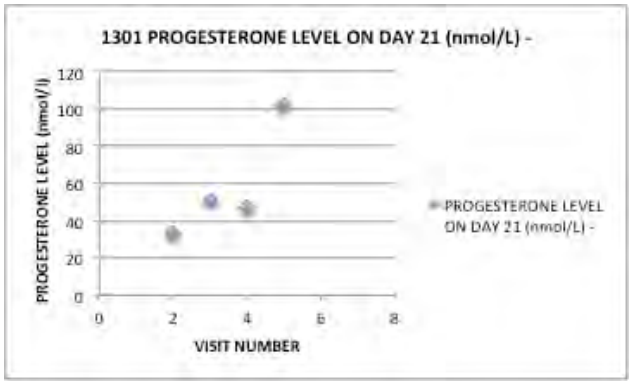


Figure 33 graph to show progesterone levels for subject 1301

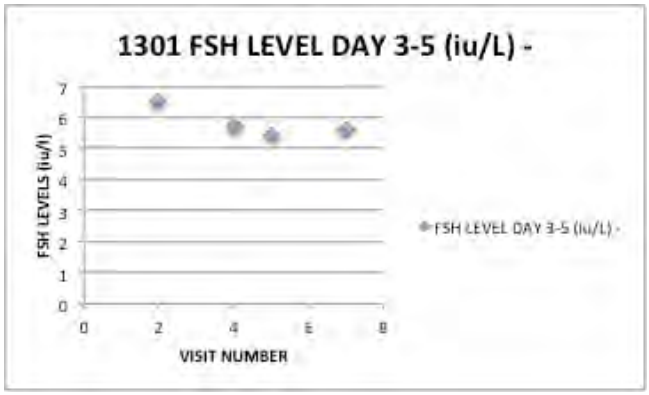


Figure 34 Graph to show FSH levels for subject 1301

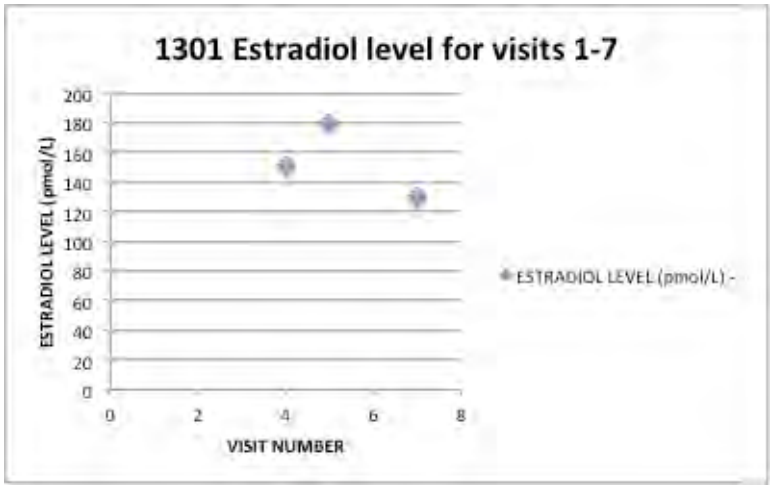


Figure 35 Graph to show Estradiol levels for subject 1301

The EHIQ for subject 1301

ID	CYCLE	GENERAL HEALTH	EMOTIONAL PROBLEMS	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	sum of domains
PATIENT ID NUMBER		Excellent=1, Very Good=2, Good=3, Fair=4, Poor =5, missing data = 9	Not at all=1, Slightly=2, Moderately =3, Quite a lot=4, Extremely= 5, missing data = 9	Definitely True = 1, Mostly True = 2, Not sure = 3, Mostly Untrue=4, Definitely Untrue =5, missing data = 9																																								
1301	1	3	3	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	4	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	199
1301	2	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	
1301	3	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	
1301	4	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	
1301	5	9	9	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	4	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	199
1301	6	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	

Figure 36 The EHIQ for subject 1301

The EQ-5D for subject 1301

VARIABLE N	ID	COUNTRY	CYCLE	MOBILITY	SELFCARE	ACTIVITY	PAIN	ANXIETY	STATE	EQ_VAS
VARIABLE DESCRIPTION	patient ID number			1=no problems, 2 = some problems, 3=extreme problems, 9=missing value	1=no problems, 2 = some problems, 3=extreme problems, 9=missing value	1=no problems, 2 = some problems, 3=extreme problems, 9=missing value	1=no problems, 2 = some problems, 3=extreme problems, 9=missing value	1=no problems, 2 = some problems, 3=extreme problems, 9=missing value		999=missing value
Data Row	1301	JERSEY	1	1	1	1	1	2	11112	70
	1301	JERSEY	2	1	1	1	1	2	11112	65
	1301	JERSEY	3	1	1	1	1	1	11111	86
	1301	JERSEY	4	1	1	1	1	1	11111	79
	1301	JERSEY	5	1	1	1	1	2	11112	86
	1301	JERSEY	6	1	1	1	1	1	11111	85

Figure 37 The EQ-5D for subject 1301

Summary

The low number of subjects recruited and the low number of appointments that they attended means that it has not been possible to perform a statistical analysis. We can see that we were able to capture both quality of life measurements and fertility outcomes with the trial design.

We are able to show changes over time for one patient and differences between each subject.

We are not able to comment on a trend or correlation as insufficient data was captured and a high degree of variation between both subjects and visits is to be expected in this clinical situation.

APPENDICES

APPENDICES

APPENDIX 11 Qualitative Data From Strand 4

Strand 4

The Work Related Concerns Of Infertile Women

Coded data from Part 1

Table 52 Table to show the quotes relating to the codes 'identity as an employee or treatment seeker' with associated sub codes

Doc	Code	Segment
TH	Identity as a treatment seeker or employee\proximity of clinic to work	P I had a good number of blood tests over the next few months. I was a nursery manager and at that point I worked in a nursery on a hospital site so didn't really need to say much as it was easy to fit in
TH	Identity as a treatment	She was fine about it, chatty, agreed the time I needed

Doc	Code	Segment
	seeker or employee\gender of boss	
TH	Identity as a treatment seeker or employee\flexibility	Any hospital appointments that followed I emailed her about to let her know, and she was happy for me to attend.
TH	Identity as a treatment seeker or employee\flexibility	I was honest about my appointments, if they were in the middle of the day I took holiday so as not to be a complete pain, if they were early or late I worked around them.
TH	Identity as a treatment seeker or employee\flexibility	He said he appreciated my being open and that I could just let the manager know when my appointments were, that was fine.
TH	Identity as a treatment seeker or employee\flexibility	The manager and director happily accommodated my appointments
TH	Identity as a	They let me book the Monday as annual leave for the

Doc	Code	Segment
	treatment seeker or employee\Using annual leave for treatment time	IUI, and then we waited.
TH	Identity as a treatment seeker or employee	(and even though that day he was telling us about how the business was developing and how our roles could grow and change within it) he made it very clear that even though it put a spanner in the works from a professional point of view, on a personal level he was really pleased.
TC	Identity as a treatment seeker or employee\company has clear policy on IVF	We have it written in our t&c that females having Ivf are allowed an extra 5 days leave in a rolling 12 mths, so if you had 1 cycle every year you can claim the extra 5 days leave, men and civil partners are allowed 2 days in a rolling 12 mths.
TC	Identity as a treatment seeker or employee\Using annual leave for treatment time	I have requested my 5 days together as I am going abroad and have taken a weeks leave before and a weeks leave after.
SW	Identity as a treatment seeker or	Yes, I got the job on merit, I had no problems whatsoever with having time off; working for a large organisation, with a terrific foundation on offering staff

Doc	Code	Segment
	employee\flexibility	a good work / life balance – I was allowed time off for egg collection and embryo transfer…
SW	Identity as a treatment seeker or employee\company has clear policy on IVF	– I was allowed time off for egg collection and embryo transfer…
SW	Identity as a treatment seeker or employee\Using annual leave for treatment time	I was able to take a combination of flexi and holiday as I felt necessary.
SOC	Identity as a treatment seeker or employee\gender of boss	luckily it was a female manager who dealt with it
ND	Identity as a treatment seeker or employee\proximity of clinic to	As we chose a clinic some distance from our home, this led to quite a lot of time off

Doc	Code	Segment
	work	
RBI	Identity as a treatment seeker or employee\proximity of clinic to work	Luckily my clinic was only 20 minutes from the office and my scans and blood tests were always first thing
RBI	Identity as a treatment seeker or employee\Using annual leave for treatment time	have now been to Cyprus twice without anyone at work having any idea of the reasons behind our trip – just a last minute holiday.
AJ	Identity as a treatment seeker or employee	When i 1st started my journey I was an assistant manager in a well know retail store. My store manager and area manager, at first, were quite sympathetic. This soon changed when i needed to go for daily bloods and scans. I was made aware that this was very inconvenient to the business and sometimes I was made to still let the cleaners in the store at 7 am and wait until another manager arrived to relieve me from my duties.
AJ	Identity as a treatment seeker or	This made me feel anxious as I had to then travel 8 miles to the hospital, get parked up and be there before 9. Whilst in the waiting area I was constantly

Doc	Code	Segment
	employee\proximity of clinic to work	aware of the time as they needed me back asap. Sometimes 2 hours would pass waiting from bloods and then onto scans, depending on how many patients were in that day. O
AJ	Identity as a treatment seeker or employee	I was very upset in front of the nurses as I knew that it would be frowned upon as saturdays are our busiest day and my area manager was visiting too.
AJ	Identity as a treatment seeker or employee	She was very annoyed and her words were "Andrea. I am very sympathetic regarding your needs but I have a business to run and your wanting to leave on a Saturday afternoon?!
AJ	Identity as a treatment seeker or employee	attitude changed towards my treatment but then from then on i thought, stuff it, they don't care about me, Im just a number and instead of having the odd day off after embyo transfer etc, i had more time off to suit my needs and not of that of the business!

2. Emotional Distress

Table 53 Table to show retrieved segments of data relating to emotional distress in the seven direct responses to forum posting

Doc	Code	Retrieved Segment
TH	Emotional distress	and to be honest I was not much fun, sometimes I'd come back to work on a high because I'd had good news, sometimes in pieces because it was not the news I'd hoped for.
TH	Emotional distress	I was absolutely broken to find out that there was only one follicle that had grown large enough and on that basis we needed to cancel my cycle. The centre suggested to give that follicle a chance and not waste the whole cycle, we could convert it to IUI. We decided to do that, and I went back to work in pieces
TH	Emotional distress\being worthy	They offered to send me home but I stayed and finished the day
SOC	Emotional distress	I had to take a day off one day because I was so upset after a terrible appointment with a gynaecologist and having to explain why was awful,
SOC	Emotional distress\fi	so I have that stress plus the stress of not getting paid for any

Doc	Code	Retrieved Segment
	nancial loss	time off I take for appointments.
SOC	Emotional distress\financial loss	proof to show work, that's also about 4 hours of wages a month I am missing out on, which doesn't sound like much but really it's the principle and I don't exactly get paid very much anyway
AJ	Emotional distress	I have been trying assisted conception now for four years. 3 failed iuis, 7 ivf with 2 pregnancies which sadly ended in miscarraige. my words that could only describe this process is its like being on an emotional roller coaster. Very stressful at times and I felt like a was the only person that understood what I was going through.
AJ	Emotional distress\feeling isolated	My partner had 2 children to a previous relation ship which made things more difficult for me to cope with, and at times i thought that he didn't even understand,as after all he had 2 children,so how could he?
AJ	Emotional distress\counselling	In time counselling helped me to see things differently
AJ	Emotional distress\being	On my return i felt that guilty that i often missed my break or lunch break as i felt i and to make the time back.

Doc	Code	Retrieved Segment
	worthy	
AJ	Emotional distress	At this point i went on to the sales floor and cried my heart ou
AJ	Emotional distress	She did her floor walk with the store manager looked at me and ignored me.
AJ	Emotional distress	I felt hurt and anxious.
AJ	Emotional distress	Whilst typing it up i was sobbing as i felt humiliated and in disbelieve that i had to do it
AJ	Emotional distress	My 1st failed ivf attempt i was that upset that my partner rang in work for me to say that i wouldn't be in work the following day. I was hysterical during the conversation
AJ	Emotional distress\financial loss	wouldn't be in work the following day. I was hysterical during the conversation and my manager could hear me in the background but because the company policy is to ring in yourself I didn't get paid.
AJ	Emotional distress	This made me feel angry and i spoke to the store manager about it saying that i felt sick and really upset
AJ	Emotional distress\putting you	attitude changed towards my treatment but then from then on i thought, stuff it, they don't care about me,Im just a number and instead of having the odd day off

Doc	Code	Retrieved Segment
	first	after embyo transfer etc, i had more time off to suit my needs and not of that of the business!

3. Trust and Support

Table 54 Table to show the retrieved code segments for Trust and Support in the seven direct responses from the forum

Doc	Code	Segment
TH	Trust and Support from Manager	She was fine about it, chatty, agreed the time I needed, and knowing my tendancy to push myself a bit hard sometimes came and did a 'welfare check' on my first day back at work.
TH	Trust and Support from Manager\empathy from boss	both the owner and the manager have two young children and understood that much as I wanted this to happen, didn't mean it ever would and did not impair my ability to do my job in the meantime.
TH	Trust and Support from Manager\empathy from boss	We got the green light to go, and my manager was almost as excited as we were, possibly more because she didn't have the fear to deal with that came with it.
TH	Trust and Support from Manager\empathy from boss	My drugs were delivered to work, she signed for them and we both squeaked with excitement, like we had just signed for a baby in a box.

Doc	Code	Segment
TH	Trust and Support from Manager\empathy from boss	we all jumped up and down about the result. Even the director
TH	Trust and Support from Manager	d I have done this with the goodwill, support, compassion and empathy of my employer.
SW	Trust and Support from Manager\empathy from boss	I have fabulous understanding bosses
SW	Trust and Support from Manager	work for a forward thinking organisation –
ND	Trust and Support from Manager\empathy from boss	tive secondary school and we have an assistant head who is responsible for staff welfare. When I told her about our IVF she was incredibly supportive and told me that I could take whatever time I needed and not to worry if appointments were sometimes at the last minute as that was the "nature of the beast".
RBI	Trust and Support from	I am a branch manager and have had to tell my MD on a couple of occasions about employees

Doc	Code	Segment
	Manager\lack of empathy	being pregnant. HER (the MD's) response has always been very negative – what it will cost the company for cover, training requirements when employees' return to work etc. She did at one point tell me she hated pregnant women! (She does have children of her own.)
RBI	Trust and Support from Manager\lack of empathy	I do not know what the response from my MD would be if I told her I was having fertility treatment.
AJ	Trust and Support from Manager\lack of empathy	This was done on a rota basis and made me feel upset as to why the store manager couldn't get the others to do it to help me out
AJ	Trust and Support from Manager\feeling let down	The 1st time i felt let down and resentful
AJ	Trust and Support from Manager\empathy from boss	The nurses were very sympathetic and apperently hear about these work related stories all of the time.
AJ	Trust and Support from Manager\lack	After that she was quite horrible about my treatment

Doc	Code	Segment
	of empathy	
AJ	Trust and Support from Manager\lack of empathy	that rules could be bent and that she should have had more empathy.
AJ	Trust and Support from Manager\empathy from boss	but I wonder to myself if he is more empathetic as he himself has friends who have had ivf treatment so he understands how difficult it can be.

Table 55 Table to show the retrieved quotes coded for 'being open' and 'non-disclosure' by the seven direct responses from the forum

Doc	Code	Retrieved Segment
TH	Being open	but I was open with my deputy manager as he and I worked very closely together and I'm not great at hiding things.
TH	Being open	My first real discussion with my line manager (Regional Operations Manager) about this was when I recieved an appointment for a laparoscopy and dye test. My letter came just before my annual appraisal, so once we had agreed our business targets etc, we discussed on a personal level that we had been trying for a year and a half for 'number 2' at that point and that this is where I was at with investigating our infertility
TH	Being open	I explained we had been trying for a second child for some time, that at this point we didn't think it would be possible but that I was taking a drug (clomid) that impacts on your hormones and I would need a blood test at day 21. They were fine with this and I think appreciated that I could have completely kept this to myself
TH	Being open	I was honest about my appointments, if they were in the middle of the day I took holiday so as not to be a complete pain, if they were early or late I worked around them.

Doc	Code	Retrieved Segment
TH	Being open	but I was open with my deputy manager as he and I worked very closely together and I'm not great at hiding things.
TH	Being open	My first real discussion with my line manager (Regional Operations Manager) about this was when I recieved an appointment for a laparoscopy and dye test. My letter came just before my annual appraisal, so once we had agreed our business targets etc, we discussed on a personal level that we had been trying for a year and a half for 'number 2' at that point and that this is where I was at with investigating our infertility
TH	Being open	I explained we had been trying for a second child for some time, that at this point we didn't think it would be possible but that I was taking a drug (clomid) that impacts on your hormones and I would need a blood test at day 21. They were fine with this and I think appreciated that I could have completely kept this to myself
TH	Being open	I had spoken to the owner/ director about the fact that we were waiting to find out if we could have IVF when we had been making an off site visit to another setting, and we had a lengthy car journey because I had an opportunity to instigate this when there was a good couple of hours available. I said I was speaking to him about this because there would be periods of

Doc	Code	Retrieved Segment
TH	Being open	but I was open with my deputy manager as he and I worked very closely together and I'm not great at hiding things.
TH	Being open	My first real discussion with my line manager (Regional Operations Manager) about this was when I recieved an appointment for a laparoscopy and dye test. My letter came just before my annual appraisal, so once we had agreed our business targets etc, we discussed on a personal level that we had been trying for a year and a half for 'number 2' at that point and that this is where I was at with investigating our infertility
TH	Being open	I explained we had been trying for a second child for some time, that at this point we didn't think it would be possible but that I was taking a drug (clomid) that impacts on your hormones and I would need a blood test at day 21. They were fine with this and I think appreciated that I could have completely kept this to myself
		time that it would be time consuming and I really needed his goodwill to be able to do it without compromising my position
TH	Being open	but safe in the knowledge that I have no big secret

Doc	Code	Retrieved Segment
TH	Being open	but I was open with my deputy manager as he and I worked very closely together and I'm not great at hiding things.
TH	Being open	My first real discussion with my line manager (Regional Operations Manager) about this was when I recieved an appointment for a laparoscopy and dye test. My letter came just before my annual appraisal, so once we had agreed our business targets etc, we discussed on a personal level that we had been trying for a year and a half for 'number 2' at that point and that this is where I was at with investigating our infertility
TH	Being open	I explained we had been trying for a second child for some time, that at this point we didn't think it would be possible but that I was taking a drug (clomid) that impacts on your hormones and I would need a blood test at day 21. They were fine with this and I think appreciated that I could have completely kept this to myself
SW	Being open	I had a job interview in October 2009, one of the questions that I was asked was “would you consider job-share?” to which I responded that I was specifically looking at a full-time role at the time, but wouldn’t rule out the possibility of being a job sharer in the future. I was asked to elaborate further! I advised the interview panel that I was hoping to undergo fertility treatment in the future, and if successful, I

Doc	Code	Retrieved Segment
TH	Being open	but I was open with my deputy manager as he and I worked very closely together and I'm not great at hiding things.
TH	Being open	My first real discussion with my line manager (Regional Operations Manager) about this was when I recieved an appointment for a laparoscopy and dye test. My letter came just before my annual appraisal, so once we had agreed our business targets etc, we discussed on a personal level that we had been trying for a year and a half for 'number 2' at that point and that this is where I was at with investigating our infertility
TH	Being open	I explained we had been trying for a second child for some time, that at this point we didn't think it would be possible but that I was taking a drug (clomid) that impacts on your hormones and I would need a blood test at day 21. They were fine with this and I think appreciated that I could have completely kept this to myself
		would like to take up a part-time role to spend as much time as possible at home.
SW	Being open	I wasn’t expecting to be handed the job on a plate, but I would have felt guilty if I had been offered the job, then handing my employers a schedule of treatment to arrange the time off. But by the same token, I wanted

Doc	Code	Retrieved Segment
TH	Being open	but I was open with my deputy manager as he and I worked very closely together and I'm not great at hiding things.
TH	Being open	My first real discussion with my line manager (Regional Operations Manager) about this was when I recieved an appointment for a laparoscopy and dye test. My letter came just before my annual appraisal, so once we had agreed our business targets etc, we discussed on a personal level that we had been trying for a year and a half for 'number 2' at that point and that this is where I was at with investigating our infertility
TH	Being open	I explained we had been trying for a second child for some time, that at this point we didn't think it would be possible but that I was taking a drug (clomid) that impacts on your hormones and I would need a blood test at day 21. They were fine with this and I think appreciated that I could have completely kept this to myself
		to be upfront and honest
RBI	Being open\non disclosure	When I discovered I would need IVF treatment, I made the decision not to tell
RBI	Being open	I told one employee who would be covering for me

Doc	Code	Retrieved Segment
TH	Being open	but I was open with my deputy manager as he and I worked very closely together and I'm not great at hiding things.
TH	Being open	My first real discussion with my line manager (Regional Operations Manager) about this was when I recieved an appointment for a laparoscopy and dye test. My letter came just before my annual appraisal, so once we had agreed our business targets etc, we discussed on a personal level that we had been trying for a year and a half for 'number 2' at that point and that this is where I was at with investigating our infertility
TH	Being open	I explained we had been trying for a second child for some time, that at this point we didn't think it would be possible but that I was taking a drug (clomid) that impacts on your hormones and I would need a blood test at day 21. They were fine with this and I think appreciated that I could have completely kept this to myself
		while I attended appointments.
RBI	Being open\non disclosure	I will admit I did come up with some ridiculous ‘white lies’ to tell to other members of staff.
RBI	Being open\non	When my IVF didn’t work and I was told I would require donor eggs I decided I didn’t want anyone in

Doc	Code	Retrieved Segment
TH	Being open	but I was open with my deputy manager as he and I worked very closely together and I'm not great at hiding things.
TH	Being open	My first real discussion with my line manager (Regional Operations Manager) about this was when I recieved an appointment for a laparoscopy and dye test. My letter came just before my annual appraisal, so once we had agreed our business targets etc, we discussed on a personal level that we had been trying for a year and a half for 'number 2' at that point and that this is where I was at with investigating our infertility
TH	Being open	I explained we had been trying for a second child for some time, that at this point we didn't think it would be possible but that I was taking a drug (clomid) that impacts on your hormones and I would need a blood test at day 21. They were fine with this and I think appreciated that I could have completely kept this to myself
	disclosure	my employment to know a
AJ	Being open	When I arrived at work that morning I had a quiet word with the area manager and explained that depending on my blood results that afternoon I may need to go infer treatment.

5. The legal position

Doc	Code	Segment
TC	The legal position\sexual discrimination	men and civil partners are allowed 2 days in a rolling 12 mths.
SW	The legal position\sexual discrimination	maybe I would have kept quiet if I was employed by a smaller company – certainly in previous jobs I was told quite candidly that they would no longer employ ladies of 'child bearing age'
SOC	The legal position\disciplinary action at work	but I had disciplinary action as a result of being off that day
SOC	The legal position\disciplinary action at work	The worst thing is that people with children are allowed time off for 'dependant care', I know more than a few people who abuse this and take days off pretending that they can't get child care and they're not disciplined for it but when I had to take a day off because I was so distressed it went through as 'sickness' and I was given a verbal warning which stays on my file for a year.

AJ	The legal position\sexual discrimination	and hurt i rang the union who gave me some really good advise and they told me what she was doing was more of sexual discrimination rather than victimisation.
AJ	The legal position	After getting advise i sort of knew where i stood, although there are no laws in place for ivf and just pregnancy laws, the advise given made me feel better.

Table 56 Table to show the retrieved segments for the legal position and sexual discrimination

6. The demands of treatment

Doc	Code	Segment
TH	The demands of treatment	Possible but that I was taking a drug (clomid) that impacts on your hormones and I would need a blood test at day 21.
SW	The demands of treatment	as the travelling alone would be a minimum of 2 hours each time.
SOC	The demands of treatment	Now I'm going to need time off twice a month for ultrasounds and blood tests and it will be extra stressful because these appointments will be made over the phone
AJ	The demands of treatment	They said that I may need to go back that day for my treatment.
AJ	The demands of treatment	This was really frustrating as it is not an exact science and all depends on your body clock

Table 57 Table to show the retrieved segments for the code 'The demands of Treatment'

7. Confidentiality

Document	Code	Segment
TC	Confidentiality	My company have been fantastic and haven't even asked to see any evidence of treatment.
SOC	Confidentiality	I had no choice but to tell work because I work in a call centre and can't just come in and leave when I like, i have to show proof and they have to photocopy everything and time off has to be approved depending on the staffing.
SOC	Confidentiality	it took me about 5 weeks to pluck up the courage to show a manager my letter from assisted conception with my first appointment on it because I was so embarrassed, my boyfriend also works in here so that makes me feel even more embarrassed - I really wish that managers in here didn't know so much about my personal life.
AJ	Confidentiality	Whislt typing it up i was sobbing as i felt humiliated and in disbelieve that i had to do it

Table 58 Table to show the retrieved segments for Confidentiality

8. Career Prospects

The concern that career or job might be jeopardized by the choice to undertake infertility treatment was only expressed once in one document in this sample.

Document	Code	Segment
RBI	career prospects	I do not know what the response from my MD would be if I told her I was having fertility treatment. It is so expensive though I cannot take the risk of letting on and then losing my job because of it – through work life just being made generally difficult, so forced out.

Table 59 Data segments for career prospects

Table 60 Coded data from forum in strand 4

Coded Data from Forum

Comment	Document	Code	Begin	End	Weight score	Segment	Author	Creation date	Document group	Page
	my story group\154	Identity as an employee or a treatment seeker	5	5	0	. It's not so much the cost of all this treatment but the cost to me emotionally, and in time off work.	Claire Haresnape	20/37/2013 11:37:00	my story group	1
	my story group\148	Identity as an employee or a treatment seeker\Using annual leave for treatment time	9	9	0	Thanks to Easter I have not had to take too much time off work but have been back a week now.	Claire Haresnape	20/44/2013 11:44:00	my story group	1
	my story group\145	Identity as an employee or a treatment seeker\Using annual leave for treatment time	4	4	0	Am just playing the waiting game now- was hoping to start asap while I am on summer holidays (I'm a teacher). If period arrives this week, embryo collection and transfer would be in the first week of the new term. Not very convenient!	Claire Haresnape	20/20/2013 12:20:00	my story group	1
	my story group\146	Identity as an employee or a treatment seeker	1	1	0	now take the pill for 39 days (my choice due to	Claire Haresnape	20/25/2013 12:25:00	my story group	1

						work and life)				
	my story group\134	Identity as an employee or a treatment seeker\medical sign off work	3	3	0	Shortly after this 2nd failed go I took some leave ill as I was suffering from anxiety/stress	Claire Haresnape	20/26/2013 12:26:00	my story group	1
	my story group\177	Identity as an employee or a treatment seeker	1	1	0	I have elderly parents I can't burden with all this and a highflying job(means very little I know - but helped at first) that means that all the friends I once had are doing bigger and better things and to busy to be there even if I could bear to talk about all this	Claire Haresnape	20/36/2013 12:36:00	my story group	1
	my story group\192	Identity as an employee or a treatment seeker\working around appointmentns	4	4	0	we finally told our families and very close friends what was going on. We'd wanted to keep it private but actually telling others was helpful - especially my family. I eventually also told work too when I requested to go part time which helped	Claire Haresnape	20/27/2013 20:27:00	my story group	1

						enormously.				
	my story group\181	Identity as an employee or a treatment seeker\Using annual leave for treatment time	12	12	0	Ive taken time off work and Im being very lazy!	Claire Haresnape	20/44/2013 20:44:00	my story group	1
	my story group\128	Identity as an employee or a treatment seeker\proximity of clinic to work	1	1	0	The waiting lists for NHS funded IVF was outside of our timescales so we chose to go privately, made easy by the fact that Bourn Hall Clinic was about 20 minutes down the road.	Claire Haresnape	10/38/2013 09:38:00	my story group	1
	my story group\126	Identity as an employee or a treatment seeker\No clear company policy in place	8	8	0	Also not sure how much time to take off from work(very stressful workplace!!) What do you think is acceptable?	Claire Haresnape	10/36/2013 09:36:00	my story group	1
	my story group\124	Identity as an employee or a treatment seeker	2	2	0	Does anyone know how long after planning how long before treatment starts roughly. How much time	Claire Haresnape	10/34/2013 09:34:00	my story group	1

						will I need off work? I am a teacher and it obviously has a big impact on the children I teach when I am continually out at appointments ?				
	my story group\120	Identity as an employee or a treatment seeker\medical sign off work	28	30	0	e finally saw the Cons again whilst I was on sick leave to talk through the treatment options and she told us we could start as soon as possible as there was in fact DS available and no waiting list	Claire Haresnape	10/26/2013 09:26:00	my story group	1
	my story group\117	Identity as an employee or a treatment seeker\medical sign off work	15	15	0	I had depression and anxiety and had been signed of work prior to our IUI commencing, the miscarriage from our IVF just compounded that	Claire Haresnape	10/22/2013 09:22:00	my story group	1
	my story group\113	Identity as an employee or a treatment seeker\proximity of clinic to work	4	4	0	Anyway fast forward a few months and we have been really lucky we have found a	Claire Haresnape	10/13/2013 09:13:00	my story group	1

						clinic 30 mins from home with excellent results and no NHS waiting list.				
	my story group\102	Identity as an employee or a treatment seeker\medical sign off work	8	8	0	So, the rollercoaster began in earnest in January last year. 2006 ended with the start of ivf cycle (icsi) number 1. It was the hardest thing i have ever done. Dr'ing was horrible, i suffered badly emotionally and didnt make it very long into treatment before needing to be signed off work.	Claire Haresnape	09/18/2013 15:18:00	my story group	1
	my story group\93	Identity as an employee or a treatment seeker	6	6	0	We haven't told friends or family, we are quite private and want to do this our way. This site really is an outlet for me to share and understand others experiences, even more so for us as our decision to keep this to ourselves will	Claire Haresnape	09/51/2013 14:51:00	my story group	1

						no doubt be difficult. I am not telling work either, my job is quite pressured and I couldn't stand the speculation. They already suspect I am pregnant as I put on weight post wedding. The irony of it isn't lost on me!!				
	my story group\93	Identity as an employee or a treatment seeker	8	8	0	Work is crazily manic and I worry about my ability to balance the relaxed zen that I need to get through the next few weeks with my need to perform and not let the side down in work.	Claire Haresnape	09/53/2013 14:53:00	my story group	1
	my story group\87	Identity as an employee or a treatment seeker\medical sign off work	8	8	0	At this point very depressed . Hit rock bottom. Sure we would not have children! Signed off work for 2 weeks	Claire Haresnape	07/11/2013 14:11:00	my story group	1
	my story group\85	Identity as an employee or a treatment seeker	1	1	0	Cycles appeared to return to normal then april to june cycle 7 weeks	Claire Haresnape	02/25/2013 18:25:00	my story group	1

						- think this is due to huge stress and unhappiness at work				
	my story group\85	Identity as an employee or a treatment seeker\working around appointmentns	1	1	0	luckily I had given up work in september so did not have to return anywhere. My husband did, but he has suffered as a result I believe, he is very depressed about the situation and buries himself in work	Claire Haresnape	07/02/2013 14:02:00	my story group	1
	my story group\78	Identity as an employee or a treatment seeker	6	6	0	But then the stress levels seem to rise Which clinic? How long to get appointment? How much time off work? (as i work as a f/t nanny difficult to get time off!) etc.....I'm sure you have all faced the same choices!	Claire Haresnape	02/07/2013 18:07:00	my story group	1
	my story group\77	Identity as an employee or a treatment seeker	3	3	0	Work wise, I am in the middle of an intensive three year training course where TTC isn't the best idea, but at the same	Claire Haresnape	02/06/2013 18:06:00	my story group	1

						time having a family means so much to us that we want all the precious time on our side that we can get				
	my story group\76	Identity as an employee or a treatment seeker\Using annual leave for treatment time	8	8	0	. We have decided though that as we have holiday in April we are going to try and tie everything in with that.	Claire Haresnape	02/02/2013 18:02:00	my story group	1
	my story group\73	Identity as an employee or a treatment seeker\working around appointmentns	1	1	0	I am 33 and DH is 36 - we got married in 2006 and had a relaxing year when first married before TTC when I came off the pill at the same time that I left a busy stressful job in London and began working for myself at home. So we were trying but not trying too hard whilst I worked on getting the business off the ground.	Claire Haresnape	02/53/2013 17:53:00	my story group	1

	my story group\70	Identity as an employee or a treatment seeker\Using annual leave for treatment time	1	1	0	I was intending on working right up to EC but I really struggled with the side effects, mainly the hot sweats, very emotional and tiredness like i've never felt before. I decided to take leave from work until after ET – my manager was wonderful, so supportive!	Claire Haresnape	02/42/2013 17:42:00	my story group	1
	my story group\67	Identity as an employee or a treatment seeker\Using annual leave for treatment time	9	9	0	April 07 - 1st IVF - this was our private one. Got 11 eggs, 8 fertilised. 2 embies transferred 2 days later on 14th November - a 4 cell b & a 3 cell b. Took the 2ww off & did all I could to optimise chances	Claire Haresnape	02/34/2013 17:34:00	my story group	1
	my story group\67	Identity as an employee or a treatment seeker\Using annual leave for treatment time	12	12	0	Again I didn't work during 2ww & I did all I did last time & a few extra things such as acupuncture, a hypnotherapy cd, paraben	Claire Haresnape	02/36/2013 17:36:00	my story group	1

						free shower gel etc, no nail polish etc. DH like the 1st time did ALL housework et				
	my story group\62	Identity as an employee or a treatment seeker\working around appointmentns	57	58	0	I can't get time off work until July so expect to start down regging June ish time.	Claire Haresnape	02/44/2013 16:44:00	my story group	1
	my story group\33	Identity as an employee or a treatment seeker	3	3	0	I went to my GP last monday and she signed me off for a week - i do not feel ready to go back to work yet but cannot get appointment at docs till tuesday....so what do i do re work and will docs renew sick note over phone.	Claire Haresnape	24/32/2013 14:32:00	my story group	1
	my story group\29	Identity as an employee or a treatment seeker\Using annual leave for treatment time	7	7	0	They have provisionally booked me in for EC and ET for week beginning feb 13th and We have both booked off that week	Claire Haresnape	24/19/2013 14:19:00	my story group	1

	my story group\29	Identity as an employee or a treatment seeker	7	7	0	Hoping that it is going to be that week as will be difficult to rearrange the time off. Plus found out recently that I am moving to a new department in work first week in March around time of end of the 2 week wait (assuming the dates don't change). Not the best timing! Will have to get to know new staff, new boss, different way of working! Not ideal but hopefully will be ok.	Claire Haresnape	24/19/2013 14:19:00	my story group	1
	my story group\282	Identity as an employee or a treatment seeker\No clear company policy in place	6	6	0	as I am the first and only woman I know they haven't had to work out maternity leave before, let alone whether they have a policy for people going through IVF treatment.	Claire Haresnape	24/16/2013 14:16:00	my story group	1

	my story group\282	Identity as an employee or a treatment seeker	6	6	0	So just hoping things will work out and I won't need too much time off for treatment. I think they would be fine about it - and my line manager has young children of his own so should understand - but I wouldn't be pleased if I was them so why should they be?	Claire Haresnape	24/16/2013 14:16:00	my story group	1
	my story group\18	Identity as an employee or a treatment seeker\Using annual leave for treatment time	6	6	0	3th August embryo put back, again not a nice experience but copable, like an extended smear test...2 weeks of pessaries, 1 week at work the other one on leave at M-I-L caravan to relax.	Claire Haresnape	24/25/2013 12:25:00	my story group	1
	my story group\9	Identity as an employee or a treatment seeker\proximity of clinic to work	6	6	0	We have found a lovely clinic nearby with	Claire Haresnape	21/18/2013 14:18:00	my story group	1

	my story group\6	Identity as an employee or a treatment seeker\proximity of clinic to work	15	15	0	In October, it was announced that my office was going to close, this really hit me as I moved to this office so that I could have mat leave, return to work part time, and be close to home, that made me really sad,	Claire Haresnape	21/13/2013 14:13:00	my story group	1

Comment	Document	Code	Begin	End	Weight score	Segment	Author	Creation date	Document group	Page
	my story group\135	Emotional distress	6	7	0	I will update this piece by piece as there is just too much to put down in one go. I think I am trying to prolong putting it all down as once it is written down then it becomes real, our story, something I wouldn't wish on my worst enemy	Claire Haresnape	20	my story group	1
	my story group\133	Emotional distress\feeling isolated	1	1	0	m fairly new on here and joined in the hope that some of you are in similar situations with male infertility. I feel very alone, but know that I'm not alone - just don't know anyone who is in the same situation. My cousin has just had a positive pregnancy test after her 3	Claire Haresnape	20	my story group	1
	my story group\133	Emotional distress	7	7	0	I still feel very , very sad that I will never have my husbands biological children, I will never look at them and think they have his nose / eyes / build etc. I still feel that I don't want another man's baby and feel guilty that my fertility (as far as we know) is fine, and cannot imagine how he feel	Claire Haresnape	20	my story group	1
	my story group\157	Emotional distress	4	4	0	Petrified I went on in, braved it but having got started it was painful, I tightned up and I just couldnt let them continue, so I never found out if my fallopian tubes were blocked.	Claire Haresnape	20	my story group	1
	my story group\157	Emotional distress	6	6	0	From my point of view I am petrified of going for blood tests, the very though of injecting daily,	Claire Haresnape	20	my story group	1

						regular trips to clinics, having eggs removed fills me with horor, I just cant see myself ever going along that route. It is expensive but we have savings that we could dip into but also to me a 25-30% chance of conceiving is still very low. I know people who have said, surely its worth the pain if you end up with a child, of course it is, but the heartache continues if you are not successful and where do you stop?				
	my story group\157	Emotional distress	7	7	0	I am sad, I feel low, not very enthusiatic about anything in life at the moment and I feel that there is something missing from me as a woman and I know I have to deal with my feelings in my head. I am a real thinker anyway so at the moment I am constanly thinking about it all and my dreams are terrible at the moment.	Claire Haresnape	20	my story group	1
	my story group\159	Emotional distress	1	2	0	Hi there - not sure where this post will take me, but here goes.....here is my story. I've been a member on INUK for the last couple of months, but have really only just managed to start responding and posting very recently. Mainly because I'm finding the reality of IF really painful and I guess I'm scared that by writing things down it makes it all so much more real. I feel now that I need to get a grip though, for my own sanity (and my DH's) as	Claire Haresnape	20	my story group	1

						well as moving forward and doing something about it. Since September I've not really done much else but cry buckets and buckets. I still do. Getting a grip is hard - it's easier to stick my head in the sand, which is probably what I've done since September 2008				
	my story group\159	Emotional distress	4	4	0	bout three years ago, we decided to start a family. I am near to tears now when I think how niaive I was in thinking it would all happen immediately. I feel guilty not just at the fact that it's me causing the IF, but also because it's because of me that we waited so long before trying.	Claire Haresnape	20	my story group	1
	my story group\159	Emotional distress	5	5	0	IVF was mentioned. So were donor eggs. It was all a blur - like being hit with a juggernaut	Claire Haresnape	20	my story group	1
	my story group\159	Emotional distress	6	6	0	I know I'm teetering on the edge of depression - I suffered from it in June 2006 following severe bullying by a senior manager at work (I left the organisation as a result ut now have my own business). I feel helpless, scared and so desperately sad.	Claire Haresnape	20	my story group	1
	my story group\159	Emotional distress	7	7	0	They (my parents) dote on him - you'd think he was their grandson. Don't want to go into that at the moment, but the way they are with him and their involvement with him, makes me angry, sad, upset, reclusive towards them.....for a whole number of different	Claire Haresnape	20	my story group	1

						reasons. I'll no doubt talk about that another time, because I know it's a major cause of my sadness and feelings of anger and helplessness whenever I see them.				
	my story group\159	Emotional distress	10	10	0	Anyway, I don't know how to finish this post - it's not really something I've done before, so I'll leave it for now and perhaps add to it another time. Hopefully, like anyone who may read this, one day the longed for result will happen and this constant ache and emptiness will go away.	Claire Haresnape	20	my story group	1
	my story group\158	Emotional distress	4	4	0	Specialist asked husband to do sp.test - to our shock it came back low - 8ml. Advised to do a secondary swim up test. Returned to the hospital in Nov for results, devastated to find DH result was even worse at 5ml.	Claire Haresnape	20	my story group	1
	my story group\158	Emotional distress	6	6	0	I just feel numb really. We haven't discussed our IF with anyone and when I try and discuss it with my DH he says everything will be ok. He is so optimistic that the results will be better in May, and I am trying to be but it is hard. Im worried that things may not improve. It seems a bit surreal that we have signed the IVF waiting list. I just have so many questions to ask and Im not sure where to start or who to ask. Not sure where to ask them on here either really.	Claire Haresnape	20	my story group	1

	my story group\151	Emotional distress	1	1	0	Unfortunately, I had a BFN in June and was utterly devestated. I couldn't believe I could feel so sad and empty. I couldn't believe that me, someone with nothing wrong with them, a youngish age and of good health, could get a BFN. I did not want to have IVF again and be so upset again	Claire Haresnape	20	my story group	1
	my story group\151	Emotional distress\counselling	1	1	0	Everything spiralled down, with me pushing Matt away at times, it was easier to grieve alone, or so I thought.Matt decided that I needed to speak to others so he joined me to this site where I have read so many stories of others, and been lucky enough to befriend some of you. On reading some of the stories, I decided I was strong enough to look to the future and I booked a counciling session for us and an appointment with the hospital nurses to discuss the next steps as I wanted to again donate my eggs	Claire Haresnape	20	my story group	1
	my story group\156	Emotional distress	4	4	0	We were devastated. We didn't realise how much we wanted the baby until we lost it. If that makes sense! It was an awful time, but slowly we picked ourselves up and everyone said at least you know you can get PG	Claire Haresnape	20	my story group	1
	my story group\154	Emotional distress	2	2	0	On Thursday I had a BFN from my 2nd IVF attempt; I still in a state of shock and feel very panic stricken.	Claire Haresnape	20	my story group	1
	my story	Emotional distress	3	3	0	Since then nothing - except a whole heap of	Claire Haresna	20	my story	1

	group\154					further loss and much suffering. Within 4 months of ttc my Grandma died, my beloved cat started his terminal illness, and then my M/C	pe		group	
	my story group\154	Emotional distress	3	3	0	However, had BFN whilst on summer holiday, and again I suffered huge distress because of the timing - precisely 2 years since M/C.	Claire Haresnape	20	my story group	1
	my story group\154	Emotional distress	5	5	0	I am currently suffering from major panic attackes and a sense of urgency as to whether to try again using a different drug to try get some eggs, or to abandon all hope of having my own and use a donor egg	Claire Haresnape	20	my story group	1
	my story group\154	Emotional distress	6	6	0	I haven't mentioned yet that my beloved cat suffered with his illness for 2 years before dying at the end of March this year, shortly before our 1st treatment, and DH's beloved cat died on the day of our 1st IVF scan. I still feel that was so outrageous of life and so unecessary to take him from us in the manner and the timing that it did. We have 1 cat and our dear little hamster left to keep us company.	Claire Haresnape	20	my story group	1
	my story group\152	Emotional distress	8	10	0	We did conceive back in October 2007 only to miscarry at 5.5 weeks. This was a complete accident and even though it wasn't planned we were of course devastated	Claire Haresnape	20	my story group	1
	my story	Emotional distress	35	36	0	Even though i am devastated I take solace	Claire Haresna	20	my story	1

	group\152					in the fact that i got pregnant again.	pe		group	
	my story group\153	Emotional distress\feeling isolated	1	1	0	, but feel that all other family members are really negiative and would rather not know what is going on. No support- I get really frustrated by this.... and makes me feel worse... especially as my parents are so supportive of my sister and her 3 children.	Claire Haresnape	20	my story group	1
	my story group\150	Emotional distress\Not feeling in control	15	17	0	I had always worked hard with determination and commitment in everything I had done in my life...but this..this was different. It didn't matter what i did I could not influence the outcome	Claire Haresnape	20	my story group	1
	my story group\149	Emotional distress	3	3	0	l. I would need IVF!! I was devastated, I had been lead to believe I would just need some pills?	Claire Haresnape	20	my story group	1
	my story group\149	Emotional distress	3	3	0	I have had to fight and got my MP behind me , harrassed my poor GP to death and it went to the Exceptional case panel. I have just found out that they have approved it and I get what I am entitled too. Whoopie doo! I should be gratefull for that! I am SO angry. I was living in ignorance, thinking that I might just need some tablets and now I am sterile! My DH is trying to understand but he has and always will have 2 lovely children. What about me? I have to heal for 3 months now before I begin the "real" journey but feel like I have been through the mill already!!!	Claire Haresnape	20	my story group	1
	my	Emotional	4	4	0	I cried and cried and think	Claire	20	my	1

	story group\149	distress				I lost the plot for a while. No-one understands as all my family and freinds have kids and if anyone else says "at least there is IVF", I think I wil hit them! lol	Haresnape		story group	
	my story group\149	Emotional distress\feeling isolated	5	5	0	I have to put a smile on my face and pretend that I am ok to everyone around me cos I think they will get sick of hearing me moaning! It would be great to hear back from anyone as I feel so very alone right now	Claire Haresnape	20	my story group	1
	my story group\146	Emotional distress	1	1	0	t.After a long wait of 25 months, one beautiful wedding and both brothers having 6 children between them and me feeling a complete failure	Claire Haresnape	20	my story group	1
	my story group\146	Emotional distress	1	1	0	I was given drugs to start that day, we were going away and my first injection ever was done in my brother in law's bedroom, I cried and really cried yet once I did it I wondered what I had panicked about it was fine	Claire Haresnape	20	my story group	1
	my story group\146	Emotional distress	1	1	0	, i started to bleed even before the blood results came so we knew, yet our heart broke when we got the phone call with the negative result	Claire Haresnape	20	my story group	1
	my story group\146	Emotional distress	1	1	0	I was given the option of waiting or having an injection called methotrexate to end it. I chose the injection I could not wait. The next day it happened. I broke my heart, I wanted to hide away and I did, the trouble with losing something so wanted and precious if it changed you forever, I wasn't sure I	Claire Haresnape	20	my story group	1

						would ever get over this but I did with time and understanding				
	my story group\134	Emotional distress\counselling	3	3	0	and started to go to the clinic counsellor which was a great help.	Claire Haresnape	20	my story group	1
	my story group\134	Emotional distress\being in control	6	6	0	During this 3rd cycle I felt more positive and more in control, I'd continued my counselling throughout and am sure this helped	Claire Haresnape	20	my story group	1
	my story group\134	Emotional distress\counselling	6	6	0	During this 3rd cycle I felt more positive and more in control, I'd continued my counselling throughout and am sure this helped	Claire Haresnape	20	my story group	1
	my story group\139	Emotional distress	1	1	0	I've got to the point where I have moments when I really struggle and feel utterly consumed with sadness at the thought of no baby	Claire Haresnape	20	my story group	1
	my story group\139	Emotional distress	1	1	0	I suffer with really bad PMS. At least I know from all the tests as a result of IVF that there appears to be nothing serious wrong, which is a plus. But I've tried pretty much everything out there to ease it, but you name it, I suffer. Once I've ovulated, for the next 2 weeks before my period, I have an absolute nightmare rollercoaster of emotions and cramps. It can put a bit of a strain me and DH, who is usually thick skinned and just goes with the flow or ducks for cover! Everything just gets so much worse during those 2 weeks – those of you who suffer will know how awful it can be. And dealing with not being a mum gets so	Claire Haresnape	20	my story group	1

						much worse. I'm so glad I've finally joined this site. I dipped in and out for so long, but got to the point where I really needed someone who properly understood. Friends and family support, but it's not the same. Knowing that what sometimes sounds like the "right" thing to say is often the worst. From feeling so alone with what I'm trying to cope with, I now feel more reassured that I'm not alone. Anyway, that's the end really. Like I say, I know I have a lot to be grateful for, and I am, but I also have this void, this huge emptiness that hits me like a kick in the stomach when I least expect. News of new babies when people seem to just blink and get pregnant. The sense of failure that I can't do something that to me is part of being a woman – being able to have children, when some people find it so, so easy. I used to get really stressed about it, but now I'm much more relaxed, but it's still something I deal with daily. I feel like I'm not living the life I thought, naively, that I would have by now – with a baby – and it's incredibly hard to deal with some days and sometimes a really good sob is what's needed – although DH gets upset seeing me upset! I'm				

						looking forward to hearing from you lovely ladies, and knowing that I've got this forum as an outlet				
	my story group\147	Emotional distress	4	4	0	.! Part of me really wanted them to find something physical so we could pin point it and fix it! Had a cry after the procedures from all the pent up anxiety, frustration and much relief that my body is in working order.	Claire Haresnape	20	my story group	1
	my story group\143	Emotional distress	2	2	0	The usual tests and scans over 2.5 years showed nothing to be wrong, incredibly frustrating in itself.	Claire Haresnape	20	my story group	1
	my story group\143	Emotional distress	4	4	0	The stress and strain took there toll I on an off over the time I suffered from depression and anxiety caused by the infertility.	Claire Haresnape	20	my story group	1
	my story group\144	Emotional distress	3	3	0	Married in 1997and started ttc in 1999, after about 9 months we went to the doctors and had all the initial blood tests and sperm samples were sent away but to be honest we didnt really think anything of it, therefore it came as a massive shock when dh sperm sample came back as no sperm in them, my blood tests were all ok.	Claire Haresnape	20	my story group	1
	my story group\171	Emotional distress	1	1	0	I've been struggling with depression for the past few years on and off - since we found out we probably couldn't have children naturally, and then, amazingly did get pregnant, only to miscarry at 12 weeks. It's nearly 2 years since then...hence the ICSI appt looming in April	Claire Haresnape	20	my story group	1
	my story	Emotional distress\feeling	1	1	0	Feel very alone with all the worry as my partner	Claire Haresna	20	my story	1

	group\171	isolated				gets upset when I get tearful about it all, so I try to keep as much of the black mood to myself as possible. Most of my friends have kids and say they feel guilty if I tell them how sad I get...so - quite isolated and blue. that's why i'm here.	pe		group	
	my story group\140	Emotional distress	2	2	0	I've been with my DH for 9 years, married for 3. We've been ttc for 16 + months now and the anger and upset each month when AF arrives certainly has not got any better over time.	Claire Haresnape	20	my story group	1
	my story group\177	Emotional distress\feeling isolated	1	1	0	is the first time I have ever really sat down and tried to tell anyone about all of this....sorry if I go on, just don't have anyone I can discuss this with and to find this network has opened my eyes so much, hopefully you won't judge me. Up until now I felt like the loneliest person in the world!	Claire Haresnape	20	my story group	1
	my story group\177	Emotional distress	1	1	0	I am a selfish, spiteful woman for not wanting to see him and as each day turns to weeks and weeks to months I find that coping with even the most mundane things in life is becoming more difficult.	Claire Haresnape	20	my story group	1
	my story group\177	Emotional distress\feeling isolated	1	1	0	Friends carry on having babies, as do family, I work in a hospital enviroment and and have to deal with seeing people who are pregnant and with children all the time, I have created a professional and cold shell I put up to allow me to function but inside I am	Claire Haresnape	20	my story group	1

						screaming, tears come late at night after my husband sleeps and when I am alone - pathetic I know, I'm doing it again now. I used to like me and I am agood person I hope, most of the time -I am a caring person, now all I see is a stressed and tired woman looking back at me at odds with the world wondering when did all this take over me and when will I ever be able to not wake to the thoughts I do and drift off to sleep without a tear stained pillow. Sorry to be moaner thanks for listening it's helped just to put this to paper so to speak. Better go and put my face on again and pretend everything is OK... am getting to be quite the expert				
	my story group\177	Emotional distress	1	1	0	Friends carry on having babies, as do family, I work in a hospital enviroment and and have to deal with seeing people who are pregnant and with children all the time, I have created a professional and cold shell I put up to allow me to function but inside I am screaming, tears come late at night after my husband sleeps and when I am alone - pathetic I know, I'm doing it again now. I used to like me and I am agood person I hope, most of the time -I am a caring person, now all I see is a stressed and tired woman looking back at me at odds with the	Claire Haresnape	20	my story group	1

						world wondering when did all this take over me and when will I ever be able to not wake to the thoughts I do and drift off to sleep without a tear stained pillow. Sorry to be moaner thanks for listening it's helped just to put this to paper so to speak. Better go and put my face on again and pretend everything is OK... am getting to be quite the expert				
	my story group\179	Emotional distress	1	1	0	I've been in tears reading some of your experiences - thank you all so much for sharing as it must have been really difficult.	Claire Haresnape	20	my story group	1
	my story group\175	Emotional distress\feeling isolated	8	8	0	I think the hardest part for me is that three of my four closest friends are all pregnant and all became pregnant in the first month of trying. I feel alienated from them as babies and pregnancy is all the talk about with each other. Sadly I feel I am avoiding situations when we are all together. I know it has affected my friendships with them. It not their fault they are pretty sensitive but they can never understand the frustrations having month after month of disapointment as then didn't even have one. Perhaps I am being mean	Claire Haresnape	20	my story group	1
	my story group\175	Emotional distress	8	8	0	I think the hardest part for me is that three of my four closest friends are all pregnant and all became pregnant in the first month of trying. I feel alienated	Claire Haresnape	20	my story group	1

						from them as babies and pregnancy is all the talk about with each other. Sadly I feel I am avoiding situations when we are all together. I know it has affected my friendships with them. It not their fault they are pretty sensitive but they can never understand the frustrations having month after month of disapointment as then didn't even have one. Perhaps I am being mean				
	my story group\170	Emotional distress	1	1	0	Well, I picked up a card for INUK 2 1/2wks ago at the hospital having ET, I desperately hoped I'd never have the need to find out what it was all about, but here I am so that says alot. I had BFN on monday and have never felt so alone in this whole IF thing, probably because this time we told no one, which I dont regret because I have just about had enough of all the sympathy and feeling sorry for us, especially surrounding the birth of my brother's beautiful baby boy in April - the first born in my family. Thats been really tough, and I have felt every emotion under the sun, including massive jealousy, anger, guilt for those feelings, and an overwhelming feeling of love and protection towards my nephew that scares me.	Claire Haresnape	20	my story group	1
	my story group\1	Emotional distress	5	5	0	The joy and tears from both my DH and I was overwhelming, but out	Claire Haresnape	20	my story group	1

	70					nurse who we had grown to know well, showed no emotion, telling us to come back a week later to look for the heart beat. A week later, we saw a flicker, but not clear. A week later, a little bigger but not developing as fast as the 7wks I should be. A week later, told not to get our hopes up, that it wasnt looking good. Needless to say I had had a missed miscarriage and my baby had died. Waited 10 days and couldnt bear it any longer, I thought I would go out of my mind with grief, I cried 24/7 and the pain in my chest with never leave me. I still cry for our baby who would have been a year old on the 1st July.				
	my story group\170	Emotional distress	7	7	0	So ..... FE cycle was crap. I was evil, felt evil and was downright evil ..... I would have left me if I had been DH !!!!! The headaches, feeling sick all the time and irritable and angry. This all eased but this time ET was really painful too, and I do have a high pain threshold ! Well, then this monday came the BFN, I'd already done 4 pg tests (even though knew it wouldnt work !!!!! Yeah but you still have hope whatever you say out loud !) I have coped this week, and I put that down to nothing being worse than my DH having meningitis and losing our darling baby, but I feel so low and angry. DH isnt coping too	Claire Haresnape	20	my story group	1

						well. He is doing the caveman bit and retreating. So I thought this would be a good way for me to get off my chest, stuff I know I want to say to DH, but cant at the moment. I am staying busy, went straight back to work after the results on monday and havent stopped, think thats the best way for me.				
	my story group\167	Emotional distress	4	4	0	this time i did nt start my period but i still got a BFN. after this try i was so depressed and low and felt awful	Claire Haresnape	20	my story group	1
	my story group\167	Emotional distress\counselling	4	4	0	. i even went for counselling at the hospital but it did nt work.	Claire Haresnape	20	my story group	1
	my story group\166	Emotional distress	1	1	0	Both DH and I were gutted but got through a tough few days.	Claire Haresnape	20†	my story group	1
	my story group\166	Emotional distress	2	2	0	The situation really hit me last October 4 days before my Nieces 1st birthday and I turned to our senior leader who was brilliant and really made a tough week as easy as it was going to be. It wasn't until end January that I started to feel better, it was when we got our review appointment through.	Claire Haresnape	20	my story group	1
	my story group\165	Emotional distress	2	2	0	I went back to GP who then informed us that DH did have a problem according to the sample he had given a year or so ago but noone had informed him. I was devastated as was he.	Claire Haresnape	20	my story group	1
	my story group\1	Emotional distress\feeling isolated	6	6	0	I get very low and because so few people around me are aware of	Claire Haresnape	20	my story group	1

	65					the problem, I often feel misundersood				
	my story group\164	Emotional distress	7	7	0	We were devastated and with my mum's help we complained to the GP and PCT and after 8 months of letters, phone calls, crying and appointments, we were transferred to another clinic.	Claire Haresnape	20	my story group	1
	my story group\164	Emotional distress	8	8	0	- when on the day we had bad news that unexpectedly my DH's sperm count and motility had drastically reduced so they couldn't go ahead with IUI - we were totally devastated and couldn't understand it and neither could the clinic because he was fine a month before. It felt like the world was falling apart.	Claire Haresnape	20	my story group	1
	my story group\164	Emotional distress	10	10	0	cycle in Feb, ready for starting IVF - and I was told by the nurse that the PCT was cutting our funding (along with 17 other couples) so we wouldn't be able to start IVF this month. I was so shocked and yet again devastated and hurt - I got straight onto the phone to my mum and then my GP - they both knew the PCT from trying to get our funding changed before, and it took a whole day and lots of phone calls for it to be agreed. (In the process they also managed to get all the other 17 couples' funding secured too - but they won't have known that!!)	Claire Haresnape	20	my story group	1
	my story group\1	Emotional distress	1	1	0	We started trying to conceive in 2004 and fell pregnant after about 6	Claire Haresnape	20	my story group	1

	60					months but sadly miscarried at 7 weeks. This hit me very hard and I was desperate to get pregnant again as soon as possible, although in retrospect perhaps I didn't allow myself time enough to grieve properly.				
	my story group\193	Emotional distress	2	2	0	DH is azoospermic (absolutely zilch). He dealt with it as only men can - very badly. He was turning 40 as well, and all that turned into a mid-life crisis of sorts. Pleased to report he's on the up, just as I lose my optimism and stamp my feet about the injustice of it all!	Claire Haresnape	20	my story group	1
	my story group\193	Emotional distress	4	4	0	After DH going to pieces initially I think he was expecting the negative result but I was, and still am, completely floored. My best friend has just had her second child and the fact I will never have DH's baby makes me feel sick. I am finding it very, very hard to accept.	Claire Haresnape	20	my story group	1
	my story group\193	Emotional distress	5	5	0	. I feel cheated and robbed and all the other horrible horrible feelings are that all of us here deal with on a daily basis.	Claire Haresnape	20	my story group	1
	my story group\194	Emotional distress	1	1	0	In the past I have had two terminations of pregnancies with people who didn't want to have children (or at least not mine!). The second of these I found particularly upsetting at the age of 35.	Claire Haresnape	20	my story group	1
	my story group\194	Emotional distress	3	3	0	After another year of trying (and lots of tears!)we went back for more tests.	Claire Haresnape	20	my story group	1

	my story group\192	Emotional distress	3	3	0	I was devastated as had found the drugs and process of scans really taxing to that point so was gutted that the chances of it working were even more reduced. We weren't surprised that it didn't work but was still very upsetting. 2 more IUI's led to BFNs in Feb and March 07 and I found it increasingly difficult to cope with.	Claire Haresnape	20	my story group	1
	my story group\192	Emotional distress\counselling	4	4	0	I found the counsellor at our clinic was great	Claire Haresnape	20	my story group	1
	my story group\191	Emotional distress	1	1	0	I'm new to INUK - I've recently been unsuccessful at ICSI (2nd attempt) and miscarried after a short time recently - 1 day before my 39th birthday so hugely disappointed and really struggled this time round - I feel a mid-life crisis coming on!	Claire Haresnape	20	my story group	1
	my story group\191	Emotional distress\feeling isolated	2	2	0	what I'm struggling with the most is how distant I now feel from a lot of my friends who were once in the same boat as me but now seem to have got on with their lives with their new familes and we just don't see so much of them or it can be a little strained - I guess they don't know what to say, others are just plain silent. It's quite painful to think the support I'd thought we'd receive just hasn't been there	Claire Haresnape	20	my story group	1
	my story group\188	Emotional distress	9	9	0	Again we had more tests and DH was asked to be a sperm donor by this clinic to which we said no	Claire Haresnape	20	my story group	1

						to straight away as I just couldnt cope with the thought of someone else having what I longed for and as his wife should be entiled to.				
	my story group\188	Emotional distress	13	13	0	BFN followed and I lost the plot, was on a plane the next day to see my parents in Spain and to give my DH a breather from the mad woman	Claire Haresnape	20	my story group	1
	my story group\188	Emotional distress	16	16	0	I am 30 in August and DH will be 39, like all of the ladies on this wonderful site I dread every birthday and every Christmas as for me it marks yet another year of ttc and for me it makes me feel a failure.	Claire Haresnape	20	my story group	1
	my story group\188	Emotional distress\Not feeling in control	17	17	0	I was a successful carrer girl and controlled all aspects of my life and this is the one thing I can't control or buy! I	Claire Haresnape	20	my story group	1
	my story group\190	Emotional distress	3	3	0	I found out a month after my wedding that i was unable to have children naturally and thought my world was ending. I had been with my husband for three years before we married and from the moment i met him i hoped to have his children one day. This news made me feel inadequate, a failure and less of a women. I couldnt understand why this was happening to m	Claire Haresnape	20	my story group	1
	my story group\190	Emotional distress	3	3	0	On my eight week scan there was a problem, the baby was not growing properly and the doctors face started to change, i had an agonising two week wait only to be told that i had had a missed miscarriage. I cried so	Claire Haresnape	20	my story group	1

						hard i couldnt breath and carried on crying for two weeks.				
	my story group\185	Emotional distress	1	1	0	ur little girl was born asleep on 25th June and we miss her so very much. She was born at 36+6 at 6.45pm and just looked so perfect and beautiful. She was conceived on our third attempt after many years of striving to become parents so her loss was particularly difficult to bear. Our little girl was a frozen embryo, created in the late summer of 2006, and so had already overcome being frozen and defrosted. We at least have the consolation that we were able to “meet” her when she was only 3 cells old	Claire Haresnape	20	my story group	1
	my story group\185	Emotional distress	1	1	0	We had lost our darling baby. They then brought through an ultrasound machine and as soon as they began you could see the chambers of my baby’s heart were still. There was no movement at all. My husband was distraught, but I had already come to accept the fact that my baby was gone. We had to wait however for a Sonographer to come on duty to confirm that we had lost our child	Claire Haresnape	20	my story group	1
	my story group\185	Emotional distress	1	1	0	. She was such a part of our lives despite our never having met her before that hour, and the devastation of her loss will remain with us for ever. We called the midwife back into the	Claire Haresnape	20	my story group	1

						room so she could wash her, as I was afraid I may hurt our little darling. The midwife weighed her and she was 5lb 10oz, she measured her head and length and we then had an opportunity to take some photographs of he				
	my story group\181	Emotional distress	9	9	0	As you can imagine i was devastated, i couldn't get my head round why this was happening, I've never been a bad person or hurt anyone why was this happening to us! Our consultant advised our best next option would be Embryo Donation.	Claire Haresnape	20	my story group	1
	my story group\181	Emotional distress	10	10	0	I was finding every day life very difficult, i would cry on the way to work and in work but the one i thing i did that did not help was i cried alone. I never have been very good at opening up, so everything just came to a head.	Claire Haresnape	20	my story group	1
	my story group\181	Emotional distress\counselling	10	10	0	I therefore starting seeing my counsellor in September 07 & am continuing to do so at present, i think without her help i would not have been ready to be where I am now.	Claire Haresnape	20	my story group	1
	my story group\180	Emotional distress	8	8	0	Two days later it is sinking in and is very painful. I am all alone away from my friends and family and honestly dont know how to get through the next few days. My husband is the silent type who says he just wants to move on... When I suggest getting a second opinion (preferably in a language we can	Claire Haresnape	20	my story group	1

						understand and in a country with few legal restrictions) he says I must not get scary and obsessed.				
	my story group\142	Emotional distress	7	7	0	Successful transfer then spotting 2 days before prgnancy test which was negative result. My husband and I were devastated..	Claire Haresnape	20	my story group	1
	my story group\142	Emotional distress	8	8	0	My husband and I were in shock and disbelief at first, I just felt numb - he was clearly devastated and angry.	Claire Haresnape	20	my story group	1
	my story group\142	Emotional distress	10	10	0	4 months on my husband wanted me to try IVF again. 6 weeks ago I told him that there is no way that I can do this again for the moment - if it did not work then this would just destroy me. I don't know when we will do it again now, but have said that if we do it again then that really is the last time I can go through this god awful process!	Claire Haresnape	20	my story group	1
	my story group\215	Emotional distress	4	4	0	We had our first consultation in Aberdeen in August 2005, I was utterly shocked to be sent away clutching my bag of injections and drugs!	Claire Haresnape	20	my story group	1
	my story group\215	Emotional distress	12	13	0	Fifth cycle in September 2006 was a natural FET with 1 embie. Ended up on anti-depressants, how much more pain could I take...	Claire Haresnape	20	my story group	1
	my story group\213	Emotional distress	1	1	0	and to my shock was told I had a probable endometrioma on my ovary and most likely had endometriosis and would need a Laparoscopy.I	Claire Haresnape	20	my story group	1
	my story	Emotional distress	4	4	0	we were both devested when we was told we	Claire Haresna	20	my story	1

	group\212					could never conceive naturally but was refered to another hospital as they didnt hold the funding for us as we lived in a diffrent county	pe		group	
	my story group\211	Emotional distress	4	4	0	First IVF attempt in May 07 - 10 eggs and no fertilisation, so advised to go for ICSI. ICSI attempt in Aug 07, which resulted in 19 eggs and no fertilisation again. Felt like the end of the world.	Claire Haresnape	20	my story group	1
	my story group\209	Emotional distress	7	7	0	The pain was beyond belief, as we had lost our little baby and our dreams were shattered. I cried for what seemed like weeks.	Claire Haresnape	20	my story group	1
	my story group\209	Emotional distress\counselling	11	11	0	. I decided to have some counselling which is one of the best things I have ever done. It was hard, very hard. But with time really helped to come to terms with what had happened and got me to a place where I am strong again and accept that there will be times when I will feel sad and that's ok but that there is much hope for the future.	Claire Haresnape	20	my story group	1
	my story group\208	Emotional distress	10	10	0	then my younger, unmarried, unattached sister announced her pg and it felt like a knife in the heart.	Claire Haresnape	20	my story group	1
	my story group\207	Emotional distress	1	1	0	Had 7th cycle using donor eggs, but donor pulled out. World then fell well and truly apart but found that leap of faith to try using donor eggs just once more. Fell pregnant!!!!	Claire Haresnape	20	my story group	1
	my story group\131	Emotional distress	1	1	0	ery rapid profound depression with clomiphene,	Claire Haresnape	20	my story group	1

	my story group\131	Emotional distress	1	1	0	With more sadness and loss my China adoption hopes have died inside, although our application is still in and we are monitoring the timescales.	Claire Haresnape	20	my story group	1
	my story group\131	Emotional distress	1	1	0	I had 3w atrocious 'baby blues'	Claire Haresnape	20	my story group	1
	my story group\130	Emotional distress	2	2	0	Probably shouldn't be writing this today as I'm feeling really tired, sore and low. But hey, ho, here goes!	Claire Haresnape	20	my story group	1
	my story group\130	Emotional distress	5	5	0	Meanwhile time is ticking and frustration building.	Claire Haresnape	20	my story group	1
	my story group\130	Emotional distress	10	10	0	I'm also having to cope with a difficult family situation. My younger (29) sister got accidently pregnant last year and chose to have an abortion. She and my mother debated not telling me, but did. So I had to bury all my own feelings to support her including listening to her complain about her pregnancy symptoms before the procedure. Didn't she realise that I'm desperate to feel like that? Life is so unfair. That little life was flushed away. My sister is incapable of offering support to me so I'm feeling angry at her (for this more than the abortion). We've now fallen-out and I don't have the emotional energy to sort it out.	Claire Haresnape	20	my story group	1
	my story group\129	Emotional distress	5	5	0	In 2009 we started our treatment. It hasn't been that bad but the emotional journey is quite hard. I	Claire Haresnape	10	my story group	1

						spend so much time trying to convince myself that we should just accept that we don't have to have children and we can get a dog or travel again but the desire for a family has become so great now that I can't see how I will accept just being the two of us.				
	my story group\128	Emotional distress	1	1	0	I hadn't had mumps as a child, nor had any viruses recently so would this be a permanent condition? My whole world came crashing down around me.	Claire Haresnape	10	my story group	1
	my story group\128	Emotional distress	1	1	0	All hope was lost. We were both devastated but with the numbness came the feeling of relief. No more unknown, no more waiting, no more clinging to hope; we could now move on.	Claire Haresnape	10	my story group	1
	my story group\128	Emotional distress	1	1	0	So how has this been emotionally? We are still going through IVF and not had much luck, therefore my feelings are still fresh and quite raw. When this is over I'm sure the benefit of hindsight will kick in but for the moment trying to have a family is still very much the focus of our lives, and coping is sometimes less than easy. My feelings this year have ranged from anger, upset, self-pity, resentment, guilt and inadequacy. On a lucky day I've felt all of these	Claire Haresnape	10	my story group	1
	my story group\128	Emotional distress\counselling	1	1	0	From speaking to the fertility counsellor I realised my feelings were normal and as a result I haven't beat myself up	Claire Haresnape	10	my story group	1

						about whether I'm being irrational.				
	my story group\128	Emotional distress	1	1	0	Of course I can't help feeling a little resentment, why do other people have a baby at the drop of a hat I ask? Likewise I know that the occasional feeling of self pity is normal. We have tried to maintain control of these feelings and I think we have made a good job of being open about all aspects of our treatment, without becoming emotional and showing any of these feelings. On the outside we've probably appeared casual, but behind closed doors it has been very different and we still get upset and get strength from each other	Claire Haresnape	10	my story group	1
	my story group\128	Emotional distress\feeling isolated	1	1	0	In an ideal world we would be open with those closest to us but people struggle with understanding how we feel and find it awkward knowing what to say. Listening to comments like "you'll be ok in the end" or "relax and stay positive" don't help but can understand why people say them	Claire Haresnape	10	my story group	1
	my story group\128	Emotional distress\counselling	1	1	0	The use of donor sperm was one of the easier things to come to term with for me. The fertility counsellor made me rethink my original idea of the student donor who was trying to make an easy £20 with a dirty magazine.	Claire Haresnape	10	my story group	1
	my story	Emotional distress	5	5	0	. He acted like it was no big deal but I know he	Claire Haresna	10	my story	1

	group\127					really felt bad.	pe		group	
	my story group\127	Emotional distress	7	8	0	I thought it would get easier the closer it got to our start date but it just gets more terrifying. I had depression in my teens & am so scared if IVF doesn't work history may repeat itself.	Claire Haresnape	10	my story group	1
	my story group\125	Emotional distress	3	3	0	So went for the scan with DH in tow, & the sonographer asked me if I knew I had ovarian cysts. Cue a bit of crying, followed by rational 'at least we know & can deal with it'.	Claire Haresnape	10	my story group	1
	my story group\125	Emotional distress	5	5	0	Managed to ask him about having children, to which he responded IVF was only hope. Needless to say I became a tad hysterical, being told that I was infertile at the age of 27.	Claire Haresnape	10	my story group	1
	my story group\123	Emotional distress	8	8	0	We started the attempt for number two end 2005, and within a few months, I started to get a bit annoyed when it wasnt happening. As the months passed, annoyance turned to bother, bother turned to anger, anger turned to confusion, confusion turned to worry. I just didnt understand why it wasn't happening.	Claire Haresnape	10	my story group	1
	my story group\123	Emotional distress	10	10	0	I was absolutely devastated. I had an overwhelming desire for another child, my friends were all having second or third children, and all anybody would ask me was 'when are you going to have another one'. I just couldn't believe this was happening - and	Claire Haresnape	10	my story group	1

						happening to me.				
	my story group\123	Emotional distress	12	12	0	was starting to feel increasingly depressed about it. Grieving for the child I couldn't have, sorrow for my son not having a sibling (I am very close to my sibling), pain at my incomplete family and feeling totally isolated dangling somewhere between the worlds of the fertile and infertile. I just didn't belong or fit in anywhere.	Claire Haresnape	10	my story group	1
	my story group\123	Emotional distress\feeling isolated	12	12	0	and feeling totally isolated dangling somewhere between the worlds of the fertile and infertile. I just didn't belong or fit in anywhere..	Claire Haresnape	10	my story group	1
	my story group\123	Emotional distress	19	19	0	The pain of infertility is so intrenched, all consuming and inexplicable, it will never ever leave me. Unless you have been there, it is really totally impossible to understand. I cannot begin to pretend to understand the depth of pain of total childlessness, but I have a fair idea of how I felt dealing with our infertility. I wouldn't wish it on my worst enemy. Its unfair, cruel and heartbreaking and nobody should have to suffer it, least of all alone	Claire Haresnape	10	my story group	1
	my story group\121	Emotional distress\feeling isolated	2	2	0	This is my story. I would really like to hear back from anyone who is in a similar position as I don't feel there is anyone I know who truly understands how I feel. I found out this week that our second attempt at IVF didn't work.	Claire Haresnape	10	my story group	1

	my story group\121	Emotional distress	6	6	0	motionally I have been demented to say the least. This is the worst experience of my life. Every month is a bereavement. The unexplained element is bewildering and not understanding why drives me demented. The prospect of facing a future without ever experiencing pregnancy and having children of my own, is horrific. Only in recent months have I come in a small way to 'accept' that this is the way it is for us right now. I have been in a state of panic and shock for most of the last 3 years. I have deep, deep feelings of failure, anger and incredulousness at our situation. The disappointment, injustice, lack of understanding I feel is overwhelming.	Claire Haresnape	10	my story group	1
	my story group\121	Emotional distress	7	7	0	I cannot stand pregnant women, especially the ones who are oblivious to the fact that someone around them may not be as lucky as them and who think everyone should fawn all over them and make a fuss of them (a so called friend who knew what I was going through thrust her positive pregnancy test under my nose a week to show me her success after I had my first failed IVF such was her lack of empathy and self absorption). I've had some pregnant friends who have been lovely and worked hard to not rub my face in it but I	Claire Haresnape	10	my story group	1

						really have difficulty being around them. When I cry, the grief comes from so deep down in my very depths and I just howl with sorrow				
	my story group\121	Emotional distress\feeling isolated	8	8	0	I could go on and in more detail but I think I've provided the general story. I really just need to be in touch with people who understand and can make me feel less lonely	Claire Haresnape	10	my story group	1
	my story group\120	Emotional distress	3	6	0	He came home devastated and the timing could not have been more ironic as it was the day before we were due to move from our little flat to a family house that we fully intended to fill with children!	Claire Haresnape	10	my story group	1
	my story group\120	Emotional distress	12	15	0	I literally felt the blood drain from my body. I think I went into a bit of a meltdown for the next few months, work was unbelievably full on, we were told that there was no DS on the NHS, we were told to go to the USA, we were told that the wait here would be 5 years.	Claire Haresnape	10	my story group	1
	my story group\120	Emotional distress\being in control	38	43	0	After that appointment we decided just to stop everything for two months, to concentrate on each other again, go on holiday in the sunshine, see our friends and find some joy in our lives again. I also found a great acupuncturist and started regular treatments to prepare my body, I started pilates again and did lots and lots of	Claire Haresnape	10	my story group	1

						walking				
	my story group\120	Emotional distress\counselling	43	46	0	We have both been having counselling and this has helped a great deal plus we got to talk to a fantastic couple from the Donor Conception Network and it was very reassuring to listen to their story and ask questions.	Claire Haresnape	10	my story group	1
	my story group\120	Emotional distress\being in control	46	47	0	have also been making efforts to reduce the stress at work.	Claire Haresnape	10	my story group	1
	my story group\119	Emotional distress	1	1	0	Every month the cycle of negative test sticks is quite wearing	Claire Haresnape	10	my story group	1
	my story group\119	Emotional distress	4	4	0	elt a bit like we were going nowhere and the constant dissapointment is really getting to me, I now seem to cry for about 3 days after my period starts.	Claire Haresnape	10	my story group	1
	my story group\118	Emotional distress	2	2	0	My first miscarriage happened last year, in August 08. I was devastated as I had thought having a baby was easy! How wrong I was! It was a blighted ovum and I had a D&C after hanging on for nearly 3 weeks and hoping that I'd just got my dates wrong. It was extremely traumatic as I just hadn't expected anything like this to happen to me.	Claire Haresnape	10	my story group	1
	my story group\118	Emotional distress	4	4	0	The very next day I had terrible pains at work - I was scared but didn't think it could be the worst.... unfortunately it was. A scan that evening showed only one heartbeat. I was so sad	Claire Haresnape	10	my story group	1

						for the first twin, afraid that something would happen to the 2nd twin, but at the same time hopeful. I had to stay in bed for 2 weeks, but after just one week I had spotting during the night. I knew immediately what was happening and was heartbroken. I had a natural miscarriage and lost the 2nd twin at 8 weeks, which was completely traumatic and devastating. I would not ever like to go through that again in my life and will never forget it.				
	my story group\117	Emotional distress	4	4	0	fter 6 months of ttc, I visited my GP for advice and said that the constant expectation each month was beginning to get me down - little did I know that was alot more expectation ahead and devastation in the future than the 6 months we had been trying for a family. The GP told me that most couples will conceive within the first 6- 8 months of ttc, and the majority by a year. Disheartened but hopeful at the same time we continued for another 3 months and nothing. I became obsessive about my cycles and stressed each month that passed.	Claire Haresnape	10	my story group	1
	my story group\117	Emotional distress\feeling isolated	4	4	0	Friends around me didn't understand and I felt lost and left out the loop or club. every announcement that was made by friends made my isolation worse.	Claire Haresnape	10	my story group	1
	my	Emotional	5	5	0	I had been to the hospital	Claire	10	my	1

	story group\117	distress				in tears and talked to the fertility nurse in the maternity/Gynae unit.	Haresnape		story group	
	my story group\117	Emotional distress\feeling isolated	5	5	0	I felt something like this may help if I had a focus each month where I could talk to others in the same situation and we could swap thoughts. I had felt so alone before this.	Claire Haresnape	10	my story group	1
	my story group\117	Emotional distress	7	7	0	The cycle was abandoned and I was devastated	Claire Haresnape	10	my story group	1
	my story group\117	Emotional distress	8	8	0	IUI was abandoned after that as a means of treatment for us and I was desperate to try IVF	Claire Haresnape	10	my story group	1
	my story group\117	Emotional distress\financial loss	8	8	0	We couldn't afford the amount being asked privately and didn't yet qualify under the NHS criteria of 3 yeas ttc, (we were 2.5 yrs) so we looked into the private system to see if we could in any way afford it possibly with some help from family.	Claire Haresnape	10	my story group	1
	my story group\117	Emotional distress	11	11	0	. My symptoms seemed to dwindle around 6 weeks and I got really worried - I was right too, on the day before our first 7 week scan I started to loose our precious miracle at the very end of April and beginning of May 07. I was devastated beyond belief. How could this happen? Why?	Claire Haresnape	10	my story group	1
	my story group\117	Emotional distress	12	12	0	After a traumatic wait in A and E at our local hospital I was told to prepare for the worst - How can you?? The next day was our scan and the clinic agreed to go ahead even though they were reluctant as they feared	Claire Haresnape	10	my story group	1

						what I already knew deep down - it was over. No picture of a heartbeat and a bean like being on the screen - nothing. I have never felt emotional pain like it. DH didn't know what to do, it was unbearable.				
	my story group\117	Emotional distress	13	13	0	We grieved and grieved and this was added to as the hospital thought there was concern over a second embryo that may have implanted in my tubes or on my ovary - an ectopic.The scans continued and more blood tests, finally after a few weeks they agreed the pregnancy was gone and I was not in danger as it had 'naturally resolved'. I was grief stricken.	Claire Haresnape	10	my story group	1
	my story group\117	Emotional distress\counselling	14	14	0	. I had counselling throughout the first cycle and through our loss, every week. Our counsellor was fantastic.	Claire Haresnape	10	my story group	1
	my story group\117	Emotional distress	15	15	0	I had depression and anxiety and had been signed of work prior to our IUI commencing, the miscarriage from our IVF just compounded that	Claire Haresnape	10	my story group	1
	my story group\117	Emotional distress	19	19	0	Slowly each week I have gained a bit more confidence but the anxiety is still there, I'm 22 weeks + 2 days pregnant, and thrilled, due on 19th May 2008, with one baby but our journey will never leave us, nor it's scars. I've seen my GP each week for anxiety. I'm now 33 and DH is 37. I am well aware some have not yet felt the joy of a positive test or worst have	Claire Haresnape	10	my story group	1

						done and lost more than we. Infertility hurts, it dissolves confidence, it rules your life, it isolates you and you loose elements of your personality				
	my story group\115	Emotional distress	2	2	0	I was devastated because losing the baby hadn't even entered my head. I have been trying again since but I had to have 2 D&C's which delayed things and then I was put on clomid again in September	Claire Haresnape	10	my story group	1
	my story group\114	Emotional distress	1	1	0	This is the first time I have written anything about what I'm feeling in relation to our 'unexplained' infertility. I have just turned 32 and we have been ttc for nearly 2 years (I know I'm still relatively young and it's only been 2 years, but it doesn't get any easier does it…). I never knew what effect this would have on our lives and on my emotions in particular. I go through days when I want to hit something with pure anger and frustration. And others when I just want to curl up under the duvet and never come out – fortunately the good days still outweigh the bad days, but the unpredictability of the bad days really gets you down.	Claire Haresnape	10	my story group	1
	my story group\114	Emotional distress\Not feeling in control	1	1	0	And now I feel like I am totally failing and there is absolutely nothing I can do to improve the situation – I can't study harder, I can't work longer	Claire Haresnape	10	my story group	1

						hours, I can't be a better daughter or wife. Usually I know the answer to things and know what I have to do to improve the situation. But not about this. I've always been known as the 'rational' friend, the person to turn to in need, the person who can work through things logically.				
	my story group\114	Emotional distress	1	1	0	And now I don't feel like that at all. In fact on the bad days I hate what I have become – I hate being the whinger, the cry-baby, the drama queen. I hate those surreptitious thoughts that go through my head when I see families with lots of children and think 'can't you give me one of those?'; or the false smile that I have to ensure is on my face when someone else tells me they are pregnant. I'm not like that – I've always been told I was a good person and loyal and a reliable friend. And I just don't feel like that any more. And the clomid is making it worse. My goodness! Talk about upsetting my emotional balances! I don't know what it is doing to me (I'm on my 5th month of it), but I'll be very glad when I can stop taking it. I feel like a loonie! Only 1 more month to go…. And then what? Then I get drawn in to the world of IUI and IVF – oh what joy. I read those other posts that you lovely ladies have written,	Claire Haresnape	10	my story group	1

						and although I'm really happy for you guys that you are moving forwards, I have to say it fills me with dread. I keep thinking of all those orphaned children in the world and wonder whether I should just accept that we can't have kids and adopt a whole host of them. Anyone else ever feel like that? I just read the factsheets today that this Network provides and they are really useful – they made me realise that it was ok to feel like this was one of the worst and hardest things I've ever had to deal with. And it really is like a bereavement – every month I feel like a little bit of me dies and disappears. Every month you have that awful wait, knowing in your heart of hearts that nothing has happened, but still that hope until the first signs of your period arrive. One friend who has been through all this uses one word to describe it, and I agree with her…..Devastating. Mayb e I'm being a drama queen again, but that's how I quite often feel – devastated. I looked up infertility support on the website today as yet another friend (who got married 2 weeks after us) told us she was pregnant.				
	my story group\1	Emotional distress	3	3	0	As i'm sure most of you will understand we were devasted and my DH	Claire Haresnape	10	my story group	1

	13					feels awful - he even told me I should leave him and find myself a 'real man'. Felt so bad and no matter how hard I tried I couldn't make him feel better. Scary to think of the journey ahead but I want children with my DH not anyone else...				
	my story group\112	Emotional distress	3	3	0	I miscarried painfully and 'completely' (as they wrote on my medical records) on the 8th January 2008 at 11 weeks and 3 days . As I lay on the bathroom floor waiting for the ambulance with T crying next to me I had that context for my fears and knew without a doubt that I would have done anything to stop that blood flowing so I could hold onto our baby. It was at that moment that I think I truly understood what it felt like to want a baby with every part of me. That feeling just grows every m	Claire Haresnape	10	my story group	1
	my story group\112	Emotional distress	6	6	0	. I remember not really understanding what she was saying and as soon as I heard menopausal I felt my heart stop- I tried to write things down but she spoke so quickly. I remember saying 'does this mean I will have an early menopause?' and she said 'yes probably'.... and I said 'but I'm 31 years old'.... then I put the phone down	Claire Haresnape	10	my story group	1
	my story group\112	Emotional distress	7	7	0	We hardly slept that night and tears came and just wouldn't stop. A badly executed phone call, delivered at the wrong	Claire Haresnape	10	my story group	1

						time in the wrong way, without a good knowledge of fertility to inform it left a legacy of fear that I don't think has left me. We got the first appointment with 'her' the next day and she seemed surprised that we were so upset and even said 'I didn't tell you that you had ovarian failure'... and so she referred us to the fertility clinic				
	my story group\112	Emotional distress	14	14	0	Friends pregnancies came and went, I trod a regular path to BabyGap and started to noticed them looking scared and sad when they told me they were pregnant and I was terrified when they told me, because I couldn't feel the happiness they deserved, the jealousy was just too strong. I now have a pregnancy radar that can spot a impending bump from a text message (How did you know from a text that said 'We are really well thanks'.. said T ?)	Claire Haresnape	10	my story group	1
	my story group\112	Emotional distress\financial loss	16	16	0	So now we need to decide when we start IVF with all the financial (not eligible despite working for the NHS!), physical and emotional baggage that is wrapped up in that package of hope.	Claire Haresnape	10	my story group	1
	my story group\111	Emotional distress	5	5	0	Started to feel really low and tearful so went to GP who said i was suffering with depression but didnt want to prescribe anything, went home and really felt i couldnt cope so rang fertility clinic to ask for help, the nurse	Claire Haresnape	10	my story group	1

						called me back and i explained how i felt, she replied "dont worry its not the end of the road for you, your DH can have a sperm retrieval opp" i explained my husbands SA was normal and she said " i am afraid not he has no sperm at all, the GP must have read it wrong" I thought i was going to faint on the phone, i only phoned to say i felt low and got this news!!! I had to break the news to my DH when he got home from work and he was devastated. We then waited two weeks to see a consultant to explain things				
	my story group\109	Emotional distress\feeling isolated	8	8	0	Has anybody out there, had a similar situation? I really feel like I need to talk about this, but like most people on here none of my family or friends understand.	Claire Haresnape	10	my story group	1
	my story group\108	Emotional distress	1	1	0	It is great to know that I am not alone in this desperate situation but sad that there are so many of us out there.	Claire Haresnape	10	my story group	1
	my story group\108	Emotional distress	8	8	0	am SO unbelievably happy for her but man was it difficult the first few months of her starting to show. It was just so hard. I just wanted to hide. With time I am getting better about it but it still is just so difficult. She is my best friend and we depend on each other so much as our families are far away but our friendship is so strained right now. She is too scared to acknowledge that she is	Claire Haresnape	10	my story group	1

						pregnant. So afraid she is going to lose this one so we just don't talk about it at all. As if it's not there. I feel like such a horrible friend. I know she doesn't feel that way and she can appreciate a bit of what I am going through having had 2mc's like me but she is now pregnant and I am not. I am so angry that it all got taken away.				
	my story group\106	Emotional distress	26	34	0	For the first time in my life I was completely devastated, I always thought I was a strong person and able to take what life threw at me – I had worked for many years in rural Africa after all – what could be worse than that!!!! But this complete destruction of my dream of adopting a child was too much. I cried solidly for a week – Kleenex shares soared!!! But there was no way we could afford it even if we only lived on bread and water for a year. So adoption is on hold until we win the Lottery.	Claire Haresnape	9	my story group	1
	my story group\106	Emotional distress	53	62	0	The world went from being unfair for the not hugely rich to just unfair - full stop!!!! Life is unfair - I know that!!!!! but I´m having a really bad time dealing with this one particular issue. I´m surrounded (it feels like) by pregnant people and I can´t relate to them anymore and more	Claire Haresnape	9	my story group	1

						importantly feel incredibly isolated, as my usual sources of help and support are pregnant and how uncomfortable for all involved to pour your heart out about being childless to someone heavily pregnant!!!! Or my mother who talks continually about my nephew!!!!!!!!!!! Or my sister who conceived the first month of trying!!!!!!!!				
	my story group\106	Emotional distress\feeling isolated	53	62	0	The world went from being unfair for the not hugely rich to just unfair - full stop!!!! Life is unfair - I know that!!!!! but I´m having a really bad time dealing with this one particular issue. I´m surrounded (it feels like) by pregnant people and I can´t relate to them anymore and more importantly feel incredibly isolated, as my usual sources of help and support are pregnant and how uncomfortable for all involved to pour your heart out about being childless to someone heavily pregnant!!!! Or my mother who talks continually about my nephew!!!!!!!!!!! Or my sister who conceived the first month of trying!!!!!!!!	Claire Haresnape	9	my story group	1
	my story group\105	Emotional distress	1	1	0	New to INUK so thought I provide some background to my story and hope to speak to individuals who	Claire Haresnape	9	my story group	1

						understand the pain I am going through.				
	my story group\105	Emotional distress	2	2	0	We also had many stresses that year, with the death of my mother-in-law, nan & auntie - so knew this might be effecting things	Claire Haresnape	9	my story group	1
	my story group\105	Emotional distress	3	3	0	Everything looked fine at the early 7 week scan and there was a lovely tiny heartbeat, however that very evening I started to bleed. I went back 4 days later and still everything looked fine, but that evening I M/C. Thankfully my husband was there with me and we grieved together.	Claire Haresnape	9	my story group	1
	my story group\105	Emotional distress\feeling isolated	5	5	0	At the moment I am feeling very low and lonely. I only have 2 friends now that don't have children and thats because they aren't yet married and ready. Our social life has come to a stand still and I really miss having girlie chats over the phone. It seems that everyone else is just too busy with their family. When people do ring, they don't know how to speak to me and keep saying it will happen or making silly little jokes like are we doing it right!!! I know they are trying to help, but really they have no idea. It seems that no one understands, I did have one friend in a similar situation but guess what! - she fell pregnant and now has a lovely daughter.	Claire Haresnape	9	my story group	1
	my story	Emotional distress	6	6	0	When will it be my turn???!!!	Claire Haresna	9	my story	1

	group\105						pe		group	
	my story group\104	Emotional distress	1	1	0	I'd stopped buying pregnancy test kits, but this time, I was late. I had to be pg - it was poetic timing, perfect symmetry from the day we came to look round the venue. Of course, life doesn't work like that and I was on the edge of tears all day, feeling terrible for focusing on my own upset and not on the couple's happy day. It took another few months for us to finally go to the GP	Claire Haresnape	9	my story group	1
	my story group\104	Emotional distress	1	1	0	We were really in denial and I regret this so much now.After initial consultations and tests with the GP, we were referred to our local hospital, but the first visit was an agonising three months later and by now the clock and the panic were ticking louder and louder in our heads	Claire Haresnape	9	my story group	1
	my story group\104	Emotional distress	1	1	0	We arrived home exhausted and tearful, took off our coats and the phone rang: DH's brother telling us we were going to have a niece or nephew. We had another nine months of hospital visits and tests, all of them involving long waits in packed waiting rooms.	Claire Haresnape	9	my story group	1
	my story group\104	Emotional distress	1	1	0	I felt really hurt, but it's hard for other people to genuinely understand the agony of IF. I know that they are probably trying to spare our feelings and don't like to bring up something that must upset us, but I wanted to	Claire Haresnape	9	my story group	1

						have those conversations and to talk with people I loved about what we'd lost. I at least wanted a hug from our parents and the chance to cry with them, but I don't think they knew how to handle it. I also think the media gives a false impression that IVF is an easy option. We had lots of comments along the lines of "you can try again" or "it'll be your turn soon". As if it was a case of keeping up with the Joneses.				
	my story group\102	Emotional distress	4	4	0	It was almost exactly a year from starting to ttc that we visited our GP and asked the questions. Luckily we had a great GP then who didnt fob us off with the whole "relax and i'm sure it'll happen" rubbish, but referred us for the inital tests straight away. That is when our whole world began to crumble..	Claire Haresnape	9	my story group	1
	my story group\102	Emotional distress	5	5	0	Dh's results however were not so reassuring and we were given the devastating news that he has an extremely low sperm count which is what was accounting for our failure thus far. Initially it was our GP that delivered the news of the result and he did so with great compassion	Claire Haresnape	9	my story group	1
	my story group\102	Emotional distress	5	6	0	we were subsequently delivered the bombshell that in order to stand any realistic chance of conceiving we would need ivf. Strangely at this stage i dont	Claire Haresnape	9	my story group	1

						remember feeling surprise d or anything other than accepting. Looking back i think there was part of us that was expecting this, after the bad initial result and given the fact that my dh has a history of undescended testes (which wasnt identified until relatively late in his childhood and therefore not corrected as early as it should have been), and another part of us that were in shock and numb really.				
	my story group\102	Emotional distress	7	7	0	After the SA results dh and i seriously grew apart. I was a like a demon possessed, desperately searching the web for info and stories of ivf and reading every book going. He on the other hand refused to discuss any of it, completely shut me out of everything and stuck his head in the sand (plus he didnt want me to talk to anyone either, got very upset if i mentioned wanting to speak to any family or friends and all but forbid me to even speak to my mum!!). Eventually the strain became too much and we split.	Claire Haresnape	9	my story group	1
	my story group\102	Emotional distress	9	9	0	We spent a weekend of tears and immense stress and actually ignored all advice to stop the medication until we were able to speak to a consultant at the colposcopy clinic, which wasnt until the Tues (we were	Claire Haresnape	9	my story group	1

						originally told all this on the Friday mid afternoon). When we finally did we discovered it wasnt necessary to interupt the cycle and any treatment for the abnormal cells could be delayed until we werent cycling or pg!				
	my story group\102	Emotional distress	10	10	0	Luckily my best friend came over to be with me when the result came in. It wasnt good. The result showed the level had dropped drastically indicating m/c was imminent. The clinic told me to stop taking the pessaries and hopefully (!!) bleeding would start within a few days. Luckily i guess, it did. Pg for one week and only a few hours of that being excited (the rest stressed and anxious) Not a happy time.	Claire Haresnape	9	my story group	1
	my story group\102	Emotional distress	13	13	0	Since then i've gone from feeling fine to feeling lost and scared, empty and devastated all over again. Initially i think i dealt with things fairly well	Claire Haresnape	9	my story group	1
	my story group\102	Emotional distress\counselling	13	13	0	The counsellor was 'happy' with how we were coping and i felt confident in the way forward.	Claire Haresnape	9	my story group	1
	my story group\102	Emotional distress	13	13	0	The last couple of weeks have seen a re-emergence of the anger and frustration, upset and tears	Claire Haresnape	9	my story group	1
	my story group\101	Emotional distress	4	4	0	At this point i'd had 2 years of monthly disappointments so said to hell with it, we'll just go for broke and go to a private clinic. Thankfully we did and in August 07	Claire Haresnape	9	my story group	1

						after an initial meeting we started 3 cycles of IUI. Unfortunately we got 3 BFN's. After hitting a big low point we decided to go for IVF and were just about to start Nov 07 when I got abnormal results back from a smear test and had to go in for a biopsy.				
	my story group\101	Emotional distress	5	5	0	was so shocked and hadn't prepared myself at all for the outcome. At this point I turned into a blubbering mess, it was just one set back too many. Thankfully my nurse (who is a total angel) phoned round all her contacts and got me booked in the next week for the dilitation which meant we could crack on with the drugs, I went from feeling totally desperate to being on cloud 9 within 24 hrs!!!	Claire Haresnape	9	my story group	1
	my story group\100	Emotional distress	6	6	0	In June 08 we started our first IVF cycle. I had just started taking the DR inhaler when I got a letter saying that a smear test I had had 3 months before showed severe abnormal results. We therefore had to cancel that cycle whilst I had treatment. I was devastated. The following week one of my closest friends announced her pregnancy. I was even more devastated! Then on the day that I got the letter saying that they had removed all of the abnormal cells, had a clear margin and there was no sign of cancer, my parents split up. More	Claire Haresnape	9	my story group	1

						devastation.				
	my story group\99	Emotional distress	3	3	0	I am desperate to know if anyone has had the New treatment, Array CGH. I am due to start the treatment in early March.	Claire Haresnape	9	my story group	1
	my story group\97	Emotional distress\being in control	3	3	0	. So I took matters into my own hands, did some research on the internet and started taking 50mg B6 daily to increase my DPO's. This worked for 3 months and I got 8/9 day LP however when realised it was giving me diarrhoea I stoped taking it and my DPO's dropped straight back down to 7.	Claire Haresnape	9	my story group	1
	my story group\97	Emotional distress	4	4	0	This time I was told under the PCT guidlines for my area I have to of been trying for 18 months for a referral as there are no grounds for me to be referred. I left very upset, without my referral, and with most of my questions unanswered	Claire Haresnape	9	my story group	1
	my story group\97	Emotional distress\being in control	5	5	0	I took matters into my own hands again - this time consulting a proffessional and started acupuncture and chinese herbal medicine.	Claire Haresnape	9	my story group	1
	my story group\97	Emotional distress	20	22	0	Over the course of the year we've had a roller coaster of emotion. If I'm honest DH isn't as worried as me. He's yonger and in less of a rush, he's more patient, he can't hear his clock ticking, he's more worried about money, he's got an exciting new job which he's really enjoying and if I'm honest he was quite dismissive and it seemed that he was releaved at the start	Claire Haresnape	9	my story group	1

						of the year when we didn't get lucky. I was really careful in approaching the subject with DH when we started out trying. I didn't want to push him into anything he wasn't ready for so I was really hurt with his attitude towards our failure, when we were supposed to be doing this together and it was a joint decision to start a family. Over the year things have moved on, I've regularly broked down - tears most month, the odd hissy fit for no reason and a couple of good heart to hearts. I'm still hurt that he never seems upset. Does that make me weird? It's not that I was to see him upset but I want to see that he cares. He's being more supportive as time goes on and I'm sure it's just a mars venus thing. Sometimes it seems he just saying the right thing but doesn't really feel it but then his family are dryer than mine emotionaly. It's not exactly the first year of married life we'de hoped for.				
	my story group\94	Emotional distress	3	3	0	. I asked my Dr if I could have Luteal Phase Defect, but was told such a condition did not exist. To cut a long story short, a series of very difficult losses happened in quick succession in 2006, meaning infertility was forced to take a back seat, although the pain continued to bubble under	Claire Haresnape	9	my story group	1

						the surface. In 2007 my marriage hit a really rough spot. The strain of everything was begining to take it's toll, and had it not of been for how strong my DH and I are as a couple, I think we could have broken up. We've managed to get our marriage back on track and despite the ongoing pain of infertility, are stronger than ever. We've moved from Swindon to Oxford, somthing we've always wanted to do and have built a new life for ourselves here. Last year, we went to a clinic called Viveka in London, which takes a holistic approach to infertility. It was confirmed through a hormone profile that I do have LPD and when I told the Dr in London that I had perviously been told it did not exist, he was horrified.				
	my story group\94	Emotional distress\being in control	3	3	0	I were so hopeful that finally we had gotten to the bottom of our infertility. (I had finally spotting). We have changed our lifestyle, I am having accupuncture, we've cut out the caffeine, booze and are eating healthily	Claire Haresnape	9	my story group	1
	my story group\94	Emotional distress	3	3	0	Since then there have been no more positives and I feel like I am loosing heart. We are due to have our first round of IVF in May, but I cannot get my hopes up. After 6 and a half years of dissapointment I feel emotionally exausted and	Claire Haresnape	9	my story group	1

						despite having a good (but v stressful) job, loving family and friends, and most importantly a wonderful husband, I still feel very low and lonely. It's like I am grieving for the child that hasn't been born. Each month is an emotional rollercoaster and I feel like I am arriving at the start of IVF exausted.				
	my story group\93	Emotional distress	4	4	0	In February of this year we were told that IVF with ICSI would be our only chance of having a family. As I drove home from the clinic my sister phoned to say she was pregnant with her first baby. I was overjoyed for her but don't mind admitting that I also shed a little tear for myself	Claire Haresnape	9	my story group	1
	my story group\92	Emotional distress	1	1	0	failed IUI attempts. We have recently had a failed IVF cycle. The awful thing was, alhtough we had 8 eggs, only 4 fertilized and none divided. The Doctors have told us that we have poor egg quality.	Claire Haresnape	9	my story group	1
	my story group\91	Emotional distress	5	6	0	I have revolutionised the diet, my partner is taking zinc and selenium and alcohol is down to a minimum. We have approx 3 months before the next step and I'm feeling more than a little overwhelmed about what's on the horizon having read various posts on this site and on others. I'll keep posting if there's anything to report, I'm a bit lost at the moment to be honest. This wasn't part of the plan!	Claire Haresnape	9	my story group	1

	my story group\91	Emotional distress\being in control	5	5	0	I have revolutionised the diet, my partner is taking zinc and selenium and alcohol is down to a minimum. We have approx 3 months before the next step and I'm feeling more than a little overwhelmed about what's on the horizon having read various posts on this site and on others.	Claire Haresnape	9	my story group	1
	my story group\89	Emotional distress	4	4	0	devastated by this blow. I burst into floods of tears and dh took me home, both of us feeling totally numb. 10 days later (July 2006) I was back in for my op. A different surgeon did the procedure and told me in the recovery room (when I was still drowsy from the drugs!) what she had found. She had removed my polyp but during the lap & dye had found that I had endometriosis. The dye drained through my right tube but my left tube was totally blocked and would not drain at all. She also found a fibroid and lasered off my endo. She said I would most likely need IVF but that we should keep trying for another 3 months before being referred for treatment! I just wanted to be with my dh - not in the recovery room on my own - and when I got back to the ward he just held me in his arms and I cried and cried	Claire Haresnape	7	my story group	1
	my story group\87	Emotional distress	8	8	0	At this point very depressed . Hit rock bottom. Sure we would not have children! Signed	Claire Haresnape	7	my story group	1

						off work for 2 weeks				
	my story group\87	Emotional distress	10	11	0	Also stopped charting cycles as absolutely obsessed with it and knew my cycles were fine! 3rd April 2007- DP first SA. Stressful++++	Claire Haresnape	7	my story group	1
	my story group\87	Emotional distress	15	16	0	22nd Jan 2008- Results of SA even lower again. Advised by reg that we need ICSI, but won't be eligible for funding until I turn 30. Only 27 at this point. Devastated. Cried all way home. Poor DP didn't know what to do! No money so self fund not an option! Also getting married in 2009! Big long gap.....continued trying. Knew when I was ovulating as cycles like clockwork by now! Lots of hope each month but nothing! Threw myself into wedding plans but hurting lots. Desperate for a baby. All my friends have at least 1 if not 2 by now! Depressed on and off over next year.	Claire Haresnape	7	my story group	1
	my story group\87	Emotional distress	34	36	0	4th Dec 2009- Scan at 7+4. No heartbeat although sac and fetal pole evident. Quite likely not alive. Wait for further scan in 3 days. Devastated. Searched online+++. Some reassuring stories but I wouldn't allow myself to get hopes up! DH more positive than me! 17th Dec 2009- Our world comes crashing down. Embie def not alive. Has started to collapse! DEVASTATED! Stop progesterone and	Claire Haresnape	7	my story group	1

						await m/c over xmas! 3rd Jan 2010- Still no m/c. The wait is now becoming unbearable . Will				
	my story group\86	Emotional distress	1	1	0	We had ICSI and it failed in the way it does for the majority of women, the embryoes failed to implant. I had been so optomistic and lost sight of us having a one in three chance of it working. I was in absolute pieces when I started bleeding - I hadn't even realised that is what would happen if it went wrong!	Claire Haresnape	7	my story group	1
	my story group\86	Emotional distress\being in control	3	3	0	I've just read a book called Taking Charge of Your Fertility by Toni Weschler - it's an International Bestseller. I wish I'd read this before going to the doctor. There's so much useful information in there about how to maximise your chances of conception. I'm going to follow it's recommendations and if they don't work I haven't wasted any money or taken any drugs - it tells you why ovulation tests might not work for you and says ttc on day 14 of your cycle might never work for you too - please read it if your ttc. It won't do you any harm and it's very insightful.	Claire Haresnape	7	my story group	1
	my story group\86	Emotional distress	19	19	0	On our 2nd cycle when we went back in for the embryo transfer we were told three embryos had survived. So they were happy to transfer two back in and wanted us to	Claire Haresnape	7	my story group	1

						decide there and then what to do with the 3rd one. Ie did we want to pay for it to go into frozen storage - which is costly and the chances of it surviving all the way through to natural birth are small - or did we consent to it being destroyed. We had to decide there and then in the waiting room (me crying and looking shocked in a room full of strangers looking scared)				
	my story group\85	Emotional distress	1	1	0	Cycles appeared to return to normal then april to june cycle 7 weeks - think this is due to huge stress and unhappiness at work	Claire Haresnape	2	my story group	1
	my story group\85	Emotional distress	1	1	0	Panic set in as thought a little bleeding not a problem, however, apparently it is if you haven't had any bleeding at all by this point. After hideous day at 2 A&E departments (won't go into that L) at 5.45pm, it is confirmed that our baby had died at about 8 weeks and that I had had a missed miscarriage i.e. your body continues to think you are pregnant after the baby has died. Total and utter devastation, I cannot describe the grief and despair and the complete and utter feeling of loss – how completely unfair to allow us to lose our miracle baby. How could that happen? I decided to have the surgical procedure, Evacuation & Removal of Products	Claire Haresnape	2	my story group	1

						related to Conception (ERPC) – how heartless a term is that? Our baby being referred to as a "Product related to Conception". This happened on the 9th October in a Day Unit where I was surrounded by people killing their babies, terminations, all of them				
	my story group\85	Emotional distress	1	1	0	I sobbed and howled, my husband and I were inconsolable, our hearts were broken. Seeing my husband cry was also extremely distressing. It took a few weeks to get back to any sense of normality,	Claire Haresnape	7	my story group	1
	my story group\85	Emotional distress	1	1	0	I am terrified of the failure again, although we do have enormous faith in our doctors this time.	Claire Haresnape	7	my story group	1
	my story group\84	Emotional distress	3	3	0	I bought a Persona and we bought a puppy – we thought it would be good practice for a baby – I have to say I'm so glad we did as she is my comforter when I have dark days and all I want to do is curl up and cry	Claire Haresnape	2	my story group	1
	my story group\84	Emotional distress	5	5	0	This was such a shock, I was only 33 and otherwise healthy, my mum did go through the menopause in her early to mid forties, but I still thought I had a couple of years before things got difficult.	Claire Haresnape	2	my story group	1
	my story group\84	Emotional distress	7	7	0	I was in shock, I bust into tears, my mind raced, did I have any eggs, would be need to consider a donor egg, where did you get one from. Would we ever have little Josh? I admit I	Claire Haresnape	2	my story group	1

						do have a habit of jumping to the worse case scenario, but when you don't know what is happening I think you do imagine the worse.				
	my story group\84	Emotional distress\feeling isolated	13	13	0	I joined IFUK to remind myself that I'm not alone, and I'm encouraged by the stories on here.	Claire Haresnape	2	my story group	1
	my story group\83	Emotional distress	1	1	0	I have had the barrage of poking, probing and tests from ultrasounds to HSG to a lap last month with the dreaded result of unexplained infertility.	Claire Haresnape	2	my story group	1
	my story group\83	Emotional distress	1	1	0	Its just starting to get to me now, with most of my friends and family being able to conceive at the drop of a hat. They are so happy with their babies that they are difficult to talk to as they don't really understand and you get the 'just relax Im sure it will happen soon' I know they mean well but it is hard to keep smiling sometimes. The doctors can be very insensitive and quite dismissive, they see you for 5 mins every 4or5 months and cant wait to get you out the door.	Claire Haresnape	2	my story group	1
	my story group\83	Emotional distress\being worthy	1	1	0	I try to think of the bigger picture, there a many people in the world a lot worse off than me.	Claire Haresnape	2	my story group	1
	my story group\82	Emotional distress	4	4	0	We have subsequently had three unsuccesful attempts at IVF using an English clinic. This was alas a really awful experience as I was put through cycles which were never going to work as my uterus was once again	Claire Haresnape	2	my story group	1

						being distorted by fibroids which had reoccured. We had asked them constantly to rescan me to check this as I feared this had happened. Nobody knows your body as you do and my periods had become so heavy and lengthy that I simply knew something wasn't right. The clinic pushed these concerns aside and seemed more interested in taking our money and pushing us onto another cycle.				
	my story group\82	Emotional distress	5	5	0	Alas we found out two weeks ago that this attempt has also failed and to be honest its really floored me. Up until now I've managed to keep quite positive and hold my head up but I really feel completely devastated. I don't know if anyone else has found this but it seems to be getting harder the more attempts we make.	Claire Haresnape	2	my story group	1
	my story group\81	Emotional distress	1	1	0	. I decided to take progestrone afterwards. lack of information caused me to believe I was pregnent as didn't know progesterone stopped period. Found out on internet. Stopped it and period came two days later. MASSIVE DISAPPOINTMENT and deep sorrow.	Claire Haresnape	2	my story group	1
	my story group\81	Emotional distress	1	1	0	feeling too confused and also want to give chinese herbs more time to work .	Claire Haresnape	2	my story group	1
	my story	Emotional distress	4	4	0	The doctor then asked me what I would like to do. I	Claire Haresna	2	my story	1

	group\80					felt under extreme pressure to make a decision then and there, which was impossible to do without DH. We hadn't really talked about IVF at this point and didn't really understand what it was all about. The doctor told me it was a very stressful and emotional thing to undergo and suggested I talk to one of the fertility nurses before leaving. This I did, and was given lots of help and advice and support-in fact she gave up a whole hour of her precious time to talk to me as she could see I was worried and upset.	pe		group	
	my story group\80	Emotional distress	5	5	0	The first time I injected I was absolutely terrified of getting something so important wrong. I wished they had given us practice injections using oranges or something. We were given a DVD about how to inject, but it's one thing understanding a DVD and another thing actually doing the practice! I will admit I got myself in a right state about it all-probably due to the DR hormones flying around my body and did my first injection in floods of tears with DH trying to calm	Claire Haresnape	2	my story group	1
	my story group\80	Emotional distress	11	12	0	On day11 I was spotting, and by day 12 I had a full blown heavy AF. I tried to stay positive as I knew that sometimes you can have implantation bleeding, but in my heart, I knew that AF was too heavy and I was losing our little "Oreos"	Claire Haresnape	2	my story group	1

						It was at that this point that everything hit me and I cried unconsolably. I am lucky enough not to be working at the moment and so was able to fall apart in the comfort of my own home. I texted DH throughout the day telling him everything as he was at work. He kept telling me to try to stay positive until after the test. I just got angry and then said I needed sometime to myself and that I was going for a walk.				
	my story group\79	Emotional distress	1	1	0	Sadly I am to follow a different route to that of my friends and family. It may sound odd but in a way I thought that we may have problems but at the time I had no reason to think this.	Claire Haresnape	2	my story group	1
	my story group\79	Emotional distress	5	5	0	At first I was excited as for the 1st time in years I felt like I have a chance of becoming a mummy but then the anxieties followed. I almost had to grieve for the fact that we cannot have a child naturally and I am also scared that my chances of having a child are now so much more limited	Claire Haresnape	2	my story group	1
	my story group\79	Emotional distress\feeling isolated	5	5	0	Knowing no one who has gone through the same thing I have found this a very lonely time.	Claire Haresnape	2	my story group	1
	my story group\78	Emotional distress	4	4	0	What a bombshell! And what a mixture of emotion. I have had many ups and downs since we were originally told last October 09. My husband has did not really speak about our news and I suppose I had to let him	Claire Haresnape	2	my story group	1

						come to terms with it in his own way as it's male factor infertility, all my tests came back normal.				
	my story group\78	Emotional distress	10	10	0	So how am I feeling??? Nervous, anxious, excited, frightened, hopeful. But mostly a bit numb. I really am not sure why I am coping with it so well. I have bad days, where I just start to cry but on the whole my opinion has been if it is going to work it will work	Claire Haresnape	2	my story group	1
	my story group\78	Emotional distress\financial loss	10	10	0	He said that my mind is overactive and no matter how many relaxation techniques I do will not stop that (plus the fact that they all cost money that we do not ha	Claire Haresnape	2	my story group	1
	my story group\78	Emotional distress\feeling isolated	12	12	0	It's just nice to have somewhere to put my thoughts and feelings. It just helps me to write about it. Can't really explain it to my friends and some of my family have not even asked me how things are since the day I told them we could not have children naturally. I suppose it's their way and they feel they don't want to ask, I don't know! I just feel like they would not understand anyway.	Claire Haresnape	2	my story group	1
	my story group\77	Emotional distress	2	2	0	We were both very upset when the results came back; his count and progressive motility were both low, but what was particularly worrying was the morphology (0% normal, summarised at the bottom of the letter as severe teratozoospermia).	Claire Haresnape	2	my story group	1

	my story group\77	Emotional distress	2	2	0	What alarmed me was his advice for us to start trying straight away, give it 6 months (not long at all!) then consider IVF with ICSI.	Claire Haresnape	2	my story group	1
	my story group\77	Emotional distress	3	3	0	This has all happened in the space of a month and I feel so overwhelmed with it all.	Claire Haresnape	2	my story group	1
	my story group\77	Emotional distress	4	4	0	. She's always there when I need a good cry or to rant about how unfair it all is. Unfortunately my Mother-in-law's reaction "Oh well, it's not the end of the world," and "well, you can always adopt then" was very unhelpful as I'm really not in a place to be thinking this way	Claire Haresnape	2	my story group	1
	my story group\77	Emotional distress	4	4	0	Mostly I feel very sad and alone, surrounded by friends who chat away about babies, and more and more announcements of pregnancies are made. Since we got married I regularly get asked the question, "so when are you having a baby?" which I never used to mind but now makes me want to burst into tears.	Claire Haresnape	2	my story group	1
	my story group\77	Emotional distress\feeling isolated	4	4	0	Mostly I feel very sad and alone, surrounded by friends who chat away about babies, and more and more announcements of pregnancies are made. Since we got married I regularly get asked the question, "so when are you having a baby?" which I never used to mind but now makes me want to burst into tears.	Claire Haresnape	2	my story group	1
	my story group\7	Emotional distress	4	4	0	As you can imagine we were devastated and I don't think I stopped	Claire Haresnape	2	my story group	1

	6					crying all weekend. Being so far away from family also was very hard, although I've kept all this away from my Dad. We lost Mum last year and he has had a lot to deal with and I don't want him worrying about me at the moment. I could have done with a good cry and natter with my wonderful Mum that day though, I can tell you.				
	my story group\76	Emotional distress	7	7	0	For me, having lost mum, I found it devastating that nothing of her/me would be passed on and that made me so very sad.	Claire Haresnape	2	my story group	1
	my story group\76	Emotional distress\being worthy	10	10	0	Gosh this story all sounds very blaze, but believe me, its all been very bleak and a hard decision to make. I know I've not been through anything compared to all you lovely ladies, but I'm hoping that things work out for us as the last couple of years have been so horrendous for us, that this was the final straw and we're just hoping that our luck changes.	Claire Haresnape	2	my story group	1
	my story group\75	Emotional distress	4	4	0	Completely freaked out that consultant thinks there could be a problem.	Claire Haresnape	2	my story group	1
	my story group\75	Emotional distress	4	4	0	Devastated, starting to drift apart from DH as he wanted me to stop trying.	Claire Haresnape	2	my story group	1
	my story group\75	Emotional distress\financial loss	4	4	0	Couldnt afford to do private without a loan so decided to wait 18mths to get to top of waiting list.	Claire Haresnape	2	my story group	1
	my story group\75	Emotional distress	5	5	0	Spring 2008, IVF 1 used buserlin and menopur and was devastated again when only got 3 follicles	Claire Haresnape	2	my story group	1

	my story group\75	Emotional distress	5	5	0	. Had second BFN just before Christmas and devastated. DH gutted too but not keen to try again. Relationship going downhill at a very rapid rate.	Claire Haresnape	2	my story group	1
	my story group\75	Emotional distress	6	6	0	2009 A new year and relationship at an all time low. At the brink of divorce, start to communicate better and eventually DH agree to one final private IVF using money saved up.	Claire Haresnape	2	my story group	1
	my story group\75	Emotional distress\counselling	6	6	0	've seen a hospital counsellor to help get my head sorted out regarding infertility diagnosis, failed IVF, dealing with family/friends and trying to be positive for this last treatment and future ahead.	Claire Haresnape	2	my story group	1
	my story group\74	Emotional distress	1	1	0	This was a bit of a shocker as I had always viewed ICSI as 'the last resort' and it took me a long time to accept that we were going straight there without trying anything else first.	Claire Haresnape	2	my story group	1
	my story group\74	Emotional distress	3	3	0	on 29th. First scan showed 11 follies which increased to 23 by day 12. Bloods still showed relatively low estradiol so after a frantic day waiting by the phone to hear if we were being cancelled we got the go ahead and our EC was arranged for 13th May.	Claire Haresnape	2	my story group	1
	my story group\73	Emotional distress	1	1	0	On the one hand I felt relieved that we had a diagnosis and could now move forward and on the other I felt crushed and slightly ashamed that we couldn't be 'normal' and	Claire Haresnape	2	my story group	1

						just get pregnant like all my friends/sister have done etc. What a horrible mix of emotions. Anyway after a week or so I picked myself up and pulled myself together and told myself to stop being ridiculous, this happens to so many people it's just that nobody really talks about it.				
	my story group\72	Emotional distress	6	6	0	By this time I was seriously depressed so I was prescribed anti-depressants for a while. Thankfully i managed to come off them a few months later.	Claire Haresnape	2	my story group	1
	my story group\72	Emotional distress	9	9	0	I am trying to remain positive and patient but it's hard.	Claire Haresnape	2	my story group	1
	my story group\71	Emotional distress	5	5	0	I have 2 sisters (and 1 brother but he can't get pregnant so is OK) and at that stage they both had one child each of about 18 months. I don't think I was upset back then as I'd only just started trying, as time went on I just started getting more stressed and my endo started becoming more painful, I got referred to specialist and had a laparoscopy.	Claire Haresnape	2	my story group	1
	my story group\71	Emotional distress	5	5	0	That was in febuary this year and I'd given myself 6 months to see if I could achieve pregnancy. Needless to say - no success - it didn't help that each of my sisters have gone on to have another child each, and they did it so easily! How can three people form the	Claire Haresnape	2	my story group	1

						same gene pool have such different experiences?				
	my story group\71	Emotional distress	6	6	0	. I thought I'd been coping reasonably well but since actually starting infertility treatment (I'm on birth control now and have a scan booked on Dec 21st) I've felt worse not better.	Claire Haresnape	2	my story group	1
	my story group\71	Emotional distress	6	7	0	I feel like I have a tenuous grip on self control, like I could cryat any moment. Hopefully once I start the cycle properly I'll feel better but I feel like I'm already waiting for it to fail. Sorry, It turned into a bit of an epic but it's so good to just be able to let it all out to someone who understands.	Claire Haresnape	2	my story group	1
	my story group\70	Emotional distress	1	1	0	Like many other couples, we were like 'if it happens, it happens' and were trying to get pregnant in a very laid back way. It wasn't long until we started using ovulation kits, trying 'properly' as we called it, and it became apparent that I wasn't ovulating at the same time each month. As the months went on, and the feeling of disappointment and upset grew I began to wonder why it wasn't 'happening' for us	Claire Haresnape	2	my story group	1
	my story group\70	Emotional distress	1	1	0	Consultant explained the only way forward for us was ICIS. We had received funding for 3 IUIs and 1 cycle of IVF - The news hit us like a ton of bricks, all sorts of things were racing around my head; would I ever be	Claire Haresnape	2	my story group	1

						able to get pregnant? would we ever be a mummy and daddy? Never before had I considered my life without a family and suddenly we were faced with that very possibility.				
	my story group\70	Emotional distress	1	1	0	week. After hearing the news that we couldn't have ET because of this, I was completely distraught!! Even though I knew we had 4 embies I felt as if everything we had been working towards had been pulled further away.....yet more waiting.....was a very strange transition period.....DP was my rock!	Claire Haresnape	2	my story group	1
	my story group\69	Emotional distress	1	1	0	My Husband and i have been trying for a family for the last 4 and half years and have gone through IVF/icsi in Devon (x2 rounds) and one round at Nottingham Care all with painfully negative outcomes	Claire Haresnape	2	my story group	1
	my story group\69	Emotional distress	1	1	0	With this round we had 5 eggs, 2 were fertilized , grade 3 quality and fragmented, and both transfered. They had developed to a 3 and 7 cell division.We are both devastated and have a huge dilema as to what to do next	Claire Haresnape	2	my story group	1
	my story group\69	Emotional distress\financial loss	1	1	0	remaining funds. We have started looking at the ARGC clinic in London but with the much higher costs we would only be able to afford one cycle	Claire Haresnape	2	my story group	1
	my story	Emotional distress\feeling	1	1	0	I am in my Mid thirties.Can ayone help	Claire Haresna	2	my story	1

	group\69	isolated				me in my isolation , i have had to carry out all past procedures in secret apart from a few close friends and famlly members	pe		group	
	my story group\68	Emotional distress	2	2	0	but slowly it began to get quite emotional - month by month, it was ovulation and then waiting to see if I came on or not. Most of the time it was on time as AF has always been like clockwork...then came the disappointment and low moods. Then poor DH would be encouraging me to say we'd try next month.. It all became really draining and stressful. At the same time the whole world was getting pregnant apart from me...	Claire Haresnape	2	my story group	1
	my story group\67	Emotional distress	9	9	0	did all I could to optimise chances. 2 days post ET ended up in gynae ward with OHSS. 30th November - did the test - BFN - totally devastated. Even worse as Christmas approaching.	Claire Haresnape	2	my story group	1
	my story group\67	Emotional distress	10	10	0	23rd december - review with our consultant - very tough as she was pregnant with her 3rd child & seeing her "bump" was such a reminder of what should have been for us	Claire Haresnape	2	my story group	1
	my story group\67	Emotional distress	12	12	0	I was crying my eyes out as I was worried we wouldn't have any embies with so few eggs.	Claire Haresnape	2	my story group	1
	my story group\67	Emotional distress	16	16	0	was in bits - Dh was ok as we knew that 3 days before there was no h/b yet Junior now had one. I was worried so we saw our private consultant	Claire Haresnape	2	my story group	1

						again on the same day en route home. Again he scanned me - no problems.				
	my story group\67	Emotional distress	18	18	0	we did the test our dreams ended. Junior has gone & with him/her all our hopes & dreams. As I'd had no bleeding & pregnancy symtoms still there the shock was crippling. Our private consultant wants to see us next week to see what we should do if I haven't bled. I guess I'll have to have an ERPC	Claire Haresnape	2	my story group	1
	my story group\67	Emotional distress	19	21	0	I used to think during 4 years of ttc that if I ever got pregnant that "at least I'd know I could conceive" What a daft thing to think. Once we got our long awaited BFP all I wanted was to hold onto it. I did everything to keep it but it wasn't to be. My Dh feels that he's happy we got pregnant & it gives us hope. I just feel I'd rather have had a BFN than this loss of our darling baby. Heartbroken we are - never knew we could feel pain like this. The bottom has fallen out of our world. Our parents & family are in pieces too. WHY WHY WHY?	Claire Haresnape	2	my story group	1
	my story group\66	Emotional distress	1	1	0	After my first unsucessesful month I started to get terrible pains, which gradually became unbearable over the next month. I contacted the doctor in Thailand and he advised me to continue as planned and if we still had	Claire Haresnape	2	my story group	1

						no luck with Clomide in 3 months fly back to Thailand to see him.After 3 very painful months we headed back to Thailand to be told that I had very large cysts on both ovaries, which had been the reason for the pain and had to stop with all medication for at least 3 months!So we traveled home in despair as in both countries we had received little advice and spent a fortune				
	my story group\65	Emotional distress	2	2	0	. But that never happened. I found out he was having an affair so ended the marriage, I could never forgive	Claire Haresnape	2	my story group	1
	my story group\65	Emotional distress\being in control	2	2	0	I was now faced with making a decision about our relationship and after a couple of years decided that having a family was more important to me than a flailing relationship so ended it. Unfortunately he is still living in my house and doesn't seem to get the hint about leaving!I was now 33 years old and beginning to believe that things were never going to happen for me.	Claire Haresnape	2	my story group	1
	my story group\65	Emotional distress	2	2	0	Only there is a very sad twist to this part of the story.....my gorgeous boyfriend can't have children despite wanting them so badly. He fought a very brave 11 year battle against leukaemia which he managed to beat but it left him unable to have children of his own. Not only was he battling the	Claire Haresnape	2	my story group	1

						illness but many other illnesses too at the same time which nearly killed him over and over again.				
	my story group\65	Emotional distress	2	2	0	It's so sad that finally I meet the man of my dreams and we can't just have a family together the way we wanted to.	Claire Haresnape	2	my story group	1
	my story group\64	Emotional distress	3	3	0	I am a successful professional and I have always held the belief that if you want something badly enough you will get it with determination and grit. Whilst that may be true of career goals, it doesn't seem to be true of fertility. I am used to being in control and calling the shots. This infertility experience has left me feeling hopelessly lost and despondent.	Claire Haresnape	2	my story group	1
	my story group\64	Emotional distress\being worthy	4	4	0	People tell me to be grateful for what I have got...I am! I know that I am lucky to have a loving relationship, a beautiful daughter, a lovely home and a great job. But does that mean I have no right to expect anything else from life?	Claire Haresnape	2	my story group	1
	my story group\64	Emotional distress	5	5	0	Every month I am filled with an optimism that turns to an overwhelming sense of grief and despair when I find out I am not pregnant AGAIN. I feel that I can't go on torturing myself and that I have to stop tryin, but then I can't let go of the dream.	Claire Haresnape	2	my story group	1
	my story group\64	Emotional distress	5	5	0	.I seem to spend a lot of time sobbing - mainly in the shower so my daughter won't hear me - and the slightest little problem at work brings on	Claire Haresnape	2	my story group	1

						the waterworks again. I feel like a failure as a woman, as a wife and as a mother. It has affected my confidence, my identity and my world belief.				
	my story group\64	Emotional distress\being worthy	6	6	0	orry, I will sto going on about it now.	Claire Haresnape	2	my story group	1
	my story group\63	Emotional distress	1	2	0	I have been ttc for six months and had a miscarriage in Jan after taking Clomid. After 17 years of going back and forth to gps/consultants I finally was diagnosed with pcos/endo and fibroids and adhesions and had major surgery. Sadly I have to abandon the Clomid as I have had major side-effects and have been in hospital. Tamoxifen has been mentioned and also ovarian drilling does anyone on the boards have any knowledge of these? I feel pretty crappy at the minute six people at work are pregnant and when I hear about others on other boards getting results I just burst into tears. I feel such a failur	Claire Haresnape	2	my story group	1
	my story group\62	Emotional distress\being worthy	1	2	0	Well it's a long story so will try not to go into loads of detail and bore anyone who reads this!	Claire Haresnape	2	my story group	1
	my story group\62	Emotional distress	19	20	0	Number 2 was December 2009. I really wouldn't recommend going through ivf this time of year. This time I felt dreadful	Claire Haresnape	2	my story group	1

	my story group\62	Emotional distress	24	54	0	Started bleeding about 10 days into the 2ww, so again no surprise bfn, 6 days before Xmas. Had a really rubbish Xmas. DH & I were told by my gay brother in law that his partner had just impregnated one of their lesbian friends with a turkey baster. They used to joke about this, and I really couldn't cope with this news as it came so out of the blue. DH & I had tried so hard and spent so money, and it works for them with a turkey baster! Ahhhhhh! Number 3 was April 2010. Everyone kept telling me "3rd time lucky", and because the weather was nice and everything was springing into life I felt much more positive this time. All 10 of my eggs fertilised, and this time I stared bleeding 2 days before my test. Again no surprises, bfn again. I seemed to be getting nowhere, and getting really depressed. Number 4 was August 2010. My consultant recommended I start asprin straight away and take heparin injections and steroids during the 2ww. This is because he thinks my nk (natural killer) cells in my blood may be too high, so were stopping embryos from implanting.	Claire Haresnape	2	my story group	1

						He decided not to actually test me for this because the results can be inconclusive and very expensive. We were lucky enough to have 2 goes on the nhs, but were rapidly running out of cash so didn't want to spend even more money on something that my be inconclusive. During the 2nd week of the 2ww I turned into a mad anxious neurotic cow. I symptom spotted all the time and was convinced I was going to start bleeding every time I went to the loo. I felt horrendous and just couldn't relax, sleep or eat! When DH & I did the pregnancy test at 5am and saw a very faint line for a bfp I couldn't believe it. I couldn't wait for Sainsbury's to open so I could buy a digital test just to make sure! We had less than one day of unbelieving elation when I started bleeding that night. Despite a weekend of bed rest, I was told by the hospital that my pregnancy was no more after a blood test, the day before my brother in laws, partner's friends baby was born. We were devastated.				
	my story group\62	Emotional distress	58	63	0	Every month that passes I am dreading it more and more – I thought I would	Claire Haresnape	2	my story group	1

						feel better about it by now but I don't. I am absolutely dreading the 2ww (the injections and flying hormones don't bother me at all, just bother DH!). If the hospital could inject me to induce me into a deep sleep for the 2nd week of the 2ww I'd jump at the chance				
	my story group\60	Emotional distress\feeling isolated	1	1	0	It's nice to find somewhere when I can finally share how I am feeling with people who truly understand	Claire Haresnape	2	my story group	1
	my story group\60	Emotional distress	3	3	0	n the mean time my DH went off for his test and we were both a little shocked at how poor the results were – weren't very many, abnormally formed, swim in circles, get lost and die!	Claire Haresnape	2	my story group	1
	my story group\59	Emotional distress	2	2	0	This is my first go, doing ivf&icsi, halfway through 2ww and feeling like a complete cliche: finding the waiting unbearable. How do people keep going through this? I'm panicking about every symptom, checking the internet too much, ringing clinic for reassurance, but finding it hard to be reassured. H	Claire Haresnape	2	my story group	1
	my story group\58	Emotional distress	3	3	0	obvious problems and SA for DH, which showed only 8% right shape. Our GP just said "well I never seen anyone get pregnant with that count so I'll refer you". DH was gutted to say the least.	Claire Haresnape	2	my story group	1
	my story	Emotional distress\feeling	7	7	0	The feeling of isolation and that your whole lives	Claire Haresna	2	my story	1

	group\58	isolated				are on hold while you go through this is one that only those who have experienced it themselves will understand. I am so grateful	pe		group	
	my story group\57	Emotional distress\being worthy	3	3	0	Went through IVF in 2007 in Oxford and conceived by beautiful, amazing DD first go. Feel very guilty writing that but hopefully it gives people hope. Dreams can come true.	Claire Haresnape	2	my story group	1
	my story group\57	Emotional distress	4	4	0	Anyway, things have been awful since then. Made extra 3 embryoes with first round of IVF. Had frozen cycle a couple of months ago. 2 died and 1 was 'barely there' on day of ET so no surprises we ended up with a BFN.	Claire Haresnape	2	my story group	1
	my story group\57	Emotional distress\financial loss	4	4	0	Things really grim now because we are out of money and my hormones are utterly messed up and periods haven't returned. Need to be scanned for cysts. Feel in quite a low place now as time is ticking, my DD is getting older and money is very low	Claire Haresnape	2	my story group	1
	my story group\57	Emotional distress	4	4	0	What an awful business this all is!To top it all, my brother and sister have both announced that they are pregnant without even trying.	Claire Haresnape	2	my story group	1
	my story group\56	Emotional distress\feeling isolated	1	1	0	Hi all - I am completely new to this and suppose I am on here looking for some friends who are going through the same thing.	Claire Haresnape	2	my story group	1
	my story group\5	Emotional distress	2	4	0	After 3 m/c's I caught with a 4th and after a small bleed was told that I was	Claire Haresnape	2	my story group	1

	6					having an ectopic. I questioned this as I didnt have any of the symptoms - never the less, I was rushed into surgery (and then waited 7 hours in a side room before going in). When I was taken back to the ward I was informed that they hadnt used any of the 'preventative' methods and had just taken out my left tube. After being discharged, and for the next week, I looked into this further and was so confused by every decision made by the hospital, I wrote to the CEO of the Hospital Trust. It was just a short 5 days late when I received a phone call asking me to return to the ward asap as they thought I may still be pregnant. Confused, we went back, to be told the worse news of my life - they had made a mistake, my baby wasnt ectopic - they had terminated it in error. The following month we were hit with the final blow - my left tube was my only 'working' tube and therefore - they left me infertile.				
	my story group\55	Emotional distress	3	3	0	his was last week, and I have spend most of the week crying and trying to except that this is it, I will never have my own baby. I have just joined this website to get more of an understanding of my problem and to talk to others that are going through this awlful	Claire Haresnape	2	my story group	1

						situation and despair. To be updated when I know what the hell to do!!!				
	my story group\55	Emotional distress\feeling isolated	3	3	0	his was last week, and I have spend most of the week crying and trying to except that this is it, I will never have my own baby. I have just joined this website to get more of an understanding of my problem and to talk to others that are going through this awlful situation and despair. To be updated when I know what the hell to do!!!	Claire Haresnape	2	my story group	1
	my story group\54	Emotional distress	1	1	0	I thought I would write about my journey as I have not posted on this section before. I talk about 'my story' not just 'my IVF story'. October 1990 – DH and I first started going out with each other. July 1991 – DH got diabetes. August 1998 – got married to DH. I got my first teaching job and DH got a job with Sky TV. August 2001 –DH started to get depression so was put on anti depressants, for the next couple of years he was on/off antidepressants but only took a bit of time off work. February 2003 – DH's depression got worse; he was having longer periods of time signed off work. April 2003 – DH's last day at Sky TV. May 2003 – DH admitted to the Priory as he was very unwell, had had a complete breakdown. Whilst he was there I found out a lot of things that I did not	Claire Haresnape	2	my story group	1

						know about him and his family! August 2003 – DH moved out for 2 weeks (whilst his parents were away – he moved into their home) as we were under so much pressure, I was walking on egg shells around DH as I never knew how he would be and how he would react to what I said or did! November 2003 – Found out SSP was going to end this month so we were under yet more pressure, DH moved out again for a month as we were unable to cope with the situation. June 2004 – DH was assigned a 'vocational rehabilitation co-ordinator' to help us try to get him to be able to cope with life. She visited every month and wrote an action plan for what DH had to try to achieve by the next visit. Looking back at this time it was just so scary as DH was unable to do anything as he just couldn't cope with anything. August 2004 – DH admitted as a day patient at the Priory for next couple of months. September 2004 – DH and I decided to separate as we felt we could not carry on emotionally hurting the other person due to the whole situation. We seriously spoke about getting a divorce (I saw a solicitor) as neither of us could see how we could cope with our situation. I still loved DH but he was hell to live				

						with! July 2005 – DH officially left Sky TV (although he had not actually been to work since April 2003) July 2005 – DH went to 'Way 2Work', it's run by MIND. They support people with mental health or emotional problems to gain employment. They recognised that taking the first steps back to work would be daunting. They helped DH think about what he could do with his life and helped him organise a CV. August 2005 – DH got a part time job as a gardener, money was cr*p but at least he was going out to work. March 2006 – Spoke to doctor with our concerns about not falling pregnant yet! As we had tried on and off since we got married (when things were tough for us of course we were not trying				
	my story group\54	Emotional distress	1	1	0	February 2007 – found out my Mum had breast cancer, it felt as though my world had fallen apart.	Claire Haresnape	2	my story group	1
	my story group\54	Emotional distress	1	1	0	une 2007 – DH's best friend died in a motorbike accident. O	Claire Haresnape	2	my story group	1
	my story group\54	Emotional distress\counselling	1	1	0	Started having counselling at my clinic as felt I was not coping at all	Claire Haresnape	2	my story group	1
	my story group\54	Emotional distress	1	1	0	DH is not coping with the result. October 2008 – For the sake of my marriage I feel I need to take a break from IVF but it is just so hard as I just want to be a Mum! 26th October 2008 - I am	Claire Haresnape	2	my story group	1

						telling everyone that I am coping with the last BFN but now I am not sure if I am; as I burst into tears whilst shoppping yesterday! This then made my DH feel more vulnerable and moody as I am usually the one who copes with everything and is the strong one, so when I don't cope he of course doesn't cope				
	my story group\53	Emotional distress	2	2	0	. I literally know nothing about it and i am very scared. I'm hoping to find some support and advice on this site as it's been a very emotional time.	Claire Haresnape	2	my story group	1
	my story group\52	Emotional distress	21	21	0	Treatment showed me to be a ‘poor responder’ - we only got 3 eggs, 1 fertilised and our grade 3 embryo was transferred on day 2. We got a devastating BFN and found the whole experience very traumatic.	Claire Haresnape	2	my story group	1
	my story group\52	Emotional distress	35	37	0	January 2010 - our fifth (frozen) cycle. Two of the 5 survived the freeze and we got a BFP but miscarried at 6 weeks. Completely heartbreaking and still very difficult to cope with, baby would have been due within days of DH’s birthday. May 2010 - our sixth cycle and feeling pretty dreadful	Claire Haresnape	2	my story group	1
	my story group\52	Emotional distress	39	39	0	Feeling weary and tired of being positive and hopeful	Claire Haresnape	2	my story group	1
	my story group\5	Emotional distress	4	4	0	The results from all of this basically mean i wont concieve without IVF and	Claire Haresnape	2	my story group	1

	1					gov wont fund it, but if i wait another 2 yrs to when gov will fund it my FSH level will be too high and they wont fund it then either, so im now at the point where im trying to get my head round the fact that we wont have children and oh im likely to start menopause early.				
	my story group\51	Emotional distress\feeling isolated	5	5	0	I would love to hear from anyone who can relate, it seems like theres no one that understands. I am dealing with this and living my life but it would realy help to chat to someone,	Claire Haresnape	2	my story group	1
	my story group\50	Emotional distress	5	5	0	This was done a fortnight ago, and nothing could have prepared us for the awful shock that awaited us that day.	Claire Haresnape	2	my story group	1
	my story group\50	Emotional distress	7	7	0	Two weeks on and I am still trying to come to terms with it. I haven't even gone back to work yet, and I'm so afraid to phone them, as I won't know what to say to them, as I only started the job a couple of mths ago. My friends and family don't seem to understand, as they have children of their own, and I come from a big family.	Claire Haresnape	2	my story group	1
	my story group\49	Emotional distress	3	4	0	We were then given the devastating news that my husband had low morphology and as I had already been diagnosed with PCOS our only hope was IVF. Just had our second IVF atttempt with ICSI, only to get the devastating news on Friday that our second IVF attempt failed. I feel so	Claire Haresnape	2	my story group	1

						disappointed and upset and a bit of a failure really.				
	my story group\49	Emotional distress	6	8	0	After ET had to endure the painful 2ww. I began to examine every pain and twinge. I was so scared that I was getting period cramps. We were also scared, becuase I was told with BFP, I could get delayed OHSS, which meant I could be seriously ill for several weeks. On the day of the blood test, I felt so sick and nervous about the outcome, although we both wanted to feel optimisitic that it had worked. however, we received devastasting news of another BFN. Just felt so shocked and was crying all afternoon. Was dreading telling our family and friends that the IVF had failed again. However after the initial shock, and because of the lovely weather at the weekend we went to the park to get some fresh air and sunshine, although it was hard seeing mums with their babies, having picnics, wishing we were in their situation	Claire Haresnape	2	my story group	1
	my story group\47	Emotional distress	2	2	0	his is my first post, my storry well didnt realise that there was anyting on the web tohelp so I have been slient with my story, I found put around 2000 that I couldnt have choldren excuess is "unexplained" which as you know reall doesnt help as you can't put	Claire Haresnape	2	my story group	1

						clousure on it I went for IVF which was funded through the NS then me and my husband (ex now) went through a really bad time and I had to pull out since then I have been able to semi accepct I will never have children after findong a new partner in 2007 we now want to try and I would love to try IVF but now my docs are not funding IVF and Im over the big 40 so I can see that ifwont happen, the only alternitive is to go to a d octors who does fund the IVF or addoption route but obivously I would love to have a go myself. Just wish I could get an answer for why I cant have children as I am sure we all would like that.				
	my story group\47	Emotional distress\being worthy	2	2	0	Thanks for listening hope I havent bored you all. just wanted to note where I am at....I have been reading some of the posts ans feels nice to know there are people worst of that me.	Claire Haresnape	2	my story group	1
	my story group\48	Emotional distress	3	3	0	I think alot of this has been tipped from not really being a problem to being one due to an incredibly awful ex-boss for 4 and a half years leading to raised stress levels most of the time (alot of psychological bullying), drinking too much as a result etc etc	Claire Haresnape	2	my story group	1
	my story group\48	Emotional distress	6	6	0	We felt better and more positive coming out (am a bit low today but that's due to every flipping time I go for tea or lunch it	Claire Haresnape	2	my story group	1

						seems to be at the same time as the enormously pregnant 3 women being there too massaging their bellies!!)				
	my story group\48	Emotional distress\being in control	12	12	0	think also would like to sort out my nutrition (any tips?) and so am going to see a nutritionist next week who specialises in fertility issues etc and may be get my weight going down a bit. I'd also like to ramp up a little my exercise - I used to go the gym/run 3 or 4 times a week and now do nothing so that isn't helping and it does make me feel better!	Claire Haresnape	2	my story group	1
	my story group\46	Emotional distress	4	4	0	On Christmas Day I felt terrible and just knew it wasn't right but couldn't get scan until Boxing Day. Long story short I had had a missed miscarriage baby had stopped developing weeks ago. This was my worst experience as I opted to wait for natural miscarriage which never happened and one evening in January I was rushed to hospital heamorraging and had to have emergency ERPC but I had lost so much blood, I was anaemic and on standby for blood transfusion.	Claire Haresnape	2	my story group	1
	my story group\46	Emotional distress	6	6	0	Our relationship has suffered a lot in the past year but we are holding it together just about!	Claire Haresnape	2	my story group	1
	my story group\44	Emotional distress\counselling	5	5	0	new and also I'm having a bad time with life in general so taking the offer of free counselling up.	Claire Haresnape	24	my story group	1
	my	Emotional	6	6	0	I'm at the point now of	Claire	24	my	1

	story group\44	distress				having to try and turn my mind to accepting that I will not be able to bear children, very hard to even write this sentance down let alone trying to start dealing it !	Haresnape		story group	
	my story group\43	Emotional distress	1	1	0	hi there my name is joy and i have been with my husband for 17years married for 15years,, we av been trying for a baby for 16years after many tests we was told that there is no way on this earth that we will be able to have a baby,,, my husband has a mental illness and is on alot of medication which has coursed him to have no good sperm we was both devestated as we both really want a baby for me as a woman it is really hard as i am reminded of it every day of my life i thought i had dealt with it but i recently found out that a couple of my mates are expecting a baby and it has brought back all that hurt i want to greive but how can you grieve for summit that is not there,,,, every time i see a baby or a young child i keep thinking wish it was me i am finding things really hard to deal with right now,,, husband and i have spoken bout ivf sperm donor but i cant do that as i would feel like that i have cheated on him we have also looked into adoption and fostering but they wont even give us a 2nd look cos of my husbands	Claire Haresnape	24	my story group	1

						mental illness which i think is wrong cos he would make a wonderful dad i went to see our doctor bout havin a histerectamy but he said that no surgeon would consider me as it is not for health reasons i told him i need to grieve and that is the only way i can think of its just so hard we you see babies and children every day of your life and wishing that they was yours,,,, any way that is my story if any one can help me i would be most greatful				
	my story group\42	Emotional distress	5	5	0	We have been referred to an infertility clinic (NHS) in Chichester, West Sussex. This week has seen me hit an all time low and I seem to have been really angry / frustrated.....most unlikem	Claire Haresnape	24	my story group	1
	my story group\41	Emotional distress	6	6	0	but I feel like christmas will be ruined, especailly if i find out that i am fully infertile, or even if they dont know what it is, all i really want is one, just one child, my partner has already got a son, he doesnt live with us but visits on the weekends, i know he really wants a family, so the pressure is so massive!	Claire Haresnape	24	my story group	1
	my story group\40	Emotional distress	73	74	0	The news that my tubes were blocked was a devastating blow. That was a very difficult week; I broke down at work, crying during a 1-2-1 with my boss,	Claire Haresnape	24	my story group	1
	my	Emotional	4	4	0	having SA re done and	Claire	24	my	1

	story group\39	distress				they we are off to Cheltenham Hospital to see a fertility specialits, I am happy and I am so so grateful for this opportunity, but at the same time I am suffering with the fact that I can't conceive naturally.	Haresnape		story group	
	my story group\38	Emotional distress	5	6	0	I've cried on and off since xmas day and am now feeling very bitter and frustrated. There are reminders everywhere! I even had someone tell me I should hurry up and have children at my age! Picking up my partner's three children and seeing the mother of his children, only added insult to injury. They do not know about what we are going through so there have been lots of excuses and brave faces, something I could have done without. My partner has been brilliant and very supportive but dare I say, this is very different for him: he has three children and he is a man so I believe his understanding is limited. No one can understand this unless you have been through it yourself.	Claire Haresnape	24	my story group	1
	my story group\38	Emotional distress\financial loss	6	6	0	We are trying again at the end of this month but I worry as my biological clock is not getting any younger and we do not have an endless pot of money (nhs will not help)	Claire Haresnape	24	my story group	1
	my story group\36	Emotional distress\financial loss	1	1	0	Hi, My name is sam and I am 28. Me and my DH have been trying now for 2yrs since our ectopic in	Claire Haresnape	24	my story group	1

						2009 which ended up me having my left tube removed. Since then we have been to the doctors and they have tested us and said we have unexplainable infertility and then referred us to private fertility clinic which we can no way afford				
	my story group\35	Emotional distress	1	1	0	Hi Im Karin (33), and together with my fiance (DF) (35), we have been trying for what seems like forever. Im not sure if i am in the right place, as we have not embarked on IVF.ICSI, but they are the considerings we are having. Im in a place right now i possibly may not come back from. My emotions are all over the place and im tired, grump, snappy & depressed - and no one i know understands, they just say stop stressing, relax all will be fine - nearly 2 years and im no further!	Claire Haresnape	24	my story group	1
	my story group\34	Emotional distress	5	5	0	i'm so angry,emotional,depressed and the wonderful group of friends as i loved going out socialising .But i feel i can't do that now all my wonderful friends are still there but they have all moved on with there little families.I feel very lost and alone	Claire Haresnape	24	my story group	1
	my story group\34	Emotional distress\feeling isolated	5	5	0	i'm so angry,emotional,depressed and the wonderful group of friends as i loved going out socialising .But i feel i can't do that now all my wonderful friends are still there but they have all moved on with there little	Claire Haresnape	24	my story group	1

						families.I feel very lost and alone				
	my story group\32	Emotional distress	3	3	0	I had 2 separate counts of less than 1 million. Other tests didn't reveal any identifiable causes. My partner and I were devastated as it seemed that conceiving naturally would be almost impossible!	Claire Haresnape	24	my story group	1
	my story group\31	Emotional distress	3	3	0	I got pregnant in October 2010 - we had been trying for a couple of months and my family had experienced a rather traumatic time earlier in the year so this was perfect. During early days I started to experience some spotting - I went to do hospital and they said it was normal for some women. I was totally distracted by this, and in the end of the day on my 10 week scan I was told I had experienced a missed miscarriage. We were devastated	Claire Haresnape	24	my story group	1
	my story group\31	Emotional distress	4	5	0	tests, we have had basic tests - all came back ok. On Thursday of next week we are going for further tests to make sure I don't have any blockages. But I still hate hearing about people being pregnant and taking it for granted. I hate feeling like this, and I live in fear of close friends telling me they are pregnant because I'll have to put on a happy face, and I won't be able to keep it up. Ugh.	Claire Haresnape	24	my story group	1
	my story	Emotional distress\being	6	6	0	I don't even know what I want to hear! And then I	Claire Haresna	24	my story	1

	group\31	worthy				feel guilty about feeling like this because it has just been over a year since my miscarriage, and so many women have been dealing with this for years - but I just don't know where to turn.	pe		group	
	my story group\31	Emotional distress	7	7	0	My husband is amazing, and so supportive - he would go to the end of the earth for me to be happy. But over the past year it's been more difficult to find happiness	Claire Haresnape	24	my story group	1
	my story group\29	Emotional distress	1	1	0	I have recently turned 35 and my DH is 39. We started TTC when we were first married in Oct 2008 (age 31 and 36). This I feel was one of the most stressful and emotional times for both of us. Each month was passing and I was buying PG tests each month and OPK's to try and time intercourse around ovulation. I was getting smiley faces on the OPK's but no smile on my face....just tears. I started temping every morning and checking cm and position of my cervix. Spent lots of money on registering with FertilityFriend and time updating all of my details. My emotions were all over the place and I spent a lot of time in tears or on the Internet searching for information on all sorts of fertility/baby sites.	Claire Haresnape	24	my story group	1
	my story group\29	Emotional distress	2	2	0	We were devastated...my poor DH. I decided to change GP surgery to same as my DH's to make things easier.	Claire Haresnape	24	my story group	1

	my story group\29	Emotional distress\being in control	5	5	0	I decided that I would be too stressed just before Christmas and had already arranged to travel to see family and that it would be too stressful to rearrange....so here we are now.	Claire Haresnape	24	my story group	1
	my story group\28 2	Emotional distress\putting you first	6	6	0	feel very conflicted a lot of the time as in June last year I started a new job which is basically my dream job working for a great charity, and don't want to be messing them around - or to give it up - but at the same time I know that having a child would be the most important thing in my life, much more important than any job	Claire Haresnape	24	my story group	1
	my story group\26 2	Emotional distress	2	2	0	That was around the time DH brother and girlfriend announced their 1st pregnancy after only being together a short while straight away i felt a pang of jelousy	Claire Haresnape	24	my story group	1
	my story group\26 2	Emotional distress	4	4	0	I rang my doctors and they said we had to be ttc for a year before they would take us seriously it seemed every day more and more of our friends had happy news i wanted to be happy for them but i felt like my world was falling apar	Claire Haresnape	24	my story group	1
	my story group\26 2	Emotional distress	5	5	0	DH had perfect fertility where as mine was non existant i took such a confidence knock i felt useless but was determined i was gonna be brave enough to do what ever it took to make this happen for us	Claire Haresnape	24	my story group	1
	my story	Emotional distress\financi	7	7	0	I turned 30 and excitedly rang the hospital to be	Claire Haresna	24	my story	1

	group\2 6 2	al loss				told i could be put on the waiting list now!!!!! i couldnt believe it but what could i do we couldnt afford to go private	pe		group	
	my story group\2 6 2	Emotional distress\Not feeling in control	7	7	0	at all i struggled with my emotions so bad i didnt know what was happening or what would happen nex	Claire Haresnape	24	my story group	1
	my story group\2 6 2	Emotional distress	7	7	0	but on the day before test i started to bleed at work i paniced and left without saying a word got home and couldnt find the words to tell DH it was as if if i said it out loud it was really happening	Claire Haresnape	24	my story group	1
	my story group\2 6 2	Emotional distress	7	7	0	i love my DH my dog and my horses but i didnt want any of them near me my doctor said i had event triggured depression i think i was in shock i felt like my life had ended i had panic attacks when people came round to see me i wouldnt go out i gave everyone quite a scare things got worse when my best friends 2nd child was due on my test date made things really hard between us	Claire Haresnape	24	my story group	1
	my story group\2 5	Emotional distress	5	5	0	At the time, DH and me were just focussing on my recovery which took months, but as the weeks went on&I began to get better it it me that we may never have the chance of having our own baby, something we have both desperately wanted for so long	Claire Haresnape	24	my story group	1
	my story group\2 5	Emotional distress	5	5	0	Now I am really scared as I had never worried about me producing the follicles before as my hormone levels have	Claire Haresnape	24	my story group	1

						always been fine, what if we fall at the first hurdle? I am not sure how we will cope.				
	my story group\24	Emotional distress	3	3	0	I had a 2 day transfer. My period came before the pregnancy test, which was a BFN. I was utterly devastated. However, the recipient had a BFP, which gave me loads of hope for future cycles	Claire Haresnape	24	my story group	1
	my story group\24	Emotional distress	5	5	0	I had a 3 day transfer. I was very positive about this cycle, but again my period came before the pregnancy test, which was a BFN. I was really upset again, but knew that the sooner we tried again, the sooner I could get over it.	Claire Haresnape	24	my story group	1
	my story group\24	Emotional distress\being in control	8	8	0	I've got lots of questions to ask at the review meeting, and will also ask for a review of my medical notes by another clinic, to see if there is anything that we can change for the next time.	Claire Haresnape	24	my story group	1
	my story group\24	Emotional distress	9	9	0	My husband has been a brilliant support throughout the process, but it is really hard to stay positive for the next cycle	Claire Haresnape	24	my story group	1
	my story group\23	Emotional distress	1	1	0	For the first time in my life I want to be pregnant and can't get pregnant. Feels like I'm being punished.	Claire Haresnape	24	my story group	1
	my story group\23	Emotional distress	1	1	0	I thought I was going to lose my mind. I can't wait to find out, I know it's my tubes, I'm hoping they can be unblocked. I	Claire Haresnape	24	my story group	1
	my story group\23	Emotional distress	1	1	0	If its not my tubes that are the problem I would be very surprised. I can feel them hurting me some times. Since being	Claire Haresnape	24	my story group	1

						infertile my sex drive is not the same, I feel to broken and sex feels pointless.				
	my story group\21	Emotional distress	2	2	0	Been married since 2000. Decided in 2002 that we were ready to have a family (how naive I was back then). Conceived 1st month of trying, very surprised but happy. Went along to scan at 9.5 weeks to have the devastating news that it had not progressed beyond the 5 week mark. Hospital gave me the choice to stay in or go home, opted to go home as didn't see the point in staying in and having the whole world and his wife watching my miscarriage. Miscarried two days later : (Then had two months of bleeding / pain / hospital visits and loads of strong antibiotics and an awful lot of upset and distress	Claire Haresnape	24	my story group	1
	my story group\21	Emotional distress	3	3	0	It had been a horrible year full of pregnancy anouncements and disappointment each month and frustration (what had changed from 1st time?). All tests said we were fine so we were another unexplained case.	Claire Haresnape	24	my story group	1
	my story group\20	Emotional distress\being worthy	2	2	0	I am very very lucky to have an amazing daughter from ivf, she is five know and time has flown by, sadly her dad and I got divorsed a year after her birth.	Claire Haresnape	24	my story group	1
	my story	Emotional distress\feeling	7	8	0	Im sick of the pregnant people, sick of new mums	Claire Haresna	24	my story	1

	group\19	isolated				with babys forcing theirs on me and the pitying smile of "it will be you soon dont stress it will happen!" Im sick of the announcements and the " i wanted to let you know im pregnant and i dont want to upset you because you cant have one!" Ive had enough of it all, i hate being the only wife alone. They all group together for mum and baby stuff and im left out on the side lines forgotten about because i dont fit into their group!	pe		group	
	my story group\19	Emotional distress\being worthy	9	9	0	It may not be as traumatic as some experiences i have read but its heartbreaking and im on the brink of giving up on the idea of ever becoming a mum and carrying our child!!!	Claire Haresnape	24	my story group	1
	my story group\19	Emotional distress	9	9	0	Adoption is an idea but so difficult for this to be agreed with army families due to the life style we lead! However i cannot be apart from my husband 5 days a week,these last 7 months have killed us.	Claire Haresnape	24	my story group	1
	my story group\18	Emotional distress	4	4	0	So back home again, tears, ice to numb leg/bum, tears, ear phones and TV for distraction, more tears, plasters so i can't see needle mark, ...I felt so sorry for hubby as he had to inject me while I was close to hysterical.	Claire Haresnape	24	my story group	1
	my story group\18	Emotional distress	5	5	0	Egg collection was booked for early as possible on 11th August, I had Emla cream on my hand to numb it (usually	Claire Haresnape	24	my story group	1

						used on kids), and i was absolutely petrified				
	my story group\18	Emotional distress	6	6	0	end of 2 weeks 27th August 2010... NEGATIVE.. deverstated...unsure whether to get up and get on with it or wither and cry forever. Having to tell the people that knew we were having treatment was horrendous.	Claire Haresnape	24	my story group	1
	my story group\17	Emotional distress	3	3	0	Was then advised to try short protocol, which I preferred, and had 4 eggs, 2 didn't mature but had the other 2 transferred back. After 2ww another BFN and was/still am gutted. This was last week.	Claire Haresnape	24	my story group	1
	my story group\16	Emotional distress\feeling isolated	1	1	0	It has taken me some time to join as I thought 'I would be ok'!! But there comes a point when you realise that your friends don't understand and you cannot keep shouting at your husband!!!	Claire Haresnape	24	my story group	1
	my story group\16	Emotional distress	4	6	0	Things had changed dramatically and there was no other option other then IVF. I was deverstated, my world fell apart, this is not how things are supposed to be. I feel like something died that day and I am trying to come to terms with it but I am so scared for the future and what it will bring for us.	Claire Haresnape	24	my story group	1
	my story group\16	Emotional distress	8	8	0	My DH and I have been through some awful times and it saddens me to think there are more to come.	Claire Haresnape	24	my story group	1
	my story	Emotional distress\financi	4	4	0	Today 04/09/12 was our first appointment at	Claire Haresna	21	my story	1

	group\15	al loss				Ninewells, the doctor explained the whole procedure and finished off with telling us if we decided to go with nhs funded treatment it would be a 3 year waiting list, if we pay it will be 8 weeks.. gutted was not the word, yes I knew there was a waiting list but never knew this long. Unfortunately we don't have the money to bring it forward.	pe		group	
	my story group\14	Emotional distress	1	1	0	Here is the story of the worst time of my life, and the loss of my son Aidan first....Aidan Irving Craig, my son, was an unexplained stillbirth at 34 weeks in Aug 23 1996. He would be turning a teen this year, and it hasnt got any easier, I was on my own then, and now after all these years, im now going thru more uncertainty and isolation with unexplained infertility I have no other family to remember my child with me, as my elderly widowed mother has suffered from vascular dementia the last 9 years, (she is now 81, been in a care home for 7 years, and nearly died this year with a severe chest infection, I was distraught with fear and worry). Aidans useless father lost touch during my pregnancy. I met him in Berlin when I played in a band I was touring with whom I played bass with) - he played guitar in another band and was	Claire Haresnape	21	my story group	1

						from Birmingham, so it was difficult to begin with(as Im in Glasgow), but he couldn't even be bothered to keep in touch even after what happened. I had already given up the band after this tour to look after myself so that was a loss in itself, but I was still looking forward to being a first time Mum at 28.I will never know the real reason why I lost Aidan, (I agreed to a post mortem, but they couldnt find anything wrong...so unexplained), but I had to move because my landlord wanted to refurbish my top floor flat so he could claim more rent money and I was up and down stairs at 7 and half months pregnant, - it so happened it was the same stressful week I got told there was no heartbeat during my usual routine scan. I had to be taken into the hospital that night knowing my baby was dead (they allowed my mother who was still well at the time thank God, to stay in the ward over night with me). The next morning they induced me, and I gave birth later that night at 10.31pm. This was when I also got told the umbilical cord was twisted round the neck and shoulder(which could have been another cause). But he weighed only 1. 32 kg (34 and half weeks).Aidans funeral				

						was a week later on Friday 30th August 1996. This was painful enough, but little did I know it was the last time I would see one of my new found friends Val, who commited suicide about 3 weeks later.The last time I saw her alive was Aidan's funeral.Then I found out another old friend Jamie died about a month after that. Needless to say this was the worst year of my life. I thought the year my Dad died was in Oct 92, but that comes a close second. As at that time, my bf then, had dumped me, I got chucked out my bedsit and had to braveface my pals wedding all in the same month! After losing Aidan, I went through several years of severe depression and chronic anxiety (which I was already prone to but never quite as bad). I also took to drink like there was no tommorrow - well I used to hope there wasn't! Plus I was on anti-depressants for over 9 years. I was just beginning to feel a bit brighter in 2000 (4 years later) but then my mum took ill with dementia and I became a carer, and this made my depression worse again. I started seeing someone who turned out to be a con man who took advantage and ripped me and my mum off - money, her engagement/wedding				

						rings, fraud, and my pets all mysteriously died and other unmentionables- another long story - he got away with it even though police knew!				
	my story group\14	Emotional distress\feeling isolated	1	1	0	im now going thru more uncertainty and isolation with unexplained infertility I have no other family to remember my child with me, as my elderly widowed mother has suffered from vascular dementia the last 9 years, (she is now 81, been in a care home for 7 years, and nearly died this year with a severe chest infection	Claire Haresnape	21	my story group	1
	my story group\14	Emotional distress\putting you first	1	1	0	since I met Graeme, that things started to get a bit better. I stopped drinking so much and stopped the long term anti-deps without the doctors help! Then started doing short courses and eventually ended up back at college, and now im qualified to do swedish massage and aromatherapy and continuing to learn other holistic therapies.	Claire Haresnape	21	my story group	1
	my story group\14	Emotional distress\being in control	1	1	0	since I met Graeme, that things started to get a bit better. I stopped drinking so much and stopped the long term anti-deps without the doctors help! Then started doing short courses and eventually ended up back at college, and now im qualified to do swedish massage and aromatherapy and continuing to learn other holistic therapies.	Claire Haresnape	21	my story group	1
	my story	Emotional distress	1	1	0	. I feel that life is passing me by and that I am just	Claire Haresna	21	my story	1

	group\14					not good enough, its very hard to explain. I also feel that I may be kidding myself on and perhaps just wanting to fill the terrible gap that not having Aidan around left behind. And perhaps I am being selfish at my age to keep trying...(As I know only too well what its like to be left without a family on my own, as I had older parents). It is also very hard keeping up the courage to keep trying after the first time that's well over 3 years now and Ill be 40 next birthday. I have to wait months inbetween tests and my next one is on Jan 21, and I think this time its about my fallopian tubes	pe		group	
	my story group\14	Emotional distress\financial loss	1	1	0	I am now too old for IVFin my area on the NHS, unless I go private and pay loads of money I don't have!	Claire Haresnape	21	my story group	1
	my story group\14	Emotional distress	1	1	0	Im now 40 and its 2009, my depression has came back with a vengeance and after all the years off them, im back on these damn anti-depressants even tho I feel they dont work. The last year and this xmas and new year have been the worst for many years since before meeting Graeme, as nothing has went right with a run of major bad luck, just feel im cursed in this life and in all honesty with no future to look forward to...still jobless, still childless and all my savings taken away and in massive debt, I cannot	Claire Haresnape	21	my story group	1

						wait to pass on to the next life. I even seriously thought of sectioning myself cos im sick of the suicidal thoughts plagueing me.				
	my story group\13	Emotional distress\feeling isolated	1	1	0	I am new to this forum, but I have decided to reach out as this process is so bloomin' isolating	Claire Haresnape	21	my story group	1
	my story group\13	Emotional distress	6	6	0	I have found this last year awfully hard. Two of my sisters got pregnant (both younger than me), and we joked about all three of us potentially being pregnant at the same time. Well, they got on that train and I was left in the waiting room. My best friend got pregnant last summer on her very first attempt, which was absolutely horrible	Claire Haresnape	21	my story group	1
	my story group\13	Emotional distress\feeling isolated	6	6	0	generally happy for her, but also very upset for several reasons - jealousy, but also I felt so lonely as her life (naturally) completely changed whereas mine stayed the same. No more sharing a bottle of wine at the pub over a girly chat, etc. I am now the Godmother of that child, which is lovely but at the same time difficult, for obvious reasons.	Claire Haresnape	21	my story group	1
	my story group\13	Emotional distress\feeling isolated	7	7	0	Where we live, most of our friends now have children or are expecting, which has left us feeling quite isolated - we sometimes joke about the fact that we need to find new friends. Of course we still spend time with our friends, but their life styles have changed and they	Claire Haresnape	21	my story group	1

						cannot do the same things as they used to. When I feel particularly lonely, I even contemplate moving, as I can't see a reason for us living here. I work from home and my husband works away 3 days a week.				
	my story group\13	Emotional distress\feeling isolated	8	8	0	I can't stand the loneliness anymore. I was initially reluctant to tell anyone because I had this idea in my head that I would get pregnant and it would be this amazing surprise to everyone	Claire Haresnape	21	my story group	1
	my story group\13	Emotional distress\feeling isolated	8	8	0	but the loneliness was just too much to bear. So we have gradually starting telling people. And this is my next step in reaching out, writing this	Claire Haresnape	21	my story group	1
	my story group\12	Emotional distress\being worthy	3	3	0	I actually do have one child already, a boy who is 9 years old. The first time round I was 27 years old and got pregnant very very easily. I took it all for granted and now realise quite what a miracle that was	Claire Haresnape	21	my story group	1
	my story group\12	Emotional distress	4	4	0	. After 2 solid years of trying every cycle we went to our GP who referred us on to a fertility clinic. It was not a very pleasant experience, the first time i turned up to the clinic the consultant came out into the waiting room and shouted loudly at me that i could not be seen at this clinic as 'I already had one kid, what more did i want?' It was awful, left totally humiliated	Claire Haresnape	21	my story group	1
	my story group\1	Emotional distress	5	5	0	I'm a pretty healthy person, I've never had anything seriously wrong	Claire Haresnape	21	my story group	1

	2					with me and i find all this a bit shocking.				
	my story group\12	Emotional distress	6	6	0	I am also struggling to cope with the idea that I may never have a 'normal' baby, one that I can take home and one that has a life expectancy beyond his teens.	Claire Haresnape	21	my story group	1
	my story group\12	Emotional distress\being worthy	6	6	0	Some people may think that i am being selfish wanting another kid but my experience with my first child has left me feeling more like a nurse than a mother and i yearn to hold a baby, feed a baby naturally not through a tube, take them home without machines etc. I have a feeling it would be very healing for us as a family to have a 'normal' healthy child, and now that this seems to be difficult its hard to consider that my only experience of motherhood is going to be one of such trial and tribulation. I know that many of you may not have children and I feel awfully guilty moaning about the experiences I have had, but let me tell you its been a tough time for my first child, and there are no guarantees that he will be with us for a long time.	Claire Haresnape	21	my story group	1
	my story group\11	Emotional distress	4	4	0	t is so frustrating not knowing what is wrong, it's been 5 yrs since we started trying again, my son is growing up and I really want him to have a sibling;	Claire Haresnape	21	my story group	1
	my story group\1	Emotional distress\being worthy	4	4	0	I know we are so lucky having him and our family of 3 is happy but I feel like	Claire Haresnape	21	my story group	1

	1					I've let him down				
	my story group\10	Emotional distress	3	3	0	In the next 7 months we had various tests done, saw an awful consultant and at the last appointment we saw a doctor who was a nightmare. We went in hoping to get my husbands second sperm analysis results (the first showed a low count & low motility) but the doctor said she hadn't got the results, when I asked when we could get them she was really rude, I burst into tears and luckily at the last minute another nurse came in with the results. They showed slight improvement, but when I asked the doctor what our chances were she just shrugged her shoulders.	Claire Haresnape	21	my story group	1
	my story group\10	Emotional distress	3	3	0	We were both shocked and felt really confused. We'd had a stressful year before for various reasons and it continued. We everything really hard to cope with	Claire Haresnape	21	my story group	1
	my story group\10	Emotional distress\being in control	3	3	0	Since then I've read up on what we can do through diet and lifestyle to improve our chances of concieving naturally. I've done daily temps etc, we had individual lifestyle plans,	Claire Haresnape	21	my story group	1
	my story group\10	Emotional distress	3	3	0	a house move & lots of close friends and family falling pregnant, being pregnant and having their babies and we're still no further, we've hit a point where we've reached our limits	Claire Haresnape	21	my story group	1
	my	Emotional	3	3	0	We're needing to protect	Claire	21	my	1

	story group\10	distress				ourselves from anymore hurt at the moment so its hard to see them. My husband has been depressed, I'm an emotional wreck its come to a point where we don't know where to tur	Haresnape		story group	
	my story group\10	Emotional distress\feeling isolated	3	3	0	feel so lonely. So after reading about I N UK and the support you all give eachother I thought we need to join. We've booked an appointment at the local private hospital to have a chat about our option	Claire Haresnape	21	my story group	1
	my story group\10	Emotional distress\financial loss	3	3	0	We can't afford private treatment	Claire Haresnape	21	my story group	1
	my story group\10	Emotional distress\being worthy	3	3	0	I feel guilty going on about how hard we're finding this when I read about some of you who have tried for much longer and have had lots of treatment. I admire your strength, I don't know if I/we can do it.	Claire Haresnape	21	my story group	1
	my story group\9	Emotional distress	5	5	0	I was told to get in touch if nothing was happening in 6 months time. I was discharged from hospital a week later with no follow up appointment scheduled and no acknowledgement of my lost baby. When my period returned 7 weeks later, after initially being unsure if we could go through that anguish again	Claire Haresnape	21	my story group	1
	my story group\9	Emotional distress\being in control	6	6	0	Meanwhile, I decided not to wait 6 months to speak to a doctor and pushed for an appointment with my gynaecologist. I had that initial appointment in	Claire Haresnape	21	my story group	1

						June 2011 and persuaded him to refer me to the local fertility clinic.				
	my story group\9	Emotional distress	6	6	0	In that time I had had 7 periods, knew when I was ovulating and every month have been left with the pain of nothing happening.	Claire Haresnape	21	my story group	1
	my story group\9	Emotional distress	6	6	0	The appointmet in Ocotber was both encouraging and devastating - they agreed not to do more surgery (no point - natural pregnancy is now highly unlikely) and have put us straight on the list for IVF (I have good ovulation levels but a low AMH and DH has borderline sperm results on top of my horribly disfigured left tube and missing right!) Unfortunately, the waiting list in my area is in excess of 2.5 years and we have been warned that in that time, the funding is likely to be - at best - severely cut, thus increasing the waiting time further, and at worst - withdrawn altogether. That same week DH was also made redundnat which heaped more stress onto the situation. DH found another job within a week (phew) and as a result, we are fortunate that, at this poitn in time, we are in a position to be able to look into private treatment	Claire Haresnape	21	my story group	1
	my story group\9	Emotional distress\financial loss	6	6	0	That same week DH was also made redundnat which heaped more stress onto the situation.	Claire Haresnape	21	my story group	1
	my	Emotional	6	6	0	It particularly feels so far	Claire	21	my	1

	story group\9	distress				away because this month is possibly the worst month of my entire life. We would have been due to meet our little son or daughter around the 29th of this month and I learned on Friday that the last of the people who were having difficulties/suffered a miscarriage at the same time as us is now nearly 5 months pregnant again and all is well.	Haresnape		story group	
	my story group\9	Emotional distress\feeling isolated	6	6	0	I am so pleased for her, and my best friend at work who is 5 1/2 months pregnant with twins but I feel so lonely. Nobody else I know is in the same position as DH and I. All of our friends are all either falling pregnant incredibly quickly or are not at the stage of starting a family. I guess in 10 years time we will be old hands dishing out the advice either way, but now it just feels like such a lonely world and quite frankly I feel like a failure as a wife!	Claire Haresnape	21	my story group	1
	my story group\8	Emotional distress	2	2	0	We went through our first IVF cycle last year and unfortunately it didnt work and thought at the time that I couldnt put myself or my husband through that again but needless to say were are starting another cycle and just started taking my nasal spray this morning. I am trying to stay positive but its so hard and if it doesnt work this time im not sure I can go through it again and to make things even	Claire Haresnape	21	my story group	1

						worse cause of all the operations and endo my cervix is in a tilted position whichmakes egg collection and embryo transfer very very painful.				
	my story group\7	Emotional distress	3	3	0	Me and my partner had a bombshell dropped on us only yesterday. It was our second appointment at the fertility clinic where the results of my day 1-4 and day 21 bloods and his sperm analysis were to be reviewed and the next steps to be discussed.	Claire Haresnape	21	my story group	1
	my story group\7	Emotional distress	5	5	0	My partner blames himself and is scared I'm going to leave him. I feel sad for my body because despite my 39 years my body released two eggs last cycle, my day 21 result was in the 80's, were we able to conceive naturally it would have been a multiple pregnancy. I feel like I'm grieving for the fact that we can't try all those other steps and have to go straight for the one-shot-40% chance IXI. I feel robbed, lost and empty. I don't feel positive and I am soooooo scared at having the face the prospect of never having a baby. I have butterflies in my stomach that are making me feel sick with anxiety. I'm scared at the prospects of the drugs, egg harvesting, and it just not working.	Claire Haresnape	21	my story group	1
	my story group\7	Emotional distress\financial loss	5	5	0	We can't afford the £5000 that has been quoted to us for further cycles	Claire Haresnape	21	my story group	1

	my story group\7	Emotional distress	5	5	0	I still find myself feeling sad and depressed. I'm grateful that we will get that 1 chance but there is soooooooooooooooooooooooo much hanging on that.	Claire Haresnape	21	my story group	1
	my story group\6	Emotional distress\being in control	8	8	0	After 2 1/4 yrs of trying, and a nice holiday to the Caribbean with no success, started looking at getting myself some further treatment - needed to do something.	Claire Haresnape	21	my story group	1
	my story group\6	Emotional distress	13	13	0	Due to test on a Saturday, on the Wednesday before this, I noticed a light spotting (which is normal before AF for me), this was worse on Thursday, started biking to work, but couldn't see the road for my tears, decided in no fit state to go to work, headed home. Spoke with my clinic, a nurse called me back, who said I could do the test a day early on the Friday, that it might not mean the end, but it could be. Terrible day, cried all day long.	Claire Haresnape	21	my story group	1
	my story group\6	Emotional distress\being in control	14	14	0	So instead, my DH and I went for a fab day out at Longleat Safari Park, and dinner in a really nice local pub, which was much better than sitting around being sad.	Claire Haresnape	21	my story group	1
	my story group\6	Emotional distress\counselling	15	15	0	so headed back to see my counsellor who helped me through it. Feeling a lot better at the moment.	Claire Haresnape	21	my story group	1
	my story group\5	Emotional distress	1	1	0	. Panic moment, so I got the GP to fax the referral to them again. Today after waiting 2 months since the 2nd referral was sent, I rang the clinic	Claire Haresnape	21	my story group	1

						again only to be told that they have never received a referral for me. I feel like I'm hitting a brick wall on what I know to be a long journey of possible brick walls. I don't know if my GP hasn't been sending them, but up to this moment they have been wonderful, even by contacting the community mental health team in regard to my clinical depression and the medication that I am on. I'm finding everything extremely overwhelming as I don't know family for support. I'm not sure what to think anymore, I feel like I'm being paranoid, but I've heard that the waiting times in regard to IVF Wales for extremely long.				
	my story group\4	Emotional distress	1	1	0	At 11weeks and 5 days I started having discharge and panicked though the GP and midwife were very matter of fact "it's an inevitable miscarriage" my world fell apart.	Claire Haresnape	21	my story group	1
	my story group\4	Emotional distress	1	1	0	. I went with my full bladder in hope, when they couldn't see anything on the ultra sound I was told "go and empty your bladder" I had to walk out in the waiting room in front of all the heavily pregnant mums with tears streaming down my face	Claire Haresnape	21	my story group	1
	my story group\4	Emotional distress	1	1	0	I cried from 7am when I went into surgery at 12am! I was devastated. We were referred to the NHS IUI clinic, the nurses were (and still are amazing). As I had clomid	Claire Haresnape	21	my story group	1

						left over we had our first couple of goes using that. The first attempt I was convinced I was going to be pregnant, but BFN again, we ended up having 7 IUI attempts some timed, some with the overtrile. I always had 2 lovely follies and was hopeful each time but all BFN's. its an emotional roller coaster doesn't even come close !!!! I told my mum who is quite ill herself and she was naturally very upset but instead of the support I thought I'd get she said "if you're trying again please don't tell me until you've had the all clear ad it's too upsetting for me"!!! Ouch. Too upsetting for her what about me? So I closed up and to that day she has no idea what we are going				
	my story group\3	Emotional distress\feeling isolated	3	3	0	Feeling quite alone in this process	Claire Haresnape	21	my story group	1
	my story group\2	Emotional distress	3	3	0	after several trips to the doctor to have various blood test which came back fine our gp sent my partner for a SA which to our surprise can back with dreaful results, morophology of only 3% we were both in total schock!	Claire Haresnape	21	my story group	1
	my story group\1	Emotional distress	1	1	0	h and myself have been ttc for 5 years-married for nearly 7. We have no children and I am 38 now so running out of time. I finally got to ivf stage on nhs earlier this year with 5 eggs at ec. Then the call to say I had zero eggs	Claire Haresnape	21	my story group	1

						fertilised I was devasted				
	my story group\1	Emotional distress	1	1	0	Devasted as cramps to so day 11 which was tues this wk I decided to do pregnancy test. As expected it was negative and bleeding heavier. Still taking progestrone suppositories and will test on fri as meant 2. I known I am wasting my time but can't help hoping for a miracle. Just can't stop crying so desperate for me and dh to have a baby. Don't know where to go from here. We said we wouldn't keep throwing money at this but I just can't accept we won't have children. The support and stories on here give me hope that miracles can happen. Just so empty at min and finding it had to carry on	Claire Haresnape	21	my story group	1

Comment	Document	Code	Begin	End	Weight score	Segment	Author	Creation date	Document group	Page
	my story group\165	Trust and Support from Manager\lack of empathy	5	5	0	Work is incredibly hard at the moment, my (female) manager does not really understand and my job is extremely stressful.	Claire Haresnape	20佷	my story group	1
	my story group\104	Trust and Support from Manager	1	1	0	I have to say though that our employers have been fantastic. My boss even looked at the INUK site and fact sheets and has been great at telling me to take as much time as I need, not to rush back to work etc. I couldn't have asked for more, so we have to count our blessings on that front. They have been incredibly understanding	Claire Haresnape	9佷	my story group	1
	my story group\104	Trust and Support from Manager\empathy from boss	1	1	0	I have to say though that our employers have been fantastic. My boss even looked at the INUK site and fact sheets and has been great at telling me to take as	Claire Haresnape	9佷	my story group	1

						much time as I need, not to rush back to work etc. I couldn't have asked for more, so we have to count our blessings on that front. They have been incredibly understanding				
	my story group\70	Trust and Support from Manager\empathy from boss	1	1	0	I was intending on working right up to EC but I really struggled with the side effects, mainly the hot sweats, very emotional and tiredness like i've never felt before. I decided to take leave from work until after ET – my manager was wonderful, so supportive!	Claire Haresnape	2佷	my story group	1
	my story group\65	Trust and Support from Manager	2	2	0	24th September 2010I was at work when I found an article in our Police Federation magazine (the Federation is like a civilian's union) which was about officers getting support through the IVF process from work.	Claire Haresnape	2佷	my story group	1

	my story group\65	Trust and Support from Manager	2	2	0	Going to speak to my Fed rep at work tomorrow and advise her of what we are doing so I can get some guarantees of support from my bosses	Claire Haresnape	2倀	my story group	1
	my story group\49	Trust and Support from Manager\empathy from boss	9	9	0	Went back to work today, which was hard, but everyone has been very sympathetic. A colleague at work, has a sister who has gone through IVF too which helps a bit, but would love to hear from anyone with words of encouragement to keep my spirits up and to hear your own experiences of IVF.	Claire Haresnape	2倀	my story group	1
	my story group\262	Trust and Support from Manager\feeling let down	7	7	0	later in 2010 i started my 1st cycle of ivf my work were awfull they didnt support me at	Claire Haresnape	24倀	my story group	1
	my story group\10	Trust and Support from Manager\lack of empathy	3	3	0	But my husbands family have found our situation hard. They have (not conciously) made it much	Claire Haresnape	21倀	my story group	1

						harder, especially this year since the birth of their first grandchild. The comments that have been made, the pressure thats put on us to attend big family get togethers and the lack of understanding even though we've tried to explain is proving really hard to deal with and causing us alot of distress				
	my story group\4	Trust and Support from Manager\lack of empathy	1	1	0	I told my mum who is quite ill herself and she was naturally very upset but instead of the support I thought I'd get she said "if you're trying again please don't tell me until you've had the all clear ad it's too upsetting for me"!!!	Claire Haresnape	21俵	my story group	1
	my story group\2	Trust and Support from Manager\lack of empathy	4	4	0	another 4 month wait to see the consultant again we were hit with more baffaling news... this	Claire Haresnape	21俵	my story group	1

						time we had a differnt consultant who proceeded to tell me the only thing would be ivf before i'd even sat down, was told after another SA partner is the problem i asked a bout my blocked tube which i had been shown to be told that that was incorrect she made me feel like i was making it up!!!				

Comment	Document	Code	Begin	End	Weight score	Segment	Author	Creation date	Document group	Page
	my story group\145	The demands of treatment	4	4	0	Am just playing the waiting game now- was hoping to start asap while I am on summer holidays (I'm a teacher). If period arrives this week, embryo collection and transfer would be in the first week of the new term. Not very convenient!	Claire Haresnape	20	my story group	1
	my story group\124	The demands of treatment	2	2	0	Does anyone know how long after planning how long before treatment starts roughly. How much time will I need off work? I am a teacher and it obviously has a big impact on the children I teach when I am continually out at appointments?	Claire Haresnape	10	my story group	1
	my story group\102	The demands of treatment	8	8	0	So, the rollercoaster began in earnest in January last year. 2006 ended with the start of ivf cycle (icsi) number 1. It was the hardest thing i have ever done. Dr'ing was horrible, i suffered badly emotionally and didnt make it very long into treatment before needing to be signed off work.	Claire Haresnape	9	my story group	1
	my story	The	4	4	0	with us purely so	Claire	9	my story	1

	group\100	demands of treatment				that we could take a morning off work and spend it shaking hands with him for 5 minutes whilst he repeated everything the nurses had told us the month before.	Haresnape		group	
	my story group\6	The demands of treatment	11	11	0	That afternoon, I felt quite rough, curled up on the sofa watching Twilgiht, insides feeling very bruised, it hit me that afternoon how big a thing IVF is.	Claire Haresnape	21	my story group	1

Comment	Document	Code	Begin	End	Weight score	Segment	Author	Creation date	Document group	Page
	my story group\157	career prospects\stressful job	2	2	0	I am a deputy manager in a day nursery (not the easiest job during this) and my husband is a bus driver	Claire Haresnape	20ヴ	my story group	1
	my story group\159	career prospects\stressful job	6	6	0	severe bullying by a senior manager at work (I left the organisation as a result ut now have my own business)	Claire Haresnape	20ヴ	my story group	1
	my story group\158	career prospects	8	8	0	To top it off Ive been offered a promotion at work but don't want to accept it if im going to start IVF this year.	Claire Haresnape	20ヴ	my story group	1
	my story group\154	career prospects\stressful job	3	3	0	I suffered greatly from my job change as in effect I was demoted - talking about kicking a man when he's down! It had a terrible effect on me as I felt I had lost everything I had worked so hard for and that was so beneficial to me	Claire Haresnape	20ヴ	my story group	1

	my story group\154	career prospects	7	7	0	My one good luck story in 3 years has been my new job, which I started 2 weeks after 1st IVF failure. So now, at least, DH and myself are both finally settled in jobs that we love, so some stability at long last.	Claire Haresnape	20ヴ	my story group	1
	my story group\150	career prospects	6	8	0	Having chased a career I finally realised I wasn't such a bad person and he was certainly a great person and what we had to offer to a new life	Claire Haresnape	20ヴ	my story group	1
	my story group\141	career prospects\stressful job	1	1	0	Instead I just feel shattered. Also worried about the effects of the drugs, about getting OHSS, about it not working and losing this one hope we have, whether to go for SET or two embryos, working full-time whilst this is all going on (although planning on taking sick	Claire Haresnape	20ヴ	my story group	1

						leave for 2 weeks)				
	my story group\179	career prospects	7	7	0	I also went on a motivational course with work in January and had to face up to some things and be honest with myself that family is more important than work for me. I think I was going for promotions as some sort of displacement for how I really feel!	Claire Haresnape	20ヴ	my story group	1
	my story group\170	career prospects	2	2	0	Both of us very career-minded and ambitious and never really thought about children, but not long after we met, we both knew we were soulmates and were engaged within a few months	Claire Haresnape	20ヴ	my story group	1
	my story group\170	career prospects	6	6	0	I got offered my boss's job, ironically to cover her maternity leave, which I started in Jan,	Claire Haresnape	20ヴ	my story group	1
	my story group\165	career prospects\stressful job	5	5	0	Work is incredibly hard at the moment, my (female) manager does	Claire Haresnape	20ヴ	my story group	1

						not really understand and my job is extremely stressful.				
	my story group\164	career prospects	2	2	0	years - I look back now and just laugh at how careful we were with contraception while we were make a go of our careers.	Claire Haresnape	20ヴ	my story group	1
	my story group\164	career prospects\stressful job	4	4	0	That's when all the hassle started - because we were both only 27 nobody took us seriously - our GP told us to go home and just relax, our parents told us to give up our stressful jobs and have a long holiday	Claire Haresnape	20ヴ	my story group	1
	my story group\188	career prospects\stressful job	17	17	0	I gave up my high flying job almost 3 years ago now and now live and work on our farm so I much more chilled and less up tight but still my body isnt doing what everyone else seems to be able to achieve so easily.	Claire Haresnape	20ヴ	my story group	1
	my story group\20	career prospects\stressf	2	2	0	he set up a new business	Claire Haresnap	20ヴ	my story group	1

	8	ul job				and I was doing a long commute to work so we just thought it was nature's way of telling us that it wasn't the right time	e			
	my story group\208	career prospects\stressful job	10	10	0	There's been lots of stress along the way - working in a workplace surrounded by 30 something women, there have been a lot of pregnancies this year	Claire Haresnape	20ヴ	my story group	1
	my story group\126	career prospects\stressful job	8	8	0	Also not sure how much time to take off from work(very stressful workplace!!) What do you think is acceptable?	Claire Haresnape	10ヴ	my story group	1
	my story group\120	career prospects\stressful job	12	15	0	I literally felt the blood drain from my body. I think I went into a bit of a meltdown for the next few months, work was unbelievably full on, we were told that there was no DS on the NHS, we were told to go to the USA,	Claire Haresnape	10ヴ	my story group	1

						we were told that the wait here would be 5 years.				
	my story group\120	career prospects\stressful job	26	28	0	At this point I was doing 70 hour weeks at work and with the stress of everything my eyesight packed up.	Claire Haresnape	10ヴ	my story group	1
	my story group\120	career prospects\stressful job	46	47	0	have also been making efforts to reduce the stress at work.	Claire Haresnape	10ヴ	my story group	1
	my story group\94	career prospects\stressful job	3	3	0	I feel emotionally exausted and despite having a good (but v stressful) job	Claire Haresnape	9ヴ	my story group	1
	my story group\93	career prospects	4	4	0	. The day after our diagnosis I started the biggest job of my career in a new company. I don't tend to do things by halves	Claire Haresnape	9ヴ	my story group	1
	my story group\93	career prospects\stressful job	6	6	0	my job is quite pressured and I	Claire Haresnape	9ヴ	my story group	1
	my story group\93	career prospects\stressful job	8	8	0	Work is crazily manic	Claire Haresnape	9ヴ	my story group	1

Comment	Document	Code	Begin	End	Weight score	Segment	Author	Creation date	Document group	Page
	my story group\127	Confidentiality	4	4	0	After about a year I persuaded DH to come along with me to our local doctors, which in itself was awkward, as I also work there	Claire Haresnape	10랭	my story group	1
	my story group\4	Confidentiality	1	1	0	At that stage I had to tell my mother in law as DH was taking me into hospital	Claire Haresnape	21랭	my story group	1

Comment	Document	Code	Begin	End	Weight score	Segment	Author	Creation date	Document group	Page
	my story group\144	Being Open\non disclosure	7	7	0	We are optimistic about this but age is against us, im 36 and dh is 37. We havent told anybody about our if so when we found this website it was a godsend and provides the needed support although to date we havent come across anyone in the exactly the same position.	Claire Haresnape	20 ÿ	my story group	1
	my story group\177	Being Open\non disclosure	1	1	0	Friends carry on having babies, as do family, I work in a hospital enviroment and and have to deal with seeing people who are pregnant and with children all the time, I have created a professional and cold shell I put up to allow me to function but inside I am screaming, tears come late at night after my husband sleeps and when I am alone - pathetic I know, I'm doing it again now.	Claire Haresnape	20 ÿ	my story group	1
	my story group\179	Being Open	7	7	0	I also went on a motivational course with work in January and had to face up to some things and be honest with myself that family is more important than work for me. I think I was going for promotions as some	Claire Haresnape	20 ÿ	my story group	1

						sort of displacement for how I really feel!				
	my story group\179	Being Open\non disclosure	10	10	0	I've not really told many people and D's parents don't know. Not sure whether it is easier to say or not - will have to see what I'm like nearer the time and decide then.	Claire Haresnape	20 ÿ	my story group	1
	my story group\165	Being Open\non disclosure	4	4	0	I have chosen not to tell many people because I do not think people understand unless they have had to deal with IF themselves. DH struggles to talk about it although he does talk more since the IVF. But I do not think men have the same need to talk as we do and of course Male Factor IF does have a big impact on the male ego	Claire Haresnape	20 ÿ	my story group	1
	my story group\192	Being Open	4	4	0	we finally told our families and very close friends what was going on. We'd wanted to keep it private but actually telling others was helpful - especially my family. I eventually also told work too when I requested to go part time which helped enormously.	Claire Haresnape	20 ÿ	my story group	1
	my story group\128	Being Open	1	1	0	In an ideal world we would be open with those closest to us but people struggle with understanding	Claire Haresnape	10 ÿ	my story group	1

						how we feel and find it awkward knowing what to say. Listening to comments like “you’ll be ok in the end” or “relax and stay positive” don’t help but can understand why people say them				
	my story group\104	Being Open	1	1	0	.We told lots of people about the ICSI. We wanted people to understand and we wanted their support and help. We knew we'd be in pieces if it didn't work. And people seemed surprised, particularly by our frankness, but supportive and encouraging	Claire Haresnape	9 ÿ	my story group	1
	my story group\104	Being Open\non disclosure	1	1	0	They have been incredibly understanding.We've had three cycles in all now, ending in BFNs, but we've really kept everything to ourselves since that first time, which I don't think is healthy - hence finally, so very late in the day, joining in the forums, although I have been reading your posts and thoughts and feelings. I can't say how much they have helped me through some dark times	Claire Haresnape	9 ÿ	my story group	1
	my story	Being	7	7	0	After the SA results	Claire	9 ÿ	my story	1

	group\102	Open\non disclosure				dh and i seriously grew apart. I was a like a demon possessed, desperately searching the web for info and stories of ivf and reading every book going. He on the other hand refused to discuss any of it, completely shut me out of everything and stuck his head in the sand (plus he didnt want me to talk to anyone either, got very upset if i mentioned wanting to speak to any family or friends and all but forbid me to even speak to my mum!!). Eventually the strain became too much and we split.	Haresnape		group	
	my story group\93	Being Open\non disclosure	6	6	0	We haven't told friends or family, we are quite private and want to do this our way. This site really is an outlet for me to share and understand others experiences, even more so for us as our decision to keep this to ourselves will no doubt be difficult. I am not telling work either, my job is quite pressured and I couldn't stand the speculation. They already suspect I am pregnant as I put on weight post wedding. The irony	Claire Haresnape	9 ÿ	my story group	1

						of it isn't lost on me!!				
	my story group\86	Being Open\non disclosure	7	9	0	When I was having treatment I didn't tell anyone at work although I was tempted on several occasions. I'm really glad I didn't. It was hard getting over the disappointment privately so dealing with other people too wouldn't have suited me. It also meant at work I could temporarily forget about it. I've told a few close friends but not a wide circle of people that we're ttc. In a way the more people you tell the more pressure you put on yourself. After all the end of your story to conceive might (sadly) be a bit of a way off. Telling my friends was hard (silly pride) but having one of two people you can really open up to aside from your partner I think is a real comfort.	Claire Haresnape	7 ÿ	my story group	1
	my story group\76	Being Open\non disclosure	4	4	0	As you can imagine we were devastated and I don't think I stopped crying all weekend. Being so far away from family also was very hard, although I've kept all this away from my Dad. We lost Mum last year and he has had a lot to deal	Claire Haresnape	2 ÿ	my story group	1

						with and I don't want him worrying about me at the moment. I could have done with a good cry and natter with my wonderful Mum that day though, I can tell you.				
	my story group\76	Being Open\non disclosure	8	8	0	So the next step is basically doing it! We have to keep things very quiet here at work, for many reasons, so getting the time/dates to do it is proving a bit of a nightmar	Claire Haresnape	2 ÿ	my story group	1
	my story group\73	Being Open\non disclosure	1	1	0	Anyway after a week or so I picked myself up and pulled myself together and told myself to stop being ridiculous, this happens to so many people it's just that nobody really talks about it.	Claire Haresnape	2 ÿ	my story group	1
	my story group\73	Being Open	1	1	0	I have since discovered a couple of close friends that are going through similar problems and realised that more people share this journey than I first imagined.	Claire Haresnape	2 ÿ	my story group	1
	my story group\69	Being Open\non disclosure	1	1	0	I am in my Mid thirties.Can ayone help me in my isolation , i have had to carry out all past procedures in secret apart from a few close friends and familly members	Claire Haresnape	2 ÿ	my story group	1
	my story group\65	Being Open	2	2	0	I've told people, I can't keep my	Claire Haresnap	2 ÿ	my story group	1

						mouth shut about anything!	e			
	my story group\29	Being Open\non disclosure	1	1	0	We have decided not to tell anyone about our situation and over time a lot of people have stopped asking us questions.	Claire Haresnape	24 ÿ	my story group	1
	my story group\282	Being Open\non disclosure	6	6	0	I haven't told work anything yet - I think I may have to but very reluctant - especially as its such a small team, there are about 10 employees	Claire Haresnape	24 ÿ	my story group	1
	my story group\13	Being Open	8	8	0	but I have gradually started to open up about this	Claire Haresnape	21 ÿ	my story group	1
	my story group\13	Being Open	8	8	0	I was so sad to give up on this surprise element	Claire Haresnape	21 ÿ	my story group	1
	my story group\13	Being Open	8	8	0	but the loneliness was just too much to bear. So we have gradually starting telling people. And this is my next step in reaching out, writing this	Claire Haresnape	21 ÿ	my story group	1
	my story group\9	Being Open\non disclosure	6	6	0	we don't want to tell people when we do it in case it doesn't work	Claire Haresnape	21 ÿ	my story group	1
	my story group\6	Being Open	13	13	0	Had to pop into work that afternoon for a meeting with my boss, let her know as best as I could.	Claire Haresnape	21 ÿ	my story group	1

Comment	Document	Code	Begin	End	Weight score	Segment	Author	Creation date	Document group	Page
	my story group\159	Medical Staff Interactions\medical let down	8	8	0	We are on the NHS waiting list for IVF (delayed because of my GP acting like God - "it's cause you're stressed" - initially saying we had to wait before he'd refer us) and hopefully it'll be sometime in September or October of this year	Claire Haresnape	20↘	my story group	1
	my story group\141	Medical Staff Interactions\medical let down	1	1	0	The consultant we saw was an odd one. He sat in his chair rocking and just said everything was "fine". We were in shock. We asked him several times to perhaps elaborate and for the actual percentages of the sperm morphology, actual results of the tests, however he is very reluctant to go into any detail whatsoever. We finally managed to get out of him that normal forms were now at 22% (although we had to do the maths ourselves to work this out). He said we come under “unexplained infertility” and offered IUI. Given this good news of now everything being “fine", we decided that maybe we should try naturally for a while longer	Claire Haresnape	20↘	my story group	1

						and so decided to put the treatment on hold for now. We were feeling really hopeful again. The “still nothing happens” bit January 2009 and still nothing had happened. We booked an appointment at the clinic to see how long they would recommend us trying for and to ask about things like nutrition, complimentary therapies (very naively thinking the clinic would offer this type of advice!). On the morning of the appointment, my DH and I decided that we would actually try the IUI. We got to the appointment and there was no expert in sight. Instead we waited for 2 hours to speak to somebody who had no idea how to answer any of our (let’s be honest, my) questions, confused IVF with IUI and just about managed to give my DH a sperm pot. Discussing nutritional advice etc was definitely out the window as the man didn’t have a clue!				
	my story group\140	Medical Staff Interactions\medical staff lack of empathy	3	4	0	To get to the fertility clinic you had to walk through the antenatal clinic. And then the waiting	Claire Haresnape	20↘	my story group	1

						room for the fertility clinic was a tiny windowless room with a load of baby toys in it! The fertility nurse I saw advised to have a laparoscopy which was an equally horrific experience. The NHS staff were unfortunately very unsympathetic and uncaring. One month after the operation I went back				
	my story group\177	Medical Staff Interactions\medical staff lack of empathy	1	1	0	My GP's answer to all of this is "just adopt, there are plenty of children out there who need a home" nice... The consultant's answer to my husbands azoospermia was in the first instance not to even offer to help him, just use donor sperm - the child won't be yours but you'll bring it up so it's as good as! This as you can imagine has not helped our relationship he won't talk to me, I am scared he will call off the whole thing if we are offered ICSI/IVF through pride, selfloathing and anger.	Claire Haresnape	20↘	my story group	1
	my story group\177	Medical Staff Interactions\medical staff lack of empathy	1	1	0	The result came back - Azoospermia, no sperm in the semen at all - we where told in a very uncaring way, it was	Claire Haresnape	20↘	my story group	1

						just announced, my husbands face was just pure shock, then anger				
	my story group\173	Medical Staff Interactions\medical staff lack of empathy	4	4	0	After a year we went to our GP and were referred to the ACU who tested us both and said everything was fine and we should go home and try and relax (argh!*&^%$£"!!!).	Claire Haresnape	20↘	my story group	1
	my story group\176	Medical Staff Interactions\medical let down	3	3	0	Our consultant said he would refer us for IVF at Leeds hospital, my hubby has a son 17 but our cons said that we would still get IVF free on the NHS cause I dont have any children, he said it wouldnt be a problem and he would fight our case....so we thought fantastic what a weight off our minds...then we got word last week that we have been rejected for IVF cause Patrick has a son!!, I was devastated so i phoned my cons secrectary and explained to her what happened, she said she would pass the info on to him, she phoned me back 3 days later and said my consultant wouldnt be appealing and that was that, she also said now they was	Claire Haresnape	20↘	my story group	1

						nothing more he can do but go and see our GP for the next step				
	my story group\162	Medical Staff Interactions\medical staff lack of empathy	1	1	0	. I was referred to a gynecologist. I feel angry when I think of him. I have always been a very thin person – size 8 and slightly under weight – however, throughout the whole appointment, he talked to me about diets and told me that I would need to cut down on the amount of carbs I was eating	Claire Haresnape	20↘	my story group	1
	my story group\165	Medical Staff Interactions\medical let down	2	2	0	I went back to GP who then informed us that DH did have a problem according to the sample he had given a year or so ago but noone had informed him. I was devastated as was he.	Claire Haresnape	20↘	my story group	1
	my story group\164	Medical Staff Interactions\medical let down	6	6	0	We were referred to a clinic and were put on the long waiting list and were told that we could pay for IUI before we reached the top of the IVF waiting list. We were all ready, and on the first day of my cycle, I rang up and.... got no answer on any of the three phone numbers. I tried again and again, all day and still no answer. The next day, the nurse rang and apologized that	Claire Haresnape	20↘	my story group	1

						everyone was on a course and we had missed our chance for that cycle!				
	my story group\164	Medical Staff Interactions\medical let down	10	10	0	cycle in Feb, ready for starting IVF - and I was told by the nurse that the PCT was cutting our funding (along with 17 other couples) so we wouldn't be able to start IVF this month. I was so shocked and yet again devastated and hurt - I got straight onto the phone to my mum and then my GP - they both knew the PCT from trying to get our funding changed before, and it took a whole day and lots of phone calls for it to be agreed. (In the process they also managed to get all the other 17 couples' funding secured too - but they won't have known that!!)	Claire Haresnape	20↘	my story group	1
	my story group\196	Medical Staff Interactions\medical let down	1	1	0	My own doctor didn't take me seriously as all tests were ok. I finally went private in 2004. He didn't take me seriously either	Claire Haresnape	20↘	my story group	1
	my story group\192	Medical Staff Interactions\medical let down	3	3	0	We started on our 1st of 3 IUI's in December 06 which went wrong when the nurse discovered that she couldn't get the catheter in the right place so just released it randomly	Claire Haresnape	20↘	my story group	1
	my story	Medical Staff	1	1	0	I was really	Claire	20↘	my story	1

	group\183	Interactions\medical staff lack of empathy				disheartened with her lack of sympathy, explanations and proposed treatment but I went away and did as I was told.	Haresnape		group	
	my story group\187	Medical Staff Interactions\medical let down	1	2	0	n Nov 08 I decided to go to the GP to discuss getting us some help in trying to conceive. He referred us to the FC and our first appt is on 7th Apr. Unfortunately I have no idea how he qualified as a GP as he hadnt referred us for any tests at all before sending us there and if it wasnt for this lifeline of a website we wouldnt know and would have been sent back for the initial tests.	Claire Haresnape	20↘	my story group	1
	my story group\214	Medical Staff Interactions\medical staff lack of empathy	1	1	0	uring the appointment the consultant was dreadful, no care, compasion, or explaination, just "well we'll have to run more tests"	Claire Haresnape	20↘	my story group	1
	my story group\212	Medical Staff Interactions\medical let down	4	5	0	At the next hospital we were told we were also at the wrong place and reffered to another hospital who then told us the local pct had cut funding and we could not have 1 cycle of icsi on the nhs but we could have 6 attemps at iui using a donor when i reached 23 years. We went to our local	Claire Haresnape	20↘	my story group	1

						newspaper who featured our story and the pct denied they had cut funding but coudnt explain why the doctors thought we could not have a cycle after trying to sort this but with no luck, we decided to move house to the county where we attended the first hospital but unfortunatley i had put the weight back on then and they refused to treat us even though they had sent us on a wild goose chase for 12 months. Then 6 months later they threatened to take us to court over sperm storage costs which they had not informed us off. the paper got involved again and the centre addmitted they was in the wrong and dropped it.				
	my story group\211	Medical Staff Interactions\medical staff lack of empathy	3	3	0	Had a lap and dye in Sep 06 which showed that both tubes were blocked and that I have endometriosis (had been complaining about painful, heavy periods form the age of 13, but the doctor had told me that this was the norm and to get on with it on several occasions). Great!	Claire Haresnape	20↘	my story group	1
	my story group\130	Medical Staff Interactions\medical	3	3	0	But classic comment from his GP 'I don't	Claire Haresnape	20↘	my story group	1

		let down				know anything about sperm but it should be enough'. Thanks for that.				
	my story group\130	Medical Staff Interactions\medical let down	4	4	0	ook months to get an appointment. When I phoned up to make the appointment the secretary told me the wrong date. A letter arrived the day of the appointment stating that it was 4 days before!!! So I phoned up - 'don't worry make another appointment after your next cycle'. Frustrating. Next cycle I phone up, but disaster! As I 'didn't turn up for the original treatment' (!!!!) my notes had been returned so NO procedure. Saw GP, made official complaint, referred to bigger central hospital.	Claire Haresnape	20↘	my story group	1
	my story group\130	Medical Staff Interactions\medical staff lack of empathy	8	8	0	I'm feeling very confused. She was so horrible!	Claire Haresnape	20↘	my story group	1
	my story group\117	Medical Staff Interactions\medical let down	8	8	0	t. With failure 2 weeks later and an awful experience with the technician doing the procedure	Claire Haresnape	10↘	my story group	1
	my story group\116	Medical Staff Interactions\medical let down	6	6	0	most recent outcome had laparoscopy on 7th jan and discovered i have both tubes blocked(which should have been picked up with having dye test done)so booked in now for tubal	Claire Haresnape	10↘	my story group	1

						reconstruction on 3rd march..				
	my story group\111	Medical Staff Interactions\medical let down	5	5	0	Started to feel really low and tearful so went to GP who said i was suffering with depression but didnt want to prescribe anything, went home and really felt i couldnt cope so rang fertility clinic to ask for help, the nurse called me back and i explained how i felt, she replied "dont worry its not the end of the road for you, your DH can have a sperm retrieval opp" i explained my husbands SA was normal and she said " i am afraid not he has no sperm at all, the GP must have read it wrong" I	Claire Haresnape	10↘	my story group	1
	my story group\111	Medical Staff Interactions\medical let down	6	6	0	I phoned my clinic four times to ask them to send both our blood test results, my DH phoned once and Addenbrooks phoned once, each time being made to feel a nuisance for keeping phoning them and when we arrived they hadnt sent our notes so our bloods had to be done again!!! The genetic councellor along with a top Doctor wrote to our clinic to tell them that there treatment DH and I had been below acceptable,	Claire Haresnape	10↘	my story group	1

						and we also made an app to complain				
	my story group\109	Medical Staff Interactions\medical let down	6	6	0	I recently asked the private clinic for a copy of my notes, and I think they have left me more confused, as they seem to suggest that my husband's sperm was ok on our very first attempt!!!	Claire Haresnape	10↘	my story group	1
	my story group\108	Medical Staff Interactions\medical staff lack of empathy	6	6	0	Well 9 weeks in she lost hers and one week later I went for a dating scan to be asked if I had a positive result. I just went cold. I knew that again I was going to have a mc. My experience with the hospitals is absolutely despicable! NO support at all! I was told to go home and let nature do it's course. No one to call, nothing.	Claire Haresnape	10↘	my story group	1
	my story group\108	Medical Staff Interactions\medical let down	6	6	0	Well 9 weeks in she lost hers and one week later I went for a dating scan to be asked if I had a positive result. I just went cold. I knew that again I was going to have a mc. My experience with the hospitals is absolutely despicable! NO support at all! I was told to go home and let nature do it's course. No one to call, nothing.	Claire Haresnape	10↘	my story group	1
	my story group\104	Medical Staff Interactions\medical	1	1	0	After a five hour wait in a crowded waiting	Claire Haresnape	9↘	my story group	1

		let down				room, we went through all the same questions and same answers as we had with our GP and were referred for the some of the same tests, which was incredibly frustrating.				
	my story group\104	Medical Staff Interactions\medical let down	1	1	0	We couldn't believe the number of people with fertility problems. We couldn't believe there seemed to be such a shortage of staff to meet their needs. At one point, some test results got lost and there was the prospect of having to wait another six months for a new test. I was on the phone non-stop, furious that due to their mistake, we would have to wait even longer to find out what was wrong. I even composed an angry letter to the chief exec of the PCT, but didn't have to send it as they managed to fit us in two weeks later.	Claire Haresnape	9↘	my story group	1
	my story group\102	Medical Staff Interactions\medical let down	6	6	0	Unfortunately on returning to our GP to discuss where we go from there we fell foul of a GP who was extremely compassionate and well-meaning but who was at the end of the day a GP and didnt have the knowledge that we needed at this time	Claire Haresnape	9↘	my story group	1

						(altho to his credit he always sought out the information we needed or pointed us in the right direction), and to this end he reassured us that there were things that could be done, it wasnt necessarily an insurmountable problem and that at least he had some sperm so hopefully he would be able to use his own sperm and not a donor (altho he did say he wasnt sure how many were needed for ivf). It was here where dh really struggled and from this moment on he couldnt see past where we were at and the mention of donor sperm				
	my story group\100	Medical Staff Interactions\medical let down	2	2	0	Our GP was sympathetic, but seemed to know less than I did about IF (from trawling the internet), and referred us to our local hospital, and the endless battery of tests began.	Claire Haresnape	9↘	my story group	1
	my story group\100	Medical Staff Interactions\medical let down	4	4	0	with us purely so that we could take a morning off work and spend it shaking hands with him for 5 minutes whilst he repeated everything the nurses had told us the month before.	Claire Haresnape	9↘	my story group	1
	my story group\100	Medical Staff Interactions\medical	5	5	0	After the second failure I therefore	Claire Haresnape	9↘	my story group	1

		let down				asked the nurse if she would put our name down on the IVF waiting list. She didn't. After our 4th failed cycle she finally decided that she had better do it				
	my story group\97	Medical Staff Interactions\medical staff lack of empathy	3	3	0	I had 21 day progesterone test in April which couldn't confirm ovulation but the Dr we saw for my results was very dismissive and told me I had to be trying for 12 months before they can do anything	Claire Haresnape	9↘	my story group	1
	my story group\97	Medical Staff Interactions\medical staff lack of empathy	4	4	0	I took my charts but she didn't even look at them.	Claire Haresnape	9↘	my story group	1
	my story group\97	Medical Staff Interactions\medical staff lack of empathy	4	4	0	This time I was told under the PCT guidlines for my area I have to of been trying for 18 months for a referral as there are no grounds for me to be referred. I left very upset, without my referral, and with most of my questions unanswered	Claire Haresnape	9↘	my story group	1
	my story group\97	Medical Staff Interactions\medical staff lack of empathy	10	10	0	I spent a few weeks not understanding if we had been reffered or not so when we went back to the Drs to get the results of the blood test (which again this could not confirm ovulation) I had intended to ask if we had been refferred but this time she was dismissive for a different reason	Claire Haresnape	9↘	my story group	1

	my story group\97	Medical Staff Interactions\Feeling supported by medical staff	11	11	0	So that was Dec 08. I got the phone number for the fertility clinic to ask how long their waiting list was (thinking it would be months again) but was amazed to here it would only be a matter of weeks before we saw someone. The nurse I spoke to was fantastic - she was very reassuring about the test results to date and was willing to listen to all of my concerns.	Claire Haresnape	9↘	my story group	1
	my story group\94	Medical Staff Interactions\medical let down	3	3	0	. I asked my Dr if I could have Luteal Phase Defect, but was told such a condition did not exist. To cut a long story short, a series of very difficult losses happened in quick succession in 2006, meaning infertility was forced to take a back seat, although the pain continued to bubble under the surface. In 2007 my marriage hit a really rough spot. The strain of everything was begining to take it's toll, and had it not of been for how strong my DH and I are as a couple, I think we could have broken up. We've managed to get our marriage back on track and	Claire Haresnape	9↘	my story group	1

						despite the ongoing pain of infertility, are stronger than ever. We've moved from Swindon to Oxford, somthing we've always wanted to do and have built a new life for ourselves here. Last year, we went to a clinic called Viveka in London, which takes a holistic approach to infertility. It was confirmed through a hormone profile that I do have LPD and when I told the Dr in London that I had perviously been told it did not exist, he was horrified.				
	my story group\93	Medical Staff Interactions\medical let down	6	6	0	For the sake of the readers of this post I will skip all the poking and prodding, the internals, the endless blood tests, the HSG and the general feeling that we were on a telecaster with no real say in when we got on or off. We have all been through it, been endlessly frustrated with the system, confused and yes sometimes very angry but lets not labour the point!!	Claire Haresnape	9↘	my story group	1
	my story group\89	Medical Staff Interactions\medical let down	4	4	0	I was gowned up, ready to go into theatre at the end of the day and I had a sinking feeling that something was going to go	Claire Haresnape	7↘	my story group	1

						wrong. Our lovely consultant came to see me to tell me that my op was cancelled due to complications with the previous patient,				
	my story group\86	Medical Staff Interactions\medical staff lack of empathy	19	19	0	On our 2nd cycle when we went back in for the embryo transfer we were told three embryos had survived. So they were happy to transfer two back in and wanted us to decide there and then what to do with the 3rd one. Ie did we want to pay for it to go into frozen storage - which is costly and the chances of it surviving all the way through to natural birth are small - or did we consent to it being destroyed. We had to decide there and then in the waiting room (me crying and looking shocked in a room full of strangers looking scared)	Claire Haresnape	7↘	my story group	1
	my story group\85	Medical Staff Interactions\medical staff lack of empathy	1	1	0	Panic set in as thought a little bleeding not a problem, however, apparently it is if you haven't had any bleeding at all by this point. After hideous day at 2 A&E departments (won't go into that L) at 5.45pm, it is confirmed that our baby had died at	Claire Haresnape	2↘	my story group	1

						about 8 weeks and that I had had a missed miscarriage i.e. your body continues to think you are pregnant after the baby has died. Total and utter devastation, I cannot describe the grief and despair and the complete and utter feeling of loss – how completely unfair to allow us to lose our miracle baby. How could that happen? I decided to have the surgical procedure, Evacuation & Removal of Products related to Conception (ERPC) – how heartless a term is that? Our baby being referred to as a "Product related to Conception". This happened on the 9th October in a Day Unit where I was surrounded by people killing their babies, terminations, all of them				
	my story group\85	Medical Staff Interactions\Feeling supported by medical staff	1	1	0	I am terrified of the failure again, although we do have enormous faith in our doctors this time.	Claire Haresnape	7↘	my story group	1
	my story group\83	Medical Staff Interactions\medical staff lack of empathy	1	1	0	The doctors can be very insensitive and quite dismissive, they see you for 5 mins every 4or5 months and cant wait to get you out the door	Claire Haresnape	2↘	my story group	1

	my story group\82	Medical Staff Interactions\medical let down	4	4	0	We have subsequently had three unsuccesful attempts at IVF using an English clinic. This was alas a really awful experience as I was put through cycles which were never going to work as my uterus was once again being distorted by fibroids which had reoccured. We had asked them constantly to rescan me to check this as I feared this had happened. Nobody knows your body as you do and my periods had become so heavy and lengthy that I simply knew something wasn't right. The clinic pushed these concerns aside and seemed more interested in taking our money and pushing us onto another cycle.	Claire Haresnape	2↘	my story group	1
	my story group\79	Medical Staff Interactions\medical let down	2	2	0	These were not really explained to us but we did not think there was anything to be concerned about.	Claire Haresnape	2↘	my story group	1
	my story group\76	Medical Staff Interactions\Feeling supported by medical staff	9	9	0	Thankfullly my Gyno here is lovely and has said that he will help me with anything that is needed....I just hope he means it !	Claire Haresnape	2↘	my story group	1
	my story group\75	Medical Staff Interactions\medical	4	4	0	Couple of months later, had lap&dye at	Claire Haresnape	2↘	my story group	1

		staff lack of empathy				another local hospital. Attitude of nurses/consultants awful and told bad news without my DH being present. Unforgiveable				
	my story group\75	Medical Staff Interactions\medical let down	5	5	0	Very confused by lack of communication, in fact, no communication, between PCT, local hospital, regional hospitals and GP. Guess work on what we were getting throughout whole process. But very grateful to get any NHS treatment as at one point very worried we wouldnt be eligble due to age and stepchild living with us. Prior to treatment had to do genetic testing again, which was long and stressful and badly organised, but eventually got complete all clear and ok to proceed with treatment.	Claire Haresnape	2↘	my story group	1
	my story group\70	Medical Staff Interactions\Feeling supported by medical staff	1	1	0	The anesthetist was fab, completely put me at ease. He was totally right, didn't feel or remember a thing! 9 eggs collected, 4 eggs fertilised successfully..... yay!	Claire Haresnape	2↘	my story group	1
	my story group\68	Medical Staff Interactions\medical let down	5	5	0	Next appt followed in Aug 09 - we were told by the consultant to take vitamins to see if they improved the	Claire Haresnape	2↘	my story group	1

						quality of DH's sperm. We were outraged as we could have been told this from the start instead of being told 8 months after our first visit to the GP.				
	my story group\68	Medical Staff Interactions\Feeling supported by medical staff	7	7	0	Next hurdle was the fact that no NHS IVF treatment is offered in Essex, so we had to choose from 5 clinics outside London. We chose Leicester as they were the only clinic not to have a waiting list. LFC have been wonderful, we have visited a few times, filled the forms and more tests done etc ...and now we are in a position where we start treatment in the next 4 days!!!	Claire Haresnape	2↘	my story group	1
	my story group\67	Medical Staff Interactions\medical staff lack of empathy	15	15	0	3rd May - standard 3 week post test scan with Fertility Clinic. Got the consultant from Hell who's never seen me before. Junior has a heartbeat!!!! BUT consultant there felt pregnancy wasn't viable as h/b faint & wanted us to see him again in a week.	Claire Haresnape	2↘	my story group	1
	my story group\66	Medical Staff Interactions\medical let down	1	1	0	After TTC for about a year we consulted a specialist in the Maldives who eventually (after a year of heavy fee's and monthly appointments) sent me for a HSG after	Claire Haresnape	2↘	my story group	1

						which she informed me that my tubes were blocked and recommended that I have microsurgery to unblock them. Unfortunately this procedure is not available in the Maldives so I traveled to Thailand with my DH to consult another specialist.Once in Thailand I performed another HSG only to be informed that my tubes were perfectly fine!!				
	my story group\66	Medical Staff Interactions\medical let down	1	1	0	After my first unsucessesful month I started to get terrible pains, which gradually became unbearable over the next month. I contacted the doctor in Thailand and he advised me to continue as planned and if we still had no luck with Clomide in 3 months fly back to Thailand to see him.After 3 very painful months we headed back to Thailand to be told that I had very large cysts on both ovaries, which had been the reason for the pain and had to stop with all medication for at least 3 months!So we traveled home in despair as in both countries we had	Claire Haresnape	2↘	my story group	1

						received little advice and spent a fortune				
	my story group\66	Medical Staff Interactions\Feeling supported by medical staff	1	1	0	From the moment I contacted the UK clinic I new we had made the right choice as finally we have been inundated with so much valuable information and friendly faces.I must admit I was a little worried as the laws have changed in the UK but after I was contacted by an Indian clinic that happily told me that they would transfer as many embryo's, as I liked up to 12!!!! As apposed to the UK's max of 2 I new I had to come home	Claire Haresnape	2↘	my story group	1
	my story group\60	Medical Staff Interactions\medical staff lack of empathy	5	5	0	The laparoscopy was awful as while in gown and waiting to go down to theatre a flippant comment was made about my tubes and womb.	Claire Haresnape	2↘	my story group	1
	my story group\58	Medical Staff Interactions\medical let down	5	5	0	But ironically due to my 'success' with Clomid that put me on a dose of Puregon that was too low and didn't stim me enough.	Claire Haresnape	2↘	my story group	1
	my story group\56	Medical Staff Interactions\medical let down	2	4	0	After 3 m/c's I caught with a 4th and after a small bleed was told that I was having an ectopic. I questioned this as I didnt have any of the symptoms - never the less, I was rushed into surgery (and then waited 7	Claire Haresnape	2↘	my story group	1

						hours in a side room before going in). When I was taken back to the ward I was informed that they hadnt used any of the 'preventative' methods and had just taken out my left tube. After being discharged, and for the next week, I looked into this further and was so confused by every decision made by the hospital, I wrote to the CEO of the Hospital Trust. It was just a short 5 days late when I received a phone call asking me to return to the ward asap as they thought I may still be pregnant. Confused, we went back, to be told the worse news of my life - they had made a mistake, my baby wasnt ectopic - they had terminated it in error. The following month we were hit with the final blow - my left tube was my only 'working' tube and therefore - they left me infertile.				
	my story group\52	Medical Staff Interactions\medical let down	19	19	0	March 2008 - our first cycle (free NHS one). Mid way through the planning appointments they realised they hadn't done any tests on me! Blood tests	Claire Haresnape	2↘	my story group	1

						showed high FSH so we were switched to the short protocol.				
	my story group\51	Medical Staff Interactions\medical let down	3	3	0	internals etc etc and said my FSH Level is too high which means my egg quality is very poor its 13.5 he said only hope would be IVF but gov wont fund it cos ive conceived within the last 3 yrs! its a joke!	Claire Haresnape	2↘	my story group	1
	my story group\48	Medical Staff Interactions\Feeling supported by medical staff	5	5	0	We saw the consultant yesterday for a good hour and she was incredibly helpful and realistic.	Claire Haresnape	2↘	my story group	1
	my story group\41	Medical Staff Interactions\medical let down	3	3	0	was diagnosed with PCOS 5 years ago, didnt really know much about it, but then nor did my DR at the time, or any since, they were pretty damn clueless which just made it worse!	Claire Haresnape	24↘	my story group	1
	my story group\41	Medical Staff Interactions\Feeling supported by medical staff	3	3	0	Luckily i have an amazing DR now	Claire Haresnape	24↘	my story group	1
	my story group\41	Medical Staff Interactions\medical let down	6	6	0	My doctor has put me in for an internal scan, and now im a sitting duck, hospitals take forever, especailly this time of year.	Claire Haresnape	24↘	my story group	1
	my story group\40	Medical Staff Interactions\medical let down	2	13	0	worst part is the waiting, waiting to see if my period will come, waiting to see the doctor, waiting for the next treatment, waiting to see if it worked... I stated puberty about aged 12-13. I	Claire Haresnape	24↘	my story group	1

						was never regular and had major problems with my "monthly" cycle. Sometimes I would go 4months without bleeding, other times I would bleed constantly for a whole month. Sometimes I was doubled up in pain sometimes I wasn't. Sometimes it would be so heavy I had to miss school or couldn't go out for a meal with my family. I knew something was wrong but 6 different GP's told me it was nothing. They gave pills to hide the pain; they strongly recommended I go on the pill, not only to mask the irregularity but also to fix it. Between the ages of 15-23 I spent most of my time on the pill (or rather several different brands of it).				
	my story group\39	Medical Staff Interactions\medical let down	3	3	0	Once we got to see him he explained that we could have blocked tubes, endometriosis, fybroids, polyps etc and wanted to do a Laparoscopy I found this so hard to deal with I thought that our problem would of been resolved easily, so he said we	Claire Haresnape	24↘	my story group	1

						could have a HSG and 3 more months of checking my progesterone and charting, so we went away and did this and after 3 months we got given the go ahead for the HSG, well they lost our paper work and I ended up waiting for another 3 months for this to be done, despite pestering the Dr and Hospital they were all happy for me to wait, until eventually my gynea's secretary decided to look into and realized my paper work had been lost so finally I am at the hospital getting into my gown ready for the HSG to be done, I found myself getting upset before hand, and wandering why we were having to go through this, it felt so unfair.				
	my story group\35	Medical Staff Interactions\medical let down	3	3	0	The whole process and after math has been a living hell, first the shambolic surgery, major swelling, massive lump, an i dont care gp, or ultrasound doctor, who says all he can see were varicous veins & carry on.	Claire Haresnape	24↘	my story group	1
	my story group\34	Medical Staff Interactions\medical let down	4	4	0	It took an age for H to back to doctors and the hospital took another 6 to 9	Claire Haresnape	24↘	my story group	1

						months. Lets just make a very long story short my hospital is awful! Brand new super hospital and very understaffed! There was originally two nurses running the subfertility clinic but one nurse retired and they never replaced her,if they did i never saw her! I have had all my records lost,the nurse has phoned in sick and they've had to rush a sectarary from another department to cancel appointments ,while i'm in reception nearly falling asleep and a number of other delays.So upset once phoned GP couldn't get to speak to him so spoke to the receptionist ,couldn't stop crying and the receptionist said if you complain they may you at back of the waitng list and/or take you off if i make to much fuss!				
	my story group\32	Medical Staff Interactions\medical let down	3	3	0	We were just told to go for ICSI/IVF and weren't given any advice about trying to improve my count.	Claire Haresnape	24↘	my story group	1
	my story group\29	Medical Staff Interactions\Feeling supported by medical staff	3	3	0	Our GP was fab! He referred us for fertility treatment straight away in the Summer of 2010 and then I had blood	Claire Haresnape	24↘	my story group	1

						tests after. All came back normal				
	my story group\29	Medical Staff Interactions\medical let down	5	5	0	We were both excited and nervous and were both geared up for it and I was just about to start down regging when I received a phone call that day informing me that our treatment had been cancelled due to staff sickness and that the next available time was week before Christmas for EC and ET	Claire Haresnape	24↘	my story group	1
	my story group\262	Medical Staff Interactions\Feeling supported by medical staff	9	9	0	I had a great doctor she signed me off work for 6 months and saw me regulally and eventually things got better i eventually visited my friend and 2nd baby a beautiful boy who is now DH and my god son.	Claire Haresnape	24↘	my story group	1
	my story group\23	Medical Staff Interactions\medical let down	1	1	0	. I've tried for a year to get my GP to give me a referral and only managed to get him to refer me to St Thomas hospital yesterday. So finally I can find our exactly what the problem is. It's all I've been thinking about for years. It's been so frustrating trying to get referred	Claire Haresnape	24↘	my story group	1
	my story group\19	Medical Staff Interactions\medical let down	5	5	0	Whilst he was gone i decided to have some further tests done! I wasnt convinced it was just him. I went in alone	Claire Haresnape	24↘	my story group	1

						and frightened but determined to get answers. I woke up in recovery and lifted my bed sheets up to find i was heamoragging all over the bed.There was blood everywhere and i sat screaming!!! They whisked me back into surgery for internal stitches, they had nicked my cervix during the first op! I woke up battered and bruised and alone. I apparently screamed for an hour none stop for my husband until they sedated me!				
	my story group\15	Medical Staff Interactions\Feeling supported by medical staff	2	2	0	Been with my partner 8 years and have now been ttc for around 4 years, after 3 years of nothing happening we went to the doctor who was very happy to get us help.	Claire Haresnape	21↘	my story group	1
	my story group\15	Medical Staff Interactions\Feeling supported by medical staff	3	3	0	After a year of tests, it was confirmed my partner had a low sperm count and that they were going to help us, next step being Ninewells for ivf treatment. Which to us was amazing news, finally getting the help we need.	Claire Haresnape	21↘	my story group	1
	my story group\12	Medical Staff Interactions\medical staff lack of empathy	4	4	0	It was not a very pleasant experience, the first time i turned up to the clinic the consultant came out into the waiting room	Claire Haresnape	21↘	my story group	1

						and shouted loudly at me that i could not be seen at this clinic as 'I already had one kid, what more did i want?' It was awful, left totally humiliated.				
	my story group\12	Medical Staff Interactions\Feeling supported by medical staff	4	4	0	. He was a bit furious and wrote a letter asking me to be seen by someone else which i was very quickly	Claire Haresnape	21↘	my story group	1
	my story group\11	Medical Staff Interactions\medical let down	3	4	0	I'm considering immune testing but I don't know if it would help me. My other concern is that I bleed from day 21 (& have done since the last m/c). The drs don't seem concerned by this but I am. My period cycle is 28 days but I start light bleeding on day 21 for 5 dys then stop for 2 dys before my actual period starts (lasting for 4 dys) - so in all bleeding for 10/11 dys each mth. The IVF consultant said it looked like there was an old follicle that hadn't disintegrated the previous mth and this was the additional bleed - but surely this can't be every mth? It is so frustrating not knowing what is wrong,	Claire Haresnape	21↘	my story group	1
	my story group\10	Medical Staff Interactions\Feeling supported by medical staff	3	3	0	We saw a lovely doctor, he referred us to the local hospital.	Claire Haresnape	21↘	my story group	1
	my story	Medical Staff	3	3	0	The consultant was	Claire	21↘	my story	1

	group\10	Interactions\medical staff lack of empathy				ok, didn't explain anything and referred us for further tests. In the next 7 months we had various tests done, saw an awful consultant and at the last appointment we saw a doctor who was a nightmare. We went in hoping to get my husbands second sperm analysis results (the first showed a low count & low motility) but the doctor said she hadn't got the results, when I asked when we could get them she was really rude, I burst into tears and luckily at the last minute another nurse came in with the results. They showed slight improvement, but when I asked the doctor what our chances were she just shrugged her shoulders. The previous doctor told us we'd need IVF, this one told us she wasnt sure, that her colleage probably knew more, but she thought we should go for IUI and asked if we wanted to go on the list. We didnt know what IUI was!! and weren't encouraged by her hesitation. We said	Haresnape		group	

						we'd think about it. We were both shocked and felt really confused.				
	my story group\10	Medical Staff Interactions\medical let down	3	3	0	The consultant was ok, didn't explain anything and referred us for further tests. In the next 7 months we had various tests done, saw an awful consultant and at the last appointment we saw a doctor who was a nightmare. We went in hoping to get my husbands second sperm analysis results (the first showed a low count & low motility) but the doctor said she hadn't got the results, when I asked when we could get them she was really rude, I burst into tears and luckily at the last minute another nurse came in with the results. They showed slight improvement, but when I asked the doctor what our chances were she just shrugged her shoulders. The previous doctor told us we'd need IVF, this one told us she wasnt sure, that her colleage probably knew more, but she thought we should go for IUI and asked if we wanted	Claire Haresnape	21↘	my story group	1

						to go on the list. We didnt know what IUI was!! and weren't encouraged by her hesitation. We said we'd think about it. We were both shocked and felt really confused.				
	my story group\5	Medical Staff Interactions\medical staff lack of empathy	1	1	0	I contacted my GP at the year mark of trying, only to be told to wait a bit longer. I changed GPs due to this flippant attitude and now have what I thought to be a wonderful GP	Claire Haresnape	21↘	my story group	1
	my story group\5	Medical Staff Interactions\medical let down	1	1	0	my GP filled in the application form for IVF Wales with us and sent it off, I was told that in 6 - 8 weeks we would receive an acknowledgement letter from them, this never arrived so I gave it a bit longer, 3 months later I gathered the courage to ring IVF Wales only to be told that never received the referral. Panic moment, so I got the GP to fax the referral to them again. Today after waiting 2 months since the 2nd referral was sent, I rang the clinic again only to be told that they have never received a referral for me. I feel like I'm hitting a brick wall on what I know to be a long journey of possible brick walls.	Claire Haresnape	21↘	my story group	1

						I don't know if my GP hasn't been sending them,				
	my story group\5	Medical Staff Interactions\Feeling supported by medical staff	1	1	0	but up to this moment they have been wonderful, even by contacting the community mental health team in regard to my clinical depression and the medication that I am on.	Claire Haresnape	21↘	my story group	1
	my story group\4	Medical Staff Interactions\medical staff lack of empathy	1	1	0	. At 11weeks and 5 days I started having discharge and panicked though the GP and midwife were very matter of fact "it's an inevitable miscarriage" my world fell apart	Claire Haresnape	21↘	my story group	1
	my story group\4	Medical Staff Interactions\medical staff lack of empathy	1	1	0	help (nobody told me this was dangerous).. I went with my full bladder in hope, when they couldn't see anything on the ultra sound I was told "go and empty your bladder" I had to walk out in the waiting room in front of all the heavily pregnant mums with tears streaming down my face. I was given the choice of waiting to pass "it" naturally or tablets to force it or "evacuation of retained products" don't these NHS healthcare 'professionsls' know what we go for?	Claire Haresnape	21↘	my story group	1
	my story group\2	Medical Staff Interactions\medical	3	3	0	we had to wait 6 months for our	Claire Haresnape	21↘	my story group	1

		let down				hospital appointment where we where told that my partners results had been read wrong, talk about emotions being all over the place, the consultant sent me for more bloods and a HSG and my partner for another SA,				
	my story group\2	Medical Staff Interactions\medical let down	4	4	0	another 4 month wait to see the consultant again we were hit with more baffaling news... this time we had a differnt consultant who proceeded to tell me the only thing would be ivf before i'd even sat down, was told after another SA partner is the problem i asked a bout my blocked tube which i had been shown to be told that that was incorrect she made me feel like i was making it up!!!	Claire Haresnape	21↘	my story group	1

APPENDICES

APPENDIX 12 memos written during thematic analysis of strand 4

Memo's Written During Thematic Analysis Of Forum Data

Memos regarding qualitative chapter

1. In vivo coding ((Charmaz, 2006) PAGE 55 that condense meanings consist of widely used terms that participants assume everyone shares.
Codes of participants special terms are in vivo codes.
Insider shorthand terms specific to this particular group are common due to the technical nature of infertility treatment and many procedures are referred to with abbreviations.

2. Triangulation was obtained by discussions with acquaintances going through infertility treatment at the time and using online forums (SSW). This helped confirm the use of some non technical abbreviations such as DH (Dear Husband) which I had assumed to be Donor Husband.

3. The literature search emerged from the coding which is the other way round than my quantitative section of the study. The work on Charmaz on identity and disability was suggested by Carol Rivas. The themes that emerged from the first smaller sample suggested the area of literature to review.

Is this an acceptable methodology?

4. reflection that symbolic interactionism is closely linked to placebo, 'we engage in a constant process of meaning making or mind action (Charon 2007)

Came across idea that Interpretive Description might be linked to my methodology. Paper by Carolyn Oliver 2011 explores the relationships between symbolic interactionism and Interpretative Description.

'An SI study must be about the ways in which people develop their lines of action in alignment with, or reaction to, those of others:' (Oliver, 2012) This quote makes me think of the forum members who are continually receiving feedback via the the reactions to their postings. There are articles about this online also see Wiki entry for SI and New Media

New Media[edit]]edit source]

New Media is a term used to define all that is related to the internet and the interplay between technology, images and sound.[10] As studies of online community proliferate, the concept of online community has become a more accepted social construct. Studies encompassed discursive communities;[11][12] identity;[13][14] community as social reality;[15] networking;[16] the public sphere;[17] ease and anonymity in interactions.[18] These studies show that online community is an important social construct in terms of its cultural, structural, political and economic character.

It has been demonstrated that people's ideas about community are formed, in part, through interactions both in online forums as well as those in face to face interactions. As a result, people act in their communities according to the meanings they derive about their environment, whether online or offline, from those interactions. This perspective reveals that online communication may very well take on different meanings for different people depending on information, circumstance, relationships, power, and other systems that make up communities of practice. People enact community the way it is conceived and the meaning of community evolves as they come up with new

ways to utilize it. Given this reality, scholars are continually challenged to research and understand how online communities are comprised, how they function, and how they are connected to offline social life.[19]

Symbolic Interaction Theory was discussed in "The Cyberself: The Self-ing Project goes online, Symbolic Interaction in the Digital Age." Robinson discusses how Symbolic Interaction theory explains the way individuals create a sense of self through their interactions with others. However, she believes advances in technology have changed this. The article investigates the manner in which individuals form their online identity. She uses symbolic interaction theory to examine the formation of the cyber "I" and a digital "generalized other." In the article, Robinson suggests individuals form new identities on the internet. She argues these cyber identities are not necessarily the way the individual would be perceived offline.[20]

5. Inductive reasoning consists of inferring general principles or rules from specific facts

6. Notes from Cardiff conference

Critical realism is presently most commonly associated with the work of Roy Bhaskar. Bhaskar developed a general philosophy of science that he described as transcendental realism, and a special philosophy of the human sciences that he called critical naturalism. The two terms were combined by other authors to form the umbrella term critical realism.

Transcendental realism attempts to establish that in order for scientific investigation to take place, the object of that investigation must have real, manipulable, internal mechanisms that can be actualised to produce particular outcomes. This is what we do when we conduct experiments. This stands in contrast to empiricist scientists' claim that all scientists can do is observe the relationship between cause and effect and impose meaning. Whilst empiricism, and positivism more generally, locate causal relationships at the level of events, Critical Realism locates them at the level of the generative mechanism, arguing that causal relationships are irreducible to empirical constant conjunctions of David Hume's doctrine; in other words, a

constant conjunctive relationship between events is neither sufficient nor even necessary to establish a causal relationship.

The implication of this is that science should be understood as an ongoing process in which scientists improve the concepts they use to understand the mechanisms that they study. It should not, in contrast to the claim of empiricists, be about the identification of a coincidence between a postulated independent variable and dependent variable. Positivism/falsification[clarification needed] are also rejected due to the observation that it is highly plausible that a mechanism will exist but either a) go unactivated, b) be activated, but not perceived, or c) be activated, but counteracted by other mechanisms, which results in its having unpredictable effects. Thus, non-realisation of a posited mechanism cannot (in contrast to the claim of positivists) be taken to signify its non-existence.

Critical naturalism argues that the transcendental realist model of science is equally applicable to both the physical and the human worlds. However, when we study the human world we are studying something fundamentally different from the physical world and must therefore adapt our strategy to studying it. Critical naturalism therefore prescribes social scientific method which seeks to identify the mechanisms producing social events, but with a recognition that these are in a much greater state of flux than those of the physical world (as human structures change much more readily than those of, say, a leaf). In particular, we must understand that human agency is made possible by social structures that themselves require the reproduction of certain actions/pre-conditions. Further, the individuals that inhabit these social structures are capable of consciously reflecting upon, and changing, the actions that produce them—a practice that is in part facilitated by social scientific research.

Critical realism has become an influential movement in British sociology and social science in general as a reaction to, and reconciliation of, so-called "postmodern" critiques.

270713.
Inspired by Charmaz model of ways of telling
Coding data for staging and spontaneous disclosure, notice that where I had used 'being open' these were quite often staged prononouments not spontaneous declarations. Not being open in the normal everyday sense.

Staging might be formalized such as asking for annual leave in order to attend appointments

New code emerging from the data

LOOKING AT SMALLER SAMPLE FIRST
Spontaneous and staged seemed inadequate to explain how they might be forced by circumstances to disclose so I added an extra code

Who did they disclose their treatment to? *Usually owner of business/ director/ manager or colleague or during interview.*
Sometimes they were sympathetic and sometimes they were not

No mention of spontaneous disclose to colleagues or friends but that is probably due to bias in my question.
Sometimes forced to disclose their need for treatment because they could not leave work easily for appointments.
What did they tell them? *Trying for a baby, waiting for treatment, needing time off for treatment, taking a fertility drug, hoping to go part time in the future. The focus is on the demands of treatment rather than internal drivers*

Social conditions affecting disclosure:
It depends on the manager, working in a child centred or friendly environment such as school or nursery, working for a forward thinking company, all had positive associations

smaller size of company, city worker, call centre, had negative associations

How did they tell them? *During annual review or job interview, as part of an application for annual leave these would be structured and staged opportunities. Also during a car journey and asking for a quiet word show premeditated intention to disclose treatment. Asking for time off to attend appointments so the demands of treatment dictate the need for disclosure.*

THOUGHT

DOES DISCLOSURE WORK DIFFERENTLY AT WORK, ARE PEOPLE USING THE FORUM FOR AN OPPORTUNITY TO HAVE SPONTANEOUS DISCLSURES BUT AT WORK THEY HAVE TO BE MORE GUARDED AND MEASURED.

HOW DOES FLAUNTING FIT IT? CHARMAZ

THE RISK OF TELLING VRS THE POSSIBLE BENEFITS RECEIVED FROM TELLING MIGHT EMERGE AS A THEME ON THE LARGER SAMPLE (82) FORUM MINIMISES THIS RISK BY PROVIDING ANONYMOUS OUTLET FOR TELLING AND RECEIVING SUPPORT

270713

If you look at the quotes for the being open codes from the large sample you can divide them into different categories depending on whom they have told:

TELLING WORK (186, 2) 186 was prompted by the need to work part time SO NOT SPONTANEOUS

I eventually also told work too when I requested to go part time which helped enormously…Had to pop into work that afternoon for a meeting with my

boss, let her know as best as I could.

NOT TELLING WORK 170,89,82,72,25,24) and the reasons for not telling include (aggregated quote): I work in a hospital environment and have to deal with seeing people who are pregnant and with children all the time, I have created a professional and cold shell I put up to allow me to function .. I am not telling work either, my job is quite pressured and I couldn't stand the speculation. When I was having treatment I didn't tell anyone at work although I was tempted on several occasions. I'm really glad I didn't. It was hard getting over the disappointment privately so dealing with other people too wouldn't have suited me. It also meant at work I could temporarily forget about it… We have to keep things very quiet here at work, for many reasons, so getting the time/dates to do it is proving a bit of a nightmare.. I haven't told work anything yet - I think I may have to but very reluctant - especially as its such a small team, there are about 10 employees.

TELLING FRIENDS AND FAMILY: 198, 186,65, 82170,186,82,72,65,100,61

AGGREGATED QUOTE

we finally told our families and very close friends what was going on. We'd wanted to keep it private but actually telling others was helpful - especially my family.. .We told lots of people about the ICSI. We wanted people to understand and we wanted their support and help. We knew we'd be in pieces if it didn't work. And people seemed surprised, particularly by our frankness, but supportive and encouraging.. I've told people, I can't keep my mouth shut about anything!.. but I have gradually started to open up about this .. I was so sad to give up on this surprise element.. but the loneliness was just too much to bear. So we have gradually starting telling people.. ….Telling my friends was hard (silly pride) but having one of two people you can really open up to aside from your partner I think is a real comfort. , i have had to carry out all past procedures in secret apart from a few close friends and family members.

NOT TELLING FRIENDS AND/OR FAMILY 144,198,89,25,24,72,65

We are optimistic about this but age is against us, im 36 and dh is 37. We havent told anybody about our if so when we found this website it was a godsend and provides the needed support although to date we havent come across anyone in the exactly the same position…I have chosen not to tell many people because I do not think people understand unless they have had to deal with IF themselves. DH struggles to talk about it although he does talk more since the IVF. But I do not think men have the same need to talk as we do and of course Male Factor IF does have a big impact on the male ego...We've had three cycles in all now, ending in BFNs, but we've really kept everything to ourselves since that first time, which I don't think is healthy He on the other hand refused to discuss any of it, completely shut me out of everything and stuck his head in the sand (plus he didnt want me to talk to anyone either, got very upset if i mentioned wanting to speak to any family or friends and all but forbid me to even speak to my mum!!). Eventually the strain became too much and we split…..We haven't told friends or family, we are quite private and want to do this our way….I've told a few close friends but not a wide circle of people that we're ttc. In a way the more people you tell the more pressure you put on yourself. After all the end of your story to conceive might (sadly) be a bit of a way off,. Being so far away from family also was very hard, although I've kept all this away from my Dad. We lost Mum last year and he has had a lot to deal with and I don't want him worrying about me at the moment. I could have done with a good cry and natter with my wonderful Mum that day though, I can tell you… I have had to carry out all past procedures in secret apart from a few close friends and family members

We have decided not to tell anyone about our situation and over time a lot of people have stopped asking us questions. we don't want to tell people when we do it in case it doesn't work

.

TELLING FORUM 144,100,89,65,9

We are optimistic about this but age is against us, im 36 and dh is 37. We havent told anybody about our if so when we found this website it was a

godsend and provides the needed support although to date we havent come across anyone in the exactly the same position… - hence finally, so very late in the day, joining in the forums, although I have been reading your posts and thoughts and feelings. I can't say how much they have helped me through some dark times. This site really is an outlet for me to share and understand others experiences, even more so for us as our decision to keep this to ourselves will no doubt be difficult. I am in my Mid thirties. Can aNyone help me in my isolation , i have had to carry out all past procedures in secret apart from a few close friends and familly members
1

1

THIS LED ME

	RISKS	*BENEFITS*
TELLING F & F	*being misunderstood* *emotional pain to self and others* *disappointment at treatment failure* *loss of privacy*	*receiving support and understanding*
NOT TELLING F & F	*not receiving support and understanding* *creates a sense of isolation*	*protects privacy*
TELLING WORK	*loss of earnings* *disapproval from manager* *career prospects damaged* *discrimination* *being misunderstood* *loss of privacy*	*support and understanding* *flexibility for time to attend treatment*
NOT TELLING WORK	*disciplinary action and* *loss of earnings for time off* *not receiving support and understanding*	*maintain privacy and professional role*
TELLING VIA FORUM	*negative experiences reported by*	*support and understanding with privacy due to*

		anonymity

NOTE SMALL COMPANY CAUSING PROBLEMS MIGHT LINK TO JERSEY BEING SMALL COMMUNITY

Telling or not telling as a form of control

to our earlier observation, all participants in the present study had access to the 28/07/13 A PRACTICAL ITERATIVE FRAMEWORK FOR QUALITATIVE DATA ANALYSIS (Srivastava, 2009)

The role of iteration is to develop a deeply reflexive processs which sparks insight and develops meaning. By visiting and revisiting the data you progressively develop refined focus and understanding. Srivastava has developed a framework of three basic questions to engage with the data analysis process.

Question one is WHAT ARE THE DATA TELLING ME?

Q2 WHAT IS IT I WANT TO KNOW?

Q3 WHAT IS THE DIALECTICAL RELATIONSHIP BETWEEN WHAT THE DATA ARE TELLING ME AND WHAT I WANT TO KNOW?

SO

Q1 What are the data telling me? That women who post their story on infertility forums are using the forum to share their story without loss of privacy. That the stories contain a lot of emotional distress and not much about employment issues. If you specifically ask for information about work stress then a small sample of women will tell you that they have experienced conflict between their identity as an employee and as a treatment seeker.

Where they have chosen to disclose their treatment status or condition they have done it in the context of the process they are engaged in and often because time was needed off work for treatment or appointments. Sometimes it is formalised as part of a performance review or interview.

If you look at the larger sample and specifically at the codes for being open/nondisclosure then you see that the reasons for not telling vary from protecting privacy, avoiding emotional pain and disappointment at failed

treatment to maintaining a professional role, avoiding additional pressure or speculation, working in a small team.

The reasons for telling work include needing to ask time off but not many quotes available

Question two , what is it I want to find out? I want to know if pressure of work inhibits women from taking part in clinical trials.

Question three what is the relationship between q1 and q2? We can see that a few women are concerned with the difficulties of managing the conflict between work and treatment but that the majority of their concerns are around emotional distress and treatment failure.

Discussion

We could detect three online behavioural styles in IVF patient couples: an 'individual information style', a 'generic information style' and a 'communication style'. There are only a limited number of correlations between these styles and demographics or coping mechanisms: patients having paid employment are significantly less attracted to individual information and significantly more to communication functions. Patients who exhibit the coping mechanism of sharing of emotions show less attraction to individual information. Although only a trend was observed, patients with a more depressive mood seem less likely to look for information concerning their own treatment and more likely to use the website to find generic information concerning the IVF treatment. A longitudinal study would explain this relationship in more detail. The positive relationship between anxiety at the start of the treatment and the 'communication style' suggests that more anxious patients are more likely to use the bulletin board (which provides asynchronous web communication) and the chatroom (for synchronous web communication) functions of the website.

It is possible that they communicate on the website as a way to relieve their anxiety. In a larger sample size, it would have been possible to investigate possible interaction effects between online behavioural style, coping mechanisms and anxiety and depression.

The lack of correlation between the behavioural styles and the demographic variables 'household income' and 'ethnic background' is notable. In previous

research by Haagen et al. (2003), both variables were significant predictors of overall internet usage, whereas in the present study, they are not. This can be attributed to differences in both study populations. In contrast Internet.(Tuil et al., 2008)

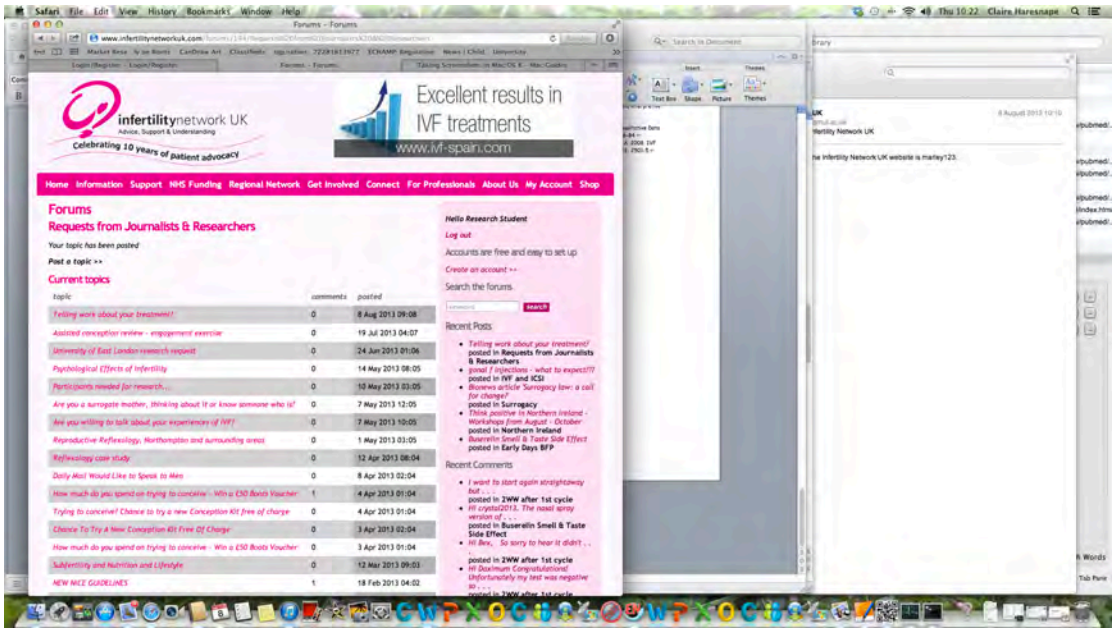
070813 just realised whilst reading (Silverman, 2013) that my focus on the work related concerns of women seeking infertility treatment could also reflect my own concerns as a working mother doing a PhD. There is the issue of the need to negotiate time off for non work activities such as Hospital appointments for self and child.

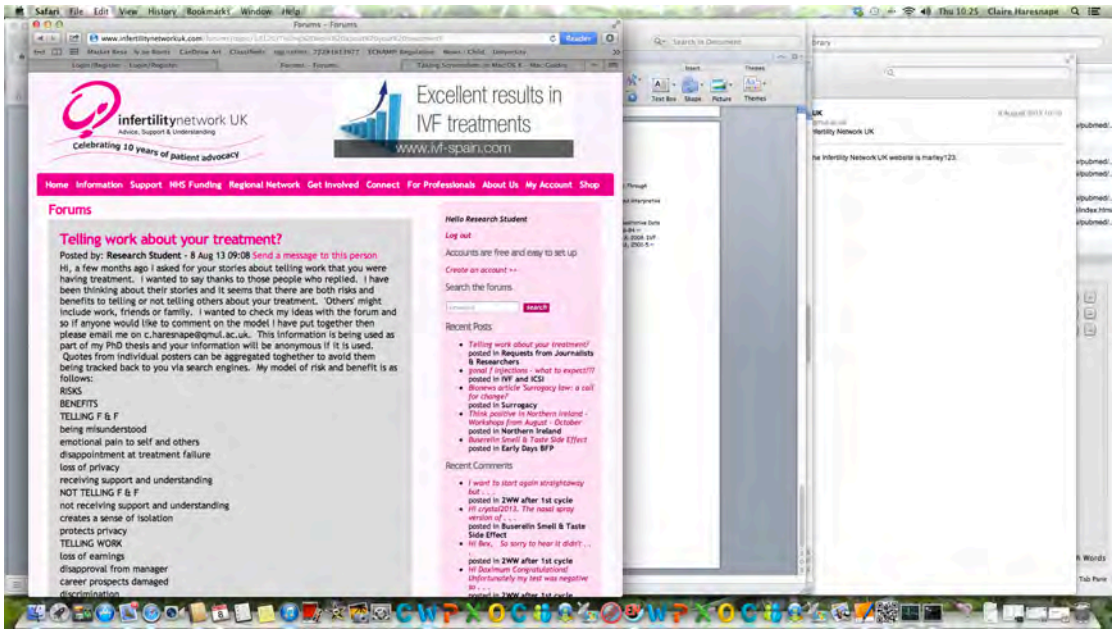
080813 Decided to use itartive analysis and check my model with the forum again. No need to ask administrators for permission as there is a special section for research questions so posted my question at 10.22 on Thursday 8th August 2013 Screeen shot attached

Hi, a few months ago I asked for your stories about telling work that you were having treatment. I wanted to say thanks to those people who replied. I have been thinking about their stories and it seems that there are both risks and benefits to telling or not telling others about your treatment. 'Others' might include work, friends or family. I wanted to check my ideas with the forum and so if anyone would like to comment on the model I have put together then please email me on c.haresnape@qmul.ac.uk. This

information is being used as part of my PhD thesis and your information will be anonymised if it is used. Quotes from individual posters can be aggregated together to avoid them being tracked back to you via search engines. My model of risk and benefit is as follows:

	RISKS	*BENEFITS*
TELLING F & F	*Being misunderstood* *Emotional pain to self and others* *Disappointment at treatment failure* *Loss of privacy*	*Receiving support and understanding*
NOT TELLING F & F	*Not receiving support and understanding* *Creates a sense of isolation*	*Protects privacy*
TELLING WORK	*Loss of earnings* *Disapproval from manager* *Career prospects damaged* *Discrimination* *Being misunderstood* *Loss of privacy*	*Support and understanding* *Flexibility for time to attend treatment*
NOT TELLING WORK	*Disciplinary action and* *Loss of earnings for time off* *Not receiving support and understanding*	*Maintain privacy and professional role*
TELLING VIA FORUM	*Negative experiences reported by others might be overwhelming.*	*Support and understanding with privacy due to anonymity*


infertilitynetwork UK
Advice, Support & Understanding
Celebrating 10 years of patient advocacy
Excellent results in IVF treatments
www.ivf-spain.com
Home Information Support NHS Funding Regional Network Get Involved Connect For Professionals About Us My Account Shop
Forums
Requests from Journalists & Researchers
Your topic has been posted
Post a topic >>
Current topics
topic
comments
posted
Hello Research Student
Log out
Accounts are free and easy to set up
Create an account >>
Search the forums
Recent Posts
Recent Comments



The tables did not come out properly so it appears as a list

The hunch that I am following is that women negotiate between the risks and benefits by disclosing information at work in a controlled and premeditated way to maximise benefit and minimise risks. The uncertainty inherent in their situation is that there is not legal framework to support their position. Perhaps the problem with taking part in a clinical trial is that it forces disclosure and maximises risks. Also the benefits to taking part in a clinical trial where they might receive a placebo might not be strong enough to balance the risks.

IDEAS FOR NEW STRUCTURE OF QUALITATIVE CHAPTER SEE RED HANDWRITTEN NOTES

Reflections on David Silverman's Doing Qualitative Research

2.1 My decision to use qualitative research methodology was because of the nature of the research question rather than starting off using qualitative

research and thus it influencing the way I defined my research problem. The method emerged from the direction that the project took. Silverman calls this 'how biographical factors play an important role in how students plan their research..' page 8

Exercise 2.2
Explain why you think a qualitative method is appropriate to your own research project?

I was trying to find out how women undergoing infertility treatment feel about attending appointments and having to ask for time off work. We wanted to know if this was stopping them being recruited for my trial. My original trial design intended to offset the advantages of a questionnaire and the rct design. I felt it would have more credibility if it included a qol questionnaire as well as just their clinical results.
I moved to investigate the reasons because I was sampling a new population to create completeness in my study. To some extent the situation in Jersey was an unexpected result and new insights needed to be found

Would quantitative methods be more appropriate and if not why not?
This would mean I needed access to numerical data for example the employment records of women showing how many days off they had requested or how many appointments were attended at the clinic. This would not answer the question about why they did NOT attend appointments due to pressures at work. It would not tell me how they perceived the trial or their feelings about taking part.

Would it make sense to combine qualitative and quantitative methods?

If we could get access to data about the number of appointments attended or we could analyse the responses of women in Jersey to a questionnaire (Qual or quan?) then that would give me a deeper understanding of the pressures they faced and the scale of the issue.

Notes on Integrating quantitative and qualitative research: how is it done? (Bryman, 2006a)

The dimensions out of which the different typologies are constructed are useful:

Are the quantitative and qualitative data collected simultaneously or sequentially? In my case the quantitative data was the primary source but was insufficient and then we moved to qualitative data as a secondary source (before analysis of the primary data).

2. Which has priority – the quantitative data or the qualitative data? In my case the qualitative data overtakes because of the failure to recruit sufficient women to the study.

3. What is the function of the integration for example triangulation, explanation or exploration. I would say mine was an exploration as we were looking for something that had been suggested. It was also an attempt to develop a theory.

At what stage in the research process does multi-strategy research occur? In my case it occurred after the initial research question and attempts at data collection and it occurred as part of the data analysis.

Is there more than one data strand? Yes we had the initial trial, the small sample and the larger sample

What are the justifications for combining quantitative and qualitative research? Greene et al 1989 has a scheme which isolates five justifications:

Triangulation: convergence, corroboration, correspondence or results from different methods. Seeking corroboration between quantitative and qualitative data.

Complementarity: seeking elaboration, enhancement, illustration, clarification of the results from one method with the results of another

Development: seeks to use the results from one method to help develop or inform the other method, where development is broadly construed to included sampling and implementation as well as measurement decisions.

Initiation: seeks the discovery of paradox and contradiction, new perspectives of frameworks, the recasting of questions or results from one method with questions or results from the other method.

Expansion : seeks to extend the breadth and range of enquiry by using different methods for different inquiry components

This scheme is parsimonious and so Bryman has devised a more detailed scheme based on the extensive review of the kinds of reasons that are frequently given for combining research methods:

1. Triangulation or greater validity refers to the traditional view that quantitative and qualitative research might be combined to triangulate findings in order that they be mutually corroborated.

2 Offset: combining methods allows the author to offset the strengths and weaknesses of each method.

3. Completeness, combining methods means that the researcher can bring together a more comprehensive account

4. Process, quan can provide an account of the structures in social life but qual can proved a sense of process.

5. Different research questions

6 Explanation one is used to help explain findings by the other

unexpected results

Instrument development

Samplings

Credibility

Context

Utility

Confirm and discover use qual data to generate hypotheses and quant research to test them

Diversity of views

Enhancement

Key points from page 41, 'treat your relations within the field as data', this study was characterised by delays and difficulties in communication with supervisor and site staff. The difficulty in setting up a reliable audit of the study via the site nurse and the effect of my expectations of her are an example. I should have made those expectations clear at the earlier

meetings with Neil. If I analyse my research diary how many times do I say that I am waiting for a response or that there is no response?

Date	*Diary Entry*
130310	*Waiting for letter of confirmation from JGH Ethics*
000510	*Waiting for AJ to arrange patient insurance*
130710	*Left message for AJ asking for tutorial*
201010	*Meeting with NM at JGH cancelled at short notice as he is flying to London to give evidence in a court case*

Page 47 I realise that I need to sort out the methodology of using internet data, although I have looked at the ethical issues around using it I also need to think about the methodological literature on analysing internet data.

http://webometrics.wlv.ac.uk

In comparison to content analysis, grounded theory has the advantage that it produces theories from the texts and the outcomes can be more interesting as a result. A key disadvantage is that the method is non-scientific in the sense that the results are not normally based upon random samples of texts and there are no real safeguards against researcher bias. In contrast, content analysis can use multiple coders to guard against bias. With grounded theory the onus is on the researcher to make the case that the findings are a valid interpretation of the texts.(Thelwall, 2009)
Silverman page 57 recommends the work of Helen Snee a British Sociologist based at Manchester. I listened to her youtube video http://www.youtube.com/watch?v=k-iBE-CLg2k and found her ideas promoted me to think about the differences between my large and small samples:

The small sample was constructed because I actively solicited information by posting a question on the forum. I am a participant observer

The large sample is naturalistic because I viewed the work that members had spontaneously posted. I am unobtrusive and an observer only.

The Methodological issues that she encountered and that resonated with me included:
The biased nature of the sample in that it only captures the views of those people who have posted on the forum.
The ethical challenges of how to view the members of the forum, are they private individuals who need to have their identity protected or are they authors whose work should be cited? She resolved this by taking a view that it is contextually dependent not black and white …
One key to this might be that the intended audience for my members is other people suffering from the same or similar conditions, who may be unknown to them, rather than friends or family known to them. In her study of gap year students the blogs were used to update people they knew about their progress.

Using a forum rather than a blog like she did reduces the amount of redundant data needing to be trawled through, it was a more focussed approach.

It has an interactive element (I post questions and become a participant observer) and also I can chose to look beyond the initial posting to view the comments made by members about each others work, (I am observing only)

10.08.13 gone back to forums to saturate categories with further data
Tried doing word searches on 'boss', 'job' saved as separate files. Also looking more closely at the conversations between forum members
11.08.13 Working on chapter 7 Using Theories of Silverman book
page 108-109 Grounded Theory

a defining strategy of grounded theory is theoretical sampling in order to flesh out the properties of a tentative category. As Charmaz and Bryant put it:
Theoretical sampling involves gathering new data to check hunches and to confirm that the properties of the grounded theorist's theoretical category are filled out…'
Theoretical sampling helps develop grounded theories based on situation and concepts which are progressively widened by :
Including social situations very different from those with which one began
Linking concepts to broader theories

This reflects two key features of the GT approach:
The constant comparative method as the analyst seeks out settings which may modify or broaden her initial categories
A continual movement between data, memos and theory so that data analysis is theoretically based and theory is grounded in data.

Because of the difficulties with my initial thesis draft I have returned to theory and returning to theory has stimulated me to revisit the data, the literature and the forums in search of theoretical sampling. I have become ITERATIVE

I now wonder if the earlier work I did on the homotoxicology treatment and the nurses focus group are indeed grounded theory?? I suspect that they do not fulfil that criteria and might be better described as a survey.

WATCHING PROF TONY BRYANT ON YOUTUBE AS SUGGESTED ON PAGE 109
Should our methods be prescriptive, advisory or heuristic?
Crtiques the Corbin book as mechanistic but it made GT popular
GT is a 'family of methods'
Grounded means theory is grounded in the data, get your data from the research context. Discovery or construction? We prefer constructionalism because it takes into account that different people will construct different meanings from the same data

Peirce the pragmatist, you try and find patterns but how you come across those patterns may be suprising (abduction) not induction or dedeuction.

Using the literature is a problem because, Glaser (keeping an open mind means don't engage with the literature). Quick and Dirty method?

110813 Reading through the forum postings one way women negotiate time off work is to be signed off for stress.

Channel Islands?

Posted by: ***Research Student*** *- 11 Aug 13 09:08 Send a message to this person*

Hi, I have already posted some details of my PhD study based at Queen Mary University of London. The data I obtained from your responses was used to help me understand the experiences of women who have to juggle work and treatment commitments. I would be interested to interview (via email) men and women based in the Channel Islands as part of my analysis. Any information provided would be used anonymously. My study has ethical approval from Jersey General Hospital. If you would be interested in sharing your experiences with me my email address is c.haresnape@qmul.ac.uk

Thanks and best wishes

Claire Haresnape

Post Graduate Research Student

Queen Mary University of London

See more at: http://www.infertilitynetworkuk.com/forums/topic/18125/Channel%20Islands?#sthash.nfavOHi9.dpuf

Key points from page 119

Models provide an overall framework for how we look at reality

Concepts are clearly specified ideas deriving from a particular model

Theories arrange sets of concepts to define and explain some phenomenon

Methodologies define how one will go about studying any phenomenon
Methods are specific research techniques

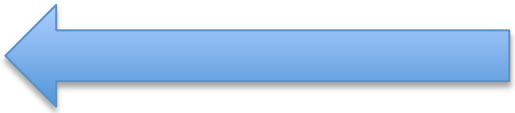
My Study

Model = Constructionism or Naturalism? If I use thematic analysis I can use both methods. See notes on thematic analysis

Concept = Definitions of the situation, how do women undergoing infertility treatment construct their reality in the face of strong emotional pressures and a lot of uncertainty about treatment success and the absence of a clear legal framework or company policy

Theory = Risks and Benefits of disclosing infertility treatment at work = consequence theory.

Hypothesis = Women undergoing infertility treatment are trying to minimise the risks of disclosure and taking part in a trial may force disclosure without producing additional benefits



Methodology = naturally occurring data (theoretical thematic analysis), and data received in response to posting on forum (theoretical thematic analysis)

Methods = observing, recording, semi structured online interview, analysis of text, iterative process of returning to forum with theory or model to share, use of theoretical thematic analysis to create a theory (Grounded Theory Charmaz style).

Findings = Concerns of women undergoing infertility treatment

Chapter 8 Choosing Methodology

There are no right or wrong methods there are only methods that are appropriate to your research topic and the model with which you are working.

Observation is fundamental to understanding another culture

Textual analysis helps understand participant's categories

Interviews consist of open ended questions to small samples

Method	*Naturalists*	*Constructionists*
Observation	*Understanding Subcultures*	*Asking both 'what' and 'how' questions to understand how interaction is organised*
Texts and Documents	*Background Material*	*Understanding of Language and other sign systems*
Interviews	*Understanding experience*	*Narrative construction*

When we analyse text from the forum how can we be sure that it reflects their social or psychological world?

Reflect that I could have approached this study with a naturalistic approach by looking at the My Story section of the forum first, immersing myself in that data and then looking for categories. Instead I took a constructionist approach because I created data by setting up a research question on the forum and then I imposed these categories on the data from 'My Story'. Or did I seek to discover them!! I sought them would be a better description..

Exercise 8.1

The data source open to me are the uk infertility forums online such as INUK and Fertility Friends.
These can give me naturally occurring data that tells participants experiences in their own words as well as interactions between different participants as they respond to posts from each other.
They can help me understand the fears and hopes, social pressures, medical treatments, relationships and physical effects of those women and men undergoing infertility treatment.
This might help me understand how they construct their reality to cope with the success and failure of treatment in a very uncertain arena with high failure rates and high expectations\high stakes.
This could help me understand how they might view taking part in a clinical trial where they might receive a placebo, how they view disclosing their treatment at work

Query: is information from a forum naturally occurring data?
Query: how might I identify deviant cases when I am trying to saturate my data?

Query: what other situations might my model fit so that I can create a generalised formal theory as opposed to a substantive theory. What about the risks and benefits of disclosing HIV status, disability, homosexuality, terminal illness?
(Rouleau et al., 2012) sheds some light on this idea:

Various conditions can influence disclosure. These include the confidant's ability to keep a secret, whether or not a climate of trust exists, a feeling of closeness and intimacy, the nature of the relationship (sexual or non-sexual), the consequences anticipated, one's perception of being stigmatized, and prior disclosure experiences [8,20,27,28]. In light of these conditions, interpersonal relations are clearly central in the decision to disclose or not. HIV-positive persons must choose carefully who they reveal their serostatus

to [27,29-31]. Moreover, it appears that there is a prior evaluation of the rewards and costs of disclosing to family and friends before disclosure occurs, which is supported by Consequence Theory [10,32]. This theoretical model proved useful in explaining disclosure in a study involving 125 HIV-positive women [10]. The principal rewards (benefits) for these WLHIV had more to do with the safety of others and their right to be informed than with oneself. The perceived costs (negative consequences) were in connection with the negative aspects of breaking the news, such as the fact of being reprimanded [10]. Disclosure occurs if the person perceives the benefits to outweigh the negative consequences and if it can thus avoid situations likely to cause harm [32](Rouleau et al., 2012)

What is consequence theory? How does this fit the theory I have devised?

(Corrigan et al., 2009) Table 1 Perceived contingencies affecting coming out Benefits

person to bring together many important people and issues into one's experience.

Participants also noticed interpersonal costs of coming out to family and friends. These are sometimes poignant and may lead people into thinking they were better in the closet. ''I am still saddened by my parent's response. I went from being the super-star daughter who does all these wonderful things to being, 'Oh well, we only expect this from you'' [Suzy]. This forces some people back into the closet. ''You know, I didn't want to hurt my mom, because she cried and she didn't talk to me for a whole month. So, if I were to stay in the closet, it would probably be because of family'' [Betsy].

Acceptance may also have meaning at the personal level; namely, recognition and acknowledgement that being gay or lesbian is part of what significantly defines the person's identity. This kind of awareness is fundamental to his or her identity.

Well, I know it's something I can't change. With enough of a career change I could start to feel like a different career person. If I move, I won't feel like a

Chicagoan and if I change religions I won't feel Jewish. But I think gay is so innate and so much a part of me that it's very close to who I am [James].

For some individuals, the many pains of acknowledging or taking on a stigmatized identity result in decisions to never come out, to never accept the experience for them- selves, and to never obtain solace from others. ''If I could choose this life again, I would be wealthy by now and I would not be gay... The lifestyle... It's too much weight for one person to carry'' [Simon]. Suzy said ''But I think at

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Acceptance: The place to begin is seeking recognition and support of key people in one's social network, most prominently including family but also friends, coworkers, peers in a faith congregation and others. This is social acceptance which is distinguished from self-acceptance. Gay men and lesbians seek to acknowledge their sexual orientation for themselves without disparagement or shame. As people learn to accept themselves, opportunities emerge for gay men and lesbians to acknowledge their multi-faceted and complex self. This kind of honesty opens the person for greater acceptance and a more integrated and positive sense of self

Community: One way in which gay men and lesbians have learned to deal with discrimination is through the development of a gay community. As gay communities matured, members sought to spread their hegemony. Groups of gay men and lesbians organized to address obvious discrimination as well as more subtle forms of prejudice. Another goal of actively participating in the gay community is to provide opportunities for peers who continue to struggle with discrimination. This kind of altruism generalizes to an overall concern about the well-being of members of the community

Comfort and Happiness: Coming out and personal acceptance have the most basic of effects on gay men and lesbians. This experience is variably enjoyed as relief, freedom, and opportunity. With comfort comes the most deep-seated experiences of life satisfactions: happiness. One way this emerges is a sense of optimism about sexual orientation

Costs

Shame and Conformity: This is the sense of failure that results from and the stigma of gays and lesbians. One way to protect one's self from the shame

and other egregious effects of public attitudes about being gay is to conform sexually, to pass as heterosexual

Harm and Discrimination: Gay men and lesbians often lose opportunities in the world of work, as well in finances, with family, and in health. Moreover, many people who are out with their sexual orientation are physically or verbally assaulted by the public. Pronounced struggles with coming out and being in the closet impact people both psychologically and physically

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110813

See below for good example of how you achieve credibility in your study.

Credibility is, according to Lincoln and Guba [43], one of the most important criteria for establishing trustworthiness. Results are credible when the phenomenon under study is recognized by participants and experts and it reflects their personal experience [43,44]. The authenticity criterion refers to the fact that results must be in line with or reflect the experiences described and lived by participants [44]. In the aim of meeting these criteria, the principal investigator: used bracketing; read the interviews many times over; went back and forth between data collection and analysis; reached data saturation; used peer reviewing and held debriefing sessions with the two research directors (supervisors) regarding the data collected, analysis and interpretation.(Rouleau et al., 2012)

Notes on Thematic Analysis (Braun and Clarke, 2006a)

Thematic analysis should be seen as a foundation method for qualitative analysis, providing core skills that will be useful for other forms of QA.
Qualitative methods can be roughly divided into two camps:
those that are tied to or stemming from a particular theoretical or epistemological position. For example conversational analysis (CA); interpretative phenomenological analysis (IPA), Grounded Theory, Discourse analysis, Narrative analysis,
Methods that are essentially independent of theory and epistemology and can be applied across a range of theoretical and epistemological approaches.

KEY TERMS
Data corpus refers to all data collected for a particular research project
Data set refers to all the data from the corpus that is being used for a particular analysis
Your data set might consist of many or all individual items within your data corpus or it might be identified by a particular analystic interest
Data item is used to refer to each individual piece of data collected
Data extract refers to an individual coded chunk of data that has been identified within and extracted from a data item.

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WHAT IS THEMATIC ANALYSIS
A method for identifying, analysing and reporting patterns (themes) within data. It minimally organises and describes your data set in (rich) details. It often goes further than this and interprets various aspects of the research topic. The range of different possible thematic analysis relate to a number of decisions regarding method.

The language of themes emerging:
'can be misinterpreted to mean that themes reside in the data …but if they reside anywhere they reside in our heads from our thinking about our data

and creating links as we understand them (Ely,Vinz, Downing, & Anzul, 1997:205-6)
((taken from page 7 of paper))

page 8: a named and claimed thematic analysis means researchers need not subscribe to the implicit theoretical commitments of a 'full-fat' grounded theory if they do not wish to produce a fully worked-up grounded theory analysis.

IMPLICATIONS FOR MY STUDY, I HAVE ACTUALLY USED THEMATIC ANALYSIS TO LOOK AT THE PRACTITIONERS AND NURSES DATA NOT GT SO NEED TO CHANGE THAT.

TA can be an essentialist or realist method which reports experiences, meanings and the reality of participants or it can be a constructionist method which examines the ways in which events, realities, meanings and experiences and so on are the effects of a range of discourses operating within society. (Page 9). The important thing is to make your theoretical position transparent.

What counts as a theme?
A theme is something which captures something important about the data in relation to the research question and represents some level of patterned response or meaning within the data set.

Prevalence of a theme might refer to the number of participants who mention it or to the number of times it appears in the total dataset.

A rich description of the data set, or a detailed account of one particular aspect

It is important to decide if you want to provide a rich thematic description of your entire data set so your reader gets a sense of the predominant or

important themes or you might wish to provide a more detailed and nuanced account of one particular theme or group of themes within the data.

Inductive vrs theoretical thematic analysis
Themes or patterns can be identified in one of two primary ways in thematic analysis:
Inductive or 'bottom up' way this means the themes are strongly linked to the data themselves it is a process of coding the data without trying to fit it into a pre-existing coding frame or the researches analytical preconceptions
Theoretical or 'top down' way means it is driven by the researchers theoretical or analytic interest in the area.
You can either code for a specific research question (theoretical approach) or the specific research question can evolve through the coding process (inductive approach).

Epistemology: essentialist/realist vs constructionist thematic analysis
The research epistemology guides what you can say about your data and informs how you theorise meaning.
For example with an essentialist/realist approach you can theorise motivations, experience and meaning in a straight forward way, because a simple, largely unidirectional relationship is assumed between meaning and experience a and language (language reflects and enables us to articulate meaning and experience).
In contrast from a constructionist perspective, meaning and experience are socially produced, rather than inhering within individuals. Therefore, thematic analysis conducted within a constructionist framework cannot and does not seek to focus on motivation or individual psychologies, but instead seeks to theorise the socio-cultural contexts and structural conditions that enable the individual accounts that are provided.

Doing thematic analysis a step by step guide

The process begins when the analyst starts to look for patterns of meaning and issues of potential interest in the data.

Writing is an integral part of analysis not something that takes place at the end

Engaging with the literature early on can sensitize you to more subtle features of the data or some would argue that it narrows your field of view.

A more inductive approach would be enhanced by not engaging with the literature in the early stages of analysis whereas a theoretical approach requires engagement with the literature prior to analysis.

question.

150813
the previous posts were removed and this was sent today
It was approved by Hannah and posted on 160813

Dear Hannah

I would like to post a research question on the INUK forum please. Last year some of your forum members responded to my enquiries about their work related stress. I have been using their responses as part of my PhD project.
The PhD was initially the design and implementation of a small clinical trial of a homeopathic product to support infertility treatment at a unit in Jersey.
The trial had to be closed down due to poor recruitment.
I then switched to investigating the reasons for poor recruitment and it was most helpful to get feedback from the forum.
I have used their responses to create a 'risk-benefit' theory that I would like to share with forum members for their feedback.

My question would look something like this:

Last year some of the forum members supported by PhD project by sharing their experiences of work related stress, I have used the data provided to generate the following theory and I would appreciate your feedback about it:

The risks of telling employers about treatment need to be balanced against the benefits of disclosure.

The risk of disclosure may include increased stress at work due to expectations of treatment success, emotional distress at treatment failure, being misunderstood, sexual discrimination for time taken off work for treatment, loss of earning or career prospects, having to use annual leave for treatment.

The benefits of disclosure at work might include support and understanding from colleagues or managers, flexible working arrangements and relief at not

having to hide a secret. Women who disclose their intention to have or participation in infertility treatment tend to do so in a controlled way, perhaps as part of formal request for time off , job interview or performance review.
If a company has a clear policy or legal framework exists then the risks of disclosure are reduced (added on 20.08.13)

This allows them to finely balance the risks and benefits of disclosure vs non disclosure. Taking part in a clinical trial that required them to attend additional appointments might force them to disclose their treatment and the benefits of taking part in a trial may not be worth this risk. Taking part in a trial may offer benefits but these are unknown particularly in a randomised trial where you might only receive a placebo.

Please can you tell me if this is an accurate representation of how you would approach the dilemma of telling your employers about your infertility treatment

Your réponses will be used as part of my PhD thesis but would be anonymised and used as an aggregated quote so that they cannot be traced back to you.

Thank you for your help and best wishes

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120813 QUERY TO SELF: SHOULD I BE OBTAINING ETHICAL APPROVAL FROM QMUL BEFORE POSTING QUESTIONS ON THE INTERNET? ASK CR AND AT AND AJ? Although the consensus was yes it was ok to proceed I removed the orginaial quotes and approached Hannah at INUK on 150813 to create a new post.

190813

Looking through my code segments of data for the original small sample I need to saturate those categories with more data but where to find it? I have then moved to a small sample of the My Story forum…

Exercise 8.1
Possible research methods and data source options:
Interviews with women who attended the clinic in Jersey. Problems with access and ethics
Questionnaire by post or phone with women who attended the clinic in Jersey, problems with access and ethics
Questionnaire to employers in Jersey, tried to do this through the chamber of commerce but no reply or response from companies
Interviews with women attending UK infertility clinics, need to form a relationship with a clinic and get ethics
Questionnaire by post or phone for women attending UK clinic , access and ethics
Posting questions on UK forum done this
Contact other researchers who have conducted trials in Jersey or trials with infertile women. Doing this already.
Interviews or questionnaires with HR and Employers
What data sources and methods of data generation are potentially available or appropriate?
The UK infertility forums
+

9 How many cases do you need?

The aim is to try and develop as full an understanding as possible
Robert Stake has identified three different types of case study

The intrinsic case study where this case is of interest in all its particularity and ordinariness. No attempt is made to generalize beyond a single case or even to build theories.
The instrumental case study in which a case is examined mainly to provide insight into an issue or to revise a generalization. Although the case is selected and studied indepth the main focus is on something else.
The collective case study where a number of cases are studied in depth in order to investigate some general phenomenon.

Qualitative research should produce explanations which are generalizable in some way or which have a wider resonance.
The Qualitative Model of Generalization
Generalizability is a standard aim in quantitative research and is normally achieved by statistical sampling procedures. Such sampling has two functions: it allows you to feel confident about the representativeness of your sample and it allows you to make inferences about the broader population.

The logic of random sampling may not work in qualitative research see page 145
In case study research:
We generalize to theoretical propositions not populations
We sample social relations not individuals
We can test theories by choosing extreme or deviant cases
We can choose new cases during our research, confident that this is not problematic but expected and useful.

Purposive sampling is guided by time and resources and researchers seek out groups settings and individuals where the processes being studied are most likely to occur.

Theoretical sampling means selecting groups or categories to study on the basis of their relevance to your research questions, your theoretical position and the explanation or account which you are developing. Theoretical sampling is concerned with constructing a sample which is meaningful theoretically because it builds in certain characteristics or criteria which help to develop and test your theory and explanation (Mason 1996 page 151 of Silverman book

Theoretical sampling has three features:
Choosing cases in terms of your theory
Choosing deviant cases
Changing the size of your sample during the research
Doubt gate keepers on principal! Page 153

Qualitative research can improve the generalizability of our findings by allowing us to include new cases after initial findings are satisfied.

Replace 'case' with instance and 'generalisatio' with 'extrapolation'.

10: Ethical Research
Voluntary participation and the right to withdraw
Protection of research participants
Assessment of potential benefit and risks to participants
Obtaining informed consent
Not doing harm

Complex Ethical Issues:
Consent to observational research
Consent to internet research
Whether there can be an 'appropriate' deception
Paying participants
The unintended consequences of good ethical practice.

Consent to internet research
Many users perceive publically accessible discourse sites as private
Anonymity is difficult to guarantee
Online discussion sites can be highly transient
Vulnerable persons are difficult to identify (age for example).

Claire,

My opinion is that if you are on this forum and you choose to answer a question posted to the forum you have consented. If you go further than that and approach a respondent outside the confines of the forum then we might to think about it.

Best wishes.

Atholl

200813 Realised that I have used the idea of keyword frequency to construct my theretical model after reading Clive Seal's work

PART THREE
Collecting and analysing your data
12: Collecting your data

290813

READING THROUGH THE SILVERMAN CHAPTER ON RELIABILITY LED ME TO GO BACK TO THE FORUM TO LOOK FOR DEVIANT CASES. CAME ACROSS AN ACCOUNT POSTED BY EMA ON 040110 ABOUT TEACHERS HAVING DIFFICULTY ASKING FOR TIME OFF. LED TO THINKING ABOUT NOT FEELING WORTHY WHICH WAS A MINOR CODE BEFORE AND HOW TIME OFF IS SANCTIONED BY AN AUTHORITY FIGURE SUCH AS BOSS OR DOCTOR. INCORPORATED THIS INTO THE MODEL SUGGESTED BY CAROL RIVAS CTY VERSION

300813
Reading charmaz paper on disclosing disability in the work place. Linking peoples proclivity to disclose with the amount of legitamancy granted to their health condition. Infertility may not be legitimised as a condition that warrents time off work but GP will validate their desire for time off by signing them off with stress or other related conditions.

Also GP is authority figure who sanctions time off and legitimises the condition.

Conflict between the role of the doctor and the role of the employer reflects the conflict between role as treatment seeker or employee

Could return to my 'medical sign off' codes to look for examples.

APPENDICES

APPENDIX 13 The References for Protocol for OVCT-001 Strand 3

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