

# **THE CLINICAL EFFECTS OF NEUROMODULATION THERAPIES IN THE TREATMENT OF FAECAL INCONTINENCE**

by

**Noel N. K. S. Thin**

Queen Mary's  
National Centre for Bowel Research and Surgical Innovation

A Thesis submitted for the Degree of  
Medical Doctorate (Research)

The University of London

November 2016

# **ABSTRACT**

## **Background and Aims**

Sacral nerve stimulation (SNS) is an established therapy for faecal incontinence (FI). Percutaneous tibial nerve stimulation (PTNS) is a newer, less-invasive treatment. The effectiveness, cost and acceptability of these treatments have not been systematically compared.

## **Methods**

A systematic review of neuromodulation interventions for FI and an investigator-blinded, randomised pilot trial of PTNS vs. SNS including parallel quantitative (clinical outcomes and cost) and qualitative studies.

## **Results**

The systematic review determined on intention-to-treat, the median success rates for SNS were 63% (range 33-66%), 58% (range 52-81%) and 54% (range 50-58%) in the short, medium and long terms respectively. The success rate for PTNS was 59% at 12 months. In the pilot trial: 40 patients (39 female; mean age 59 years) met eligibility criteria. As designed, 23 were randomised to receive SNS and 17 PTNS. 15 patients progressed to permanent SNS implantation and 16 patients received a full course of PTNS. Within group effect sizes were marginally greater for SNS than PTNS on available case analysis. FI episodes per week at baseline, 3 months and 6 months follow-up: SNS median 5.75 (IQR 5.75-15.5 ) [mean 11.4 (SD 12.0)], 2.5 (2-4.5) [4.0 (4.0)], 1.75 (1.5-5) [4.9 (6.9)], vs. PTNS median 6.5 (IQR 2.5-16.5) [mean 10.6 (SD 11.2)], 3.5 (0.75-7.25) [5.8 (6.9)], 2.5 (0.75-10.75) [6.3

(6.9)]. At least 50% improvement in FI episodes per week at 6 months: SNS 61% vs. PTNS 47%. Effect estimates for SNS with chronic implanted stimulation were larger (67% at 6 months). Clinical FI scores and quality of life improvements complemented these results. Qualitative analysis demonstrated a very high acceptability and safety profile for both treatments. Total costs were £2,906 (SD £122) per patient for PTNS and £12,748 (SD £4,175) for SNS.

## **Conclusions**

Definitive trial data between SNS or PTNS is lacking. This RCT pilot study determined that in the short-term, SNS confers a small clinical benefit over PTNS for FI but is much more expensive.

## **ACKNOWLEDGEMENTS**

I am forever indebted to my supervisors, Professor Charles H. Knowles, Professor Norman S. Williams and Professor Stephanie J. Taylor for their tireless patience, motivation, encouragement and support throughout my studies, without which completion of this thesis would not have been imaginable. I would also like to personally thank Dr Paul Allen for his support and understanding in ensuring that I am able to complete my studies. I am most grateful for the willingness and enthusiasm with which they have all offered their advice, time and assistance. Further, I should like to pay special tribute to Professor Charles Knowles for providing me with invaluable career guidance, academic advice and personal help in writing this thesis.

I am immensely honoured and proud to have been given the opportunity to conduct my studies within the National Centre for Bowel Research and Surgical Innovation within Queen Mary University, London. I have admiration for all those who been part of the incredible work that is being undertaken in that unit. The integration of scientific, pathological, medical and surgical research within the department to combat colorectal disease has been a true revelation.

I am grateful to the National Institute of Health Research for providing the funding for these studies (Research for Patient Benefit Grant).

I should like to thank my clinical and academic colleagues for their encouragement and camaraderie. Also importantly to all the patients who consented to take part in these studies. Particularly for their compliance and willingness to undertake sometimes prolonged treatment regimens, follow-up and investigations; without which these studies could not be possible.

Last but not least I would especially like to thank my wife and family who have been incredibly supportive and understanding, enduring every key stroke of this thesis along with me.

***I should also like to thank the following:***

Ms Barbara Braithwaite and Ms Debbie Hanson for their administrative support.

Ms Sybil Bannister for her assistance as a research nurse.

Ms Tatenda Marunda for her assistance as a SNS specialist nurse.

Dr Emily Heavy as an independent research assistant conducting the qualitative interviews themselves.

Dr Stephen Bremner as a statistician and assisting with the design and conduct of the statistical analysis.

Dr Natalia Hounscome as a health economist and assisting with the design and conduct of the health economic analysis.

Mr Mike Waring as the database developer and data manager.

Dr SM Scott, fellow researchers and all the staff within the GI Physiology Unit at the Royal London Hospital, particularly those involved in the investigation of study patients referred for physiological assessment.

Dr Ahsan Alam and Dr Anton Emmanuel within the GI Physiology Unit at University College Hospital, London

Mr Gregory Thomas and Miss Caroline Vaizey within the GI Physiology Unit at St. Marks Hospital, London

*To my parents Dr and Mrs Thin, my wife Dr Mei-Ling Thin and  
daughters Amelie and Nicole*

## **STATEMENT OF ORIGINALITY**

All studies within this thesis were undertaken between December 2009 and October 2013. A breakdown of each component (work packages) of the studies and the time taken to undertake each, is further represented in a Gantt chart (Table 2.02, Chapter 2). The author wishes to certify that all the work and opinions presented in this thesis are original in concept, design and execution, although the techniques and methods have been described previously, and are in use in clinical practice. All the interventions, acquisition and analysis of resulting data, as well as the subsequent production of this manuscript were performed by the author unless clearly stated otherwise.

In particular the author contributed to the design, conduct and management of every aspect of the study; delivering the timely completion of the trial whilst ensuring patient safety. The author's duties consisted of but were not limited to; securing funding for the project, securing ethical approval, day-to-day administration and conduction of the trial, organisation and chairing of steering group meetings, recruitment of patients and provision of front line clinical care, administration of both treatments, collection of unblinded data, data storage, analysis of data and reporting of data outcomes.

Of note the author recruited all patients with the aid of the research nurse (Ms Sybil Bannister) and other clinical research fellows (Mr Ahsan Alam and Mr Gregory Thomas) from other hospitals. The author operated on all patients undertaking SNS intervention himself apart from in four patients, who were from University College London Hospital (London). The author enlisted the help of another research fellow at UCLH (London) but in the majority of cases performed all PTNS interventions himself also. Outcome measure data collection was completed by the research nurse at baseline, 3 months and 6 months to reduce observation bias. Qualitative interviews took roughly an hour to undertake and were conducted by a trained external research assistant (Dr Emily Heavy). The interview audio recordings were transcribed and



analysed by the author. It is noted that this in itself was a resource intensive process taking an estimated 10-15 hours of work on each interview. The Senior supervisor Professor Taylor supervised the design, conduct and analysis of the qualitative data and gave guidance to the author. To understand qualitative methodology better, the author also undertook a 2 day qualitative data (Interpretative Phenomenological Analysis) course before undertaking any interviews.

Support for the study was provided by the Pragmatic Clinical Trials Unit, QMUL (including Prof Taylor, Dr Natalia Hounscome, Dr Stephen Bremner and Dr Emily Heavy). Statistical analysis was blinded and conducted by Senior Statistician, Dr. Stephen Bremner. A descriptive data sheet including medians, interquartile ranges, means and standard deviations were created by the statistician but all figures and tables were produced by the author. Health economic data capture and analysis was guided by the Senior Health Economist, Dr Natalia Hounscome. Dr Hounscome and the author together created the data capture tools and analysed the subsequent cost utility of each procedure. Presentation of data was advised by Dr Hounscome but the mathematical analysis was conducted by the author with guidance. The trial database design and management including encryption was conducted by Mr Mike Waring, the Database Manager. Data input into the database was completed by both the author and the research nurse. Checking, cleaning and unlocking of the data was undertaken by the Database Manager.

The author was responsible for completing and reporting studies and maintaining subsequent contact with patients throughout the duration of the study. In keeping with good clinical practice the author was charged with keeping both general practitioners and referring consultants informed of patient progress.

The author, with the aid of staff within the surgical units of participating hospitals and the GI Physiology Unit ( Royal London Hospital), was involved in the initial clinical assessments of the participants including their anorectal physiology testing before recruiting them for the trial.

## PUBLICATIONS

Some of the results presented in this thesis have already been published, in part, in the following journals:

## PAPERS

1. **Thin NN**, Taylor SJ, Bremner SA, Emmanuel AV, Hounscome N, Williams NS, Knowles CH. Randomized clinical trial of sacral versus percutaneous tibial nerve stimulation in patients with faecal incontinence. *Br J Surg.* 2015;102:349-58
2. **Thin NN**, Horrocks EJ, Hotouras A, Palit S, Thaha MA, Chan CL, Matzel KE, Knowles CH. Systematic review of the clinical effectiveness of neuromodulation in the treatment of faecal incontinence. *Br J Surg.* 2013;100:1430-47
3. **Thin NN**, Knowles CH, Alison ME. Sacral nerve stimulation in patients with faecal incontinence. *Gastroint Nurs: 2012;10:36-44.*

## ABSTRACTS

1. **Thin NN**, Taylor S, Bremner S, Bannister S, Williams NS, Allison ME, Emmanuel A, Vaizey C, Alam A, Thomas G, Knowles CH. A Randomised Mixed Methods Pilot Trial Of Sacral and Percutaneous Tibial Nerve Stimulation For Faecal Incontinence. (abstr.).
2. **Thin NN**, Taylor S, Bremner S, Bannister S, Williams NS, Allison ME, Emmanuel A, Vaizey C, Alam A, Thomas G, Knowles CH. A Randomised Mixed Methods Pilot Trial Of Sacral and Percutaneous Tibial Nerve Stimulation For Faecal Incontinence. (abstr.).

3. **Thin NN**, Taylor S, Bremner S, Bannister S, Williams NS, Allison ME, Emmanuel A, Vaizey C, Alam A, Thomas G, Knowles CH. A Randomised Mixed Methods Pilot Trial Of Sacral and Percutaneous Tibial Nerve Stimulation For Faecal Incontinence. (abstr.).

## **PRESENTATIONS TO LEARNED SOCIETIES**

### ***INTERNATIONAL***

1. A Randomised Mixed Methods Pilot Trial Of Sacral and Percutaneous Tibial Nerve Stimulation For Faecal Incontinence. **Thin NN**, Taylor S, Bremner S, Bannister S, Williams NS, Allison ME, Emmanuel A, Vaizey C, Alam A, Thomas G, Knowles CH. *Digestive Disease Week, Orlando, USA, May 2014*
1. A Randomised Mixed Methods Pilot Trial Of Sacral and Percutaneous Tibial Nerve Stimulation For Faecal Incontinence. **Thin NN**, Taylor S, Bremner S, Bannister S, Williams NS, Allison ME, Emmanuel A, Vaizey C, Alam A, Thomas G, Knowles CH. *Tripartite Colorectal Meeting, Birmingham, UK, Feb 2014*
2. A Randomised Mixed Methods Pilot Trial Of Sacral and Percutaneous Tibial Nerve Stimulation For Faecal Incontinence. **Thin NN**, Taylor S, Bremner S, Bannister S, Williams NS, Allison ME, Emmanuel A, Vaizey C, Alam A, Thomas G, Knowles CH. , *Barcelona, Spain, October 2003.*

### ***NATIONAL***

1. A Randomised Mixed Methods Pilot Trial Of Sacral and Percutaneous Tibial Nerve Stimulation For Faecal Incontinence. **Thin NN**, Taylor S, Bremner S, Bannister S, Williams NS, Allison ME, Emmanuel A, Vaizey C, Alam A, Thomas G, Knowles CH. *SARS , Cambridge, UK, Jan 2014.*

# CONTENTS

	Page No.
Title	1
Abstract	3
Acknowledgements	5
Statement of originality	8
Publications	10
Contents	12
Figures	19
Tables	20
Abbreviations	22

## **CHAPTER 1**      **INTRODUCTION: FAECAL INCONTINENCE**

1.1.	DEFINITION	24
1.2.	EPIDEMIOLOGY	26
1.3.	AETIOLOGY	27
	1.3.1. Obstetric Injury	28
	1.3.2. Traumatic Injury	29
	1.3.3. Colorectal Disease	30
	1.3.4. Neuropathic Disease	30
	1.3.5. Congenital Malformations	31
	1.3.6. Aetiological Differences In Male FI	32
1.4.	PATHOPHYSIOLOGY	32
1.5.	COST AND BURDEN	36

1.6.	CLINICAL EVALUATION OF FAECAL INCONTINENCE	39
1.6.1.	Focused History	40
1.6.2.	Clinical Examination	41
1.6.3.	Investigations	42
1.6.3.1.	Standard investigations	43
1.6.3.2.	Advanced and novel investigations	47
1.7.	TREATMENT	50
1.7.1.	Conservative Management	51
1.7.1.1.	Diet and medication	50
1.7.1.2.	Bowel management	51
1.7.1.3.	Anal plugs	52
1.7.1.4.	Physiotherapeutic interventions	52
1.7.2.	Operative Management	53
1.7.2.1.	Traditional surgical approaches	54
1.7.2.2.	Anal encirclement procedures	56
1.7.2.3.	Stomas	58
1.7.2.4.	Minimally invasive therapies	60
1.8.	SACRAL NERVE STIMULATION (SNS)	63
1.9.	PERCUTANEOUS TIBIAL NERVE STIMULATION (PTNS)	65
1.10.	STUDY RATIONAL AND AIMS	70
1.11.	SPECIFIC PROJECT AIMS	72
1.11.1.	A Review Of Clinical Effectiveness Of Neuromodulation In Faecal Incontinence	72
1.11.2.	Randomised Pilot Trial Of Sacral And Percutaneous Tibial Nerve Stimulation In Patients With Faecal	

Incontinence	72
1.11.3. Qualitative Interview Study Of Sacral And Percutaneous Tibial Nerve Stimulation In Patients With Faecal Incontinence	73

## **CHAPTER 2            MATERIAL AND METHODS**

2.1. INTRODUCTION	75
2.2. GENERAL TECHNICAL, CLINICAL AND ORGANISATIONAL PRINCIPLES OF SNS THERAPY	76
2.2.1. Patient Selection And Pre-Operative Considerations	77
2.2.2. Intra-Operative Considerations	78
2.2.3. Post-Operative Considerations	84
2.3. GENERAL TECHNICAL, CLINICAL AND ORGANISATIONAL PRINCIPLES OF PTNS THERAPY	85
2.4. GENERAL PROJECT MANAGEMENT	87
2.4.1. Management Structure	88
2.4.2. Membership Of The Study Steering Group	88
2.5. RESEARCH PLAN	89
2.6. DATA MANAGEMENT	94
2.7. PROJECT FUNDING	94
2.8. SPECIFIC STUDY METHODS	95
2.8.1. A Review Of Clinical Effectiveness Of	

Neuromodulation In Faecal Incontinence	95
2.8.1.1. Protocol Development	95
2.8.1.2. Inclusion Criteria	96
2.8.2. Randomised Pilot Trial Of Sacral And Percutaneous Tibial Nerve Stimulation	100
2.8.2.1. Setting and patients	101
2.8.2.2. Interventions	104
2.8.2.3. Preliminary data	106
2.8.2.4. Sample size calculation and feasibility	106
2.8.2.5. Randomisation, allocation and blinding	108
2.8.2.6. Outcome measures	109
2.8.2.7. Statistical analysis	111
2.8.3. Qualitative Interview Study Of Sacral And Percutaneous Tibial Nerve Stimulation In Patients With Faecal Incontinence	112
2.8.3.1. Consent	112
2.8.3.2. Sampling	112
2.8.3.3. Interviews	113
2.8.3.4. Data collection	113
2.8.3.5. Pilot interview study and topic guide development	114
2.8.3.6. Data analysis	114
2.8.3.7. Validation	115

## **CHAPTER 3 RESULTS**

3.1. A REVIEW OF CLINICAL EFFECTIVENESS OF NEUROMODULATION IN FAECAL INCONTINENCE	117
3.1.1. Summary Of Study Characteristics	118
3.1.2. Primary Outcome	124

3.1.3. Secondary Clinical Outcomes	124
3.1.4. Quality Of Life	125
3.2. RANDOMISED PILOT TRIAL OF SACRAL AND PERCUTANEOUS TIBIAL NERVE STIMULATION IN PATIENTS WITH FAECAL INCONTINENCE	133
3.2.1. Patient Recruitment And Baseline Characteristics	133
3.2.2. Clinical Outcome Data	137
3.2.3. Health Economic Data	139
3.2.4. Adverse Events	153
3.3. QUALITATIVE INTERVIEW STUDY OF SACRAL AND PERCUTANEOUS TIBIAL NERVE STIMULATION IN PATIENTS WITH FAECAL INCONTINENCE	154
3.3.1. Participant Description	154
3.3.2. Experience Of SNS Therapy	155
3.3.2.1. Acceptability of therapy	156
3.3.2.2. Results of therapy	161
3.3.2.3. Psychological impact	168
3.3.3. Experience of PTNS therapy	170
3.3.3.1. Acceptability of therapy	171
3.3.3.2. Results of therapy	178
3.3.3.3. Psychological impact	182

## **CHAPTER 4**      **DISCUSSION, LIMITATIONS AND CONCLUSION**

4.1. STUDY 1: A REVIEW OF CLINICAL EFFECTIVENESS OF NEUROMODULATION IN FAECAL INCONTINENCE	185
-----------------------------------------------------------------------------------------------	-----



4.1.1.	Summary Of Evidence	185
4.1.2.	Previous Literature Reviews	187
4.1.3.	The Place Of SNS And PTNS In Current Treatment Algorithms	188
4.2.	STUDY 2: QUANTITATIVE OUTCOMES FROM THE EXPLORATORY STUDY	190
4.2.1.	Critical Appraisal Of Other SNS And PTNS Comparison Studies	196
4.2.1.1.	Clinical outcomes and effectiveness	197
4.2.1.2.	Cost effectiveness of SNS vs. PTNS	199
4.3.	STUDY 3: QUALITATIVE OUTCOMES - EXPERIENCES AND ACCEPTABILITY OF SNS AND PTNS	202
4.3.1.	Acceptability Of Therapy	203
4.3.2.	Results Of Therapy	204
4.3.3.	Psychological Impact	206
4.3.4.	Comparisons With Other Novel Qualitative Studies	207
4.4.	LIMITATIONS	210
4.4.1.	Limitations Of The Systematic Review	210
4.4.1.1.	Intention-to-treat analysis	210
4.4.1.2.	Review methods	211
4.4.1.3.	Safety data review	212
4.4.2.	Limitations Of The Quantitative And Qualitative Exploratory Studies	214
4.4.2.1.	Small sample size	215
4.4.2.2.	Sample population	217
4.4.2.3.	Short follow up period	218
4.4.2.4.	Limited economic analysis	218
4.4.2.5.	Lack of placebo control	220

4.4.2.6. Lack of investigation into mechanism of action	222
4.4.2.7. Limitation of available outcome measures	223
4.4.2.8. Use of qualitative methodology	239
4.4.2.9. An optimum PTNS treatment protocol	241
4.4.3. Summary Of Limitations	241
4.5. CONDUCTING A FULL MULTICENTRE TRIAL: SAMPLE SIZE AND FEASIBILITY	242
4.6. THE CLINICAL IMPACT OF THESE EXPLORATORY STUDIES	244
4.7. FUTURE TRENDS AND FURTHER RESEARCH	248
4.8. CONCLUSION	251
<b>REFERENCES</b>	254

## **APPENDIX**

- i. QUANTITATIVE OUTCOME MEASURES USED
- ii. ANNOTATED QUALITATIVE INTERVIEWS (On CD)

## FIGURES

1.01	Factors contributing to the maintenance of faecal continence	34
1.02	High-resolution anorectal manometry	44
1.03	Normal endoanal ultrasound scan image	46
1.04	Normal evacuation proctography image	47
1.05	Normal dynamic MRI proctogram images	50
1.06	Intraoperative views of sphincter repair	55
1.07	Diagrammatic representation of the artificial anal sphincter device	56
1.08	Magnetic anal sphincter device	57
1.09	Diagram of a gracilis neosphincter wrap	58
1.10	Schematic diagram of different approaches for colonic irrigation	59
1.11	Schematic diagrams of possible placement of biomaterials	60
1.12	SECCA radiofrequency device	61
1.13	Diagrammatic representation of in-situ SNS and a neurostimulator	64
1.14	Placement of percutaneous tibial nerve stimulation (PTNS)	66
1.15	Diagrammatic representation of the mechanism of PTNS	69
1.16	Transcutaneous tibial nerve stimulation (TTNS)	69
2.01	Temporary peripheral nerve evaluation (PNE) set up with monopolar lead	77
2.02	Insertion of tined lead into the S3 foramen	79
2.03	Urgent PC system	87
2.04	Study design flow chart	103
3.01	SNS PRISMA flow diagram	119
3.02	PTNS and TTNS PRISMA diagram	120
3.03	Study 1: trial patient CONSORT diagram	136
3.04	Main outcomes of percutaneous tibial nerve stimulation (PTNS) & sacral nerve stimulation (SNS) at 3 and 6 months compared to baseline	146
3.05	Patient centred outcomes of PTNS & SNS at 3 and 6 months compared to baseline	148

## TABLES

1.01	Faecal incontinence sub-types and possible mechanisms	25
1.02	Risk factors for faecal incontinence	28
1.03	Pathophysiological mechanisms leading to faecal incontinence	32
1.04	Assessment of anorectal function maintaining continence	42
2.01	Key differences in test and permanent SNS techniques	80
2.02	Gantt chart of work packages undertaken	92
2.03	Inclusion and exclusion criteria	102
3.01a	SNS study characteristics (all undertaking PNE)	121
3.01b	SNS study characteristics (permanent implants only)	122
3.02	PTNS study characteristics	123
3.03	Effect of SNS on success and cure rates	128
3.04	Effect of PTNS on clinical outcomes	129
3.05	Effect of SNS on Cleveland Clinic Incontinence Score	130
3.06	Effect of SNS on faecal incontinence episodes per week	131
3.07	Numbers and percentages in means and standard deviation of baseline characteristics by treatment type	134
3.08	Outcomes of eighteen eligible non-participants	135
3.09	Numbers of patients analysed and medians and interquartile ranges (means and standard deviations) of pre- and post-treatment clinical outcome data	141
3.10	Numbers of patients analysed proportions of "success" of pre- and post-treatment clinical outcome data	142
3.11	Means of within patient changes and 95% confidence intervals, by treatment group	143
3.12	Direct intervention costs of SNS and PTNS	149
3.13	Thematic coding for experience of SNS	155
3.14	Thematic analysis of experience of PTNS	170
4.01	Browning and Park's incontinence score	227
4.02	Cleveland Clinic incontinence score	228

4.03	The St. Marks (Vaizey) incontinence score	229
4.04	The Pescatori incontinence score	230
4.05	The faecal incontinence severity index	231
4.06	Alternative outcome measures of success for SNS	236

## **ABBREVIATIONS**

3D	Three Dimensional
A&E	Accident and Emergency Department
ACE	Antegrade Continence Enema
BLT	Barts and London NHS Trust
CCIS	Cleveland Clinic Incontinence Score
CI	Confidence Interval
CT	Computerised Tomography
EAS	External Anal Sphincter
EMG	Electromyography
EQ-5D	EuroQoL 5D Questionnaire
FI	Faecal Incontinence
FICA	Faecal Incontinence and Constipation Assessment
FIE	Faecal Incontinence Episodes
FIQL	Faecal Incontinence Quality of Life
GP	General Practitioner
IAS	Internal Anal Sphincter
ICER	Incremental Cost Effectiveness Ratio
ICIQ-B	International Consultation of Incontinence questionnaire
IPG	Implantable Pulse Generator
ITT	Intention to Treat
IQR	Interquartile Range
MAS	Magnetic Anal Sphincter
MRI	Magnetic resonance imaging
NASHA Dx	Dextranomer in stabilized hyaluronic acid
NHS	National Health Service
NICE	National Institute of Health and Clinical Excellence
NM	Neuromodulation
PCOM	Patient Centred Outcome Measure
PCT	Primary Care Trust

PCTU Pragmatic Clinical Trials Unit  
PMG Project Management Group  
PNE Percutaneous Nerve Evaluation  
PNTML Pudendal Nerve Terminal Motor Latency  
PP Per-Protocol (Permanent SNS Protocol only)  
PRISMA Preferred Reporting Items for Systematic Reviews and Meta-Analyses  
PSSRU Personal Social Services Research Unit  
PTNS Percutaneous Tibial Nerve Stimulation  
QALY Quality Adjusted Life Years  
QMUL Queen Mary University, London  
QoL Quality of Life  
R&D Research and Development  
RAIR Recto-Anal Inhibition Reflex  
RCT Randomised Control Trial  
SD Standard Deviation  
SECCA Radiofrequency Ablation Procedure  
SF-36 Social Function 36  
SNS Sacral Nerve Stimulation  
SSG Study Steering Group  
TASR Transient Anal Sphincter Relaxation  
TENS Transcutaneous Electrical Nerve Stimulation  
TTNS Transcutaneous Tibial Nerve Stimulation  
UCH University College Hospital  
UK United Kingdom  
UKCRN UK Clinical Research Network Portfolio Number  
UPC Urgent PC (Uroplasty)  
USA United States of America  
WP Work Package

# 1 INTRODUCTION

## 1.1 FAECAL INCONTINENCE



Faecal incontinence (FI) can be defined as the involuntary and recurrent uncontrolled passage of faecal material from the anus for a least one month in individuals with a developmental age of at least four years old <sup>1, 2</sup>. The

International Continence Society have defined anal incontinence to be the involuntary loss of flatus, liquid or solid stool that is a social or hygienic problem <sup>3</sup>. Although sometimes used interchangeably, there is a widely accepted distinction between "anal incontinence" denoting any loss of stool or flatus per anus and "FI" indicating loss of solid or liquid stool.

Being both devastating and common, FI remains a taboo subject with only about a third to half of symptomatic patients discussing their problems with a medical professional <sup>4, 5</sup>. Embarrassment, hopes of spontaneous resolution, assumptions that FI is normal with aging and poor expectations of treatment often prevent patients from seeking appropriate and timely intervention <sup>6, 7</sup>. The consequences of this



underreported and undertreated “silent affliction”<sup>4</sup> can be devastating, leading to low self esteem, social isolation and an impaired quality of life (QoL)<sup>8</sup>.

Clinically, FI can be categorised into three different types: urge incontinence, passive incontinence, and post defaecatory faecal seepage<sup>9</sup>. Urge incontinence occurs when a strong desire to defaecate cannot be deferred appropriately, passive incontinence is the involuntary loss of faecal material without awareness, and faecal seepage (or post defaecatory FI) is leakage after evacuation, usually presenting as undergarment staining<sup>10</sup> [Table 1.01]. Although categorisation may be useful in indicating any underlying pathophysiology, in reality FI often presents with a combination of symptoms substantiating the aetiological complexity of this condition. Furthermore, the severity of FI can range from unintentional passing of flatus to complete elimination of bowel contents<sup>10</sup>. The patient's ability to cope and motivation to seek treatment is usually dependant on the severity of symptoms, therefore accurate assessment is imperative.

**Table 1.01:** Faecal incontinence sub-types and possible mechanisms

	<b>Sphincter impairment</b>	<b>Rectal impairment</b>
Passive FI	Internal sphincter weakness or tear	Loss of rectosigmoid perception and/or anorectal reflexes
Urge incontinence	Disruption of external anal sphincter function	Diminished rectal capacity
Post defaecatory faecal soiling	Normal anal sphincter function	Incomplete evacuation of stool and/or impaired rectal sensation

## 1.2 EPIDEMIOLOGY OF FAECAL INCONTINENCE

Since 2004, there have been several large studies on the epidemiology of FI <sup>11-18</sup>. International population-based studies have provided varying estimates of prevalence, showing that up to 18% of adults are affected by FI <sup>19-21</sup>. It is also estimated that 0.5-1.0% of adults experience regular severe FI effecting their QoL <sup>20</sup>. In England the prevalence of FI is approximately 200,000 people as a crude estimate of those currently presenting to the NHS <sup>22</sup>. FI can affect both men and women of all ages and most epidemiological studies have shown an approximate equivalence in sex distribution <sup>20, 21, 23, 24</sup>. Despite this, some reported clinical series have a substantial predominance of female sufferers <sup>25</sup>. Variations in the prevalence of FI among studies may partly reflect differences in the populations sampled, survey methods (e.g., by phone or in person), the screening questions used, the reference time frame, patient underreporting and the definition of incontinence (e.g. anal incontinence vs. FI).

There is good evidence that the prevalence of FI increases steadily with age, even after controlling for concurrent illnesses, activity levels, and overall health <sup>26, 27</sup>. Reports have demonstrated a rise in daily or weekly FI, from about 1-2% of the adult population to approximately 7% in healthy independent adults over the age of 65 <sup>4, 28, 29</sup>. Patients aged 80 years and older demonstrate a prevalence reaching 11%; with frequency and severity also increasing <sup>20</sup>. In particular, patients living in institutions

---

have an extremely high prevalence of FI with reports of between 33 and 65% of nursing home residents being afflicted <sup>30-32</sup>. Despite not being a life threatening condition, studies have found an association between severe FI and increasing mortality <sup>24, 33</sup>. It is clear that FI is a growing problem in an aging global population and will become a more prominent health issue in the future.

### **1.3 AETIOLOGY OF FAECAL INCONTINENCE**

FI may be caused by any disturbance of the mechanisms that are required to maintain continence: sphincter function, rectal sensation, rectal capacity, colonic transit time, stool consistency, and cognitive factors <sup>34</sup>. In community surveys, bowel disturbances, especially diarrhoea (mean odds ratio 53 [95% Confidence Interval (CI) 6.1–471]), the symptom of rectal urgency, and the burden of chronic illness but not obstetric history (e.g., forceps use, complicated episiotomy) were the most important independent risk factors for FI <sup>1, 17, 35-38</sup>. Other factors associated with FI include previous cholecystectomy, current smokers, rectocele, stress urinary incontinence, obesity, advanced age, co-morbid disease, anal sphincter trauma (obstetrical injury, prior surgery), and decreased physical activity <sup>1, 12, 17, 18, 28, 39</sup>. Due to the complex and overlapping function of continence mechanisms, there is usually an underlying combination of impaired pelvic floor mechanisms and/or disordered bowel habit.

---

Nevertheless, traditionally FI aetiology has been classified into the following categories: obstetric, traumatic (including iatrogenic), inflammatory or neoplastic colorectal disease, neurologic diseases (cerebral, spinal, peripheral), congenital and idiopathic conditions<sup>40</sup>.

**Table 1.02:** Risk factors for faecal incontinence

Category	Examples of condition
Lifestyle	Obesity, Cigarette smoking, COPD, Cholecystectomy, Bariatric surgery, Institutionalisation, Limited mobility, Laxative abuse
Obstetric	Parity, Birth trauma, Tear, Episiotomy, Forceps delivery, Prolonged labour
Traumatic	Haemorrhoidectomy, Sphincterotomy, Fistulotomy, Anal instrumentation, Low anterior resection, Penetrating/blunt force perineal trauma, Iatrogenic
Colorectal conditions	Colon cancer, Inflammatory bowel disease, Anal fistula, Chronic anal sepsis, Large haemorrhoids, Radiation proctitis, Rectal prolapse, Systemic sclerosis
Neurological	Dementia, Stroke, Cauda equina, Diabetes, Multiple sclerosis, Neuropathy, Brain injury
Congenital	Imperforate anus, Hirschsprung disease, Cloacae, Spina bifida, Meningomyelocele
Idiopathic	Diarrhoea, Faecal impaction, Urinary incontinence, Female, Age, Comorbid illness, Irritable Bowel Syndrome

### **1.3.1 OBSTETRIC INJURY**

Obstetric trauma has historically been thought to be a significant cause of FI in women. The most frequent type of injury reported, is direct mechanical sphincter disruption; occurring in approximately 0.6–16%<sup>21</sup> of vaginal deliveries with women undergoing forceps delivery being at particular risk<sup>41-43</sup>. The disruption of the

sphincter complex (even occult) may be associated with diminished anal canal pressures<sup>44</sup>, and therefore FI. Isolated pudendal nerve damage is rare<sup>29</sup> but traction injury to the pudendal nerve can accompany obstetric sphincter lacerations, lengthy vaginal deliveries (particularly second stage) and forceps use<sup>45, 46</sup>. Other obstetric risk factors include primiparity, baby weight over 4 kg, and deliveries in the occipitoposterior position<sup>47</sup>. Among women in the community, the median age of onset of FI is the 7th decade<sup>11</sup>. Interestingly, current evidence indicates that obstetric anal sphincter injury is not, after adjusting for bowel disturbances, a major risk factor for FI occurring many decades after vaginal delivery in women<sup>38</sup>.

### **1.3.2 TRAUMATIC INJURY**

Sphincter damage from anal surgery may be unavoidable after some surgical procedures: for example, in complex anal fistula or chronic anal fissure surgery. FI may also occur as a complication of common operations such as haemorrhoidectomies, anal advancement flaps or from transanal surgery<sup>46</sup>. Other less common causes of sphincter damage are with low anterior resections (particularly after neoadjuvant radiotherapy), accidental penetrating trauma, perineal lacerations, pelvic fractures, spinal injuries, and anal foreign body insertions.

### **1.3.3 COLORECTAL DISEASE**

Rectal inflammation and/or irritability causing faecal urgency and incontinence can provide subtle symptoms of underlying colorectal disease necessitating further investigation. Colorectal conditions associated with FI include inflammatory bowel disease, intestinal malabsorption, malignancies, infectious diseases and internal rectal prolapse. Patients with progressive systemic sclerosis<sup>48</sup> or chronic idiopathic intestinal pseudo-obstruction may also develop degeneration and fibrosis of the internal anal sphincter leading to passive FI.

### **1.3.4 NEUROPATHIC DISEASE**

Acquired neurological conditions affecting the brain, spinal cord, or peripheral nerves such as strokes, tumours, spinal-cord injury, multiple sclerosis, and diabetic autonomic neuropathy can all be causes FI. Often in these longstanding conditions, the combination of anal sphincter weakness, blunted rectoanal sensation and diarrhoea predispose to FI<sup>49</sup>. Patients with severe learning difficulties and many patients with dementia may be incontinent because of a lack of interest or awareness of their bowel function.

### **1.3.5 CONGENITAL MALFORMATIONS**

Congenital malformations such as imperforate anus, rectal agenesis, cloacal defect, Hirschsprung's disease, spina bifida, meningocele, and myelomeningocele may also cause FI. The severity depends on the bulk and development of pelvic-floor muscles and the degree of impairment of the sensory mechanisms. Even children with normal anal sphincters can pass stool inappropriately (encopresis), or may leak faeces as a result of faecal impaction with overflow <sup>2</sup>.

### **1.3.6 AETIOLOGICAL DIFFERENCES IN MALES**

Only a few studies have focused on investigating FI aetiology in men <sup>50</sup>. Disruption of the anal sphincter complex in males is most commonly caused by anal trauma (see section 1.3.2). In addition existing anorectal diseases, including haemorrhoids, fissures or fistula have been reported as significant risk factors, even in the absence of surgery <sup>51</sup>. Reports suggest that male FI most often takes the form of passive leakage with faecal staining of underwear <sup>52</sup>. In the absence of any anatomical abnormality, the presence of a long anal canal leading to trapping of stool and subsequent expulsion <sup>52, 53</sup>, pelvic dyssynergia resulting in incomplete evacuation <sup>54</sup>, abnormal rectal sensation <sup>55, 56</sup> and isolated degeneration of the internal anal sphincter <sup>57</sup> may all be possible mechanisms.

---

#### 1.4 PATHOPHYSIOLOGY OF FAECAL INCONTINENCE

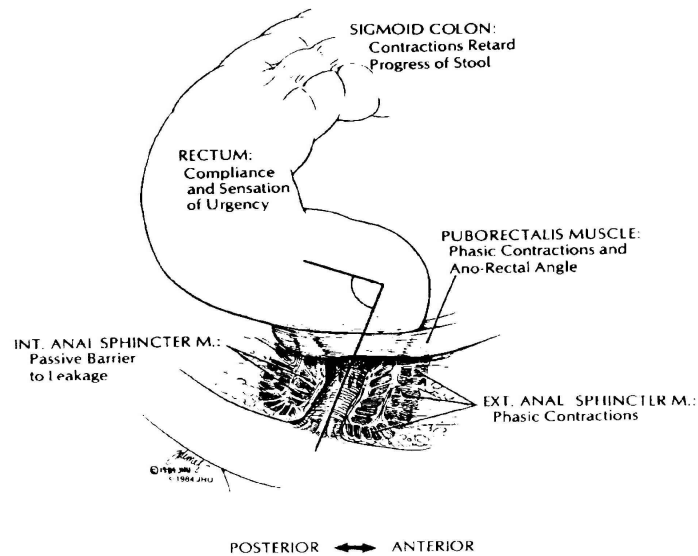
The ability to maintain continence requires structural and functional integrity of the neuromuscular apparatus of the anorectum including: the internal and external anal sphincters, pelvic floor musculature and anorectal angle, pudendal nerve function, rectal compliance and rectal sensation. In addition, adequate colonic transit time, stool volume, stool consistency, cognitive function and appropriate ability to access bathroom facilities are necessary<sup>58</sup>. When one or more of these continence mechanisms are disrupted to an extent that others are unable to compensate, then FI can occur<sup>59</sup>.

**Table 1.03:** Pathophysiological mechanisms leading to faecal incontinence

Structure	Function	Stool	Mechanism	Cause
Anal sphincter	High pressure zone		Sphincter weakness	Obstetric injury, Haemorrhoidectomy, Anal trauma/dilatation, Infection, IBD
Rectum	Rectal sensation	Volume and consistency, Irritants	Diarrhoea and urgency, Impaired accommodation, Rapid stool transport, Faecal impaction and overflow	Infection, IBD, IBS, Prolapse, Aging, Drugs, Metabolic, Bile salt malabsorption, laxatives, dyssynergic defaecation
Pudendal nerve	Anorectal sensation		Sphincter weakness, Sensory loss, Impaired Reflexes	Obstetric injury, Anal trauma/dilatation, Excessive straining/perineal descent
CNS, Spinal cord, Autonomic nervous system	Anorectal sensation		Loss of sensation, Impaired Reflexes, Secondary myopathy, Loss of accommodation	Spinal cord injury, Back surgery/trauma, Multiple sclerosis, Diabetes, Stroke
Miscellaneous	Physical mobility/cognitive function	Volume and consistency	Multifactorial changes, Diarrhoea, Alter sensation, Relaxed sphincter tone	Aging, Dementia, Antidepressants, Caffeine/muscle relaxants, Laxatives



The anal sphincter is comprised of the internal anal sphincter (IAS), which is a 0.3-0.5 cm expansion of the circular smooth muscle layer of the rectum and the external anal sphincter (EAS), a 0.6-1.0 cm expansion of the levator ani muscles. Anal sphincter weakness is the most frequently identified disturbance in incontinent patients. In controlled studies, approximately 40% of older women with FI have reduced anal resting pressure and 80% had reduced squeeze pressure<sup>60</sup>. The IAS is chiefly responsible for maintaining continence at rest and contributes approximately 70-80% of the resting sphincter tone. Decreased anal resting pressure may be associated with structural disturbances (i.e., defects and/or thinning) of the internal sphincter or anal sphincter dysfunction which may be characterized by exaggerated spontaneous relaxation of the internal anal sphincter (sampling reflex)<sup>61</sup>. At rest, the levator ani muscles and external anal sphincter are in a unique state of continuous tonic activity by a spinal reflex, 'the postural reflex'. This status is changed in response to different stimuli and conditions (rectal distension, increase of intra-abdominal pressure) to facilitate defecation or to prevent FI<sup>62</sup>. This high pressure zone is further reinforced by anal mucosal folds, endovascular cushions and voluntary squeezing of the EAS. External anal sphincter weakness may result from one or more of the following factors: sphincter damage, neuropathy, myopathy, or reduced cortico-spinal input.



**Figure 1.01:** Factors contributing to the maintenance of faecal continence (*reproduced from Whitehead & Schuster. Am J Gasroenterol 1987; 82: 487-497 © 1987 Blackwell Publishing, with permission from Blackwell Publishing*).

The puborectalis muscle slings around the rectum and acts like a "flap valve" pulling the anorectal junction forward to reinforce the anorectal angle (approximately 90 degrees at rest). During squeeze, the puborectalis contracts further to make the angle more acute, whereas during defecation, the puborectalis relaxes. Evidence suggests that the inward traction exerted by the puborectalis can be reduced in FI, correlating more closely with symptoms than changes in squeeze pressure<sup>63</sup>.

Continence requires the complex integration of signals among the smooth muscle of the colon and rectum, the puborectalis muscle, and the anal sphincters. Innervation of the EAS is from the pudendal nerve, a mixed motor and sensory nerve that arises from the second, third, and fourth sacral nerves (S2, S3, and S4). Innervation of the

puborectalis arises from a branch directly from the sacral plexus (levator ani nerve)<sup>64</sup>. Stool is transferred into the rectum by colonic high-amplitude propagated contractions, which tend to occur after awakening or meals<sup>65</sup>. As colonic contents are presented to the rectum, the rectum distends. The sensation of rectal distension is most likely transmitted along the S2, S3, and S4 parasympathetic nerves. This results in a parasympathetically mediated relaxation of the IAS (rectoanal inhibitory reflex) and a contraction of the EAS (rectoanal contractile reflex). The epithelial lining of the upper anal canal has a rich supply of sensory nerve endings, especially in the region of the anal valves. The rectal contents are sampled as to their nature (i.e., gas, liquid, or solid) seen as an equalisation of the rectal and upper anal canal pressures. Decreased anorectal sensation and less frequent sampling have been hypothesised to contribute to the pathogenesis of FI<sup>66</sup>. If evacuation of the rectum is not socially appropriate, sympathetically mediated inhibition of the smooth muscle of the rectum and voluntary contraction of EAS and puborectalis musculature occur increasing the high pressure zone and narrowing the anorectal angle.

Rectal hypersensitivity may also be associated with reduced rectal compliance which has been found to be reduced in women with FI, and associated with the symptom of urgency and anal incontinence<sup>60, 67</sup>. Again the exact mechanism of this is not fully understood and debate continues as to whether it is a cause or effect of FI. Furthermore sphincter pressures do not always distinguish continent from

---

incontinent patients, emphasising the complex interplay and importance of rectal compliance and sensation in maintaining continence<sup>68</sup>.

## **1.5 COSTS AND BURDEN OF FAECAL INCONTINENCE**

Although FI is a major public health problem with varying degrees of severity, little is known about the exact cost burden to patients and to the NHS in the UK. This lack of knowledge is compounded the fact that many patients are reluctant to reveal the full extent of their disorder. They may instead attempt to hide and bear the brunt of the social and financial burden by themselves. Even though only estimates can be calculated, it is thought that the socio-economic burden of the disease is substantial. Considering direct medical costs alone i.e. those incurred by obtaining medical care for prevention, diagnostics, therapeutics, rehabilitation and care; adult urinary and faecal incontinence account for 2% of total UK healthcare budget with an annual NHS spend in excess of £500 million<sup>69</sup>. If FI is compared to the better-studied disease of urinary incontinence (with which it is closely associated), it could account for a mean cost per patient (females) per year of at least £218 in the UK.

Unlike other conditions FI does not lead to extensive inpatient hospitalisations. Most of the investigations and treatments are undertaken on an outpatient basis. In the USA, the annual average cost per patient with either urinary or faecal

---

incontinence in the outpatient setting is estimated at \$17,166<sup>70</sup>. The main expense coming from a build up of extensive investigations and repeated outpatient treatments.

Direct healthcare costs include expenditure on pharmaceutical drugs, which in patients with FI are mainly antidiarrhoeal and laxatives. These drugs do not have a high unit costs and account for less than 10% of the total costs. The items weighing most heavily on the total cost undoubtedly concern incontinence protection (disposable pads and pants, washable nappies, anal tampons, under blankets and waterproof sheets, faeces bags, etc.), which account for approximately 25% of total expenditure<sup>71</sup> and may be born both or totally by the healthcare provider or the patient. In the United States approximately \$400 million/year is spent on adult incontinence diapers<sup>4</sup> and between \$1.5 and \$7 billion/year is spent on care for incontinence among institutionalised elderly patients<sup>72, 73</sup>. During 1999 the direct costs of pads, appliances and other prescription items throughout hospitals and long term care settings in the UK for incontinence in general was estimated at £82.5million<sup>74</sup>. Studies by National Institute of Health and Clinical Excellence (NICE) suggest that 10–20% of the total identified population presenting with FI (200,000 people) use incontinence pads. Assuming a midpoint of 15%, it can be estimated that approximately 30,000 patients are using incontinence pads. At an average of 4 incontinence pads per day for each patient<sup>75</sup>, this would work out as a cost of approximately £21,024,000 per year to the NHS. In the NHS the patient can receive

---

incontinence pads free of charge and, theoretically at least, do not have to bear this burden. Other direct non-medical costs are those associated with travel/time for the purpose of obtaining health care and extra costs of cleaning or skincare products. These include but are not limited to over the counter antidiarrhoeal medication (26%), skin care products (11%), special articles of clothing (10%), cleaning products (9%), and special foods (6%)<sup>76</sup> Many patients are either too embarrassed to ask or do not know that they can obtain these products from the NHS and therefore put a large long-term financial burden on themselves.

In terms of direct and indirect costs, cleaning after incontinence accounts for a large proportion of the total cost involved in the disorder. Indeed, taking into account how much time is spent cleaning patients who are permanently in institutions, it has been estimated that the personnel in charge of caring for incontinent patients devote 13% of their time to this duty. Therefore, the loss of the same percentage of the carer's salary should be regarded as a indirect costs generated by FI.

Indirect non-medical costs are costs due to productivity losses associated with paid and unpaid work<sup>22</sup>. These costs vastly outstrip direct costs to the NHS in terms of working days lost and decreased productivity in other areas of social functioning<sup>77-79</sup>. In essence FI can jeopardise employment, and may lead to institutionalisation<sup>80-82</sup>. The population of FI patients can be relatively young and of working age, the cost of the disorder in terms of lost working hours can be high in terms of absenteeism

---

or, in the very severe cases, early retirement. Moreover, these indirect costs are not attributable exclusively to the patients themselves; they may also be generated by those assisting them. Particularly with congenital incontinence, there is a heavy impact on parents, who often have to restrict their own employment to care for their children.

Intangible costs are related to pain, suffering, and discomfort. Whereas these effects cannot be evaluated in monetary terms, they nevertheless contribute to the overall burden of the disorder. With FI, intangible costs primarily concern impaired social activity resulting from shame and embarrassment. The socio-economic combined cost of healthcare utilisation <sup>83</sup> is indicative of the unmet clinical need in this area with attendant high economic costs to both patients and the NHS <sup>84</sup>. Management of FI is a major problem due to not only to a high prevalence but also to a lack of widespread expertise. A true panacea for this difficult condition which is both clinically and cost effective remains elusive.

## **1.6 CLINICAL EVALUATION OF FAECAL INCONTINENCE**

Baseline evaluation of FI should include a detailed clinical assessment together with appropriate physiological tests and imaging of the lower gastrointestinal tract. Results can provide information regarding severity, impact and possible aetiology.

---

Due to the overlap and complexity of continence mechanisms previously discussed, no one test is superior. Therefore it must be considered that FI arises from multiple contributory factors rather than a single diagnosis and consequently one may need a combination of different modes of investigation and treatments to manage this condition effectively.

#### **1.6.1. FOCUSED HISTORY**

Initially clinicians need to establish a favourable rapport with their patient and approach the whole subject with sensitivity. Thereafter, a thorough assessment of the features of FI: the onset (timing and duration); nature of symptoms (flatus, liquid, or solid faeces); frequency of episodes; and related changes in bowel function or stool consistency can be explored<sup>21</sup>. Personal questions about the current impact of FI on QoL, sexual health, daily activity, the use of pads or other devices and co-existing urinary incontinence are also essential. Further inquiry into the patient's medical background, including an assessment of their: obstetric history, social history, co-existing medical problems, dietary history, concurrent medications and family history must also be completed. Co-existing physical and cognitive disabilities can exacerbate the effect of FI by impeding access to toilets, interfering with transfers to the commode, or preventing adequate cleaning after defaecation<sup>21</sup>. Most importantly, any possibilities of an organic condition particularly a colorectal cancer must be explored and treated before focusing on FI management.



### **1.6.2 CLINICAL EXAMINATION**

A detailed general physical and neurological examination should be performed to rule out systemic or neurological disorders. Following this, a meticulous perineal inspection and digital rectal examination are critical. Upon inspection, the presence of soiling, prolapsed haemorrhoids, dermatitis, deformities, anal stenosis, fistula, abscesses or a gaping anus may be identified <sup>34</sup>. Other pertinent findings include a thinned or deformed perineal body and scars from previous surgery or trauma. A rectal prolapse and excessive perineal descent can be demonstrated by a Valsalva's manoeuvre with an outward bulge exceeding 3 cm usually abnormal <sup>85</sup>. The perianal sensation should also be assessed by eliciting the anocutaneous reflex. This reflex examines the integrity of the connection between the sensory nerve and the skin, the intermediate neurones in the spinal cord segments S2, S3, and S4 and the motor innervation of the EAS. A digital rectal examination assesses the anal resting tone, the strength of the sphincters, length of anal canal, the integrity of the puborectalis, the acuteness of the anorectal angle, and the elevation of the perineum during voluntary squeezing <sup>86</sup>. Finally a vaginal examination should be performed to evaluate the presence of rectoceles, cystoceles, enteroceles or a vaginal prolapse.

### 1.6.3 INVESTIGATIONS

Established first line tests: colonoscopy/CT colonography, anorectal manometry, rectal sensory testing, endoanal ultrasonography, pudendal nerve terminal latency testing and evacuation proctography are generally used in combination by any specialist investigating FI. They are relatively cheap, readily available, easy to perform and interpret and are informative especially when analysed in combination. In the UK they have been approved by NICE as standard investigation for ongoing FI<sup>87</sup>. If cases are more complex they may need further assessment using novel techniques.

**Table 1.04:** Assessment of anorectal function maintaining continence

Function	Standard assessment method	Advanced assessment method
Anal sphincter complex	Anal manometry, Endoanal ultrasound, Evacuation proctography, Pudendal nerve latency MRI	High definition manometry, Saline continence test, Dynamic MRI proctography Sphincter EMG
Rectal sensation	Rectal perception of distension by manual syringe, RAIR (balloon distension and anal manometry)	Barostat Evoked potentials Magnetic stimulation
Rectal accommodation	Evacuation proctography, Balloon expulsion test	Barostat Integrated MRI
Anal sensation	-	Anal mucosal electrical / temperature sensation

### **1.6.3.1 Standard investigations**

#### ***Endoscopy***

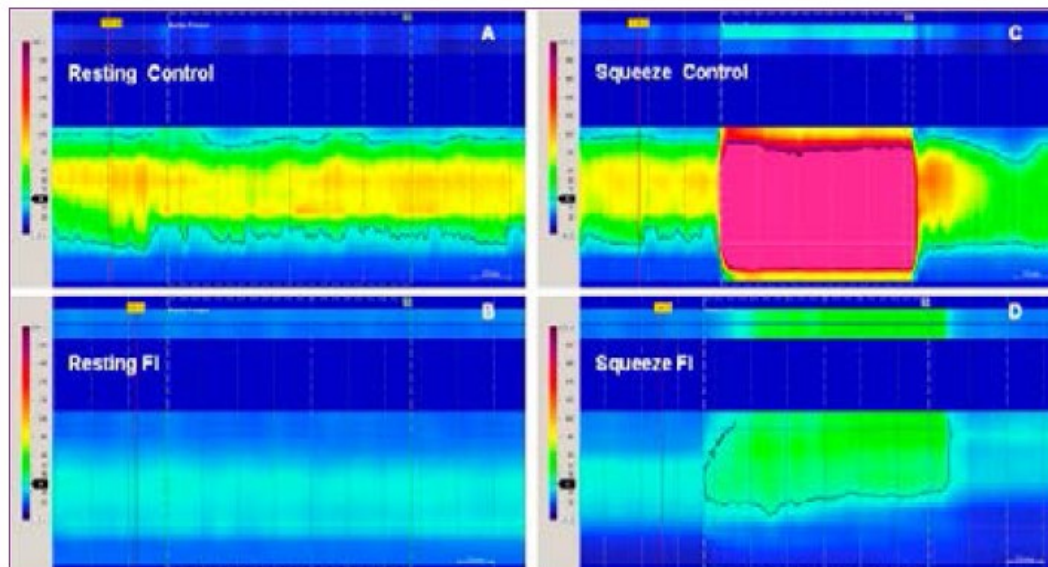
A colonoscopy or flexible sigmoidoscopy is usually the first investigation of choice when evaluating any abnormal bowel condition<sup>88</sup>. The ability to directly visualise the lumen of the colon and rectum ensures that colonic polyps, inflammatory bowel disease and cancer are detected and histological confirmation undertaken. In patients who cannot tolerate these investigations CT colonography may be an appropriate alternative test. Most patients attending specialist consultation will already have completed these tests and therefore the next investigational step is a combination of standard anorectal physiology studies and imaging.

#### ***Anorectal manometry***

Anorectal manometry measures the resting pressure, squeeze pressures and canal length of the anal sphincter complex<sup>57</sup>. If required, further evaluation of canal pressures can be conducted during coughing, Valsalva and straining manoeuvres. With traditional water perfused manometry, pressures are recorded via a transducer introduced into the rectum and withdrawn through the anal canal (pull through technique). Nowadays, different types of solid state transducers, pressure-recording devices and computer software are able to conduct high resolution or high definition stationary manometry. High resolution catheters provide a single averaged circumferential pressure, at 6-mm intervals along the

---

entire length of the anal canal<sup>89</sup>. High definition catheters use 256 circumferentially distributed pressure sensors and therefore can provide greater definition of sphincter morphology and defects<sup>90</sup>. Despite advances in techniques, measurement of anal canal pressures can still only determine the function of the anal complex without differentiation between different causes of sphincter weakness<sup>89</sup>. Variations in catheter designs, overlapping values between patient groups, and lack of standardised methods of analysis between centres mean that the value of this utility as an independent investigation has been debated. However, anal manometry is technically undemanding and widely available and is most usefully interpreted in correlation with other physiological test findings<sup>91</sup>.



**Figure 1.02:** High-resolution anorectal manometry, comparisons between resting and squeeze pressures in a control patient and one with FI. (*reproduced from Costilla et al. Gastroenterol Hepatol 2012; 9: 423-433 © 2012 Wiley Publishing, with permission from Wiley Publishing*).

***Rectal sensory testing***

Rectal sensation can be assessed using progressive air or water distension of either a latex balloon manually, or more accurately a polyethylene balloon attached to a barostat machine, situated in the rectum. Volume thresholds of sensation are recorded at first perception, desire to defecate, and severe discomfort intervals<sup>92</sup>. Rectal balloon distension together with anal manometry can also be used to evaluate the recto-anal inhibition reflex (RAIR). An impaired or absent reflex suggests either afferent or efferent neuronal injury<sup>10, 86</sup>.

***Simple neurophysiological testing***

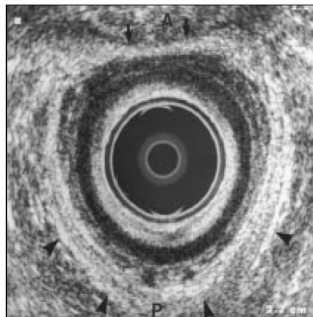
The pudendal nerve terminal motor latency (PNTML) measures the conduction time of the right and left pudendal nerve (ms), via a stimulating electrode mounted on the index finger of the glove of the examiner. Long latencies are associated with neuropathy or traction injury to the nerve. Despite its common use, uncertainty exists on the accuracy of PNTML and its predictive value on outcomes<sup>21</sup>.

***Endoanal ultrasonography***

This technique provides real time, detailed information about the general integrity of the sphincter muscles and remains the standard for identifying anal sphincter injuries, including tears, scars, atrophy, and anal fistulae<sup>93, 94</sup>. Several ultrasound devices are currently available including those with 3D reconstruction. In general scanning provides excellent resolution of the IAS but is less accurate in assessing the

---

EAS; this is operator-dependent and the analysis is subject to substantial interoperator variability<sup>95, 96</sup>. The use of endoanal ultrasound has certainly increased the detection of occult injuries and scarred sphincters. The extent to which these clinically occult isolated sphincter defects are responsible for FI is still unclear, although some have advocated surgical repair<sup>97</sup>. Anal endosonography is often one of the first preferred investigations for FI as it is easy to perform, safe, cheap and readily available<sup>10 86</sup>.



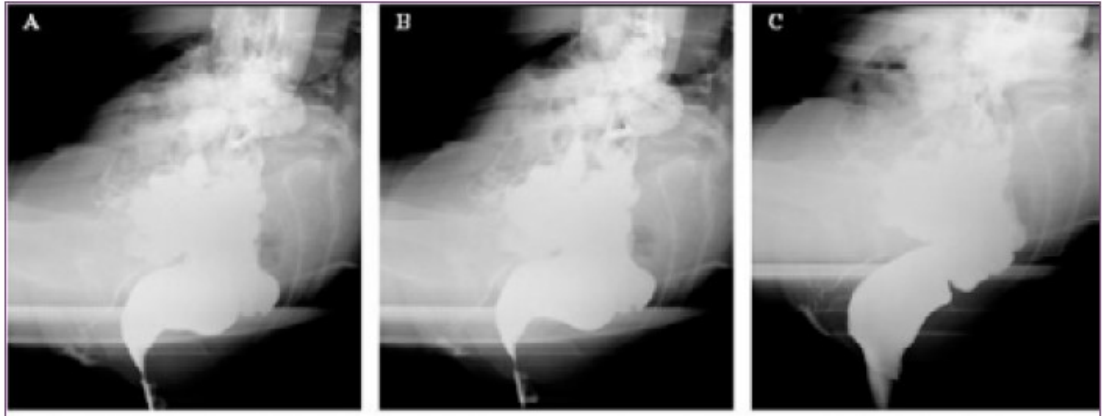
**Figure 1.03:** Normal endoanal ultrasound scan image (*reproduced from Kamm. BMJ 1998; 316: 528-532 © 1998 BMJ Publishing, with permission from BMJ Publishing*).

### ***Evacuation proctography (defaecography)***

Evacuation proctography is a dynamic radiological study of attempted rectal evacuation in the natural defecating position<sup>98</sup>. Thickened barium contrast is introduced into the rectum and whilst the patient defaecates seated on a commode, their anorectal anatomy and pelvic floor motion are recorded via X-ray images. During imaging at rest, coughing, squeezing, and straining to evacuate; the anorectal angle and position of the anorectal junction can be assessed. Defaecography can also reveal a poorly distensible rectum suggesting capacity abnormalities<sup>99</sup>. Evacuation proctography may be most useful in the diagnosis of incontinent

---

patients with anatomical abnormalities such as intussusception, rectal prolapse, excessive perineal descent, and rectocele.



**Figure 1.04:** Normal evacuation proctography images (*reproduced from Costilla et al. Gastroenterol Hepatol* 2012; **9**: 423-433 © 2012 Wiley Publishing, with permission from Wiley Publishing).

### 1.6.3.2 Advanced and novel investigations

#### ***Anal sensory testing***

Anal sensation is a summation of properties of central and peripheral nerve function of the submucosa and mucosa. Anal sensation is assessed by determining the perception threshold to a thermo or electrical stimulus in the anal canal. With both techniques, an altered anal sensation has been demonstrated in patients with FI which may play a part in its pathophysiology<sup>100</sup>.

***Further neurophysiological testing***

Electromyography (EMG), uses a concentric needle electrode or a surface electrode, to demonstrate functional muscle tissue in the anus by quantifying motor unit potentials. EMG provides a sensitive measure of denervation (fibrillation potentials) and can usually identify myopathic, neurogenic, or mixed injury<sup>101</sup>. Using novel techniques to assess somatic pathways, evoked potentials elicited by peripheral or central electrical or magnetic stimulation can provide information about the neural pathways mediating anorectal function. Depending on the site of stimulation and recording, afferent and efferent pathways can be evaluated<sup>102, 103</sup>. These techniques are still experimental and further investigation and validation is necessary before more widespread use<sup>104</sup>.

***Rectal pressure and compliance testing***

If the pressure applied to the rectal wall is also recorded when using the balloon distension technique, the compliance of the rectum can be determined by calculating rectal pressure-volume relationships. Abnormal rectal compliance is felt to be associated with FI<sup>105</sup>. Rectal pressure and diameter, hence rectal stress-strain relationships (or stiffness) can be directly measured by integrating MRI with rectal balloon distension; the application of this novel test is still under investigation<sup>106</sup>.



***Magnetic resonance imaging (MRI)***

MRI, like anal endosonography, can give an excellent impressions of the anatomy of the anus and pelvic floor. MRI plays a major role in establishing atrophy of the external anal sphincter by demonstrating the amount of fat present and revealing the thickness and surface area of the external anal sphincter. This estimate is useful for predicting success of sphincter repairs<sup>107</sup>. In addition, MRI is preferred in cases with high anorectal malformations (anorectal atresia and related urogenital abnormalities).

***Magnetic resonance proctography***

With the advent of rapid MRI sequences, dynamic MRI imaging can visualise both anal sphincter anatomy and global pelvic floor motion in real-time, without radiation exposure. The anal sphincters are visualised by axial T2-weighted fast spin-echo images and corresponding T1-weighted spin-echo images with a disposable endorectal colon coil<sup>108</sup>. The dynamic images of defaecation are acquired providing a unique appreciation of global pelvic floor motion, i.e., in addition to the anorectum, the bladder and genital organs are also visualised. This examination can be performed using conventional, closed-configuration MRI systems because there is little difference in the detection of clinically relevant findings between supine MRI and seated MRI<sup>109</sup>.



**Figure 1.05:** Normal dynamic MR proctogram images (*reproduced from Costilla et al. Gastroenterol Hepatol 2012; 9: 423-433 © 2012 Wiley Publishing, with permission from Wiley Publishing*).

## 1.7 TREATMENT OF FAECAL INCONTINENCE

Management of FI is a major problem, not only due to its high prevalence but also to a lack of widespread expertise. Treatment must always be tailored to the specific needs of the individual but in general a stepwise approach should be undertaken. Initially, conservative measures are recommended. Although these treatments can improve symptoms in more than half of patients, they may not be universally successful or long lasting<sup>110, 111</sup>. Therefore, patients with intractable symptoms and impaired QoL, may seek a surgical solution. Operative intervention to the anorectum is not to be undertaken lightly and is usually only considered after appropriate assessments have indicated a surgically correctable problem. Despite enthusiasm and evolution in operative techniques, these procedures are still invasive, irreversible, and have at best variable success rates with significant risk of morbidity<sup>87, 112</sup>.

### **1.7.1 CONSERVATIVE MANAGEMENT**

#### **1.7.1.1 Diet and medication**

First-line measures are mainly dietary and pharmacological modification. Dietary changes (e.g. avoidance of foods causing diarrhoea or urgency), a high fibre intake, sufficient fluids and stool-bulking agents (psyllium products or methylcellulose) may all help to improve stool volume and consistency. In addition, medical management using: Loperamide (Imodium), Diphenoxylate Hydrochloride plus Atropine Sulphate (Lomotil) or Codeine Phosphate, can help alter colonic transit. With these simple lifestyle modifications, many patients can manage their FI independently, monitoring their diet and titrating their medication as required.

#### **1.7.1.2 Bowel management**

Cleansing rectal irrigation, rectal enemas, laxatives and suppositories can be used in patients with overflow incontinence for disimpaction: emptying the rectum and diminishing the chance of FI during the day. Although these measures are easy to learn, safe and have only minor side effects, they may be inconvenient and uncomfortable in the long term and therefore their use can be limited<sup>113</sup>.

### **1.7.1.3 Anal plugs**

A foam anal plug is designed to block the loss of stool<sup>114</sup>. Patients with anal seepage and subsequent faecal odour seem most effectively managed with this device. Although simple to use, the achievement of continence is only possible if the plug is supported by a functioning pelvic floor<sup>114, 115</sup>.

### **1.7.1.4 Physiotherapeutic interventions**

Pelvic physiotherapeutic interventions are generally non-invasive, inexpensive, have few complications and require no sophisticated equipment<sup>116</sup>. Moreover, all other therapeutic options are still available while physiotherapy is being used<sup>117</sup>. Kegal exercises form the mainstay of therapy, activating latent motor units to allow these muscles to become functional again<sup>118</sup>. Other physiotherapeutic techniques used to improve FI include biofeedback and direct electrical stimulation.

#### ***Biofeedback and rectal balloon training***

Nowadays, three modalities of biofeedback in the treatment of FI are recognised<sup>119</sup>. The first technique uses either an intra-anal electromyographic (EMG) sensor, an anal manometric probe (measuring intra-anal pressure), or a perianal surface electrode to inform the patient about the activity of the pelvic floor muscles by way of a visual display and/or an auditory signal. The second technique involves the use

---

of a distended manometric rectal balloon (rectal balloon training) to imitate rectal contents and aid defaecation practice. The third modality is a three-balloon system used to train forceful external anal sphincter contraction after a stimulus of rectal distension<sup>116, 120</sup>. Although biofeedback requires a series of outpatient attendances, it is simple, easily accessible, painless and risk-free<sup>110, 120</sup>. The benefit of biofeedback can be variable but improvements have been cited in around 64-89% of patients<sup>120, 121</sup>.

### ***Direct electrical stimulation***

Direct electrical stimulation is achieved by applying an electrical current via probes in either the vagina or anal canal, or through surface electrodes on the perineum; passively stimulating the pelvic floor muscles, sphincters and accompanying nerve structures<sup>122</sup>. The purpose of electrical stimulation is to re-educate and strengthen weakened or poorly functioning pelvic floor muscles by increasing awareness and contractions of the targeted muscles<sup>122</sup>. Any abnormalities or infections of the perineum may contraindicate the use of this type of therapy<sup>123</sup>.

### **1.7.2 OPERATIVE MANAGEMENT**

A wide range of operative techniques have been developed through the ages. Most traditional surgical approaches target deficits in the pelvic floor or anal sphincters. Although a place in the treatment algorithm for these operations still exist, they do

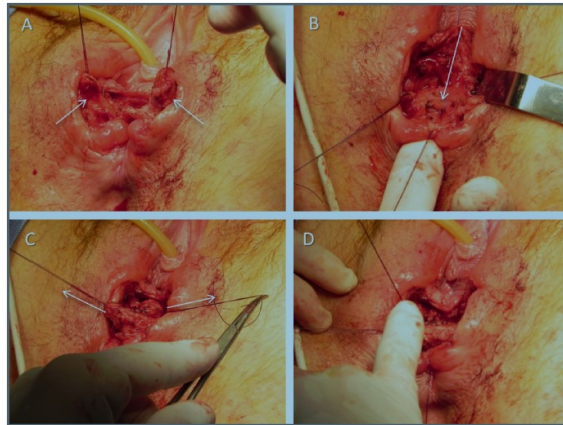
---

carry a significant risk of severe complication and morbidity. Nowadays after conservative measures have failed, a minimally invasive approach is most often advocated. These techniques have gained widespread popularity and are evolving quickly. Unlike, traditional approaches, they may prevent surgery to the perineum and its associated morbidity. More and more, direct "open surgery" is now being left as a second-line operative option. To decide which surgical therapy is most suitable, the causal determinants of an anatomical or functional nature need to be analysed and matched to the expertise of the surgeon.

#### **1.7.2.1 Traditional surgical approaches**

##### ***Sphincteroplasty***

Immediate anal sphincter repair is an established operation in acute situations (e.g., when an obstetric sphincter injury is recognised). Unfortunately, as many as 75% of women have persistent external anal sphincter defects after primary repair, and about 60% have some degree of incontinence <sup>124</sup>. For incontinent patients with established sphincter defects, overlapping sphincteroplasty is an option. Overlapping sphincteroplasty yields substantial clinical improvement in approximately 65 to 80% of patients <sup>125, 126</sup>. Unfortunately, current data indicates that the results deteriorate significantly over time <sup>127, 128 112</sup> although sphincteroplasty can be repeated <sup>129</sup>.



**Figure 1.06:** Intraoperative views of sphincter repair (reproduced from Meurette. *J Visc Surg* 2014; **154**: 29-39 © 2014 Elsevier Masson Publishing, with permission from Elsevier Masson Publishing)

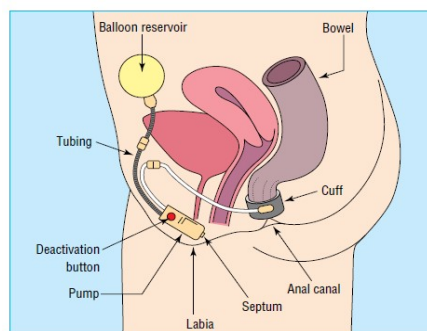
### ***Pelvic floor repairs***

Sir Alan Parks devised the postanal repair in the 1970s to treat FI in the absence of sphincter defects<sup>130</sup>. The aim is to strengthen the posterior pelvic floor including the puborectalis and accentuate the flap valve effect of the puborectalis sling. The initial results were encouraging but were found to deteriorate over time and therefore this operation is rarely performed today<sup>131, 132</sup>. An alternative operation is the anterior sphincter levatorplasty. In this procedure, the dissection plane is found anterior to the anus, and the levator ani is plicated. The surgeon can also repair occult anterior sphincter injuries, coexisting rectoceles and increase the length of the anal canal<sup>133</sup>. A total pelvic floor repair combines both procedures. Although this is not a common operation, it may be an option for the treatment of post obstetric neurogenic FI<sup>134</sup>.

### 1.7.2.2 Anal encirclement procedures

#### **Artificial anal sphincters**

The artificial anal sphincter is an implantable system consisting of three parts: an inflatable perianal cuff, a pressure-regulating balloon, and a control pump that is implanted in the scrotum or the labia majora. The artificial sphincter is placed around the native sphincter and is kept inflated until the patient wishes to defecate, at which time the device is deactivated<sup>135</sup>. Good results (approximately 50%) have been reported in individual case series but device infection and the risk of erosion have also been a problem<sup>136-138</sup>.



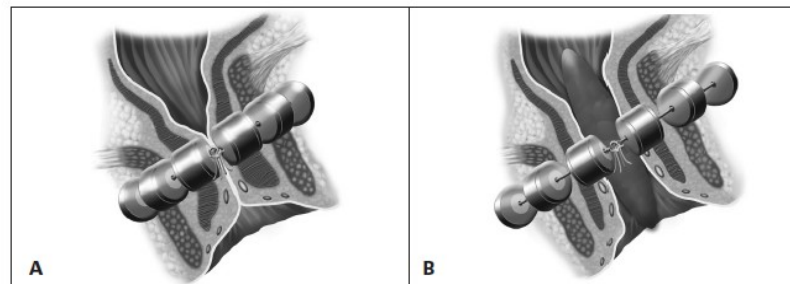
**Figure 1.07:** Diagrammatic representation of the artificial anal sphincter device (*reproduced from Kamm. BMJ 1998; 316: 528-532 © 1998 BMJ Publishing, with permission from BMJ Publishing*).

#### **Magnetic anal sphincters**

A magnetic anal sphincters is a new device consisting of a ring of 14–20 magnetic titanium beads that are placed to surround and reinforce the anal sphincter. This magnetic device may prevent FI by supporting the closure of the sphincter muscles.



Recent comparative studies indicates that MAS may be as effective as the artificial bowel sphincter in improving FI and the QoL of patients<sup>135, 139</sup>.



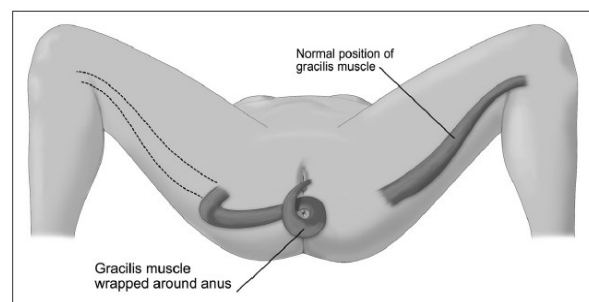
**Figure 1.08:** Magnetic anal sphincter device (a) in a closed position (b) in an open position (reproduced with permission from Torax Medical, Shoreview, MN).

### ***Electrically stimulated neosphincter procedures***

Procedures creating a neosphincter from transposed skeletal muscle date back to the early 20th century and mostly surgeons have made use of either the gluteus maximus<sup>140</sup> or the gracilis muscles<sup>141</sup>. To overcome the long-term muscle fatigue issues with static muscular transposition, stimulated neosphincters were pioneered. The first successful electrically stimulated gracilis neosphincter procedure was reported in 1988<sup>142</sup>. Chronic stimulation of the muscle, with a neurostimulator, alters its morphological, physiological and biochemical characteristics, resulting in two main effects. Firstly, conversion of the fast-twitch, rapidly fatigable gracilis muscle to a slow-twitch, fatigue-resistant muscle capable of prolonged tonic contraction<sup>143</sup>. Secondly, electrical stimulation maintains tonic muscle contraction

---

without the need for continuous voluntary control. In this way, an imitation of normal anal function is achieved, which enables the patient to maintain continence for a prolonged period of time<sup>144</sup>. Gracilis neosphincter operations are often complex and are undertaken in stages. They can be considered a salvage option in well motivated patients, at centers with the requisite expertise and experience. However, three large multicenter trials have reported less encouraging results with prohibitive morbidities, limiting the popularity of this technique<sup>145-147</sup>.



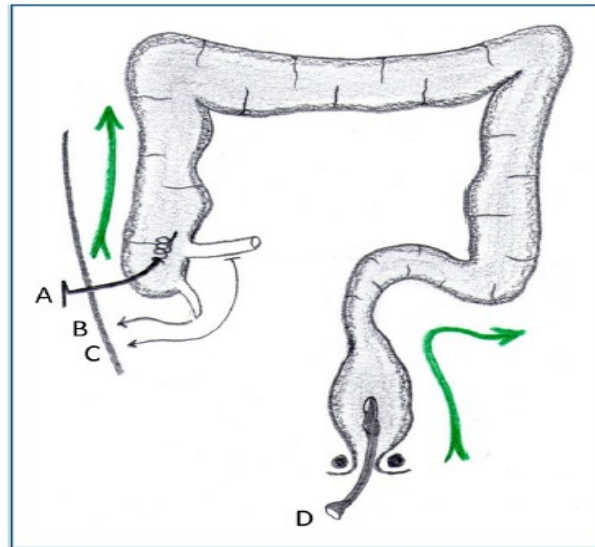
**Figure 1.09:** Diagram of a gracilis neosphincter wrap (reproduced from Meurette. J Visc Surg 2014; 154: 29-39 © 2014 Elsevier Masson Publishing, with permission from Elsevier Masson Publishing).

### 1.7.2.3 Stomas

#### ***Antegrade continence enema (ACE)***

This rare procedure requires a stoma formation (appendicostomy, caecostomy, or sigmoidostomy) and antegrade irrigation of the colon and rectum. Like retrograde irrigation, cleansing the distal bowel may prevent involuntary loss of enteric content. However, some patients may still have fluid leakage from rectum or the

stoma, or may develop stomal strictures. Despite these complication, ACEs can result in improvements in symptoms and QoL for carefully selected patients <sup>148</sup>.



**Figure 1.10:** Schematic diagram of different approaches for colonic irrigation (a) Caecostomy (b and c) Antegrade continence enemas (d) retrograde irrigation (*reproduced from Meurette. J Visc Surg 2014; 154: 29-39 © 2014 Elsevier Masson Publishing, with permission from Elsevier Masson Publishing*).

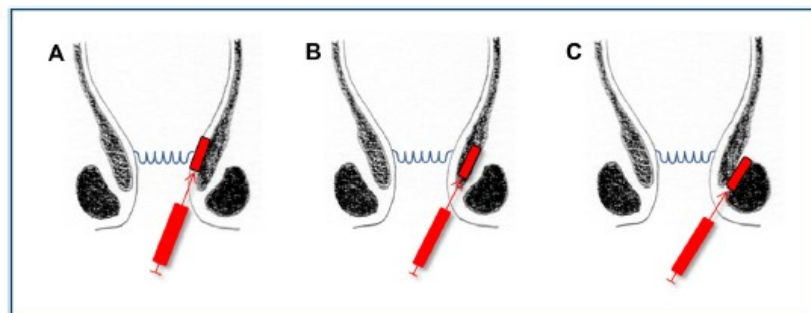
## Colostomy

If all other treatments fail or if the patient wishes, a colostomy can be fashioned. Colostomies provide a degree of bowel control in a manner that allows patients to resume normal activities and improve their QoL <sup>149, 150</sup>. Adverse effects of stoma creation may include significant psychosocial issues and stoma-related complications. Little data is available regarding colostomy for incontinence; however, in one survey, 83 percent of patients reported a significant improvement in lifestyle and would choose to have the stoma again <sup>150</sup>.

#### 1.7.2.4 Minimally invasive therapies

##### ***Injectable biomaterials***

Injection of biomaterials either around the internal anal sphincter or into defects to provide bulk can be simple surgical procedures<sup>151</sup>. The materials employed include autologous fat, cross-linked collagen, silicone, Teflon paste and carbon-coated beads<sup>151, 152</sup>. Positive results have been found in a pivotal trial of 206 patients, assessing dextranomer in stabilized hyaluronic acid (NASHA Dx). The 6-month response based on 50% FI episode reduction was higher for NASHA Dx (52%) than sham injections (31%)<sup>153</sup>. This is now an approved treatment by the food and drug administration in the USA.



**Figure 1.11:** Schematic diagrams of possible placement of biomaterials (a) submucosal, (b) intramuscular, (c) intermuscular (*reproduced from Meurette. J Visc Surg 2014; 154: 29-39 © 2014 Elsevier Masson Publishing, with permission from Elsevier Masson Publishing*)

**Radiofrequency ablation (SECCA)**

The SECCA device delivers temperature-controlled circumferential radiofrequency energy directly to the anal sphincters via the anal canal <sup>154</sup>. Aimed at improving passive FI, the radiofrequency energy causes collagen contraction, healing, and remodelling of the anal sphincter, thereby increasing the outlet resistance. Recent studies have shown that the 'Secca procedure' can be a successful (approximately 60%), safe, minimally invasive, procedure which can be performed under local anaesthesia <sup>155, 156</sup>. However, no changes in anorectal manometry or anal sonography after treatment have been seen and long-term results are less convincing <sup>157</sup>.



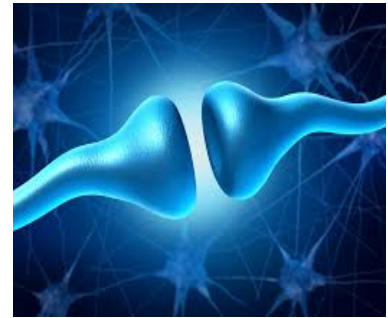
**Figure 1.12:** SECCA radiofrequency device (Reprinted with permission from Mederi Therapeutics, Greenwich, CT.)

**Stem cell injection**

Recent studies have proposed stem cell injection as an alternative new therapeutic approach with low morbidity. In these studies, autogenous bioproducts, such as myoblasts, have been used to enhance sphincter muscle cell growth. This therapy is still very much in the investigational stages of use <sup>158</sup>.

### **Neuromodulation**

Minimally invasive neuromodulation methods have been developed to bridge the treatment gap between conservative and surgical management for FI. Neuromodulation (NM) therapies encompasses any technology that impacts upon neural interfaces to



produce benefit, and is one of the fastest growing areas of medicine. NM is defined by the International Neuromodulation Society as "the alteration of nerve activity through the delivery of electrical stimulation or chemical agents to targeted sites of the body" <sup>159</sup>. NM devices stimulate nerves using pharmaceutical agents, electrical signals and other forms of energy by modulating abnormal neural pathway behaviour caused by the disease process and "normalising" them. The use of NM therapies has been common since the 1980s, with indications in all facets of medicine expanding. Common treatments include: spinal cord stimulation for neuropathic pain, deep brain stimulation for Parkinson's disease and epilepsy, sacral nerve stimulation for neurogenic bladder and bowel conditions as well as miniature implants for auditory and visual sensory impairment.

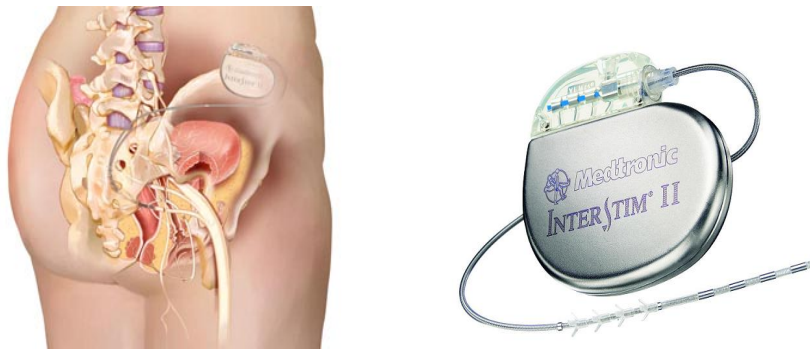
In the last 30 years, neuromodulation has gained support as a treatment for FI employing chronic, low-voltage electrical stimulation to recruit residual function of pelvic organs by direct or indirect stimulation of the sacral spinal nerves <sup>160</sup>. It is based on the concept that residual anorectal neuromuscular function pertinent to

continence can be recruited by electrical stimulation of its peripheral nerve supply. NM treatments bridge the gap between conservative therapies and potentially hazardous surgery to the bowel or anal sphincter. The most established of these is sacral nerve stimulation (SNS) and the next most popular technique is percutaneous tibial nerve stimulation (PTNS). This thesis focuses on evaluating the clinical effectiveness of these two interventions.

## **1.8 SACRAL NERVE STIMULATION (SNS)**

Sacral spinal nerve stimulation was originally investigated as a possible treatment for paraplegic patients with the intention of assisting rehabilitation and walking<sup>161</sup>. In the late 1970s, as a consequence of his early work, Brindley found that this treatment had a more profound effect on inducing micturition in neurogenic urinary retention<sup>162</sup>. The first series of implanted sacral nerve stimulators was undertaken by Tanagho *et al.* in 1989 for the treatment of urinary voiding disorders<sup>163</sup>. Subsequently it was found that stimulation of the sacral nerve had a concomitant effect on the bowel and was reported as a successful treatment of FI by Matzel 1995<sup>164</sup>. Since then indications for sacral neuromodulation therapy have significantly widened and now include many functional pelvic pathologies including constipation, irritable bowel syndrome, and chronic pelvic pain<sup>165</sup>. Despite these developments, the most compelling data for its success, has been from the treatment of FI<sup>166</sup>.

---



**Figure 1.13:** Diagrammatic representation of in-situ SNS and a neurostimulator (*reproduced with permission from Medtronic PLC*)

SNS has gained popularity and acceptance due to the advantages of a minimally invasive technique, high cited success rates (approximately 70%)<sup>7</sup>, minimal morbidity (overall complications rates of 5% to 26%<sup>8</sup>) and no reported mortality<sup>9</sup>. SNS is a safe and effective option for most patients failing non-interventional therapies regardless of FI aetiology e.g. sphincter injury, neurological impairment<sup>167-171</sup>. A temporary percutaneous nerve evaluation (PNE) allows patients to trial the SNS system and test the feasibility of success before an expensive and slightly invasive permanent stimulator is implanted. The technique of PNE followed by permanent tined lead implantation has been well described in the literature (and below in section 2.2.2). With impressive reported success rates for a very challenging condition, SNS has become the "gold standard" treatment to which other treatments are now being compared.

---



Internationally SNS has been shown to be a cost effective treatment overall <sup>11, 12</sup>, with reports of the financial advantage over colostomy and dynamic graciloplasty at 5 years <sup>13, 14</sup>. Despite these reports, costs of SNS still remain an issue of on-going discussion. The initial outlay is still considerable both in terms of direct equipment cost (approximately £7,000 in the UK) and indirect hospital admission costs (£12,959 in the UK) <sup>11</sup>. Particularly given the high equipment costs, patients who require SNS in the UK often necessitates prior individual funding approval which can delay treatment. Since other treatments for FI are reported to lose effectiveness over time, for example sphincteroplasty <sup>15</sup>, there is a great deal of interest into whether SNS has sustained benefits and remains cost effective. Data on long-term effectiveness are now available <sup>16, 17</sup>. At a time when many institutions face financial constraints, it is increasingly important to clarify the long-term success rate of this technique.

## **1.9 PERCUTANEOUS TIBIAL NERVE STIMULATION (PTNS)**

Over the last few years, cheaper, less invasive and technically simpler neuromodulatory therapies have been developed. These aim to achieve minimally invasive therapy in the outpatient setting, easily performed by specialists without the need for surgical training. Currently the commonest form of distal neuromodulation treatment in clinical practice is percutaneous tibial nerve

---

stimulation (PTNS) <sup>172</sup>. PTNS uses a small electrode needle to stimulate the tibial nerve near the ankle in order to achieve effects via its origin, which is common to the spinal roots that control bowel function. The idea of stimulating the tibial nerve is based upon the knowledge of traditional Chinese acupuncture points over the common peroneal or tibial nerves inducing reflex inhibition to the pelvic organs <sup>173</sup>. Similar to the development of SNS, neuromodulation of the tibial nerve was first shown to have an effect on bladder continence in 1983 by Nakamura <sup>174</sup> and McGuire *et al.* <sup>175</sup> In 2000 the method was further modified by Stoller in San Francisco by stimulation of a percutaneously placed needle electrode at the level of the ankle and was soon popularised as an effective treatment for urinary incontinence. It was first described as a treatment of FI in 2003 by Shafik, who achieved a reported 78% functional success in 32 patients <sup>172</sup>.



**Figure 1.14:** Placement of percutaneous tibial nerve stimulation (PTNS) (*reproduced from [www.uroplasty.com](http://www.uroplasty.com) © Uroplasty PLC, with permission from Uroplasty*)

It has been hypothesised that PTNS and SNS treatments may have the same outcomes because the mode of action on the sacral nerve plexus is thought to be the same. In principle, PTNS aims to use peripheral neuromodulation to recruit and retrain latent nerve fibres in the sacral plexus via stimulation of the tibial nerve. In turn this may allow improved innervation to the muscles of the pelvic floor and therefore improved continence.

Although definitive trial data, which are available for over-active bladder therapy<sup>176</sup>, is currently not available for FI, limited published case series have shown an approximate 60-78% success rate<sup>172, 177, 178</sup>. The cost of PTNS is estimated to be less than one-tenth that of SNS; in the presence of a trained healthcare specialist, the setup costs for PTNS are less than £1000 for the stimulator (which can be used on multiple patients) and a cost of £500 per patient for the disposable equipment for the treatment course<sup>178</sup>. PTNS is simple to perform in the outpatient clinic without anaesthesia or radiation exposure. The optimal protocol for FI using PTNS is still not standardised and various treatment frequencies have been described. As mentioned already the effects of PTNS may wear off in time and therefore intermittent "top-up" treatments may be required to maintain its effectiveness, the exact number of these and the long term effectiveness and cost of repeated treatment is still yet to be determined. It is suspected that depending on the frequency of PTNS top-up treatments, a large number of hospital visits may be required, which might limit its use to patients living near specialist hospitals. Unlike SNS there is no prescribed

---

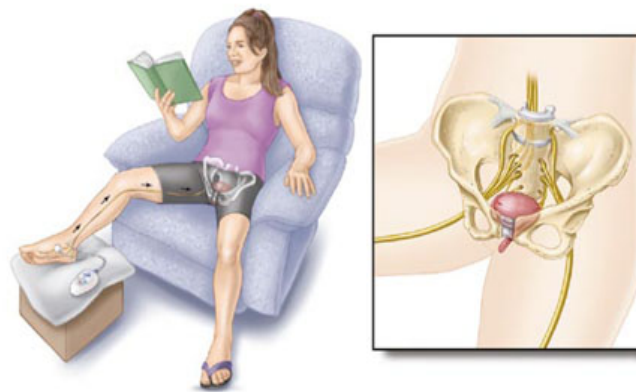
evaluation phase to determine treatment responders therefore a lengthy and potentially resource intensive programme of treatment may be needed to assess its effectiveness.

Akin to SNS, there are relatively few contraindications to PTNS however these include: the presence of a pacemaker or implantable defibrillator, bleeding disorders, the presence of a painful or total peripheral neuropathy (which may result in over or under stimulation), and patients who are pregnant or intending to become pregnant whilst receiving the treatment. Prior to commencement of PTNS, patients should be counseled regarding expectations and must be motivated to comply with ongoing sessions of therapy. Side effects can include occasional tenderness at the site of needle insertion, swelling and inflammation around the needle site, toe/foot pain and small haematomas<sup>178, 179</sup>. So far this therapy has been found to be completely reversible, if the effects are not adequate or adverse reactions occur then the treatment course can simply be halted with spontaneous resolution.

More recently attempts to make this therapy needleless have resulted in the development of devices using adhesive surface electrodes placed over the tibial nerve. This form of transcutaneous electrical nerve stimulation (TENS) is based on the principle of PTNS but is even less invasive allowing delivery of the electrical stimulus to the tibial nerve without piercing the skin<sup>180</sup>. Transcutaneous tibial nerve

---

stimulation (TTNS) involves electrical stimulation which is delivered via two-pad electrodes placed over the tibial nerve just above the ankle. This is usually delivered via a TENS machine. Treatment regimens vary considerably, although administration is usually in 20- to 30-minute sessions over a period of weeks or months. The main advantage of PTNS over TTNS is the proximity of the needle to the tibial nerve, enabling higher treatment amplitude to be delivered while avoiding the painful skin sensations associated with transcutaneous treatment. To avoid confusion, as this technique is sometimes also abbreviated to PTNS, it will be referred to as TTNS.



**Figure 1.15:** Diagrammatic representation of the mechanism of PTNS (*reproduced from [www.uroplasty.com](http://www.uroplasty.com) © Uroplasty PLC, with permission from Uroplasty*)



**Figure 1.16:** Transcutaneous tibial nerve stimulation (TTNS) (*reproduced from Thomas. Colorectal Dis 2013; 15:519-26 © 2013 Wiley publishing, with permission from Wiley publishing*)

## **1.10 STUDY RATIONALE AND AIMS**

Although PTNS is gathering popularity as a minimally invasive treatment for FI, it is still not clear where it stands within the algorithm of FI treatment. Knowledge of the efficacy of PTNS is paramount to informing NHS (National Institute of Health and Clinical Excellence - NICE) policy on the management of patients with FI. Accepting the limitations of available data (absence of pivotal randomised control trial data for either treatment), PTNS has the potential to be a very attractive alternative to SNS, at the very least in the short-term. In order to confirm this possibility, it would have to be proven that PTNS is largely equivalent in clinical effectiveness and is more cost effective when compared to an established comparator (SNS). Such results may have enormous relevance to patients both within the NHS and internationally. Specifically, the adoption of PTNS would have the potential to:

- Expand treatment choice for patients
- Enable treatment of patient groups currently marginalised from interventional therapy e.g. the very elderly / care home residents (PTNS could be provided in the future as a visiting specialist service)
- Reduce need for operative surgery
- Reduce need for inpatient stays
- Reduce operative morbidity including hospital acquired infections
- Reduce waiting times for treatment

Such information has the potential to change the current algorithm of management of FI and thus impact on future NHS resource utilisation; PTNS could thus become the routine first 'invasive' intervention in patients with FI failing prior conservative physician- and nurse-led approaches. Furthermore, PTNS could be relatively easily implemented within the NHS, requiring only modest training and expertise, and little financial outlay on specialist equipment.

The primary aim of this thesis is to provide a broad overview, determining the short term clinical effectiveness, costs and patient acceptability of PTNS when compared directly to the more established neuromodulation method of SNS. To our knowledge a prospective randomised comparison of clinical outcomes and full health-related costs between these two treatments has never before been undertaken but is clearly relevant to future health provision and policy making. The studies within this thesis therefore aims to provide pilot data which may aid the planning of further definitive studies on this topic. In keeping with the convention of pilot studies, a hypothesis is unable to be offered but there seems to be current equipoise in the literature between the effectiveness of each technique. By directly comparing SNS and PTNS, the series of studies within this thesis may provide some evidence that PTNS in the short term can have comparable clinical outcomes and patient acceptability to SNS but at a lower cost.

### **1.11 SPECIFIC PROJECT AIMS**

To achieve our primary aim, we devised three studies to assess both PTNS and SNS.

1. A systematic review of clinical effectiveness for both neuromodulation techniques in FI.
2. A pilot randomised control trial (RCT) comparing SNS and PTNS.
3. A qualitative interview study of SNS and PTNS patients

#### ***1.11.1 A REVIEW OF CLINICAL EFFECTIVENESS OF NEUROMODULATION IN FAECAL INCONTINENCE***

The aim of this study is to (1) systematically review the current literature clinical outcomes of SNS in the short, medium and long term on an intention-to-treat (ITT) basis, (2) describe outcomes of PTNS and TTNS; and (3) to report congruence of clinical outcome measures in the evaluation of success for FI therapies.

#### ***1.11.2 RANDOMISED PILOT TRIAL OF SACRAL AND PERCUTANEOUS TIBIAL NERVE STIMULATION IN PATIENTS WITH FAECAL INCONTINENCE***

The overall aim for this exploratory study is to acquire, using a phase II mixed methods pilot trial design, the necessary quantitative and qualitative data to inform a subsequent definitive randomised control trial (RCT) comparing SNS and PTNS. In

---



keeping with the pilot design, endpoints are selected to give an indication of the short-term effectiveness and acceptability of both treatments with no pre-specified primary outcome. For the same reason, no specific hypotheses are provided.

### ***1.11.3 QUALITATIVE INTERVIEW STUDY OF SACRAL AND PERCUTANEOUS TIBIAL NERVE STIMULATION IN PATIENTS WITH FAECAL INCONTINENCE***

Qualitative methodology concerns the detailed examination of personal change. With this innovative research technique we hope to provide an aid to understanding our patient's experiences and views of the two FI treatments <sup>181</sup>. This study is designed to conduct a robust qualitative analysis to complement the quantitative study of neuromodulation treatments running in parallel. By analysing the personal accounts of our participants, we anticipate acquiring a unique insight into the lived experience of those undergoing NM treatments for FI. We can foresee that the data attained will give those interested in managing FI a new perspective on the two presented treatments.

Our aim is to use the inductive and deductive principles of qualitative research to find out the patient's experience of their "life world" <sup>182</sup>. It is accepted and encouraged that the course and content of the interview is not laid down in advance. The aim of the interviews are to provide a snapshot of the patient's attempts to make sense of their experiences. The thoughts accessed in the

---

interviews are not necessarily held to be the truth but instead are personally “meaning-full” originating from the situated concerns of the participants <sup>183</sup>. Through this study we want to explore patients' experiences, acceptability and preferences around the two treatments (SNS and PTNS) for FI.

# **2 MATERIALS AND METHODS**

## **2.1 INTRODUCTION**

This chapter covers two main aspects of the project. In the first part we discuss the materials, methods and considerations required in preparing patients and delivering both SNS and PTNS as clinical treatments. Both interventions are newer minimally invasive techniques and therefore many healthcare professionals may not yet be familiar with the concept of NM. Moreover, it is imperative to understand the technical, clinical and organisational considerations for each technique, therefore maximising the benefit, safety and satisfaction for all patients. As with all procedures there is a learning curve in perfecting each approach. As a method of validation, the Clinical Research Fellow (CRF) undertook a training period of approximately 12 months studying the SNS technique. The CRF was then assessed by the Senior Investigator (Professor Charles Knowles) and was approved to be competent to perform the intervention independently. Similarly a three month training period was required for PTNS, after which a certification of proficiency was awarded by Uroplasty (the company producing PTNS).

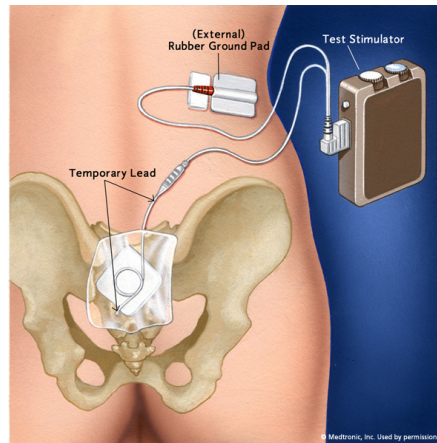
The second section of this chapter covers the material and methods for the proposed pilot studies. The three studies were designed to be undertaken simultaneously with the two prospective studies using the same cohort of recruited patients. Where organisational and recruitment methods are common to all three studies, they have been included in the generalised methodology section with specific study methods described individually thereafter.

## **2.2    *GENERAL TECHNICAL, CLINICAL AND ORGANISATIONAL PRINCIPLES OF SNS THERAPY***

SNS can be considered as a two stage procedure comprising of a 2-3 week test phase known as the PNE followed by the surgical implantation of a permanent implantable pulse generator (IPG). The InterStim system<sup>© Medtronic</sup> can be simplified into its two main functioning parts: the lead (or wire) and the stimulator, also known as the IPG or battery. The lead is percutaneously inserted and positioned in an appropriate sacral foramen (usually S3 or S4) to lie adjacent to the sacral nerve. The stimulator, lead and nerve form a conducting circuit whereby mild electrical impulses generated by the stimulator pass along the lead and stimulate the nerves to innervate organs that contribute to bowel function; such as the anus, rectum and pelvic floor. Any complications breaking or impeding the continuity of this electrical circuit can cause the system to fail; including lead displacement, lead breakage,

---

stimulator failure or high resistance caused by excess fibrosis. Hetzer *et al.* reported that the percutaneous technique, first described by Spinelli and colleagues<sup>184</sup>, had a low morbidity rate and could be performed easily as a day-case procedure<sup>185</sup>.



**Figure 2.01:** Temporary peripheral nerve evaluation (PNE) set up with monopolar lead (*reproduced from <http://www.rcsed.ac.uk> © Medtronic PLC, with permission from Medtronic*)

### 2.2.1 PATIENT SELECTION AND PRE-OPERATIVE CONSIDERATIONS

Before undertaking SNS, patients should undergo a full assessment of their condition including anorectal physiology testing (see section 1.6)<sup>87</sup>. Although the procedure is not technically complicated, a permanent implant can have a significant impact on individual lifestyle. Implanted patients may need to make adjustments to their usual routines and therefore need to be counselled of the possible restrictions of living with a permanent implant. Although the aim of successful control of FI is to allow the patients to regain their "freedom", a permanent implant will bring about restrictions similar to those for other implanted

devices such as cardiac pacemakers. Absolute contraindications to implantation can be considered to be: requirements for MRI scanning, participation in contact or extreme sports (especially with changes in atmospheric pressure) and pregnancy. Other patient considerations include adjustment of air travel routines with particular reference to airport security gates: this requires the deactivation of implants when going through detectors and informing security staff appropriately. In addition invasive medical procedures may need cover with antibiotics.

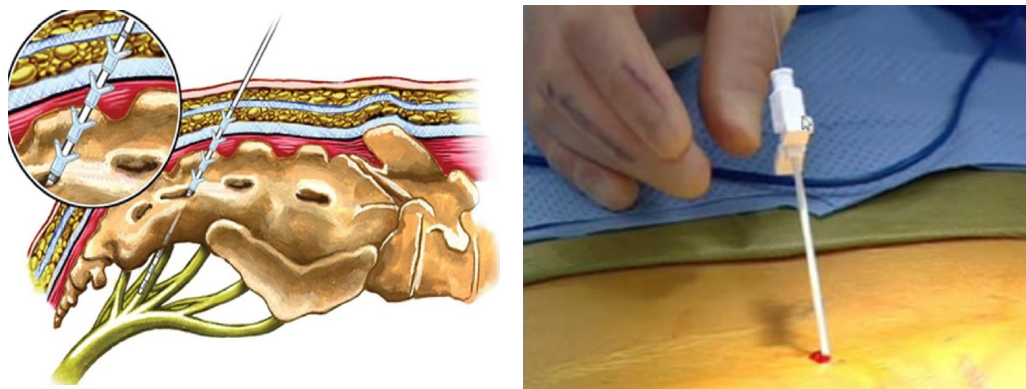
From our own experience, time set aside from busy clinics prior to surgery, in a dedicated counselling session is very worthwhile. Not only does it give healthcare professionals the chance to discuss expectations of the treatment but it also allows patients to voice concerns over changes which may affect their lifestyle. These in-depth sessions help patients build a rapport with the SNS team and aim to improve post operative compliance. The author echoes the sentiments of other authors<sup>186</sup> who feel that SNS should be conducted in a suitable multidisciplinary environment with specific points of contact within the hospital and access to rapid outpatient consultation.

### **2.2.2 INTRA-OPERATIVE CONSIDERATIONS**

The technique of SNS placement can be carried out effectively and safely under both general and local anaesthetic with/without sedation<sup>187</sup>; however it is important to

---

appreciate the variations in equipment and surgical skill required at each stage. Of course both stages require careful aseptic technique and correct positioning of the lead. This can be achieved at the time of insertion by careful skin marking, optimal lead positioning using cross table lateral intra-operative X-rays and acute lead testing, ensuring either perineal sensation or anal muscle contraction (Bellow's response) +/- plantar flexion of the ipsilateral great toe is elicited. All muscle blocking agents should be avoided at this stage to avoid false negative responses.



**Figure 2.02:** Insertion of tined lead into the S3 foramen (*reproduced from <http://www.rcsed.ac.uk> © Medtronic PLC, with permission from Medtronic*)

To facilitate successful SNS, familiarity with the equipment and careful consideration for its organization whilst in theatre is essential. Below is a brief outline of the operative steps at each stage. The equipment required and key differences between the procedures are outlined in Table 2.01.

**Table 2.01:** Key differences in test and permanent SNS techniques

	Equipment		Intra-operative Consideration			General Consideration		
	Lead	Stimulator	Anaesthetic	Antibiotics	Diathermy	Tunnelling of lead and Subcutaneous pocket	Test Duration	Removal
<b>Monopolar Lead test (PNE)</b>	3065USC - temporary lead kit	3625 External Pulse Generator	5-10 ml of 1% lignocaine with 1:200,000 adrenaline +/- sedation	None	None	None	2 weeks	Outpatient setting
<b>Tined Quadripolar Lead test (Stage 1)</b>	3093-28 - tined lead kit 3550-18 - lead introducer kit	3625 External Pulse Generator	20-40 ml of 1% lignocaine with 1:200,000 adrenaline + sedation/GA	Induction Co-amoxiclav and 3 post op doses	Required	Subcutaneous tunnel for lead. 4cm pocket for internal to external interconnector	Up to 6 weeks	Operative in theatre
<b>Permanent Implant (Stage 2)</b>	3093-28 - tined lead kit 3550-18 - lead introducer kit	3058 (InterStim II) Indwelling IPG	20-40 ml of 1% lignocaine with 1:200,000 adrenaline + sedation/GA	Induction Co-amoxiclav and 3 post op doses	Required	Subcutaneous tunnel for lead. 7cm pocket for IPG	Permanent	Operative in theatre



***Test stimulation***

There are two methods of performing the test phase. The first uses a non-tined monopolar lead (3065USC; Medtronic, Minneapolis, Minnesota, USA) and is known as the PNE method. At our institution unilateral percutaneous insertion of this lead is performed under local anaesthetic with or without sedation. The lead is inserted percutaneously through a needle introducer positioned in the appropriate sacral foramen. After correct positioning and acute testing, the needle introducer is removed leaving the lead in place. Approximately  $\frac{3}{4}$  of the lead remains outside the skin. The free end of the lead is connected to an extension wire and earth pad secured with dressings. Care must be taken to secure this properly, preventing lead displacement for the duration of the PNE period. The extension wire is then connected to an external pulse generator (3625; Medtronic) approximately the size of a pager; then stimulation is commenced the same day at 14Hz, pulse width 210 $\mu$ s for a total of 14 days. The amplitude is controlled at a comfortable sub-sensory level by the patient (usually 1-3 mA). Patients assess their own response to PNE through 2 week bowel diaries and then the lead is removed in the outpatient setting. The disadvantage of this technique is that even though a response is found, the carefully placed lead has to be removed. If the patient goes on to have a permanent implant, a new lead will need to be sited, attempting to replicate the exact position and response again. This is not always possible and may be made more difficult by scarring around the sacral foramen following the initial procedure.

The alternative test stimulation method uses the tined quadripolar lead (3093-28; Medtronic) to perform the chronic test. It is also known as the first stage procedure in a 2 staged implantation method. This procedure is slightly more challenging and some surgical skill is required for its insertion. The tined lead is designed to be more permanent and has little barbs (plastic hooks) on the lead to allow anchoring to the sacrum as it passes through the foramen. Before implantation the tined lead is soaked in antibiotic solution (4ml of 80mg Gentamicin diluted in a saline solution). Insertion of the tined lead is performed under local anaesthetic with sedation. First an introducing needle is used to locate the optimum response from the sacral nerve. A guide wire then replaces the needle and a rigid dilator and lead introducer is inserted over the guide wire into position. It is important to assess the depth of the introducer with intra-operative X-ray to ensure safe and accurate positioning of the lead. The lead is placed through the introducer and then the introducer is removed leaving the tined lead in position. The tined lead is then tunnelled subcutaneously to a small pocket created in the ipsilateral buttock. This pocket will house an interconnector to an exteriorised wire which will allow connection to an external stimulator (3625; Medtronic). With this set up, the testing phase can be lengthened to 6 weeks rather than two.

The clear advantages of using the permanent tined quadripolar lead are (1) the longer test period gives the patient a more accurate representation of the effect of the permanent system and (2) the placement of the lead remains constant. The

---

disadvantages are that (1) the tined lead is more expensive than the unipolar lead and (2) a small surgical procedure is required to remove the tined lead if unsuccessful. Therefore whether an implant is required or not, careful planning and co-ordination of available theatre space must be undertaken at 6 weeks to ensure that there are no unnecessary delays to the second stage procedure.

### ***Permanent stimulation***

If a monopolar lead test had been carried out previously, unilateral percutaneous insertion of a permanent tined quadripolar lead (3093-28; Medtronic) and implantable pulse generator (3023; Medtronic) is required. Again the author prefers to perform this under local anaesthesia with sedation but this can also be done under general anaesthetic. Where possible this should be inserted in the same sacral foramen as the temporary lead. The technique for the insertion of the tined quadripolar lead is the same as has been described above. After correct insertion and positioning of the lead, a subcutaneous tunnel is created allowing the lead to be connected to the IPG placed in a subcutaneous pocket in the ipsilateral buttock of the implanted electrode. The key to a patient friendly implant is to get the depth of the subcutaneous pocket right. Too shallow and it will be uncomfortable for the patient, too deep and it will be difficult for the patient to use with their hand held controller (3037; Medtronic). It is important to ensure that the lead is tucked deep to the implant before closure as this will protect the lead when IPG replacement is necessary.

If the tined lead is already in position then the second stage procedure is even simpler. The subcutaneous pocket already fashioned can be re-opened and the interconnector located. The interconnector and externalised wire can be removed and the free end of the lead can be attached to the IPG. The subcutaneous pocket may require widening to house the IPG; at all times care must be taken to protect the lead from injury. Once the implant has been inserted, stimulation can be commenced the same day using the stimulation parameters mentioned previously. At our institution an intra-operative dose Co-Amoxiclav is given at induction with 3 post operative doses for all permanent implants. Short-term complications include bleeding, wound and lead infection. Medium-term complications include sleep disturbance, perineal or leg pain, lead displacement or damage<sup>188</sup>. The implant should not be visible and does not restrict normal activities although rigorous activities again should be avoided for the first three to six weeks.

### **2.2.3 POST-OPERATIVE CONSIDERATIONS**

After the patient is suitably alert and recovered on the ward, the initial set up of the IPG can be undertaken along with patient programmer training (InterStim Icon 3037, Medtronic). In the initial post operative period before natural tissue fibrosis has occurred to anchor the lead, it is imperative to ensure that the lead does not become displaced. Again the importance of a multidisciplinary team approach cannot be overemphasised. The patient should have a point of contact at the unit

---

and mechanisms in place to ensure prompt follow up. SNS is still a relatively new concept and healthcare services outside specialists unit may be unfamiliar with its set up and equipment. Upon discharge we provide our patients with written information detailing the restrictions for the immediate post operative period and contact details for our unit. Post operatively we follow up our patients at 6 weeks and then at suitable regular intervals. At these appointments it is important to review the stimulator and electrode settings. It is often necessary to adjust electrode settings more frequently in the early stages of the therapy to ensure that optimum stimulation parameters are achieved. The IPG is equipped with a battery which discharges with time, lasting approximately seven years. At the end of the batteries life, a small operation is required to replace the IPG.

### **2.3    *GENERAL TECHNICAL, CLINICAL AND ORGANISATIONAL PRINCIPLES OF PTNS THERAPY***

Since 2005, Uroplasty has marketed the Urgent<sup>®</sup> PC Neuromodulation System, the only presently available commercial device to deliver PTNS (Uroplasty Ltd., Manchester, UK)<sup>178, 179, 189</sup>. The system comes in two parts: a single use disposable pack of two needle electrodes and a lead wire set (UPC250), and the reusable battery operated Urgent PC stimulator (UPC200).

Unlike SNS no surgical skill is required for performing this procedure and the technique itself is easy to learn. The patient is seen in an Outpatient clinic room, ideally sitting up on a comfortable examination couch. Either leg can be used for the procedure and preference is usually left up to the patient. Shoes and socks of the preferred foot are removed and the trouser leg rolled up to approximately mid calf. The site of needle insertion is identified at a location on the lower inner aspect of the patient's leg, three finger breaths (5 cm) cephalad to the medial malleolus and one fingerbreadth (2 cm) posterior to the tibia. The area is cleaned with ethanol and the needle electrode-guide tube assembly is placed over the identified insertion site at a 60-degree angle between electrode and ankle. The fine 34 gauge needle electrode is gently tapped to pierce the skin and then advanced using a rotating motion approximately 2cm. The lead wire is connected to the needle and the calcaneal reference electrode placed on the ipsilateral calcaneum. The lead wire is then connected to the Urgent PC stimulator. The PTNS stimulator (UPC200) is an external pulse generator that provides visual and auditory feedback. It has an adjustable current setting from 0-9mA in pre-set 0.5mA increments, a fixed-pulse frequency of 20Hz and a pulse width of 200 microseconds. The setting for therapy is determined by increasing the current whilst observing the patient response. Stimulation of the tibial nerve produces a motor (plantar flexion or fanning of the toes) and/or sensory (tingling in the ankle, foot or toes) response. Once the appropriate level for therapy is found, the 30-minute treatment is started. Therapy is given for a period of 12 weeks, in weekly 30-minute sessions, although others

---

have used alternative treatment protocols. Following the 12 initial weekly treatments, some patients may need intermittent 'top-up' sessions. At our institution 3 top-up sessions are given at 2 weeks, 4 weeks and 8 weeks after the completion of the initial 12 weekly sessions. Further top-up sessions may be offered to those who require them on an approximately 6 monthly basis.



**Figure 2.03:** Urgent PC system (reproduced from [www.uroplasty.com](http://www.uroplasty.com) © Uroplasty PLC, with permission from Uroplasty)

## 2.4 GENERAL PROJECT MANAGEMENT

All three studies were performed in conjunction with the 'Pragmatic Clinical Trials Unit' (PCTU). This unit, situated within the Centre for Health Science at QMUL, leads and supports clinical trials when the primary question of interest relates to intervention effectiveness i.e. whether complex interventions work under real-life conditions.

#### **2.4.1 MANAGEMENT STRUCTURE**

The project was overseen by a Study Steering Group (SSG).

The SSG met/teleconferenced, on a quarterly basis throughout the project. The remit of the SSG was to ensure:

- 1) That views of users and carers are always taken into consideration
- 2) The scientific rigour of the study
- 3) That project milestones are met
- 4) Expertise / advice are provided to the Project Management Group (PMG)

#### **2.4.2 MEMBERSHIP OF THE STUDY STEERING GROUP**

The applicants, 2 user group representatives, the Executive Director of Bladder and Bowel Foundation, Health Economist, Senior Clinical Physiologist and 2 peer experts in this field: internal: Mr Peter Lunniss, Consultant Colorectal Surgeon (Barts and Royal London) and external: Dr Anton Emmanuel, Consultant Gastroenterologist with interest in neuromodulation (University College, London).

A PMG was responsible for the day to day project delivery. It met fortnightly and included the Senior Investigator (Professor Knowles), Research Nurse (RN), CRF, study nursing leads and a Project Finance Officer from the joint (Trust and Medical



College) R&D Office. This group was informed by the SSG. The group was responsible for overseeing and managing:

1. trial recruitment and retention rates
2. site initiation, training, monitoring, compliance and correction/preventative actions
3. data management (collection, quality control, entry and query management)
4. adverse and serious adverse event (SAE) reporting
5. study milestones
6. study reporting
7. budget expenditure and accruals

A Patient Advisory Group was also established to advise the SSG and the PMG via representation (2 nominated members) at meetings. The project acted under the auspices of the PCTU.

## **2.5 RESEARCH PLAN**

The research plan comprised of six work packages (WP)

WP1: Ethical permission was attained prior to the study start date. The research team undertook final public consultation and research governance checks. The PMG and SSGs were convened.

WP2: Training (0-6 months): The CRF received formal training in qualitative methodologies by attending a short course run by Aston University, Birmingham. The CRF was also trained to perform both SNS and PTNS treatments. The CRF had already been training to perform SNS 6 months before the start of the project. The RN was trained in all other outcome assessment tools (and in aspects related to maintaining blinding).

WP3: Trial roll out (7-31 months). During this phase of the study, the clinical trial was formally opened and conducted by the CRF. Active recruitment of patients for a 9-10 month period (months 7-17) with interventions thence administered by specialist surgical and nursing staff. All treatments were conducted over a 12 month duration and were completed by end of month 22. Blinded data acquisition was undertaken by the RN for all quantitative outcome measures. Qualitative interviews were undertaken by the research assistant and analysed iteratively by the CRF. This period of follow up finished at end month 28 with a minimum of 6 months follow up after completion of either treatment arm. Regular 2 weekly meetings by the were conducted by the PMG to continue to guide and when necessary make modifications to the protocol detail as well as to monitor satisfactory recruitment targets. On-going discussions with trial participants and their carers allowed a feedforward analysis throughout the trial.

Milestones were: start month 6 - first recruitment, end month 17 - last recruitment, end month 23 - end last treatment, end month 28 - last FU visit.

WP4: Data analysis and start of process of dissemination. During this phase of the study, the research team commenced the task of data analysis. Qualitative (unblinded) data analysis had a rolling process of analysis from 24 month. In conjunction with the trial statistician, quantitative data was cleaned and locked after 3 and 6 months follow ups, with the randomisation coding only broken after month

---

30, and all outcomes analysed. The data was disseminated after end month 36 by national and international presentation as well as by publication [British Journal of Surgery].

WP5: Project management (0-36 months). This was a continuous phase of managerial meetings to ensure quality control.

WP6: Systematic Review (0-36 months). This was a continuous background activity along with the prospective studies. The review was devised to provide background supportive evidence on both treatment modalities on an intention-to-treat basis. To the authors' knowledge this had not previously been undertaken.

**Table 2.02:** Gantt Chart of Work Packages Undertaken

	09	2010												2011												2012													
Month	D	J	F	M	A	M	J	J	A	S	O	N	D	J	F	M	A	M	J	J	A	S	O	N	D	J	F	M	A	M	J	J	A	S	O	N			
	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			
STAFFING																																							
RN																																							
CRF																																							
S&HE																																							
WP1	TRIAL FINALISATION																																						
Public consult																																							
Convene SSG																																							
WP2	TRAINING																																						
RN																																							
CRF																																							
WP3	TRIAL ROLL OUT & QUALITATIVE STUDY																																						
Recruitment																																							
Random-isation																																							
Interventions																																							
Follow up																																							
Qualitative																																							

	09	2010												2011												2012											
Month	D	J	F	M	A	M	J	J	A	S	O	N	D	J	F	M	A	M	J	J	A	S	O	N	D	J	F	M	A	M	J	J	A	S	O	N	
	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	
WP4	DATA ANALYSIS AND START DISSEMINATION																																				
Qualitative analysis																																					
Clean / lock down 3/12																																					
Clean / lock down 6/12																																					
Code break & analysis																																					
Plan dissemination																																					
WP5	PROJECT MANAGEMENT																																				
PMG meetings																																					
SSG meetings																																					
WP6	SYSTEMATIC REVIEW																																				
CRF																																					

Abbreviations: RN = Research Nurse, CRF = Clinical Research Fellow, S&HE = Statistician & Health Economist, WP = work package, PMG = project management group, SSG = study steering group, Qualitative = qualitative interviews and analysis

## **2.6 DATA MANAGEMENT**

The PCTU data manager designed a secure database for entering, storing and transferring all pertinent patient data. Automated validation checks were carried out at the point of data entry. Data entry and cleaning was done by the researchers and further checks performed on receipt by the study statistician. The database was locked for analysis once the data manager and statisticians were satisfied with the quality and completeness.

## **2.7 PROJECT FUNDING**

This exploratory project was funded by a £160,000 Research for Patient Benefit Programme grant awarded in open competition from the National Institute of Health Research (ref: PB-PG-0909-20150). Queen Mary University of London acted as study sponsor. Neither relevant commercial organization (Medtronic Inc. or Uroplasty) had any role in the design, conduct or analysis of the trial.

## **2.8 SPECIFIC STUDY METHODS**

### **2.8.1 A REVIEW OF CLINICAL EFFECTIVENESS OF NEUROMODULATION IN FAECAL INCONTINENCE**

A systematic review was performed, adhering as closely as possible to the PRISMA<sup>190</sup> framework, which provides clear guidance on the methodology by which empirical evidence should be collated, therefore minimising bias and providing for reliable conclusions.

#### **2.8.1.1 Protocol development**

Two primary investigators (CRF and another independent researcher) and Senior Investigator (Professor Knowles) developed the protocol for review, detailing pre-specified methods of the analysis and eligibility for the study. Final decisions upon the scope of the review and search methodology were made by the Senior Investigator.

### **2.8.1.2 Inclusion criteria**

#### ***Report eligibility***

All published studies reporting results of permanent SNS, PTNS and other NM therapies from January 1995 until July 2012 were eligible for inclusion. Non-English language papers were excluded unless they contained an abstract in English providing sufficient information to meet inclusion criteria. It was stipulated that each study must provide data for at least 10 patients treated with permanent SNS or other NM therapy. Only reports which (a) clearly documented the number of patients having permanent SNS or other NM therapy performed (b) reported at least one chosen outcome measure (baseline and post intervention) and (c) recorded a clear follow up period were eligible for inclusion. Studies reporting solely on the PNE and chronic testing phase of SNS were excluded.

#### ***Participants***

No exclusions were placed upon study centre or patients regarding age, gender, ethnicity or aetiology of FI.

#### ***Interventions***

All eligible studies required a definitive intervention by permanent SNS, PTNS or other NM technique in patients with FI. Reports which included a NM therapy

---



together with a concurrent operative procedure for FI were excluded as were reports of NM therapies for primary urinary symptoms.

### ***Outcomes***

The chosen primary outcome was "success rate" of therapy based on a  $\geq 50\%$  improvement in FI episodes. Secondary outcomes were: (a) cure rates of the therapy i.e. 100% reduction in FI episodes (b) improvement of CCIS <sup>191</sup> (c) ordinal reductions in faecal incontinence episodes (FIE) per week; (d) other success measures of incontinence based on individual symptoms or scores and (e) QoL measures (generic and condition-specific). Outcome measures have been presented according to the median length of follow-up of the study data: short-term (0-12 months), medium-term (>12-36 months) and long-term (>36 months).

### ***Study selection***

Eligibility assessment was performed independently by three review authors, in an un-blinded but standardised manner. Methodological quality of included studies was assessed independently using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) assessment criteria. Disagreement between reviewers was resolved by consensus and by the Senior Investigator. The CRF and other research investigator independently undertook data extraction. Exact duplicate data sets generated from the same cohort of patients were excluded. In instances of doubt, authors from the relevant institutions were contacted to confirm

---

or refute any repetition of results. Because SNS and other NM therapies have in general been performed in specialist centres, it is accepted that results may have been published at more than one time point as experience developed. Inevitably there may be some longitudinal overlap in patient data sets, but in keeping with previous reviews<sup>188</sup> such data were not excluded. This represents a necessary trade-off between the benefit of greater numbers (of patients and studies) and length of follow-up against the significant likelihood that some of the data will be a continuation of those previously published (this has been highlighted in tables where the numbers of such patients were documented).

### ***Search***

For SNS studies, two authors individually carried out comprehensive searches of the literature in July 2012 using PubMed, Medline, Embase and Evidence Based Medicine reviews (including the Cochrane database of systematic reviews and the Cochrane central register of controlled trials). Full-text copies of all studies deemed to be potentially relevant were obtained and assessed for inclusion. Where papers cited other potentially important references, these were assessed. For other NM studies two authors individually carried out comprehensive searches in July 2012. Systematic reviews, randomised controlled trials, controlled clinical trials, comparative observational studies, population-based registry studies, case series, case reports and narrative reviews on patients with FI who had received NM were

extracted and then hand searched for relevant data sets. The reviewers were not blinded to the names of studies, authors, institutions or publications.

For SNS data the initial search terms used were 'sacral nerve stimulation faecal incontinence' and 'sacral neuromodulation faecal incontinence ("sacrum"[MeSH Terms] OR "sacrum"[All Fields] OR "sacral"[All Fields]) AND nerve [All Fields] AND stimulation [All Fields] AND ("faecal incontinence"[All Fields] OR "fecal incontinence"[MeSH Terms] OR ("fecal"[All Fields] AND "incontinence"[All Fields]) OR "fecal incontinence"[All Fields]). Search results were hand searched and cross referenced with bibliographies of relevant papers. One author was contacted and further clarification on the data was provided. For PTNS and other NM techniques, search terms 'percutaneous tibial nerve stimulation', 'percutaneous tibial nerve neuromodulation', 'posterior tibial nerve stimulation', 'posterior tibial nerve neuromodulation'. Further search terms for other NM strategies, 'Tibial Nerve Stimulation', 'percutaneous', 'transcutaneous', 'electrical', 'neuromodulation', 'faecal incontinence', 'fecal incontinence', and 'anal incontinence', were used.

### ***Risk of bias***

It is acknowledged that by limiting the inclusion criteria to English series with only greater than 10 patients, selection bias may have been introduced. This search strategy however ensured that individual case reports and smaller series would not

bias the results towards specific patient sub-populations or to investigators with limited experience.

### ***Summary measures and analysis***

Meta-analysis of data was not deemed appropriate because of heterogeneity between study designs and outcome measures and the absence of any genuine comparator for nearly all studies (the only published meta-analysis of SNS used baseline values as a comparator denoting these as maximum conservative therapy<sup>192</sup>). Summary measures (for individual outcome variables across roughly homogeneous studies) were limited to percentages, with use of medians and ranges.

## ***2.8.2 RANDOMISED PILOT TRIAL OF SACRAL AND PERCUTANEOUS TIBIAL NERVE STIMULATION IN PATIENTS WITH FAECAL INCONTINENCE***

The study was designed as a 24 month, mixed methods project involving two studies: (1) a pilot randomised single-blinded, external<sup>193</sup>, comparison trial of SNS and PTNS and (2) a qualitative study of patients' experiences and preferences around the two procedures. The overall design is shown in figure 2.04.

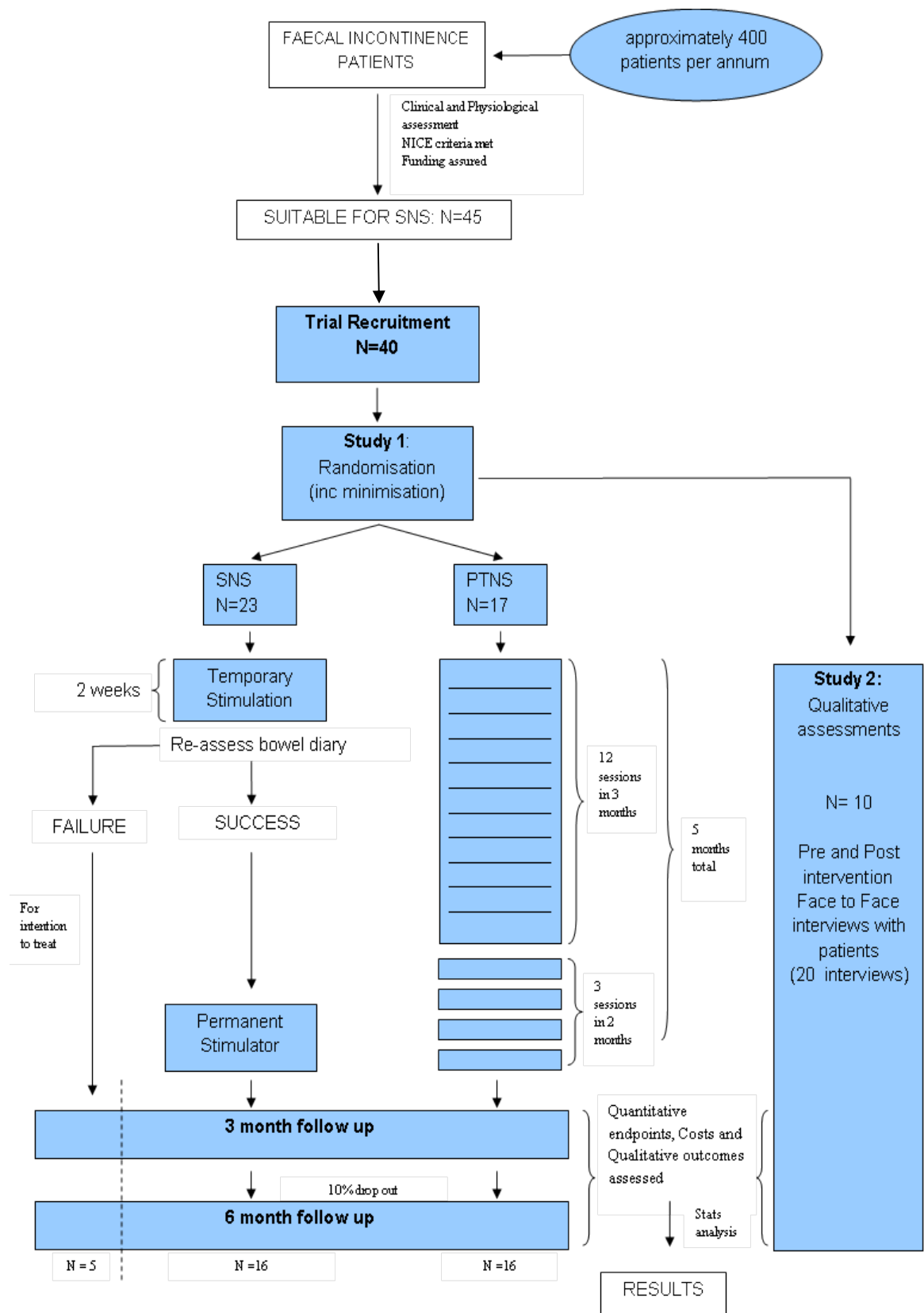
### **2.8.2.1 Setting and patients**

The study was undertaken across 2 sites with recruitment over 12 months of patients attending the Royal London Hospital (Barts Health) and University College Hospital - London (UCLH) NHS trusts for specialist investigation and treatment for FI. Ethics approval was granted by King's College Hospital Research Ethics Committee (Dulwich): NREC REF: 10/H0808/38 with local approvals at participating hospitals. The trial was registered on the UK clinical research network portfolio database (UKCRN ID: 10479 and European Clinical Trials Database (EduraCT) number: 2010-018728-15). Patients were eligible for inclusion based on meeting NICE criteria<sup>87</sup> for symptom severity and failure of prior conservative therapy; patients with specific contraindications to either therapy were excluded [Table 2.03]. All patients had NICE-recommended appropriate specialist investigations including structural and functional anorectal assessments<sup>87</sup>. Baseline data and eligibility were assessed and informed consent obtained at a clinical visit 2-4 weeks before treatments were assigned. All patients participating in the trial had funding approved for SNS from their Primary Care Trusts before randomisation.

**Table 2.03:** Inclusion and exclusion criteria

Inclusion	Exclusion
Aged > 18 years	Inability to provide informed consent for the research study
Meets NICE criteria for SNS treatment (2007)	Severe concomitant medical conditions precluding randomization to operative treatment
(Faecal incontinence sufficiently severe to warrant investigation and failure of all appropriate conservative measures)	Neurological diseases, such as diabetic neuropathy, multiple sclerosis and progressing Parkinson's disease
	Other medical conditions precluding stimulation: e.g. bleeding disorders, certain cardiac pacemakers, peripheral vascular disease
	Congenital anorectal anomalies or absence of native rectum due to surgery
	Present evidence of external full thickness rectal prolapse
	Previous rectal surgery (rectopexy / resection) < 12 months ago (24 months for cancer)
	Stoma <i>in situ</i>
	Chronic bowel diseases such as inflammatory bowel disease, chronic uncontrolled diarrhoea
	Anatomical limitations that would prevent successful placement of electrodes
	Pregnancy or intention to become pregnant
	Previous experience of SNS or PTNS

Figure 2.04: Study design flow chart



### **2.8.2.2 Interventions**

#### ***Sacral Nerve Stimulation (SNS)***

SNS was performed by the standard two stage approach<sup>164</sup> as detailed earlier in this chapter (section 2.2). For test stimulation, unilateral percutaneous insertion of a stimulating electrode (3065USC; Medtronic, Minneapolis, Minnesota, USA) into the sacral foramen was performed under local or occasionally (n=2) general anaesthesia. The unipolar PNE was used over the 2 stage quadripolar testing technique previously mentioned because (a) funding for each SNS treatment was easier to attain for PNE with a unipolar lead as the equipment was cheaper, (b) the unipolar technique was more established at the time of study and therefore easier to standardise across all units, (c) any externalised quadripolar leads require operative removal/IPG insertion within 6 weeks to minimise the infection risks. Pragmatically theatre sessions dedicated to SNS were limited and this could not be guaranteed at the investigator's institution.

Stimulation was then commenced the same day at 14 Hz and at a pulse width of 210  $\mu$ s for a total of 14 days using an external pulse generator (3625; Medtronic). Amplitude was controlled at a comfortable sensory level by the patient (1-3mA). Patients progressed to permanent stimulation if a  $\geq 50\%$  decrease in FI episodes was determined on 2 week bowel diary review<sup>164</sup>. Permanent stimulation used unilateral percutaneous insertion of a permanent tined lead (3093-28; Medtronic)

---



and implantable pulse generator (3058; Medtronic) under general or local anaesthesia, and where possible on the same side as temporary stimulation. Stimulation was commenced the same or following day using similar stimulation parameters as those described above. Meticulous attention was made to asepsis throughout, and Co-Amoxiclav given for 3 post-operative doses<sup>194</sup>.

### ***Percutaneous Tibial Nerve Stimulation (PTNS)***

PTNS was administered by a nurse consultant with the assistance of the CRF using the Urgent<sup>®</sup> PC neuromodulation system (Uroplasty, Minneapolis, USA)<sup>195</sup>. The patient was positioned in a comfortable supine or sitting position on an outpatient couch and the procedure performed as described in detail previously in this chapter (section 2.3)<sup>196</sup>. If the patient had no preference, the right ankle was usually used for ease of ergonomic insertion (positioned on a couch with left side of patient adjacent to the wall). Amplitude of stimulation was determined by increasing the current slowly whilst observing the participant's sensory (appropriate response being in great toe or sole of foot) or motor response (plantar-flexion of foot or great toe). Current was then reduced by one level for therapy, and continued for 30 minutes. Stimulation parameters were set to pulse width 200µs, frequency of 20Hz and average treatment amplitude was 7mA (range 1-10). Treatment was repeated for 12 initial sessions within 3 months with an interval tolerance of 1 week. Three maintenance treatments were then given to all patients over a 2 month period i.e. in total, patients received 15 sessions over a 5 month period.

---

### **2.8.2.3 Preliminary data**

Prior to the study commencing, audited data showed 51 patients completing the treatment cycle of SNS at Barts and The London with median follow up of 14 months. The treatment cycle consisted of patients having temporary stimulation for 2 weeks with an intention to proceed to permanent stimulation. 37 patients proceeded to have permanent stimulation. The dropout rate from failures of temporary stimulation was estimated at 27% ( $n = 14$ ) and patient choice 10% ( $n = 10$ ). In the trial the SNS group was therefore over recruited to account for the substantial temporary test failure rate and therefore dropout rate.

Similar departmental data from 42 patients was also analysed from those completing PTNS with a median of 5 months follow up at Barts and The London suggested a success rate at of  $27/42 = 64\%$  with no complications. Dropout rates from treatment were only 5%.

### **2.8.2.4 Sample size calculation and feasibility**

Formal sample size calculations for a fully powered RCT revealed that >2000 patients would be required to detect a difference in proportions of at least 5%. Since such a study would prove impracticable even on a multicentre basis (a realistic figure for a multi-centre trial would be nearer 200 patients), this pilot was needed to determine

---

the variability and distribution of a variety of quantitative endpoints as well as qualitative data to inform the most suitable/responsive outcome measures for a subsequent well designed and sufficiently powered RCT. If, accepting the difficulties of design and conduct, a full equivalence trial were planned, the equivalence margins could be determined from the results of the trial.

Based on the experience and throughput of the unit, approximately 45 patients were broadly eligible for recruitment over a 9 month period [Department data 9 month period 2008: n = 22 permanent SNS and n = 30 PTNS]. Therefore, allowing for refusal/specific exclusions, a total starting sample size of 40 was feasible for the 9 month recruitment period. The randomisation allowed for a 25% failure rate of temporary stimulation. Despite our previous experience of very high compliance for both treatments (near 100%) the study also allowed for an overall additional dropout rate off 10% for both interventions during treatment or follow-up. This yielded an estimated final figure of 15-16 patients for each group with complete data for analysis.

**2.8.2.5 Randomisation, allocation and blinding**

Eligible patients were allocated to receive either SNS or PTNS by restricted randomisation. Minimisation by sex and by symptom severity [2 groups: 1-6 and 6+ FIE per week] was used to balance the groups on these potential confounding factors. The figure of 6 FIE per week was chosen as an arbitrary figure locally agreed by the steering group that denoted severe FI if >6 episodes (i.e. daily episodes) were determined on initial questioning. A pre-determined allocation ratio allowed for a greater number of patients in the SNS group (n = 23 vs. 17 in PTNS group) to negate the established failure rate (approximately 25%) at the temporary SNS evaluation stage in order to have approximately equal numbers of patients having a full course of treatments. The randomisation sequence was generated remotely by a statistician uninvolved in recruitment and requests were made and actioned by email. A dedicated member of the study team (research nurse) recruited participants, collected all baseline and follow up data, and (the research nurse) remained blind to patients' allocation throughout the study. This allowed the direct clinical care of the patients to be undertaken by the research fellow, who remained unblinded to the intervention.

### **2.8.2.6 Outcome measures**

#### **Clinical outcomes**

The following assessments were undertaken 2-4 weeks pre-intervention, and at 3 and 6 months post-intervention completion (copies of these questionnaires can be found in Appendix i.):

- a) FIE per week: 2 week bowel diaries recorded number and type of incontinence episodes per week (and associated symptoms). These have formed the basis of the established <sup>166</sup> definition of 'success' in previous studies:  $\geq 50\%$  reduction in FIE per week <sup>197</sup>.
- b) validated and reliable patient-rated quantitative outcomes including symptom severity score (CCIS) <sup>191</sup>, validated disease-specific: American Society of Colon and Rectal Surgeons Faecal Incontinence Quality of Life (FIQL) <sup>82</sup> and generic: Social Function 36 (SF-36) <sup>198</sup> and EQ-5D <sup>199</sup> quality of life measures.
- c) novel patient centred outcome measure (PCOM) developed specifically for this study. This outcome measure consists of one specific question about the effectiveness of current treatment and a further five questions regarding the general effects of FI on patient wellbeing.

#### **Cost utility data**

Economic evaluation methods adhered, as far as possible, to the NICE Guide to the Methods of Technology Appraisal 2013 <sup>200</sup>. The costs of the SNS and PTNS

---

treatments included both the cost of the respective intervention and the cost of healthcare services and medication. A micro-costing of the intervention included a bottom-up construction of the costs associated with delivering SNS and PTNS in the NHS setting. These included SNS and PTNS equipment, consultations, physiology testing and investigations, counselling, pre-assessment for operation, SNS and PTNS procedures, post-operative medication, re-programming of the pulse generator and post-operative checks. Data on the use of healthcare services and medication by participants over the past three months was extracted from participants' questionnaires. These included: number of contacts with GP, nurse and consultants (including telephone consultations), outpatient attendances, inpatient stays and A&E admissions. Questions were also asked about the use of pre-specified medication for managing incontinence and gastrointestinal disorders. Individual-level resource use data were combined with unit costs to calculate the total cost of healthcare service use for each participant. Primary care unit costs were taken from the UK Unit Costs of Health and Social Care, PSSRU 2012 <sup>201</sup>. The unit costs for secondary care were based on the National Schedule of Reference Costs 2011-2012 <sup>202</sup>. The unit costs for medications were obtained from the British National Formulary <sup>203, 204</sup>.

### **2.8.2.7 Statistical analysis**

#### ***Sample size considerations***

A sample size of 40 was selected based on recruitment feasibility over a 12 month period (no sample size calculation was performed in keeping with pilot study). The randomisation schedule allowed for a 25% failure rate of temporary SNS stimulation and a drop-out rate of 10% from either intervention. Thus recruitment of 23 patients for SNS and 17 for PTNS would yield a final figure of 15-16 patients for each group potentially having complete data for analysis of effects of chronic stimulation.

#### ***Quantitative clinical outcome data***

Data were summarised to provide estimates of the variability of outcomes. We also estimated within group effects, and 95% confidence intervals, rather than between group effects as the two treatments were expected to be similar to each other. Statistical hypothesis testing was not carried out, following principles of pilot studies<sup>193</sup>, and no formal comparison of interventions was undertaken. All available cases were analysed in the groups to which they were randomised without imputation of missing data. A per protocol analysis was also performed for SNS patients considering only those patients receiving complete protocol of therapy i.e. progression to permanent implantation.

***Health economics analysis***

We considered that the economic analysis, like the other clinical outcomes in this pilot, was not designed to find a definitive answer. In keeping with the exploratory nature of the study, a cost utility analysis only was undertaken with no intention of directly comparing cost effectiveness. Instead estimates of costs could be used to inform a future trial design. In this pilot study, we collected all micro costings to aid calculation of an economic analysis on an "all-available-cases" basis. A sensitivity analysis was conducted to address uncertainties and to provide upper and lower limits of costs.

***2.8.3 QUALITATIVE INTERVIEW STUDY OF SACRAL AND PERCUTANEOUS TIBIAL NERVE STIMULATION IN PATIENTS WITH FAECAL INCONTINENCE******2.8.3.1 Consent***

Because of the sensitive and personal nature of the interviews, patients who wanted to participate were consented separately for the qualitative study.

***2.8.3.2 Sampling***

We aimed to reflect the diversity within the population with FI <sup>205</sup>. We used purposive (theoretical) <sup>206</sup> sampling with interest to include "outliers" conventionally

---



discounted in quantitative approaches<sup>207</sup>. The two equivalent groups were: those undergoing SNS and another undergoing PTNS. We examined the comparable groups following the principles of purposive homogeneous sampling<sup>208</sup>. For each treatment arm we found a small group of patients (5 in each group, total number of 10) who were willing to undertake interviews.

### **2.8.3.3 Interviews**

Semi-structured in-depth interviews were conducted as an exploration of the patient's personal experience of their treatment (SNS or PTNS). A topic guide using a set of pre-determined open-ended questions was developed and used to provide some structure to the interviews. With this framework, the interviews aimed to collect appropriate data whilst retaining the flexibility to allow patients to speak freely about their experiences. Each interview was approximately one hour long, was digitally recorded throughout and undertaken by a trained independent research assistant.

### **2.8.3.4 Data collection**

The goal of data collection was to engage in conversational dialogue until the experience was fully depicted; this process is described as listening fully in the moment<sup>182, 209</sup>. All interviews were undertaken over a period of 24 months. To

---

capture a wealth of experiences at different stages of each therapy, the patients were analysed as a case series with each interview conducted at an interval at least three months after the treatment had been completed.

#### **2.8.3.5 Pilot interview study and topic guide development**

The development of our topic guide was informed by existing literature and our patient advisors. The questions were non-directive, open-ended, and designed to encourage participants to express themselves without feeling constrained. The topic guide was developed by the CRF and the research assistant. Before interviews on patients were carried out, a single pilot interview was conducted using the topic guide on a volunteer from our patient advisory group with experience of SNS at the Royal London Hospital. The pilot interview was critically appraised for content by the CRF, research assistant and Senior Supervisor (Professor Taylor) to ensure the style and depth of the interview was appropriate. After refinement of the interview topic guide the interviews were conducted on the 10 recruited participants. The data from the pilot interview was not included in the analysis.

### 2.8.3.6 Data analysis

Through in depth analysis of the transcripts, the CRF examined the patent's experiences in a high level of detail collating the rich source of data (all annotated transcripts can be found in appendix ii [CD included]). The analysis using a thematic content analysis methodology was conducted iteratively <sup>182</sup>. This study was constructed from the outset to be partly phenomenological and heavily idiographic collecting the data from a relatively small number of subjects rather than surveying a large sample. Because the CRF identified closely with the stories being told by participants, immersion in the data was facilitated <sup>210</sup>. Thematic Content Analysis involved identifying themes and categories that 'emerged from the data'. This involved discovering themes in the interview transcripts and attempting to verify, confirm and qualify them by searching through the data and repeating the process to identify further themes and categories <sup>211</sup>. A process of open coding followed by grouping of categories was undertaken. Words and phrases used by participants were coded according to meaning and these concepts were then grouped into categories based on shared characteristics. Themes were identified by examining and grouping these categories. Once the themes and categories were identified, the data was again examined and further categories and themes searched for. From these categories emergent sub-ordinate and super-ordinate themes were identified and described <sup>182</sup>.

#### **2.8.3.7 Validation**

The interviews themselves were carried out by an independent fully trained researcher who was not involved in the clinical treatment of the participants. This ensured that the information given by the interviewee was completely voluntary and impartial. To validate the interview analysis, we used multiple coding for each theme and a process of inter-rater reliability<sup>206</sup>. Cross checking of coding strategies and interpretation of data was independently undertaken by both the CRF and RN in a random sample of three transcripts. Furthermore the RN analysis found them to be accurate reflections of the original digital recordings and confirmed the themes to be credible and faithful descriptions as interpreted from the transcripts. A meeting between the CRF, RN and Senior Supervisor Professor Taylor reviewed the three triangulated transcripts discussing themes and coding. Any significant disagreements between the CRF or RN's subjective coding was resolved by the Senior Supervisor's (Professor Taylor) decision. The rest of the transcripts were solely coded by the CRF and analysis reviewed by the Senior Supervisor.

# 3 RESULTS

## 3.1 A REVIEW OF CLINICAL EFFECTIVENESS OF NEUROMODULATION IN FAECAL INCONTINENCE

For SNS, 321 citations were identified on the basis of initial electronic search terms and eligibility criteria, of which 214 were selected for retrieval for detailed evaluation [Figure 3.01]. Ten articles did not have abstracts to view; their full texts were reviewed and the articles excluded for not meeting the inclusion criteria. After detailed evaluation of all remaining 204 abstracts, 132 more citations were excluded. The reasons for exclusion are shown in Figure 3.01. Seventy-two full text articles were assessed in detail and a further 11 studies were also excluded. The reasons for these exclusions were: one study used mixed urinary and faecal incontinence indications for implantation<sup>212</sup>, one study did not have original clinical outcome data<sup>213</sup>, 2 studies had PNE data only<sup>214, 215</sup>, 3 studies had no documented baseline of the chosen outcome measures<sup>216-218</sup>, 2 studies had no follow up terms documented<sup>219, 220</sup>, 1 study did not clearly document the results of the chosen outcome measures<sup>221</sup> and 1 study was excluded<sup>170</sup> as it exactly duplicated the data set of another included study<sup>169</sup>; further clarification was not possible. This left 61 SNS studies that were appropriate for inclusion [Table 3.01a and Table 3.01b]. In

---

order to present data on ITT analysis, we separated studies into (a) those including all consecutive patients (including failures) attempting PNE [Table 3.01a] from (b) those who only reported outcomes of positively responding patients to the test phase [Table 3.01b]. Patients who were still awaiting permanent implantation despite a successful PNE were excluded from the analysis. The initial electronic search for PTNS and TTNS revealed 22 relevant citations of which 11 remained when eligibility criteria were applied [Figure 3.02]. Of these, 7 studied PTNS and 4 TTNS.

### **3.1.1 SUMMARY OF STUDY CHARACTERISTICS [TABLE 3.01a, 3.01b AND 3.02]**

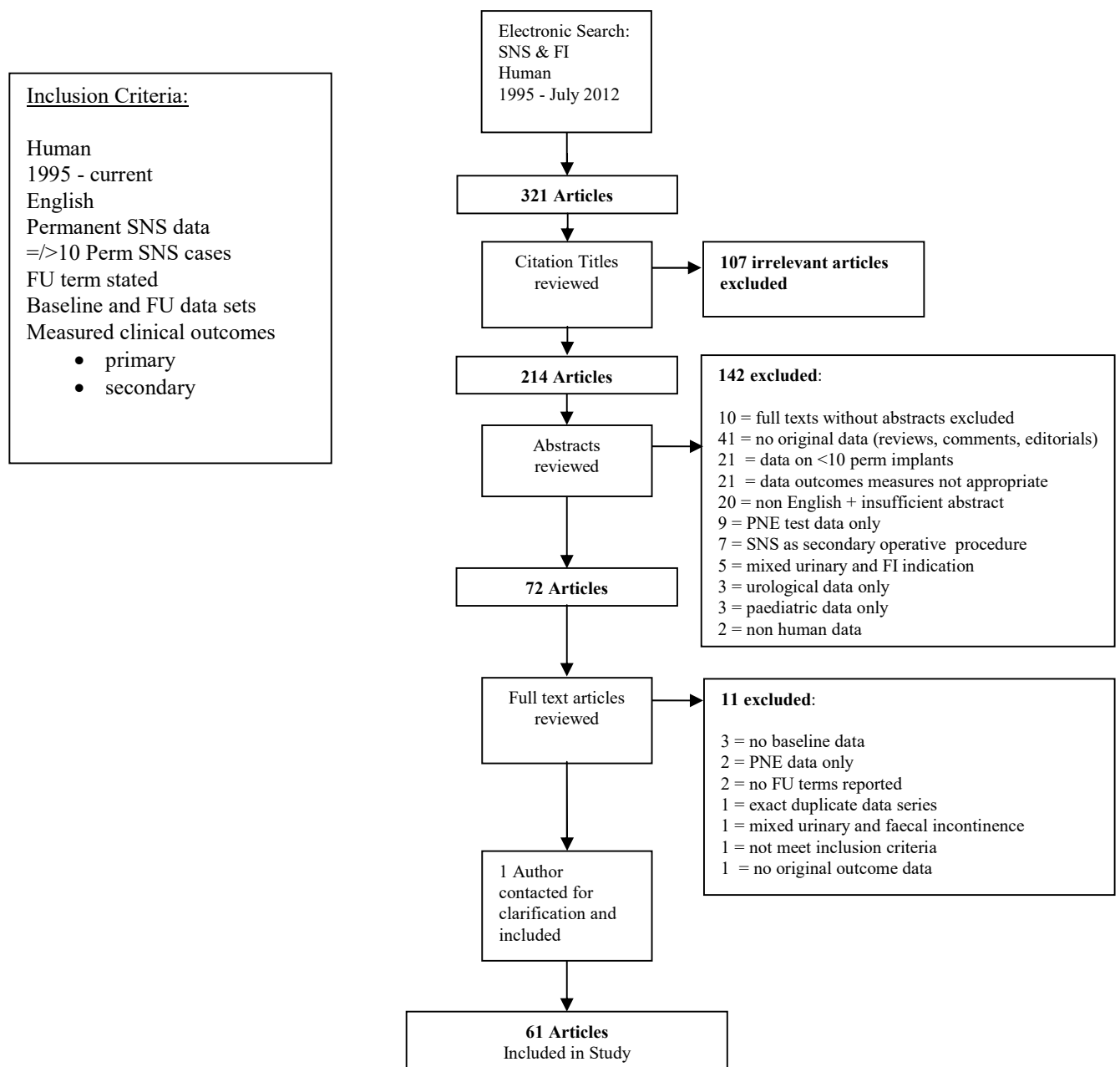
Of 61 SNS studies reviewed, the majority (50 studies) were prospective case series. Only two randomised controlled trials were eligible for inclusion<sup>168, 169</sup>. Each study was graded for its quality of evidence upon guidance set out by the Oxford Centre of Evidence-based Medicine<sup>222</sup>. The majority (N=55) of the studies were evaluated as only level 4 evidence [Table 3.01a and 3.01b]. The combined median follow up duration of all SNS studies was 24 months, with a median of 77% (40-100) implantation rate from PNE to permanent stimulators.

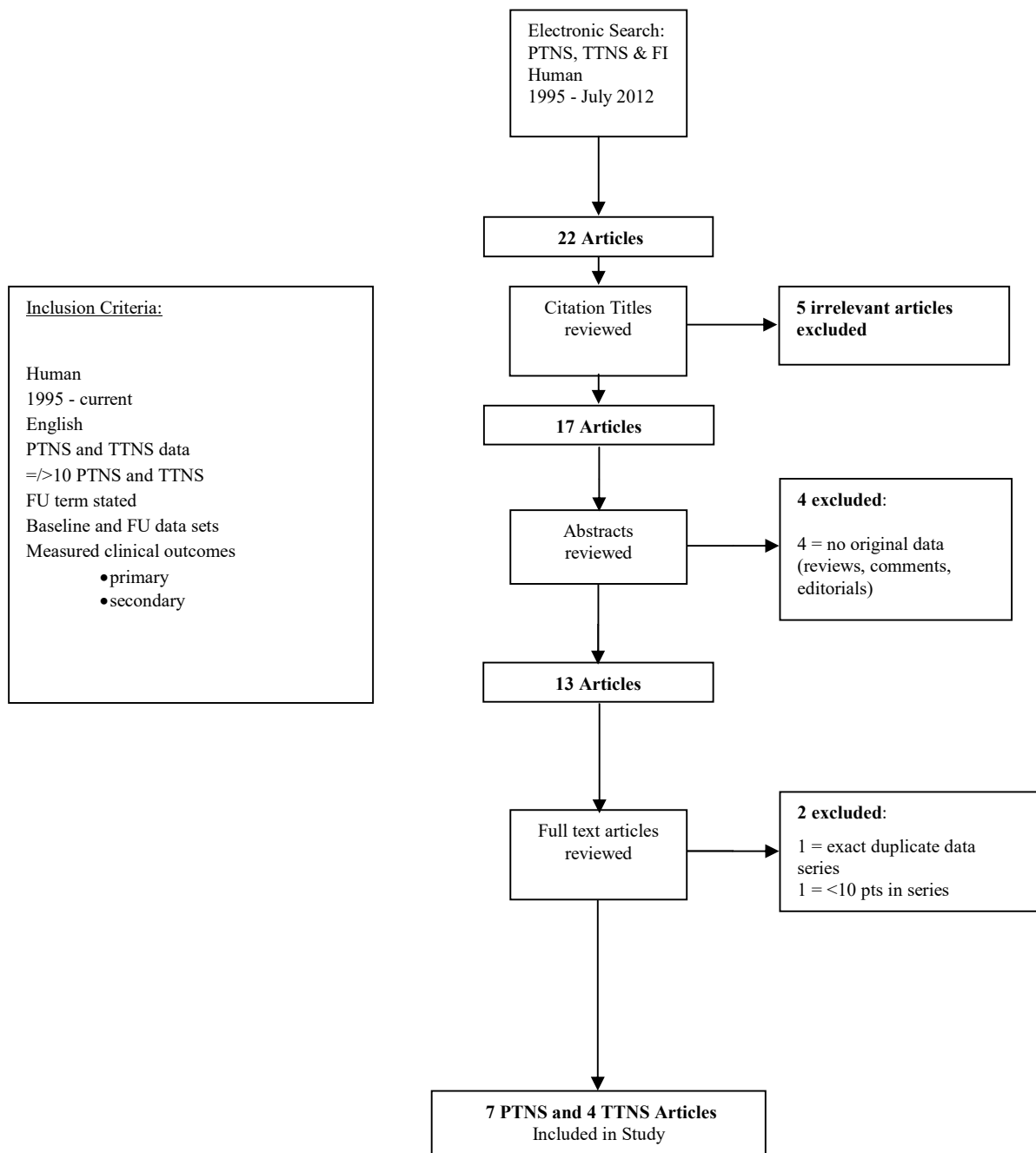
Of 7 PTNS case series, 6 were prospective and one retrospective [Table 3.02]. A total of 216 patients (181 female) were studied with a median duration of treatment of 3 months (range 1-11 months). Follow-up ranged from 0 to 29 months after

---

treatment. The 4 included TTNS studies<sup>180, 223-225</sup> were prospective case series with a total of 78 patients (median 18, range 10-32). Their treatment durations were 3 months in three studies and 6 months in one, with follow-up ranging from 0 to 15 months post treatment.

**Figure 3.01:** SNS PRISMA flow diagram



**Figure 3.02:** PTNS and TTNS PRISMA flow diagram



**Table 3.01a:** SNS study characteristic (all undertaking PNE)

Author	Year	Centre (No. Hosp)	Study type	LoE	Median Study FU (months)	PNE (n)	Perm SNS (n)	% of Perm implants
Rosen H <sup>226</sup>	2001	SC	PCS	4	15	20	16	80
Kenefick N <sup>227</sup>	2002	SC	PCS	4	24	15	15	100
Altomare D <sup>228</sup>	2004	SC	PCS	4	14	40	16	40
Jarrett M <sup>229</sup>	2004	MC (3)	PCS	4	12	59	46	78
Matzel KE <sup>230</sup>	2004	MC (8)	PCS	4	24*	37	34	92
Rasmussen O <sup>231</sup>	2004	SC	PCS	4	6	45	37	82
Uludag O <sup>232</sup>	2004	SC	PCS	4	12	63	50	79
Hetzer FH <sup>185</sup>	2005	SC	PCS	4	13	20	13	65
Jarrett M <sup>233</sup>	2005	SC	PCS	4	12	13	12	92
Faucheron J <sup>234</sup>	2006	SC	PCS	4	6†	40	29	73
Kenefick N <sup>235</sup>	2006	SC	PCS	4	24	19‡	19	100
Gourcerol G <sup>236</sup>	2007	SC	PCS	4	12	61	33	54
Hetzer FH <sup>237</sup>	2007	SC	PCS	4	13	44	37	84
Holzer B <sup>238</sup>	2007	SC	PCS	4	35	36§	28	77
Melenhorst J <sup>239</sup>	2007	SC	PCS	4	26*	134\\	100	75
Navarro J <sup>240</sup>	2007	SC	PCS	4	12†	26	24	92
Dudding T <sup>241</sup>	2008	SC	PCS	4	24	60	51	85
Melenhorst J <sup>242</sup>	2008	SC	CCS	2b	A: 29 B: 23	A: 20 B: 20	A: 16 B: 14	80 70
Munoz-Duyos A <sup>243</sup>	2008	SC	PCS	4	35	43	29	67
Stelzner S <sup>244</sup>	2008	SC	PCS	4	10	20	13	65
Tjandra J <sup>169</sup>	2008	SC	RCT	1b	12†	60	53	88
Altomare D <sup>245</sup>	2009	SC	PCS	4	74 *	94	60	64
Boyle DJ <sup>246</sup>	2009	SC	PCS	4	6†	15	13	87
Govaert B <sup>247</sup>	2009	ns	PCS	4	31*	208	145	70
Govaert B <sup>248</sup>	2009	SC	RCS	4	35 *	245	173	71
Vallet C <sup>249</sup>	2009	SC	PCS	4	37 *	45	32	71
Faucheron J <sup>250</sup>	2010	SC	PCS	4	45	123	87	71
Hollingshead J <sup>251</sup>	2010	SC	PCS	4	22	113	86	76
Koch SM <sup>252</sup>	2010	MC (16)	PCS	4	24 *	35	19	54
Michelsen HB <sup>253</sup>	2010	SC	PCS	4	24	167¶	126	75
Oom D <sup>254</sup>	2010	SC	PCS	4	32	46	37	80
Sharpe A <sup>255</sup>	2010	SC	PCS	4	50	54	44	79
Wexner SD <sup>256</sup>	2010	MC (6)	PCS	4	28*	133**	120	90
George AT <sup>257</sup>	2011	SC	PCS	4	44	30	23	77
Lim JT <sup>258</sup>	2011	SC	PCS	4	51*	80††	53	66
Leroi AM <sup>259</sup>	2011	MC (20)	PCS	4	24†	94	60	64
Maeda Y <sup>260</sup>	2011	SC	RCS	4	33	245	176	72
Pascual I <sup>261</sup>	2011	MC (4)	RCS	4	13	50§§	48	96
Wong MT <sup>262</sup>	2011	SC	RCS	4	31	91	61	67
Mellgren A <sup>263</sup>	2011	MC (16)	PCS	4	37	133\\	120	90
Duelund-Jakobsen J <sup>264</sup>	2011	MC (2)	RCS	4	46	ns (87)	158 (70)	n/a (80)
Boyle DJ <sup>265</sup>	2011	SC	PCS	4	17†	50	37	74
Wong MT <sup>266</sup>	2012	SC	PCS	4	22	28	16	57
Devroede G <sup>267</sup>	2012	MC (16)	PCS	4	39	133\\	120	90
George AT <sup>268</sup>	2012	SC	PCS	4	114	25	23	92
Santoro GA <sup>269</sup>	2012	SC	PCS	4	18	28	28	100

Key: LoE = Level of Evidence; RCT = randomized controlled study; DBC = double blind cross over study; CCS = case controlled study; PCS = prospective case series; RCS = retrospective case series; MC= multi centre; SC = single centre; \* = mean values (integer values); † = values taken at time point; ‡ = 15 patients included from previous study<sup>227</sup>; § = 15 patients included from previous study<sup>226</sup>; \\ = 63 patients included from previous study<sup>232</sup>; ¶ = 19 patients used tined PNE; \*\* = 112 patients used tined PNE; †† = 28 patients included from previous study<sup>169</sup>; §§ = all used tined lead for PNE; \\\ = 120 patients included from previous study<sup>256</sup>; ns = not stated; n/a = not able.

**Table 3.01b:** SNS study characteristic (permanent implants only)

Author	Year	Centre (No. Hosp)	Study type	LoE	Median Study FU (months)	PNE (n)	Perm SNS (n)
Ganio E <sup>270</sup>	2001	MC (ns)	PCS	4	16*	ns	16
Leroi AM <sup>168</sup>	2005	MC (ns)	RCT (DBC)	1b	6†	ns	34
Michelsen HB <sup>271</sup>	2006	SC	PCS	4	6†	ns	29
Uludag O <sup>272</sup>	2006	SC	PCS	4	1†	ns	14
Roman S <sup>273</sup>	2008	SC	PCS	4	3†	ns	18
Dudding T <sup>274</sup>	2009	SC	CCS	2b	A: 51 B: 8	ns	18 30
Matzel KE <sup>197</sup>	2009	SC	PCS	4	118*	ns	12
Brouwer R <sup>275</sup>	2010	SC	PCS	4	37	ns	55
Lombardi G <sup>276</sup>	2010	SC	RCS	4	38	ns	11
Otto S <sup>277</sup>	2010	SC	PCS	4	6†	ns	14
Ratto C <sup>278</sup>	2010	SC	CCS	2b	33	ns	10
Uludag O <sup>279</sup>	2010	SC	PCS	4	6†	ns	12
Gallas S <sup>280</sup>	2011	MC (9)	PCS	4	12	ns	200
Soria-Aledo V <sup>281</sup>	2011	SC	PCS	4	6†	ns	23
Uludag O <sup>282</sup>	2011	SC	PCS	4	85	ns	50

Key: LoE: Level of Evidence; RCT: randomized controlled study; DBC: double blind cross over study; CCS: case controlled study; PCS: prospective case series; RCS: retrospective case series; MC: multi centre; SC: single centre; \* = mean values (integer values); † = values taken at time point, ns = not stated.

**Table 3.02:** PTNS study characteristics

Author	Year	Centre (No. Hosp)	Study type	LoE	No. of initial weekly treatments (n)	No. of “top up” treatments (n)	Median FU from start of treatment (months)	No. of patients starting treatments (n)	No. of patients continuing therapy after initial phase (n)	% of patients continuing therapy (%)
Shafik <sup>172</sup>	2003	SC	NCT	3b	14	8	22*	32	25	78
De la Portilla <sup>177</sup>	2009	SC	PCS	4	12	8	6†	16	11	69
Govaert <sup>283</sup>	2009	SC	PCS	4	12‡	>72	12†	22	18	82
Boyle <sup>178</sup>	2010	SC	PCS	4	12	3	14	31	21	68
Findlay <sup>284</sup>	2010	SC	PCS	4	12	0	3†	13	12§	92§
Hotouras <sup>285</sup>	2011	SC	PCS	4	12	0	3	100	ns	n/a
Hotouras <sup>286</sup>	2012	SC	PCS	4	12	0	3†	88	ns	n/a

Key: LoE = Level of Evidence; NCT = non-randomised controlled trial, PCS = prospective case series; SC = single centre; \* = mean value; † = at specific time point; ‡ = twice weekly sessions over 6 weeks; § = completed initial course; ns = not stated; n/a = not available. All values are calculated to nearest integer.

### **3.1.2 PRIMARY OUTCOME**

The success rates for SNS based on a  $\geq 50\%$  improvement in FIE per week are shown in Table 3.03. On ITT, the median success rates were 63% (range 33-66%), 58% (range 52-81%) and 54% (range 50-58%) in the short, medium and long terms respectively. Only two long-term SNS studies, following up a total of 86 permanent implants, could be used to calculate ITT. The per-protocol median success rates were also 79% (range 69-83%), 80% (range 65-88%) and 84% (range 75-100%) in the short, medium and long terms. The success rates of PTNS are shown in Table 3.04. Only short-term follow-up data was reported. The 2 studies<sup>178, 283</sup> which reported this outcome, used different treatment protocols (6 weeks and 3 months) although the longest follow-up showed a 59% success rate at 12 months<sup>283</sup>. There were no reports of this outcome for TTNS.

### **3.1.3 SECONDARY CLINICAL OUTCOMES [TABLES 2.05, 2.06 AND 2.07]**

For SNS, the median rates of perfect continence through all follow-up durations are shown in Table 3.03. Five long-term studies reported perfect continence rates that could be analysed on ITT with median of 20% (2-48%). The rate of perfect continence following PTNS therapy was reported only with short-term follow-up in one study of 31 patients as 39% immediately following treatment [Table 3.04]. The composite scores for the CCIS and the number of FIE per week after SNS in the short, medium and long terms are shown in Tables 3.05 and 3.06 respectively. The equivalent short-

---

term results are shown for PTNS in Table 3.04. All PTNS studies reported a statistically significant improvement in aggregate CCIS scores post compared to pre-treatment. All four of the TTNS studies used the CCIS as an endpoint. Two studies did not perform statistical analysis of results due to small patient numbers<sup>180, 224</sup>. In the remaining two studies, one showed a significant improvement in the mean CCIS at 3 months and 6 months following treatment<sup>223</sup> and the other showed no statistically significant improvement at a mean follow-up of 15 months<sup>225</sup>.

### **3.1.4 QUALITY OF LIFE**

Although not used exclusively, the FIQL<sup>82</sup> and the SF-36<sup>198</sup> scores were the commonest QoL outcome measures reported throughout the SNS literature. Thirteen studies using FIQL<sup>168, 169, 226, 228-230, 233, 238, 243, 256, 259, 275, 287</sup> reported short-term results (median 12 months) with median score improvements for each category post SNS of: 1 (0-2) lifestyle, 1 (0-2) coping/behaviour, 1 (0-2) depression/self-perception, 1 (0-2) embarrassment. Statistically significant improvements in all categories were reached in 11 studies<sup>168, 169, 226, 228-230, 238, 243, 256, 275, 287</sup>. In the medium-term (median 36 months), 8 series<sup>230, 238, 243, 256, 259, 262, 263, 275</sup> reported a median score increase of: 2 (1-2) lifestyle, 1 (0-2) coping/behaviour, 1 (0-2) depression/self-perception, 1 (0-2) embarrassment. All medium-term reports presented a statistically significant FIQL score increases in all categories except for Leroi's non randomised study<sup>259</sup>, where the increase was not statistically significant for depression/self-perception. Four

---

studies had follow-up periods of more than 36 months; Matzel<sup>197</sup> reported on 4 patients at a follow-up of 84 months, Munoz-Duyos<sup>243</sup> documented FIQL scores in 5 patients at 60 months, Brouwer<sup>275</sup> reported on 13 patients followed up at 48 months and Uladag<sup>282</sup> 50 patients at a median of 85 months. All four studies showed an increase in FIQL scores post SNS with an aggregate median score change of 2 (1-2) points in lifestyle, 2 (1-2) points in coping/behaviour, 1 (0-2) point in depression/self-perception and 1 (1-2) point in embarrassment subcategories. Eleven studies measured generic changes in quality of life using the SF-36 score. Although there was variability in reports, there was a strong trend towards an overall improvement in the aggregate scores post SNS. Four studies reported long-term results with a median follow up of 61 (46-85) months, showing an increase in the overall SF-36 scores and improvements in all SF-36 domains<sup>245, 275, 276, 282</sup>. In particular, statistically significant improvements were reported in the mental health component scores which were not found in the physical component scores<sup>245, 276, 282</sup>.

Four studies, all short-term, included data on quality of life both before and after PTNS treatment<sup>177, 283-285</sup> and all used the disease-specific FIQL scale. In one study, the FIQL results were grouped by aetiology so no comparison was possible<sup>285</sup>. Govaert<sup>283</sup> showed statistically significant improvements in coping/behaviour and embarrassment immediately post-treatment, and in lifestyle and coping/behaviour at 1 month after treatment cessation and De la Portilla<sup>177</sup> showed significant improvements in the domains of coping/behaviour, depression/self-perception and

---

embarrassment at 6 months follow-up. The fourth study showed a statistically significant improvement in the mean score in the lifestyle domain only <sup>284</sup>. Three other QoL measures were also reported in three studies <sup>177, 283, 284</sup>. These include the SF-36, a Visual Analogue Scale for QoL and the ICIQ-B <sup>78</sup>. PTNS studies using these QoL scores showed significant improvements in most of their domains at their latest follow-up. Only Eléouet's study <sup>223</sup> reported QoL measures pre and post TTNS, with significant improvements found in all 4 categories of the FIQL scores at 3 months although this decreased to only 2 categories at 6 months.

**Table 3.03:** Effect of SNS on success and cure rates

Author	Median FU (months)	Perms at Base (N)	Perms at FU (N)	% Perm at FU	>50% imp in FI episodes per week (%)	100% cont (%)	ITT >50% imp in FI episodes per week (%)	ITT 100% cont (%)
Short Term Follow Up (up to and including 12 months)								
Jarrett M <sup>233</sup>	12	12	12	100	ns	42	ns	8
Leroi AM <sup>168</sup>	6*	34	19	56	ns	26	ns	n/a
Gourcerol G <sup>236</sup>	12	33	29	89	69	21	33	10
Tjandra J <sup>169</sup>	12*	53	53	100	71	47	63	42
Boyle D <sup>246</sup>	6*	13	13	100	77	46	66	40
Dudding T <sup>274</sup>	8	30	30	100	80	40	n/a	n/a
Hollingshead J <sup>251</sup>	12	86	86	100	81	Ns	62	ns
Wexner SD <sup>256</sup>	12*	120	106	88	83	41	66†	32
Santoro GA <sup>269</sup>	6*	28	28	100	ns	68	ns	68
Medium Term Follow Up (between 12 and 36 months)								
Kenefick N <sup>227</sup>	24	15	15	100	ns	73	ns	73
Matzel KE <sup>230</sup>	24	34	34	100	88	35	81	32
Kenefick N <sup>235</sup>	24	19	19	100	ns	74	ns	74
Melenhorst J <sup>239</sup>	26‡	100	100	100	79	Ns	59	Ns
Dudding T <sup>241</sup>	24	51	48	94	65	40	52	32
Munoz-Duyos A <sup>243</sup>	35	29	29	100	86	48	58	33
Govaert B <sup>247</sup>	31‡	145	145	100	80	Ns	56	ns
Govaert B <sup>248</sup>	35‡	173	169	98	77	Ns	53	ns
Koch SM <sup>252</sup>	24‡	19	19	100	ns	21	ns	11
Oom D <sup>254</sup>	32	37	37	100	81	5	65	4
Mellgren A <sup>263</sup>	36*	120	77	64	86	40	59†	26
Boyle DJ <sup>265</sup>	17	37	37	100	73	35	54†	26†
Long Term Follow Up (more than 36 months)								
Altomare D <sup>245</sup>	74‡	60	52	87	ns	18	ns	10
Dudding T <sup>274</sup>	51	18	18	100	94	39	n/a	n/a
Matzel KE <sup>197</sup>	118	12	9	75	78	44	58	33
Vallet C <sup>249</sup>	44‡	32	23	72	ns	4	ns	2
Hollingshead J <sup>251</sup>	60*	86	18	21	83	Ns	n/a	n/a
Lombardi G <sup>276</sup>	46‡	11	11	100	100	27	n/a	n/a
Duelund-Jakobsen J <sup>264</sup>	46	158	91	58	75	36	n/a	n/a
Uludag O <sup>282</sup>	85	50	50	100	84	Ns	n/a	n/a
Devroede G <sup>267</sup>	48*	120	77	64	87	34	50	20
George AT <sup>268</sup>	114	23	19	83	ns	52	ns	48
Summary (median and ranges)								
Short term	12 (6-12)		29 (12-106)	100 (56-100)	79 (69-83)	42 (21-68)	63 (33-66)	36 (8-42)
Medium term	25 (13-36)		37 (15-169)	100 (64-100)	80 (65-88)	40 (5-74)	58 (52-81)	32 (4-74)
Long term	56 (44-118)		21 (9-91)	79 (21-100)	84 (75-100)	35 (4-52)	54 (50-58)	20 (2-48)

Key: \* = values taken at time point; † = intention to treat reported; ‡ = mean values (integer values); ns = not stated; n/a = not able. All values are calculated to nearest integer.



**Table 3.04:** Effect of PTNS on clinical outcomes

Author	Follow up (months)	>50% imp in FI episodes per week (%)	100% cont (%)	CCIS (med) [baseline to follow up]	Score diff	Significance	Weekly FI episodes (med) [baseline to follow up]	Episode diff	Significance
Short Term Follow Up (up to and including 12 months)									
Shafik <sup>172</sup>	22*	ns	ns	a) 17 to 2*	-15	<0.001	ns	ns	ns
				b) 18 to 3*	-15	<0.05			
				c) 19 to 15*	-3	not sig			
De la Portilla <sup>177</sup>	3	ns	ns	13 to 9*	-4	<0.0005	ns	ns	ns
	8			13 to 8*	-5	0.001			
	14			13 to 9*	-4	0.001			
Govaert <sup>283</sup>	6 weeks	63	ns	12 to 8*	-3	<0.001	7 to 3	-4	p=0.082
	12	59		12 to 6*	-5	0.001	7 to 1	-6	p=0.029
Boyle <sup>178</sup>	5	71	39%	13 to 7	-6	<0.0001	4 to 0	-4	p<0.0001
Findlay <sup>284</sup>	4	ns	ns	Ns	Ns	ns	L: 3 to 0	-3	not sig
							S: 5 to 0	-5	not sig
Hotouras <sup>285</sup>	3	ns	ns	U= 11 to 8*	-3	0.0188	4 to 0	-4	0.047
				P= 12 to 9*	-3	0.3293	4 to 3	-1	0.2839
				M=13 to 9*	-4	<0.0001	5 to 1	-4	<0.0001
Hotouras <sup>286</sup>	3	ns	ns	12 to 9*	-4	<0.0001	4 to 1	-3	<0.0001
Summary (median and ranges)									
Short term	5 (3-22)	59-71%	39%	13 to 9	-4 (-4 to -15)		5 to 1	-4 (-3 to -6)	

Key: \* = mean value; ns = not stated; a) = good response group; b) = fair response group; c) = poor response group; L= liquid incontinence; S= solid incontinence; not sig = reported as no statistically significant difference. All values are calculated to nearest integer.

**Table 3.05:** Effect of SNS on Cleveland Clinic Incontinence Score

Author	Med FU month	Base Perm (n)	FU Perms (n)	% Perm FU	Baseline score (median)	FU score (median)	Score Diff	Stat Sig (P value)
Short Term Follow Up (up to and including 12 months)								
Jarrett M <sup>229</sup>	12	27	27	100	14 (5-20)	6 (1-12)	-8	<0.001
Rasmussen O <sup>231</sup>	6	37	37	100	16 (9-20)	6 (0-20)	-10	<0.0001
Hetzer FH <sup>185</sup>	1*	13	13	100	14 (6-20)	4 (0-12)	-10	<0.001
Leroi AM <sup>168</sup>	1*	28	28	100	16 (8-20)	9 (0-19)	-7	0.0002
Michelsen HB <sup>271</sup>	6*	29	29	100	16 (6-20)	4 (0-12)	-12	<0.0001
Hetzer FH <sup>237</sup>	6*	37	30	81	14 (6-20)	5 (0-13)	-9	<0.001
Navarro J <sup>240</sup>	12*	24	24	100	15 (+/- 1.81) <sup>†</sup>	5 (+/- 2.54) <sup>†</sup>	-10	=0.0018
Tjandra J <sup>169</sup>	12*	53	53	100	16 (+/- 1.3) <sup>†</sup>	1 (+/- 1.8) <sup>†</sup>	-15	<0.0001
Boyle D <sup>246</sup>	6*	13	11	85	12 (9-18)	9 (4-14)	-3	0.0005
Brouwer R <sup>275</sup>	12*	55	48	87	15 (13-18)	6 (4-8)	-9	=0.001
Gallas S <sup>280</sup>	12*	200	130	65	14 (2-20)	7 (0-19)	-7	=0.0011
Otto S <sup>277</sup>	6*	14	14	100	16 (+/- 3.1) <sup>†</sup>	10 (+/- 5.9) <sup>†</sup>	-6	=0.002
Medium Term Follow Up (between 12 and 36 months)								
Brouwer R <sup>275</sup>	36*	55	31	56	15 (13-18)	7 (5-8)	-8	=0.001
Hollingshead J <sup>251</sup>	33	86	86	100	15 (+/- 3) <sup>†</sup>	9 (+/- 5) <sup>†</sup>	-6	<0.001
Michelsen HB <sup>253</sup>	24	126	126	100	16 (6-20)	10 (0-20)	-6	<0.0001
Ratto C <sup>278</sup>	33	10	10	100	18 (+/- 2.0) <sup>†</sup>	10 (+/- 3.7) <sup>†</sup>	-8	=0.0001
Pascual <sup>261</sup>	13	48	48	100	18 (ns)	4 (ns)	-14	<0.01
Boyle DJ <sup>265</sup>	17	37	33	89	15 (3-20)	8 (0-17)	-7	<0.0001
Gallas S <sup>280</sup>	24*	200	54	27	14 (2-20)	7 (0-19)	-7	=0.0011
Wong MT <sup>262</sup>	31	61	61	100	14 (ns)	8 (ns)	-6	ns
Wong MT <sup>266</sup>	22	16	16	100	15 (11-18)	12 (0-14)	-3	=0.0001
Santoro GA <sup>269</sup>	18*	28	16	57	16 (12-20)	3 (1-8)	-13	=0.0017
Long Term Follow Up (more than 36 months)								
Altomare D <sup>245</sup>	74 <sup>†</sup>	60	52	87	15 (+/- 4) <sup>†</sup>	5 (+/- 5) <sup>†</sup>	-10	<0.001
Matzel KE <sup>197</sup>	118	12	9	75	17 (12-19)	10 (3-14)	-7	<0.007
Vallet C <sup>249</sup>	37 <sup>†</sup>	32	23	72	16 (+/- 3) <sup>†</sup>	10 (+/- 4.7) <sup>†</sup>	-6	ns
Brouwer R <sup>275</sup>	48*	55	13	24	15 (13-180)	6 (2-8)	-9	=0.008
Faucheron J <sup>250</sup>	45	87	87	100	13 (6-19) <sup>†</sup>	8 (1-17) <sup>†</sup>	-5	ns
Lombardi G <sup>276</sup>	46	11	11	100	13 (11-18) <sup>†</sup>	5 (3-9) <sup>†</sup>	-9	<0.018
Michelsen HB <sup>253</sup>	72*	126	10	9	20 (12-20)	7 (2-11)	-13	<0.0001
Sharpe A <sup>255</sup>	50	44	37	73	16 (9-20)	4 (0-10)	-12	ns
Lim JT <sup>258</sup>	51 <sup>†</sup>	53	41	77	12 (9-15)	8 (5-11)	-4	0.001
Summary (median and ranges)								
Short term	6 (1-12)		29 (11-130)	100 (65-100)	15 (12-16)	6 (1-10)	-9 (-3 to -15)	
Medium term	24 (13-36)		41 (10-126)	100 (27-100)	15 (14-18)	8 (3-12)	-7 (-3 to -14)	
Long term	50 (37-118)		23 (9-87)	75 (9-100)	15 (12-20)	7 (5-10)	-8 (-4 to -13)	

Key: \* = values taken at time point; <sup>†</sup> = mean values (integer values); ns = not stated. All values are calculated to nearest integer.

**Table 3.06:** Effect of SNS on faecal incontinence episodes per week

Author	FU month	Base Perm N	FU N	% Perm at FU	Baseline: median Episodes	FU: median episodes	Episode Change	Stat Sig (P value)
Short Term Follow Up (up to and including 12 months)								
Altomare D <sup>228</sup>	12*	14	8	57	7 (n/a)	1 (n/a)	-6	<0.01
Jarrett M <sup>229</sup>	12	46	46	100	8 (1-78)	1 (0-39)	-7	<0.001
Matzel KE <sup>230</sup>	12*	37	30	81	16 (+/- 19.3)†	3 (+/- 5.5)†	-13	<0.0001
Uludag O <sup>232</sup>	12*	50	27	54	8 (ns)	1 (ns)	-7	<0.001
Jarrett M <sup>233</sup>	12	13	12	92	9 (+/- 7.64)†	2 (+/- 3.69)†	-7	=0.012
Leroi AM <sup>168</sup>	1*	28	28	100	7 (0-17)	1 (0-10)	-6	<0.05
Kenefick N <sup>235</sup>	12*	19	12	63	12 (ns)	2 (ns)	-10	<0.01
Uludag O <sup>272</sup>	1*	14	14	100	9 (ns)	0 (ns)	-9	<0.01
Gourcerol G <sup>236</sup>	12*	33	15	45	5 (ns)†	1 (ns)†	-4	<0.05
Hetzer FH <sup>237</sup>	6*	37	30	81	8 (ns)	2 (ns)	-6	0.07
Melenhorst J <sup>239</sup>	12*	100	76	76	10 (n/a)†	2 (n/a)†	-8	<0.0001
Munoz-Duyos A <sup>243</sup>	12*	29	25	86	1 (0-16)	0 (ns)	-1	<0.001
Stelzner S <sup>244</sup>	10	13	11	85	10	5	-5	0.045
Tjandra J <sup>169</sup>	12*	53	53	100	10 (+/- 12.8)†	3 (+/- 10.1)†	-7	<0.0001
Boyle D <sup>246</sup>	6*	13	13	100	8 (n/a)	2 (n/a)	-6	=0.01
Dudding T <sup>274</sup>	8	30	30	100	3 (0-28.5)	0 (0-25)	-3	<0.001
Michelsen HB <sup>253</sup>	12*	126	49	39	8 (n/a)	1 (n/a)	-7	<0.0001
Uludag O <sup>279</sup>	6*	12	12	100	6 (ns)	1 (ns)	-5	=0.001
Wexner SD <sup>256</sup>	12*	120	106	88	9 (+/- 7.3)†	2 (+/- 3.8)†	-7	<0.0001
Soria-Aledo V <sup>281</sup>	6*	23	23	100	3 (+/- 1.1)†	1 (+/- 0.6)†	-2	<0.001
Medium Term Follow Up (between 12 and 36 months)								
Ganio E <sup>270</sup>	16	16	16	100	6 (n/a)†	0 (n/a)†	-6	ns
Rosen H <sup>226</sup>	15	16	16	100	2 (n/a)	1 (n/a)	-1	ns
Kenefick N <sup>227</sup>	24	15	15	100	11 (2-30)	0 (0-7)	-11	<0.001
Altomare D <sup>228</sup>	24*	14	5	36	7 (n/a)	1(n/a)	-6	<0.01
Matzel KE <sup>230</sup>	24*	37	21	57	16 (+/- 19.3)†	2 (+/- 3.3)†	-14	<0.0001
Uludag O <sup>232</sup>	24*	50	6	18	8 (ns)	1 (ns)	-7	not sig
Kenefick N <sup>235</sup>	36*	19	5	26	12 (ns)	0 (ns)	-12	<0.05
Gourcerol G <sup>236</sup>	36*	33	5	15	5 (ns)†	1 (ns)†	-5	<0.05
Holzer B <sup>238</sup>	35	29	29	100	2 (n/a)	1(n/a)	-1	0.002
Melenhorst J <sup>239</sup>	36*	100	33	33	10 (n/a)	2 (n/a)	-8	<0.0001
Dudding T <sup>241</sup>	24	51	48	94	6 (0-81)	1 (0-59)	-5	ns
Melenhorst J <sup>242</sup>	24*	A: 20 B: 20	A: 10 B: 8	50 40	A: 9 (n/a)† B: 8 (n/a)†	A: 4 n/a)† B: 1 (n/a)†	-5 -7	=0.001 =0.008
Munoz-Duyos A <sup>243</sup>	36*	29	13	45	1 (0-16)	0 (ns)	-1	0.002
Hollingshead J <sup>251</sup>	33	86	86	100	9 (+/-7.3)	1 (+/-2.4)	-8	<0.001
Koch SM <sup>252</sup>	24^	35	35	100	11 (+/- 11.7)†	2 (+/- 2.6)†	-7	<0.0001
Oom D <sup>254</sup>	32	37	37	100	9 (3-35)	0 (0-15)	-9	ns
Ratto C <sup>278</sup>	33	10	10	100	26 (ns)†	1 (ns)†	-25	=0.0001
Mellgren A <sup>263</sup>	36*	120	77	64	9 (ns)†	2 (ns)†	-7	<0.0001
Boyle DJ <sup>265</sup>	17	37	33	89	7 (n/a)	1 (n/a)	-6	<0.0001
Santoro GA <sup>269</sup>	18*	28	16	57	14 (+/- 8)†	0 (+/- 0.8)†	-14	<0.001
Long Term Follow Up (more than 36 months)								
Kenefick N <sup>235</sup>	48*	19	4	21	12 (ns)	0 (ns)	-12	not sig
	60*	19	2	11	12 (ns)	0 (ns)	-12	not sig
Melenhorst J <sup>239</sup>	48*	100	15	15	10 (n/a)†	2 (n/a)†	-8	<0.0001
	60*	100	6	6	10 (n/a)†	2 (n/a)†	-8	<0.0001

Author	FU month	Base Perm N	FU N	% Perm at FU	Baseline: median Episodes	FU: median episodes	Episode Change	Stat Sig (P value)
Munoz-Duyos A <sup>243</sup>	48*	29	6	21	1 (0-16)	0 (ns)	-1	not sig
	60*	29	5	17	1 (0-16)	0 (ns)	-1	0.040
Altomare D <sup>245</sup>	74^	60	52	87	4 (n/a)†	1 (n/a)†	-3	=0.004
Dudding T <sup>274</sup>	51	18	18	100	6 (0-80)	0 (0-8.5)	-6	<0.001
Matzel KE <sup>197</sup>	118	12	9	75	9 (2-58)	0 (0-29)	-9	<0.001
Lombardi G <sup>276</sup>	46	11	11	100	5 (3-8.5)	1 (0-2.5)	-4	<0.018
Duelund-Jakobsen J <sup>264</sup>	46	147	147	100	6 (n/a)	1(n/a)	-5	<0.0001
George AT <sup>257</sup>	44	23	23	100	5 (n/a)	0 (n/a)	-5	<0.001
Uludag O <sup>282</sup>	60	50	Ns	Ns	8 (n/a)	0 (n/a)	-8	<0.002
Devroede G <sup>267</sup>	48	120	77	64	9 (n/a)	2 (n/a)	-7	<0.001
George AT <sup>268</sup>	114	23	19	83	11 (2-35)	0 (0-2)	-11	0.001
Summary (median and ranges)								
Short term	12 (1-12)		27 (12-106)	88 (39-100)	8 (1-16)	1 (0-5)	-7 (-1 to -13)	
Medium term	24 (15-36)		16 (5-86)	64 (15-100)	8 (1-12)	1 (0-4)	-7 (-1 to -25)	
Long term	51 (44-118)		13 (2-147)	70 (6-100)	8 (1-12)	1 (0-2)	-7 (-1 to -12)	

Key: \* = values taken at time point; † = mean values (integer values); ns = not stated; n/a = not able; not sig = reported as no statistically significant difference. All values are calculated to nearest integer

### **3.2     *RANDOMISED PILOT TRIAL OF SACRAL AND PERCUTANEOUS TIBIAL NERVE STIMULATION IN PATIENTS WITH FAECAL INCONTINENCE***

#### **3.2.1   *PATIENT RECRUITMENT AND BASELINE CHARACTERISTICS***

Of 91 consecutive patients screened, 58 met the eligibility criteria and 40 patients (39 female, mean age 59 years) agreed to participate. As pre-determined, 23 patients were randomised to SNS and 17 to PTNS. Baseline demographic, medical and physiological findings were similar in both groups [Table 3.07]. Eighteen patients that were eligible but did not participate in the trial, the reasons for not doing so and consequent management are presented in Table 3.08. Before any intervention had been carried out, 4 patients dropped out from the SNS group. Two patients chose not to undergo surgery after being randomised to SNS (one patient did not wish to be contacted further by our services and another elected to maintain her conservative management only); one patient declined further treatment because her symptoms had resolved and another had inter-current disease requiring urgent medical management. From the PTNS group one patient chose not to undergo the procedure because of spontaneous improvements in her symptoms. Thus 19 patients underwent temporary SNS procedure. Of these, a further four patients did not progress to permanent implantation; three did not meet required success criteria to progress and one withdrew from therapy due to need for investigation (MRI) and surgical treatment of a para-rectal cyst]. These patients were referred back to the specialist nursing services for further conservative management but follow up data at 3 months and 6 months were collected to enable available case analysis [based on n = 19]. This left 15 patients undergoing definitive (permanent) SNS implantation. 16 PTNS patients underwent a full course of 15 PTNS therapies. See flowchart [Figure 3.03].

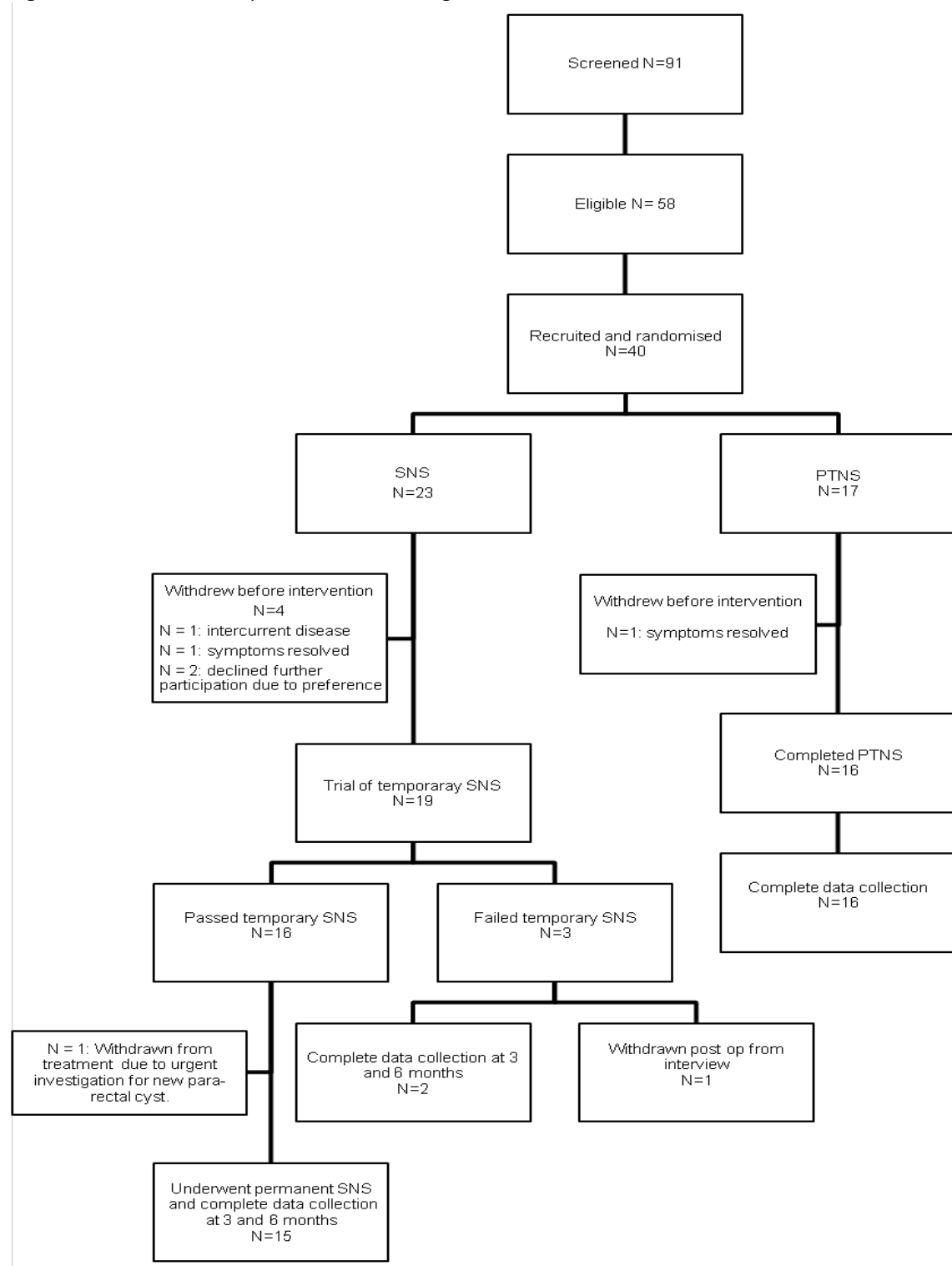
**Table 3.07:** Numbers and percentages or means and standard deviations of baseline characteristics by treatment type

	PTNS (N=17)	SNS all (N=23)
<b>Demographic</b>		
Barts Health NHS Trust	15	20
University College Hospital London	2	3
Female	17 (100%)	22 (96%)
Age (years)	59 (SD 11.1)	59 (SD 13.2)
<b>History</b>		
Post-partum aetiology	10 (59%)	10 (45%)
Traumatic deliveries	7 (41%)	8 (34%)
Hysterectomy	7 (41%)	12 (55%)
<b>Previous / on-going treatments</b>		
Previous anal sphincter repair	0 (0%)	2 (9%)
Nurse led conservative management	12 (71%)	17 (74%)
Biofeedback	4 (24%)	11 (48%)
Incontinence pad usage	9 (53%)	23 (100%)
Anal plug	0 (0%)	1 (4%)
Anti-diarrhoeal medications	8 (47%)	17 (74%)
Suppository use	2 (12%)	7 (30%)
Enema use	1 (9%)	1 (4%)
Irrigation	2 (12%)	2 (9%)
<b>Main Symptoms</b>		
Severity $\leq$ 6 FI episodes/week	12 (71%)	16 (70%)
Severity $>$ 6 FI episodes /week	5 (29%)	7 (30%)
Urge Incontinence	14 (82%)	21 (91%)
Passive Incontinence	15 (88%)	20 (87%)
Flatus Incontinence	16 (94%)	20 (87%)
Unable to defer defaecation	13 (76%)	20 (87%)
Soiling	16 (94%)	21 (91%)
Evacuatory difficulties	11 (65%)	10 (43%)
<b>Baseline Physiology</b>		
Anal canal length (cm)	2.3 (SD 1.5)	2.0 (SD 1.2)
Max rest pressure (mmH20)	43.6 (SD 27.7)	54.9 (SD 43.0)
Max squeeze pressure	36.1 (SD 19.5)	44.0 (SD 47.8)
FCS	41.6 (SD 23.9)	57.5 (SD 37.5)
DDV	77.5 (SD 35.1)	119.0 (SD 73.3)
MTV	120(SD 45.7)	163 (SD 80.8)
L PTML	2.8 (SD 0.5)	2.6 (SD 0.3)
R PTML	2.7 (SD 0.6)	2.7 (SD 0.5)
Anal Sphincter def	21.8% (SD 11.2)	23.2% (SD 6.0)

Key: SD = standard deviation

**Table 3.08:** Outcomes of eighteen eligible non-participants

<b>Candidate</b>	<b>Reason for non participation</b>	<b>Further management</b>
1	FI symptoms manageable	Discharge back to GP
2	Actively losing weight and operation not appropriate	Referral to specialist nurse for further conservative management
3	Happy with conservative management	Referral to specialist nurse for further conservative management
4	Symptoms improved	Discharged back to GP
5	Back pain and due MRI (contraindication SNS)	Referral to specialist nurse for further conservative management
6	Happy with conservative management	Referral to specialist nurse for further conservative management
7	Did not want operation	Referral to specialist nurse for further conservative management
8	Happy with conservative management	Referral to specialist nurse for further conservative management
9	Pacemaker in situ	Referral to specialist nurse for further conservative management
10	Symptoms improved	Discharged back to GP
11	Symptomatic diverticular disease	Awaiting colectomy
12	Only wanted PTNS	Referred to specialist nurse for PTNS
13	Difficulty with transportation to hospital	Discharged back to GP for local treatment
14	Symptoms improved	Discharged back to GP
15	Learning difficulties and dyslexia	Referral to specialist nurse for further conservative management
16	Only wanted PTNS	Referred to specialist nurse for PTNS
17	Only wanted PTNS	Referred to specialist nurse for PTNS
18	Having In Vitro Fertilisation	Referral to specialist nurse for further conservative management

**Figure 3.03:** Pilot RCT trial patient CONSORT diagram



### **3.2.2 CLINICAL OUTCOME DATA**

Within group effect estimates for SNS were greater than PTNS especially in those patients progressing to permanent implantation [Tables 3.08 and 3.09]. On available case analysis, in the SNS group, FIE per week improved from a median (interquartile range (IQR)) of 5.75 (5.75-15.5) [mean (SD) of 11.4 (12.0)] at baseline to 2.5 (2-4.5) [4.0 (4.0)] and 1.75 (1.5-5) [4.9 (6.9)] at 3 months and 6 month follow up, respectively vs. the PTNS group who had improvements from median (IQR) 6.5 (2.5-16.5) [means 10.6 (SD: 11.2)] to 3.5 (0.75 -7.25) [5.8 (6.9)] and 2.75 (0.75 to 10.75) [6.3 (6.9)], respectively [Figure 3.04a]. Using the CCIS as a global incontinence measure, improvements were evident in the SNS group from median (IQR): 16.5 (14-19) [mean (SD) 16.2 (3.0)] points (baseline) to 13 (8-16) [11.1 (5.2)] and 12 (6-16) [10.4 (5.6)] vs. in PTNS group, 14 (13-17) [15.1 (2.7)] to 12.5 (7.5-15) [11.7 (4.4)] and 12 (9-16.5) [12.1 (5.2)] at 3 months and 6 months respectively [Figure 3.04b]. Using the 50% reduction in FIE as a measure of clinical response, in all available cases, this was achieved in 47% and 61% at 3 months and 6 months in the SNS group compared with 40% and 47% at 3 and 6 months in the PTNS group. We note that there were only 15 patients available for analysis in the PTNS group because during their 2 week baseline assessment, one of the participants in the PTNS group was found not have any FIE (although enrolled on their reported severe FI symptoms) and therefore was excluded from this analysis. More marked differences in categorical differences were observed for the 75% improvement

---

quartile [Figure 3.04c]. Three patients in both groups had no episodes of incontinence during the 2 week bowel diary period at 6 months follow up. Analysis of the implanted SNS group demonstrated a greater effect of treatment than was observed with inclusion of all available cases. This pattern was upheld for most of the main measures and led to a 50% reduction in FI episodes in 53% and 67% patients at 3 and 6 months respectively [Figure 4.02].

The two parts of the PCOM were analysed separately and therefore results presented for questions 1 and questions 2-6 respectively. In keeping with other clinical outcomes, the specifically developed patient satisfaction Likert scale for FI treatment (question 1 of PCOM) demonstrated median (IQR) [mean (SD)] score improvements in both neuromodulation therapy groups: 1 (1-3) [1.7 (1.5)] to 4.5 (3-8) [5.3 (3.0)] and 6 (4-8) [5.8 (2.9)] for SNS vs. 2.5 (2-4) [3.2 (2.3)] to 5.5 (3-8) [5.2 (3.0)] and 5 (3-7) [4.8 (2.9)] for PTNS patients at baseline, 3 months and 6 months respectively. The within group effects were notably larger for SNS and proved even greater when analysed with permanent SNS responders only: 1 (1-3) [1.4 (1.5)] at baseline improving to 7 (4-8) [6.7 (2.2)] and 7 (5-8) [7.2 (1.5)] at 3 and 6 months. Total aggregate median (IQR) [means (SD)] scores for PCOM questions 2-6 also followed this pattern and demonstrated improvement in all groups: 6 (3-15) [8.7 (7.5)] to 23 (13-40) [26.5 (14.9)] and 30 (20-42) [28.7 (14.3)] for SNS on all available cases analysis vs. 13 (9-22) [16.1 (11.6)] to 28.5 (13-38.5) [25.9 (14.9)] and 23.5 (12.5-36) [24.2 (14.5)] for PTNS at baseline, 3 months and 6 months respectively.

---

In both groups, the FIQL measure showed improvements from baseline in all four domains (lifestyle, coping/behaviour, depression/self-perception and embarrassment), at both follow up points. In the SNS group, the change in aggregated means (SD) was from 7.2 (2.3) at baseline to 10.1 (2.9) at both 3 months and 6 months. The PTNS group also demonstrated an improvement in FIQL scores from 8.5 (2.9) at baseline to 10.2 (3.1) and 9.4 (3.1) respectively. Effect estimates in the SNS group were larger across all domains than PTNS [Table 3.09]. SF-36 and EQ-5D scores (global health scores) showed little improvement after treatment [Table 4.04]. Changes in scores for EQ-5D (calculated using computer algorithm and expressed using descriptive system as a weighted index<sup>199</sup> from -0.594 to 1.0 where 0 represents death and 1.0 = perfect health) varied between 0.0 and 0.11 with no in group significant changes). On reviewing the SF-36 scale subscales (each scale ranges from 0-100% where 100 = perfect health), increases in physical role were observed for SNS, particularly after permanent implantation; modest increases were also observed in emotional role and social functioning for both interventions.

### **3.2.3 HEALTH ECONOMIC DATA**

The direct intervention cost of PTNS was £2,260 compared to the cost of SNS of £13,922 per patient (£1,613 for temporary SNS plus £12,309 for permanent SNS). The breakdown of intervention costs is shown in Table 3.10. Sensitivity analyses

---

were conducted to address uncertainty around major assumptions used for costing the intervention. Using minimum and maximum parameters estimates for uncertain variables (e.g. number of patients sharing PTNS stimulator; the proportion of patients failing permanent SNS; number of patients re-using temporary SNS device; number of re-programming sessions for SNS), the total cost of the intervention per person varied from £2,218 to £2,297 for PTNS and from £12,139 to £14,238 for SNS. The use of health care resources by participants was also analyzed. The total cost of treatment (including the cost of the intervention and resource use by participants) estimated on an intention-to-treat basis were £2,356 (SD £122) per person for PTNS and £12,748 (SD £4,175) per person for SNS (four participants failed temporary SNS). The health outcome of treatment estimated in quality adjusted life years (QALYs) was 0.299 (0.170) for PTNS and 0.343 (SD 0.102) for SNS. No treatment-related adverse events were found in the trial and therefore no such costs could be assigned.

**Table 3.09:** Numbers of patients analysed and medians and interquartile ranges (means and standard deviations) of pre- and post-treatment clinical outcome data

Intervention		PTNS			SNS (all)			SNS (permanent implant)		
Visit		Base-line	3 months	6 months	Base-line	3 months	6 months	Base-line	3 months	6 months
<b>N</b>		16	16	16	22	19	18	15	15	15
<b>Total FI episodes p/w</b>	med	6.5	3.5	2.75	5.75	2.5	1.75	5	2	1.5
	(IQR)	(2.5-16.5)	(0.75-7.25)	(0.75-10.75)	(5.75-15.5)	(2-4.5)	(1-5.5)	(2.5-19)	(1.5-3)	(0.5-5.5)
	mean (SD)	10.6 (11.2)	5.8 (6.9)	6.3 (6.9)	11.4 (12.0)	4.0 (4.0)	4.9 (6.9)	12.1 (13.7)	2.8 (2.5)	3.1 (4.0)
<b>Urge FI episodes p/w</b>	med	1.5	1.5	1	2	0.5	0.75	2.5	0.5	0.5
	(IQR)	(0.25-4.25)	(0.25-4)	(0.25-4.25)	(0-6.5)	(0-2)	(0-1.5)	(0-7)	(0-2)	(0-1.5)
	mean (SD)	3.2 (5.0)	2.3 (3.0)	2.3 (2.7)	4.0 (4.7)	0.8 (1.0)	1.5 (3.1)	4.5 (5.3)	0.9 (1.0)	0.8 (1.0)
<b>Passive FI episodes p/w</b>	med	4.25	1.75	2	3.25	2	1	2.5	2	1
	(IQR)	(1-10)	(0.25-4)	(0-6.5)	(1.5-11)	(0.5-4.5)	(0-4)	(1-11)	(0-2)	(0-3.5)
	mean (SD)	7.4 (8.8)	3.5 (4.4)	3.9 (4.6)	7.4 (9.6)	3.2 (3.7)	3.4 (5.2)	7.5 (10.6)	1.9 (1.9)	2.3 (4.0)
<b>N CCIS</b>	med	14	12.5	12	16.5	13	12	18	10	8
	(IQR)	(13-17)	(7.5-15)	(9-16.5)	(14-19)	(8-16)	(6-16)	(14-19)	(7-14)	(5-13)
	mean (SD)	17 (15.1)	16 (11.7)	16 (12.1)	22 (16.2)	19 (11.1)	19 (10.4)	15 (16.3)	15 (10.0)	15 (9.1)
<b>PCOM Q1 (score)</b>	med	2.5	5.5	5	1	4.5	6	1	7	7
	(IQR)	(2-4)	(3-8)	(3-7)	(1-3)	(3-8)	(4-8)	(1-3)	(4-8)	(5-8)
	mean (SD)	3.2 (2.3)	5.2 (3.0)	4.8 (2.9)	1.7 (1.5)	5.3 (3.0)	5.8 (2.9)	1.4 (1.5)	6.7 (2.2)	7.2 (1.5)
<b>PCOM Q2-6 (total score)</b>	med	13	28.5	23.5	6	23	30	3	32	38
	(IQR)	(9-22)	(13-38.5)	(12.5-36)	(3-15)	(13-40)	(20-42)	(2-14)	(16-44)	(21-42)
	mean (SD)	16.1 (11.6)	25.9 (14.9)	24.2 (14.5)	8.7 (7.5)	26.5 (14.9)	28.7 (14.3)	6.5 (5.8)	30.3 (14.0)	32.6 (12.7)

Key: med = median, IQR = interquartile range, PCOM = Patient Centred Outcome Measures

**Table 3.10:** Numbers of patients analysed proportions of "success" of pre- and post-treatment clinical outcome data

Intervention	PTNS			SNS (all)			SNS (permanent implant)		
	Baseline	3 months	6 months	Baseline	3 months	6 months	Baseline	3 months	6 months
<b>N</b>		15*	15*		19	18		15	15
<b>≥ 50% reduction in FI episodes p/w</b>	-	6 (40%)	7 (47%)	-	9 (47%)	11 (61%)	-	8 (53%)	9 (67%)
<b>≥ 75% reduction in FI episodes p/w</b>	-	3 (20%)	4 (27%)	-	7 (37%)	8 (44%)	-	7 (47%)	8 (53%)
<b>100% reduction in FI episodes</b>	-	2 (13%)	3 (19%)	-	2 (11%)	3 (17%)	-	2 (13%)	2 (13%)
<b>N</b>		16	16		19	19		15	15
<b>≥ 50% reduction in CCIS</b>	-	(19%)	(19%)	-	(26%)	(37%)	-	(33%)	(47%)

Key: FI = faecal incontinence, p/w = per week, CCIS = Cleveland Clinic Incontinence Score, \* one patient with no episodes at baseline excluded by definition

**Table 3.11:** Means of within patient changes (baseline to 3 months, and baseline to 6 months), and 95% confidence intervals, by treatment group

Intervention	PTNS (n = 17)				SNS all (n = 19)				SNS permanent implant (n = 15)			
Visit	3 months		6 months		3 months		6 months		3 months		6 months	
N	16		16		19		19		15		15	
	mean	95% CI	mean	95% CI	mean	95% CI	mean	95% CI	mean	95% CI	mean	95% CI
<b>Change in total FI episodes p/w</b>	-4.8	(-9.5 to 0.0)	-4.3	(-10.5 to 1.9)	-7.9	(-13.6 to -2.2)	-6.6	(-12.4 to -0.7)	-9.3	(-16.2 to -2.3)	-9.0	(-15.2 to -2.8)
<b>Change in urge FI episodes p/w</b>	-0.9	(-4.0 to 2.2)	-0.9	(-4.1 to 2.3)	-2.9	(-5.2 to -0.7)	-3.5	(-6.3 to -0.1)	-3.6	(-6.4 to -0.8)	-3.8	(-6.7 to -0.8)
<b>Change in passive FI episodes p/w</b>	-3.9	(-6.9 to -0.9)	-3.5	(-8.0 to 1.0)	-5.0	(-9.4 to -0.6)	-4.3	(-8.9 to 0.2)	-5.6	(-11.0 to -0.2)	-5.2	(-9.7 to -0.8)
<b>Change in CCIS</b>	-3.6	(-5.4 to -1.9)	-3.2	(-4.8 to -1.5)	-5.1	(-7.6 to -2.5)	-6.4	(-9.3 to -3.5)	-6.3	(-9.2 to -3.3)	-7.2	(-10.3 to -4.1)
<b>Change in PCOM Q1</b>	1.6	(-0.4 to 3.6)	1.4	(-0.9 to 3.7)	3.9	(2.1 to 5.8)	4.3	(2.7 to 5.9)	5.5	(4.0 to 6.9)	5.7	(4.6 to 6.7)
<b>Change in PCOM Q2-6</b>	9.4	(3.9 to 14.9)	7.7	(1.3 to 14.1)	17.9	(9.1 to 26.7)	20.4	(12.4 to 28.5)	23.8	(15.0 to 32.6)	26.1	(18.4 to 33.8)

<b>Change in EQ-5D</b>	.05	(-.09 to .18)	.08	(-.05 to .21)	.00	(-.12 to .13)	.09	(-.01 to .19)	.02	(-.15 to .18)	.11	(-.02 to .24)
<b>Change in EQ-5D VAS</b>	4.5	(-1.7 to 10.7)	5.03	(-4.2 to 14.3)	5.3	(-5 to 15.6)	8.9	(-3.1 to 20.9)	7.7	(-5 to 20.4)	8.6	(-6.9 to 24.0)
<b>Change in FIQL (lifestyle)</b>	0.2	(-0.2 to 0.5)	0.2	(-0.2 to 0.5)	0.8	(0.3 to 1.2)	0.8	(0.4 to 1.2)	1.0	(0.5 to 1.4)	0.9	(0.5 to 1.3)
<b>Change in FIQL (coping)</b>	0.5	(0.1 to 0.9)	0.2	(-0.3 to 0.7)	0.8	(0.4 to 1.2)	0.9	(0.5 to 1.3)	1.0	(0.5 to 1.4)	1.0	(0.6 to 1.4)
<b>Change in FIQL (depression)</b>	0.6	(0.3 to 0.8)	0.3	(0.0 to 0.5)	0.5	(0.2 to 0.8)	0.6	(0.2 to 0.9)	0.7	(0.3 to 1.0)	0.7	(0.3 to 1.0)
<b>Change in FIQL (embarrassment)</b>	0.3	(-0.2 to 0.5)	0.1	(-0.4 to 0.5)	0.8	(0.4 to 1.2)	1.0	(0.5 to 1.4)	1.0	(0.5 to 1.4)	1.1	(0.6 to 1.6)
<b>Change in SF-36 (physical functioning)</b>	9.1	(-3.4 to 21.7)	9.1	(-3.3 to 21.4)	-9.0	(-21.4 to 3.4)	-6.4	(-19.5 to 6.8)	-9.8	(-24.2 to 4.7)	-9.1	(-25.4 to 7.3)
<b>Change in SF-36 (physical role)</b>	6.7	(-23.6 to 36.9)	0	(-22.3 to 22.3)	19.7	(-0.2 to 39.6)	22.3	(-1.7 to 46.4)	26.7	(3.6 to 49.8)	25	(-5.5 to 55.5)

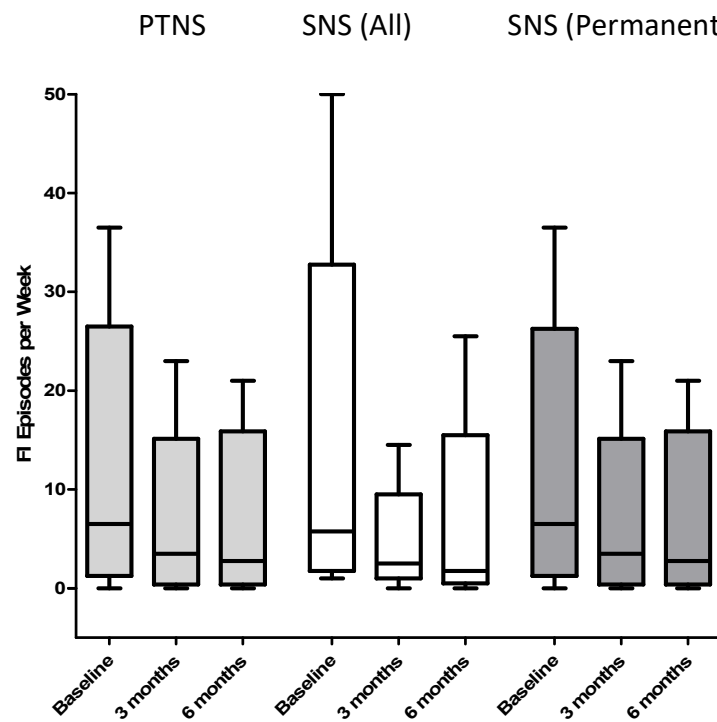


<b>Change in SF-36 (bodily pain)</b>	-5.5	(-20.5 to 9.5)	0.9	(-8.8 to 10.6)	1.4	(-12.7 to 15.6)	3.8	(-11.9 to 19.5)	2.7	(-15.7 to 21.0)	7.2	(-12.7 to 27)
<b>Change in SF-36 (general health)</b>	-4.0	(-12.1 to 4.1)	-7.5	(-14.7 to -0.3)	-6.4	(-16.8 to 4.0)	-4.2	(-13.5 to 5.0)	-6.8	(-20.2 to 6.7)	-4.8	(-15.4 to 5.8)
<b>Change in SF-36 (vitality)</b>	2	(-3.7 to 7.7)	0	(-8.9 to 8.9)	1.6	(-7.5 to 10.7)	6.8	(-3.3 to 17.0)	2.7	(-8.9 to 14.3)	8.7	(-4.3 to 21.6)
<b>Change in SF-36L (emotional role)</b>	20	(-15.4 to 55.4)	16.7	(-0.5 to 33.8)	14.0	(-11.8 to 39.9)	19.3	(-6.0 to 44.6)	11.1	(-19.8 to 42.1)	17.8	(-12.5 to 48.1)
<b>Change in SF-36 (social functioning)</b>	13.3	(1.2 to 25.5)	10.9	(-0.7 to 22.6)	13.8	(0.8 to 26.8)	13.2	(-1.3 to 27.6)	19.1	(3.7 to 34.6)	17.5	(-0.4 to 35.4)
<b>Change in SF-36 (mental health)</b>	8.3	(1.2 to 15.3)	10.5	(5.1 to 15.9)	-2.1	(-10.7 to 6.5)	3.2	(-8.0 to 14.3)	-2.7	(-13.8 to 8.4)	1.7	(-12.2 to 15.5)

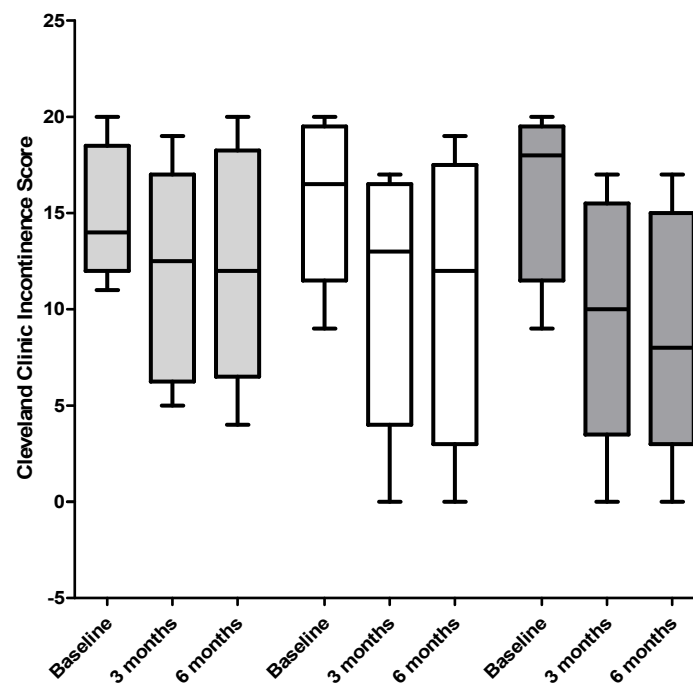
Key: FI = faecal incontinence; p/w = per week; CCIS = Cleveland Clinic Incontinence score; EQ-5D = EuroQol questionnaire; EQ-5D VAS = EuroQol Visual Analog Scale; FIQL = faecal incontinence quality of life; SF-36 = social form 36 questionnaire.

**Figure 3.04:** Main outcomes of percutaneous tibial nerve stimulation (PTNS) and sacral nerve stimulation (SNS) at 3 and 6 months compared to baseline

(a)

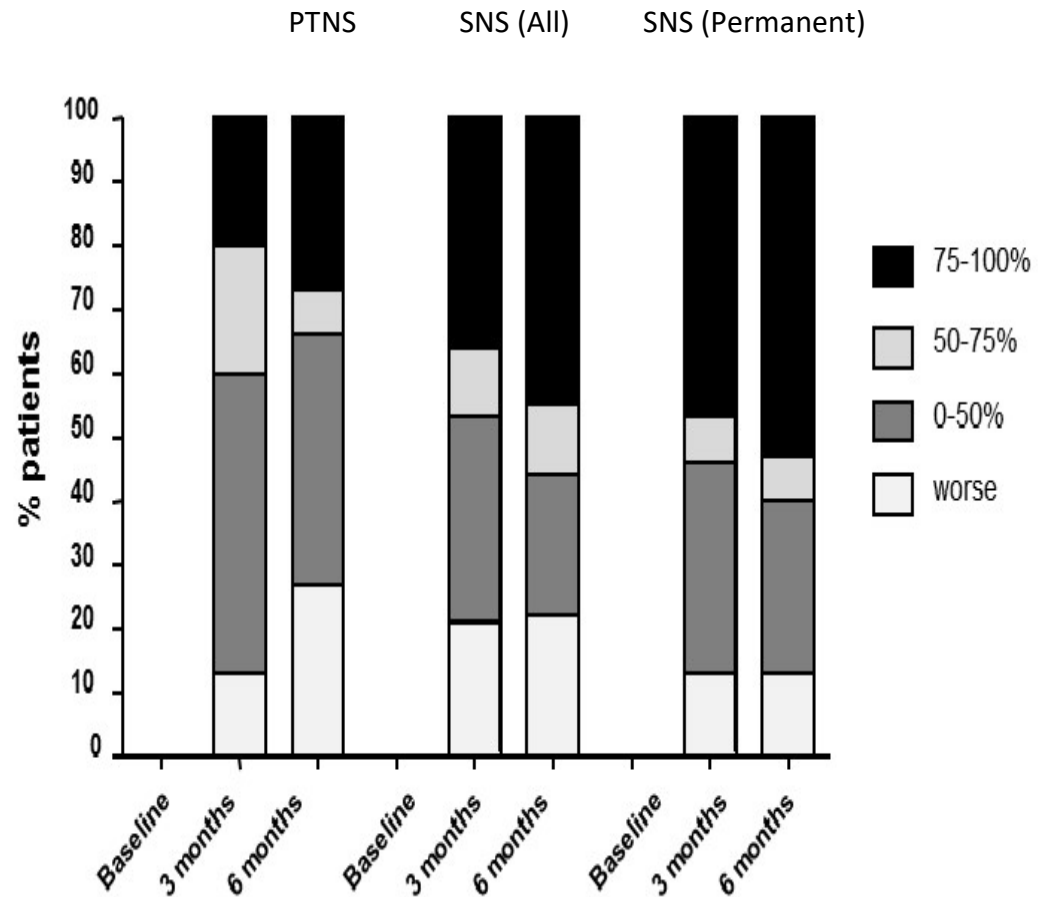


(b)



(a) prevalence of faecal incontinence episodes per week; (b) Cleveland clinic incontinence scores. Box and Whiskers charts represent medians + interquartile range + range.

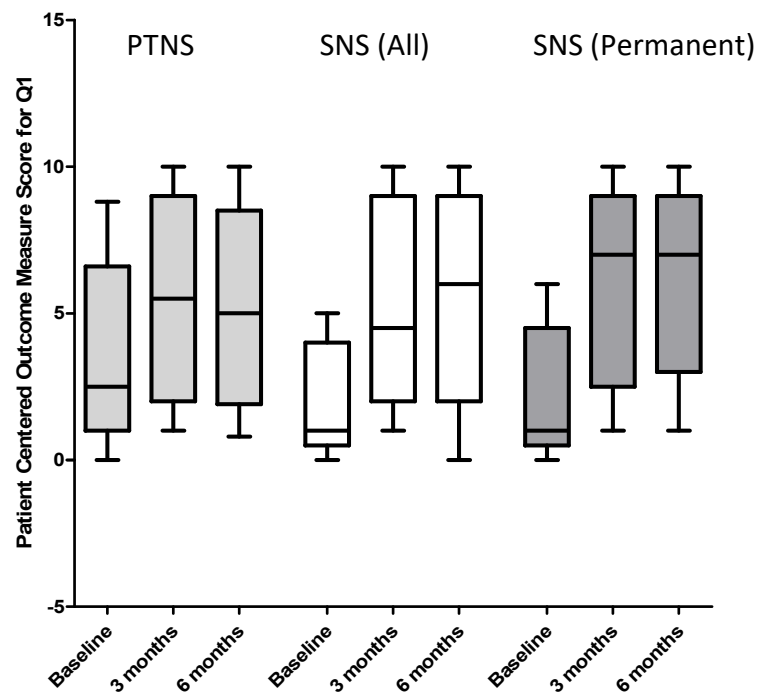
(c)



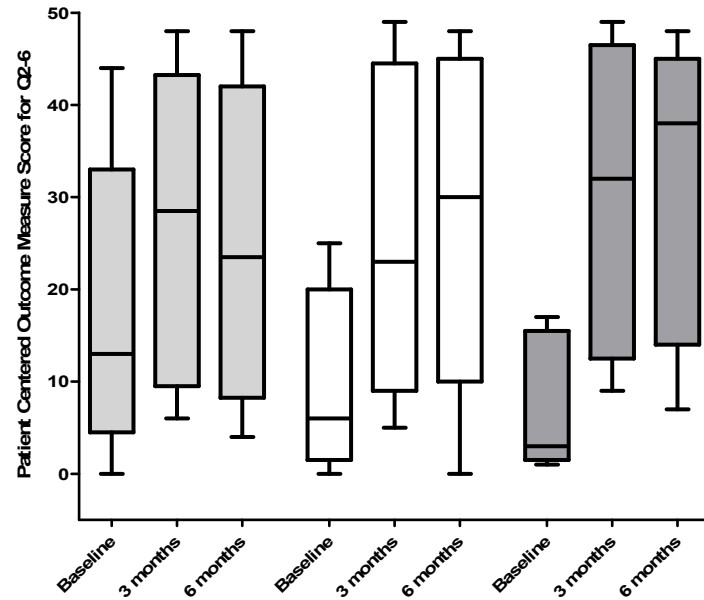
(c) bar frequency chart showing quartiles of percentage change in FI episodes per week from baseline.

**Figure 3.05:** Patient centred outcomes of percutaneous tibial nerve stimulation (PTNS) and sacral nerve stimulation (SNS) at 3 and 6 months compared to baseline

(a)



(b)



(a) patient centred outcomes scores for question one only; (b) patient centred outcome summative scores for questions 2-6 only. Box and Whisker charts represent medians + interquartile range + range

**Table 3.12:** Direct intervention costs of SNS and PTNS

Expenditure type	Unit Cost (£)	Reference	Cost per patient (£)	Assumptions
<b>Device costs</b>				
<b>Temporary SNS</b>				
Temporary SNS kit (Medtronic)	210.00	[a]	210.00	Includes 9 cm needles x 2, single use
12.5 cm needles pack of 6 (Medtronic)	135.00	[a]	0.45	Single use, assumes 2 needles per patient, requires for 1% of patients
Power source (Medtronic)	335.00	[b]	18.61	Multiple use, assumes 18 patients as per trial
<b>Total cost temporary SNS</b>			<b>229.06</b>	
<b>Permanent SNS</b>				
Patient programmer (Medtronic)	500.00	[a]	500.00	Single use
Pulse generator (Medtronic)	5,700.00	[a]	5,700.00	Single use
Tined lead (Medtronic)	1,350.00	[a]	1,350.00	Single use
Lead introducer kit (Medtronic)	200.00	[a]	200.00	Single use
<b>Total cost permanent SNS</b>			<b>7,750.00</b>	
<b>Total device cost SNS:</b>			<b>7,979.06</b>	
<b>PTNS</b>				
UPC stimulator (Uroplasty)	868.84	[c]	51.11	Multiple use, assumes 17 patients as per trial
UPC lead set of 12 (Uroplasty)	417.88	[c]	522.35	Single use, assumes 15 leads per patient
<b>Total device cost PTNS:</b>			<b>573.46</b>	
<b>Resource use costs</b>				
<b>Temporary SNS</b>				
Initial consultation	123	[d]	123	Consultant Led: First Attendance Non-Admitted Face to Face, Colorectal Surgery
Physiology testing				

Expenditure type	Unit Cost (£)	Reference	Cost per patient (£)	Assumptions
Outpatient appointment	99	[d]	99	Non-Consultant Led: Follow up Attendance Non-Admitted Face to Face, Colorectal Surgery
Ultrasound	51	[d]	51	Diagnostic Imaging: Outpatient. Ultrasound Scan, less than 20 minutes
Fluoroscopy	119	[d]	119	Diagnostic Imaging: Outpatient. Contrast Fluoroscopy Procedures, less than 20 minutes
Second consultation	93	[d]	93	Consultant Led: Follow up Attendance Non-Admitted Face to Face, Colorectal Surgery
Counselling	99	[d]	99	Non-Consultant Led: Follow up Attendance Non-Admitted Face to Face, Colorectal Surgery
Pre-assessment for operation	99	[d]	99	Non-Consultant Led: Follow up Attendance Non-Admitted Face to Face, Colorectal Surgery
Procedure	599.00	[d]	599.00	Intermediate pain procedure, day case
Post-operative medication: Paracetamol 500mg for 7 days	100-tab pack = £2.88	[e]	2.88	Non-proprietary, 0.5–1 g every 4–6 hours
Specialist nurse review	99	[d]	99	Non-Consultant Led: Follow up Attendance Non-Admitted Face to Face, Colorectal Surgery
<b>Total cost temporary SNS</b>			<b>1,383.88</b>	

Expenditure type	Unit Cost (£)	Reference	Cost per patient (£)	Assumptions
<b><i>Permanent SNS</i></b>				
Pre-assessment for operation	99	[d]	99	Non-Consultant Led: Follow up Attendance Non-Admitted Face to Face, Colorectal Surgery
Procedure	4,268.00	[d]	4,268.00	Insertion of neurostimulator or intrathecal drug delivery device, day case
Post-operative medication				
Co-codamol 8/500 mg for 14 days	100-tab pack = £3.40	[e]	6.80	Non-proprietary, 1–2 tablets every 4–6 hours
Co-amoxiclav 500/125 mg for 5 days	21-tab pack = £3.03	[e]	3.03	Sandoz, one tablet every 12 hours
Re-programming pulse generator	99	[d]	89.10	Requires for 90% of patients. Non-Consultant Led: Follow up Attendance Non-Admitted Face to Face, Colorectal Surgery
Post-operation check at 6 weeks	93	[d]	93	Consultant Led: Follow up Attendance Non-Admitted Face to Face, Colorectal Surgery
<b><i>Total cost permanent SNS</i></b>			<b><i>4,558.93</i></b>	
<b><i>Total resource use SNS:</i></b>			<b><i>5,942.81</i></b>	
<b><i>PTNS</i></b>				
Initial consultation	123	[d]	123	Consultant Led: First Attendance Non-Admitted Face to Face, Colorectal Surgery
Physiology testing				

Outpatient appointment	99	[d]	99	Non-Consultant Led: Follow up Attendance Non-Admitted Face to Face, Colorectal Surgery
Ultrasound	51	[d]	51	Diagnostic Imaging: Outpatient. Ultrasound Scan, less than 20 minutes
Fluoroscopy	119	[d]	119	Diagnostic Imaging: Outpatient. Contrast Fluoroscopy Procedures, less than 20 minutes
Second consultation	93		93	Consultant Led: Follow up Attendance Non-Admitted Face to Face, Colorectal Surgery
15 PTNS procedures	99	[d]	1,485.00	Non-Consultant Led: Follow up Attendance Non-Admitted Face to Face, Colorectal Surgery
2 top-up PTNS procedures at 6 months	99	[d]	198.00	Non-Consultant Led: Follow up Attendance Non-Admitted Face to Face, Colorectal Surgery
<b>Total resource use PTNS:</b>			<b>2,168.00</b>	

Key: [a] Medtronic Ltd UK. List prices 2012. Personal enquiry; [b] NHS purchasing and Supply Agency 2010. Economic report. Sacral nerve stimulation for faecal incontinence; [c] Uroplasty Ltd UK. List prices 2012. Personal enquiry; [d] National Schedule of Reference Costs 2011-2012 - NHS trusts and NHS foundation trusts. Available at <https://www.gov.uk/government/publications/nhs-reference-costs-financial-year-2011-to-2012>. Accessed 30 July 2013; [e] British National Formulary 2013. Available at <http://www.bnf.org/bnf/index.htm>.



### **3.2.4 ADVERSE EVENTS**

There were no unexpected serious adverse events relating to either treatment. Three patients from the SNS group had procedure related complications. One had mild ipsilateral leg pain during temporary testing but this resolved after removal of the temporary lead. This patient's improvement in FI was marked and therefore she elected to proceed with a permanent operation. Further implantation of the permanent device did not lead to a recurrence of this problem. Two further patients had stimulator site pain after the insertion of their neurostimulators which resolved with the adjustment of their stimulator settings. In the PTNS group, one patient had paraesthesia and another mild discomfort in the foot directly after sessions of stimulation. Both adverse events resolved spontaneously within 24 hours. In subsequent therapy sessions, the stimulation level for these patients was decreased slightly to alleviate the unwanted symptoms. These mild adverse events did not discourage either patient from completing their full course of PTNS. There were no infective complications and no premature treatment termination in either group.

### **3.3 QUALITATIVE INTERVIEW STUDY OF SACRAL AND PERCUTANEOUS TIBIAL NERVE STIMULATION IN PATIENTS WITH FAECAL INCONTINENCE**

#### **3.3.1 PARTICIPANT DESCRIPTION**

Out of 40 participants eligible for the study, 10 agreed to participate in qualitative interviews. Five participants were from the group undertaking SNS and five from the PTNS group. After an iterative process of review after each interview the steering group decided that 10 participants would be enough to reach data saturation. In the SNS group four patients successfully passed their temporary testing phase and therefore proceeded to a permanent implant. One patient however failed their temporary test and although invited for a post treatment interview, she declined. All participants in the PTNS group completed a full course of treatment and returned for a post treatment interview. Therefore 19 interviews were completed, transcribed and analysed. All the participants were female aged from 34 to 72 years. There were a mixture of those who were still currently working and those who had retired in both groups. There was also a mixture of participants in stable intimate relationships and those without partners at the time of the interviews.

### 3.3.2 EXPERIENCE OF SNS THERAPY

Five participants undertook SNS therapy. Four participants completed the therapy and returned for a post therapy interview. The three main super-ordinate themes were: acceptability of therapy, results of the therapy and feelings of psychological support.

**Table 3.13:** Thematic coding for experience of SNS

Super-ordinate theme	Sub-ordinate theme	Codes
<b>Acceptability of therapy</b>	Physical	Operation was fine, No side effects, No negatives, Easy to get used to, Control of therapy, System just continues to work, Easier than previous treatments, Confusion with the temporary system, Discomfort, Implant could be better positioned, Worried about remote controller
	Social and Economical	Concerns Going abroad, Time off work, Cost, Specialist centre, Helpful to have treatment at local hospital, Go through a lot of batteries, 6 weeks of reduced activity
	Emotional	Scared , Unsure, Prepared, Good trade off, Positive outlook, Good experience, Feels at home, Praise to staff
<b>Results of therapy</b>	Positive	More optimistic / hope, Freedom, Success, Feel in control, No concerns, Psychologically much better, Not worried about incontinence, Toilet not a second thought, Able to socialise, Better than other treatments, Improved Confidence, Improved self esteem, Can get on with life, Warning to visit toilet, Doesn't feel isolated, can fulfil role at work, Relaxed, Open, Dress appropriately, Able to socialise, more spontaneous, Psychologically happier, Not so self deprecating, Improved Intimate relations, Psychological control, Better attitude to her health, Becoming normal, Stopped support aids, Met expectation
	Negative	Not 100%, temporary system had only little effect, In between temporary and permanent therapy back to normal
<b>Psychological impact</b>		Accessible service, Paradoxical food mapping, Still wears padding, Still planning/preparing

### **3.3.2.1 Acceptability of therapy**

The acceptability of SNS based on the physical, social and economic and emotional sub-ordinate themes drawn from the coding was analysed. In general there seemed to be a high acceptability of this type of treatment despite the patient undergoing two operations.

#### ***Physical***

The participants found the operations themselves easy to tolerate. They were pleased that the operation was carried out under local anaesthetic and that they could be discharged on the same day. Some patients had felt some pain or discomfort around the site of the operation after the procedure but they did not view this as a limiting problem or a side-effect.

*"The actual operation itself was fine, they put you to sleep don't they and you wake up and it's done. The operation itself was quite fine and there weren't any complications afterwards or anything. I had a time, I think it was about 3 weeks after the operation, it all got a bit red and inflamed and I went to the GP and he said it was just dry, there wasn't anything, it was alright, it was healing, don't worry. And it all healed up quite well"*

On first use, participants were nervous that they may set the stimulator incorrectly or may somehow damage the implant but after some practice they started to enjoy the control they had over their new therapy. They felt the stimulator was easy to tolerate and after some time even became unaware of its presence.

*"Initially I think you are a little bit nervous at first turning it on and off it is new, but I think once I had done it a few times, like now if you told me to do it, I would do it and it beeps and I can play with it and I like it. It is alright, I feel quite in control."*

One patient found the temporary system confusing and uncomfortable but was pleased with the permanent implant which was much more discreet. Some of the participants interviewed found SNS treatment easier to use than previous conservative measures and had a sense that once it was set up it would continue to work for them without problems.

*"I just think it will get better. Yes I think I will get more and more used to it being there. I mean to be honest sometimes I forget it is there. You forget it is there and then some days I don't give it a second thought."*

*"I wouldn't dare not to be honest. Just in case it went back like before. I presume that this will stay in forever and it will just get checked and everything is ok, it will just stay as it is, that is my understanding,"*

***Social and economical***

There were some concerns about the need to attend a specialist hospital in London for their treatment rather than a local hospital. This meant that they required more time off work and extra costs for travel. For convenience they expressed a wish to have a service setup locally that could provide this type of operation and follow-up.

*"So although sometimes it is a bit inconvenient when you come and have time off work and come for your appointments because it is not just down the road it is a fair way to come. So I have to have a day off work, but I think, the treatment from the beginning up until now has been closely monitored and sort of been aware of what is going on, so as far as I am concerned, it has been marvellous."*

*"I think obviously coming up to London is a fair way to come. I mean I feel lucky that I have been asked to come up and it is working, but it is a shame that there aren't more local things, maybe there might be some people in my position as well, but who maybe couldn't get to London on a regular basis, so it is a shame that there are no opportunities like this in other hospitals."*

Another concern for those with an implant was the ability to proceed through a flight terminal with the implant. Although they had appropriate documentation there were still some concern that they might be stopped at the security check in and would be interrogated about their medical device.

*"No, there is no down side. On my mind, I am thinking about going on holiday and things like that. Obviously I have got my card, I have got my letter. I wouldn't say I'm stressed, but it is in the back of my mind. The process of going through of saying "Look I can't walk through that" it's do I turn it off, you know what I mean, but no worry. When the time comes I will deal with it."*

For those that had already ventured abroad they found that this was usually a more discreet process than they had anticipated. The enforced six weeks of reduced activity after implantation was limiting but not too onerous for our participants. They expressed the opinion that these small inconveniences were an acceptable trade-off for the benefits of the therapy.

*"Yes I am fine. Yes. I think whatever I have had to do, on balance, it will always pay for the life that I am leading now"*

### ***Emotional***

Initially some of the patients did delay the therapy because they were scared of having an operation for their condition. They were apprehensive about the possible complications of the procedures and also unsure whether it would give them any real benefit.

*"I was quite scared, really scared. Anyone I spoke to so, because nobody knows about it only me I suppose, I was scared of having the operation, quite scared. I put it off for quite a few months, like dragging my heels thinking "I don't know, having an operation, what if this and what if that"*

*"It's of little while to decide whether to go ahead with little not. I really wanted to stick my head in the sand and forget about it"*

Despite their initial reservations they all felt well prepared and once they had undertaken it, generally found it to be a positive experience.

*"Um, yes it has been much better and much easier, yes I mean I haven't had a lot of treatment as such but yes it has been much better, there seems to be a minimum of fuss and that was very pleasing"*

The participants praised the staff and found them to be attentive, kind and professional. This allowed patients to feel well looked after and even comfortable when attending for appointments at the Royal London Hospital.

*"I felt the staff everyone has been so kind and helpful"*

*"It has all been fine and if I had any problems I have got a phone number, I can ring Tatenda or whatever, she will get back to me and they will every time, they have been really really good"*



### 3.3.2.2 Results of therapy

In general the results of the therapy in the four patients who completed SNS were remarkably good. In all cases the treatment had met the expectations of the patient and they were pleased with the results. As the their FI improved there was a significant impact on their psychological health and lifestyle.

#### **Positive**

Our participants found the treatment of FI was very successful with SNS. They describe improvements in both the constant leakage of stool and also urgency symptoms.

*"I personally think that it has worked. I mean, like I said I have had the odd blip and it seems to go into, like I have a couple of days and I think I hope things are not going back to how they used to be, but then it just seems to pick up again"*

*"But overall, no major accidents. Even today, in the car and going places and getting on the train, I have got no concerns"*

*"Yes, in fact it has exceeded my expectations. Because it was a trial, you have to keep thinking to yourself oh whatever. You have to keep thinking this might not work. Some patients it doesn't work. But it really really 100% has worked for me, because I was just leaking diarrhoea all the time. Now I can sit here comfortably"*

They describes feelings of abdominal discomfort which acted as a warning sign to alert them to a need to evacuate imminently. Patients also felt they could defer defecation longer and this allowed them to visit the toilet in a controlled fashion.

*"And I think to myself in my mind, it that wasn't in there I would have had an accident. Because I would have sat there and it would have happened. Because that it is there telling me now, it is giving me that uncomfortable feeling like it is there and it is coming, I feel confident that I will not have accidents"*

*"Yes, I feel in control. I think overall, going to the toilet and that, I know when I am going to the toilet now. I think for some reason, whatever that's doing, sending messages to my brain, I haven't had an accident since I have had it in"*

*"But it is control and knowing and knowing that I am going to be alright, do you know what I mean. It takes the panic and embarrassment and that kind of thing away"*

*"That is the control. I feel like I have got the control back in my life and I will know when I have to go to the toilet"*

*"I know I want to go to the toilet, so psychologically, 10 times better, 100 times better, because I have got no fear now. I might have to go quickly sometimes, but I know I will get to the toilet"*

*"I think basically, I think mentally, physically, it has made a big difference. I think the key word is "control". I think I have got control in my life"*

Participants found that SNS yielded better results than the other previous treatments they have tried.

*"Nothing else worked. Even before this .... So this is actually the first thing that has worked"*

They all expressed benefits to both their symptoms and also their lifestyle. For the first time since the start of their condition our participants expressed a feeling of control in their lives which led them to be less anxious and worried about their incontinence. They felt much more relaxed, open and sociable. They felt that they could get on with their life and they felt freedom to be more spontaneous without giving extra thought to the need for a toilet.

*"Whereas now, in the summer, when my sister says let's go here, let's go there, it will be like "Yes". So I think it will make a big difference and I think in the summer I will notice it more"*

*"it's just made it less anxious life which is a good thing and it has given me more confidence. I think those are the two things mainly. Yes more optimism I think"*

*"It's oh my gosh I am late to the appointment, I must get on the train, let's do this, let's do that." But the toilet was not even a second thought, whereas two years before the operation, it was like my whole life revolved about going to the toilet and the need to go to the toilet"*

---

*"but I don't worry so much if I do go out now, so if it is something unplanned and on the spur of the moment, you know, I think, well ok, I don't need to pack a bag of pants and pads and everything else. I mean I am not saying that accidents don't happen because they do. I have had a couple of blips, but it is nothing like it was and you feel like you can actually do more and not embarrass myself"*

They became optimistic and had hope that the treatment might even improve with time. They had improved self-confidence and self-esteem and began to feel normal again.

*"But I feel so much more confident and happier"*

*"I do feel more confident in the fact that I haven't had an accident, a big accident for a long time*

*"So you tend to feel that they are happening a lot lot less so, yes, you are more confident, you know it is, fingers crossed, not going to happen like it did"*

*"It's funny, I think my self-esteem has risen. I am a different case, because I had been widowed just before the treatment, but my confidence, but mostly my self-esteem has been raised, yes, by this treatment, knowing that I am not going to get whatever. Yes it has, it has made a hell of a difference"*

Physically they are able to stop some of their support aids such as pads, pants and spare clothes and did not need to hide behind baggy clothes any longer.

---

*"I am going on holiday soon with my pal and I can off not wearing anything. No sorry, I didn't mean not wearing anything. No incontinent protection"*

*"and I am not having to keep checking on myself, that is much better, I feel confident to go out now. Whereas before I would still go out but I would be sort of worrying about certain stuff, about finding the right loo."*

*"Honestly I can't explain how wonderful it is not to be encased by Tena lady incontinence pants"*

*"No I don't carry knickers or anything, all I have got is a pad. A normal Tena pad as well. So it is just in case of a little bit of leakage"*

*"Yes, yes, and now like before I was having proper big what I call nappy pads now it is just like a panty liner pad, so I feel better"*

They were able to be more open about their condition and no longer felt isolated or fed up with life. Our participants reported improved intimate relations with their partners although many were still wary that they could still have accidents. They felt that they would gain confidence and be more relaxed in these situations over time.

*"So have you told them [workplace] about the treatment? Yes, they are all like in shock because they have never known anybody, because I say to people I've got a pacemaker. I say it's in my bum! It is a standing joke that I have got a pacemaker in my arse! But they are quite – ooh. And I say it is all connected to the nerves and muscles, because it is new and nobody has heard of it."*

*"Yes, I am not as miserable anymore. Because I was quite miserable and depressed and things like that. Whereas now I feel a lot better"*

*"I think I have been looking it in a positive way, because I wanted it to be positive. I don't know. It is like a whole cloud over you where you can't go out because you know you might mess yourself, embarrass yourself, and it is almost like someone has taken that away, you can go out"*

*"Because obviously after the operation and to be honest I think we are just getting back on track now, but I mean ideally, because before I had a couple of accidents on him, like I would have an accident while I was having sex, so I think ideally I don't worry about having accidents now, but at the moment we are just getting back on track.....but I can imagine once we get back into the swing of things it will be much better."*

Overall the expectations of the patients were met by the treatment results and therefore they were generally very pleased with the control they had with their condition. Overall SNS seem to give them the immediate and impactful change in their symptoms that they had hoped for.

*"And you know, like before I would walk places because I knew I could get back in time and it sounds really stupid, but you can go further, you can walk a bit more, you can do a bit more..... I honestly don't think there is anything negative at all. It is so nice just to be able to do things that everyone else takes for granted you know"*

---

**Negative**

During the interviews, there were a few negative comments regarding the results of SNS. Although the treatment was successful in the eyes of the patients, they did comment that they still continued to have occasional incontinence episodes and therefore the treatment could not be considered a cure.

*"I still have little bits of problem completely opening my bowels and then through that I will have 2-3 days where I get a little bit of leakage and that I think is when I haven't emptied my bowels properly and it will be a couple of days later at work, I feel uncomfortable and I need to go, but it is a little bit of leakage, but not much."*

*"Sometimes my bowels don't empty; sometimes I do have a little bit of leakage, so the physical side just needs a little bit of time"*

*"now I have the odd blip, but it is nothing to what I used to have"*

*"Um, well I still have the odd accident from time to time but then I think it's dietary based"*

They also mentioned discrepancies between the effect of the PNE which in some cases was deemed not to be as effective as the permanent implant. Another drawback of the treatment was the period between the PNE and permanent implantation which meant that symptoms returned to their normal baseline levels.

*"the temporary one I had a few problems with, because I really didn't know what I should be doing. And it didn't seem to have a lot of effect"*

*"We went up Romford and I had this hell day, because I didn't have the temporary one on and it was like back to hell and there was one point where I was rushing to the toilet and sitting down with pains, do you know what I mean, having accidents, getting panicky. Just like I can't cope, I've got to go home, I've got to go home. Just miserable"*

As the second operation needed to be scheduled, there could be a slight delay until final therapy could be instigated. All in all these negative feelings were minor compared to the success that they had felt the treatment had provided.

### **3.3.2.3 Psychological impact**

It was well recognised by patients' themselves that the process of having SNS treatment had given them some emotional and psychological support in their battle against incontinence. They felt comforted that they had a service which was accessible and expertise that could help them with their symptoms even if the therapy started to fail.



*"I am yet to see if it keeps on; if not I know I can ring up and say "I am having a problem here". I know that I will be seen; well I know Dr Thin has already seen me for a year, but I do know I can ring and if I have a problem they will do all they can"*

Patients could not completely rely on the therapy only as they had still encountered incontinence episodes. Many still felt they had to wear underwear padding whilst planning their public outings carefully in order to maximise their chance of successfully avoiding incontinence accidents. In some cases this was done more out of habit and was difficult to give up completely.

*"Yes, physically comfortable, mentally. I think it is habit. Like I said I get up in the morning, shower, dress put on a pad, so it is habit, but then it's like my little safety thing cos if I do have a little leak"*

*"Oh yes, I do slightly still yes. I take Imodium from time to time and I feel I need it, um, and I always take precautions anyway and that's just me I think so that is yes, how I feel about it"*

*"Like before when I used to go out, it would be planning where you are going, how long is it going to take. To some extent I still do that, because old habits die hard"*

Despite these measures the patients felt much more comfortable with the use of these safety aids becoming rarer. Overwhelmingly these patients felt that

prevention of incontinence episodes was due to the actions of the device rather than psychological support they had received.

### 3.3.3 EXPERIENCE OF PTNS THERAPY

In a more deductive approach to this analysis, we use the super-ordinate themes already accounted for in the SNS group as a framework for analysis of the PTNS group. These included: acceptability of therapy, results of therapy and psychological support. This allowed us the ability to loosely compared these two treatments.

**Table 3.14:** Thematic analysis of experience of PTNS

Super-ordinate theme	Sub-ordinate theme	Codes
<b>Acceptability of therapy</b>	Physical	No problems with treatment, Simple treatment, Not painful, Needle treatment acceptable, some discomfort, No negative effects, Minimal physical restriction
	Social and Economical	Could fit around other responsibilities, Hospital appointments take priority, Valid treatment, Less self directed treatment preferred, preference for local treatment options, Preference for medically trained person administer their treatment
	Emotional	Glad to have tried therapy, Less invasive than other treatments - seen as entry level treatment, Praise for staff, Literature was a well explained but scared the patient, Providing hope
<b>Results of therapy</b>	Positive	Gained More confidence, Success - good treatment, had better control of bowels, Better effect than other

treatments, Keen to continue treatments,

Negative

Subtle improvements difficult to attribute to PTNS treatment, Possible temporary effect, Sceptical, expectations of results, Not met expectations, Not had big impact of daily living, Some patients didn't want to continue therapy, Unexpected treatment effects, Seeking next step

**Psychological impact**

Psychological aspects of treatment, Positive effects on confidence, Keen for group therapy, Still using coping strategies to combat FI, Still concerned about intimate relationships, Still worried when going to new environments, Still embarrassed about therapy

---

### **3.3.3.1 Acceptability of therapy**

On the whole there was a high acceptability of PTNS therapy for faecal incontinence. Exploring the participants attitudes to the treatment we found that their opinions could be further subdivided into the physical acceptability, social and economic acceptability and emotional acceptability of this treatment.

#### ***Physical***

Although PTNS is minimally invasive, it is a treatment that needs to be repeated initially on a weekly basis for 12 weeks. Currently this is administered by a trained medical health professional in a specialist clinic setting. Although this was a new technique participants were generally happy having the treatment carried out. They found that there were no significant problems in the treatment done and felt that it was generally a simple process.

---

*"It was quite easy going to be honest. I didn't know it was going to be that simple.*

*Yes it has been good"*

*"The actual treatment itself was made as comfortable as possible and it wasn't a terrible thing. I felt comfortable about having that"*

Most participants found that the needle placement was well tolerated although there were some who felt that there was some discomfort on stimulating the needle.

*"Sometimes it was, it depends whereabouts in the nerve it was. If it was really painful. The needle was alright, but it was when they turned the electric on, it would be really painful, not all the time. So if that was the case, they would take the needle out and put it somewhere else"*

Despite this the patients generally felt comfortable having control of the stimulator and settings which they could increase and decrease as they tolerated. Patients cited only very minimal restriction to their movements with this stimulate connected.

*"it wasn't you know painful or anything, I mean sometimes you could have a little bit too high and it would be uncomfortable but um, you know you could always adjust it, um setting and um, and it seemed to, you know it wasn't any trouble"*

*"Yes. Initially you didn't know what you were looking for, but as soon as you got to grips and what you should be looking for and how you were able to tolerate it, it was fine. You just switch it on and I sat there reading my book"*

In general the physical process of nerve stimulation was well tolerated without any ill effects. Even those who cited a needle phobia were able to tolerate the process without any difficulty.

*"I didn't mind it, no, I didn't mind it, it didn't cause any problems, I don't like needles so I was quite surprised that I was, you know, all right"*

Conversely when asked directly if there were any negative effects some did report some discomfort in their feet after the treatment episode, although this was also well tolerated.

*"I did get sometimes and achy afterthought feeling I think from it, um, but it only lasted a day or so and that's it. um, but it wasn't any trouble"*

This simple process did make some sceptical of how this treatment could happen effect on their faecal incontinence.

*"I think I was a bit sceptical. You know, how on earth is this going to do any stimulating, because I was almost hoping that I would get the implant. I was very*

*open minded and when you have had this problem for so long, you are willing to try anything"*

### ***Social and economical***

The social and economic burden to the patient to attend appointments was very much dependent on how far they lived away from the specialist Hospital where the treatments took place. Some participants lived up to a two-hour train journey away and therefore their weekly travel burden was greater. Some participants expressed the wish that the treatment could be carried out at a local facility because of the time and expense needed to make the journey.

*"and apart from the journey up here you know it was fine. That was the only thing, it's a shame they can't do this sort of thing at your local hospital"*

*"Well, I made it convenient, because I so wanted it to work. You could say travelling up here, I mean I got subsidised, but the fare was quite expensive, I had to leave early in the morning, so because I wanted the treatment, I didn't look at that side of it. And up here they made it so nice and easy"*

Although it was an inconvenience to travelling long distances, this group of participants were well motivated and when given a theoretical choice of completing treatment independently at home; they preferred to have their treatment conducted in a medical facility by train medical professional.

---

*"No I mean obviously you've got to make the time to come down, especially from where I live, I had to clear it with work, but obviously hospital treatment they can't really say anything um they have been good and supportive time really just flies by and I have tried to make it an early appointment or a late appointment to accommodate with work. But I have the end of the day you've got to put your health first and so um, it shouldn't really be seen as negative to make time for your own health."*

*"I think is err better because you're coming down to an appointment and someone is doing it for you, you know you don't have to be disciplined to do it, if you see what I am saying, so it has been good."*

*"In one sense, this treatment I found more comfortable because I felt the doctor was there and if there was any problems there was 1:1 discussions, doesn't matter how small or how big. That was one of the comforting factor in terms of away from the medication aspect."*

Paradoxically because the treatment was done in a hospital facility it seemed that the participants could more easily make plans to attend. There was some validation to the disease and also for the treatment. During the trial participants did not mind attending therapy once a week but there was some concern over the number of the therapies required and whether they could keep up with the "top-up" therapies.

*"Thinking about the top ups now that I've spoken to the doctor about it really depends on how many of those I may have, you know it's difficult when you work full time"*

If the patients are unable to attend therapies, it will obviously decrease compliance and therefore the effectiveness of the treatment.

### ***Emotional***

The participants were glad to have tried the therapy as they had felt that it had provided hope that their condition could be treated.

*"Yeah it's been a good thing I'd rather have had a rather not have had an if you see what I mean"*

*"But you know apart from that time when I wasn't getting any treatment even like the thought of getting treatment I think probably psychologically helps you to some extent to think that you know that you are not just having to deal with it and accept that it is problem that can't be solved sort of thing"*

Participants also felt that because of the simplicity of the treatment it should be offered as a initial therapy on which to build on.



*"One thing I was quite pleased about was that I had this stimulation, because it was the lowest treatment if you like and I thought well, it's a start. If that works and is not invasive, that is a good start"*

With regular treatments the patients felt comfortable in the environment and praised the staff for their role in providing support and professionalism in their treatment.

*"So I mean I've only got praise for them here, all very efficient, I come and I am seen straightaway and it takes half an hour. I think they were all very good and made it easy, um, any questions I had it all answered, no problems whatsoever"*

*"The main thing was how exceptionally, whether it was Noel or somebody else, how professional they were. Within that professionalism they were really really kind, that's not quite the word, but in tune and how they approached it and they made it very comfortable and talk about it. It was excellent. So firstly, everything was made so easy and everybody was so very very nice and nobody was difficult or abrupt or anything. That was really good"*

With a prolonged treatment schedule, it was very important that the patients felt comfortable and benefitted from attending the service. When patients attend appointments at regular intervals, it is not unusual for a friendly relationship to develop between the patient and health worker. Just knowing there is someone

---

supportive in clinic may also indirectly increase the benefit of therapy to patients. Obviously this human interaction may not be so evident in other treatments where personal interactions are limited.

### **3.3.3.2 Results of therapy**

Results were generally positive or negative depending on degree of benefit they received from the therapy versus the expectation of the patient.

#### ***Positive***

Some participants had positive accounts of how the treatment had worked for them. They found that control of their bowels had improved and were pleased to have had the treatment.

*"I think I've noticed a difference in how long I can hold it and I do credit to that"*

*"but I think with the treatment I have had that little bit longer where I can, so I definitely think it's been successful"*

*"But I do feel better and myself, definitely. I think it has helped"*

Although their accounts were positive, our patients' did not report remarkable improvements in their control. In some patients this small improvement in control made a huge difference in their perception of their symptoms. Despite this, our

participants found it difficult to credit all the improvements on just the PTNS treatment.

*"So I think that where before I had lots more, it is hard to accredit it just to this because lifestyle is a big part it, I know looking back and analysing it, ...Errm now my life is kind of changed away from that, errm yes I do think that when I go out and if I do drink a lot I have got that couple of minutes or five minutes more to think I need to go to the toilet.... So I kind of think a lot more about that and it has given me that little window of opportunity not to have that accident. And that is a matter of pride and you know the night going really badly wrong then you know having a good night out so even that five minutes is life changing for me."*

*"I have just thought a lot more about it but umm, it has had an effect because it just gives me that little more opportunity to get to the toilet without having an accident if I need it, I mean now I don't have it, as many things anyway, so that is definitely an improvement, umm, but as I say I don't think it is one hundred percent the treatment but who knows it could be errm but also my lifestyle changed"*

*"I suppose the change of having the treatment is that I use those precautions less, that's how I gauge that it has actually worked.....Yes I think it has um, it was explained to me that it was not going to be um, a cure. And I think I will always have a weakness but I do think it's less severe than it was before.....but I feel that it is better than it was and I guess that's probably the main thing"*

*"Yes, um, that I would see an improvement but um, not necessarily a total cure. I mean I had to keep a bowel diary um, at the start, I think I have done three overall actually in the last one I don't, I think Dr was a bit disappointed that I had had a couple of accidents but I felt that it wasn't as bad as before, so I think is a good treatment"*

Despite only subtle improvements, the patients with positive results wanted to continue their treatment to ensure that the severity of their symptoms did not return. The consideration for these patients was the balance between the social economic burden of travelling and giving time to have further treatment and the positive effect it had on their lives.

*"I think I will have to top up, again it might just be peace of mind or psychological but I don't think there is any harm is there really, because I have seen an improvement in the time I have been able to, the urgency that I have had errm I think I would be silly not to have a top ups.*

*And do you see it continuing to like work and effect, quite positively affect stuff?*

*Errm, I only gauge that I don't have so many incidents so I think that is a positive effect yeah"*

**Negative**

Although the overall experience of the treatment seemed mostly to be positive throughout, some patients did not find the benefits they had expected from their treatment.

*"No not really, it hasn't made the difference, I thought that it was going to make. I would say I am marginally better. I have got a little more control than I did have. It was the improvement I thought I was going to get, but it is better I would say marginally better"*

*"I didn't meet the expectation, and I still have days when it is not so good, but I would say that it is definitely, I will have to think back now because it is more than 6 months. I would say that I am probably 30% better"*

It seemed that this slight benefit could not make a difference to their overall quality of life and therefore they did not feel it was worth continuing their treatment. They felt that they could manage the symptoms adequately themselves.

*"No I don't think so at the minutes, no, it hasn't made a dramatic difference, so I don't think, unless it gets worse or anything. At the minute I am not looking at carrying on with it"*

*the participants looked for the next stage of treatment which they assumed to be sacral nerve stimulation.*

*"If they felt that having the implant may give me additional control, well I would go for it"*

One patient although improved in their incontinence started have symptoms of constipation instead which she attributed to the treatment. She therefore also didn't want to continue the treatment in case it was caused by PTNS.

### **3.3.3.3 Psychological impact**

Just as with SNS, there was a feeling from these patients that they had been supported psychologically and emotionally by the process of seeking and instigating treatment. This produced a positive result in increasing our participant's confidence levels. This may have been a product of going through the process rather than just improvements in symptoms.

*"Yes it has had an effect. I am more confident to go out. It is still there, it hasn't gone away totally, but not as much as before. It is coming back to where I was before when I would think about if I need to go out and I would just go out. Like today, just before coming today, I rang my sister to see if she was available and would want to go out. So these are the things I wouldn't have possibly done. Yes."*

*"No I have gained confidence in one respect because of the support from you all here and knowing there are other people, I know you know there are other people like me,*

---

*but knowing there are a lot of other people like me. With socialising. I think I have got a bit more courage to do a bit more"*

*"You make it easy and you and Noel, it is emotional really and it has helped my confidence and even if this hasn't improved, you have helped me mentally. You have helped me thank you"*

One suggestion was to have a group session with other FI sufferers in order to share experiences. Despite improved confidence in the participants they were not confident enough to stop relying on the crutch of their coping mechanisms.

*"it is not too bad now I don't think it has now been too bad just need to be sure that there is a toilet on standby. I do panic a bit if I'm going somewhere and it isn't but I mean especially when I'm going out with my boyfriend he thinks I've got bladder problems I reckon because I'm always going ooh you know where is the toilet, better go and check like an old lady."*

Despite the participants improvement in symptoms and confidence, they were still unable to resume intimate relationships or feel open about their condition.

*"I am still very wary you know because if I have had a day where it has been physical, or I have not emptied myself, my bowel and it is all to do with control.... then the pressure. So I am like, I can't put myself through that"*

*"they are okay about time off but you always feel a bit a little bit awkward asking for time off and obviously you don't want to go into discussion about what treatment having, and they are always wondering why you're having to go all the way up to London when there's a hospital just 10 min away, you know what I mean"*

PTNS did seem to bring about an improvement in patient symptoms but it did not seem to be the dramatic improvement in symptoms and daily living that some of our patients were striving for. Despite this, some found this improvement to be enough to want to return for ongoing treatments.



# **4**

## ***DISCUSSION, LIMITATIONS AND CONCLUSION***

### **4.1 STUDY 1: A REVIEW OF CLINICAL EFFECTIVENESS OF NEUROMODULATION IN FAECAL INCONTINENCE**

#### **4.1.1 SUMMARY OF EVIDENCE**

From the data summarised, the initial success rate of SNS based on ITT was found to be 63%; with a long-term success rate of 54% (median of 56 months). Although an approximately 10-20% loss in effectiveness was demonstrated within 5 years, SNS still appeared to be an effective long-term treatment option. To put this figure into context, most patients seeking treatment for FI can be successfully managed with conservative measures alone; in over half of the remainder of patients, SNS can provide a  $\geq 50\%$  improvement in continence maintained into the long term. With regards to PTNS, success rates could only be determined in a limited number of studies reporting short-term outcomes, which seemed comparable to that of SNS. Two PTNS studies reported a 63%<sup>283</sup> and 71%<sup>178</sup> success rate immediately after treatment. Only one study reported a 59%<sup>283</sup> success rate at the longest reported follow-up term of 1 year. A single study<sup>178</sup> also reported a 39% cure rate at 5 months after PTNS treatment, although this has not been replicated in any other

---

series. There was no current data on the medium-term and long-term clinical effectiveness of PTNS or TTNS.

Further support for the long-term clinical effectiveness of SNS was also demonstrated by changes in the CCIS and the number of FIE per week, with improvements of 8 points and 7 episodes respectively at a median of 50 months. Furthermore 20% of all patients undergoing SNS continued to have perfect continence at 56 months. With respect to QoL, both disease-specific and generic QoL measures demonstrated improvements in aggregate scores after SNS throughout all terms, although the magnitude of this improvement declined slightly with time. In the long-term, the FIQL assessments corresponded to results found with clinical continence measures much more closely than the generic QoL measures (SF-36), substantiating Matzel's opinion<sup>288</sup> that the therapeutic impact of SNS was most evident when disease-specific QoL instruments were applied. The most significant long-term improvements were found in the mental health component scores of the SF-36 questionnaire. This is an important finding as often these patients are anxious and self-conscious; with the fear of embarrassment rather than the actual number of episodes limiting their social interactions. SNS therapy may be able to return lasting confidence to these patients.

With PTNS, short-term improvements in the CCIS (median score change of 4 points), weekly FIE (median change of 4 episodes per week) and QoL outcomes were

---

demonstrated. In comparison to SNS the magnitudes of these improvements were less. This may indicate that PTNS could be more suitable in targeted patients with less severe FI in the first instance. Indeed the median baseline CCIS and number of FIE per week were lower for PTNS than those for SNS (13 vs. 15 and 5 vs. 8 respectively). The evidence for TTNS is equivocal with only one of four studies showing a statistically significant improvement in the CCIS at 6 months. In the other three studies there was a general trend towards clinical improvement but this could not be proven statistically.

#### **4.1.2 PREVIOUS LITERATURE REVIEWS**

There have been five systematic reviews<sup>167, 171, 188, 265, 289</sup> and another 35 review articles on SNS for the treatment of FI. Despite enthusiasm to summarise the available evidence, the lack of homogeneous outcomes and the uncertainty of possible duplication within reported data sets have been a consistent problem. Attempts to limit bias have led to the exclusion of the majority of the available reports leaving only a paucity of evidence for review. For example, two systematic reviews published in 2004<sup>171, 289</sup> considered only the most recently published series from each country to avoid double counting, leaving only 6 case series and one cross-over study (of only 2 patients). Similarly a Cochrane review in 2007, due to very strict inclusion criteria included only 2 cross-over studies with a total of 36 patients<sup>167</sup>. In 2011, Boyle *et al.*<sup>265</sup> reviewed SNS success and perfect continence

---

rates based on an ITT analysis. This review reported success rates in 19 studies and perfect continence rates in 8 studies. At the time of writing, available data may have been limited since the reviewers included four reports containing only five patients or fewer and only two reports with a median follow-up of more than 36 months. Previously there has only been one review article on PTNS and TTNS for FI <sup>290</sup>; reporting eight case series which were not systematically assessed.

#### **4.1.3 THE PLACE OF SNS AND PTNS IN CURRENT TREATMENT ALGORITHMS**

In 2004 NICE published guidance (Interventional Guidance Procedure 99) <sup>291</sup> for the use of SNS after a systematic review commissioned by the institute. They found the evidence on the safety and efficacy of sacral nerve stimulation for FI to be adequate to support its use. They further specified that SNS should only be performed in specialist units by clinicians with a particular interest in the assessment and treatment of FI. Since then SNS has become an established treatment in the UK for FI. Further to their previous guidance, NICE Guideline 49 (2007) <sup>1</sup> recommended SNS first line surgical option for people with FI who had failed conservative treatment and for whom sphincter surgery was deemed inappropriate <sup>292</sup>. Certainly in the UK and in Europe, SNS had established itself as the main first line surgical therapy after failure of conservative measures in almost all cases of FI. In the USA the Food and Drug Administration approved its use for the treatment of FI in 2011 after a pivotal US multicenter trial showed good results <sup>256</sup>. In 2010, there were 20 specialist

---

centres providing SNS treatment across the UK <sup>293</sup>. Until more recently, there has not been a viable alternative to this type of therapy.

In these times of financial constraint, those looking for a cheaper, simpler and even less invasive method of delivering neuromodulation championed the use of PTNS in FI. Initial studies found that the success rates were somewhat comparable to SNS and therefore it became another exciting potential treatment for FI. Even today, evidence regarding PTNS is somewhat limited but interest and momentum is gaining. In 2011 NICE brought out guidance on PTNS (Procedure Guidance 395) <sup>294</sup>, which reported the evidence on PTNS for faecal incontinence raised no major safety concerns. There was evidence of efficacy in the short term in a limited number of patients and therefore, PTNS should only be used with special arrangements for clinical governance, consent and audit or research. Similar to SNS guidance they further stated that this procedure should only be carried out in units specialising in the assessment and treatment of faecal incontinence, as one of a range of treatment options.

Despite the increasing use and popularity of these treatments, questions about how and where SNS and PTNS should feature in the treatment algorithm of FI have not been answered. Like other countries, commissioning in the UK has been confusing <sup>294, 295</sup>. The initial draft of the UK commissioning policy included that a trial of PTNS must be undertaken as a requirement before SNS commissioning, although later this

was amended <sup>295</sup>. The current commissioning position of NHS England states that PTNS and/or other conservative measures should have been tried and not yielded adequate continence before SNS can be considered. The RCS commissioning document has been firmer in its commitment to PTNS, publishing an algorithm including PTNS as nurse led therapy to be undertaken before SNS <sup>296</sup>. They advocated the use of SNS as a specialist surgical intervention after these conservative measures had been exhausted.

Conflicting statements from different regulatory bodies prove that there is still uncertainty regarding the role of PTNS as an adjunct prior to SNS or as a viable alternative, and whether the same specialist centres should be offering both treatments or whether PTNS could be undertaken in community settings, making it more accessible. Although the position of PTNS in the FI care pathway remains unclear due to limited evidence <sup>14</sup> offering PTNS as second line treatment may, potentially, reduce the need for SNS treatments.

## **4.2 STUDY 2: QUANTITATIVE OUTCOMES FROM THE EXPLORATORY STUDY**

The results of the randomised exploratory study determined that both treatments provide some short-term patient benefit (manifest in reduction in main symptom frequencies, validated summative symptom scores, as well as disease-specific and

---

generic QoL measures). The pilot design did not allow for direct statistical comparison of SNS and PTNS, however for nearly all outcomes, the within group effect estimates were larger for SNS than PTNS. This was especially true at 6 months, when SNS effects were either maintained or increased compared to 3 month data; in contrast, the effect of PTNS on some clinical and QoL variables appeared to decline at 6 months. The analysis of permanent implanted patients (per protocol) undergoing SNS showed that outcomes were better still than on available case analysis.

The outcomes obtained for SNS were comparable to those in published case series where the denominator used was the number starting treatment at the temporary phase. The systematic review <sup>166</sup> described in Chapter 3 (section 3.1.2), of 61 published series demonstrated a median short-term 'success rate' (based on proportion of patients with a 50% reduction in FIE per week) of 63% (range 33-66%) compared to 61% in the current study. Reported as the proportion of patients undergoing permanent implantation (as has been the fashion for most previous series), our success rate at 6 months was 67% which compares less favourably with published short-term follow-up results of 79% (range 69-83%) <sup>166</sup> from European <sup>230,</sup> <sup>251</sup> and US <sup>256</sup> specialist centres identified by the systematic review. This may be accounted for by several factors including: the use of the temporary (unipolar) rather than tined quadripolar lead for the test phase leading to failure to reproduce outcomes at permanent implantation; patient preference; and more objective

---

recording and interpretation as a result of third party blinded acquisition and analysis of data <sup>297</sup>. However the mean difference in FIE per week (9 episodes per week) and CCIS (7.2 points) on this analysis were in keeping with improvements found in reviewed short term series conducted in this thesis (see Chapter 3, section 3.1): median 7 (range 1 to 13) FIE per week and 9 (range 3 to 15) points respectively <sup>166</sup>. Further, the median CCIS in implanted patients at 6 months reduced below the notional threshold of 10 points which has been considered to equate with improved quality of life <sup>298</sup> (noting the general limitations of such scoring systems including the possibility of scoring 12 points on the CCIS without having incontinence to faeces).

The results for PTNS were disappointing compared to published data found in our review. Based on the same notional measure of 'success' a 6 month positive outcome was achieved in only 47% patients: c.f. 65% (range 59-71%) at review <sup>166</sup>. This cannot be explained by analysis of all available cases, since 16 of 17 recruited patients completed the treatment regime. Changes in raw symptom measures e.g. FIE per week (mean change of -4.3 [CI: -10.5 to 1.9]) and CCIS (-3.2 [-4.8 to -1.5]) were, however, comparable with nearly all previous studies <sup>196, 299</sup>. Changes in FIQL scores were greater for patients receiving SNS than PTNS [Table 3.10]. The FIQL scale <sup>82</sup> defines 4 subscales all of which are calculated from the mean response to specific sets of individual scale items giving a range of 1 to 4 points for each where a score of 1 indicates lowest functional status. PTNS patients had negligible improvements in subscale scores (0.1 to 0.3) at 6 months compared to values of 0.7

---



to 1.1 for SNS patients. The differences with SNS equate almost to those between FI patients and controls in the original validation of the scale<sup>82</sup>. In common with other studies of either therapy, effects on generic QoL measures (SF-36 and EQ-5D) were small for both SNS and PTNS. This finding is consistent with the lack of specificity of these measures to patients with FI<sup>300</sup>.

Results from the health economics analyses suggest that SNS is associated with significantly higher short-term costs compared to PTNS: £12,748 (SD 4,175) versus £2,356 (SD 122). These figure did not include the cost of treatment-specific adverse events, which would be higher for SNS compared to PTNS according to published studies<sup>196, 245, 301, 302</sup>. Published studies have previously evaluated the costs and consequences of treating patients with SNS for FI<sup>213, 218, 241, 243, 259, 302, 303</sup>. These studies from multiple different countries (England, Spain, Italy, France and Switzerland) have concluded that SNS is cost-effective compared to conservative measures when offset by the quality-adjusted life-years (QALY) gained. The associated incremental cost per QALY fell within the threshold range of £20,000 - £30,000 used by NICE, and therefore SNS was considered as a cost-effective treatment for FI. As PTNS is certainly cheaper than SNS (with no overlap in average total costs) with little difference in QALY over 6 months, our results would also suggest that PTNS is a cost effective treatment for FI in the short term.

Despite the exploratory nature of this study and the inadequacies of the presented health economic data, to test the above theory and in keeping with other studies<sup>218, 302-304</sup> there may still be some value in estimating the cost effectiveness between these two therapies. If one was to try to make a decision about which strategy to employ given limited financial resources, there would be a need to compare the cost effectiveness between the two strategies. In actual fact there are three strategies to choose from: (1) conservative management only, (2) SNS after conservative management and (3) PTNS after conservative management. The alternatives to SNS therapy for FI cannot be ignored and therefore these are found to be mutually exclusive strategies<sup>305</sup>. In this setting, the incremental cost effectiveness ratio (ICER) exposes the true cost of more expensive medical interventions<sup>306</sup>. Therefore analysing the cost effectiveness of SNS and PTNS by calculating the ICER between them is appropriate.

Using the in-trial health care resources for the 6 month period, on an intention-to-treat basis, the total costs of the intervention were £2,356 (SD £122) per person for PTNS and £12,748 (SD £4,175) per person for SNS with QALYs of 0.299 (0.170) for PTNS and 0.343 (SD 0.102) for SNS. In the absence of a full trial and longer follow up, we elect to use our own data to extrapolate an ICER. To calculate the ICER between SNS and PTNS, the following formula where SNS is the established strategy can be used:

$$ICER = \frac{Cost_{Strategy\ 1} - Cost_{Strategy\ 2}}{Effect_{Strategy\ 1} - Effect_{Strategy\ 2}}$$

*Strategy 1 = SNS, Strategy 2 = PTNS*

$$ICER = \frac{12,748 - 2,356}{0.343 - 0.299}$$

Calculating the available data, there is an ICER of £236,182 per QALY, more expensive for SNS when compared with PTNS. These results suggest that PTNS is economically dominant.

The small differences in EQ-5D results has led to relatively small changes in QALYs, with an impact on ICER, which was calculated to be higher than previously reported estimate for SNS versus conservative treatment (£25,070 per QALY)<sup>218, 241, 293</sup>. The use of the EQ-5D to calculate the QALY in this study may have further limited our results. In common with other studies of either therapy, the effect on generic QoL (SF-36 and EQ-5D) was small. This finding is consistent with the lack of specificity of these measures to patients with FI<sup>300</sup>. It should be advised that the above calculated ICER using only short term data be viewed with caution.

#### **4.2.1 CRITICAL APPRAISAL OF OTHER SNS AND PTNS COMPARISON STUDIES**

To the authors knowledge, at the time of study inception there were no ongoing studies comparing clinical and/or cost measures between these two neuromodulation therapies for FI. Since then, three studies have been published broadly attempting to compare SNS against PTNS, based on treatment efficacy and cost. Recently Al Asari *et al.*<sup>307</sup> published their results from a single centre non-randomised case controlled study in France concentrating on the comparative clinical effectiveness of the two neuromodulation therapies for FI. From our own centre in the UK, Hotouras *et al.*<sup>308</sup> also described a non randomised prospective audit of FI patients treated with either SNS or PTNS and attempted comparisons of clinical efficacy and costs between groups. The final study from Martinson *et al.*<sup>304</sup> was the first to attempt comparisons of direct healthcare costs and cost effectiveness between SNS and PTNS, using a hypothetical economic model for the treatment of over active bladder. Although the this condition differs from FI, the technical aspects of treatment are similar and thus similar costs may be incurred. We can therefore reasonably extrapolate the comparative costs from this study and consider them for FI. Below we attempt to critically appraise these studies with comparisons to our own work.

#### 4.2.1.1 Clinical outcomes and effectiveness

Clinical effectiveness was evaluated in Al Asari *et al.*'s non-randomised case controlled study of 78 patients with chronic severe FI. The study included 21 patients having PTNS and 57 patients having SNS from a single centre in France. The main outcome measures were the CCIS and FIQL scores at 6 and 12 months post intervention. Their results showed improvements from baseline CCIS, means (SD) for; PTNS 14.9 (2.4) and SNS 14.4 (2.75) to mean post-treatment CCIS at 6 months; PTNS 8.1 (3.2) and SNS 7 (4.8) respectively. Their denoted "success measure" was a  $\geq 50\%$  improvement in CCIS. This was identified at 6 and 12 months in 47% and 30% of PTNS patients and in 50% and 58% of SNS patients. Overall mean FIQL scores at baseline were PTNS 2.1 (0.5) and SNS 2.1 (0.5) improving to PTNS 3.2 (0.6) and SNS 3.1 (0.8) at 6 months.

In this study the results of SNS treatment were similar to the ones presented in this theisi. However, Al Asari's treatment response from PTNS was notably superior to ours. The author's results using the same success measure showed only 19% of PTNS patients gaining a  $\geq 50\%$  improvement in CCIS at 6 months. Looking at mean changes in CCIS, Al Asari's study demonstrated a 6.8 point mean improvement in CCIS in the PTNS group, double that of the curently presented results (an improvement of 3.2 points at 6 months). A difference in treatment protocols meant that Al Asari's patients undertook approx 19 sessions in 6 months where the current study's

patients had only 15 sessions. Although increasing the number of stimulation sessions may have increased the effectiveness of PTNS, it is difficult to tell whether this could have improved the CCIS by more than double. In both studies FIQL scores improved with PTNS and SNS at 6 months in all domains although these results could not be directly compared because we did not feel it appropriate to synthesise the data as average summative scores.

Hotouras *et al.* also attempted to compare clinical outcomes between SNS and PTNS at 3 months using CCIS and FIEs <sup>196</sup>. In their pseudo case matched model: the mean pre-treatment CCIS score (SD) for permanent SNS 14 (4) and PTNS 13 (3) improved to 9 (5) vs. 9 (4); a mean score improvement of 5 points for SNS and 4 points for PTNS. These mean changes were in keeping with the current study's results. In the SNS group, Hotouras *et al.* reported a more impressive median reduction of FIEs of almost double that of PTNS but unexpectedly found that this was not statistically significant ( $p = 0.07$ ). It is felt that due to the limited sample size, this statistical calculation must be treated with caution. Given the results from both studies SNS seems more effective for patients with higher number of baseline FIEs. Hotouras *et al.* did not describe any QoL measures or denotations of success in their analysis.

As both Al Asari's and Hotouras' studies were not blinded or randomised, the effect of substantial selection bias was a concern. There was no mention as to why or how patients were stratified to receive either PTNS or SNS in either study. From the

---

presented qualitative study results, patient preference and expectations of therapy can have a large impact on the effect of treatment. Furthermore the article authors themselves felt that the patient samples included were small and the follow-up times short. In both studies the SNS analysis was only conducted on a per-protocol (PP) basis and therefore no ITT analysis (or equivalent) was attempted. In Al Asari's study four patients (28%) shifted from PTNS to SNS during the course of the study. A description of their course of treatment was included but how this affected the analysis was not clear.

#### **4.2.1.2 Cost effectiveness of SNS vs. PTNS**

Although it is strongly suspected that PTNS is an altogether cheaper intervention than SNS, there have not been any authoritative studies comparing the cost effectiveness between the two therapies for FI. The costs of PTNS are less well established compared to SNS, however from the current literature direct medical costs would be expected to be reduced, if PTNS replaced SNS, by an estimated £9,787 (£11,594 SNS to £1,807 PTNS <sup>179, 265</sup>). This would clearly have major cost implications in respect of the £3.7 million spent on SNS implementation in the UK.

Martinson *et al.*'s single institution study involved a simulated cost-effectiveness analysis using a Markov model to compare the cost-effectiveness of PTNS and SNS as second line therapies for overactive bladder from the perspective of the health

---

care payer. The simulation modelled a 2 year period using available outcome measures from previously published data<sup>309</sup>. Similar to our study, uncertainties on probability variables and cost variables were varied in 1 and 2-way sensitivity analysis, varied at half the rate estimated from the literature and also at twice the rate. Costs were varied from the minimum Medicare payment in the United States to the maximum.

They calculated that for PTNS, the costs of initial therapy were \$1,773 (approx £1,171) for 12 weekly percutaneous tibial nerve stimulation treatments and \$1,857 (approx £1,226) for PNE. For ongoing therapy the cost of the SNS implant was \$22,970 (approx £15,167). Effectiveness was measured as the percent of patients still on therapy at a given time. Effectiveness rates were therefore 48% for PTNS and 49% for SNS, respectively, at 2 years. From the model, the incremental cost-effectiveness ratio (ICER) was \$573,000 (approx £378,343) per additional patient on sacral nerve stimulation over 2 years (therefore £189,171 per year). This figure is congruent with our own study data, predicting an ICER for SNS vs. PTNS to be £236,182 more expensive for SNS per QALY gained, using an all available case analysis. When considering a PP analysis, Martinson *et al.* demonstrated the costs were \$24,342 (approx £16,072) and \$4,867 (approx £3,211) for SNS and PTNS respectively with an ICER of \$99,872 (approx £65,944).



Base costs increased with time, primarily due to the accumulating costs of therapy sessions for PTNS, and for adverse events and explantation with SNS. When the number of PTNS treatments per month was varied from 0.5 to 2 during ongoing therapy, ICERs were \$639,333 (approx. £422,142) and \$516,667 (approx. £341,147), respectively. Using sensitivity analyses, when PTNS was at its lowest predicted value of 34% success and SNS was at its high value of 78% success, the cost difference was greater by only \$16,400 (approx. £10,828). Thus, the cost-effectiveness of SNS was more favourable at an ICER of \$35,900 (23,704) per additional patient on SNS. This suggests that to become a cost effective treatment over PTNS, SNS would have to be at least twice as effective as PTNS.

One key criticism of Martinson's study is their choice of effectiveness outcome, presented as the percentage of patients continuing treatment. Despite good rates of compliance, patients may choose to continue therapy without having any real benefit in symptoms. This has been found to occur in SNS patients previously (approximately 33% of patients with a permanent implant<sup>310</sup>). However PTNS patients may also want to continue ineffective therapy because they want to avoid surgery.

The limitations of Hotouras *et al.* study design have been previously discussed, but the cost analysis also demonstrated several limitations. Only initial direct healthcare costs were analysed with a cost difference shown of treating a patient for 1 year of

---

£11 374 (\$18 223) for permanent SNS vs. £1740 (\$2784) for PTNS. It may be considered that some of the costs had been neglected without mention of: ad hoc phone calls, extra clinic appointments, GP appointments or hospitalisation in relation to these interventions which could add to NHS costs. Although there was an attempt to extrapolate these costs to ten years by multiplication and itemised hypothetical costing, there does not seem to be any economic modelling to include alternative decision making pathways, analysis of treatment failures or adverse events leading to other therapies or surgical revision. There was no mention of patient drop outs, patients changing treatments, patients not wishing to undergo a battery change which would all have consequent costs implications. Indeed no comparative cost effectiveness analysis were performed, only descriptions of "up-front" costs of each procedure. This is a simplistic attempt at costing and is at best a financial audit of one units operational costs rather than a reproducible cost analysis for the whole NHS.

#### **4.3 STUDY 3: QUALITATIVE OUTCOMES - EXPERIENCES AND ACCEPTABILITY OF SNS AND PTNS**

The experiences of both SNS and PTNS could be demonstrated through the three super-ordinate themes of: the acceptability of the therapy, results of therapy and psychological support that were found to be correlating features of both therapies.

---

#### **4.3.1 ACCEPTABILITY OF THERAPY**

In both therapies the author was able to categorise the open codes into physical, social and economical and emotional sub-ordinate themes. In general both treatments had very high physical acceptability levels which were largely equivalent. As SNS was undertaken as a day-case operation, all participants tolerated it well. Our PTNS participants described their therapy to be very simple and easy to undertake. Both groups of patients enjoyed having control over their therapy, allowing them to set their own stimulation parameters. It is possible that this gave them the first sense of control over the disease. Many of the patients felt validated in coming to hospital for treatments and preferred these treatments to previous therapies tried. Both groups did mention some stimulation discomfort either from the needle or sacral electrode causing aching or pain in leg or foot. This was most often well tolerated and self-limiting and did not dampen the enthusiasm for either treatment.

In both groups the social and economic burden of treatments were considerable. Most of our participants did not live nearby to the hospital which made appointments inconvenient. Many had to travel for one to two hours on the train to reach the hospital and some had to request time off from work because of hospital appointments. In both groups our participants had quite a considerable number of hospital appointments either for the treatments directly or for peri-operative care.

They expressed a wish for these services to be conducted at local hospitals and GP practices. Interestingly when asked if they would have self-administered treatments in their own homes, they felt this may be inappropriate and that the treatment should be undertaken in a professional environment supported by appropriately expert staff. Both sets of participants were pleased with the discreetness of the therapies especially with the implant. In the SNS group, one particular concern was the ability to travel through the security terminals without commotion. Those who had already experienced foreign travel had not found this to be problematic. Emotionally all participants felt well supported and prepared for their treatments; mainly put this down to the kindness, attentiveness and professionalism of all the staff involved in the process. Two of the patient's in the SNS group admitted that they had been scared of the operation and had delayed the therapy for a short time. Once they had undertaken their procedure they were pleased that they had done so.

#### **4.3.2 RESULTS OF THERAPY**

In this super-ordinate theme there were some marked differences between the accounts of those undergoing SNS and those having PTNS. Regardless of this it must be kept in mind that one of the SNS candidates did not complete her therapy because of a lack of effect, also declining to participate in a follow up interview to discuss her therapy. Although there is no firm evidence, it can only be hypothesised

---

that her experience of the therapy was not a positive one and her account would have significantly changed the dynamics of this study. From the four remaining participants who underwent SNS, there were extremely positive reflections on the improvements in their condition. They described stark results with impressive improvements in both leakage and urgency symptoms. They felt that SNS had yielded much better results than other previous therapies and became much more optimistic about their lives, explaining that their experience of the treatment had resulted in improved self-confidence and self-esteem. The participants also expressed some negative feelings on still not having a cure for the disease but overall they were pleased with the results of their treatment. The PTNS participants in general also found their treatment was effective but the change was more subtle when compared to the accounts of SNS. In some PTNS cases, symptoms had improved marginally but this led to a larger impact on QoL. In other cases it was difficult for our participants to separate the positive effects of PTNS from other lifestyle or dietary changes. A proportion of participants in the PTNS group did not find that the treatment had improved their symptoms at all and therefore it had not meet their expectations. Although this was disappointing, this was still acceptable because of the ease of having the treatment. Many thought that PTNS was a good initial stage treatment but considered that they may have had more benefit from an implanted device. This was an interesting conclusion from our PTNS participants as we had always maintained that the effectiveness of both therapies was equivalent.

#### **4.3.3 PSYCHOLOGICAL IMPACT**

Along with both SNS and PTNS therapies, the study participants found psychological and emotional support through participating in the process of seeking and undertaking treatment for their condition. They felt an understanding and support network from the healthcare professionals at the specialist hospitals and appreciated that this had aided improvements in the psychological aspects of their disease. They felt validated in their condition and gained hope that there were treatments that could improve their condition. Overall self-confidence improved in both groups although in the PTNS group our participants felt this was more overtly due to support provided by the service rather than just the effects of the treatment. It can be hypothesised that the human interaction of healthcare professions was much greater during the treatment of the PTNS group as there were many more treatment sessions. Despite reporting improvements in symptoms, participants also found old habits of wearing pads and checking for toilets difficult to break. Again the use of these 'emotional crutches' were less evident in the SNS group. In both groups, participants found that intimate relationships were most difficult to re-establish even if they felt more confident about themselves. This may be because in those circumstances they were most likely to give up control of their bodies and any incontinence episodes would be seen as a major setback in their progress.

#### **4.3.4 COMPARISONS WITH OTHER NOVEL QUALITATIVE STUDIES**

The data regarding both SNS and PTNS for FI currently exists only as quantitative measures focussing on quantifying success<sup>284, 311</sup>. Qualitative research has already been used to inform therapeutic outcomes in other surgical disciplines<sup>312</sup> but as yet, has not been widely adopted in the surgical field of FI treatment. The taboo subject of FI and its treatments lends itself well to personal analysis and investigation into the patient's psychological, physical and social well-being<sup>78</sup>. Previously Cotterill *et al.* had demonstrated that a patient centred approach was fundamental for understanding the true nature of these issues which are poorly explored by quantitative measures alone<sup>78</sup>. Issues regarding FI as a condition have been explored through qualitative analysis in a few studies previously<sup>78, 313-319</sup>. None have yet looked at the psychological and emotional implications of the results of therapies in a qualitative way.

To the author's knowledge, this is the only study that has attempted to compare two treatments for FI in a qualitative way. Ultimately the aim of treatment is for the patients to gain freedom, control and feel normal again. Rasmussen<sup>319</sup> claimed that the health of a human being depended on whether he/she had a 'repertoire', i.e. a capacity to reduce the divergence between the actual and the ideal ego. Even though neither treatment was seen as a cure, our participants' improved control

over FI decreased the distance between their actual and ideal egos. The treatment bringing them closest to attaining their targets was the one subjectively identified to be most successful.

Two published studies have investigated the aspects of treatment which seem most important to patients living with FI. The first study by Manthey *et al.*<sup>320</sup> used semi-structured interviews in 189 subjects and the method of content analysis to code and theme data. The findings of Manthey's study suggest that even when complete continence of stool may not be possible, individuals could identify goals of management that were important to them. The study showed that patients with FI have numerous management goals with the most important ones being: decreases in liquid consistency, decrease frequency of stool leaks and having greater confidence in controlling FI. A further study by Cichowski *et al.*<sup>321</sup> conducted focus group discussions with 11 women on non-surgical treatments. The data was analysed using the constructivist, grounded theory methodology and revealed 12 themes: embarrassment, worry, ability to do things that you enjoy, effect on lifestyle, smell, no treatment recommendations from physicians, wanting to be/feel healthy, will to get better, desire to get better, personal effort, hope, and living life.

Interestingly these two studies highlighted themes that were also important for our own participants. The subjects in Manthey's study mainly focused on the physical results of treatment. They described the top priority for successful treatment as

---



being "a decrease in the frequency of leakage and having more confidence in controlling FI". Participants in both of our treatment groups gained positive results with concerns to these physical issues although this seemed to be achieved to a greater degree in the SNS group. Once our patients felt that the amount of leakage and frequency of incontinence episodes had improved significantly, as a secondary phenomenon we found that their other measures to disguise or protect themselves from accidents were being used less often.

Chicowki's study highlighted psychological themes that his subjects had been concerned about. These were very similar to our own theme of psychological support. In Chicowki's overarching themes, his patient's wanted doctors to communicate hope, to tell them to continue to live their lives and to advise them on personal coping strategies. Concerning these issues PTNS treatment seems to have provided greater support which we could attribute to the longer human contact between the healthcare workers and the patient's. This highlights the importance to the patients of well trained, knowledgeable and empathetic staff. This adds further weight to the suggestion patients may prefer to attend outpatient clinics rather than to have self-administered treatment at home.

## **4.4 LIMITATIONS**

### **4.4.1 LIMITATIONS OF THE SYSTEMATIC REVIEW**

#### **4.4.1.1 Intention-to-treat analysis**

To be able to compare differing modalities of treatment adequately, it is crucial that there is parity in the way outcomes are measured. Most previously reported SNS data were assessed on a per-protocol basis including only patients already responding to a successful PNE. The per-protocol approach uses PNE as a diagnostic test to identify patients who may benefit from permanent stimulation and may also be used to identify potential new indications for treatment. An alternate analysis uses ITT, which considers the PNE phase as part of the treatment. The success of PNE itself is variable, with an approximate 25% failure rate<sup>262</sup> and therefore impacts upon the ITT analysis. Failure of PNE may be due to several factors: 1) technical issues, 2) patient selection: especially in the early phase of the evolution of SNS when new indications were explored 3) issues related to the monitoring of the clinical effect or 4) patients' own preferences for implantation. Centres who have reported a higher drop out from temporary testing to permanent SNS will have a lower overall success rate. As an example, in Govaert's study of 245 patients<sup>248</sup> who underwent SNS testing, the success rate of permanent SNS at an average of 35

---

months on a per protocol basis was 77%. If results from the same cohort are based on ITT, because of a 29% failure at the testing phase, the overall success rate decreases to 53%. Although both ways of assessment are meaningful, other treatments do not have an evaluation phase, so it is not possible to compare them to SNS using existing data; rather, to be an effective comparator, the success of SNS must be presented on an ITT basis. This was calculated where possible from the reported number of patients undergoing PNE.

#### **4.4.1.2 Review methods**

We acknowledge that there were methodological limitations to conducting this systematic review. The most obvious being study heterogeneity in relation to data collection and method of analysis. Some studies reported average outcomes for a whole cohort with an average follow-up period whereas others reported outcomes at specific time points. The heterogeneity of reported outcomes (some reporting means and some medians) and the wide variety of reporting styles made statistical formal synthesis impossible. We acknowledge also that the evidence base was poor (especially for PTNS and TTNS), mostly made up of case series with low patient numbers and only short-term follow-up. Even when long-term follow-up was available for SNS there was an approximately 25% drop out rate to follow-up. A selection bias could not be excluded, as it is possible that patients with the longest follow-up maintained the most treatment benefits and therefore remained keen to

---

be included in their respective studies. Regrettably on detailed evaluation of these long-term series, none have used strategies such as 1) the last observation carried forward or 2) worse case scenarios (considering missing data as failures) to represent any data loss, avoiding this potential bias.

The paucity of randomised controlled trial data has deterred us from attempting to summarise the data using the meta-analysis method. We note that this has been attempted before using baseline data as a comparator to treatment<sup>192</sup>. Uncertainty concerning the validity of using baseline data as treatment controls led us to provide only summary variables as median and range data. Along with this it was difficult to ascertain if large cohorts from the same centres contained duplicate series which had already been previously reported. We have attempted to minimise this by separating each series into different follow-up terms (short, medium and long) therefore expecting a minimal amount of repetitive data within each category.

#### **4.4.1.3 Safety data review**

The remit of the original systematic review presented in this thesis was to detect the true clinical effectiveness of SNS and PTNS with the most current published evidence at the time. The safety profile had previously been highlighted in a systematic review<sup>188</sup> as an important issue regarding SNS and therefore this was not repeated in thesis. However it is important to comment on suboptimal therapeutic effects

---

and complications following SNS especially as Maeda et al. found that there was significant underreporting of complications throughout the literature<sup>188</sup>. Out of 94 articles included in the review only 48 were identified as studies reporting on adverse events and suboptimal outcomes. From Maeda et al.'s review it was determined that during PNE, there was an adverse event rate of 6.3% with the most commonly reported event being lead displacement in 5.3% of patients<sup>188</sup>. The incidence of suboptimal therapeutic response was identified in 12.1% of the pooled data. The most common attributed causes were problems relating to the implant lead displacement or mechanical damage. Thirteen percent of patients reported pain around the stimulator site, attributed to haematoma, device protrusion and suboptimal programming. Management was usually analgesia, repositioning of the stimulator, reprogramming and explantation of the device. The incidence of infective complications was 3.9%. Other complications included lead displacement, dislodgement, dislocation, migration or fracture. This often necessitated reoperation of explantation. Other less frequent complications sited included perineal, leg and foot pain. Complications associated with the existence of the device and surgical techniques such as skin erosion, hematoma, cellulitis, local allergic reaction, and seroma and wound dehiscence have been reported<sup>188</sup>. Functional adverse effects from stimulation included constipation and urinary retention that required deactivation during defecation and urination, sleep disturbance that required switching off the stimulation during the night time, and increased sexual drive. There is also a report that a patient reported the sensation of minor electric shock

when passing through an ambient electric or magnetic field <sup>188</sup>. In a more recent publications the surgical revision rate in SNS patients has been shown to be around 20% <sup>322, 323</sup>.

Although the safety profile of PTNS treatment has not been systematically reviewed, the largest recent study demonstrated that there were only 7 related adverse events and another out of 43 possibly related adverse effects from PTNS treatment in 107 patients having weekly PTNS treatments for 12 weeks <sup>324</sup>. All adverse events were minor and resolved with little or no intervention. No PTNS interventions were withheld or stopped during the study <sup>324</sup>. Although PTNS does seem advantageous in relation to its safety profile, it is important to note that SNS complications tend to occur in the medium and long term for which the safety profile of PTNS has yet to be studied.

#### **4.4.2 LIMITATIONS OF THE QUANTITATIVE AND QUALITATIVE EXPLORATORY STUDIES**

As the two prospective studies were devised to run in parallel and from the same pool of recruited patients, the limitations of the studies are generally shared by their design. Therefore the limitations of both studies have been discussed together.

#### **4.4.2.1 Small sample size**

The limitations of the exploratory RCT study are implicit in its pilot design and small number of recruits. As designed, the number of recruits reflect a compromise between a meaningful sample size for data analysis and the feasibility of project completion within the elected 24 month period. The calculations behind the sample size for this study have already been discussed within Chapter 2 (section 2.9.2.4). The author is aware that as a pilot, the small number of participants did not allow statistical comparisons between groups to be made which limits the informative nature of the outcomes measured.

Even with this small sample size there were challenges to recruitment. As mentioned in Chapter 2 (section 2.9.2.1) individual Primary Care Trust (PCT) funding approvals were required prior to SNS therapy. Our inclusion criteria ensured that every recruited participant was equally eligible for either SNS or PTNS and therefore all 40 patients had funding approved (for SNS) before randomisation. These individual funding requests were often complex and time consuming requiring the PCT to convene and discuss authorisation on an individual case basis. Midway through the recruitment process, some of the local PCTs could not afford to maintain their support for SNS. This made the recruitment of patients from our own trust very difficult. As a solution we decided to enlist the aid of another hospital

(University College Hospital, London) with the requisite expertise in neuromodulation. The expansion of the trial allowed us to recruit the required amount of patients to cost and schedule. Our detailed protocol ensured that all aspects of the trial were conducted in a standardised manner. Another difficulty that arose was that many patients that were otherwise eligible to have either procedure did not want to be randomised to an intervention. Often FI patients are well informed and have strong views as to which therapy they can commit to. As has been discussed within the qualitative interviews, patients personal circumstances often guide patients to one treatment over another.

With respects to the qualitative aspect of the study; in contrast to quantitative research, a “small” sample size is typical of the nature of this work and sampling is stopped when “a thorough understanding of the phenomenon studied has been reached” <sup>206</sup>. While the number of patients having interviews was purposely less than the whole (10 of 40 patients), this is usual in qualitative research <sup>325</sup>, the sample chosen was considered adequate based on qualitative methods literature <sup>325</sup>. Our study indeed achieved data saturation and determined by the clinical research fellow and Senior Supervisor Professor Stephanie Taylor (Professor in Public Health and Primary Care) who reviewed all the transcripts iteratively, the findings are described in Chapter 3 (section 3.3). Although this study was informative, the small number of participants limited the generalisation of results. However, it did fulfil its aim as an insight into the minutiae of the participants’

---



experiences, adding a new dimension to the understanding of those who are treated for FI.

#### **4.4.2.2 Sample population**

Due to our selected sample, the trial results may not have been truly representative for the general population of FI sufferers. Having been recruited from tertiary hospitals with a special interest in FI, our participants were all well motivated and had made conscious decisions to seek further investigation and treatment. All of our participants had already experienced treatment with conservative measures and therefore were deemed to have sufficiently severe FI to warrant NM therapy. This exposed the study to a degree of self-selection bias. When compared to others with less severe FI, it is likely that our patient sample had a greater knowledge of treatment options and furthermore, their expectations, views and perceptions of care may have differed significantly. Incidentally all the participants in the qualitative study were female. Out of 40 available recruits, there was only one male participant (who had SNS). He was approached to partake in the qualitative study but unfortunately he declined because of personal time constraints. We can only speculate whether the result would have been different if more men had participated in this study. We may also wonder whether men and women deal with their medical conditions in different ways. It may be hypothesised that women put a

heavier emotional emphasis on the effects of their condition; consequently benefitting more from the counselling aspects of therapy.

#### **4.4.2.3 Short follow up period**

We accept that the short follow-up interval, due primarily to resource constraints, also present a significant limitation. A longer follow-up interval of one year and ideally two years, even for a pilot study, would have been preferable. FI is a chronic disease and the interest in terms of clinical outcomes and cost are in the medium and long term. The durability of these treatments is extremely important and the long-term clinical and cost effectiveness including adverse events and treatment compliance rates, are still to be determined. The effects of long-term PTNS are unknown, and although unlikely, it is unclear whether there are any associated chronic adverse effects. Furthermore, it is not known how many patients having PTNS ultimately go on to have SNS therapy and whether there is a cost burden or benefit from delaying this process.

#### **4.4.2.4 Limited economic analysis**

Considering the above limitations and exploratory design of this study, the appropriateness of a cost effectiveness analysis, rather than the cost utility presented in the results (Chapter 3, section 3.2.3) can be questioned. It is already

---

known that the cost of SNS seems to be greatest up-front (discussed in Chapter 1, section 1.8) and therefore, in a short-term study there is a large bias favouring PTNS. Admittedly like almost all other economic studies on FI interventions, we only collected short-term direct health care costs from the view point of the NHS. Although an assessment of indirect costs has not been performed, it could be hypothesised that the societal costs with PTNS are greater over the long-term; due to requirements for repeated hospital attendances and an overall more modest effect. In a fully powered study, direct and indirect costs from the patients perspective (transportation, loss of earnings) and unit costs of protective measures (incontinence pads and clothing etc bought by the patient) should be collected.

Cost-effectiveness ratios between treatments should be measured over a time frame which can determine loss of efficacy of treatment with time and also for any cost of additional interventions that may be required due to complications or drop outs. From other studies it is likely that SNS patients will develop some complication lead (displacement, simulator re-setting and changing the battery) during the first year of treatment and also in subsequent years<sup>260, 326</sup>. Ideally a full scale analysis should be performed over a seven-year window, this being roughly equivalent to the time that the average InterStim implant battery lasts. If medium-term data had been collected then modelling the predicted outcome of the two therapies would be appropriate. In the long-term, PTNS patients would require top-up sessions at least every 6 months and therefore additional outpatient appointments. However, these

visits may be partially offset by 6 to 12 month review appointments of SNS patients for auditing purposes recommended by NICE for the management of patients with FI<sup>87</sup>.

Further criticism could be targeted towards the reproducible application of our data for those outside the UK. As this study was funded by the NHS, the health economic evaluation was conducted from its perspective. However this data would also be relevant for other countries with public funded single-payer healthcare systems such as Canada, Norway, and Taiwan and indeed the itemised cost could be useful in all countries.

#### **4.4.2.5 Lack of placebo control**

Another limitation of this trial, was the lack of a placebo comparison arm. The placebo effect of NM treatments has been an ongoing concern for many because the true mechanism of NM treatment has not yet been consistently identified. In this randomised trial, it would almost be impossible to design a plausible placebo control arm that would faithfully recreate a sham stimulus, comparable with both techniques. Although SNS is now well-established as an effective therapy for FI, patient trials of this treatment vs. placebo are limited to short-term cross-over studies<sup>168, 327</sup>. Furthermore, the use of 'stimulator off' as a placebo is questionable since described 'subsensory' stimulation is in reality still usually perceivable in most

---

patients. In addition, there has been only one trial to date of SNS vs. a comparator (optimal medical treatment) <sup>169</sup>. However, the long-term positive effects of SNS, with data more than 10 years has also shown sustained improvements in FI with the system <sup>197, 268, 328</sup>. This would suggest that SNS does not work through a placebo effect. Sham studies for PTNS have been designed and undertaken in the urological literature by Peters *et al.* <sup>329</sup> and these have demonstrated that PTNS is more effective than sham. A UK multicentre randomised controlled trial: CONFIDeNT has just been completed which aimed to address this knowledge gap in FI; published results are still pending. In our parallel arm study design we used SNS (current established therapy), as a positive control for the evaluation of PTNS. As long-term effectiveness data for PTNS is not available, at this present time a substantial placebo effect cannot be excluded. From the qualitative study, our participants did identify a psychological effect from undertaking treatments. Even the process of obtaining treatment and interaction with staff within treatment sessions provided substantial positive psychological effects. As the number of treatment sessions and therefore personal interaction with PTNS was greater, it could be hypothesised that PTNS could provide a greater placebo effect. Long-term effectiveness data for PTNS in addition to the results of CONFIDeNT will be pivotal in assessing the magnitude of any such placebo effect.

#### 4.4.2.6 Lack of investigation into mechanisms of action

It was beyond the scope of this thesis to identify possible mechanisms of action for either SNS or PTNS. It was also felt that the patients in the study would not benefit from the burden of extra hospital attendances and repeated invasive anorectal assessment. Although baseline physiology tests were performed (Table 3.07), available resources were limited and repeated anorectal physiology tests on these patients after therapy was not undertaken. In fact during the period of the project the anorectal manometry testing facilities changed from a standard water perfused pull through system to high resolution manometry using a solid-state probe. As discussed previously (Chapter 1 section 1.6.3.1) these different methods of assessment could not reliably be calibrated against each other and therefore pre- and post-intervention changes would not have been accurately detected.

Reviewing the literature on both SNS and PTNS mechanisms of action<sup>173, 271, 330-332</sup>, there have been no widely reproducible changes in anorectal physiology/neurophysiology in humans to support a particular or even a shared mechanism of action for SNS or PTNS. Most of the hypothesised mechanisms of NM therapies have been deduced from the studies of SNS<sup>214, 220, 279, 333-337</sup>. The exact mechanism of SNS's effects are uncertain, as there is a discrepancy between symptom-improvement and the relatively minor changes on easily measurable anorectal function<sup>338, 339</sup>. Recent data suggest that SNS, but not sham stimulation,

---

increased the frequency of retrograde propagated sequences throughout the colon. In contrast, SNS increased colonic propagating sequences in constipation<sup>340</sup>. Perhaps differences in baseline colonic motor activity partly explain why SNS may have different effects on colonic motility in constipation and FI but this seems counter-intuitive. While SNS has no consistent effect on basic anal motor functions (contractile force)<sup>339</sup>, some FI patients may have reduced rectal sensation which is rapidly restored after SNS<sup>341</sup>. Several studies now indicate modulation of afferent functions including effects on ano- and recto-cortical signalling<sup>342, 343</sup>. It is also likely that SNS modulates the afferent limb of local and spinal reflexes that participate in transient anal sphincter relaxations (TASRs), anal sampling and rectal emptying akin to those observed in bladder and urethral functioning<sup>344</sup>.

#### **4.4.2.7 Limitation of available outcome measures**

The planning of investigations and subsequent treatment requires a judgment on the severity of incontinence. To provide objective assessment, most previous studies have employed the use of a combination of either FI bowel diaries (usually over a 2 or 3 week period), symptom severity score/indices and/or quality of life measures (either symptom specific or global).

***Faecal incontinence bowel diaries***

With self completed FI diaries, patients record the number of controlled defaecation episodes, urgent FI episodes, passive FI episodes and use of pads per day (see Appendix i). Despite the popular utilisation of this assessment instrument there has been criticism of its usefulness. Individual FI episodes can be difficult to categorise and measure discretely. Standardising definitions such as the subtle differences between episodes of passive incontinence and soiling can depend on patient's interpretation, expectation and judgement<sup>186</sup>. In fact, even unconscious behavioural modification can greatly influence diary recordings. As a simple example, patients who stay close to a toilet or avoid leaving home can reduce the frequency of incontinence episodes despite having no real improvement in symptoms<sup>186</sup>. It can also be considered that the accuracy of self recorded data entry may not always be optimal, as paper diaries can be damaged/lost and data entered retrospectively/incompletely before submission.

Despite their limitations, patient completed bowel diaries are still widely used both clinically and in the research setting. Of possible outcomes, the most frequently used and probably least affected by subjective reporting differences is the number of FIE per unit time (usually per week). This outcome, obtained directly from the mean of 2 or 3 week bowel diary frequencies has been employed in almost all contemporary studies of FI interventions including recent SNS studies<sup>167-169, 171, 218, 230, 237, 241, 345</sup>. The problem with this variable is that, being a count, it has a Poisson



distribution and is over-dispersed i.e. has greater variability than expected. This raises major difficulties in defining a clinically significant mean reduction in FIE within a population of patients with widely dispersed starting FI frequencies. To counter this problem, contemporary studies have adopted a primary outcome for "success" using a categorical measure of percentage reductions i.e. the proportion of patients who have a 50% or greater reduction in FIE per week<sup>167-169, 171, 218, 230, 237, 241, 345</sup>. The most accepted criterion for "successful treatment" has previously been defined as a greater than 50% improvement in the number of FI episodes per week<sup>164</sup>.

The principal use of this outcome measure is at the PNE stage to identify patients, in whom continence is adequately controlled and might therefore benefit from an implanted neurostimulator for chronic treatment (accepting the expense and limitations of a permanent implant). This criterion has been taken as received wisdom, born from the urology literature from which much of SNS FI methodology has been developed. Because of the life altering consequences and expense of a permanent implant, it is necessary to carefully select patients in whom continence is adequately controlled and can gain lasting benefit from a second stage operation.

As demonstrated from the systematic review findings, there is still an approximately 20% [Table 3.03] medium to long term failure rate, i.e. those unable to maintain the original PNE effectiveness (>50% improvement in FIE) with their permanent

---

implantation. With this consideration the 50% improvement criteria, based on objective measurements, may give a false evaluation of the success of therapy. In addition, patients with severe incontinence who obtain a “successful” reduction in incontinent episodes may continue to experience incontinence at a level that continues to impair social functioning and quality of life<sup>186</sup>.

### ***Faecal incontinence severity scores***

To overcome the problems with subjective self reporting, many have developed and employed FI symptom grading instruments to provide objective measures of FI severity. A universally agreed upon standard scoring/grading system does not exist. Authors have often devised their own systems in an effort to describe baseline patient symptomatology before and after interventions. These classification systems are numerous and diverse. Many are not validated and have been used only by the author who devised them. Therefore reproducibility across clinicians, patients, procedures and treatments remains unknown. Many of the grading/scoring systems recorded in the current literature suffer from a variety of shortcomings including: a lack of objectivity, being descriptive in nature<sup>346, 347</sup>, using objective parameters such as anal manometry or difficult to classify subjective parameters<sup>348</sup> which often do not correlate with clinical conditions, or do not account for frequency of the incontinent episodes in individual patients<sup>349, 350</sup>. Several anal incontinence grading or scoring systems have been prospectively developed and tested.

The simplest scale method was initially presented by Browning and Parks in 1983 (Table 4.01)<sup>130</sup>. This scale includes four main categories in which the lowest grade is normal continence and the highest is total incontinence: it was originally used to assess the success (or otherwise) of a posterior Parks' anal sphincter repair. The Parks' scale, whilst easy to use and remember, had several major shortcomings as it did not address symptom severity or the frequency of incontinence episodes.

**Table 4.01:** Browning and Parks' incontinence scale

Grade	Severity of incontinence
I	Normal continence (i.e. continent for solids, liquid stools and flatus)
II	Continent for solid and liquid stools but not for flatus
III	Continent for solid stools only. Usually presented with faecal leakage
IV	Complete incontinence

Later scoring systems have added more relevant parameters pertaining to severity of incontinence. Currently four FI instruments - Cleveland Clinic Incontinence Score (CCIS)<sup>191</sup> [Table 4.02], St Marks (Vaizey)<sup>351</sup> [Table 4.03], Pescatori Anal Incontinence Score<sup>352</sup> [Table 4.04] and the Faecal Incontinence Severity Index (FISI)<sup>353</sup> [Table 4.05] - are the most established and are commonly used in clinical studies to rate the severity of FI<sup>11, 354, 355</sup>. All these scales for rating the severity of FI incorporate the type and frequency of leakage.

**Table 4.02:** Cleveland Clinic incontinence score

Type of incontinence	Frequency				
	Never	Rarely	Sometimes	Usually	Always
Solid	0	1	2	3	4
Liquid	0	1	2	3	4
Gas	0	1	2	3	4
Wears pads	0	1	2	3	4
Lifestyle alteration	0	1	2	3	4

0, perfect continence, 20, complete incontinence

Never, 0; rarely, <1/month; sometimes, <1/week and >1/month; usually, <1/day and >1/week; always, >1/day

Perhaps the most widely used scale or grading system is the CCIS developed by Jorge and Wexner<sup>191</sup>. This was the first system to account for the use of pads, changes or alterations to lifestyle, consistency and frequency of incontinence. The CCIS is derived from numerical values assigned to the frequency of occurrence (scored 0-4) in each of several categories including type of incontinence (solid, liquid, gas), pad use, and lifestyle alteration. A minimum score of 0 indicates perfect continence, and a maximum score of 20 indicates complete incontinence [Table 4.02]. Each of the incontinence presentations is graded equally in this scoring system and no psychometric items are included, other than the non-specific 'Lifestyle Alterations' item.

Criticisms of the CCIS may be that it does not take specific account of faecal urgency, even in the absence of specific incontinence episodes, nor of the importance of the use of a pad in terms of continence, which are both given equal weighting. Pad use

may also reflect urinary incontinence or patients' hygienic concerns, independently of episodes of incontinence; further, it does not assess the use of specific anti-diarrhoeal medications. These deficiencies are addressed in the St. Mark's (Vaizey) score, published in 1999 <sup>351</sup>, is also commonly used in clinical studies and reports and was based on the CCIS but added two further items for assessment: the use of constipating medication and the presence of faecal urgency. The relative weighting of pad (or anal plug) use was decreased in this score, where the designers felt that such use may represent more the subjective fear of social embarrassment, rather than actual frequency. This revised score was validated against clinical expert assessment in the primary evaluation as well as in estimations of therapeutic efficacy and in pre- and post-surgical assessments [Table 4.03].

**Table 4.03:** The St. Marks (Vaizey) incontinence score

Type of incontinence	Frequency				
	Never	Rarely	Sometimes	Usually	Always
Solid	0	1	2	3	4
Liquid	0	1	2	3	4
Gas	0	1	2	3	4
Lifestyle alteration	0	1	2	3	4
				No	Yes
Need to wear a pad or plug				0	2
Taking constipating medicines				0	2
Lack of ability to defer defecation for 15 minutes				0	4

Never = no episodes in the past four weeks; Rarely = 1 episode in the past four weeks; Sometimes =>1 episode in the past four weeks but <1 a week; Usually = 1 or more episodes a week but <1 a day;

Always = 1 or more episodes a day.

Add one score from each row.

Minimum score is 0 = perfect continence; maximum score is 24 = totally incontinent.

The Pescatori Anal Incontinence (AI) score <sup>352</sup> [Table 4.04] is another grading system widely used throughout Italy and also combines both degree of incontinence (flatus–mucus/liquid stool/solid stool) with frequency. Incontinence ratings of A, B and C indicate AI for flatus/mucus, liquid stool, and solid stool, respectively; frequency scores of 1, 2 and 3 indicate occasional, weekly, and daily AI. A score of zero is given for normal continence. The combined score is the sum of the degree and the frequency (e.g. A3 = 1 + 3 = 4; C2 = 3 + 2 = 5). The minimum score is 0 and the maximum score is C3 (= 6).

**Table 4.04:** The Pescatori incontinence score

Degree		Frequency	
A	Incontinence for flatus/mucous	Less than once a week	1
		At least once a week	2
		Every day	3
B	Incontinence for liquid stool	Less than once a week	1
		At least once a week	2
		Every day	3
C	Incontinence for solid stool	Less than once a week	1
		At least once a week	2
		Every day	3

Anal Incontinence (AI) score = AI degree (A = 1, B = 2 or C = 3) + AI frequency.

The Faecal Incontinence Severity Index (FISI) [Table 4.05] developed by Rockwood *et al.* <sup>353</sup> applies an external weighting scheme to a 20 cell matrix table and has been evaluated as a questionnaire for assessing the severity of AI <sup>353</sup>. The researchers constructed the FISI by looking at type (gas, mucus, liquid and solid) and frequency

(5 categories) of incontinence episodes. The FISI was then distributed to both physicians and patients for weighting and scoring. Although there was good correlation between the two groups, clearly some aspects of FI were more important to patients than to clinicians, generating two different graded numerical results. The final weighted score is therefore dependant on who is completing the FISI assessment tool. The severity score ranges from 0 to 61 when using the recommended patient-derived weights and from 0 to 59 when using the surgeon-derived weights. In this approach there is an assumption that the frequency with which different types of FI events occur, the coping mechanisms used and how lifestyle is altered, is not equal and because of that weighting mechanisms are valuable<sup>353, 356</sup>. Although the weighted approach probably provides for making more accurate and valid inferences regarding severity, it is not known if such accuracy is truly required.

**Table 4.05:** The Faecal Incontinence Severity Index

Patient checklist	2 or more times a day		Once a day		2 or more times a week		Once a week		1-3 times a month		Never	
Weights	A	B	A	B	A	B	A	B	A	B	A	B
a. Gas	12	9	11	8	8	6	6	4	4	2	0	0
b. Mucus	12	11	10	9	7	7	5	7	3	5	0	0
c. Liquid stool	19	18	17	16	13	14	10	13	8	10	0	0
d. Solid stool	18	19	16	17	13	16	10	14	8	11	0	0

NOTE. A denotes patient rating of severity, and B denotes surgeon rating of severity. "Never" always receives a score of 0.

The bowel version of the International Consultation of Incontinence questionnaire (ICIQ-B), the Faecal Incontinence and Constipation Assessment (FICA) and the Revised Faecal Incontinence scale are the most recently developed and validated instruments; however, they have not been widely used in clinical studies<sup>357-360</sup>. Out of these newer grading systems the most innovative is the ICIQ-B which will be discussed in more detail later in this section.

### ***Faecal incontinence quality of life measures***

Clinical outcome measurement tools such as prospective bowel diaries and clinical grading systems have been suggested as helpful aids in the assessment of FI severity but in contrast to many other disorders, currently no universally accepted symptomatic index of FI accurately reflects clinical severity<sup>91</sup>. Therefore, conflicting opinions remain regarding the most suitable assessment measures for determining intervention outcomes with questions over their accuracy and utility<sup>168, 237</sup>. Problems with, leakage, hygiene, social embarrassment and the ability to reach the toilet in time are all other limiting factors to patients' daily living which may not be formally assessed through these measures<sup>168</sup>. Inadequate clinical outcome measures may not reflect changes to individual patient's lives and this raises problems when evaluating treatments.

It is believed that even the most commonly used scoring method, CCIS<sup>191</sup>, may not be sensitive enough to pick up subtle improvements in patient condition<sup>168</sup>. Leroi

---



argues that two criteria (used to calculate the CCIS), wearing protection and the impact on social life often require more than 6 months to change, even if the treatment is effective, as patients may need time to regain confidence<sup>168</sup>. Some authors have felt that the success of interventions cannot be measured by changes of involuntary stool loss alone and strongly advocate analysing QoL<sup>227, 237</sup>. Previous studies have shown there to be correlation between QoL variables such as depression/embarrassment and symptom measures (i.e., frequency of FI episodes, of urgency and delay to postpone defecation and CCIS); demonstrating the emotional improvement that accompanies incontinence recovery<sup>168</sup>

Self recorded bowel diaries and severity scores do not account for any quality of life improvements which often depend on the patient's confidence and ability to interact within society. Inadequate clinical outcome measures may not reflect changes to individual patient's lives and this raises problems when evaluating FI treatments. Some authors have felt that the success of SNS cannot be measured by changes of involuntary stool loss alone and strongly advocate analysing QoL measures<sup>227, 237</sup>. Although many different QoL measures have been used to assess the impact of FI, FIQL score, SF-36 and EuroQoL EQ-5D assessment instruments are the most commonly used and therefore chosen to be employed in this study.

The FIQL<sup>82</sup> is a disease specific QoL measure providing subscale scores for each of the four domains: lifestyle, coping/behaviour, depression/self-perception and

---

embarrassment. A higher score within the domain signifies an improved QoL. The SF-36<sup>198</sup> is a generic QoL assessment tool; it rates quality of life on a scale of 1–100 (a high score indicates better function) in eight subscales: physical functioning; physical role; bodily pain; general health; vitality; social functioning; emotional role; and mental health. These subscale scores can be summarised to provide scores within the physical component and mental component categories. The EuroQoL EQ-5D<sup>199</sup> assessment tool comprises of five dimensions of health including mobility, self-care, usual activities, pain/discomfort and anxiety/depression. It has been found that the EQ-5D scale substantially correlates with selective scales of the SF-36<sup>361</sup>. Each dimension comprises three levels including no problems, moderate problems and extreme problems.

Several issues must be resolved before an ideal scoring system is developed: the definition of incontinence must be standardised; the optimum method of data collection must be decided on (i.e., diaries and severity scores versus patients' recall); the need for data beyond type and frequency must be assessed; and the assignment of numerical values to the combinations of type and frequency must be validated<sup>21</sup>.

Another limitation of our study could include our choice of outcome measures and denotation of success in FI treatment. Research into treatment of FI is currently hampered by the lack of a valid and reliable tool that allows standardisation of

---

outcomes. Inadequate clinical outcome measures may not reflect changes in individual lives and thus raises problems when evaluating FI therapies. With these considerations the 50% improvement criteria, based on objective measurements, may give a false evaluation of the success of therapy in this study. With this type of measure the starting point of severity of symptoms or number of FIE is the overriding factor. For instance, patients with severe incontinence who obtain a “successful” reduction in incontinent episodes may continue to experience incontinence at a level that continues to impair social functioning and QoL<sup>186</sup>. Even those with less severe baseline symptoms may find it relatively easier to attain 50% reduction in symptoms without a change in effect.

The use of multiple different clinical measures within the literature reflect efforts to compensate for the known limitations of this success measure with many institutions electing to use their own definitions of treatment success (from: a  $\geq 50\%$  improvement in CCIS to patient satisfaction with SNS)<sup>253, 260, 287, 362</sup>; particularly in the evaluation of the medium and long-term effects of SNS. These reports may provide a more realistic rate of treatment success, but without consensus across studies, results remain inconclusive [see Table 4.06] .

**Table 4.06:** Notable alternative outcome measures of success for SNS

Author	Median FU	Base Perm (N)	Perms at FU (N)	% Perm at FU	Outcome measure of success	Success (n)	Success of perms (%)	ITT success (%)
<b>Short Term Follow Up (up to and including 12 months)</b>								
Jarrett M <sup>229</sup>	12	46	46	100	Improved continence	44	96	75
Rasmussen O <sup>231</sup>	6	37	37	100	Functioning SNS system	32	86	71
Uludag O <sup>232</sup>	12	50	50	100	Improved continence	48	96	76 <sup>+</sup>
Hetzer FH <sup>185</sup>	1*	13	13	100	Decrease in CCIS	13	100	65
Jarrett M <sup>233</sup>	12	12	12	100	Improvement in FIE	9	75	69
Leroi AM <sup>168</sup>	6*	34	27	79	Chosen as "on" stimulation	19	70	n/a
Faucheron J <sup>234</sup>	6*	29	29	100	Improvement in continence	24	83	60
Navarro J <sup>240</sup>	12*	24	24	100	Decrease in CCIS	16	68	62
Roman S <sup>273</sup>	3*	18	18	100	Sig imp in FI	14	78	n/a
Gallas S <sup>280</sup>	6*	200	189	95	>30% imp in CCIS	103	54	52
Uludag O <sup>279</sup>	6*	12	12	100	>50% imp in continence	12	100	n/a
<b>Medium Term Follow Up (between 12 and 36 months)</b>								
Kenefick N <sup>235</sup>	24	19	19	100	Improved continence	19	100	100
Hetzer FH <sup>237</sup>	13	37	37	100	Sig imp in continence	34	92	77 <sup>+</sup>
Holzer B <sup>238</sup>	35	29	29	100	Marked improvement in continence	28	97	78
Melenhorst J <sup>242</sup>	A: 29	16	A: 16	100	FU success	12	75	60
	B: 23	14	B: 14	100		12	86	60
Koch SM <sup>252</sup>	24‡	19	19	100	Persisting continence	17	89	49 <sup>+</sup>
Michelsen HB <sup>253</sup>	36*	126	107	85	Decrease in CCIS scores	87	81	52
Ratto C <sup>278</sup>	33	10	10	100	Sig imp in FI	10	100	n/a
Maeda Y <sup>260</sup>	33	176	163	93	Good and Acceptable outcome (some clinical benefit)	103	63	44
Pascual I <sup>261</sup>	13	48	48	100	Patient perceived success	45	94	90
Wong MT <sup>262</sup>	31	61	61	100	CCIS <8 or failed if > 1 FIE per week	36	59	40
<b>Long Term Follow Up (more than 36 months)</b>								
Altomare D <sup>245</sup>	74‡	60	50	83	>50% improvement of CCIS,	37	74	39
		60	50	83	>70% improvement of CCIS	25	50	27
Vallet C <sup>249</sup>	44‡	32	23	72	Patient satisfaction with "Good result"	12	38	27
Sharpe A <sup>255</sup>	50	44	44	100	Patient satisfied + CCIS 10 or less	37	84	62

Key: \* = values taken at time point; † = intention to treat reported; ‡ = mean values (integer values); n/a = not able; FU = follow up; SNS = Sacral Nerve Stimulation; FIE = faecal incontinence episodes; CCIS = Cleveland Clinic Incontinence Score; Sig imp = significant improvement; A = group with anal sphincter defects; B = group without anal sphincter defects. All values are calculated to nearest integer. This table demonstrates the multiple methods of determining "successful SNS treatment" as found in the SNS literature; ranging from subjective improvements in symptoms to arbitrary percentage improvement in clinical outcome scores.

***Current study outcome measures used***

Despite the considerable limitations of current clinical outcome measures, we have shown that the reporting of CCIS, FIE and "success measures" are prevalent and provides most of the evidence for the effectiveness of SNS. This is most likely due to their ease-of-use and standardised methods, with this outcome data providing readily interpretable discreet numerical scores or counts. As many of the centres providing SNS have also investigated the use of other NM systems for incontinence, it is not surprising that these outcome measures have also been integrated into the assessments of alternate FI therapies.

In keeping with the tenets of the pilot design, there was no pre-specified primary outcome. To try and address limitations of specific outcome measures we used a range of alternative measures of success including proportional reductions in FIEs  $\geq 75\%$  and  $100\%$  and also  $\geq 50\%$  reduction in CCIS. Akin to previous reports on NM, we further measured the effectiveness of each treatment by presenting the mean changes in total FIE, mean changes in CCIS and changes in QoL scores. These data outcomes may better represent improvements in severe incontinence which may in turn reflect patient perception of treatment outcome more accurately.

Unsure of whether available outcome measures would adequately capture patient perspective symptom changes, due to NM treatment; the PCOM assessment tool was developed especially for the trial. The PCOM was designed as a two part

---

questionnaire. The first part (question 1), a simple Likert type scale between 1-10 (1 being least effective and 10 most), aimed to demonstrate subjective satisfaction of the patient's current therapy. All recruits had received maximal conservative management (i.e. physiotherapeutics, dietary advice and medications) for their FI, changes in this score from baseline would indicate patient satisfaction with NM intervention as compared to previous therapies. Likert type scales in questions 2-6 of the PROM focused on exploring the current effect of FI on different aspects of patient wellbeing regardless of treatment. These five questions were loosely based on the assessment of factors found to be of particularly importance to FI patients as determined by Cotterill *et al.* in 2008 <sup>78</sup>. The formal International Consultation on Incontinence Questionnaire for anal incontinence (ICIQ-B) assessment tool was the primary development from Cotterill's original studies but was only published in entirety in 2011 <sup>363</sup> (see Appendix i for full questionnaire). The PROM assessment tool used specifically in our pilot trial in 2009 was developed completely independently from the ICIQ-B. Despite this, the similarities between the two outcome tools focussing on patients' subjective assessment of the consequences of their FI are marked. It may be consequently considered that our PROM assessment tool provides an alternative modified short form version of the ICIQ-B questionnaire.

Unlike other validated and globally used symptom scores in this trial, the PCOM provides a completely subjective outcome measure based on the opinions of the patients in the trial only. There can be no inference of meaningful comparisons

---

between the PCOM scores and other outcome clinical or QoL scores as there have not been any prospective rigorous tests or assessments to prove its validity. The authors expect that the within group differences may represent a degree of change in satisfaction with treatment but also cannot be sure that there is any statistical usefulness in analysing these changes as Likert type scores are notoriously subject to "central tendency bias". However, there is a pattern of PCOM score improvements after treatment as compared to baseline, with greater within group improvements found in the SNS group over PTNS. This correlates with all other clinical scores and the FIQL measure used in the trial. The authors found that being brief (one side of A4) the patients did not find it difficult or onerous to complete this questionnaire which was reflected in its 100% completion rate for those that remained in the trial. This was equivalent to all other clinical measures used.

#### **4.4.2.8 Use of qualitative methodology**

Given the aim of the study and participant numbers, the authors considered it was appropriate to use "thematic content analysis" as the method of data analysis. Alternative methodologies already used for these types of interviews have been Interpretative Phenomenological Analysis and Grounded Theory approaches. The aim was to maintain a phenomenological perspective although the larger number of our participants and the comparative analysis between interviews would be too complex to undertake with these methods. In the project's qualitative interview

---

design, there was a trade-off between having a deeper emersion into exploring the life world of our participants and allowing them to provide honest unbiased accounts. To this end its was felt that the flexible and highly idiographic method of thematic content analysis was the most suitable and achievable method of analysis for this study.

An added complexity was the conduct of interviews by a neutral person (independent research assistant) and then subsequent analysis by a different member of the team (CRF). The SSG felt that given the resource restrictions (especially as each interview transcription and analysis taking many hours each), it would be difficult to find an independent researcher who could undertake the study in entirety. Therefore the division of labour was the most appropriate arrangement for ensuring all information given was as valid, truthful and complete. It is conceivable that when the CRF analysed the audio recorded interviews, expressions and emotions which are usually acknowledged through non-verbal communication may be lost. In truth some information such as gestures may be significant, most subtle interactions could be determined through analysis of the use of language and tone of voice from both interviewer and patients. A preferred set-up may have been to use video recorded interviews for data collection. However, it could be argued that patients may have found a video camera to be more intrusive and therefore when being recorded become self conscious and less open; defeating the ideals of the study.

---



#### **4.4.2.9 An optimum PTNS treatment protocol**

A further criticism of the study regards the optimal interval between maintenance sessions required to maintain symptom relief. Hotouras *et al.* have acknowledged that the lack of published data on the long-term efficacy of PTNS may require some patients to require therapy sessions more frequently than the recommended 6-monthly intervals. In fact in both Martinson's<sup>304</sup> and Al Asari's studies<sup>307</sup> (discussed earlier in this chapter, section 4.2.1), maintenance therapies of approximately once a month was required to maintain benefit. In these studies the effectiveness of PTNS may have been greatly improved because of frequent "top-up" therapies. There is still no consensus agreement over a standard protocol for PTNS therapy making long-term cost effectiveness impossible to model.

#### **4.4.3 SUMMARY OF LIMITATIONS**

As pilot studies, the limitations of the small sample size, short follow up and lack of comparative placebo on the ability to determine meaningful conclusions over treatment superiority are undisputed. The investigators have avoided attempting to analyse the data in directly comparative way and have instead provided descriptive statistics using median and mean estimates, interquartile ranges and confidence intervals, only as a guide for informing further studies (see Chapter 3, section 3.2). The results demonstrated that for all clinical outcome measures there have only

been small differences in within group mean improvements between SNS and PTNS at both 3 and 6 months with overlapping confidence intervals indicating that neither treatment was clearly superior in clinical effectiveness. A full equivalence trial would be necessary to test this hypothesis. However this unique study has attempted to be innovative in its use of a mixed method design including the use of established and novel clinical outcome measures, qualitative interview studies and an analysis of costs. The study was completed as designed, to cost and time and therefore has been successful in accomplishing its designated remit in producing detailed feasibility information, both quantitative and qualitative, upon which decisions to undertake a fully powered randomised study can be based.

#### **4.5 CONDUCTING A FULL MULTICENTRE TRIAL: SAMPLE SIZE AND FEASIBILITY**

Before conducting the trial, an estimated sample size calculation for a suitably powered RCT of SNS vs. PTNS revealed that more than 2000 patients would be required to detect a difference in proportions of at least 5% (see Chapter 2 section 2.9.2.4). The overall rationale for our pilot study was to acquire, using an exploratory trial design, the necessary quantitative and qualitative data to inform a subsequent definitive RCT comparing SNS and PTNS. We aimed to determine the variability and distribution of clinical endpoints as well as qualitative data to inform the most

suitable and responsive outcome measures for a subsequent well designed and sufficiently powered RCT.

If, accepting the difficulties of design and conduct, a full equivalence trial would be required to provide meaningful results, the equivalence margin would first need to be determined. While the effect estimates from this pilot trial, which included all common currently used outcome measures, are undoubtedly useful, the interquartile ranges (and large standard deviations) will have a significant impact on future trial design. It must be accepted that an adequately powered randomised trial of these two complex interventions would be a major and costly undertaking. The current data could be used to design such an equivalence trial but the sample size would need to be very large. Even using the simplest outcome measure, the binary responder (>50% improvement in weekly FI episodes) and a non-inferiority margin of 20%, assuming 40% success in PTNS and 50% in SNS, we would require 506 patients in each group <sup>364</sup>. However, assuming that a third fail temporary stimulation or withdraw from treatment (as in the current data): the SNS group would need 759 patients. With further attrition in both groups of 10%, 843 patients would be required in the SNS and 562 in PTNS. Extrapolated back from the current data, 3189 patients would need to be screened to recruit to the trial. Such a trial would also need to address the other major weakness of the current study, that of the short follow up time (6 months only). It is well-acknowledged that the outcomes of interventions for functional disorders in the short-term may not reflect accurately

those at later follow-up. While a minimum of 1 year follow-up would have been desirable, there are sufficient data for SNS to suggest that accepting a degree of long-term attrition in outcome (10-20%) and need for re-intervention and re-programming<sup>260</sup>, benefit is usually maintained in the long-term, with some patients now having implants for over 15 years<sup>197, 268</sup>. Such data do not exist for PTNS and it will be important to know whether short-term outcomes are maintained and at what intensity (and therefore cost) of top-up treatments are required to sustain benefit. Detailed cost-effectiveness modelling would then be required to fairly compare SNS and PTNS to a long-term time horizon. Qualitative findings support concern that for some patients, repeat hospital visits for treatment might prove onerous for patients who have a life-long illness. In contrast, other patients expressed a clear preference (2 withdrawals before therapy) against surgical intervention with SNS. These factors will also be considered in any future studies. A definitive RCT directly comparing SNS and PTNS even in a international multicentre trial would probably be unfeasible.

#### **4.6 THE CLINICAL IMPACT OF THESE EXPLORATORY STUDIES**

The review adds to the literature by presenting summaries of the available short, medium and long-term clinical scores and success rates of two of the most popular NM therapies: SNS and PTNS. We believe that these summarised outcomes may be

---

useful in informing both clinicians and patients considering NM therapy for FI. The simple estimates presented in this review may be used as a counselling aid, enabling patients to understand the true effectiveness of each technique. This information together with consideration for individual circumstances may help determine the most suitable treatment options. We have presented data for SNS both on an ITT and per-protocol basis with the rationale that each is useful depending on whether the patient has already undertaken PNE.

Given the cheaper initial outlay of PTNS and a possible delay in gaining funding for SNS, PTNS could offer a relatively affordable 'first line' outpatient treatment to many FI patients who have failed conservative management. It could also be considered as an adjunct to SNS and a useful 'stop-gap' treatment for those awaiting the more permanent solution of SNS. As well as providing some form of treatment above conservative measures to those unable or unwilling to have surgery, it would be a very useful treatment if there is a delay in gaining SNS funding. TTNS is an attractive alternative to PTNS but at present it is still in the evaluation phase (see section 4.7).

This randomised trial has provided the first direct comparison of clinical outcome and health economic data for both SNS and PTNS, contextualising quantitative findings with qualitative appraisal of acceptability of both the interventions and the outcome measures. Our exploratory study is a step towards providing the evidence

---

base to expand treatment choice for patients including those currently marginalised from interventional therapy e.g. elderly care home residents. Indeed, our results and others discussed, have demonstrated that PTNS could become the routine first ‘invasive’ intervention in patients with FI failing prior conservative physician- and nurse-led approaches with significant reductions in operations, hospital stay, complications, waiting times and cost of treatment. In the absence of a fully powered equivalence study, and with the assistance of appropriate regulatory bodies e.g. NICE, it is likely that this project can provide some background evidence for the accelerated roll-out of PTNS nationally, with significant impact on NHS policy and resource utilisation. PTNS improves clinical outcomes in FI in the short term although it may not be as effective as SNS. It is also a highly acceptable treatment for patients and is certainly less invasive than SNS. It is notable that in a recent study comparing percutaneous with transcutaneous PTNS, which showed the superiority of the former technique, some patients responded so well to PTNS that they were taken off the SNS waiting list <sup>365</sup>.

Due to the paucity of long-term data we cannot recommend PTNS as a complete alternative to SNS. Accurate cost-effectiveness studies in long term timescales will be very important to determine if PTNS is a true financial competitor for SNS especially with the need to have regular ongoing top-up treatments. At the moment the optimum interval of top-up treatments to maintain affect whilst preserving resource is still being investigated. The other suggestion that PTNS can be a

---

predictive or evaluative tool for SNS is so far unfounded. As we are unsure of the mechanisms of both SNS and PTNS, we cannot determine whether they effect a shared neurological pathway. In fact akin to Thomas's observations <sup>366</sup>, no PTNS studies have ever been proven to elicit an anal motor reflex seen with SNS. Furthermore a previous study at the author's centre <sup>367</sup> could not determine whether patients who had initial success with PTNS but needed frequent top-up treatments had a greater chance of success with SNS than those who failed PTNS outright.

It would make sense that patients who failed the more conservative PTNS proceed to SNS therapy but there have not been any studies that have trialled the effect of PTNS in those failing SNS. It is possible that if these treatments worked via different mechanisms that PTNS could offer some treatment benefit to this group. An alternative theory may be that SNS innervates nerves more centrally and therefore provides a larger stimulation "dose" to the end neural interface providing improved action. The use of pudendal nerve stimulation is also of interest as this technique claims to provide even more focused stimulation to the pudendal nerve, although this has not been proven to be effective in all patients who failed SNS <sup>368</sup>. Unfortunately the pudendal nerve stimulation is no longer licensed for use in FI and therefore cannot be further investigated this point.

#### **4.7 FUTURE TRENDS AND FURTHER RESEARCH**

Currently, the largest centres internationally<sup>197, 245, 253, 268</sup> are able to report their long-term experience with SNS; demonstrating a maintained clinical benefit. Furthermore there is growing interest in the potential of newer, less invasive and less costly NM techniques (like PTNS and TTNS). Unfortunately, direct comparisons with more established surgical therapies (e.g. sphincter repair) are almost impossible given the heterogeneity of current NM outcome reporting; as demonstrated in the review. To enable fair comparisons with other interventions; all future outcome reporting must include an ITT analysis.

As mentioned, there is continuing controversy regarding the classification of 'treatment success' for FI therapies and it is likely that a combination of outcome tools will continue to be used for this purpose. It is recommend that a consensus to standardise the use of outcome measures and indicators of success for FI in order that further reports can be compared in a meaningful way. This could be attained by the enrolment of all patients undergoing SNS into a national registry.

Currently only 8-10 UK centres offer PTNS as an NHS treatment and some feel it is still an underutilised treatment option. In the future, as PTNS is simple to administer and easy to learn, it may become available in local hospitals or community-based settings. From the results of the presented qualitative study

---



there has been some reservations about the use of self-administered "home" PTNS; as many of the participants expressed a preference for treatment to be undertaken by trained experts. It is also difficult to know whether the efficacy of treatment would be better or worse than current published data if it were self-administered. Further studies will have to be undertaken to provide validation for self-administration methods. This does not preclude however a mobile or outreach service which could be conducted either in secondary care or in community practice. The main advantage of PTNS are its initial costs and simple mobile equipment especially when compared with SNS. It is therefore a particularly good alternative to for those currently marginalised, i.e. nursing home residents or house-bound patients.

Patient selection and the mechanism of action of NM therapies are topics that have not been specifically addressed in these studies, but a deeper understanding of these may help to improve clinical outcomes. Currently, the unknown mechanisms of NM and concerns over the high numbers of case series and selection bias due to lack of clear reporting of subsequent withdrawals or losses to follow up, mean a placebo effect still cannot be confidently excluded. Understanding the mechanism of action of these treatment will be key in determining the correct FI aetiologies to focus on and therefore improve outcomes. As anorectal physiological assessment techniques and aetiological understanding evolve, FI stratification will be improved and therefore therapy can become more targeted. In fact two pivotal PTNS studies

<sup>324, 369</sup> demonstrated that when patients were stratified into those with predominantly urgent FI, their outcomes with PTNS were superior to those of passive FI. In Hotouras *et al.*'s prospective case series on short term outcomes, patients were stratified into either passive, urgent or mixed FI. In the urgent FI group, following treatment, there were statistically significant improvements in the CCIS, from 11.0 (SD:4.1) to 8.3 (4.8), the time to postpone defaecation (from 1.0 to 5.0 min) and the average number of weekly incontinence episodes (from four to zero per week). Whereas in the passive FI group, the mean CCIS improved from 11.5 (4.1) to 9.4 (4.3), accompanied by similar improvements in the median defaecation deferment time (5.0 to 12.5 min) and median number of weekly incontinence episodes (from four to three per week) which were not significant on statistical testing. Equally in the eagerly awaited Horrock *et al.*'s multicentre study (CONFIDeNT) of 227 patients randomised to either PTNS treatment or sham, PTNS did not show significant clinical benefit over sham electrical stimulation in the treatment of FI based on number of patients who received at least a 50% reduction in weekly FIE. There was, however, a significantly greater decrease in total weekly FIEs in the PTNS arm than in the sham arm (difference in means  $-2.3$ , 95% CI  $-4.2$  to  $-0.3$ ;  $p = 0.02$ ). This included a reduction in the number of urge FIEs weekly ( $-1.5$ , 95% CI  $-2.7$  to  $-0.2$ ;  $p = 0.02$ ) but not in the number of passive FIEs ( $-0.64$ , 95% CI  $-1.67$  to  $0.40$ ;  $p = 0.23$ )<sup>324</sup>. In view of the results, there may be a justification in continuing to treat a subgroup of patients with troublesome urge FI symptoms in whom directed therapy may cause symptomatic improvement<sup>324, 369</sup>. Further studies

of PTNS should be directed at those with urge FI to determine the clinical effectiveness.

On the horizon, it is predicted that even more non invasive methods of neuromodulation using skin contact devices will be increasingly used. We have already presented some data with small participant numbers detailing the use of TTNS. Although they have not yet managed to prove their effectiveness against the more established PTNS for FI<sup>173, 370</sup>, TTNS treatments are attractive because of the ease of use, non invasive technique and now ambulatory devices. A pilot study on an ambulatory device has been published recently by Rimmer *et al.*<sup>371</sup> Many are looking forward to more details and usage of these types of devices and their FI outcomes.

#### **4.8 CONCLUSION**

Long-term equivalence between the effectiveness of SNS and PTNS outcomes would have to be proven before PTNS can be recommended as a complete alternative to SNS. Despite PTNS being seemingly cheaper than SNS, the true long term patient costs of either treatment are still unknown; particularly as PTNS requires regular repeated treatments for an unknown and potentially prolonged period of time. Further well-conducted randomised trials comparing different therapies, using

standardised protocols and outcome measures, may supply the high quality clinical evidence required to design a definitive treatment algorithm.

This body of work including a pilot randomised trial suggests that in the short-term, both SNS and PTNS confer some clinical benefit for patients with FI. Within group effect estimates were in general larger for SNS based on analysis of all patients embarking on treatment with greater effects seen when focussing the analysis to only those who progressed to permanent implantation. This finding is in keeping with non-randomised comparisons of SNS and PTNS identified in the review with results presented in Chapter 3 <sup>166</sup>. The qualitative study revealed some of the personal difficulties that living with FI brings and demonstrated that appropriate treatment can make a real difference to many aspects of individual life. In terms of the two treatments available, our participants were pleased with both novel therapies although SNS seemed to produce more noticeable symptomatic benefits. Both treatments were highly acceptable and well tolerated by patients although some had expressed a wish for more expertise to be available locally. The minimal invasiveness and positive side effect profiles of these treatments seem to have contributed greatly to the enthusiasm for both treatments. Even if the treatment did not work as well as participants had expected, they found confidence and comfort in the process of treatment. This helped them to cope better and be more open about their problems.

These studies provide evidence that SNS analysed on an all-available-cases principle (similar to intention-to-treat) was a more expensive treatment in the short term with only a potential small treatment benefit over PTNS. Unfortunately the pilot has revealed that a definitive full scale non inferiority RCT would probably be unfeasible. While longer-term outcomes and economic modelling will be required to make firm conclusions. However, as the short term costs are advantageous and the technique easily tolerated and accepted, it may be considered that PTNS can be employed for patients with FI failing prior conservative approaches or are awaiting SNS. Furthermore, the author believes localised/mobile PTNS treatments could be relatively easily implemented throughout primary care settings requiring only modest training and little financial outlay. The author believes that these types of community services would greatly assist those who are currently marginalised because of time, financial or physical restraints. Excitingly, further work on ambulatory transcutaneous devices is being undertaken which if prove to be effective, would also make a welcome addition to the armamentarium against FI.

**REFERENCES**

1. Bharucha AE, Zinsmeister AR, Schleck CD, Melton LJ, 3rd. Bowel disturbances are the most important risk factors for late onset fecal incontinence: a population-based case-control study in women. *Gastroenterology* 2010;**139**(5): 1559-1566.
2. Whitehead WE, Wald A, Norton NJ. Treatment options for fecal incontinence. *Dis Colon Rectum* 2001;**44**(1): 131-142; discussion 142-134.
3. Christiansen J, Nelson R, Pemberton J. Anal Incontinence: International Continence Society. In: [http://www.wic.org/Publications/ICI\\_2/chapters/Chap15pdf](http://www.wic.org/Publications/ICI_2/chapters/Chap15pdf) accessed 26/02/2015.
4. Johanson JF, Lafferty J. Epidemiology of fecal incontinence: the silent affliction. *Am J Gastroenterol* 1996;**91**(1): 33-36.
5. Edwards NI, Jones D. The prevalence of faecal incontinence in older people living at home. *Age Ageing* 2001;**30**(6): 503-507.
6. Heymen S. Psychological and cognitive variables affecting treatment outcomes for urinary and fecal incontinence. *Gastroenterology* 2004;**126**(1 Suppl 1): S146-151.
7. Rizk DE, Hassan MY, Shaheen H, Cherian JV, Micallef R, Dunn E. The prevalence and determinants of health care-seeking behavior for fecal incontinence in multiparous United Arab Emirates females. *Dis Colon Rectum* 2001;**44**(12): 1850-1856.
8. Gallagher DL, Thompson DL. Identifying and managing fecal incontinence. *J Wound Ostomy Continence Nurs* 2012;**39**(1): 95-97.
9. Sailer M, Bussen D, Debus ES, Fuchs KH, Thiede A. Quality of life in patients with benign anorectal disorders. *Br J Surg* 1998;**85**(12): 1716-1719.
10. Rao SS. Diagnosis and management of fecal incontinence. American College of Gastroenterology Practice Parameters Committee. *Am J Gastroenterol* 2004;**99**(8): 1585-1604.
11. Bharucha AE, Zinsmeister AR, Locke GR, Seide B, McKeon K, Schleck CD, Melton LJ. Prevalence and burden of fecal incontinence: A population based study in women. *Gastroenterology* 2005;**129**: 42-49.
12. Melville JL, Fan MY, Newton K, Fenner D. Fecal incontinence in US women: a population-based study. *Am J Obstet Gynecol* 2005;**193**(6): 2071-2076.
13. Quander CR, Morris MC, Melson J, Bienias JL, Evans DA. Prevalence of and factors associated with fecal incontinence in a large community study of older individuals. *American Journal of Gastroenterology* 2005;**100**(4): 905-909.
14. Varma MG, Brown JS, Creasman JM, Thom DH, Van Den Eeden SK, Beattie MS, Subak LL, Reproductive Risks for Incontinence Study at Kaiser Research G. Fecal incontinence in females older than aged 40 years: who is at risk? *Diseases of the Colon and Rectum* 2006;**49**(6): 841-851.
15. Siproudhis L, Pigot F, Godeberge P, Damon H, Soudan D, Bigard MA. Defecation disorders: a French population survey. *Diseases of the Colon and Rectum* 2006;**49**(2): 219-227.

16. Nygaard I, Barber MD, Burgio KL, Kenton K, Meikle S, Schaffer J, Spino C, Whitehead WE, Wu J, Brody DJ, Pelvic Floor Disorders N. Prevalence of symptomatic pelvic floor disorders in US women. *JAMA* 2008;**300**(11): 1311-1316.
17. Whitehead WE, Borrud L, Goode PS, Meikle S, Mueller ER, Tuteja A, Weidner A, Weinstein M, Ye W, Network PFD. Fecal incontinence in US adults: epidemiology and risk factors. *Gastroenterology* 2009;**137**(2): 512-517.
18. Matthews CA, Whitehead WE, Townsend MK, Grodstein F. Risk factors for urinary, fecal, or dual incontinence in the nurses' health study. *Obstet Gynecol* 2013;**122**(3): 539-545.
19. Macmillan AK, Merrie AE, Marshall RJ, Parry BR. The prevalence of fecal incontinence in community-dwelling adults: a systematic review of the literature. *Dis Colon Rectum* 2004;**47**(8): 1341-1349.
20. Perry S, Shaw C, McGrother C, Matthews RJ, Assassa RP, Dallosso H, Williams K, Brittain KR, Azam U, Clarke M, Jagger C, Mayne C, Castleden CM. Prevalence of faecal incontinence in adults aged 40 years or more living in the community. *Gut* 2002;**50**(4): 480-484.
21. Madoff RD, Parker SC, Varma MG, Lowry AC. Faecal incontinence in adults. *Lancet* 2004;**364**(9434): 621-632.
22. Faecal incontinence, Costing report: Implementing NICE guidance in England. <http://www.nice.org.uk/guidance/cg49/resources/faecal-incontinence-costing-report2> [21/02/15].
23. Kalantar JS, Howell S, Talley NJ. Prevalence of faecal incontinence and associated risk factors; an underdiagnosed problem in the Australian community? *Med J Aust* 2002;**176**(2): 54-57.
24. Nakanishi N, Tatara K, Shinsho F, Murakami S, Takatorige T, Fukuda H, Nakajima K, Naramura H. Mortality in relation to urinary and faecal incontinence in elderly people living at home. *Age Ageing* 1999;**28**(3): 301-306.
25. Probst M, Pages H, Riemann JF, Eickhoff A, Raulf F, Kolbert G. Fecal incontinence: part 4 of a series of articles on incontinence. *Dtsch Arztebl Int* 2010;**107**(34-35): 596-601.
26. Rey E, Choung RS, Schleck CD, Zinsmeister AR, Locke GR, 3rd, Talley NJ. Onset and risk factors for fecal incontinence in a US community. *Am J Gastroenterol* 2010;**105**(2): 412-419.
27. Whitehead WE, Borrud L, Goode PS, Meikle S, Mueller ER, Tuteja A, Weidner A, Weinstein M, Ye W. Fecal incontinence in US adults: epidemiology and risk factors. *Gastroenterology* 2009;**137**(2): 512-517, 517 e511-512.
28. Nelson R, Norton N, Cautley E, Furner S. Community-based prevalence of anal incontinence. *JAMA* 1995;**274**(7): 559-561.
29. Kamm MA. Faecal incontinence. *BMJ* 1998;**316**(7130): 528-532.
30. Markland AD, Goode PS, Burgio KL, Redden DT, Richter HE, Sawyer P, Allman RM. Incidence and risk factors for fecal incontinence in black and white older adults: a population-based study. *J Am Geriatr Soc* 2010;**58**(7): 1341-1346.
31. Nelson R, Furner S, Jesudason V. Fecal incontinence in Wisconsin nursing homes: prevalence and associations. *Dis Colon Rectum* 1998;**41**(10): 1226-1229.

32. Hagglund D. A systematic literature review of incontinence care for persons with dementia: the research evidence. *J Clin Nurs* 2010;**19**(3-4): 303-312.
33. Chassagne P, Landrin I, Neveu C, Czernichow P, Bouaniche M, Doucet J, Denis P, Bercoff E. Fecal incontinence in the institutionalized elderly: incidence, risk factors, and prognosis. *Am J Med* 1999;**106**(2): 185-190.
34. Cameron JL. *Current surgical therapy* (9th edn). Mosby Elsevier: Philadelphia, 2008; xxxii, 1397 p., [1322] p. of plates.
35. Bharucha AE, Zinsmeister AR, Locke GR, Seide B, McKeon K, Schleck CD, Melton LJ. Risk Factors for Fecal Incontinence: A Population Based Study in Women. *American Journal of Gastroenterology* 2006;**101**: 1305-1312.
36. Bharucha AE, Seide B, Zinsmeister AR, Melton JL. Relation of bowel habits to fecal incontinence in women. *American Journal of Gastroenterology* 2008;**103**(6): 1470-1475.
37. Rey E, Choung RS, Schleck CD, Zinsmeister AR, Locke GR, 3rd, Talley NJ. Onset and risk factors for fecal incontinence in a US community. *American Journal of Gastroenterology* 2010;**105**(2): 412-419.
38. Bharucha AE, Fletcher JG, Melton LJ, 3rd, Zinsmeister AR. Obstetric Trauma, Pelvic Floor Injury And Fecal Incontinence: A Population-Based Case-Control Study. *American Journal of Gastroenterology* 2012;**107**(6): 902-911.
39. Rommen K, Schei B, Rydning A, H Sultan A, Morkved S. Prevalence of anal incontinence among Norwegian women: a cross-sectional study. *BMJ Open* 2012;**2**(4).
40. Corman ML. *Colon and rectal surgery* (5th edn). Lippincott Williams & Wilkins: Philadelphia, Pa. ; London, 2005; xvii, 1741 p.
41. Sultan AH, Kamm MA, Hudson CN, Thomas JM, Bartram CI. Anal-sphincter disruption during vaginal delivery. *N Engl J Med* 1993;**329**(26): 1905-1911.
42. Varma A, Gunn J, Gardiner A, Lindow SW, Duthie GS. Obstetric anal sphincter injury: prospective evaluation of incidence. *Dis Colon Rectum* 1999;**42**(12): 1537-1543.
43. Varma A, Gunn J, Lindow SW, Duthie GS. Do routinely measured delivery variables predict anal sphincter outcome? *Dis Colon Rectum* 1999;**42**(10): 1261-1264.
44. Zetterstrom J, Mellgren A, Jensen LL, Wong WD, Kim DG, Lowry AC, Madoff RD, Congilosi SM. Effect of delivery on anal sphincter morphology and function. *Dis Colon Rectum* 1999;**42**(10): 1253-1260.
45. Sorensen M, Tetzschner T, Rasmussen OO, Bjarnesen J, Christiansen J. Sphincter rupture in childbirth. *Br J Surg* 1993;**80**(3): 392-394.
46. Wolff BG. *The ASCRS textbook of colon and rectal surgery*. Springer: New York, N.Y. ; [London], 2007.
47. Sultan AH, Kamm MA, Hudson CN, Bartram CI. Third degree obstetric anal sphincter tears: risk factors and outcome of primary repair. *BMJ* 1994;**308**(6933): 887-891.
48. Engel AF, Kamm MA, Talbot IC. Progressive systemic sclerosis of the internal anal sphincter leading to passive faecal incontinence. *Gut* 1994;**35**(6): 857-859.



49. Epanomeritakis E, Koutsoumbi P, Tsiaoussis I, Ganotakis E, Vlata M, Vassilakis JS, Xynos E. Impairment of anorectal function in diabetes mellitus parallels duration of disease. *Dis Colon Rectum* 1999;**42**(11): 1394-1400.
50. Qureshi MS, Rao MM, Sasapu KK, Casey J, Qureshi MU, Sadat U, Hick D, Ambrose S, Jayne DG. Male faecal incontinence presents as two separate entities with implications for management. *Int J Colorectal Dis* 2011;**26**(12): 1589-1594.
51. Hayden DM, Weiss EG. Fecal incontinence: etiology, evaluation, and treatment. *Clinics in colon and rectal surgery* 2011;**24**(1): 64-70.
52. Sentovich SM, Rivela LJ, Blatchford GJ, Christensen MA, Thorson AG. Patterns of male fecal incontinence. *Dis Colon Rectum* 1995;**38**(3): 281-285.
53. Parellada CM, Miller AS, Williamson ME, Johnston D. Paradoxical high anal resting pressures in men with idiopathic fecal seepage. *Dis Colon Rectum* 1998;**41**(5): 593-597.
54. Rao SS, Ozturk R, Stessman M. Investigation of the pathophysiology of fecal seepage. *Am J Gastroenterol* 2004;**99**(11): 2204-2209.
55. Lubowski DZ, Nicholls RJ. Faecal incontinence associated with reduced pelvic sensation. *Br J Surg* 1988;**75**(11): 1086-1088.
56. Hoffmann BA, Timmcke AE, Gathright JB, Jr., Hicks TC, Opelka FG, Beck DE. Fecal seepage and soiling: a problem of rectal sensation. *Dis Colon Rectum* 1995;**38**(7): 746-748.
57. Vaizey CJ, Kamm MA, Bartram CI. Primary degeneration of the internal anal sphincter as a cause of passive faecal incontinence. *Lancet* 1997;**349**(9052): 612-615.
58. Rasmussen OO. Anorectal function. *Dis Colon Rectum* 1994;**37**(4): 386-403.
59. Cheetham MJ, Malouf AJ, Kamm MA. Fecal incontinence. *Gastroenterol Clin North Am* 2001;**30**(1): 115-130.
60. Bharucha AE, Fletcher JG, Harper CM, Hough D, Daube JR, Stevens C, Seide B, Riederer SJ, Zinsmeister AR. Relationship between symptoms and disordered continence mechanisms in women with idiopathic fecal incontinence. *Gut* 2005;**54**: 546-555.
61. Sun WM, Donnelly TC, Read NW. Utility of a combined test of anorectal manometry, electromyography, and sensation in determining the mechanism of 'idiopathic' faecal incontinence. *Gut* 1992;**33**(6): 807-813.
62. Porter NH. A physiological study of the pelvic floor in rectal prolapse. *Ann R Coll Surg Engl* 1962;**31**: 379-404.
63. Fernandez-Fraga X, Azpiroz F, Malagelada JR. Significance of pelvic floor muscles in anal incontinence. *Gastroenterology* 2002;**123**(5): 1441-1450.
64. Percy JP, Neill ME, Swash M, Parks AG. Electrophysiological study of motor nerve supply of pelvic floor. *Lancet* 1981;**1**(8210): 16-17.
65. Bassotti G, Crowell MD, Whitehead WE. Contractile activity of the human colon: lessons from 24 hour studies. *Gut* 1993;**34**(1): 129-133.
66. Miller R, Bartolo DC, Cervero F, Mortensen NJ. Anorectal sampling: a comparison of normal and incontinent patients. *Br J Surg* 1988;**75**(1): 44-47.
67. Felt-Bersma RJ, Sloots CE, Poen AC, Cuesta MA, Meuwissen SG. Rectal compliance as a routine measurement: extreme volumes have direct clinical impact

and normal volumes exclude rectum as a problem. *Diseases of the Colon & Rectum* 2000;**43**(12): 1732-1738.

68. Bharucha AE. Fecal incontinence. *Gastroenterology* 2003;**124**(6): 1672-1685.

69. NICE. The Management of Faecal Incontinence in Adults: Final Scope. In: London: National Institute for Clinical Excellence (NICE); 2005.

70. Mellgren A, Jensen LL, Zetterstrom JP, Wong WD, Hofmeister JH, Lowry AC. Long-term cost of fecal incontinence secondary to obstetric injuries. *Dis Colon Rectum* 1999;**42**(7): 857-865; discussion 865-857.

71. Ratto C, Doglietto GB. *Fecal incontinence : diagnosis and treatment*. Springer: Milan ; New York, 2007; xxi, 362 p.

72. Ouslander JG, Kane RL. The costs of urinary incontinence in nursing homes. *Med Care* 1984;**22**(1): 69-79.

73. Szurszewski JH, Holt PR, Schuster M. Proceedings of a workshop entitled "Neuromuscular function and dysfunction of the gastrointestinal tract in aging". *Dig Dis Sci* 1989;**34**(7): 1135-1146.

74. BBF. Integrated continence service 2000 Bladder and Bowel Foundation. Making the case for an integrated continence service; 2000.

75. Royal-College-of-Physicians-England. Report of the National Audit of Continence Care for Older People (65 years and above) in England, Wales and Northern Ireland. London: Royal College of Physicians England; 2006.

76. Ratto C, Doglietto GB. *Fecal incontinence : diagnosis and treatment*. Springer: Milan ; [London], 2007.

77. Collings S, Norton C. Women's experiences of faecal incontinence: a study. *Br J Community Nurs* 2004;**9**(12): 520-523.

78. Cotterill N, Norton C, Avery KN, Abrams P, Donovan JL. A patient-centered approach to developing a comprehensive symptom and quality of life assessment of anal incontinence. *Dis Colon Rectum* 2008;**51**(1): 82-87.

79. Damon H, Guye O, Seigneurin A, Long F, Sonko A, Faucheron JL, Grandjean JP, Mellier G, Valancogne G, Fayard MO, Henry L, Guyot P, Barth X, Mion F. Prevalence of anal incontinence in adults and impact on quality-of-life. *Gastroenterol Clin Biol* 2006;**30**(1): 37-43.

80. Crowell MD, Schettler VA, Lacy BE, Lunsford TN, Harris LA, DiBaise JK, Jones MP. Impact of anal incontinence on psychosocial function and health-related quality of life. *Dig Dis Sci* 2007;**52**(7): 1627-1631.

81. O'Keefe EA, Talley NJ, Zinsmeister AR, Jacobsen SJ. Bowel disorders impair functional status and quality of life in the elderly: a population-based study. *J Gerontol A Biol Sci Med Sci* 1995;**50**(4): M184-189.

82. Rockwood TH, Church JM, Fleshman JW, Kane RL, Mavrantonis C, Thorson AG, Wexner SD, Bliss D, Lowry AC. Fecal Incontinence Quality of Life Scale: quality of life instrument for patients with fecal incontinence. *Dis Colon Rectum* 2000;**43**(1): 9-16; discussion 16-17.

83. Miner PB, Jr. Economic and personal impact of fecal and urinary incontinence. *Gastroenterology* 2004;**126**(1 Suppl 1): S8-13.

84. Finne-Soveri H, Sorbye LW, Jonsson PV, Carpenter GI, Bernabei R. Increased work-load associated with faecal incontinence among home care patients in 11 European countries. *Eur J Public Health* 2008;**18**(3): 323-328.
85. Harewood GC, Coulie B, Camilleri M, Rath-Harvey D, Pemberton JH. Descending perineum syndrome: audit of clinical and laboratory features and outcome of pelvic floor retraining. *Am J Gastroenterol* 1999;**94**(1): 126-130.
86. Tuteja AK, Rao SS. Review article: Recent trends in diagnosis and treatment of faecal incontinence. *Aliment Pharmacol Ther* 2004;**19**(8): 829-840.
87. Faecal Incontinence: The management of faecal incontinence in adults. <http://guidance.nice.org.uk/CG49/NICEGuidance/pdf/English> [15/03/2014].
88. Bharucha AE, Rao SS. An update on anorectal disorders for gastroenterologists. *Gastroenterology* 2014;**146**(1): 37-45 e32.
89. Noelting J, Ratuapli SK, Bharucha AE, Harvey DM, Ravi K, Zinsmeister AR. Normal values for high-resolution anorectal manometry in healthy women: effects of age and significance of rectoanal gradient. *Am J Gastroenterol* 2012;**107**(10): 1530-1536.
90. Lee YY, Erdogan A, Rao SS. High resolution and high definition anorectal manometry and pressure topography: diagnostic advance or a new kid on the block? *Curr Gastroenterol Rep* 2013;**15**(12): 360.
91. Felt-Bersma RJ, Klinkenberg-Knol EC, Meuwissen SG. Anorectal function investigations in incontinent and continent patients. Differences and discriminatory value. *Dis Colon Rectum* 1990;**33**(6): 479-485; discussion 485-476.
92. Whitehead WE, Palsson OS. Is rectal pain sensitivity a biological marker for irritable bowel syndrome: psychological influences on pain perception. *Gastroenterology* 1998;**115**(5): 1263-1271.
93. Bharucha AE. Update of tests of colon and rectal structure and function. *J Clin Gastroenterol* 2006;**40**(2): 96-103.
94. Pinski I, Brown J, Phang PT. Assessment of sonographic quality of anal sphincter muscles in patients with faecal incontinence. *Colorectal Dis* 2009;**11**(9): 933-940.
95. Enck P, Heyer T, Gantke B, Schmidt WU, Schafer R, Frieling T, Haussinger D. How reproducible are measures of the anal sphincter muscle diameter by endoanal ultrasound? *Am J Gastroenterol* 1997;**92**(2): 293-296.
96. Hussain SM, Stoker J, Lameris JS. Anal sphincter complex: endoanal MR imaging of normal anatomy. *Radiology* 1995;**197**(3): 671-677.
97. Nielsen MB, Hauge C, Pedersen JF, Christiansen J. Endosonographic evaluation of patients with anal incontinence: findings and influence on surgical management. *AJR Am J Roentgenol* 1993;**160**(4): 771-775.
98. Mahieu P, Pringot J, Bodart P. Defecography: I. Description of a new procedure and results in normal patients. *Gastrointest Radiol* 1984;**9**(3): 247-251.
99. Jones HJ, Swift RI, Blake H. A prospective audit of the usefulness of evacuating proctography. *Ann R Coll Surg Engl* 1998;**80**(1): 40-45.

100. Salvioli B, Bharucha AE, Rath-Harvey D, Pemberton JH, Phillips SF. Rectal compliance, capacity, and rectoanal sensation in fecal incontinence. *Am J Gastroenterol* 2001;**96**(7): 2158-2168.
101. Cheong DM, Vaccaro CA, Salanga VD, Wexner SD, Phillips RC, Hanson MR, Waxner SD. Electrodiagnostic evaluation of fecal incontinence. *Muscle Nerve* 1995;**18**(6): 612-619.
102. Harris ML, Hobson AR, Hamdy S, Thompson DG, Akkermans LM, Aziz Q. Neurophysiological evaluation of healthy human anorectal sensation. *Am J Physiol Gastrointest Liver Physiol* 2006;**291**(5): G950-958.
103. Remes-Troche JM, Tantiphlachiva K, Attaluri A, Valestin J, Yamada T, Hamdy S, Rao SS. A bi-directional assessment of the human brain-anorectal axis. *Neurogastroenterol Motil* 2011;**23**(3): 240-248, e117-248.
104. Di Lazzaro V, Oliviero A, Pilato F, Saturno E, Dileone M, Mazzone P, Insola A, Tonali PA, Rothwell JC. The physiological basis of transcranial motor cortex stimulation in conscious humans. *Clin Neurophysiol* 2004;**115**(2): 255-266.
105. Tantiphlachiva K, Attaluri A, Valestin J, Yamada T, Rao SS. Translumbar and transsacral motor-evoked potentials: a novel test for spino-anorectal neuropathy in spinal cord injury. *Am J Gastroenterol* 2011;**106**(5): 907-914.
106. Bharucha AE, Holmes D, Haider C, Carrascal CA, Edge J, Manduca A, Zinsmeister AR. Increased rectal stiffness in women with urge-predominant fecal incontinence. *Gastroenterology* 2013;**144**(S-82).
107. Briel JW, Stoker J, Rociu E, Lameris JS, Hop WC, Schouten WR. External anal sphincter atrophy on endoanal magnetic resonance imaging adversely affects continence after sphincteroplasty. *Br J Surg* 1999;**86**(10): 1322-1327.
108. Fletcher JG, Busse RF, Riederer SJ, Hough D, Gluecker T, Harper CM, Bharucha AE. Magnetic resonance imaging of anatomic and dynamic defects of the pelvic floor in defecatory disorders. *Am J Gastroenterol* 2003;**98**(2): 399-411.
109. Bertschinger KM, Hetzer FH, Roos JE, Treiber K, Marincek B, Hilfiker PR. Dynamic MR imaging of the pelvic floor performed with patient sitting in an open-magnet unit versus with patient supine in a closed-magnet unit. *Radiology* 2002;**223**(2): 501-508.
110. Norton C, Kamm MA. Anal sphincter biofeedback and pelvic floor exercises for faecal incontinence in adults--a systematic review. *Aliment Pharmacol Ther* 2001;**15**(8): 1147-1154.
111. Sun WM, Read NW, Verlinden M. Effects of loperamide oxide on gastrointestinal transit time and anorectal function in patients with chronic diarrhoea and faecal incontinence. *Scand J Gastroenterol* 1997;**32**(1): 34-38.
112. Malouf AJ, Norton CS, Engel AF, Nicholls RJ, Kamm MA. Long-term results of overlapping anterior anal-sphincter repair for obstetric trauma. *Lancet* 2000;**355**(9200): 260-265.
113. Gosselink MP, Darby M, Zimmerman DD, Smits AA, van Kessel I, Hop WC, Briel JW, Schouten WR. Long-term follow-up of retrograde colonic irrigation for defaecation disturbances. *Colorectal Dis* 2005;**7**(1): 65-69.

114. Norton C, Kamm MA. Anal plug for faecal incontinence. *Colorectal Dis* 2001;**3**(5): 323-327.
115. Deutekom M, Dobben AC. Plugs for containing faecal incontinence. *Cochrane Database Syst Rev* 2012;**4**: CD005086.
116. Engel BT, Nikoomanesh P, Schuster MM. Operant conditioning of rectosphincteric responses in the treatment of fecal incontinence. *N Engl J Med* 1974;**290**(12): 646-649.
117. Miner PB, Donnelly TC, Read NW. Investigation of mode of action of biofeedback in treatment of fecal incontinence. *Dig Dis Sci* 1990;**35**(10): 1291-1298.
118. Kegel AH. Physiologic therapy for urinary stress incontinence. *J Am Med Assoc* 1951;**146**(10): 915-917.
119. Norton C. Behavioral management of fecal incontinence in adults. *Gastroenterology* 2004;**126**(1 Suppl 1): S64-70.
120. Heymen S, Jones KR, Ringel Y, Scarlett Y, Whitehead WE. Biofeedback treatment of fecal incontinence: a critical review. *Dis Colon Rectum* 2001;**44**(5): 728-736.
121. Jensen LL, Lowry AC. Biofeedback improves functional outcome after sphincteroplasty. *Dis Colon Rectum* 1997;**40**(2): 197-200.
122. Hosker G, Cody JD, Norton CC. Electrical stimulation for faecal incontinence in adults. *Cochrane Database Syst Rev* 2007(3): CD001310.
123. Understanding electrical stimulation for incontinence. [http://www.seekwellness.com/incontinence/electric\\_stim.htm](http://www.seekwellness.com/incontinence/electric_stim.htm).
124. Pinta TM, Kylanpaa ML, Salmi TK, Teramo KA, Luukkonen PS. Primary sphincter repair: are the results of the operation good enough? *Dis Colon Rectum* 2004;**47**(1): 18-23.
125. Engel AF, Kamm MA, Sultan AH, Bartram CI, Nicholls RJ. Anterior anal sphincter repair in patients with obstetric trauma. *Br J Surg* 1994;**81**(8): 1231-1234.
126. Karoui S, Leroi AM, Koning E, Menard JF, Michot F, Denis P. Results of sphincteroplasty in 86 patients with anal incontinence. *Dis Colon Rectum* 2000;**43**(6): 813-820.
127. Halverson AL, Hull TL. Long-term outcome of overlapping anal sphincter repair. *Dis Colon Rectum* 2002;**45**(3): 345-348.
128. Lamblin G, Bouvier P, Damon H, Chabert P, Moret S, Chene G, Mellier G. Long-term outcome after overlapping anterior anal sphincter repair for fecal incontinence. *Int J Colorectal Dis* 2014;**29**(11): 1377-1383.
129. Pinedo G, Vaizey CJ, Nicholls RJ, Roach R, Halligan S, Kamm MA. Results of repeat anal sphincter repair. *Br J Surg* 1999;**86**(1): 66-69.
130. Browning GG, Parks AG. Postanal repair for neuropathic faecal incontinence: correlation of clinical result and anal canal pressures. *Br J Surg* 1983;**70**(2): 101-104.
131. Setti Carraro P, Kamm MA, Nicholls RJ. Long-term results of postanal repair for neurogenic faecal incontinence. *Br J Surg* 1994;**81**(1): 140-144.
132. van Tets WF, Kuijpers JH. Pelvic floor procedures produce no consistent changes in anatomy or physiology. *Dis Colon Rectum* 1998;**41**(3): 365-369.
133. Lamah M, Kumar D. Fecal incontinence. *Dig Dis Sci* 1999;**44**(12): 2488-2499.

134. Yoshioka K, Ogunbiyi OA, Keighley MR. A pilot study of total pelvic floor repair or gluteus maximus transposition for postobstetric neuropathic fecal incontinence. *Dis Colon Rectum* 1999;**42**(2): 252-257.
135. Wong MT, Meurette G, Stangherlin P, Lehur PA. The magnetic anal sphincter versus the artificial bowel sphincter: a comparison of 2 treatments for fecal incontinence. *Dis Colon Rectum* 2011;**54**(7): 773-779.
136. Lehur PA, Roig JV, Duinslaeger M. Artificial anal sphincter: prospective clinical and manometric evaluation. *Dis Colon Rectum* 2000;**43**(8): 1100-1106.
137. Parker SC, Spencer MP, Madoff RD, Jensen LL, Wong WD, Rothenberger DA. Artificial bowel sphincter: long-term experience at a single institution. *Dis Colon Rectum* 2003;**46**(6): 722-729.
138. Malouf AJ, Vaizey CJ, Kamm MA, Nicholls RJ. Reassessing artificial bowel sphincters. *Lancet* 2000;**355**(9222): 2219-2220.
139. Lehur PA, McNevin S, Buntzen S, Mellgren AF, Laurberg S, Madoff RD. Magnetic anal sphincter augmentation for the treatment of fecal incontinence: a preliminary report from a feasibility study. *Dis Colon Rectum* 2010;**53**(12): 1604-1610.
140. Devesa JM, Madrid JM, Gallego BR, Vicente E, Nuno J, Enriquez JM. Bilateral gluteoplasty for fecal incontinence. *Dis Colon Rectum* 1997;**40**(8): 883-888.
141. Faucheron JL, Hannoun L, Thome C, Parc R. Is fecal continence improved by nonstimulated gracilis muscle transposition? *Dis Colon Rectum* 1994;**37**(10): 979-983.
142. Baeten C, Spaans F, Fluks A. An implanted neuromuscular stimulator for fecal continence following previously implanted gracilis muscle. Report of a case. *Dis Colon Rectum* 1988;**31**(2): 134-137.
143. Konsten J, Baeten CG, Havenith MG, Soeters PB. Morphology of dynamic graciloplasty compared with the anal sphincter. *Dis Colon Rectum* 1993;**36**(6): 559-563.
144. Konsten J, Baeten CG, Spaans F, Havenith MG, Soeters PB. [Anal dynamic plastic surgery of the gracilis muscle; a new surgical technique for the treatment of fecal incontinence]. *Ned Tijdschr Geneeskd* 1992;**136**(44): 2178-2182.
145. Mander BJ, Wexner SD, Williams NS, Bartolo DC, Lubowski DZ, Oresland T, Romano G, Keighley MR. Preliminary results of a multicentre trial of the electrically stimulated gracilis neoanal sphincter. *Br J Surg* 1999;**86**(12): 1543-1548.
146. Baeten CG, Bailey HR, Bakka A, Belliveau P, Berg E, Buie WD, Burnstein MJ, Christiansen J, Collier JA, Galandiuk S, LaFontaine LJ, Lange J, Madoff RD, Matzel KE, Pahlman L, Parc R, Reilly JC, Seccia M, Thorson AG, Vernava AM, 3rd, Wexner S. Safety and efficacy of dynamic graciloplasty for fecal incontinence: report of a prospective, multicenter trial. Dynamic Graciloplasty Therapy Study Group. *Dis Colon Rectum* 2000;**43**(6): 743-751.
147. Madoff RD, Rosen HR, Baeten CG, LaFontaine LJ, Cavina E, Devesa M, Rouanet P, Christiansen J, Faucheron JL, Isbister W, Kohler L, Guelinckx PJ, Pahlman L. Safety and efficacy of dynamic muscle plasty for anal incontinence: lessons from a prospective, multicenter trial. *Gastroenterology* 1999;**116**(3): 549-556.

148. Chereau N, Lefevre JH, Shields C, Chafai N, Lefrancois M, Tiret E, Parc Y. Antegrade colonic enema for faecal incontinence in adults: long-term results of 75 patients. *Colorectal Dis* 2011;**13**(8): e238-242.
149. Madoff RD. Surgical treatment options for fecal incontinence. *Gastroenterology* 2004;**126**(1 Suppl 1): S48-54.
150. Norton C, Burch J, Kamm MA. Patients' views of a colostomy for fecal incontinence. *Dis Colon Rectum* 2005;**48**(5): 1062-1069.
151. Kenefick NJ, Vaizey CJ, Malouf AJ, Norton CS, Marshall M, Kamm MA. Injectable silicone biomaterial for faecal incontinence due to internal anal sphincter dysfunction. *Gut* 2002;**51**(2): 225-228.
152. Kumar D, Benson MJ, Bland JE. Glutaraldehyde cross-linked collagen in the treatment of faecal incontinence. *Br J Surg* 1998;**85**(7): 978-979.
153. Graf W, Mellgren A, Matzel KE, Hull T, Johansson C, Bernstein M. Efficacy of dextranomer in stabilised hyaluronic acid for treatment of faecal incontinence: a randomised, sham-controlled trial. *Lancet* 2011;**377**(9770): 997-1003.
154. Takahashi T, Garcia-Osogobio S, Valdovinos MA, Mass W, Jimenez R, Jauregui LA, Bobadilla J, Belmonte C, Edelstein PS, Utley DS. Radio-frequency energy delivery to the anal canal for the treatment of fecal incontinence. *Dis Colon Rectum* 2002;**45**(7): 915-922.
155. Efron JE. The SECCA procedure: a new therapy for treatment of fecal incontinence. *Surg Technol Int* 2004;**13**: 107-110.
156. Ruiz D, Pinto RA, Hull TL, Efron JE, Wexner SD. Does the radiofrequency procedure for fecal incontinence improve quality of life and incontinence at 1-year follow-up? *Dis Colon Rectum* 2010;**53**(7): 1041-1046.
157. Kim DW, Yoon HM, Park JS, Kim YH, Kang SB. Radiofrequency energy delivery to the anal canal: is it a promising new approach to the treatment of fecal incontinence? *Am J Surg* 2009;**197**(1): 14-18.
158. Frudinger A, Kolle D, Schwaiger W, Pfeifer J, Paede J, Halligan S. Muscle-derived cell injection to treat anal incontinence due to obstetric trauma: pilot study with 1 year follow-up. *Gut* 2010;**59**(1): 55-61.
159. international neuromodulation society. <http://www.neuromodulation.com/> [26.03.15].
160. Matzel KE. The role of sacral nerve stimulation in treating faecal incontinence and refractory constipation. Editorial. *Colorectal Dis* 2011;**13** Suppl 2: iii-iv.
161. Brindley GS. History of the sacral anterior root stimulator, 1969-1982. *Neurol Urodyn* 1993;**12**(5): 481-483.
162. Brindley GS, Polkey CE, Rushton DN. Sacral anterior root stimulators for bladder control in paraplegia. *Paraplegia* 1982;**20**(6): 365-381.
163. Tanagho EA, Schmidt RA, Orvis BR. Neural stimulation for control of voiding dysfunction: a preliminary report in 22 patients with serious neuropathic voiding disorders. *J Urol* 1989;**142**(2 Pt 1): 340-345.
164. Matzel KE, Stadelmaier U, Hohenfellner M, Gall FP. Electrical stimulation of sacral spinal nerves for treatment of faecal incontinence. *Lancet* 1995;**346**(8983): 1124-1127.

165. Dudding TC. Future indications for sacral nerve stimulation. *Colorectal Dis* 2011;**13 Suppl 2**: 23-28.
166. Thin NN, Horrocks EJ, Hotouras A, Palit S, Thaha MA, Chan CL, Matzel KE, Knowles CH. Systematic review of the clinical effectiveness of neuromodulation in the treatment of faecal incontinence. *Br J Surg* 2013;**100**(11): 1430-1447.
167. Mowatt G, Glazener C, Jarrett M. Sacral nerve stimulation for faecal incontinence and constipation in adults. *Cochrane Database Syst Rev* 2007(3): CD004464.
168. Leroi AM, Parc Y, Lehur PA, Mion F, Barth X, Rullier E, Bresler L, Portier G, Michot F. Efficacy of sacral nerve stimulation for fecal incontinence: results of a multicenter double-blind crossover study. *Ann Surg* 2005;**242**(5): 662-669.
169. Tjandra JJ, Chan MK, Yeh CH, Murray-Green C. Sacral nerve stimulation is more effective than optimal medical therapy for severe fecal incontinence: a randomized, controlled study. *Dis Colon Rectum* 2008;**51**(5): 494-502.
170. Chan MK, Tjandra JJ. Sacral nerve stimulation for fecal incontinence: external anal sphincter defect vs. intact anal sphincter. *Dis Colon Rectum* 2008;**51**(7): 1015-1024; discussion 1024-1015.
171. Jarrett ME, Mowatt G, Glazener CM, Fraser C, Nicholls RJ, Grant AM, Kamm MA. Systematic review of sacral nerve stimulation for faecal incontinence and constipation. *Br J Surg* 2004;**91**(12): 1559-1569.
172. Shafik A, Ahmed I, El-Sibai O, Mostafa RM. Percutaneous peripheral neuromodulation in the treatment of fecal incontinence. *Eur Surg Res* 2003;**35**(2): 103-107.
173. Thomas GP, Dudding TC, Rahbour G, Nicholls RJ, Vaizey CJ. A review of posterior tibial nerve stimulation for faecal incontinence. *Colorectal Dis* 2013;**15**(5): 519-526.
174. Nakamura M, Sakurai T, Tsujimoto Y, Tada Y. [Transcutaneous electrical stimulation for the control of frequency and urge incontinence]. *Hinyokika Kiyo* 1983;**29**(9): 1053-1059.
175. McGuire EJ, Zhang SC, Horwinski ER, Lytton B. Treatment of motor and sensory detrusor instability by electrical stimulation. *J Urol* 1983;**129**(1): 78-79.
176. Peters KM. Alternative approaches to sacral nerve stimulation. *Int Urogynecol J Pelvic Floor Dysfunct* 2010;**21**(12): 1559-1563.
177. de la Portilla F, Rada R, Vega J, Gonzalez CA, Cisneros N, Maldonado VH. Evaluation of the use of posterior tibial nerve stimulation for the treatment of fecal incontinence: preliminary results of a prospective study. *Dis Colon Rectum* 2009;**52**(8): 1427-1433.
178. Boyle DJ, Prosser K, Allison ME, Williams NS, Chan CL. Percutaneous tibial nerve stimulation for the treatment of urge fecal incontinence. *Diseases of the colon and rectum* 2010;**53**(4): 432-437.
179. Allison M. Percutaneous tibial nerve stimulation for patients with faecal incontinence. *Nursing standard* 2011;**25**(24): 44-48.
180. Queralto M, Portier G, Cabarrot PH, Bonnaud G, Chotard JP, Nadrigny M, Lazorthes F. Preliminary results of peripheral transcutaneous neuromodulation in



- the treatment of idiopathic fecal incontinence. *Int J Colorectal Dis* 2006;**21**(7): 670-672.
181. Smith JA, Eatough V. Interpretative phenomenological analysis. In: *Research methods in psychology*, Breakwell GM, Hammond S, Fife-Shaw C, Smith JA (eds). Sage: London, 2006; 322-341.
182. Burnard P, Gill P, Stewart K, Treasure E, Chadwick B. Analysing and presenting qualitative data. *Br Dent J* 2008;**204**(8): 429-432.
183. Harding G, Gantley M. Qualitative methods: beyond the cookbook. *Fam Pract* 1998;**15**(1): 76-79.
184. Spinelli M, Giardiello G, Gerber M, Arduini A, van den Hombergh U, Malaguti S. New sacral neuromodulation lead for percutaneous implantation using local anesthesia: description and first experience. *J Urol* 2003;**170**(5): 1905-1907.
185. Hetzer FH, Hahnloser D, Knoblauch Y, Lohlein F, Demartines N. New screening technique for sacral nerve stimulation under local anaesthesia. *Tech Coloproctol* 2005;**9**(1): 25-28.
186. Dudding TC, Hollingshead JR, Nicholls RJ, Vaizey CJ. Sacral nerve stimulation for faecal incontinence: patient selection, service provision and operative technique. *Colorectal Dis* 2011;**13**(8): e187-195.
187. Mitchell PJ, Cattle K, Saravanathan S, Telford KJ, Kiff ES. Insertion under local anaesthetic of temporary electrodes for sacral nerve stimulation testing is reliable and cost effective. *Colorectal Dis* 2011;**13**(4): 445-448.
188. Maeda Y, Matzel K, Lundby L, Buntzen S, Laurberg S. Postoperative issues of sacral nerve stimulation for fecal incontinence and constipation: a systematic literature review and treatment guideline. *Dis Colon Rectum* 2011;**54**(11): 1443-1460.
189. Peters KM, Carrico DJ, Perez-Marrero RA, Khan AU, Wooldridge LS, Davis GL, Macdiarmid SA. Randomized trial of percutaneous tibial nerve stimulation versus Sham efficacy in the treatment of overactive bladder syndrome: results from the SUMiT trial. *The Journal of urology* 2010;**183**(4): 1438-1443.
190. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gotzsche PC, Ioannidis JP, Clarke M, Devereaux PJ, Kleijnen J, Moher D. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. *BMJ* 2009;**339**: b2700.
191. Jorge JM, Wexner SD. Etiology and management of fecal incontinence. *Dis Colon Rectum* 1993;**36**(1): 77-97.
192. Tan E, Ngo NT, Darzi A, Shenouda M, Tekkis PP. Meta-analysis: sacral nerve stimulation versus conservative therapy in the treatment of faecal incontinence. *Int J Colorectal Dis* 2011;**26**(3): 275-294.
193. Lancaster GA, Dodd S, Williamson PR. Design and analysis of pilot studies: recommendations for good practice. *J Eval Clin Pract* 2004;**10**(2): 307-312.
194. Thin NN, Carrington EV, Grimmer K, Knowles CH. Advancement anoplasty and sacral nerve stimulation: an effective combination for radiation-induced anal stenosis. *International journal of colorectal disease* 2011;**26**(2): 211-213.

195. Hotouras A, Allison M, Currie A, Knowles CH, Chan CL, Thaha MA. Percutaneous tibial nerve stimulation for fecal incontinence: a video demonstration. *Diseases of the colon and rectum* 2012;**55**(6): 711-713.
196. Hotouras A, Murphy J, Walsh U, Allison M, Curry A, Williams NS, Knowles C, Chan CL. Outcome of Percutaneous Tibial Nerve Stimulation (PTNS) for Fecal Incontinence: A Prospective Cohort Study. *Annals of surgery* 2013.
197. Matzel KE, Lux P, Heuer S, Besendorfer M, Zhang W. Sacral nerve stimulation for faecal incontinence: long-term outcome. *Colorectal Dis* 2009;**11**(6): 636-641.
198. Ware JE, Jr., Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care* 1992;**30**(6): 473-483.
199. Rabin R, de Charro F. EQ-5D: a measure of health status from the EuroQol Group. *Ann Med* 2001;**33**(5): 337-343.
200. Guide to the Methods of Technology Appraisal. <http://www.nice.org.uk/media/D45/1E/GuideToMethodsTechnologyAppraisal2013.pdf>. [15/03/2014].
201. Unit Costs of Health and Social Care 2012. <http://www.pssru.ac.uk/project-pages/unit-costs/2012/> [15/03/2014].
202. National Schedule of Reference Costs 2011-2012 - NHS trusts and NHS foundation trusts. <https://www.gov.uk/government/publications/nhs-reference-costs-financial-year-2011-to-2012> [15/03/2014].
203. British National Formulary. <http://www.bnf.org/bnf/index.htm> [15/03/2014].
204. Peeters B, Benninga MA, Hennekam RC. Childhood constipation; an overview of genetic studies and associated syndromes. *Best practice & research Clinical gastroenterology* 2011;**25**(1): 73-88.
205. Kuzel AJ. Sampling in qualitative inquiry. In: *Doing qualitative research*, Crabtree BF, Miller WL (eds). Sage: London, 1992; 31-44.
206. Mays N, Pope C. Rigour and qualitative research. *BMJ* 1995;**311**(6997): 109-112.
207. Barbour RS. The case for combining qualitative and quantitative approaches in health services research. *J Health Serv Res Policy* 1999;**4**(1): 39-43.
208. Ritchie J, Lewis J. *Qualitative research practice : a guide for social science students and researchers*. Sage Publications: London, 2003.
209. Wengraf T. *Qualitative research interviewing : semi-structured, biographical and narrative methods*. SAGE: Thousand Oaks, Calif. ; London, 2001.
210. Powell JH. The reflective practitioner in nursing. *J Adv Nurs* 1989;**14**(10): 824-832.
211. Pope C, Mays N. *Qualitative research in health care* (3rd ed. edn). Blackwell ; London : BMJ Books: Oxford, 2006.
212. El-Gazzaz G, Zutshi M, Salcedo L, Hammel J, Rackley R, Hull T. Sacral neuromodulation for the treatment of fecal incontinence and urinary incontinence in female patients: long-term follow-up. *Int J Colorectal Dis* 2009;**24**(12): 1377-1381.
213. Indinnimeo M, Ratto C, Moschella CM, Fiore A, Brosa M, Giardina S. Sacral neuromodulation for the treatment of fecal incontinence: analysis of cost-effectiveness. *Dis Colon Rectum* 2010;**53**(12): 1661-1669.

214. Uludag O, Morren GL, Dejong CH, Baeten CG. Effect of sacral neuromodulation on the rectum. *Br J Surg* 2005;**92**(8): 1017-1023.
215. Altomare DF, De Fazio M, Giuliani RT, Catalano G, Cuccia F. Sphincteroplasty for fecal incontinence in the era of sacral nerve modulation. *World J Gastroenterol* 2010;**16**(42): 5267-5271.
216. Meurette G, La Torre M, Regenet N, Robert-Yap J, Lehur PA. Value of sacral nerve stimulation in the treatment of severe faecal incontinence: a comparison to the artificial bowel sphincter. *Colorectal Dis* 2009;**11**(6): 631-635.
217. Michelsen HB, Krogh K, Buntzen S, Laurberg S. A prospective, randomized study: switch off the sacral nerve stimulator during the night? *Dis Colon Rectum* 2008;**51**(5): 538-540.
218. Hetzer FH, Bieler A, Hahnloser D, Lohlein F, Clavien PA, Demartines N. Outcome and cost analysis of sacral nerve stimulation for faecal incontinence. *Br J Surg* 2006;**93**(11): 1411-1417.
219. O'Riordan JM, Healy CF, McLoughlin D, Cassidy M, Brannigan AE, O'Connell PR. Sacral nerve stimulation for faecal incontinence. *Ir J Med Sci* 2008;**177**(2): 117-119.
220. Michelsen HB, Christensen P, Krogh K, Rosenkilde M, Buntzen S, Theil J, Laurberg S. Sacral nerve stimulation for faecal incontinence alters colorectal transport. *Br J Surg* 2008;**95**(6): 779-784.
221. Dudding TC, Pares D, Vaizey CJ, Kamm MA. Predictive factors for successful sacral nerve stimulation in the treatment of faecal incontinence: a 10-year cohort analysis. *Colorectal Dis* 2008;**10**(3): 249-256.
222. Oxford Centre for Evidence-based Medicine Levels of Evidence. <http://www.cebm.net/index.aspx?o=1025>.
223. Eleouet M, Siproudhis L, Guillou N, Le Couedic J, Bouguen G, Bretagne JF. Chronic posterior tibial nerve transcutaneous electrical nerve stimulation (TENS) to treat fecal incontinence (FI). *Int J Colorectal Dis* 2010;**25**(9): 1127-1132.
224. Vitton V, Damon H, Roman S, Nancey S, Flourie B, Mion F. Transcutaneous posterior tibial nerve stimulation for fecal incontinence in inflammatory bowel disease patients: a therapeutic option? *Inflamm Bowel Dis* 2009;**15**(3): 402-405.
225. Vitton V, Damon H, Roman S, Mion F. Transcutaneous electrical posterior tibial nerve stimulation for faecal incontinence: effects on symptoms and quality of life. *Int J Colorectal Dis* 2010;**25**(8): 1017-1020.
226. Rosen HR, Urbarz C, Holzer B, Novi G, Schiessel R. Sacral nerve stimulation as a treatment for fecal incontinence. *Gastroenterology* 2001;**121**(3): 536-541.
227. Kenefick NJ, Vaizey CJ, Cohen RC, Nicholls RJ, Kamm MA. Medium-term results of permanent sacral nerve stimulation for faecal incontinence. *Br J Surg* 2002;**89**(7): 896-901.
228. Altomare DF, Rinaldi M, Petrolino M, Monitillo V, Sallustio P, Veglia A, De Fazio M, Guglielmi A, Memeo V. Permanent sacral nerve modulation for fecal incontinence and associated urinary disturbances. *Int J Colorectal Dis* 2004;**19**(3): 203-209.

229. Jarrett ME, Varma JS, Duthie GS, Nicholls RJ, Kamm MA. Sacral nerve stimulation for faecal incontinence in the UK. *Br J Surg* 2004;**91**(6): 755-761.
230. Matzel KE, Kamm MA, Stosser M, Baeten CG, Christiansen J, Madoff R, Mellgren A, Nicholls RJ, Rius J, Rosen H. Sacral spinal nerve stimulation for faecal incontinence: multicentre study. *Lancet* 2004;**363**(9417): 1270-1276.
231. Rasmussen OO, Buntzen S, Sorensen M, Laurberg S, Christiansen J. Sacral nerve stimulation in fecal incontinence. *Dis Colon Rectum* 2004;**47**(7): 1158-1162; discussion 1162-1153.
232. Uludag O, Koch SM, van Gemert WG, Dejong CH, Baeten CG. Sacral neuromodulation in patients with fecal incontinence: a single-center study. *Dis Colon Rectum* 2004;**47**(8): 1350-1357.
233. Jarrett ME, Matzel KE, Christiansen J, Baeten CG, Rosen H, Bittorf B, Stosser M, Madoff R, Kamm MA. Sacral nerve stimulation for faecal incontinence in patients with previous partial spinal injury including disc prolapse. *Br J Surg* 2005;**92**(6): 734-739.
234. Faucheron JL, Bost R, Duffournet V, Dupuy S, Cardin N, Bonaz B. Sacral neuromodulation in the treatment of severe anal incontinence. Forty consecutive cases treated in one institution. *Gastroenterol Clin Biol* 2006;**30**(5): 669-672.
235. Kenefick NJ. Sacral nerve neuromodulation for the treatment of lower bowel motility disorders. *Ann R Coll Surg Engl* 2006;**88**(7): 617-623.
236. Gourcerol G, Gallas S, Michot F, Denis P, Leroi AM. Sacral nerve stimulation in fecal incontinence: are there factors associated with success? *Dis Colon Rectum* 2007;**50**(1): 3-12.
237. Hetzer FH, Hahnloser D, Clavien PA, Demartines N. Quality of life and morbidity after permanent sacral nerve stimulation for fecal incontinence. *Arch Surg* 2007;**142**(1): 8-13.
238. Holzer B, Rosen HR, Novi G, Ausch C, Holbling N, Schiessel R. Sacral nerve stimulation for neurogenic faecal incontinence. *Br J Surg* 2007;**94**(6): 749-753.
239. Melenhorst J, Koch SM, Uludag O, van Gemert WG, Baeten CG. Sacral neuromodulation in patients with faecal incontinence: results of the first 100 permanent implantations. *Colorectal Dis* 2007;**9**(8): 725-730.
240. Navarro JM, Arroyo Sebastian A, Perez Vicente F, Sanchez Romero AM, Perez Legaz J, Serrano Paz P, Fernandez Frias AM, Candela Polo F, Calpena Rico R. [Sacral root neuromodulation as treatment for fecal incontinence. Preliminary results]. *Rev Esp Enferm Dig* 2007;**99**(11): 636-642.
241. Dudding TC, Meng Lee E, Faiz O, Pares D, Vaizey CJ, McGuire A, Kamm MA. Economic evaluation of sacral nerve stimulation for faecal incontinence. *Br J Surg* 2008;**95**(9): 1155-1163.
242. Melenhorst J, Koch SM, Uludag O, van Gemert WG, Baeten CG. Is a morphologically intact anal sphincter necessary for success with sacral nerve modulation in patients with faecal incontinence? *Colorectal Dis* 2008;**10**(3): 257-262.
243. Munoz-Duyos A, Navarro-Luna A, Brosa M, Pando JA, Sitges-Serra A, Marco-Molina C. Clinical and cost effectiveness of sacral nerve stimulation for faecal incontinence. *Br J Surg* 2008;**95**(8): 1037-1043.

244. Stelzner S, Kohler K, Hellmich G, Witzigmann H. [Indications and results of sacral nerve stimulation in faecal incontinence]. *Zentralbl Chir* 2008;**133**(2): 135-141.
245. Altomare DF, Ratto C, Ganio E, Lolli P, Masin A, Villani RD. Long-term outcome of sacral nerve stimulation for fecal incontinence. *Dis Colon Rectum* 2009;**52**(1): 11-17.
246. Boyle DJ, Knowles CH, Lunniss PJ, Scott SM, Williams NS, Gill KA. Efficacy of sacral nerve stimulation for fecal incontinence in patients with anal sphincter defects. *Dis Colon Rectum* 2009;**52**(7): 1234-1239.
247. Govaert B, Melenhorst J, van Gemert WG, Baeten CG. Can sensory and/or motor reactions during percutaneous nerve evaluation predict outcome of sacral nerve modulation? *Dis Colon Rectum* 2009;**52**(8): 1423-1426.
248. Govaert B, Melenhorst J, Nieman FH, Bols EM, van Gemert WG, Baeten CG. Factors associated with percutaneous nerve evaluation and permanent sacral nerve modulation outcome in patients with fecal incontinence. *Dis Colon Rectum* 2009;**52**(10): 1688-1694.
249. Vallet C, Parc Y, Lupinacci R, Shields C, Parc R, Tiret E. Sacral nerve stimulation for faecal incontinence: response rate, satisfaction and the value of preoperative investigation in patient selection. *Colorectal Dis* 2010;**12**(3): 247-253.
250. Faucheron JL, Voirin D, Badic B. Sacral nerve stimulation for fecal incontinence: causes of surgical revision from a series of 87 consecutive patients operated on in a single institution. *Dis Colon Rectum* 2010;**53**(11): 1501-1507.
251. Hollingshead JR, Dudding TC, Vaizey CJ. Sacral nerve stimulation for faecal incontinence: results from a single centre over a 10 year period. *Colorectal Dis* 2010.
252. Koch SM, Melenhorst J, Uludag O, Deutekom M, Stoker J, van Gemert WG, Baeten CG. Sacral nerve modulation and other treatments in patients with faecal incontinence after unsuccessful pelvic floor rehabilitation: a prospective study. *Colorectal Dis* 2010;**12**(4): 334-341.
253. Michelsen HB, Thompson-Fawcett M, Lundby L, Krogh K, Laurberg S, Buntzen S. Six years of experience with sacral nerve stimulation for fecal incontinence. *Dis Colon Rectum* 2010;**53**(4): 414-421.
254. Oom DM, Steensma AB, van Lanschot JJ, Schouten WR. Is sacral neuromodulation for fecal incontinence worthwhile in patients with associated pelvic floor injury? *Dis Colon Rectum* 2010;**53**(4): 422-427.
255. Sharpe A, Read A. Sacral nerve stimulation for the management of faecal incontinence. *Br J Nurs* 2010;**19**(7): 415-419.
256. Wexner SD, Collier JA, Devroede G, Hull T, McCallum R, Chan M, Ayscue JM, Shobeiri AS, Margolin D, England M, Kaufman H, Snape WJ, Mutlu E, Chua H, Pettit P, Nagle D, Madoff RD, Lerew DR, Mellgren A. Sacral nerve stimulation for fecal incontinence: results of a 120-patient prospective multicenter study. *Ann Surg* 2010;**251**(3): 441-449.
257. George A, Kalmar K, Goncalves J, Nicholls RJ, Vaizey CJ. Sacral Nerve Stimulation in the Elderly. *Colorectal Dis* 2011.
258. Lim JT, Hastie IA, Hiscock RJ, Shedda SM. Sacral Nerve Stimulation for Fecal Incontinence: Long-term Outcomes. *Dis Colon Rectum* 2011;**54**(8): 969-974.
-

259. Leroi AM, Lenne X, Dervaux B, Chartier-Kastler E, Mauroy B, Normand LL, Grise P, Faucheron JL, Parc Y, Lehur PA, Mion F, Damon H, Barth X, Leriche A, Saussine C, Guy L, Haab F, Bresler L, Sarramon JP, Bensadoun H, Rullier E, Slim K, Sielezneff I, Mourey E, Ballanger P, Michot F. Outcome and cost analysis of sacral nerve modulation for treating urinary and/or fecal incontinence. *Ann Surg* 2011;**253**(4): 720-732.
260. Maeda Y, Lundby L, Buntzen S, Laurberg S. Suboptimal outcome following sacral nerve stimulation for faecal incontinence. *Br J Surg* 2011;**98**(1): 140-147.
261. Pascual I, Gonzalez Gomez CC, Ortega R, Jimenez Toscano M, Marijuan JL, Lomas Espadas M, Fernandez Cebrian JM, Garcia Olmo D, Pascual Montero JA. Sacral nerve stimulation for fecal incontinence. *Rev Esp Enferm Dig* 2011;**103**(7): 355-359.
262. Wong MT, Meurette G, Rodat F, Regenet N, Wyart V, Lehur PA. Outcome and management of patients in whom sacral nerve stimulation for fecal incontinence failed. *Dis Colon Rectum* 2011;**54**(4): 425-432.
263. Mellgren A, Wexner SD, Collier JA, Devroede G, Lerew DR, Madoff RD, Hull T. Long-term efficacy and safety of sacral nerve stimulation for fecal incontinence. *Dis Colon Rectum* 2011;**54**(9): 1065-1075.
264. Duelund-Jakobsen J, van Wunnik B, Buntzen S, Lundby L, Baeten C, Laurberg S. Functional results and patient satisfaction with Sacral Nerve Stimulation for idiopathic faecal incontinence. *Colorectal Dis* 2011.
265. Boyle DJ, Murphy J, Gooneratne ML, Grimmer K, Allison ME, Chan CL, Williams NS. Efficacy of sacral nerve stimulation for the treatment of fecal incontinence. *Dis Colon Rectum* 2011;**54**(10): 1271-1278.
266. Wong MT, Meurette G, Wyart V, Lehur PA. Does the magnetic anal sphincter device compare favourably with sacral nerve stimulation in the management of faecal incontinence? *Colorectal Dis* 2012;**14**(6): e323-329.
267. Devroede G, Giese C, Wexner SD, Mellgren A, Collier JA, Madoff RD, Hull T, Stromberg K, Iyer S. Quality of life is markedly improved in patients with fecal incontinence after sacral nerve stimulation. *Female Pelvic Med Reconstr Surg* 2012;**18**(2): 103-112.
268. George AT, Kalmar K, Panarese A, Dudding TC, Nicholls RJ, Vaizey CJ. Long-term outcomes of sacral nerve stimulation for fecal incontinence. *Dis Colon Rectum* 2012;**55**(3): 302-306.
269. Santoro GA, Infantino A, Cancian L, Battistella G, Falco GD. Sacral nerve stimulation for fecal incontinence related to external sphincter atrophy. *Dis Colon Rectum* 2012;**55**(7): 797-805.
270. Ganio E, Ratto C, Masin A, Luc AR, Doglietto GB, Dodi G, Ripetti V, Arullani A, Frascio M, BertiRiboli E, Landolfi V, DelGenio A, Altomare DF, Memeo V, Bertapelle P, Carone R, Spinelli M, Zanollo A, Spreafico L, Giardiello G, de Seta F. Neuromodulation for fecal incontinence: outcome in 16 patients with definitive implant. The initial Italian Sacral Neurostimulation Group (GINS) experience. *Dis Colon Rectum* 2001;**44**(7): 965-970.

271. Michelsen HB, Buntzen S, Krogh K, Laurberg S. Rectal volume tolerability and anal pressures in patients with fecal incontinence treated with sacral nerve stimulation. *Dis Colon Rectum* 2006;**49**(7): 1039-1044.
272. Uludag O, Koch SM, Dejong CH, van Gemert WG, Baeten CG. Sacral neuromodulation; does it affect colonic transit time in patients with faecal incontinence? *Colorectal Dis* 2006;**8**(4): 318-322.
273. Roman S, Tatagiba T, Damon H, Barth X, Mion F. Sacral nerve stimulation and rectal function: results of a prospective study in faecal incontinence. *Neurogastroenterol Motil* 2008;**20**(10): 1127-1131.
274. Dudding TC, Pares D, Vaizey CJ, Kamm MA. Comparison of clinical outcome between open and percutaneous lead insertion for permanent sacral nerve neurostimulation for the treatment of fecal incontinence. *Dis Colon Rectum* 2009;**52**(3): 463-468.
275. Brouwer R, Duthie G. Sacral nerve neuromodulation is effective treatment for fecal incontinence in the presence of a sphincter defect, pudendal neuropathy, or previous sphincter repair. *Dis Colon Rectum* 2010;**53**(3): 273-278.
276. Lombardi G, Del Popolo G, Cecconi F, Surrenti E, Macchiarella A. Clinical outcome of sacral neuromodulation in incomplete spinal cord-injured patients suffering from neurogenic bowel dysfunctions. *Spinal Cord* 2010;**48**(2): 154-159.
277. Otto SD, Burmeister S, Buhr HJ, Kroesen A. Sacral nerve stimulation induces changes in the pelvic floor and rectum that improve continence and quality of life. *J Gastrointest Surg* 2010;**14**(4): 636-644.
278. Ratto C, Litta F, Parello A, Donisi L, Doglietto GB. Sacral nerve stimulation is a valid approach in fecal incontinence due to sphincter lesions when compared to sphincter repair. *Dis Colon Rectum* 2010;**53**(3): 264-272.
279. Uludag O, Koch SM, Vliegen RF, Dejong CH, van Gemert WG, Baeten CG. Sacral neuromodulation: does it affect the rectoanal angle in patients with fecal incontinence? *World J Surg* 2010;**34**(5): 1109-1114.
280. Gallas S, Michot F, Faucheron JL, Meurette G, Lehur PA, Barth X, Damon H, Mion F, Rullier E, Zerbib F, Sielezneff I, Ouaisi M, Orsoni P, Desfourneaux V, Siproudhis L, Mathonnet M, Menard JF, Leroi AM, Club N. Predictive factors for successful sacral nerve stimulation in the treatment of faecal incontinence: results of trial stimulation in 200 patients. *Colorectal disease : the official journal of the Association of Coloproctology of Great Britain and Ireland* 2011;**13**(6): 689-696.
281. Soria-Aledo V, Mengual-Ballester M, Pellicer-Franco E, Aguayo-Albasini JL. Improvement in the quality of life of faecal incontinent patients after sacral root stimulation treatment. *Cir Esp* 2011;**89**(9): 581-587.
282. Uludag O, Melenhorst J, Koch SM, van Gemert WG, Dejong CH, Baeten CG. Sacral neuromodulation: long-term outcome and quality of life in patients with faecal incontinence. *Colorectal Dis* 2011;**13**(10): 1162-1166.
283. Govaert B, Pares D, Delgado-Aros S, La Torre F, Van Gemert WG, Baeten CG. A prospective multicentre study to investigate percutaneous tibial nerve stimulation for the treatment of faecal incontinence. *Colorectal Dis* 2010;**12**(12): 1236-1241.

284. Findlay JM, Yeung JM, Robinson R, Greaves H, Maxwell-Armstrong C. Peripheral neuromodulation via posterior tibial nerve stimulation - a potential treatment for faecal incontinence? *Annals of the Royal College of Surgeons of England* 2010;**92**(5): 385-390.
285. Hotouras A, Thaha MA, Boyle D, Allison ME, Currie A, Knowles CH, Chan CL. Short-term outcome following percutaneous tibial nerve stimulation (PTNS) for faecal incontinence: a single-centre prospective study. *Colorectal disease : the official journal of the Association of Coloproctology of Great Britain and Ireland* 2011.
286. Hotouras A, Thaha MA, Allison ME, Currie A, Scott SM, Chan CL. Percutaneous tibial nerve stimulation (PTNS) in females with faecal incontinence: the impact of sphincter morphology and rectal sensation on the clinical outcome. *International journal of colorectal disease* 2012.
287. Gallas S, Michot F, Faucheron JL, Meurette G, Lehur PA, Barth X, Damon H, Mion F, Rullier E, Zerbib F, Sielezneff I, Ouaisi M, Orsoni P, Desfourneaux V, Siproudhis L, Mathonnet M, Menard JF, Leroi AM. Predictive factors for successful sacral nerve stimulation in the treatment of faecal incontinence: results of trial stimulation in 200 patients. *Colorectal Dis* 2011;**13**(6): 689-696.
288. Matzel K. Sacral Nerve Stimulation. In: *Fecal Incontinence: Diagnosis and Treatment*, Ratto C, Doglietto GB (eds). Springer: Milan, 2007; 244.
289. Fraser C, Glazener C, Grant AM, Mowatt G. Systematic Review of the Efficacy and Safety of Sacral Nerve Stimulation for Faecal Incontinence. In: Procedures RBfI, editor. Aberdeen: National Institute for Clinical Excellence; 2004.
290. Findlay JM, Maxwell-Armstrong C. Posterior tibial nerve stimulation and faecal incontinence: a review. *Int J Colorectal Dis* 2011;**26**(3): 265-273.
291. Sacral nerve stimulation for faecal incontinence. <http://www.nice.org.uk/IPG099>.
292. Faecal Incontinence: The management of faecal incontinence in adults. <http://guidance.nice.org.uk/CG49/NICEGuidance/pdf/English>.
293. Sprange K, Clift M, Burke MJ, Whitehead S, Hutton J. Evidence review: Sacral Nerve Stimulation for faecal incontinence. In: (HITEC) HlaTEC, editor. London: Centre for Evidence Based Purchasing; 2010.
294. Percutaneous tibial nerve stimulation for faecal incontinence. <http://www.nice.org.uk/nicemedia/live/13159/54508/54508.pdf> [March 2014].
295. Clinical Commissioning Policy: Sacral nerve stimulation (SNS) for faecal incontinence (Adult) ref NHSE/A08/P/b. <http://www.england.nhs.uk/wp-content/uploads/2013/08/a08-p-b.pdf> [15/03/2014].
296. Royal-College-of-Surgeons. Commissioning guide: Faecal Incontinence; 2014.
297. Tillin T, Gannon K, Feldman RA, Williams NS. Third-party prospective evaluation of patient outcomes after dynamic graciloplasty. *The British journal of surgery* 2006;**93**(11): 1402-1410.
298. Rothbarth J, Bemelman WA, Meijerink WJ, Stiggelbout AM, Zwinderman AH, Buyze-Westerweel ME, Delemarre JB. What is the impact of fecal incontinence on quality of life? *Diseases of the colon and rectum* 2001;**44**(1): 67-71.
-



299. Horrocks EJ, Thin N, Thaha MA, Taylor SJ, Norton C, Knowles CH. Systematic review of tibial nerve stimulation to treat faecal incontinence. *Br J Surg* 2014.
300. Thin NN, Knowles CH, Allison ME. Sacral Nerve Stimulation for Faecal Incontinence. *Gastrointest Nursing* 2012;**10**(1): 36-44.
301. NHS. Economic report: Sacral nerve stimulation for faecal incontinence. In: Purchasing and Supply Agency, NHS; 2010.
302. Brosa M, Munoz-Duyos A, Navarro-Luna A, Rodriguez JM, Serrano D, Gisbert R, Dziekan K, Segu JL. Cost-effectiveness analysis of sacral neuromodulation (SNM) with Interstim for fecal incontinence patients in Spain. *Curr Med Res Opin* 2008;**24**(3): 907-918.
303. van Wunnik BP, Visschers RG, van Asselt AD, Baeten CG. Cost-effectiveness analysis of sacral neuromodulation for faecal incontinence in The Netherlands. *Colorectal Dis* 2012;**14**(12): e807-814.
304. Martinson M, MacDiarmid S, Black E. Cost of neuromodulation therapies for overactive bladder: percutaneous tibial nerve stimulation versus sacral nerve stimulation. *J Urol* 2013;**189**(1): 210-216.
305. Gray AM, Clarke PM, Wolstenholme JL, Wordsworth S. *Applied Methods of Cost-effectiveness Analysis in Healthcare*. Oxford University Press: Oxford, 2011.
306. Hershey JC, Asch DA, Jepson C, Baron J, Ubel PA. Incremental and average cost-effectiveness ratios: will physicians make a distinction? *Risk Anal* 2003;**23**(1): 81-89.
307. Al Asari S, Meurette G, Mantoo S, Kubis C, Wyart V, Lehur PA. Percutaneous tibial nerve stimulation vs sacral nerve stimulation for faecal incontinence: a comparative case-matched study. *Colorectal Dis* 2014;**16**(11): O393-399.
308. Hotouras A, Murphy J, Allison M, Curry A, Williams NS, Knowles CH, Chan CL. Prospective clinical audit of two neuromodulatory treatments for fecal incontinence: sacral nerve stimulation (SNS) and percutaneous tibial nerve stimulation (PTNS). *Surg Today* 2014;**44**(11): 2124-2130.
309. Peters KM, Carrico DJ, Wooldridge LS, Miller CJ, MacDiarmid SA. Percutaneous tibial nerve stimulation for the long-term treatment of overactive bladder: 3-year results of the STEP study. *J Urol* 2013;**189**(6): 2194-2201.
310. McMullin CM, Jadav AM, Hanwell C, Brown SR. Resource implications of running a sacral neuromodulation service: a 10-year experience. *Colorectal Dis* 2014;**16**(9): 719-722.
311. Matzel KE. Sacral nerve stimulation for faecal incontinence: its role in the treatment algorithm. *Colorectal Dis* 2011;**13 Suppl 2**: 10-14.
312. Cadogan J, Bennun I. Face value: an exploration of the psychological impact of orthognathic surgery. *Br J Oral Maxillofac Surg* 2010.
313. Tucker J, Clifton V, Wilson A. Teetering near the edge; women's experiences of anal incontinence following obstetric anal sphincter injury: an interpretive phenomenological research study. *Aust N Z J Obstet Gynaecol* 2014;**54**(4): 377-381.
314. Johnsen V, Skattebu E, Aamot-Andersen A, Thyberg M. Problematic aspects of faecal incontinence according to the experience of adults with spina bifida. *J Rehabil Med* 2009;**41**(7): 506-511.

315. Olsson F, Bertero C. Living with faecal incontinence: trying to control the daily life that is out of control. *J Clin Nurs* 2014.
316. Peden-McAlpine C, Bliss D, Hill J. The experience of community-living women managing fecal incontinence. *West J Nurs Res* 2008;**30**(7): 817-835.
317. Wilson M, McColl E. The experience of living with faecal incontinence. *Nurs Times* 2007;**103**(14): 46-49.
318. Wilson M. Living with faecal incontinence: follow-up to a research project. *Br J Nurs* 2013;**22**(3): 147-150, 152-144.
319. Rasmussen JL, Ringsberg KC. Being involved in an everlasting fight--a life with postnatal faecal incontinence. A qualitative study. *Scand J Caring Sci* 2010;**24**(1): 108-115.
320. Manthey A, Bliss DZ, Savik K, Lowry A, Whitebird R. Goals of fecal incontinence management identified by community-living incontinent adults. *West J Nurs Res* 2010;**32**(5): 644-661.
321. Cichowski SB, Dunivan GC, Rogers RG, Komesu YM. Patients' experience compared with physicians' recommendations for treating fecal incontinence: a qualitative approach. *Int Urogynecol J* 2014;**25**(7): 935-940.
322. Bielefeldt K. Adverse events of sacral neuromodulation for fecal incontinence reported to the federal drug administration. *World J Gastrointest Pharmacol Ther* 2016;**7**(2): 294-305.
323. Zeiton M, Faily S, Nicholson J, Telford K, Sharma A. Sacral nerve stimulation-hidden costs (uncovered). *Int J Colorectal Dis* 2016;**31**(5): 1005-1010.
324. Horrocks EJ, Bremner SA, Stevens N, Norton C, Gilbert D, O'Connell PR, Eldridge S, Knowles CH. Double-blind randomised controlled trial of percutaneous tibial nerve stimulation versus sham electrical stimulation in the treatment of faecal incontinence: CONTROL of Faecal Incontinence using Distal Neuromodulation (the CONFIDENT trial). *Health Technol Assess* 2015;**19**(77): 1-164.
325. Kuper A, Lingard L, Levinson W. Critically appraising qualitative research. *BMJ* 2008;**337**: a1035.
326. Maeda Y, Lundby L, Buntzen S, Laurberg S. Outcome of Sacral Nerve Stimulation for Fecal Incontinence at 5 Years. *Ann Surg* 2013.
327. Vaizey CJ, Kamm MA, Roy AJ, Nicholls RJ. Double-blind crossover study of sacral nerve stimulation for fecal incontinence. *Dis Colon Rectum* 2000;**43**(3): 298-302.
328. Hull T, Giese C, Wexner SD, Mellgren A, Devroede G, Madoff RD, Stromberg K, Collier JA. Long-term durability of sacral nerve stimulation therapy for chronic fecal incontinence. *Dis Colon Rectum* 2013;**56**(2): 234-245.
329. Peters K, Carrico D, Burks F. Validation of a sham for percutaneous tibial nerve stimulation (PTNS). *Neurourol Urodyn* 2009;**28**(1): 58-61.
330. Vaizey CJ, Kamm MA, Turner IC, Nicholls RJ, Woloszko J. Effects of short term sacral nerve stimulation on anal and rectal function in patients with anal incontinence. *Gut* 1999;**44**(3): 407-412.
331. Carrington EV, Evers J, Grossi U, Dinning PG, Scott SM, O'Connell PR, Jones JF, Knowles CH. A systematic review of sacral nerve stimulation mechanisms in the

- treatment of fecal incontinence and constipation. *Neurogastroenterol Motil* 2014;**26**(9): 1222-1237.
332. Thomas G, Norton C, Nicholls R, Vaizey C. Sacral transcutaneous stimulation for faecal incontinence may have a different mechanism of action to sacral nerve stimulation. *Colorectal Dis* 2013.
333. Giani I, Novelli E, Martina S, Clerico G, Luc AR, Trompetto M, Malaguti S, Nicholls J, Ganio E. The effect of sacral nerve modulation on cerebral evoked potential latency in fecal incontinence and constipation. *Ann Surg* 2011;**254**(1): 90-96.
334. Gourcerol G, Vitton V, Leroi AM, Michot F, Abysique A, Bouvier M. How sacral nerve stimulation works in patients with faecal incontinence. *Colorectal Dis* 2011;**13**(8): e203-211.
335. Michelsen HB, Worsoe J, Krogh K, Lundby L, Christensen P, Buntzen S, Laurberg S. Rectal motility after sacral nerve stimulation for faecal incontinence. *Neurogastroenterol Motil* 2010;**22**(1): 36-41, e36.
336. Abdel-Halim MR, Crosbie J, Engledow A, Windsor A, Cohen CR, Emmanuel AV. Temporary sacral nerve stimulation alters rectal sensory function: a physiological study. *Dis Colon Rectum* 2011;**54**(9): 1134-1140.
337. Damgaard M, Thomsen FG, Sorensen M, Fuglsang S, Madsen JL. The influence of sacral nerve stimulation on gastrointestinal motor function in patients with fecal incontinence. *Neurogastroenterol Motil* 2011;**23**(6): 556-e207.
338. Patton V, Wiklendt L, Arkwright JW, Lubowski DZ, Dinning PG. The effect of sacral nerve stimulation on distal colonic motility in patients with faecal incontinence. *British Journal of Surgery* 2013;**100**(7): 959-968.
339. Carrington EV, Evers J, Grossi U, Dinning PG, Scott SM, O'Connell PR, Jones JFX, Knowles CH. A systematic review of sacral nerve stimulation mechanisms in the treatment of fecal incontinence and constipation. *Neurogastroenterology & Motility* 2014;**26**(9): 1222-1237.
340. Dinning PG, Hunt LM, Arkwright JW, Patton V, Szczesniak MM, Wiklendt L, Davidson JB, Lubowski DZ, Cook IJ. Pancolonic motor response to subsensory and suprasensory sacral nerve stimulation in patients with slow-transit constipation. *The British journal of surgery* 2012;**99**(7): 1002-1010.
341. Knowles CH, Thin N, Gill K, Bhan C, Grimmer K, Lunniss PJ, Williams NS, Scott SM. Prospective randomized double-blind study of temporary sacral nerve stimulation in patients with rectal evacuatory dysfunction and rectal hyposensitivity. *Ann Surg* 2012;**255**(4): 643-649.
342. Knowles CH, Thin N, Gill K, Bhan C, Grimmer K, Lunniss PJ, Williams NS, Scott SM. Prospective randomized double-blind study of temporary sacral nerve stimulation in patients with rectal evacuatory dysfunction and rectal hyposensitivity. *Annals of Surgery* 2012;**255**(4): 643-649.
343. Evers J, Devane L, Carrington EV, Scott SM, Knowles CH, O'Connell PR, Jones JF. Effects of stimulation frequency and intensity in sacral neuromodulation on anorectal inputs to the somatosensory cortex in an experimental model. *The British journal of surgery* 2014;**101**(10): 1317-1328.
-

344. Osman NI, Chapple CR. Fowler's syndrome--a cause of unexplained urinary retention in young women? *Nat Rev Urol* 2014;**11**(2): 87-98.
345. Gladman MA, Knowles CH. Surgical treatment of patients with constipation and fecal incontinence. *Gastroenterology clinics of North America* 2008;**37**(3): 605-625, viii.
346. Hiltunen KM, Matikainen M, Auvinen O, Hietanen P. Clinical and manometric evaluation of anal sphincter function in patients with rectal prolapse. *Am J Surg* 1986;**151**(4): 489-492.
347. Broden G, Dolk A, Holmstrom B. Recovery of the internal anal sphincter following rectopexy: a possible explanation for continence improvement. *Int J Colorectal Dis* 1988;**3**(1): 23-28.
348. Keighley MR, Fielding JW. Management of faecal incontinence and results of surgical treatment. *Br J Surg* 1983;**70**(8): 463-468.
349. Rudd WW. The transanal anastomosis: a sphincter-saving operation with improved continence. *Dis Colon Rectum* 1979;**22**(2): 102-105.
350. Womack NR, Morrison JF, Williams NS. Prospective study of the effects of postanal repair in neurogenic faecal incontinence. *Br J Surg* 1988;**75**(1): 48-52.
351. Vaizey CJ, Carapeti E, Cahill JA, Kamm MA. Prospective comparison of faecal incontinence grading systems. *Gut* 1999;**44**(1): 77-80.
352. Pescatori M, Anastasio G, Bottini C, Mentasti A. New grading and scoring for anal incontinence. Evaluation of 335 patients. *Dis Colon Rectum* 1992;**35**(5): 482-487.
353. Rockwood TH, Church JM, Fleshman JW, Kane RL, Mavrantonis C, Thorson AG, Wexner SD, Bliss D, Lowry AC. Patient and surgeon ranking of the severity of symptoms associated with fecal incontinence: the fecal incontinence severity index. *Dis Colon Rectum* 1999;**42**(12): 1525-1532.
354. Rockwood TH. Incontinence severity and QOL scales for fecal incontinence. *Gastroenterology* 2004;**126**(1 Suppl 1): S106-113.
355. Nevler A. The epidemiology of anal incontinence and symptom severity scoring. *Gastroenterol Rep (Oxf)* 2014;**2**(2): 79-84.
356. Violi V, Boselli AS, De Bernardinis M, Costi R, Trivelli M, Roncoroni L. A patient-rated, surgeon-corrected scale for functional assessment after total anorectal reconstruction. An adaptation of the Working Party on Anal Sphincter Replacement scoring system. *Int J Colorectal Dis* 2002;**17**(5): 327-337.
357. Bharucha AE, Zinsmeister AR, Locke GR, Schleck C, McKeon K, Melton LJ. Symptoms and quality of life in community women with fecal incontinence. *Clin Gastroenterol Hepatol* 2006;**4**(8): 1004-1009.
358. Bharucha AE, Locke GR, 3rd, Seide BM, Zinsmeister AR. A new questionnaire for constipation and faecal incontinence. *Aliment Pharmacol Ther* 2004;**20**(3): 355-364.
359. Cotterill N, Norton C, Avery KNL, Abrams P, Donovan JL. A patient-centered approach to developing a comprehensive symptom and quality of life assessment of anal incontinence. *Diseases of the Colon & Rectum* 2008;**51**(1): 82-87.

360. Sansoni J, Hawthorne G, Fleming G, Marosszeky N. The revised faecal incontinence scale: a clinical validation of a new, short measure for assessment and outcomes evaluation. *Diseases of the Colon & Rectum* 2013;**56**(5): 652-659.
361. Brazier JE, Harper R, Jones NM, O'Cathain A, Thomas KJ, Usherwood T, Westlake L. Validating the SF-36 health survey questionnaire: new outcome measure for primary care. *BMJ* 1992;**305**(6846): 160-164.
362. Altomare DF, Giuratrabocchetta S, Knowles CH, Munoz Duyos A, Robert-Yap J, Matzel KE. Long-term outcomes of sacral nerve stimulation for faecal incontinence. *Br J Surg* 2015.
363. Cotterill N, Norton C, Avery KN, Abrams P, Donovan JL. Psychometric evaluation of a new patient-completed questionnaire for evaluating anal incontinence symptoms and impact on quality of life: the ICIQ-B. *Dis Colon Rectum* 2011;**54**(10): 1235-1250.
364. Jones B, Jarvis P, Lewis JA, Ebbutt AF. Trials to assess equivalence: the importance of rigorous methods. *BMJ* 1996;**313**(7048): 36-39.
365. George AT, Kalmar K, Sala S, Kopanakis K, Panarese A, Dudding TC, Hollingshead JR, Nicholls RJ, Vaizey CJ. Randomized controlled trial of percutaneous versus transcutaneous posterior tibial nerve stimulation in faecal incontinence. *Br J Surg* 2013;**100**(3): 330-338.
366. Thomas GP, Norton C, Nicholls RJ, Vaizey CJ. Sacral transcutaneous stimulation for faecal incontinence may have a different mechanism of action to sacral nerve stimulation. *Colorectal Dis* 2014;**16**(1): 68-69.
367. Hotouras A, Murphy J, Thin NN, Allison M, Horrocks E, Williams NS, Knowles CH, Chan CL. Outcome of sacral nerve stimulation for fecal incontinence in patients refractory to percutaneous tibial nerve stimulation. *Dis Colon Rectum* 2013;**56**(7): 915-920.
368. Thomas GP, George AT, Dudding TC, Nicholls RJ, Vaizey CJ. A pilot study of chronic pudendal nerve stimulation for faecal incontinence for those who have failed sacral nerve stimulation. *Tech Coloproctol* 2014;**18**(8): 731-737.
369. Hotouras A, Thaha MA, Boyle DJ, Allison ME, Currie A, Knowles CH, Chan CL. Short-term outcome following percutaneous tibial nerve stimulation for faecal incontinence: a single-centre prospective study. *Colorectal Dis* 2012;**14**(9): 1101-1105.
370. Thomas GP, Norton C, Nicholls RJ, Vaizey CJ. A pilot study of transcutaneous sacral nerve stimulation for faecal incontinence. *Colorectal Dis* 2013;**15**(11): 1406-1409.
371. Rimmer CJ, Knowles CH, Lamparelli M, Durdey P, Lindsey I, Hunt L, Nugent K, Gill KA. Short-term Outcomes of a Randomized Pilot Trial of 2 Treatment Regimens of Transcutaneous Tibial Nerve Stimulation for Fecal Incontinence. *Dis Colon Rectum* 2015;**58**(10): 974-982.

# **APPENDIX i**

## **QUANTITATIVE OUTCOME MEASURES USED**



## **Health Questionnaire**

**English version for the UK  
(validated for Ireland)**

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**

Best  
imaginable  
health state

100

90

80

70

60

50

40

30

20

10

0

Worst  
imaginable  
health state

# Patient Diary

Patientcode:

center code - patient no - 1<sup>st</sup> initial last name 1<sup>st</sup> initial first name

Start date:

d d m m y y y y

Please mark appropriate visit:

Follow-up visits:

☐ Baseline  
☐ Screening

☐ 1 Month  
☐ 3 Months

☐ 6 Months  
☐ 12 Months

☐ 24 Months  
☐ 36 Months

☐ 48 Months  
☐ Months

Unscheduled visit:

Important document for hospital chart



**Medtronic**

**InterStim**

Diary, version 1.0, July 18, 01 English

[illegible]

[illegible]

Dear Patient,

You should have been completing two weeks of diary. Please verify that all fields have been completed as this information is very important. Finally, I am asking you to please complete the following six questions. This will be very helpful information for me as your physician to allow a better assessment of your bowel as well as urinary (if any) symptoms.

Thank you for your cooperation.

- |                                                                                      |                                     |                                    |                                     |                                   |                                  |
|--------------------------------------------------------------------------------------|-------------------------------------|------------------------------------|-------------------------------------|-----------------------------------|----------------------------------|
| 1. When you get the urge, how long can you defer defecation (on average)?            | <input type="checkbox"/> not at all | <input type="checkbox"/> <1 min    | <input type="checkbox"/> 1-5 min    | <input type="checkbox"/> 5-15 min | <input type="checkbox"/> >15 min |
| 2. Do you have to strain to empty your bowel?                                        | <input type="checkbox"/> never      | <input type="checkbox"/> sometimes | <input type="checkbox"/> frequently | <input type="checkbox"/> always   |                                  |
| 3. Are you able to empty your bowel completely?                                      | <input type="checkbox"/> never      | <input type="checkbox"/> sometimes | <input type="checkbox"/> frequently | <input type="checkbox"/> always   |                                  |
| 4. Do you experience urinary incontinence?                                           | <input type="checkbox"/> never      | <input type="checkbox"/> sometimes | <input type="checkbox"/> frequently | <input type="checkbox"/> always   |                                  |
| 5. If yes, how many pads (for urinary incontinence) do you use per day (on average)? | <input type="checkbox"/> 0          | <input type="checkbox"/> 1-3 pads  | <input type="checkbox"/> 4-7 pads   | <input type="checkbox"/> >7 pads  |                                  |
| 6. Please rate the degree of (urinary) urgency prior to voiding?                     | <input type="checkbox"/> none       | <input type="checkbox"/> mild      | <input type="checkbox"/> moderate   | <input type="checkbox"/> severe   |                                  |

Please have this diary with you at your next applicable follow-up visit.

## Appendix

Q 1: In general, would you say your health is:

- 1 ☐ Excellent  
 2 ☐ Very Good  
 3 ☐ Good  
 4 ☐ Fair  
 5 ☐ Poor

Q 2: For each of the items, please indicate how much of the time the issue is a concern for you due to accidental bowel leakage. (If it is a concern for you for reasons other than accidental bowel leakage then check the box under Not Apply, (N/A).)

Q2. Due to accidental bowel leakage:	Most of the Time	Some of The Time	A Little of the Time	None of the Time	N/A
a. I am afraid to go out	1	2	3	4	<input type="checkbox"/>
b. I avoid visiting friends	1	2	3	4	<input type="checkbox"/>
c. I avoid staying overnight away from home	1	2	3	4	<input type="checkbox"/>
d. It is difficult for me to get out and do things like going to a movie or to church	1	2	3	4	<input type="checkbox"/>
e. I cut down on how much I eat before I go out	1	2	3	4	<input type="checkbox"/>
f. Whenever I am away from home, I try to stay near a restroom as much as possible	1	2	3	4	<input type="checkbox"/>
g. It is important to plan my schedule (daily activities) around my bowel pattern	1	2	3	4	<input type="checkbox"/>
h. I avoid traveling	1	2	3	4	<input type="checkbox"/>
i. I worry about not being able to get to the toilet in time	1	2	3	4	<input type="checkbox"/>
j. I feel I have no control over my bowels	1	2	3	4	<input type="checkbox"/>
k. I can't hold my bowel movement long enough to get to the bathroom	1	2	3	4	<input type="checkbox"/>
l. I leak stool without even knowing it	1	2	3	4	<input type="checkbox"/>
m. I try to prevent bowel accidents by staying very near a bathroom	1	2	3	4	<input type="checkbox"/>



Q 3: Due to accidental bowel leakage, indicate the extent to which you AGREE or DISAGREE with each of the following items. (If it is a concern for you for reasons other than accidental bowel leakage then check the box under Not Apply, N/A).

Q3. Due to accidental bowel leakage:	Strongly Agree	Somewhat Agree	Somewhat Disagree	Strongly Disagree	N/A
a. I feel ashamed	1	2	3	4	<input type="checkbox"/>
b. I can not do many of things I want to do	1	2	3	4	<input type="checkbox"/>
c. I worry about bowel accidents	1	2	3	4	<input type="checkbox"/>
d. I feel depressed	1	2	3	4	<input type="checkbox"/>
e. I worry about others smelling stool on me	1	2	3	4	<input type="checkbox"/>
f. I feel like I am not a healthy person	1	2	3	4	<input type="checkbox"/>
g. I enjoy life less	1	2	3	4	<input type="checkbox"/>
h. I have sex less often than I would like to	1	2	3	4	<input type="checkbox"/>
i. I feel different from other people	1	2	3	4	<input type="checkbox"/>
j. The possibility of bowel accidents is always on my mind	1	2	3	4	<input type="checkbox"/>
k. I am afraid to have sex	1	2	3	4	<input type="checkbox"/>
l. I avoid traveling by plane or train	1	2	3	4	<input type="checkbox"/>
m. I avoid going out to eat	1	2	3	4	<input type="checkbox"/>
n. Whenever I go someplace new, I specifically locate where the bathrooms are	1	2	3	4	<input type="checkbox"/>

Q 4: During the past month, have you felt so sad, discouraged, hopeless, or had so many problems that you wondered if anything was worthwhile?

- 1 ☐ Extremely So - To the point that I have just about given up
- 2 ☐ Very Much So
- 3 ☐ Quite a Bit
- 4 ☐ Some - Enough to bother me
- 5 ☐ A Little Bit
- 6 ☐ Not At All

**Patient Centred Outcomes Measure Form**

Patient Identification:

Hospital Number:

Date:

Please answer each statement by circling the most appropriate answer:

1. I feel my **current treatment is helping** me with my faecal incontinence.Strongly  
Disagree

0 1 2 3 4 5 6 7 8 9

Strongly  
Agree

10

2. I feel I can **cope** with my faecal incontinence problems.Strongly  
Disagree

0 1 2 3 4 5 6 7 8 9

Strongly  
Agree

10

3. I feel confident to go out in public without feeling **embarrassed**.Strongly  
Disagree

0 1 2 3 4 5 6 7 8 9

Strongly  
Agree

10

4. I feel I can **predict and prepare** for any incontinence accidents.Strongly  
Disagree

0 1 2 3 4 5 6 7 8 9

Strongly  
Agree

10

5. I feel I am no longer looking for the **nearest toilet**.Strongly  
Disagree

0 1 2 3 4 5 6 7 8 9

Strongly  
Agree

10

6. I feel my incontinence problems no longer **restrict my social activity**.Strongly  
Disagree

0 1 2 3 4 5 6 7 8 9

Strongly  
Agree

10



**Name:**

**Study number:**

**Date when completing form:**

## SF-36 Health Survey

**INSTRUCTIONS:** This survey asks your views about your health. This information will help keep track of how you feel and how well you are able to do your usual activities.

Please answer every question by marking the answer as indicated. If you are unsure about how to answer a question, please give the best answer you can.

When complete, please return the questionnaire in the envelope provided.

---

1. In general, would you say your health is:

(circle one)

Excellent .....	1
Very good .....	2
Good .....	3
Fair .....	4
Poor .....	5

2. Compared to one year ago, how would you rate your health in general now?

(circle one)

Much better now than one year ago .....	1
Somewhat better than one year ago .....	2
About the same as one year ago .....	3
Somewhat worse than one year ago .....	4
Much worse now than one year ago .....	5

3. The following questions are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

(circle one number on each line)

Activities	Yes, limited a lot	Yes, limited a little	No, not limited at all
Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports.	1	2	3
Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling or playing golf	1	2	3
Lifting or carrying groceries	1	2	3
Climbing several flights of stairs	1	2	3
Climbing one flight of stairs	1	2	3
Bending, kneeling or stooping	1	2	3
Walking more than a mile	1	2	3
Walking half a mile	1	2	3
Walking one hundred yards	1	2	3
Bathing or dressing yourself	1	2	3

4. During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

(circle one number on each line)

	Yes	No
Cut down on the amount of time you spent on work or other activities	1	2
Accomplished less than you would like	1	2
Were limited in the kind of work or other activities	1	2
Had difficulty performing the work or other activities (for example, it took extra effort)	1	2

5. During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

(circle one number on each line)

	Yes	No
Cut down on the amount of time you spent on work or other activities	1	2
Accomplished less than you would like	1	2
Didn't do work or other activities as carefully as usual	1	2

6. During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbours or groups?

(circle one)

Not at all	.....	1
Slightly	.....	2
Moderately	.....	3
Quite a bit	.....	4
Extremely	.....	5

7. How much bodily pain have you had during the past 4 weeks?

(circle one)

None	.....	1
Very mild	.....	2
Mild	.....	3
Moderate	.....	4
Severe	.....	5
Very severe	.....	6

8. During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?

(circle one)

Not at all	.....	1
A little bit	.....	2
Moderately	.....	3
Quite a bit	.....	4
Extremely	.....	5

9. These questions are about how you feel and how things have been with you during the past 4 weeks. For each question please give the one answer that comes closest to the way you have been feeling. How much of the time during the past 4 weeks...

	All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	None of the time
Did you feel full of life?	1	2	3	4	5	6
Have you been a very nervous person?	1	2	3	4	5	6
Have you felt so down in the dumps that nothing could cheer you up?	1	2	3	4	5	6
Have you felt calm and peaceful?	1	2	3	4	5	6
Did you have a lot of energy?	1	2	3	4	5	6
Have you felt downhearted and low?	1	2	3	4	5	6
Did you feel worn out?	1	2	3	4	5	6
Have you been a happy person?	1	2	3	4	5	6
Did you feel tired?	1	2	3	4	5	6

10. During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting friends, relatives, etc.)?

(circle one)

All of the time	.....	1
Most of the time	.....	2
Some of the time	.....	3
A little of the time	.....	4
None of the time	.....	5

11. How TRUE or FALSE is each of the following statements to you?

(circle one number on each line)

	Definitely true	Mostly true	Don't know	Mostly false	Definitely false
I seem to get ill more easily than other people	1	2	3	4	5
I am as healthy as anybody I know	1	2	3	4	5
I expect my health to get worse	1	2	3	4	5
My health is excellent	1	2	3	4	5

Date:

Follow Up Term: 3 or 6 months

**PILOT SNS vs PTNS STUDY****Patient Cost Analysis  
(Health Economics)****Questionnaire**

## Section A: Resource use questionnaire

This section is about the health care you have received

All questions refer to the **three months** before completing this questionnaire.

We would like to know about contacts you have had with health professionals in the last three months. **This is just in regard to your faecal incontinence.**

1. In the last **3 months**, have you been seen by any of the following **at your GP surgery?**

- *Your own or another GP*
- *Nurse*
- *Any other health professional (e.g. dietician, physiotherapist, health visitor)*

No  Please go to Question 2

Yes  Please enter the number of times

GP

Nurse

Other (please specify)

2. In the last **3 months**, have you been seen by any of the following at home?

- *Your own or another GP*
- *Nurse*
- *Any other health professional (e.g. dietician, physiotherapist, health visitor)*

No  Please go to Question 2

Yes  Please enter the number of times

GP

Nurse

Other (please specify)

3. In the last **3 months**, have you discussed your health over the telephone with any health professional (apart from to make or change appointments).

No ☐ Please go to Question 4

Yes ☐ Please enter number of times

With anyone at your GP surgery  
 With anyone at the hospital  
 With NHS Direct (NHS 24 in Scotland)


4. In the last **3 months**, have you visited an accident and emergency department **for problems related to the faecal incontinence or its treatment** ?

No ☐ Please go to Question 4

Yes ☐ Please enter the number of times

5. In the last **3 months**, have you been admitted as an in-patient (i.e. stayed overnight in hospital) for **problems related to the faecal incontinence or its treatment**

No ☐ Please go to Question 5

Yes ☐ Please enter the number of **nights** you spent in hospital

Number of nights	Reason

6. **If you are in work**, did you take any time off work *either* due to illness or in order to see any health professional, for **your incontinence problems**, in the last **3 months**?

No ☐ Please go to Section F

Yes ☐ Please enter the number of day (to the nearest **half day**)

7. In the last **3 months**, have you visited the Colorectal Outpatient department **for problems related to the faecal incontinence or its treatment** ?

No ☐ Please go to Question 4

Yes ☐ Please enter the number of times

### Section B: Drugs use questionnaire

Have you taken any of the following **prescribed** drugs in the last **3 months**?

#### Drugs for incontinence (prescribed in the last 3 months)

Name of Drug	Strength	Number taken per day	Number of days	Total number in 3 months
Imodium (Loperamide)				
Codeine Phosphate				
Other				



### Suppositories (prescribed in the last 3 months)

	Strength	Number taken per day	Number of days	Total number in 3 months
<b>Glycerine</b>				
<b>Bisocodyl</b>				
<b>Other</b>				

### Enemas (prescribed in the last 3 months)

	Strength	Number used per day	Number of days	Total number in 3 months
<b>Fleet</b>				
<b>Microlette</b>				
<b>Phosphate</b>				
<b>Other</b>				

### Medication for general GI disorders (prescribed in the last 3 months)

	Strength of tablet	Number of tablets prescribed	Number of Prescriptions used	Total number in 3 months
<b>Sennokot</b>				
<b>Lactulose</b>				
<b>Fybrogel</b> (Ispaghula Husk)				
<b>Dulcolax</b> (Sodium Docosate)				
<b>Movicol</b>				
<b>Buscopan</b> (hyoscine)				
<b>Colpermine</b> (peppermint oil)				
<b>Maxolon</b> (Metoclopramide)				
Other				

### Medication not listed (prescribed in the last 3 months)

Have you been **prescribed** any other drugs regularly in the last **3 months** that have not been listed here (excluding paracetamol, aspirin and ibuprofen)?

If so, please tell us the:

- **name**
- **strength**
- **number of tablets you take per dose and dose frequency (e.g. two tablets four times a day, etc)**

If the medication is not taken continuously over the last three months, please tell us whether it is taken “**as required**” or whether it was a **short course**.

Please also indicate the **average** number taken per day and the average frequency (N<sup>o</sup> days per week) for drugs taken “as required” or the number of days it was taken for if a short course.

**Thank you for completing this questionnaire**

## **Wexner faecal incontinence score**

Patient identification:

Hosp No:

Date:

Pre – treatment ☐      3 months after ☐      6 months after ☐

The aim of this questionnaire is to find out about the severity of your bowel incontinence. This information will help us to follow your progress as you have treatment.

Please answer each question by ticking the statement that **most** relates to you:

1. I accidentally lose control of solid motion from my bowel:

- ☐ Every day
- ☐ More than once a week but not every day
- ☐ More than once a month but less than once a week
- ☐ Less than once a month
- ☐ Never

2. I accidentally lose liquid motions from my bowel:

- ☐ Every day
- ☐ More than once a week but not every day
- ☐ More than once a month but less than once a week
- ☐ Less than once a month
- ☐ Never

3. I accidentally leak wind/gas from my bowel:

- ☐ Every day
- ☐ More than once a week but not every day
- ☐ More than once a month but less than once a week
- ☐ Less than once a month
- ☐ Never

4. I have to wear a pad/plug of cotton wool or toilet paper:

- ☐ Every day
- ☐ More than once a week but not every day
- ☐ More than once a month but less than once a week
- ☐ Less than once a month
- ☐ Never

5. Losing bowel motion or gas from my bowel makes me alter my daily life:

- ☐ Every day
- ☐ More than once a week but not every day
- ☐ More than once a month but less than once a week
- ☐ Less than once a month
- ☐ Never

Thank you for completing this form