Chronic illness in childhood and adolescence: A longitudinal exploration of co-occurring mental illness

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Statement of Originality

I, Ann Marie Brigid Brady, confirm that the research included within this thesis is my own work or that where it has been carried out in collaboration with, or supported by others, that this is duly acknowledged below and my contribution indicated. Previously published material is also acknowledged below.

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Details of collaboration and publications:

This work was supported by the National Institute of Health Research (NIHR) Collaboration for Leadership in Applied Health Research and Care (CLAHRC) North Thames at Barts Health NHS Trust. The views expressed are those of the author and not necessarily those of the NHS, the NIHR or the Department of Health.

This thesis has been entirely written by the author. All analysis and written work carried out by the author as part of this research has been under the supervision of Professor Stephen Stansfeld, of the Centre for Psychiatry, Queen Mary University of London, and Dr. Jessica Deighton, of the Anna Freud National Centre for Children and Families, University College London. The concept for this thesis originated with the author, and was developed with the guidance of Professor Stansfeld and Dr. Deighton. All measures selected for this study were approved by Professor Stansfeld and Dr. Deighton, before an official request was sent to the board of the 'Avon Longitudinal Study of Parents and Children' (ALSPAC).

The methodology of this study was approved by a board representing the team of the 'Avon Longitudinal Study of Parents and Children' (ALSPAC), before access to the relevant data was granted.

The search strategy for the systematic review overviewed in chapter 1 was developed with assistance from Paula Funnell, the faculty liaison library for medicine and dentistry at Queen Mary University of London. Findings relating to this study have been accepted for publication in the 'Journal of Adolescence':

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Abstract

Chronic health problems are hypothesised to be a risk factor to child and adolescent mental health, due the consistent and continuing stress these health problems pose to normative patterns of development. However, this theory remains to be substantiated by empirical research. Moreover, a systematic review conducted as part of this research indicated that the empirical body is not one on which the validity of this theory can be adequately tested. The major question posed is whether the lack of high quality epidemiological data in the field is obscuring a true psychiatric risk associated with chronic illness in childhood and adolescence, or whether, in contrast, the theory of chronic health problems as a particular risk factor to child and adolescent mental health, is based on false premises.

In order to provide a stronger insight into the association of chronic health problems to mental ill-health across the late childhood and adolescent period, this study used data from a large, representative British sample (the Avon Longitudinal Study of Parents and Children (ALSPAC)) and sensitive measures of mental health outcomes. Mediating factors in these associations were also identified, and a model of the association of chronic health problems to poor mental health outcomes in early adolescence was developed. In order to ensure that all findings were applicable across chronic health conditions, outcomes over this period for children with chronic illness more generally were compared to outcomes for children with asthma diagnoses.

Children with chronic health problems presented with a disproportionate rate of psychiatric illness at 10 years, and these chronic health problems continued to be associated with poor mental health outcomes across the early to mid-adolescent period. The outcomes at 10 and 13 years were suggested to be mediated by factors non-specific to any diagnosis, specifically peer victimisation and health-related school absenteeism. Limitations to external validity in the research, and implications for public health and future research are discussed.

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CHAPTER 1

Literature Review and Introduction to the Thesis

1.1 Introduction to the Literature Review

It has been estimated that an adult living with a long-term illness in the United Kingdom (i.e. “those conditions that cannot at present be cured, but can be controlled by medication and/or other therapies” (Department of Health, 2012)) is two to three times more likely to have a psychiatric illness than an adult in the general population (Naylor et al., 2012). Although long-term illness in childhood and adolescence is commonly hypothesised as having a similarly negative association with mental health, a closer look at the literature indicates that such a strong position remains, as of yet, unsubstantiated by the body of empirical research. The major question posed as a result is whether the lack of high quality epidemiological data in the field is obscuring a true psychiatric risk associated with chronic illness in childhood and adolescence, or whether, in contrast, the theory of chronic health problems as a risk factor to child and adolescent mental health is based on false premises.

At a time when chronic illness has come to the forefront of public health discourses, and psychiatric comorbidities among patients living with long-term conditions have, in particular, become a target area for healthcare intervention, it is vitally important that we have more insight into the associated rates of psychiatric illness amongst younger age groups living with chronic illness, a group which represents approximately 10% of the population aged under 18 years in England and Wales (Department of Health, 2012). Psychiatric comorbidities in the context of chronic illness are associated with poorer clinical outcomes, adverse health problems, and poorer self-management (Naylor et al., 2012), and it is estimated that comorbid psychiatric illness has a greater impact on patient quality of life that any other co-morbid physical health problem, with the exception of neurological conditions (Mujica-Mota et al., 2015). This thesis aims to learn from the limitations of previous empirical investigations, by providing a more balanced test of the current theory of chronic illness as a risk factor to the mental health of children and adolescents, using longitudinal data from a large, representative sample of children living in the United Kingdom.

This opening chapter will provide a thorough overview of the literature to provide a context for this research. To give some initial grounding to this discussion, it will first outline the prevalence and the characteristics of chronic health conditions in childhood and adolescence, highlighting why they have become such a major focus in the field of child health. It will then detail why these conditions have come to be viewed as a specific risk factor for the mental health of children and adolescents, in balance with what is known about the aetiological factors of childhood and adolescent onset psychopathology. The supporting evidence for this theory will also be reviewed, both in terms of the proposed mechanisms, and in terms of previous empirical investigations examining the association between chronic health problems and mental illness in children and adolescents. It is hoped that an overview of the methodological practices in the field, and how these may have affected the insight of previous overviews of the research, will provide a logical reason for the undertaking of the systematic review of the literature, which will be subsequently outlined. The conclusion of this chapter will open with an overview of all literature reviewed, and will outline how the research gaps identified indicate that a more thorough testing of the hypothesised relationship of chronic health problems in childhood and adolescence to poor mental health is vitally needed. The research undertaken as part of this thesis will then be introduced, with emphasis on how the study design was built upon the limitations identified in previous empirical investigations.

It is hoped that this review of the literature will illuminate the reasoning behind the chosen research topic, by outlining the reasons why the mental health outcomes of children and adolescents living with chronic health problems is a worthy topic of research investigation, and by highlighting the major research gaps that exist in knowledge regarding the nature of this association. It is also hoped that it will make clear that this research investigation was built on a grounded sense of the literature, in order to provide an insight into this relationship beyond that which is available based on current research and knowledge.

1.1 The prevalence and characteristics of long-term illness in childhood and adolescence

The significant advancements in medical technology and understanding over the course of the past two centuries have led to a momentous shift in the prevalence and course of disease within the past number of decades (e.g. Michaud, Surís, & Viner, 2007). Consequently, the World Health Organisation has defined this current milieu as one of "epidemiological transition" where conditions defined as "chronic" diseases have come to replace acute and infectious disease as the greatest challenge to public health and national healthcare resources (Michaud et al., 2007). This section will open by examining the contribution of epidemiological transition to childhood and adolescent health. This section of the thesis will provide a contextual understanding of what defines chronic illness, the substantial prevalence of such conditions within the childhood and adolescent populations, and the particular characteristics of these diseases. It is hoped such insight will provide initial grounding to the subsequent discussion of the associated mental health outcomes of chronic disease in this age group. Please note that throughout this section, and indeed throughout this thesis, the terms "chronic illness", "chronic disease", "chronic health conditions" and "long-term illness" will be treated as synonymous, and will be used inter-changeably.

1.1.1 The prevalence of long-term illness in children and adolescents

Exact prevalence estimates of rates of chronic disease in any given population are difficult to determine (e.g. Michaud et al., 2007). The reasons for these difficulties lie in the fact that terms such as "chronic disease" and "long-term conditions" were developed as a response to illness patterns rather than stemming from naturally occurring pathologies (see Weisz, 2014). As Weisz (2014) highlights these terms came into common usage, in their current forms, in the mid-twentieth century to describe a growing population of patients that had a broad range of presenting problems. These patients included those living with previously fatal illnesses, such as diabetes mellitus type 1, which were now survivable with the intervention of lifelong medication, as well as an increased population of elderly citizens who

required prolonged care for the multiple infirmities associated with old age. The mid-twentieth century also saw a growth in patients presenting with several conditions with chronic medical presentations, such as cardiac illness, which were a consequence of exceedingly prevalent lifestyle behaviours, such as physical inactivity, high blood pressure, and smoking (Remington & Brownson, 2011). Despite the differences in individual symptomatology, all these conditions presented the healthcare system with a common challenge – namely to finance the provision of services and medical resources over an extensive period of time (Weisz, 2014). Therefore, when these challenges were discussed within public healthcare discourse, any conditions requiring prolonged medical intervention came to be referred to as "chronic diseases" for convenience, with the equivalent terms "chronic illness" and "degenerative disease" also emerging in this period (see Weisz, 2014).

Defining the exact parameters of "chronicity" is exceedingly difficult. As Bynum (2015) highlights, there is simply no easy means of distinguishing acute from chronic conditions, as many conditions that could be viewed as acute, such as tuberculosis, have prolonged natural histories that may extend beyond those traditionally viewed as chronic. Furthermore, the outcomes of many primary acute illnesses, such as cancer, are lifelong monitoring and medical treatment regardless of the primary treatment's success (e.g. McCorkle et al., 2011). Indeed, the Department of Health (2012) notes that their official guideline definition of chronic illness – "those conditions that cannot at present be cured, but can be controlled by medication and/or other therapies" – does not have strict boundaries for this very reason. However, these arbitrary boundaries pose challenges to the understanding of the prevalence of chronic conditions in children and adolescents.

As detailed in the opening to this section, this milieu has been described as one of "epidemiological transition" by the World Health Organisation, and official statistics indicate that this historic shift has been reflected in child health, with similarly improved outcomes for acute health conditions, and increases in chronic health impairments among children and adolescents

(Halfon & Newacheck, 2010). Despite variations in prevalence rates due to methods and definitions, it is clear that rates of chronic illness in young people are substantial and rising (e.g. Berntsson & Köhler, 2001). However, a systematic review by Van der Lee and colleagues (Van der Lee, Mokkink, Grootenhuis, Heymans, & Offringa, 2007) indicated that prevalence estimates of chronic illness in young people age 0 to 18 years ranged vastly depending on the definition used, from a low of 0.22% to a high of 44%. Moreover, prevalence rates of chronic diseases and disabilities (defined by the World Health Organisation as "a restriction or lack of ability to perform an activity in the manner or within the range considered normal for a human being" (p.19, Barlow & Ellard, 2006) are often amalgamated in population estimates (see Newacheck & Halfon, 1998; Barlow & Ellard, 2006), causing further limitations in our understanding of the prevalence of chronic conditions in younger populations.

Basing their estimates on data from the 2010/2011 Quality and Outcomes Framework (QOF) and the 2009 General Lifestyle Survey, the Department of Health of England and Wales (Department of Health, 2012) estimate that in the region of 15 million people in England have at least one long-term condition, a figure representing approximately 30% of the population. When breaking these figures down by age group, it is estimated that this figure accounts for 10% of those aged 0-9 years, and approximately 12% of those age 10 to 19 years (Department of Health, 2012), which remains a substantial proportion of 8% and 10% of these age groups respectively when only those living with chronic physical health conditions, rather than mental health conditions, are taken into consideration. These population prevalence figures remain the most frequently cited in official reports (e.g. Department of Health, 2015), yet, the Department acknowledges that these figures are likely to be an underestimate of the true population prevalence due to the lack of QOF disease registers for many conditions. Moreover, it has been argued that many of the most challenging chronic health issues – such as chronic pain – are not reflected in population prevalence estimates (Torsheim, Valimaa, & Danielson, 2004). A study by Barnett, Mercer, Norburg, Watt, Wyke, and Guthrie (2012), which extracted data on 40 separate morbidities

from a database of 1, 751, 841, patients registered with 314 medical practices in Scotland as of March 2007, indicated a much higher prevalence rate of 27.4% in younger age groups, although this survey subsumed the data of children and adolescents with young adults (18 to 24 years). Therefore, it should be kept in mind that although these figures indicate that chronic disease has a substantially high prevalence among children and adolescents living in England and Wales, it is likely that actual prevalence rates are much higher.

1.1.2 The characteristics of chronic illness in children and adolescents

A clear increasing gradient in rates of chronic illness can be seen when examining the indicated proportion of people in England living with long-term conditions in the Department of Health (2012) figures by their allocated age group (see Figure 1.1). Past the age of nineteen, the estimated incidence of all conditions examined increase substantially (Department of Health, 2012). In addition, although a growing prevalence of people living with multiple long-term conditions has been repeatedly highlighted as a source of concern in official reports (e.g. Department of Health, 2012; Naylor et al., 2016), the incidence of multiple long-term conditions is also relatively low in those aged 18 years or younger. This is as many chronic diseases in adult age groups are acquired because of lifestyle factors and established health risk behaviours (cf. Sawyer Drew, Yeo, & Britto, 2007; La Greca, 1992). Although the rise in chronic illness in childhood over the past 50 years does seem to correlate with a fall in activity levels in this age group, as well as rising levels of obesity, even having considered the likely influence of improved medical treatments (see Halfron & Newacheck, 2010), behavioural factors are seen to play a lesser role in the incidence of chronic illness among these younger age groups (Sawyer et al. 2007). This perhaps underlies the relatively lower incidence of these conditions among young people in comparison with older populations. Moreover, it has been observed that the proportion of children in any specific disease category form a small percentage of the total population - for example, diabetes, one of the most common endocrine disorders of childhood, affected 2.55 youths per 1000 young people in the United States in 2009, and this was the highest prevalence since medical records began

(Dabelea et al., 2014) . The only exception to this general rule is the respiratory condition of asthma, the most common chronic disease of childhood and adolescence, which is estimated to be prevalent amongst 5% to 10% of children internationally (Looijmans-van den Akker, van Luijn, & Verheij, 2016). Therefore, it is only when viewed collectively that children with long-term conditions can be considered a substantial proportion of the juvenile population (Stein & Jessop, 1989; Williams, Holmbeck, & Greenley, 2002).

Figure 1.1 Proportion of people in England with a long-term condition by age, based on data from the General Lifestyle Survey 2009 (*Source: Department of Health, 2012)*

As well as being generally low in incidence, childhood chronic illness is characterised by relatively unobtrusive symptomatology - 66% of the childhood population living with chronic illness are estimated to have relatively mild symptoms, resulting in minimal disruption to daily activities (Newacheck & Taylor, 1992; Barlow & Ellard, 2006). For example, only 27.5% of those identified as having a chronic illness in a large survey of American adolescents reported any impact of their condition on their everyday activities, and only 7.6% reported that their condition had any form of impact on their socialization patterns (Denny et al., 2004). Based on data from a large, representative American population in 1988, Newacheck & Taylor (1992) estimated that, at that time, only 1 in 8 children with chronic

illness could be seen as having a severe degree of impairment. It is important to keep in mind that functionality of children with chronic illness has probably only improved since this time given medical advances (Shaw & McCabe, 2008).Furthermore, while an initial adjustment period has been identified as pivotal in helping adults to cope with the treatment regimen of their condition (e.g. Charmaz, 1995; Sawyer et al., 2007), this initial adjustment period has been argued to be less instrumental in young people who are developing and are therefore constantly in a state of re-adjustment (Bennett, 1994). Indeed, it has been found that children and adolescents have quite different perceptions regarding the cause of their illness and their ability to cope with their treatment regimens when compared with adults (Schmidt, Petersen, & Bullinger, 2003). However, it has also been found that the adherence to medical regimens declines as children enter their adolescent years (e.g. Holmbeck, 2002; Viner & Davies, 2012).

Chronic illness in childhood and adolescence also shows socio-economic gradients, with children from less privileged social classes showing higher incidence rates across international prevalence studies (Michaud et al., 2007; Perrin, Bloom, & Gortmaker, 2007; Halfon & Newacheck, 2010). Price and colleagues (Price, Khubchandani, McKinney, & Braun, 2013) posit that low birth weights amongst more socially deprived mothers could in some way explain these socio-economic discrepancies. However, this socio-economic gradient is not a specific characteristic of chronic illness in childhood and adolescence. In fact, this socio-economic bias in incidence is found in rates of chronic illness across age groups, with many official reports highlighting that those living with a long-term condition in the United Kingdom, and, in particular, those living with multiple long-term conditions, disproportionately reside in more socio-economically deprived areas (Naylor et al., 2012).

1.1.3 Summary

A large-scale epidemiological transition in the characteristics of disease has been reflected in childhood and adolescent groups, with the rates of young people living with conditions that require prolonged healthcare growing substantially over the past fifty years. Although the exact parameters of the categorisation of “chronic disease” are hard to define, and this creates

difficulties in estimating population prevalence, it is estimated that at least 8% of those aged nine years or younger in England and Wales, and 10% of those aged ten to nineteen years, are living with such conditions. However, although these children and adolescents cumulatively subsume a substantial proportion of the juvenile population, the incidence of specific conditions is relatively low, with the exception of the respiratory condition of asthma, which affects approximately 5% to 10% of the childhood and adolescent population. Moreover, childhood and adolescent chronic disease is mainly characterised by quite mild symptomatology, with relatively little impairment to daily functioning. Children are argued to assimilate relatively more easily to their condition than adults, although adherence to medical regimens has been found to decline in adolescence. Socio-economic gradients have been noted in the incidence of chronic disease, with children living with long-term health conditions disproportionately more likely to reside in socio-economically deprived areas.

1.2 Chronic Illness as a Risk Factor for the Mental Health of Children and Adolescents

In the past number of years, psychiatric comorbidities affecting people living with chronic illness have become a prominent focus in public healthcare circulars in England and Wales (e.g. Naylor et al., 2012; Academy of Royal Colleges, 2009; Mental Health Network/NHS Confederation, 2012). As stated in the opening of this chapter, it has been found that an adult living with a chronic illness is two- to three- times more likely to present with a psychiatric illness than a person in the general population (Naylor et al., 2012). Moreover, this association has been established for a broad range of primary diagnoses (Patten, 1999), although this relationship is particularly strong for patients living with chronic obstructive pulmonary disease and musculoskeletal disorders (Academy of Medical Royal Colleges, 2009). These disproportionately high rates of psychiatric illness have a detrimental impact on patient quality of life and physical health outcomes (see Naylor et al., 2012; Mujica-Mota et al., 2015), and it is estimated that they result in a 45% to 75% increase in service costs annually (Naylor et al., 2012; Mental Health Network/NHS Confederation, 2012). Consequently, the mental health of patients living with chronic illness has become a priority area within the National Health System in England and Wales (Department of Health, 2012).

However, although these findings are stark and indicate a strong relationship between chronic illness and psychiatric illness in adulthood, it cannot be seen as an indication of the relationship between chronic health problems and mental health in childhood and adolescence. There is a tendency within healthcare discourse to view children and adolescents as “small adults” (p. 357, Grey & Sullivan-Bolyai, 1999), and, as such, to frequently apply learning based on adults with chronic illness to younger populations (e.g. Grey & Sullivan-Bolyai, 1999; Williams, Holmbeck, & Greenley, 2002; Sawyer et al., 2007). However, the disproportionate rate of psychiatric comorbidities in adulthood have been largely attributed to pre-existing lifestyle and health-related risk factors, which are common aetiological factors in the onset of both chronic physical illness and adult psychopathology (e.g. Churchill, 2001; Naylor et al., 2012; Mental Health Network/NHS Confederation, 2012). There

are also variations in the characterisation of childhood and adolescent psychopathology as opposed to adult psychiatric disorders (e.g. Kaufman, Martin, King, & Charney, 2001; Jaffee et al., 2002), in addition to the relatively lower incidence and unique characteristics of childhood and adolescent chronic illness. Consequently, it is vitally important that any discussion of psychiatric illness in the context of childhood and adolescent psychopathology is separated from investigations of this relationship in adulthood. Therefore, it is important to highlight that chronic health conditions in childhood and adolescence have been independently proposed as a risk factor for poor mental health outcomes for these younger age groups.

This section of the literature review will examine why chronic illness in childhood and adolescence has been hypothesised as being a risk factor for the mental health of these age groups. It will open with an overview of existing theory regarding this association, which will be balanced with current understanding of risk factors in mental health. It will then examine the support for these theories from existing empirical investigations, both in terms of support for the underlying mechanisms proposed and in terms of the associated mental health of children and adolescents living with chronic health problems. It should be highlighted that some methodological concerns have been raised concerning the design of many studies in the field. These methodological artefacts will be reviewed and it will be queried the extent to which these study limitations have biased the directionality of results. It is hoped that this overview will explain the rationale for a more methodologically balanced systematic review of the literature, which will be outlined in the subsequent section of this literature review.

1.2.1 The theory of chronic illness as a risk factor to the mental health of children and adolescents

From the first recognition of the epidemiological shift to a growing prevalence of chronic illness in the field of paediatric healthcare, chronic health problems have been theorised as having a negative impact on child and adolescent mental well-being (Wallander & Varni, 1998). This theory is consistently reflected in more recent discussions of the impact of chronic illness in adolescence by Michaud, Suris, and Viner (2007) and Sawyer and

colleagues (2007), where the main impetus behind the call for further research in this age group is the hypothesised negative impact of chronic health problems on adolescent psychological well-being. So why are chronic medical health problems in youth and adolescence considered to be such a risk factor for the mental health of this age group, especially given that such problems are found to be generally characterised by quite mild symptomatology and impairment (e.g. Newacheck & Taylor, 1992)? Early theorists in the field of paediatric chronic illness (e.g. Pless & Pinkerton, 1976; Stein & Jessop, 1982) argued that chronic health problems, regardless of the primary diagnosis, are associated with a number of common stressors which lead to poor familial and psychosocial outcomes for children and adolescents. This is why Michaud and colleagues (2007) and Sawyer and colleagues (2007) in particular hypothesise adolescence to be an acute risk area in the development of mental health problems in children living with chronic illness. These papers argue that the demands of chronic medical problems may come into acute conflict with the main developmental milestones of adolescence, such as increased autonomy from parents and identity formation. Therefore, it is hypothesised that chronic illness in childhood and adolescence is associated with poor mental health outcomes as a consequence of the continuing stress chronic ill health places on normal patterns of development.

When examining the papers of the original proponents of this "non-categorical" view of chronic illness (e.g. Stein & Jessop, 1982; 1989; Pless & Pinkerton, 1976), it is clear that a generalised association of chronic health conditions to childhood and adolescent mental ill-health was not proposed. Rather, these theorists argued that common aspects of chronic illness – such as increased healthcare contact and activity limitations – provide the strongest insight into mental health outcomes, relative to diagnosis alone. This is clear from an early study Stein and Jessop (1989) used to support their hypothesis. This study used data from two American studies – the Pediatric Ambulatory Care Treatment Study (an institutional study) (n=2000) and the National Health Examination Survey Cycles II and III (a population-based study) (n=1946) – to test the utility of diagnoses in predicting a range

of psychological, social, and educational outcomes. Rather than finding that chronic health problems ubiquitously predicted poor outcomes regardless of diagnosis, they found that there was more variation within diagnostic groups than between them. They, therefore, concluded that it may be more insightful to focus on common dimensions of long-term conditions in the prediction of psychosocial outcomes. Moreover, these theories were also guided by a form of pragmatism, with Stein and Jessop (1982) highlighting the difficulties in understanding the psychosocial impact of such a wide range of conditions with such low incidence rates in the general population. However, this more nuanced view of the impact of chronic illness on child development, and, subsequently, on mental health, has not been reflected in the underlining theories guiding much of the research in the field of child and adolescent chronic illness in the following years. It is clear from a review paper by Wallander and Varni (1998), which overviewed research focusing on the psychosocial outcomes of paediatric chronic health disorders in the preceding 5 to 8 years, that researchers had commonly assumed a generalised negative psychosocial impact of chronic disease in childhood and adolescence, theorising that any role of specific disease characteristics was moderating rather than mediating. A more recent review of the literature by Van der Lee and colleagues (2007) also found that the clear majority of the research studies assumed a common impact of chronic illness on psychological and social outcomes regardless of the primary diagnosis or severity of impairments.

It should be noted that the theory that the mechanisms underlying the association of chronic health problems to mental-ill health are characterised by continuous stress, is compatible with current knowledge regarding the aetiological factors of child and adolescent psychopathology. For example, although the root causes of mental health disorders are complex and heterogeneous, Henje-Blom and colleagues (Henje Blom et al., 2016) and Hayden and Mash (2014) argue, that, at their essence, all can be seen as resulting from increased neural susceptibility to stress. Such patterns of neural sensitivity have been used to explain the female preponderance of emotional disorders in adolescence, with females releasing a high level of

gonadal steroid hormones following puberty which affects cortisol reactivity (Henje Blom et al., 2016). However, the roots of such stress are complex, and are often accumulative and dynamic. For example, the mental health risk consistently attributed to socio-economic deprivation is attributed to the fact that socio-economic deprivation is a marker for a multitude of developmental risk factors and stressors, such as parental substance abuse and marital breakdown (e.g. Patel, Flisher, Hetrick, & McGorry, 2007). In addition, some individuals are more susceptible than others to the impact of contextual stressors (Henje Blom et al., 2016). For example, depression is moderately heritable (Thapar, Collishaw, Pine, & Thapar, 2012) and, in addition, early experiences may shape neurobiological structures and functions, and may make individuals more sensitive to the effects of emotional distress at adolescence (e.g. Cicchetti & Walker, 2001; Fox, Zeanah, & Nelson, 2012). Moreover, protective factors, such as strong supportive social relationships, may provide resilience in children with strong predisposition to mental illness (e.g. Holmbeck, 2002). Therefore, the onset of mental illness, in particular from early adolescence onwards, is best understood, not as a direct result of the impact of a single risk factor, or set of risk factors, but as a developmental trajectory, with the unique interplay of risk and protective factors giving rise to mental illness across different developmental milestones (e.g. Holmbeck, 2002). Therefore, if chronic medical issues are indeed associated with a common and continuing stress on normal developmental processes, it would suggest that long-term conditions may indeed be a risk factor for poor child and adolescent mental health in a proportion of children who may be more susceptible to the effects of lifestyle stressors. It would also lend some support to the view of adolescence as being a risk period for mental health in children living with chronic health conditions, given the increased neural susceptibility to contextual stressors during this period. However, this is only if the current theory of chronic health problems as having a generalised negative impact on a range of developmental outcomes is supported.

It should be noted that there have been theoretical models developed to describe the association between the thoughts and behaviours in adolescent presenting with chronic illness and mental ill-health, mostly for use in clinical practice. For example,

Verhoof, Maurice-Stam, Heymans, Evers and Grootenhuis (2014) overview evidence which has linked illness cognitions – i.e. the ways in which people give meaning to their illness and illness symptoms – to feelings of anxiety and depression. Although they note that much of this research was developed in adults with chronic illness, their research shows that cross-sectionally, negative illness cognitions are associated with lower health related quality of life and well-being in a sample of young adults who had developed chronic illness in their early years. Therefore, they argue that tackling these negative illness cognitions could be key to improving mental well-being among people with chronic illness. It should be noted that Sint Nicolaas and colleagues (2016) argue in a more recent paper, that in children with chronic illness, the role of parental illness cognitions must also be considered in order to develop psychotherapeutic interventions. Although such a model is supported from the association between illness cognitions and symptoms of mental ill-health in empirical studies (see Verhoof et al., 2014), and therefore has a pragmatic clinical value, it does not answer the crucial question of how these negative illness cognitions form in children and adolescents, or their families.

The catastrophising theory has also been used to understand symptoms of anxiety and depression in children and adolescents with chronic illness, but has mainly been used to understand reactions to painful symptomatology (see Leung, 2012). Catastophising is a cognitive style whereby the individual displays an irrationally negative forecast of current and future events (Leung, 2012). In the context of chronic illness, it is theorised that patients have exaggerated and ruminating cognitions regarding the painful stimuli that they may be experiencing, or may experience in future (Leung, 2012). Similar to the illness cognition model, it has been argued that when applying this theory to younger children that clinicians should consider the possibility of parents catastrophising physical symptoms, and the impact that this may have their children's perceptions of their illness (Langer, Romano, Levy, Walker, & Whitehead, 2009; Langer, Romano, Liu, Levy, Nielson, & Brown, 2016). Although it is clear that this catastrophising style could be generalised to other symptoms of chronic illness, it should be kept in mind that catastrophising was first used to describe a cognitive style involved in the maintenance of anxiety and depression symptoms (Leung, 2012). Therefore, as in the illness cognition model, focusing on catastrophising could limit insight into how this cognitive style, and related symptoms of anxiety and depression, first emerge. It should be noted that catastrophising of symptoms is also an element of another theoretical model that has principally been used to understand reactivity to painful symptoms of chronic illness: the fear-avoidance model (Crombez, Eccleston, Van

Damme, Vlaeyon, & Karoly, 2012). This model posits that if pain is understood in a catastrophising manner, the person will turn to safety seeking behaviours to avoid future occurrences, such as avoidance of any activities perceived to elicit the painful symptoms (Crombez et al., 2012). Although this model was developed to explain symptoms of avoidance in adults with conditions such as chronic back pain, it was later applied to behaviours seen in children and adolescents (Asmundson, Noel, Peter, & Parkerson, 2012). Again, this model has mainly been used to understand the maintenance of anxiety and depression symptoms in the context of chronic illness (e.g. Crombez et al., 2012).

The risk resilience model of pediatric chronic illness (e.g. Cousins, Kalapurakkel, Cohen, & Simons, 2015) is more in line with contemporary views of the development of mental illness. Although it has again been mainly used to consider reactivity to painful symptoms, it also employs a dynamic model which considers personal and social resilience mechanisms in addition to illness risks (see Cousins et al., 2015). This is very much a strengths-based model, which argues for a focus on individual resilience and protective factors, and has been developed with clinical presentations and treatments in mind (Cousins et al., 2015). As in the case of the previous models overviewed, the risk resilience model is supported by empirical investigations, and has been shown to have great practical utility in clinical settings (see Cousins et al., 2015). However, in terms of understanding the relationship between chronic illness and the development of mental ill-health, it is argued that a more developmental view is required with consideration of biopsychosocial factors, as is put forward in contemporary theories. However, it is argued that such a view is especially important to understanding the impact of chronic illness on well-being in adolescence.

1.2.1.1 Chronic illness and adolescent development

As suggested by this overview, particular emphasis has been placed on why chronic illness may specifically pose a risk to mental health in adolescence (e.g. Sawyer et al., 2007). The overview of contemporary views of adolescent mental health emphasised that such views are highly dynamic in nature, and consider the ways in which the interaction between risk and protective factors may change across the lifespan (e.g. Holmbeck, 2002). This dynamic view of developmental outcomes has been generally accepted by theorists across the field of psychology, who view development as an interaction between biological, personal, contextual and social factors which interact in a variable fashion over the lifespan (see Lerner, Theokas, & Bobek, 2012). The role of biological and social factors in personal development and

well-being is seen to be particularly acute during the period of adolescence (Sawyer et al., 2007). The World Health Organisation (e.g. 2015) defines adolescence as the period between 10 and 19 years, which is normatively marked by the initiation of puberty, and characterised by increasing independence and social awareness. The adolescent period has traditionally been a relatively understudied period in medical research (see Viner & Davies, 2012; Patton et al., 2016), a factor which been attributed to the low mortality risk during these years from naturally occurring pathology (see Viner & Davies, 2012; Patton et al., 2016). However, increased understanding of the period of adolescence as a critical period of social development and identity formation has led many to view this period as being of significant import to lifespan health and future well-being, especially in the context of treating a long-term condition (Michaud et al., 2007). As Blakemore (2008) overviews, the initiation of puberty, and the release of related pubertal hormones, not only marks rapid external physical development, but also gives rise to changes in brain chemistry. These neural changes not only enhance social understanding and self-awareness, but also have a significant impact on the systems which control individual reactivity to rewards and danger (Blakemore, 2008). In addition, as highlighted, increased neural susceptibility to cortisol leads to adolescents reporting elevated stress levels, with this being seen particularly in adolescent girls (Nelson, Leibenluft, McClure, & Pine, 2005). Given the very dynamic changes occurring during this period, Miauton, Narring and Michaud (2003) argue that adolescent health, or health behaviours, cannot be understood without reference to a biopsychosocial model, which understands health outcomes to be a reciprocal interaction between the characteristics of the illness and the developmental changes that occur during this period, in addition to the social context. The importance of considering such contextual factors is made clear when examining what is known about the ways in which adolescents living with a chronic illness respond to their medical regimens and related demands during these years.

It has been long identified that there is a particular issue in maintaining adherence to medical regimens amongst children with chronic health conditions as they progress into the adolescent years (see Geist, Valerie & Otley, 2003). For example, numerous sources of data would suggest that approximately only 21% of American teenagers with type 1 diabetes mellitus meet the recommended medically instituted guidelines for haemoglobin A1c levels (see Dayte, Moore, Russell & Jaser, 2015). Significantly, it has been highlighted that this lack of adherence does not seem to be linked to health beliefs, in the same fashion that is seen in adults (Geist et al., 2003). In contrast, Borus and Laffel (2010) argue that the barriers to self-

management and adherence amongst this age group come from the increased social awareness and identity searching that is characteristic of this dynamic period of development. As part of their identify formation, adolescents are given more independence from parents and experiment with adult behaviour (e.g. sexual acts, substance use) (Michaud et al., 2007). Qualitative data would suggest that adolescents see the demands and restrictions imposed by their treatment regimen as a barrier to this experimentation (Michaud et al., 2007). It is hypothesised that although adolescents recognise the importance of managing their condition, decreased neural reactivity to danger, and increased reactivity to social rewards, means that adolescents with chronic illness are likely to perform risky behaviours if they perceive that there is a social reward to doing so (Michaud et al., 2007; Miauton et al., 2003). Therefore, it is theorised that due to this perceived conflict of disease management with social and personal goals, adolescents fail to maintain the treatment adherence demonstrated at earlier stages in development (Borus & Laffel, 2015; Michaud et al. 2007). Moreover, it is argued that such risky health behaviours are reinforced by the increased social acceptance perceived to be garnered by these behaviours. However, as Sawyer and colleagues (2007) and Patten and colleagues (2016) note, although initial exploratory data supports this theoretical position, longitudinal data examining the impact of social, educational and pubertal transitions on adolescents with chronic illness is needed in order to fully validate this biopsychosocial view of disease management in adolescence.

The dynamics of adolescent development can also cause young people to change their existing view of their illness and its' impact on their lives (Michaud et al., 2007; Sawyer et al., 2007). Chronic disease and medical interventions can affect the timing of puberty, and this can have a substantial impact on the development of adolescents in terms of the way that they are treated by their parents and the ways in which they are seen by their peers (Patton and Viner, 2007). This impact is viewed as possibly even more detrimental for adolescent boys, given that late developing boys have been shown to have poorer social outcomes than their early developing counterparts (Michaud et al., 2007). Furthermore, increased social self-awareness as a result of neural changes may lead to more negative illness cognitions in conditions where there are physical manifestations of the chronic illness, such as stomas, scars, and insulin pumps (Michaud et al., 2007). Therefore, it is clear that to work with young people with chronic illness in the adolescent years requires a knowledge of the dynamics of adolescent development and the way this may interact with health beliefs and disease management. Evidence regarding self-management behaviours would suggest a conflict between illness management and

related coping skills, and the rapid developmental changes and growth that are characteristic of this stage in the lifespan. This would reinforce the view of chronic illness as an acute stressor during this stage of the lifespan, and would again support the integral importance of examining the impact that chronic illness has on mental health and well-being in these transitional years.

1.2.2 Support for existing theory of chronic illness as a risk factor to child and adolescent mental health

This section will examine support for the existing theory of chronic illness as a specific risk factor to child and adolescent health, firstly by focusing on the empirical support for the mechanisms proposed, and then by looking at what is known about the associated psychological health of children and adolescents with chronic health conditions.

1.2.2.1 Support for the theory of chronic illness as a continuing stressor throughout child development

As Sein (2001) highlights, much of the early research focusing on the stressors associated with chronic illness focused on the family context. Researchers hypothesised that the presence of a paediatric chronic illness in a family unit, and the related treatment burdens involved, would have a detrimental impact on family functioning and that this be one way in which chronic illness is associated with poor mental health outcomes for children (Eiser, 1990). This theory has had a continuing presence in the progression of research in the field, and, as a consequence, family functioning in the context of childhood chronic illness has been investigated more than any other key variable in development (Williams et al., 2002; McClellan & Cohen, 2007). Recent discussions of the possible impact of chronic illness on family functioning have become increasingly aware of how this relationship may vary with age, with a particularly nuanced relationship suggested for the adolescent period (e.g. Sawyer et al., 2007). It is generally hypothesised that chronic illness leads to a high amount of dependence on parents, and that this may conflict with the desire for increased independence during this developmental phase (Surís, 2003; Schmidt et al., 2003; Jones & Lollar, 2008). However, the support for such theories is mixed.

An early review of the field by Eiser (1990) found evidence that the presence of chronic illness may indeed have a deleterious effect on family functioning, with mothers being perceived as more restrictive, families showing higher levels of conflict, support networks being smaller and denser, and siblings demonstrating patterns of maladjustment. Yet, it was noted that many of these studies were qualitative in nature, or based on small, possibly unrepresentative samples. A more recent review by Barlow and Ellard (2006) indicated that no strong conclusions could be made based on existing research regarding the impact of chronic illness on parental well-being and the parent-child relationship. However, there was some evidence to suggest that siblings of children living with chronic illness may be at risk of experiencing poor psychosocial outcomes, and that this may be suggestive of some degree of malfunctioning within the family system. In contrast, a nearly concurrent review by McClellan and Cohen (2007) concluded that there was no evidence to suggest that childhood chronic illness has a negative impact on any aspect of family functioning, but, again, similar to Barlow and Ellard's (2006) review, they note that the general quality of the research in this area is quite poor.

Family functioning does play a crucial role in children's mental health in the context of chronic illness (e.g. Geist, Grdisa, & Otley, 2003). A recent meta-analysis by Leeman and colleagues (Leeman et al., 2016) found that, of the 719 dimensions of family functioning investigated, all showed significant correlations with child outcomes. However, cohesion and inter-familial conflict showed the strongest association with child psychosocial outcomes, inclusive of mental well-being, social competence and quality of life. In addition, excessive parental control in adolescence has been found to lead to reduced feelings of autonomy, and increased demonstrations of problem behaviour (Holmbeck, 2002). Yet, the lack of consistent evidence for a pathway from chronic illness to impairments in family functioning may mean that the role of family functioning in psychiatric comorbidities among children with chronic illness may be moderating rather that mediating, if such an association exists.

It should be noted that there is evidence to suggest that there may be some fluctuations in the impact of chronic illness on family functioning depending on disease characteristics. For example, research indicates that the parents of children with cystic fibrosis have two to three times higher rates of depression than those found in broader community samples (Quittner et al., 2014). It should be noted that this finding may not suggest that the theory of common stressors attributable to chronic illness is invalid, but may suggest that a more nuanced view of the association of chronic illness to family functioning may be needed. For example, Silver, Westbrook and Stein (1998) found that, based on data from an American population-based national sample (n=298), parents of children with functional limitations were more distressed than other parents of children with chronic illness. Therefore, it may be that functional limitations in the context of chronic illness presents as a stressor to family functioning, and that these effects in turn lead to poor mental health of children and adolescents. Yet, such a finding would seem to invalidate the view that chronic health problems generally present as a risk factor to child and adolescent mental health, given that most children experience quite mild levels of impairment (e.g. Newacheck & Taylor, 1992). However, it should be noted that in Silver and colleagues (1998) study, a separate analysis of an inner-city community-based sample (n=380) found that the presence of paediatric chronic illness predicted greater levels of parental distress, regardless of the particular impairments associated with the condition. This raises concerns about the possibility of bias within the sample being represented in the study findings.

Therefore, as Wood (1999) argues, the quality of family functioning and inter-family relationships does seem to have a strong impact on the mental health of children and adolescents with chronic illness. However, it is not clear if chronic illness has a general negative impact on family functioning. This lack of clarity may be driven by methodological limitations within the research. As McClellan and Cohen (2007) argue family functioning is a very broad concept, and perhaps there needs to be a more articulate theory put forward of how, specifically, chronic health problems negatively impact on families. Moreover, there is limited focus on age-related variations in family

functioning within this research, which contrasts with the more nuanced discussions of how the impact of chronic illness on psychosocial outcomes may vary with age (e.g. Sawyer et al., 2007). Above all, issues regarding the quality of the research were continuously highlighted in reviews of the literature, which may mean that biased methodological practices, such as the use of small samples (e.g. Barlow & Ellard, 2006) are obscuring insight into a true association between chronic health problems and poor family outcomes.

More recent studies have focused on how chronic illness may present as a stressor to patterns of normative social development, with the view that such impairments would lead to a decline in psychological well-being (see Geist, et al., 2003) A lot of this research has focused on the period of adolescence, when, social variables, such as school connectedness, personal autonomy, and peer relationships, become important determinants of psychological well-being (Viner & Davies, 2012). Indeed, as discussed, recent theoretical articles have envisioned chronic illness as being a specific impairment to well-being during this developmental period in particular (Michaud et al., 2007; Sawyer et al., 2007). It should be noted that adherence to medical regimens is at its lowest in adolescence, when compared to both children and adults (e.g. Holmbeck, 2002; Viner & Davies, 2012), which would suggest that the major developmental processes of this time interact with illness outcomes (Holmbeck, 2002).

Yet, similar to the findings regarding family functioning, the support to a pathway from chronic illness to psychosocial disruptions in adolescence is inconsistent. Williams, Holmbeck & Greenley (2002) argue that most research findings suggest that peer relationships among adolescents with chronic illness are similar to their healthy peers. However, a systematic review of rates of peer victimisation by Sentenac and colleagues (Sentenac, et al., 2012) indicated that children and adolescents with chronic conditions (aged between five and seventeen years) were overall more likely to be identified as victims of bullying across a wide number of research investigations. The researchers hypothesise this may be a consequence of how chronic health conditions noticeably differentiate children with chronic illness from their healthy peers. Yet, it should be noted that when rates of

peer victimisation among specific conditions were isolated, children with conditions such as asthma and eczema were less likely to report victimisation, which raises questions about the wider applicability of this finding to specific diagnostic categories. Furthermore, as noted, Denny and colleagues (Denny et al., 2014) found that only 7.6% of adolescents in their national sample reported that their condition had an impact on their social activities. However, a meta-analysis by Martinez, Carter and Legato (2011), focusing specifically on social competence, found that successful socialisation varied by diagnosis, with children with neurological disorders (e.g. epilepsy) displaying significantly lower levels of competence than peers, and conditions such as asthma and diabetes having no discernible association.

Stam and colleagues (Stam, Hartman, Deurloo, Groothoff, & Grootenhuis, 2006) found delayed attainment of developmental milestones (inclusive of autonomy, psychosexual and social milestones) amongst a Dutch sample of 650 young adults who had grown up with a chronic illness when compared to a general population comparative group. However, the trends showed significant variation by disease type, with young adults with oesophageal atresia demonstrating no identifiable differences with the comparative group, and survivors of childhood cancer and patients with end-stage renal disease most delayed. The authors attribute the diversity in outcomes to variations in the medical consequences of the primary diagnosis. In a cross-sectional national study in the United States (Jones & Lollar, 2008) and in Sweden (Nylander, Seidel, & Tindberg, 2014) youths with chronic illness were found to demonstrate higher levels of health-risk behaviours, such as smoking, drug experimentation and early sexual debut. However, it should be noted that in the studies of Jones and Lollar (2008), the sample was inclusive of youths with self-reported disability, and that the group with chronic illness were also more likely to have reported being sexually assaulted and being overweight. Such sample characteristics suggest that there may have been confounding factors in the association identified.

Jones and Lollar (2008) and Nylander and colleagues (2014) hypothesised that the disproportionate rates of health-risk behaviours found amongst their

samples of adolescents with chronic illness were indicative of adolescents trying to “fit in” with peers, and gain their approval, a hypothesis also put forward by Valencia and Cromer (2000). This largely fits in with qualitative accounts of the lived experience of paediatric chronic illness, where the major themes to consistently emerge are the children’s desire to appear normal and similar to their peers (e.g. Yates et al., 2010; Sartain, Clarke & Heyman, 2000; McCormack, Norrish, Parker, & Framptom, 2010; Taylor, Gibson, & Franck, 2008; Lambert & Keogh, 2015; Ferguson & Walker, 2014; Hopkins, Green, Henry, Edwards-Wang, 2014; Venning, Eliot, Wilson, & Kettler, 2008). Moreover, it has been found that children and their parents see the impact of the illness on daily activities, inclusive of social activities, as the most stressful aspect of the disease, even in life-threatening conditions such as cancer (Compas, Jaser, Dunn, & Rodriguez, 2012). Taylor, Gibson and Franck’s (2008) systematic review of the qualitative literature also found that the importance of developing and maintaining friendships was the most common theme to emerge in qualitative accounts of the lived experience of chronic illness in childhood and adolescence. Therefore, on the whole, it does appear that peer relationships are highly important to adolescents living with a chronic illness, with adolescents striving to live as normally as their condition permits. However, the impact of living with a chronic condition on the normative trajectory of psychosocial development remains unclear, and it is queried whether deleterious patterns are only associated with certain conditions. It should also be noted that Geist, Grdisa and Otley (2003) have concluded that insight is once again limited by the general poor design of studies in this extensive body of research, inclusive of issues regarding small samples and lack of adjustment for possible confounding factors.

Therefore, overall, these studies provide, at best, mixed support for a view of chronic illness as being associated with continuing stress on normative trajectories of development. As it is the view that this impact on development is the mechanism by which chronic physical problems result in poor child and adolescent mental health outcomes, this raises concerns about the validity of the primary theory of the relationship of chronic health problems to

psychological well-being in the field. Of particular concern are findings of inter-disease variations in psychosocial outcomes. Even if variation could be explained, as Stein and Jessop (1989) suggest, by factors present in all chronic illness conditions to a varying degree, this would still suggest that only a minority of children living with chronic health conditions are at an increased risk of developing psychopathology. However, continuous suggestions of quality issues within the research field means that no strong conclusions can be made regarding the associated impairments to normative psychosocial development as a consequence of chronic ill health in childhood and adolescence.

1.2.2.2 Support for the hypothesised association of chronic health problems in childhood and adolescence to poor mental health outcomes

It is hard to identify prevalence studies examining the specific rates of psychiatric illness among children and adolescents living with chronic illness. The Department of Health (2012) supports the position that chronic illness may a risk factor for poorer mental health outcomes in younger age groups based on data from the United Kingdom National Survey of Children's Mental Health and Wellbeing, which indicates that young people with a physical illness are at a twofold increased risk of developing mental health disorders (see Parry-Langdon, 2008). However, the effects of the chronicity of the condition were not examined explicitly in these analyses which is limiting given that chronic conditions in childhood and adolescence are suggested to be more acutely characterised by mild symptomatology and impairment than other physical illness conditions (Newacheck & Taylor, 1992). A study of multimorbidities amongst Scottish patients registered with GP's, found that the mental-chronic physical health comorbidities were at their lowest in younger age groups – representing a proportion of 0.5% of the overall patients aged 0 to 24 years (95% CI: 0.5 - 0.6), compared to 5.7% of patients aged 25-44 years (95% CI: 5-6-5.7%) (see Barnett et al., 2012). However, in addition to subsuming a large age range of patients this study did not compare rates of psychiatric disorders among this cohort to same-aged peers from the general population of patients. Therefore, these prevalence

studies do not provide clear insight into the incidence of psychiatric illness among children and adolescents living with chronic illness.

A number of meta-analyses focusing on the related mental health outcomes of chronic illness have been undertaken. One of the earliest of these meta-analyses was by Lavigne and Faier-Routman (1992). This investigation was named in the review by Wallander and Varni (1998) as the single greatest contribution to the understanding of the mental health outcomes of paediatric chronic illness. The over-arching indication of this meta-analysis was that children and adolescents affected by chronic illness demonstrate a relatively increased prevalence of emotional symptoms and externalising behavioural issues when compared to their healthy peers. The association between chronic illness and the prevalence of emotional symptoms was, in particular, very strong. Lavigne and Faier-Routman (1992) noted that these associations varied as a function of the informant used and the degree of matching with controls, with studies comparing scores against peers in the general population showing lower effect sizes than studies which used scale norms. There also appeared to be some inter-disease variations in the strength of associations, although Lavigne and Faier-Routman (1992) noted that the number of studies in each disease cluster were too small to statistically analyse effects by diagnosis. Yet, based on descriptive statistics, it was not possible to categorise the conditions in a logical pattern based on their association with mental health outcomes, both in terms of symptomatology and even in terms of relative risk of fatality. Wallander and Varni (1998) highlight that this finding, in particular, was taken as supportive evidence against a view of diagnosis as being particularly insightful to the associated mental health outcomes of chronic illness. It should be noted that although the included studies contained samples from three to nineteen years, age variations were not examined in this meta-analysis.

Wallander and Varni (1998) note that, in the years following the publication of Lavigne and Faier-Routman's (1992) meta-analysis, the number of papers focusing on the mental well-being of children living with chronic illness were quite small in number. This was due to a general belief that consensus on the negative impact of chronic health problems on the mental health of

children and adolescents had been reached (Wallander & Varni, 1998). Yet, criticising Lavigne and Faier-Routman's review for using non-specific outcome measures, Bennet (1994) published a meta-analysis focusing on rates of depression in this population. Reviewing over 60 studies, Bennet (1994) concluded that, although children and adolescents living with chronic illness appeared to be at a slightly increased risk of experiencing depressive symptomatology (although this risk was higher in studies using parental ratings and community-based comparative samples), there was no evidence to suggest that there was a higher incidence of depressive disorders among this population. The findings were also suggestive of not only great variation in symptomatology within conditions, but also across conditions, with a higher risk associated with asthma, recurrent abdominal pain and sickle cell anaemia. Moreover, the trends suggested inconsistent relationships with severity and time since diagnosis, with gender and age found to have limited impact on outcomes.

More recent updates mimic the findings of their predecessors. In 2011, Pinquart and Shen published a series of three meta-analyses which focused on the impact of chronic illness on anxiety (2011a), depression (2011c), and emotional symptoms and externalising behaviour problems (2011b).Chronic illness was associated with higher levels of anxiety overall, but , when looking at specific diagnoses, anxiety levels were only significantly elevated in children with chronic fatigue syndrome (d=0.46), migraine/tension headache (d=0.42), sensory impairment (d=0.35), epilepsy (d=0.34) and asthma (d=0.13) (Pinquart & Shen, 2011a). In addition, elevated levels of anxiety were only observed if illness duration was below the median. In weighted multiple linear regression models, type of illness, year of publication, age, informant, and basis of comparison collectively accounted for approximately 20% of variance in effect sizes. Similar to Bennett (1994), Pinquart and Shen (2011c) also found a small effect size (d=0.19) for the effects of chronic illness on depressive symptomatology, a significant finding in light of the study's focus on depressive symptomatology rather than clinical diagnoses. The authors found that no increased risk was indicated for many conditions such as diabetes and cancer, and that the highest effect

sizes found for chronic fatigue syndrome (d=-.94), fibromyalgia (d=0.59), cleft lip and palate (d=0.54), migraine/tension headache (d=0.51) and epilepsy (d=0.39). They again found variations dependent on gender, year of publication, informant, measure of depression used, country, and target of comparison. The final meta-analysis suggested that young people with chronic illness have a higher level of emotional symptoms (g=0.47), externalising behavioural symptoms (g=0.22) and total behavioural problems (g=0.42) than healthy controls, with chronic fatigue syndrome having the strongest association with emotional symptoms and epilepsy having the strongest association with externalising behavioural symptoms (Pinquart & Shen, 2011b). Elevations were more pronounced in studies using parental ratings. On the ratings of emotional symptoms, all conditions showed significantly elevated rates, with the Q scores indicating some level of inter-disease variation. However, on the scales of externalising behaviour disorders, only 10 out of 17 conditions showed significantly elevated rates. Gender effects were also noted, with emotional symptoms being more prevalent in girls. Throughout the reviews, Pinquart and Shen (2011a; 2011b; 2011c) noted extensive use of samples which subsumed the data of children and adolescents, with the lack of age specific data limiting the possibility of looking at risk variations across age groups. However, including age of the study child as a covariate did not seem to have a significant impact on outcomes, with the only age-related effects being noted were a reduction in anxiety disorders with age (Pinquart & Shen, 2011a) and an early childhood reduction of internalising and externalising behavioural symptoms (Pinquart & Shen, 2011b).

Therefore, these reviews suggest that although there may be a comparatively higher rate of emotional and externalising behaviour symptoms amongst children living with chronic illness conditions, with small to moderate effect sizes consistently identified, the extent to which this impact is generalised across conditions, or the degree to which the impact is clinically relevant is unclear. Moreover, the focus on broad age ranges in these reviews means that age-specific risks may be obscured. Therefore, as was concluded in the overview of the empirical support for the mechanisms

proposed, the theory of chronic health problems in childhood and adolescence being a particular risk factor for the psychological well-being of these age groups remains to be substantiated by empirical research focusing specifically on psychological outcomes.

1.3.2 Quality issues in the study of the related mental health outcomes of long-term conditions in childhood and adolescence

As is clear, although the theory of chronic health problems as being a risk factor to child and adolescent mental health aligns well with what we know about the aetiological factors in child- and adolescent- psychopathology, support for this theory from empirical data is mixed and weak at best. This raises concerns about the validity of the underlying hypothesis in the clear majority of research focusing on the psychosocial outcomes of chronic health problems in this group (e.g. Van der Lee et al., 2007). However, throughout the discussion of the empirical support for this position concerns regarding methodological practices, and how these may have impacted on the direction of findings, were consistently raised.

One of the most substantial concerns highlighted regarding research in this area, is the pervasive dependence on small samples within this research. The meta-analyses reviewed accumulated studies focusing on many different chronic illness conditions, and such research poses significant challenges to researchers given the generally low prevalence of many chronic illness conditions (e.g. La Greca & Varni, 1993). Yet, much research in the area of chronic illness has responded to these challenges by focusing on small, selective samples of a wide age range - a practice further complicated by the lack of attention to the representative nature of these samples, and the validity of chosen comparative groups (Eiser, 1990; Sawyer et al., 2007). Barlow and Ellard (2006) have gone as far as to argue that these sampling issues are endemic in this field, with Boekaerts and Roder (1999) furthermore noting that adjustment for, or even attention to, possible confounding factors is lacking, limiting the comparability of findings across studies. In a further complicating factor, McClellan and Cohen (2007) note that much research includes only young people who demonstrate active symptoms of the disease, limiting the insight into the outcomes of chronic

illness more generally, given that this is usually characterised by quite unobtrusive symptomatology. It is clear that many authors of the meta-analyses overviewed felt that these sampling practices may have biased the direction of their findings – for example, Lavigne and Faier-Routman (1992) hypothesised that these sampling issues could possibly be driving the large intra-disease differences found in their analysis.

One other limitation introduced by the pervasive dependence on small sample sizes is that it negates the possibility of examining possible age-related variations in outcomes. Child and adolescent groups were considered as an amalgamated grouping across the meta-analyses, perhaps as a reflection of the frequent use of broad age groups across the eligible studies. However, these are very distinct developmental stages, with unique psychiatric profiles. For example, in a longitudinal study of 1420 American children aged nine to thirteen years, Costello, Mustillo, Erkanli Keeler, and Angold (2003) found dynamic changes in the prevalence rates of psychiatric disorders across childhood and adolescence. The highest prevalence of mental disorders was among children aged nine to ten years, with levels falling through the age of twelve, and rising steadily again throughout adolescence. The authors later concluded that this trend may be due to a fall in rates of what could be characterised as childhood disorders (e.g. ADHD, separation anxiety disorder) by adolescence, and the gradual emergence of characteristic adult conditions (e.g. major depressive disorder) in the teenage years (Costello, Foley, & Angold, 2006). In addition, as highlighted, chronic illness has been theorised as being particularly tied to poor mental health outcomes in adolescence (e.g. Sawyer et al., 2007), due to the likely disruption these conditions pose to social predictors of mental health during this period, such as increased autonomy from parents (e.g. Schmidt et al., 2003; Surís, 2003). This period has also been identified as a phase of particular susceptibility to neurological stress in studies examining the aetiological factors of psychopathology (e.g. Fox et al., 2012; Cicchetti, & Walker, 2001). Although age of the study child is often included as a covariate in statistical analyses, Williams, Holmbeck and Greenley (2002) argue that most of the samples are too underpowered to accurately assess

age-related effects. Please note that this was the methodology used in the meta-analyses of Pinquart and Shen (2011a; 2011b; 2011c), who did not find that the age of the study child impacted the direction of their findings. Moreover, a lack of longitudinal research focusing on children and adolescents living with chronic illness has been highlighted (see Sawyer and colleagues, 2007), meaning that there is also a limited ability to study age-related variations in outcomes from this perspective. Consequently, current sampling methodologies may be obscuring true age-related variations in the related psychological outcomes of chronic illness.

The second aspect of these study methodologies that must be highlighted relate to the measurement of mental health outcomes. The meta-analyses overviewed have indicated substantial variations in outcomes based on the responder used, with parents generally presenting more negative appraisals of their child's adjustment (e.g. Pinquart & Shen, 2011a; 2011b; 2011c). It has been argued that parental reports on these assessments reveal as much about the parent as they do about the adjustment of their children, and, therefore, multiple psychometric measures, collected from a range of informants, may be more insightful approximations of child well-being (McClellan & Cohen, 2007). However, a further concern has been raised regarding the sensitivity of many psychometric measures specifically in the context of childhood and adolescent chronic illness. These scales include somatic symptoms as indicators of emotional problems. This is because depressive symptomatology presents in many children as physical symptoms, such as excessive fatigue (see Perrin, Stein, & Drotar, 1991; Bennet, 1994). An early review by Canning and Kelleher (1994) compared the indications of these measures against those of rigorous clinical interviews, and noted a lack of sensitivity and precision in the case of children and adolescents living with a chronic illness. The authors, therefore, advised against the use of these measures in studies of populations living with paediatric chronic illness, arguing that findings may be misleading, leading researchers to overestimate the prevalence of mental ill-health in these age groups. Therefore, the relatively small increases in rates of emotional and behavioural symptomatology indicated among the meta-

analyses may just reflect the somatic symptomatology associated with living with a chronic condition. Yet, it should be noted that, despite these concerns, Pinquart and Shen (2011b) found similar trends in responses for somatic versus non-somatic scales amongst chronic illness samples in their analysis of measures of depressive symptomatology.

Having overviewed the methodological concerns underlining research in the field, it is clear that the research reviewed, and in particular the meta-analyses overviewed (e.g. Lavigne & Faier-Routman, 1992; Pinquart and Shen, 2011a; 2011b; 2011c), were based on studies that may have been open to methodological bias, such as the use of small, selective samples and single-informant assessments of child psychological adjustment. Therefore, these reviews cannot be taken as a conclusive and reliable insight into the relationship between chronic health problems and related mental health outcomes. Therefore, learning from the limitations identified in these overviews, it was clear that a more selective approach to reviewing the available research was needed.

1.3.3 Summary

Chronic health problems in childhood and adolescence, regardless of the underlying diagnosis, have been hypothesised as a risk factor to the mental health of these younger age groups. The underlying theory suggests that chronic health problems are associated with a consistent and continuing stress on normative patterns of development, and that this mediates the association of chronic health problems to poor mental health outcomes. More recent discussions have in particular focused on the period of adolescence, and how chronic health problems may conflict with the major developmental processes of this time, such as increased autonomy from the family unit. This theory is strongly compatible with what is known about the aetiological factors of childhood and adolescent psychiatric illness, with many epidemiological overviews arguing that such disorders are best understood as a consequence of neural susceptibility to contextual stressors, which are often dynamic and cumulative. However, it should be noted that although this theory dominates current research in the field, it contrasts with the originating views, which were more nuanced. Rather than assuming chronic illness

symptomatology to be generally associated with poor mental health outcomes in younger age groups, early theorists in the field suggested that factors common to all chronic illness conditions may provide the greatest insight into the associated mental health outcomes of chronic illness in child and adolescent groups.

Support for the theory of chronic health problems as presenting as a continuing source of stress throughout child and adolescent development is very much mixed. Family functioning in the context of childhood chronic illness has been broadly studied, and it is clear that this is an integral factor in child psychological well-being. However, it is unclear if there is a distinct pathway from chronic illness to poor family functioning. This is complicated by the issues of quality within the research, and the lack of focus on possible age-related variations in family outcomes. Findings of impairment to normative trajectories of social development, in particular during adolescence, are also decidedly mixed, and may suggest inter-disease variations. This is a concern as it would suggest that the underlining theory which is guiding much of the current research is invalid. However, no strong conclusions on the basis of these studies can be made, as quality issues were again identified in much of the research in this field. Therefore, the theory of chronic health problems as being associated with a constant and consistent stress on the normative trajectory of child and adolescent development, and this being the mechanism behind poor mental health in this patient group, remains to be substantiated by the empirical research.

As chronic health problems in childhood and adolescence have been proposed as a risk factor to mental health in younger age groups, much research has focused on measuring the mental health outcomes of childhood and adolescent long-term conditions. Consequently, many meta-analyses of this research were identified. These reviews suggest that there may be a comparatively higher rate of emotional and externalising behaviour symptoms amongst children living with chronic illness conditions relative to their healthy peers, with small to medium effect sizes indicated. However, the extent to which this association is generalised across conditions, or the degree to which the impact is clinically relevant, remains unclear. Concerns

have been raised regarding the quality of many of the studies which have been used in this field, and how this may affect the ability to sensitively detect differences between groups of children living with chronic health problems and children who are relatively healthy, even within meta-analyses. Dependence on small and possible unrepresentative samples may be driving findings of substantial intra-disease variation, and limit the possibility of examining age-related variations in outcomes. Moreover, the measures of psychological outcomes may be over-inflating somatic symptomatology as a consequence of the primary diagnosis and parental concerns. Therefore, these reviews have been open to methodological bias and may not provide objective indications of the association of chronic health problems to psychological outcomes. Learning from the limitations in these overviews, it was clear a more selective approach to reviewing the research was needed.

1.4 A Systematic Review of the Literature

Chronic health problems in childhood and adolescence, regardless of the primary diagnosis, have been theorised as presenting as a continuous source of stress throughout child and adolescent development, with these related impairments mediating an association between chronic health problems and poor mental health outcomes for these younger age groups. However, the theory of chronic health problems as having a generally negative impact on family relationships and social development is weakly supported by the literature. Moreover, research focusing on the associated mental health outcomes of chronic illness is also decidedly mixed, with suggestions of inter-disease variation. Yet, such substantial concerns have been raised regarding the quality this research, that even meta-analyses could be open to a degree of methodological bias. This suggested that a more selective approach to reviewing previous research was needed. Such an approach is not unprecedented in the research area. For example, due to the inconsistencies and often contradictory findings of empirical investigations, Opolski and Wilson's (2005) review of the relationship between asthma and depression simultaneously appraised the quality of the literature. This review considered research findings in balance with methodological practices, in an approach that was termed a "pragmatic review". Moreover, reviews in the field of epidemiology always give a higher weighting to studies focusing on representative samples and high quality measures (e.g. Merikangas & Ho, 2014), and as a result, researchers in this field have developed many quality measures to assess the risk of methodological bias in studies. Therefore, a decision was made to undertake an extensive systematic review of the literature with an explicit focus on the quality of methodological procedures. It was hoped that by identifying methodologically rigorous explorations of the association of chronic physical health problems to poor mental health outcomes in childhood and adolescence, a more balanced view of the evidence base would be needed.

The over-arching question of this review was: "Is there evidence to suggest that living with a chronic illness in childhood and adolescence is associated with the co-occurrence of psychiatric illness?" The reason for focusing on

psychiatric illness rather than impairments to normative patterns of development was that, within the remits of the theory under investigation, these outcomes were only of interest as mediators within the larger association of chronic health problems to mental health outcomes. Moreover, such a broad range of developmental factors have been implicated as possibly mediating the association between chronic illness and poor psychological outcomes that it is inconceivable that a thorough exploration could be conducted within a single systematic review. Furthermore, it should be also noted that it was decided to focus on psychiatric illness as an outcome, rather than mental health symptomatology more generally, given that previous reviews (e.g. Bennett, 1994) had explicitly questioned the clinical significance of the relatively higher level of emotional and behavioural symptomatology attributed to living with a chronic illness in childhood and adolescence.

This section will open with an overview of the methodology of this systematic review, eligibility criteria, search process, study selection, data collection process and assessment of risk of bias. The results of this systematic review of the literature will then be presented inclusive of details of the study selection process, the assessment of study quality, the characteristics of the studies that achieved the quality criteria, and what these studies would suggest about the association between chronic health problems and rates of psychiatric illness. Trends in studies that did not reach the quality criteria will also be reviewed. The findings of this review will then be compared to the indications of previous literature.

1.4.1 Methodology of the systematic review

This section will outline the methodology of the systematic review, the overviews of the eligibility criteria, search process, study selection, data collection process and assessment of risk of bias. The write-up of this methodology is in accordance with PRISMA statement guidelines (see Liberati et al., 2009), with the exception that the discussion of risk of bias in individual studies and risk of bias across studies is amalgamated in one section entitled “Quality Assessment” (1.4.1.7)

1.4.1.1 Eligibility criteria

For inclusion, studies had to meet the following criteria: (a) be an original research study that measures a mental health outcome in a sample of young people affected by chronic illness; (b) contain specific analyses relating to a sample aged between birth and nineteen years; (c) compare the levels of psychological adjustment or the frequency of psychiatric diagnoses between children and adolescents with chronic physical illness and their healthy peers, or, alternatively, scale norms; and (d) base analyses on data collected in the year 2000 or later. Please note that, based on these criteria, studies that focused on the mental health outcomes associated with a particular diagnosis were eligible in addition to studies that examined the overall association of chronic illness to mental health outcomes. This was to fully explore the theory that the impact of chronic health conditions on mental health outcomes is reflected across conditions. The date criterion was imposed to ensure that the medical regimens of the young people in the chronic illness sample would be approximately representative of current cohorts of adolescents living with these chronic health conditions. This criterion would also ensure that the review was not merely re-analysing studies that had been included in existing meta-analyses. A specific criterion relating to a separation of age groups in analyses was not specified, although it was hoped that more methodologically balanced research would provide greater insight into possible age related variations in psychological outcomes.

An initial challenge under this quality criterion was to delineate the exact boundaries of what would constitute a chronic illness. Wider discussions have highlighted the debate underlining the inconsistencies in the definition of such conditions (e.g. van der Lee et al., 2007) arising from the lack of somatic comparability between such conditions (e.g. Weisz, 2014). Previous systematic reviews in paediatric chronic illness have often merely focused on a small number of the more prevalent conditions as exemplars (e.g. Didsbury et al., 2016). However, to get a broader sense of possible variations between conditions, it was decided to include as vast a range of long-term physical health disorders as could be identified. Consequently, among studies with a

non-categorical framework, all studies were included regardless of what specific conditions the study's chosen definition would include. Among studies which looked at the specific associations of a named chronic illness condition, a stricter inclusion criterion was imposed. Given the large number of studies identified in pilot studies, this review departed from previous reviews by excluding conditions where although the primary diagnosis may be treatable, follow-on medical treatment may be required (e.g. various forms of cancer), and where psychological processes have been proposed as primary aetiological factors (e.g. chronic pain). This decision was based on suggestions that the psychiatric sequelae of mental health outcomes in these conditions require a unique framework of analysis – for example, the consideration of the effects of cranial radiation in cancer (e.g. Stuber, 1996). It was hoped that such an exclusion criterion would allow for a stricter focus on the similarities and contrasts between more prevalent forms of chronic illness among this age group, such as asthma (e.g. Hagell, Coleman, & Brooks, 2015)

1.4.1.2 Information sources

Pilot searches, undertaken to guide the final search protocol, identified a sizable number of articles which were eligible for screening. In consideration of the review objective and the large number of original empirical studies being returned in trial searches, it was decided to focus the search on academic databases, rather than consulting the grey literature for relevant material.

The following four online databases were searched to identify studies assessing the mental health of children and adolescents with chronic illness: PsycInfo; Medline; Embase; and Web of Science. These databases were selected following consultation with the faculty librarian, and were chosen based on the reasoning that they would provide the widest variety of journals from both the field of medicine and the field of psychology, therefore providing the best opportunity to find a large number of relevant articles. The databases were limited to articles published from the year 2000 onwards.

The databases were searched from the following time periods:

- PsycInfo: 13th November 2014 – 1st December 2014
- Medline: 29th November 2014 – 16th December 2014
- Embase: 16th December 2014 – 6th January 2015
- Web of Science: 6th January 2015 – 22nd January 2015

In addition, all four databases were searched for a final time on the date of 23rd of January 2015 to identify any relevant studies that may have been published in the intervening time period.

1.4.1.3 Search

The following search terms was used uniformly for all four databases:

"chronic illness" OR "chronic disease" OR "long term physical" OR asthma OR diabetes OR "musculoskeletal disorder" OR epilepsy OR anaemia OR anemia

AND

"conduct disorder" OR "conduct problem" OR emotional and behav* difficulties OR emotional and behav* problems OR "mental health" OR depress* OR anxiety OR internali* AND externali*

The named physical conditions (i.e. asthma, diabetes etc.) were selected based on the recurring identification of these conditions in discussions of chronic illness in young people (e.g. Compas et al., 2012; Pinquart & Shen, 2012a; 2012b; 2012c), keeping the study's definition of chronic illness in mind. The age range was filtered to child and adolescent on the PsycInfo, Medline and Embase database. As there was no age filter on the Web of Science database the following search terms were added to those already stated:

AND

child* OR adolesc* OR pediatric OR youth

Search area was limited to the title and abstract, with the exception of the 'Web of Science' database, where this option was not available. In addition, the following filters were used for all databases:

- *Timespan:* Year 2000 Onwards
- *Language:* English
- *Document Type:* Journal Article

On the Medline and Embase databases, results were additionally filtered to only identify studies conducted with human subjects.

1.4.1.4 Study selection

After the four databases were searched, duplicate records were noted and removed. The remaining records were then screened based on title and abstract. In this screening stage, studies that obviously breached the pre-defined eligibility criteria were eliminated. The full texts of the remaining records were then closely examined to ensure that they fulfilled the inclusion criteria. The articles that were deemed eligible were subsequently analysed, and the data abstracted was used to form the systematic analysis. A summary of the study selection process can be seen in the study flowchart (Figure 1.2).

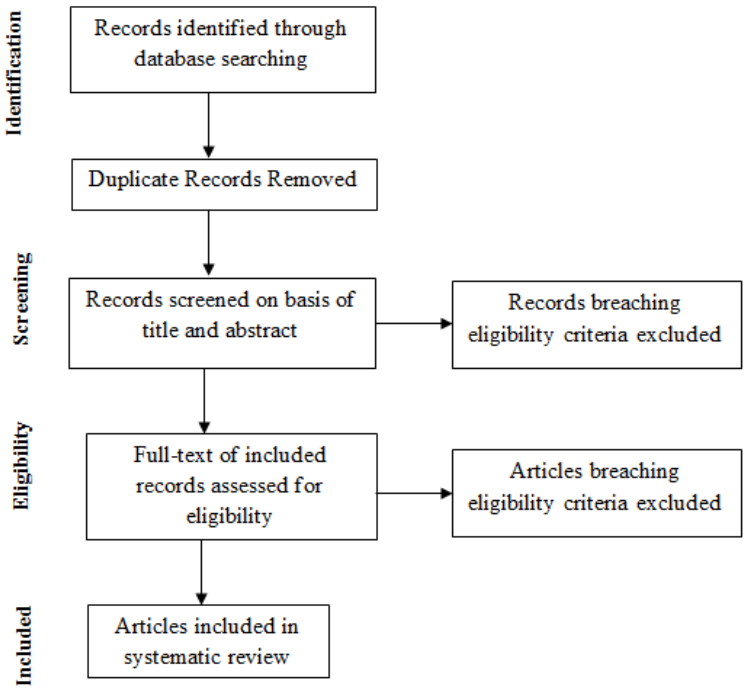


Figure 1.2 Selection process through the different phases of the systematic review

1.4.1.5 Data collection process

Published templates for data extraction forms were reviewed (e.g. the Cochrane Consumers and Communication Review group's data extraction template) and a data extraction form was developed with the focus of this systematic review in mind. It was designed to be used only with articles that fulfilled the eligibility criteria. This form was first pilot-tested on a set of twelve studies, and then refined accordingly to be as concise, yet comprehensive, as possible (a copy is included in Appendix I).

1.4.1.6 Data items

The following headings were included on each data extraction form to structure data abstraction from each study:

(1) Author & Date
(2) Date of Data Collection
(3) Study Design
(4) Sample Size (n)
(5) Description of Sample
(6) Response Rate
(7) Adjustment for Confounding Factors
(8) Measure of Chronic Illness/Specific Chronic Illness
(9) Outcome Mental Health Variable and Measure
(10) Summary of Results
(11) Conclusions
(12) Quality Rating

1.4.1.7 Quality assessment

To make the judgements regarding possible risks of methodological bias as objective as possible, the 'Newcastle-Ottawa Quality Assessment Scale for Cohort Studies' was used. This scale was designed specifically to assess the quality of cohort studies included in epidemiological systematic reviews and was selected based on its application to observational and non-randomised trials, an advantage given the breadth of the studies included in this review. In a review of sixty quality assessment tools designed for use with non-randomised studies by Deeks and colleagues (2003), the Newcastle-Ottawa scale was selected as one of the best tools, with its major drawback being

identified as its lack of measure of the quality of the study analysis. As the study authors note, this drawback would have the biggest impact on reviews assessing the effectiveness of interventions. As this review was focused on the co-occurrence of mental health disorders in long-term physical health conditions, this was not considered to be a reason to reject the scale. As detailed by Wells and colleagues (2014), the content validity and inter-rater reliability of the scale have been established, with analyses into criterion validity on-going. In the scale, stars are awarded for each quality item to aid quick visual assessment of quality.

Under the 'Newcastle-Ottawa Quality Assessment Scale' rating system, each study was judged on three categories of quality criteria: 'Selection'; 'Comparability'; and 'Outcome'. The categories of 'Selection' and 'Outcome' were originally planned to assess bias within studies. The category of 'Comparability' was planned to assess quality across studies.

The 'Selection' category contained four items: (i) the representativeness of the exposed cohort (i.e. were the participants in the chronic illness cohort representative of the average person living with that chronic illness in the population); (ii) the selection of the non-exposed cohort (i.e. were the control/comparison group drawn from the same community as the exposed cohort and were the groups truly comparable in terms of demographics); (iii) ascertainment of exposure (i.e. was the presence of chronic illness ascertained on the basis of physical examination or medical diagnosis); and (iv) demonstration that outcome of interest was not present at the start of study (i.e. were youths with pre-existing mental health problems excluded or were pre-existing mental health issues controlled for in analyses). One star was awarded for each item if the study fulfilled that quality criterion.

The 'Outcome' category contained three items: (i) assessment of outcome (i.e. if the mental health variable was assessed by a structured psychiatric interview or medical record linkage); (ii) was follow-up long enough for outcomes to occur (i.e. in longitudinal studies, were cohorts followed for long enough to ensure there could be a variation in psychological adjustment [minimum pre-determined period: six months]); and (iii) adequacy of follow-

up cohorts (i.e. in longitudinal studies was there a complete follow up cohort, or was the attrition rate likely to introduce bias). Again, one star was awarded for each item if the study fulfilled that quality criterion.

The final category of the 'Newcastle-Ottawa Quality Assessment Scale for Cohort Studies', 'Comparability', aims to identify the comparability of studies on the basis of design or analysis, and contains two items: (i) Study controls for demographic variables; and (ii) Study controls for any additional factor. One star was awarded for each item if the study fulfilled that quality criterion.

Although it was originally envisioned that this scale would be the only measure of study quality across the review, and each study eligible was assigned a rating based on this scale, the quality of the studies were too low to use this scale to isolate studies for the main review. Therefore, a more limited quality criteria, based on the exclusion of certain items from the 'Newcastle-Ottawa Quality Assessment Scale for Cohort Studies', was used to assess study quality. It was decided that only studies that fulfilled the following criteria would be included in the main literature review:

1. **A representative exposed cohort:** In line with the quality ratings of 'Newcastle-Ottawa Quality Assessment Scale for Cohort Studies', the exposed sample should somewhat represent the average young person living with that illness condition in the community
2. **A high quality comparative group:** The comparative group should be comparable to the exposed cohort in terms of demographic characteristics and suffering from no major medical issues, in order to enable unbiased comparisons between the groups.
3. **An independent measure of illness diagnosis:** The exposure measure should not be reliant on parent- or self- report of diagnosis.
4. **A high quality assessment of psychological outcomes:** The mental health measure should be at low risk of introducing subjective bias or inflating somatic symptoms

5. **Control for demographic variables:** The study should have adjusted for the confounding effects of demographic variables. This criterion was imposed to reduce the risk of bias when comparing findings across-studies.

As outlined, the 'Newcastle-Ottawa' rating scale gives a higher quality rating to studies that use a longitudinal methodology. Although it is true that longitudinal research provides a better insight into the stability of associations over time, as well as insights into possible mediating factors, a lack of longitudinal data in the research area was identified at the outset of the assessment of the study criteria. Therefore, the quality criteria that would only apply to longitudinal analyses were not used as a basis to exclude studies from the main review. Baseline controls for mental health were also not prioritised as a quality criterion as, in the case of studies using cross-sectional methodology, this would be unnecessary. It should be noted that these quality ratings negated original plans to perform a meta-analysis of studies that met the quality criteria. A lack of high quality studies was noted, and the variation in outcome measures meant that the under-taking of a meta-analysis would not provide additional insight beyond a qualitative synthesis.

1.4.1.8 Summary measures

All comparative data relating to mental health in chronic illness (including mean differences, risk ratios, odds ratios etc.) were abstracted from the study, regardless of the nature of the summary measure. The magnitude of scores was also extracted when reported. Any information on possible moderating factors in the associations identified were also extracted to provide further insight, although it was acknowledged that this insight would be limited given the predominant use of cross-sectional methodology across the studies.

1.4.2 Results of the systematic review

Many studies were identified in the initial search process, but methodological limitations were pervasive, and, as a result, only five studies met the pre-determined quality criteria. This section will present an overview of the study

selection process before outlining the findings relating to these five studies. The trends in the studies that failed to meet the quality criteria will also be overviewed, in balance with their relative methodological constraints.

1.4.2.1 Study selection process

The search yielded 5205 unique citations. Of these, 4922 did not meet the inclusion criteria based on titles and abstracts. Of the remaining 283 articles, 146 additional papers did not meet the inclusion criteria on reading the full text. Please note that included in these 146 papers were papers that looked at chronic health conditions with a neurological aetiology. This exclusion was based on initial readings which indicated a clear qualitative difference in the mental health outcomes associated with such conditions. Although a disproportionate rate of psychiatric disorders among both children and adolescents living with neurological-based conditions was indicated, these were indicated to be in some part attributable to the typology of the condition. For example, longitudinal studies identifying precedents of epilepsy among children indicated marked differences in mental health and externalising behaviour symptoms in the months preceding the first recognised seizure (e.g. Austin et al., 2001; Austin et al., 2011; Jones et al., 2007). Moreover, it was indicated that internalising and externalising issues vary across time as a function of seizure frequency (Austin et al., 2002; Kobayashi et al., 2013). Similarly, it has been suggested that the psychological profile of children with tuberous sclerosis shows strong associations with the underlining neurological impact of the condition (de Vries, Hunt, & Bolton, 2007). Therefore, although it was clear that there was an elevated rate of psychiatric comorbidities in conditions with a neurological aetiology, the findings suggested these were not so much associations, but a related symptom of the condition, therefore suggesting that the psychiatric comorbidities of such conditions are qualitatively unique relative to those of other chronic conditions. Please note, that psychiatric comorbidities in conditions with a neurological aetiology have also often been frequently distinguished from other chronic conditions in older generations due to the similar indications (see Academy of Medical Royal Colleges, 2009). Therefore, it seemed that

there was a strong rationale for side-lining these studies away from the main review.

Consequently, the exclusion process resulted in 137 articles that met the inclusion criteria (a flow diagram of this search process is presented in Fig. 1.3). 102 of these studies examined the outcomes associated with a specific condition; 26 studies examined the non-specific effects of chronic illness without reference to the conditions being examined (a non-categorical method of analysis); and 9 studies cross-referenced the outcomes associated with different long-term conditions.

Of the 102 studies that focused on the outcomes associated with specific conditions, 72 of the studies focused on the conditions of asthma and diabetes. Therefore, there was a notable shortage of identifiable research concerning many conditions at the outset of this review.

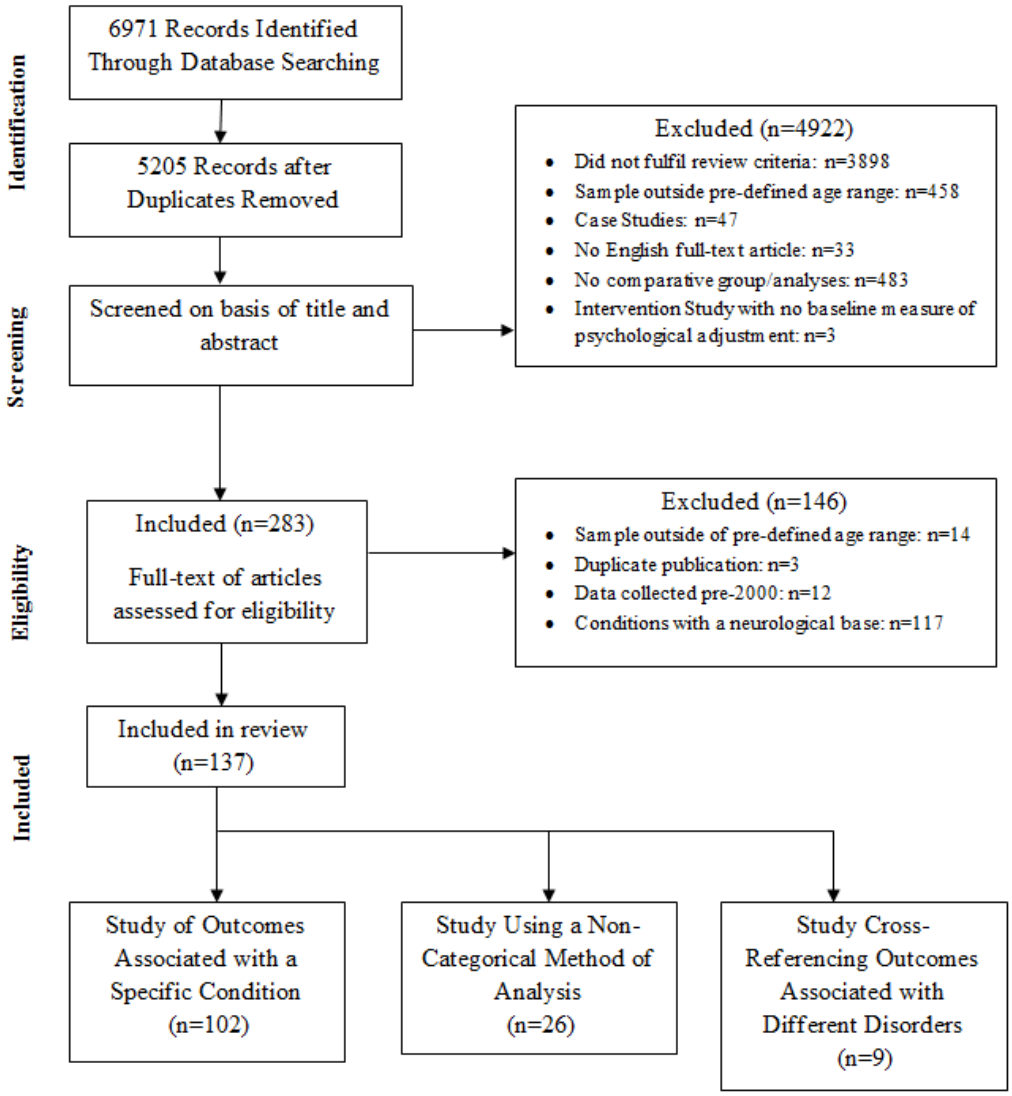


Figure 1.3 Flowchart of the results of the study selection process for the systematic review

1.4.2.2 Assessment of study quality

Several notable methodological issues were found among many of the eligible studies following the application of the quality criteria. Amongst the studies that examined the mental health associations of specific diagnoses, the most notable issue was the use of small, selective samples, with further reliance on comparison groups of convenience, or scale norms. For example, the only study which examined psychiatric associations of Cystic Fibrosis was based on 43 children who received check-ups at the Danish Cystic Fibrosis Centre in a set time period and the comparison was based on scale norms (see Bregnballe, Thastum, & Schiotz, 2007). Furthermore, some studies recruited their comparative samples from other clinical groups – for

example, in studies of the associations with Systematic Lupus Erythematosis (Louthrenoo, Krairojananan, Chartapisak, & Opastirakul, 2012), Sickle Cell Disease (Amr, Amin, & Hablas, 2010) and Juvenile Arthritis (Brace, Smith, McCauley, & Sherry, 2000) at least some members of the comparative groups were recruited from other medical clinics. Furthermore, there was limited adjustment for the effects of confounding variables among these studies. Therefore, there are significant concerns regarding the external validity of such studies given their dependence on possibly biased samples.

It should be noted that among the 26 studies that looked at generalised mental health associations of chronic illness conditions, regardless of the specific diagnosis (a 'non-categorical' method of analysis) samples were generally larger and more representative. However, assessments of physical and mental health were generally of a lower quality amongst these studies, with many studies dependent on single-item outcome measures (e.g. Blackman & Conaway, 2013; Curtis & Luby, 2008). It should also be noted that there were wide variations in the definitions of chronic illness used, and indeed the conditions examined, across this set of studies (see Appendix II).

When the pre-determined quality criteria were applied, only 5 of the 137 studies were indicated to be at a low risk of introducing bias in the review. Four of these studies examined the mental health outcomes associated with asthma, while one study examined the outcomes associated with diabetes. The findings of these five studies will be reviewed in depth. The trends in the remaining studies will be overviewed in balance with their identifiable limitations. However, please note that a full and detailed overview of the trends in these studies is to be found in Appendix III.

1.4.2.3 Characteristics of studies that achieved the quality criteria

Characteristics of the five highlighted studies are shown in Table 1.1. The two studies conducted by Chen and colleagues (Chen et al., 2014a, 2014b) utilised data from the National Health Insurance Research Database of Taiwan, which is a database of the medical claims of 100,000 subjects (approximately 4.3% of the population). As of 2014, 99.9% of Taiwan's population were enrolled in this insurance programme, and it is, therefore,

believed that this database is representative of the general population. Delmas and colleagues (Delmas et al., 2011) used data from a national school survey conducted with students across France, while Katon and colleagues (Katon et al., 2007) identified their sample from the administrative data of a health maintenance organisation in the state of Washington in the United States. This data included a large proportion of the state's population, ensuring that it was characteristic of the population of this area. The participant's records had to have fulfilled one or more of the following criteria for youth to be deemed as having an active asthma diagnosis: (a) hospitalization with an asthma diagnosis and one or more asthma prescription; (b) one or more emergency room or urgent care visit with an asthma diagnosis and one or more asthma prescription; (c) 2 office visits with an asthma diagnosis and one or more asthma prescriptions; (d) only 1 asthma visit, but 2 asthma prescriptions filled on different days; (e) four or more prescriptions for asthma medication; (f) one or more visit with an asthma diagnosis in the past year and another in the past 18 months and one or more asthma prescription during that year. Wandell and colleagues (2014) used data from an in-depth survey of health and demographic characteristics of all living persons in Stockholm County in Sweden collected on January 1st, 2011.

The included studies represented cohorts from a variety of locations internationally, namely within Asia, Europe, and North America. Moreover, all samples were somewhat representative and contained relatively large samples overall, with all the respective cohorts with a chronic condition of a substantial size to provide adequate power to the analyses. In addition, two of the five studies were longitudinal, which added extra explanatory strength to the associations identified, although both studies were focused on quite similar cohorts from Taiwan. However, the significant variation in location between the studies means that cross-cultural factors may need to be taken into consideration. It is known that the patient's culture plays a significant role in both their experience and perception of their physical illness (Turner, 1996) and in the expression of mental illness (Patel, Flisher, Hetrick, & McGorry, 2007)

Table 1.1 Characteristics of the studies that achieved the pre-determined quality criteria of the systematic review

Study	Condition Examined	Country of Origin	Study Design	Sample Size (n)	Age Range (Mean)	Asthma Measure	Psychological Outcome	Psych. Outcome Measure
Chen et al. (2014a)	Asthma	Taiwan	Cross-Sectional	7265 (1453 with asthma)	10-15 years (M=11.69)	Recorded diagnosis of asthma by a paediatrician, pulmonologist, or rheumatologist between Jan 1, 1998, and Dec 31, 2000 in medical claims	Mood Disorders	Recorded diagnosis by psychiatrist within medical claims during the period from baseline to December 31, 2010
Chen et al. (2014b)	Asthma	Taiwan	Longitudinal	9449 (725 with asthma)	10-15 Years (M=11.69 (SD:1.59))	Recorded diagnosis of asthma by a paediatrician, pulmonologist, or rheumatologist in the year 2003 in medical claims	Mood Disorders	Recorded diagnosis by psychiatrist within medical claims during the period from baseline to December 31, 2010
Delmas et al. (2011)	Asthma	France	Cross-Sectional	7000 (8.5% approx. with asthma)	9th grade students (approx. 13-16 years) (M=15.1)	Medical examination (inclusive of anthropometric measures) by school doctor and nurse, and response patterns on the French version of the standardised International Study of Asthma and Allergies in Childhood (ISSAC) Questionnaire	Major Depressive Episodes	The Composite International Diagnostic Interview – Short Form

Katon et al. (2007)	Asthma	United States	Cross-Sectional	1379 (781 with asthma)	11-17 years (M=14)	Fulfilling no. of criteria relating to prescriptions and healthcare use	Anxiety and Depressive Diagnoses	The Diagnostic Interview Schedule for Children NIMH DISC 4.0
Wandell et al. (2014)	Type 1 Diabetes Mellitus	Sweden	Cross-Sectional	471685 (1989 with diabetes)	0-18 Years	Diagnosis Recorded in Linked Medical Records	Mental Health Diagnoses	Diagnoses recorded in linked Medical Records

1.4.2.4 The indications of studies that achieve the quality criteria

The four studies which examined the mental health outcomes associated with asthma included adolescent samples only. These studies predominantly measured the prevalence of emotional disorders. The study of Wandell and colleagues (2014) included a wider range of psychiatric diagnoses, however the younger age group subsumed all young people aged from 0 to 18 years. The main findings of these studies can be seen in Table 1.2.

The four studies focusing on asthma unanimously indicated a strong association between the presence of this condition in adolescents and emotional disorder diagnoses, inclusive of depressive and anxiety disorders. Adjusted odds ratios between the studies indicated a substantially increased risk for both anxiety and depression, which was at least 50% higher than that of the comparative samples. The study of Katon and colleagues (2007) highlighted a particularly high prevalence of social phobia (adjusted OR: 2.28 (95% CI: 0.99 – 5.26)) and agoraphobia (adjusted OR: 1.92 (95% CI: 1.13-3.28)) among American adolescents living with asthma, but the wide confidence intervals for the adjusted odds ratios indicate that the samples may have not been large enough to examine the exact prevalence of specific psychiatric disorders with precision. Therefore, based on these four studies, it does appear that asthma in adolescence is associated with psychiatric illness, underlined by emotional symptomatology.

These four studies suggested that the association between anxiety and depressive disorders and asthma may be particularly acute in some asthma sub-groups. Chen and colleagues (2014b) found that the presence of asthma, in the absence of comorbid conduct disorders at baseline, was not associated with a statistically significant increase of emotional disorders among their sample, suggesting that comorbid behavioural symptomatology was a key factor in the associated emotional disorder outcomes. However, it should be noted that this study was based on a Taiwanese population and that this finding was not replicated in the remaining three samples, meaning that this may be a culturally-specific finding. Yet, Katon and colleagues (2007) did find that externalising behaviour scores were predictive of the prevalence of anxiety and depressive disorders in their sample of North

American adolescents. Therefore, the role of comorbid behavioural problems in the related association of asthma to emotional disorders warrants further investigation.

The findings of Delmas and colleagues (2011) indicated that those who had been diagnosed with asthma, but were not currently experiencing symptoms of their condition, did not have a higher prevalence of major depressive episodes, meaning that the strong association indicated (approximately 70% increased prevalence) was applicable to only the adolescents currently experiencing symptoms of their condition. It should be noted that quite strict definitions of asthma were used in the remaining three studies, raising concerns about how applicable these findings are to adolescents with an asthma diagnosis in general. Moreover, the findings of Katon and colleagues (2007) highlight the important moderating role of contextual factors in the association between asthma and mental health outcomes among the American adolescents in their sample, such as living with an unmarried parents and low physical health scores. However, the cross-sectional nature of the study means that it was not possible to elucidate whether these factors played a cumulative or moderating role in this association.

Wandell and colleagues (2014) indicated that there was a higher prevalence of psychiatric diagnoses among both females and males in the diabetes cohort in comparison to their healthy peers. There was a 10% increased prevalence rate of any psychiatric diagnosis among these children and adolescents. As in the asthma studies, this increased prevalence extended in particular towards mood disorders, inclusive of anxiety, depression and bipolar disorder (approximately 50% higher prevalence across both genders), with the exception that males aged 0-18 years with Type 1 diabetes had a lower prevalence of bipolar disorders. This study only considered the impact of age by including it as a covariate in the regression models focusing on the prevalence of psychiatric disorders across the lifespan. This makes it difficult to distinguish unique variations in mental illness associations between children and adolescents. However, the covariate analyses indicated increasing odds of 5–6% for each added life-year in the population of Stockholm County, suggesting that adolescents

living with Type 1 Diabetes may be experiencing a higher prevalence of mental health disorders than children of a younger age. Yet, this age effect should be considered in context. Despite the overall low prevalence rates of schizophrenia in youth with diabetes, the age-adjusted odds ratios show a substantially increased prevalence of schizophrenia in the diabetic sample, with the age-adjusted odds ratios calculated as 3.439 (95% CI: 3.057-3.868) for women and 2.787 (2.514-3.089) for men. The authors isolated this association between schizophrenia and diabetes in the cohort, from that found between diabetes and other psychiatric disorders, due to the weight gain caused by antipsychotics – which increases the risk of developing diabetes – and the common genetic links identified for the two disorders. Therefore, the association between Diabetes Type 1 disease in adolescence specifically and poorer mental health outcomes requires further elucidation.

Finally, it should be noted that the increased prevalence of anxiety and depressive disorders among females noted consistently amongst the samples studied is consistent with the general female preponderance associated with the juvenile-onset of such disorders (e.g. Thapar et al., 2012).

Table 1.2 Comparative risk indicated in studies that achieved the pre-determined quality criteria of the systematic review

Study	Condition Examined	Mental Health Outcome	Comparative Risk	Moderators of Association
Chen et al. (2014a)	Asthma	Major Depression	*Prevalence:* 2.8% versus 1.1% *Adjusted Hazard Ratios*:* 1.81 (95% CI: 1.14-2.89)	None Detailed
		Any Depressive Disorder	*Prevalence:* 6.1% versus 2.6% *aHR*:* 1.74 (95% CI: 1.27-2.37)	
		Bipolar Disorder	*Prevalence:* 1% versus 0.3% *aHR*:* 2.27 (95% CI: 1.01-5.07)	
Chen et al. (2014b)	Asthma without Comorbid Diagnosis of ADD/ADHD	Major Depression	No longer significant association	Comorbid Diagnosis of ADD/ADHD (Fully mediated association between asthma and psychological outcomes)
		Any Depressive Disorder	No longer significant association	
		Bipolar Disorder	No longer significant association	
Delmas et al. (2011)	Asthma	Major Depressive Episodes	*Prevalence*: 14.2% versus 9.2% *aOR**:* 1.7 (95% CI: 1.2-2.3)	Current Patterns of Symptomatology The incidence in children with past asthma symptomatology was not statistically significant (aOR: 1.2; 95% CI: 0.7 – 2.0)
Katon et al. (2007)	Asthma	Anxiety and Depressive Disorders (Overall)	*Prevalence:* 16.3% versus 8.3% *aOR***:* 1.83 (95% CI: 1.28-2.62)	Being female (aOR: 1.96; 1.27-3.03) Living with a currently unmarried parent (aOR: 1.96; 1.26-3.07)

		Major Depression	*Prevalence:* 4% versus 7.2% *aOR***:* 1.65 (95% CI: .99-2.76)	A more recent diagnosis of asthma (aOR: 0.94; 0.89- 0.98)
		Dysthymia	*Prevalence:* 0% versus 0.1% *aOR***:* -	Higher externalizing scores on the CBCL (aOR 1.03; 1.01-1.05)
		Panic Disorder	*Prevalence:* 1.2% versus 2.5% *aOR***:* 1.93 (95% CI: 0.78-4.77)	A lower physical health score on the asthma-specific functional impairment scale (aOR: 0.95; 0.94-0.96)
		Generalised Anxiety Disorder	*Prevalence:* 2.2% versus 1.2% *aOR***:* 1.8 (95% CI: 0.71-4.56)	
		Social Phobia	*Prevalence:* 3.3% versus 1.4% *aOR***:* 2.28 (95% CI: 0.99-5.26)	
		Separation Anxiety	*Prevalence:* 3.4% versus 1.9% *aOR***:* 1.69 (95% CI: 0.82-3.48)	
		Agoraphobia	*Prevalence:* 7.5% versus 3.4% *aOR***:* 1.92 (95% CI: 1.13-3.28)	
Wandell et al. (2014)	Type 1 Diabetes Mellitus	Any Psychiatric Diagnosis	*Prevalence:* 25.31% versus 14.18% Female 27.47% versus 18.46% Male *Age-Adjusted Lifetime Odds Ratio:* 1.296 (95% CI: 1.267-1.326) Female 1.3999 (95% CI: 1.368-1.432) Male	Increasing odds of 5-6% of any psychiatric diagnosis for each added life-year
		Schizophrenia	*Prevalence:* 0.01% versus 0% Female 0.09% versus 0.01% Male	

	Age-Adjusted Lifetime Odds Ratio: 3.439 (95% CI: 3.057-3.868) Female 2.787 (95% CI: 2.514-3.089) Male
Bipolar Disorders	*Prevalence:* 0.33% versus 0.12% Female 0% versus 0.06% Male
	Age-Adjusted Lifetime Odds Ratio: 1.714 (95% CI: 1.54-1.905) Female 1.6 (95% CI: 1.429-1.792) Male
Depression	*Prevalence:* 5.24% versus 2.1% Female 2.93% versus 1.06% Male
	Age-Adjusted Lifetime Odds Ratio: 1.412 (95% CI: 1.365-1.46) Female 1.531 (95% CI: 1.474-1.591) Male
Anxiety	*Prevalence:* 4.68% versus 2.94% Female 3.21% versus 1.51% Male
	Age-Adjusted Lifetime Odds Ratio: 1.276 (95% CI: 1.227-1.327) Female 1.35 (95% CI: 1.289-1.414) Male

* Adjusted by gender, age at enrolment, level of urbanisation, and comorbid allergic diseases
** Adjusted for current asthma, gender, age, family structure, and the father's employment status
*** Adjusted for ethnicity, education, marital status, Medicaid and Pediatric CDS

1.4.2.5 Trends in remaining studies

The trends among the studies that did not achieve the quality criteria can be seen in Table 1.3. The only consistent associations identified were between the conditions of asthma, diabetes mellitus and thalassemia, and depressive and emotional symptomatology. In the remaining conditions, small to moderate associations were identified which often varied based on the informant used – for example, when considering the associations of inflammatory bowel disease to emotional symptomatology, significant associations were identifiable based on parental ratings only. Yet, severity of the conditions was suggested as a moderating factor in many of the associations identified, with children with more severe symptoms of their primary condition and a greater degree of functional impairments also demonstrating higher levels of emotional and behavioural symptoms. However, the role of symptom severity was suggested to be nuanced. In conditions such as juvenile arthritis and inflammatory bowel disease, the presence of more severe sub-types of the condition did not predict mental health outcomes, but concurrent symptomatology and disease activity did. However, these findings may be an artefact of low analytic power. Moreover, it should be noted that the vast majority of these data are cross-sectional. Based on what is known about the relationship of psychiatric comorbidities to physical health outcomes, it is also feasible to hypothesise that children with a higher rate of emotional and behavioural symptoms develop or perceive functional impairments because of their mental illness. Therefore, it is not plausible to propose causal links about mediation based on this data. It is also important to note that moderating factors varied based on diagnosis. Although this may reflect varying focuses within the studies, Mubarek and colleagues (2010) suggested moderating factors in mental health outcomes may vary between sub-types of anaemia.

The literature review indicated that most children living with chronic illness have very mild forms of their conditions. Therefore, the possibility was considered that the findings of non-significant associations among many conditions overviewed in the studies are due to an over-representation of children with diagnoses in the absence of active symptoms of the condition.

This may suggest that severity of symptomatology plays a key role in the association of chronic health problems to poor mental health outcomes. However, it should be noted that many of these samples were recruited from hospital clinics, which suggests that these children would have some degree of disease activity. Moreover, as noted, some of the comparative groups were recruited from other outpatient clinics, so it is likely that these non-significant findings may be also be an artefact of the point of reference. Finally, it should be noted that severity of symptoms was suggested to play an inconsistent role in the prediction of mental health outcome across studies, although again it must be highlighted that these variations may be an artefact of limited analytic power.

The studies which examined the impact of chronic illness non-categorically uniformly indicated an increased prevalence of both emotional symptomatology and behavioural symptomatology, consistent with the findings of previous reviews. Such a contrast raises questions of whether it is only a small number of conditions that is driving these associations. Indeed, inter-disease variability in prevalence was noted amongst many of the studies, and neurological conditions were often named as having the strongest association with mental health outcomes. However, given the risks of methodological bias indicated among the studies focusing on the outcomes of specific diagnoses, it could equally be queried whether the widespread dependence on small samples is obscuring identifiable associations between chronic illness in adolescence and poor mental health outcomes, by inflating intra-disease variation. It should be noted that studies which used a non-categorical methodology did not indicate that symptom severity played a substantial role in the associated mental health outcomes. However, this may reflect the difficulty in measuring symptom severity across such a broad range of conditions. Indeed, some variations were shown in associations dependent on the measure used and the informant. Yet, it is important to highlight that these studies suggested that functional impairment, as a consequence of the condition, was the most consistent insight into the associated mental health outcomes. However, as many of these studies were also cross-sectional in nature it was, again, not feasible

to start speculating about the nature of the role of functional impairments relative to symptom severity in mental health outcomes.

No identifiable age-related variations were found in terms of mental health outcomes across these studies, with the exception that adolescents with diabetes were consistently found to be more maladjusted than their younger counterparts. Moreover, associations between asthma and poor mental health outcomes were stronger based on adolescent samples relative to younger samples. However, this may reflect the generally low quality of research focusing on the childhood period. Most of the studies overviewed were based on small samples and included age as a covariate in statistical models, meaning that analyses may not have been adequately powered to sensitively detect age-related changes. Moreover, there was a lack of longitudinal studies among this cohort, meaning that it was also not possible to explore possible age-related variations in mental health outcomes based on this study design.

Table 1.3 Trends among the remaining studies that did not achieve the pre-determined quality criteria of the systematic review

Condition	Number of Studies	Emotional Outcomes	Behavioural Outcomes	Moderators of Associations
Asthma	42	Increased prevalence of depression and anxiety (Approximately 50% - 70% higher prevalence)	Findings were mixed but, overall, it was suggested that there was approximately a 20% increase in the prevalence of conduct disorders	Functional Impairment High risk of juvenile-onset psychopathology (Full mediators of association in many studies) Age (Association stronger in adolescent samples)
Diabetes (Type I Sub-Type Only)	26	Likely increase in prevalence of emotionally-predominated disorders	Likely increase in prevalence of conduct disorders	Age (Adolescents showing higher levels of maladjustment) Glycaemic control (Findings mixed) Functional Impairment

				Family Climate
Sickle Cell Disease	6	Mixed Evidence (Parent ratings support but this is contradicted by self-report and teacher ratings) Slight increase in anxiety disorders only based on psychiatric interview (However, poor quality comparative group)	Mixed evidence (Parent and teachers reports support, but not self-report or ratings of secondary caregivers)	Gender (Females at higher risk) Low Family Income Experience of Frequent Painful Crises More severe sub-types of the condition (Associated with maternal ratings only)
Thalassemia	3	Increase in emotional symptoms above clinical threshold	Increase in prevalence of conduct disorders	More severe symptoms of thalassemia
Juvenile Arthritis	3	No association	No association	Active status of arthritis symptoms

Inflammatory Bowel Disease	3	Increase in Emotional Symptoms above Clinical Threshold (Parents Ratings Only)	No association	More severe sub-types of the condition Time of onset of condition (Adolescent-Onset having stronger association with somatisation)
Haemophilia	2	Increase in depressive symptoms, but below clinical thresholds	No association	Severe sub-types of the condition (However, means still below a level of clinical significance)
Chronic Kidney Disease	3	No association	No association	Reliance on Dialysis
Non-Alcoholic Fatty Liver Disease	2	Increase in emotional symptoms (Clinical Significance not examined)	No association	BMI (Only supported by one of the two eligible studies; other found no association)

Cystic Fibrosis	1	Increase in anxiety symptoms in boys aged 7-10 years	No association	Socio-economic factors
Epidermolysis Bullosa	1	Increase in emotional symptoms (Means not in clinical range)	No association	Severity (However, this was not a statistically significant association)
Oesophageal Atresia	1	No association	No association	None identified
Familial Mediterranean Fever	1	Increase in depressive symptoms of clinical significance No relationship with anxiety	No association	Condition severity (but not condition duration or genotype)
Systematic Lupus Erythematosus	1	No association	No association	None identified

Primary Ciliary Dyskinesia	1	Increase in emotional symptoms in borderline clinical range	No association	None identified
Eosinophil-Associated Gastrointestinal Disorders	1	Increase in emotional symptoms	Increase in behavioural difficulties	None identified
Non-Categorical Examination of Chronic Illness	26	Increased prevalence of emotional symptomatology	Increased prevalence of conduct problems	Diagnosis (Higher risk associated with neurological conditions) Functional Impairments Child's Perception of Severity Socio-Economic Deprivation Social Development

Cross-Reference of Mental Health Outcomes Between Disorders	9	n/a (due to significantly high risks of methodological bias)	n/a (due to significantly high risks of methodological bias)	-

1.4.3 A comparison of the findings of this systematic review to previous reviews

This systematic review aimed to provide a degree of insight into psychiatric comorbidities of paediatric chronic illness beyond the scope of existing overviews. Even though there was not sufficient evidence to answer the underlying question of the review – i.e. "Is there evidence to suggest that living with a chronic illness in childhood and adolescence is associated with the co-occurrence of psychiatric illness?" – it is clear that this review has still fulfilled this purpose. The meta-analyses outlined in the literature review indicated small to moderate effect sizes of chronic illness on mental illness symptomatology, and it was questioned whether these effects were indicative of effect sizes which would warrant clinical intervention. Similar conclusions would probably be made in this review if a more exclusionary approach to the literature was not taken. Yet, the findings of the studies indicated to be at a low risk of bias in this review indicated strong and positive associations between asthma in adolescence and the prevalence of psychiatric disorders, and in particular anxiety and depressive disorders. In addition, a significant association between diabetes mellitus Type 1 and an increased rate of psychopathology in youth aged from childhood to 18 years was also identified, albeit on the basis of a single cross-sectional study. Given that studies that failed to reach the quality criteria also indicated positive associations for these conditions to mental ill-health, and such associations were also indicated in previous meta-analyses, it might suggest that these conditions, unique from other chronic illness conditions, are associated with a disproportionate rate of psychiatric illness. This could suggest the uniform findings of higher levels of both emotional and behavioural symptomatology amongst the non-categorical studies reviewed could possibly be driven by an escalated risk associated with a minority of conditions. However, alternatively, it may also indicate that the reliance on small and possible unrepresentative samples is driving intra-disease variation, and obscuring indications of true disproportionate levels of psychiatric illness among this cohort.

Comparisons of the results of this review with previous meta-analyses suggest that the theory of small and possibly unrepresentative samples obscuring true associations may be in some way supported. In a meta-analysis of studies examining the mental health outcomes of Type 1 diabetes mellitus, Reynolds and Helgeson (2011) did find that children with Type 1 diabetes were more likely to be rated as experiencing emotional symptoms and demonstrating external behavioural symptoms than their healthy peers. However, the effects sizes were of a small to medium magnitude, with the weakest effect sizes indicated amongst more recent studies and samples that were well-matched with the control group. Yet, in Wandell and colleagues (2014) study there was a clear and strong association identified between diabetes and mental ill-health, even though this study, consistent with the meta-analysis of Reynolds and Helgeson (2011), amalgamated the data of children and adolescents. However, the generally lower magnitude of the associations to psychological outcomes identified amongst studies using a non-categorical method of analysis suggests that a potential over-inflation of disproportionate rates of psychiatric comorbidities associated with only a minority of conditions cannot be fully discounted. However, it should be kept in mind that the direction of findings amongst these studies may have also been impacted by methodological artefacts, such as the use of single-item measures of mental health. Therefore, the generally high risk of bias amongst studies in the field is severely limiting any insight that can be gained into the validity of the theory of a generalised negative impact of chronic health problems.

This review again raised questions regarding the role of symptom severity and functional impairment in the associated psychological outcomes observed. The studies focusing on the rates of emotional disorders in asthma used quite strict definitions of asthma diagnosis, and Delmas and colleagues (2011) suggested that asthma without active symptomatology was not associated with any increase in rates of emotional disorders. However, this was the only study to examine the role of active versus inactive symptomatology on psychological outcomes. Yet, severity of symptoms and, more consistently, functional impairments were consistently identified as

moderators of associated mental health outcomes in many studies. It is unclear, given this finding, if there is a general association of chronic disease, or indeed certain disease conditions, to poor mental health outcomes, with symptom severity or related impairments moderating this association, or whether, in contrast, in a reflection of early hypotheses in the field, symptom severity and functional impairments are the key variables in understanding mental health outcomes. Again, it should be noted that, due to the cross-sectional nature of the vast majority of the studies, it is also a feasible possibility that this association is mediated by the impact of psychiatric comorbidities on consequent physical health outcomes. Therefore, the role of symptom severity and functional impairment in the associated psychiatric comorbidities of childhood and adolescent chronic health problems cannot be ascertained within the boundaries of this review.

Studies that did not reach the quality criteria suggested that pre-existing risk factors for childhood- and adolescent- onset psychopathology, such as a history of parental mental illness and socio-economic deprivation, may fully mediate the association between asthma and poor mental health outcomes. However, although the studies which reached the quality criteria controlled for the possible confounding impact of demographic factors on the associated mental health outcomes of asthma in adolescence, it is possible that all predisposing risk factors were not fully accounted for. Socio-economic status and related socio-economic variables were also indicated to moderate the strength of the association between psychiatric illness and many of the remaining chronic health conditions, such as sickle cell anaemia and cystic fibrosis, and were also isolated as a possible moderating factor in studies using a non-categorical method of analysis. The role of family history of mental illness was not explored in these studies. As socio-economic gradients have been observed in the incidence of childhood and adolescence chronic illness, it may be important to explore the role of socio-economic variables, and other predisposing risks to childhood and adolescent mental health, in the association of chronic health problems to mental ill-health.

The findings of Chen and colleagues (2014b) found that the presence of asthma, in the absence of comorbid conduct disorders at baseline, was not associated with a statistically significant increase of emotional disorders among their sample, suggesting that comorbid behavioural symptomatology was a key factor in the associated mental health outcomes. It should be noted that this study was based on a Taiwanese population and may be a culturally-specific finding. However, Katon and colleagues (2007) did find that externalising behaviour scores were predictive of the prevalence of anxiety and depressive disorders in their sample of North American adolescents. A discussion of this finding again highlights major limitations in the scope of research in the area. It could signify a unique role of pre-existing behavioural symptomatology in the occurrence of emotional disorders in adolescents living with asthma, or it could also just reflect the fact that the role of pre-existing behavioural symptomatology has not been examined in research looking at other chronic health conditions. It should be noted much of the research overviewed in this review was focused on emotional symptomatology rather than behavioural disorders. This finding may also signify some form of developmental pathway in the occurrence of psychopathology among children living with asthma and other chronic health conditions, but the lack of longitudinal data limits our ability to test this hypothesis. Similarly, the findings of an age gradient in the association of asthma to poor mental health outcomes, with adolescents showing elevated levels of psychopathology relative to children, may be a consequence of the minimal exploration of age-related variations in research focusing on other chronic health conditions and the generally low quality of research looking at the childhood period. Therefore, overall, these findings again highlight the significant limitations caused to insight by the pervasive nature of methodological limitations in the field.

Finally, it should be noted that the finding that conditions with a neurological aetiology may have a unique association with mental health outcomes, in comparison to other chronic health conditions, is not a novel finding. Turkel and Pao (2007) have highlighted the unique pattern of psychiatric

comorbidities that have been observed in adults living with chronic conditions that have a neurological aetiology.

Therefore, this systematic review provided a degree of insight into the association of chronic health problems to mental health beyond existing research. It suggested that more methodologically balanced research may support the theorised link between chronic health problems and mental ill-health. However, many other aspects of the findings of the review – such as findings of inter-disease variations, and frequent indications of symptom severity and impairments playing a moderating role in psychological outcomes – raise concerns about the underlying validity of the theory of chronic health problems as being a specific risk factor to the mental health of child and adolescent groups. However, the research was just too limited by methodological artefacts to reliably assess the validity of the current over-arching theory in the field. Therefore, this review highlighted that the over-arching theory of the paediatric chronic illness field cannot be fully tested or validated within the scope of current research.

1.5 Introduction to the Thesis and Research Overview

This literature overview presented a major gap in research knowledge. Although there is a pervasive theory of chronic health problems having a general association with poor mental health outcomes for children and adolescents, with this association being mediated by the continuing stress chronic health problems present to normative patterns of development, this theory has not, as of yet been, in any way, substantiated by empirical studies in the field. Moreover, it highlighted that this theory cannot be fully tested within the boundaries of current research. Due to pervasive methodological limitations, it remains unclear whether the consistent findings of an association between chronic health problems and disproportionate rates of mental illness symptomatology are an over-inflation of an acute risk associated with a small number of conditions, or whether reliance on small and possible unrepresentative samples is driving intra-disease variation, and obscuring true disproportionate levels of psychiatric illness among this cohort. It is also unclear what role severity of the condition, and functional impairments, play in the association of chronic illness to mental ill-health outcomes for this younger age group. Moreover, it is unclear if adolescence is a particular risk period for the development of psychopathology in children with chronic illness, as is commonly hypothesised. Therefore, while the literature overviewed presented a lot of different possibilities about the association of chronic health problems in childhood and adolescence to poor mental health outcomes, it was of too poor a quality to provide definite insight into patterns in this association.

Learning from this review, and the limitations identified in previous investigations, this research was built with the aim of providing a more reliable test of the theory of chronic health problems as being a specific risk factor for the psychological health of children and adolescents. To provide a better understanding into the generalised association of chronic health problems to poor mental health outcomes, it will first examine the cross-sectional and longitudinal associations of chronic health problems to mental ill-health outcomes in childhood and adolescence, beyond the impact of possible confounding factors, using data from a large, representative sample

from the United Kingdom and high quality measures of mental health. It will then aim to identify the mediators in this association, first by examining whether indicators of symptom severity and functional impairments play a mediating role, either fully or partially, in the associated mental health outcomes observed, as well as exploring the mediating role of several factors, indicative of impairments to normative development trajectories. This exploration will be then be used to create a model of the association of chronic health problems to rates of psychiatric illness across the childhood and adolescent period, which will be tested for goodness of fit to the data. In order to ensure that this pattern is applicable to specific chronic illness conditions, both the cross-sectional and longitudinal analyses will be compared to analyses using asthma diagnosis as the primary predictive factor, and the model developed will also be tested for goodness of fit to the patterns in mental health seen in this condition.

In overview, the steps in the research described in this thesis are as such:

I. To examine the cross-sectional and longitudinal associations of chronic health problems to mental ill-health across childhood and adolescence, using data from a large, representative sample, high quality measures of mental health, and controlling for the possible influence of confounding factors.
II. To identify mediators in the associations identified. Specifically, to explore the role of symptom severity and functional impairment in this association, and to also look at the mediating role of a number of variables indicative of impairments to normative trajectories of development.
III. To build a model of the association of chronic health problems to mental ill-health outcomes across the childhood and adolescent period, and test this for goodness of fit to the data.
IV. To examine the applicability of these findings to specific chronic conditions by comparing the indications of the cross-sectional and longitudinal associations to a similar set of analyses using asthma diagnosis as the independent variable. The mediation model will also

be tested for goodness of fit to the mental health outcomes associated with asthma diagnosis.

Asthma was selected as a point of comparison for many reasons. Asthma is one of the most prevalent conditions affecting child and adolescent groups (Department of Health, 2012), meaning that a large, representative sample could be identified in the dataset chosen, reducing the possibility of the introduction of methodological bias. In addition, van Gent and colleagues (2008) report that the "silent" majority of children with asthma (up to 70%) are affected by mild persistent asthma, a state in which symptomatology is responsive to medical intervention, and contact with healthcare services is minimal, if not comparable to healthy peers. This suggests that asthma is an optimal condition in which to explore the role of symptom severity and functional impairment in associated mental health outcomes. In addition, there were many unique patterns noted in the mental health outcomes attributable to asthma in the review, such as a possible role of pre-existing behavioural symptomatology and an age-related gradient in risk. However, these indications must be balanced with the awareness that this was the most common chronic condition to be studied in a rigorous fashion. Yet, in conclusion, there were many characteristics of asthma which suggested that this condition would be a good point of comparison when studying the effects of chronic health problems more generally.

One limitation to this research should be noted at the outset. One of the concerns raised in the review regarded whether non-categorical methods of analysis were over-inflating an acute risk associated with only a small number of chronic illness conditions, inclusive of asthma. However, it was not feasible within the constraints of this study to examine whether all chronic health conditions of childhood and adolescence were associated with poor mental health outcomes. Yet, one of the aims of this study was to identify a mediation model of the associations of chronic health problems to mental health outcomes. If this model suggests that factors common to all chronic illness conditions mediate the associations identified, and this model is also applicable to the patterns of co-occurrence in mental health outcomes seen

in asthma, then this would suggest chronic health problems are a specific risk factor to child and adolescent mental health, regardless of diagnosis.

As Van der Lee and colleagues (2007) review highlighted, a theory that chronic health problems in childhood and adolescence as having a negative impact on mental health in these age groups, regardless of primary diagnosis or symptom severity, underlies the majority of research in this field. However, as this literature review has highlighted, this position remains to be substantiated by empirical research. The design of this research has carefully considered the methodological limitations identified in previous investigations in the field, and it has aimed to build a research study that will overcome these methodological artefacts, and provide a clearer, and more balanced, insight into the association of chronic health problems to mental ill-health. It is hoped that, in this way, it will provide a stronger test of the validity of the current, over-arching theory within the research field.

CHAPTER 2

Methodology

2.1 Chapter Overview

As outlined in the conclusion of the second chapter of this report, this research aims to explicitly investigate the validity of the theory that chronic health problems in childhood and adolescence pose a specific risk to mental health in these age groups, through the mediating effects of the stress such conditions place on child development. This investigation will examine the cross-sectional and longitudinal associations of chronic health problems to poor mental health outcomes in a large, representative dataset, and will identify key mediating variables in this association. It will also compare the applicability of these findings to analyses based on children with an asthma diagnosis.

This methodology chapter highlights how insight gained from both the opening literature review and the consequent systematic review were used to design a study which would provide a balanced insight into mental ill-health amongst children and adolescents living with chronic illness. The outline of the research design (section 2.2) and subsequent selection of survey data (section 2.3), choice of measurement instruments (2.4) and overview of the various stage of the statistical analyses (section 2.5) will highlight how each element of this research was measured and considered in order to select methods that would provide the most thorough testing of the hypotheses within the limits of the data and current statistical techniques.

2.2 Research Design

It was a priority of this study to recruit a large sample of children living with chronic health problems, and to examine them longitudinally using a thorough and comprehensive range of measures, which would provide a broad insight into the child's functioning by a range of different informants. Therefore, to achieve this aim within the time constraints of the project (approximately three years), the scope for data collection within a novel sample was extremely limited, and would negate the possibility of exploring trajectories of associations over a sufficient time period. Therefore, it was decided at a very early stage that the research should be designed around secondary analysis of a dataset that has already been collected, with the view that this selected dataset size should be sufficient to power complex analyses.

To achieve the study aims, the dataset would have to contain a measure of chronic illness somewhere in the childhood period, in order to define this study's timeline. A measure of asthma diagnosis would also have to be administered at this time in allow for the comparative analyses. The mental health of the sample would then have to be examined over a follow-up period that extended into the adolescent years. It was also desired that the dataset would contain consistent measures of factors relating to family functioning, peer relationships, and activity limitations.

2.3 Dataset

A number of longitudinal datasets from the United Kingdom were considered for use in the secondary analyses that underline this study. The dataset selected was the 'Avon Longitudinal Study of Parents and Children' (ALSPAC). The ALSPAC dataset was chosen by virtue of the fact that, as the core aim in the design of this study was to identify moderators of health, the dataset contains a broad range of mental and physical health measures, which vary in scope from parent- and self-report to clinical data. Multiple indicators of developmental outcomes, and in particular psychosocial variables, were also collected. The study cohort is of substantial size and largely representative of the chosen catchment area. Moreover, as data is available for the sample from birth until young adulthood, it is possible to examine the influence of variables from multiple time-points. The relatively recent period of data collection for this study was also a decided advantage.

The two alternative datasets, which were also strongly considered, were the Olympic Regeneration in East London (ORiEL) project dataset and the Millennium Cohort Study (MCS) dataset. In brief, the ORiEL project dataset, which consists of data from a major longitudinal research project which evaluated the impact of the London 2012 Olympic Games legacy and regeneration activities on the health and well-being of young people and their families in East London, had only limited data concerning medication usage and health-related factors, such as functional impairments. In addition, although the Millennium Cohort Study (MCS), a multi-disciplinary research project following the lives of around 19,000 children born in the United Kingdom in 2000-01, is nationally representative, with high participant retention, and a wealth of lifestyle and health measures, complete data was only available for children up to the age of twelve years at the time of the dataset selection. This would have been a significant restraint on the scope of this study, given that adolescent psychosocial development in the context of chronic illness was highlighted as a priority area for research within the literature review.

A full description of the selected dataset – the 'ALSPAC' study - will be provided in this section, in line with a consideration of the advantages and limitations of using this dataset in the context of the aims of this study. Unless otherwise stated, all reported information on the ALSPAC sample and the study itself has been extracted from two detailed methodological reports (Boyd, et al., 2012; Fraser et al., 2012).

2.3.1 Survey description

The 'Avon Longitudinal Study of Parents and Children' (ALSPAC) was one of a larger series of Pan-European longitudinal birth cohorts investigating moderators of child health and development, which were initiated following a World Health Organisation (WHO) recommendation. Jean Golding, the principal investigator on the original ALSPAC study, designed the methodology for this series of studies, collectively termed the 'European Longitudinal Study of Pregnancy and Childhood' (ELSPAC). In the United Kingdom, the county of Avon was selected as the area for sample recruitment, specifically three South-West Regional Health Authorities (Southmead District Health Authority, Frenchay District Health Authority, and Weston District Health Authority) which are now encompassed under the 'Bristol and District Health Authority'. This area captured residents in the city of Bristol, as well as residents in town, village and farming communities in the surrounding area, but excluded residents in the area around the city of Bath. All pregnant women resident in this catchment area with an estimated delivery date that fell between the 1st of April 1991 and the 31st of December 1992 were eligible to participate in ALSPAC.

WHO Europe provided the originally seed funding for the ELSPAC studies, and in line with the common methodology designed for these studies, ALSPAC was originally conceived as a study of pregnancy and early childhood. To reflect this early focus, the original ALSPAC acronym denoted the 'Avon Longitudinal Study of Pregnancy and Children', rather than its modern connotation, the 'Avon Longitudinal Study of Parents and Children'. However, following the initiation of the study, the ALSPAC investigators pursued funding from a number of funders within the United Kingdom, which

extended the initially envisioned timeframe for the ALSPAC data collection. At the time of the publication of this thesis, the ALSPAC sample were still engaged in routine data collection under the study proviso, and funding secured in the 2011/2012 enabled the collection of extensive genetic and phenotypic material from the study cohort, in addition to the participants' parents and offspring, in order to establish ALSPAC as a notable multi-generational cohort study.

2.3.2 Eligible sample and recruitment

Due to the dynamic nature of the original ALSPAC target population, no convenient sampling frame could be developed at the design phase of the study. Therefore, the sampling methods in the early pregnancy study were more opportunistic than systematic. ALSPAC attempted to contact eligible women through local media drives, visits to community locations, and promotion at centres of routine antenatal and maternity health services. Pregnant women migrating into the study catchment area were eligible up to the point of delivery, whereas women migrating out of the area prior to delivery were excluded unless they had completed the questionnaire scheduled for the third trimester of pregnancy.

The eligible study sample was defined in retrospect, based on maternity, birth and child health records, in addition to ALSPAC recruitment records. The later delineation of the eligible sample allowed for the use of more sophisticated geocoding resources than those that would have been available to researchers at the design stage of the study. As a reflection of the limitations of the original sampling procedure, the use of these more sophisticated techniques identified 229 pregnancies (223 live births) living on the geographical periphery of the study area that were incorrectly believed to be eligible. Please note, as these individuals had contributed a substantial amount of data, they are continued to be included in both the 'eligible sample' and 'enrolled sample', and are eligible for continuing follow-up. This later analysis indicated that recruitment was not complete. However, due to the methods employed as part of the ALSPAC recruitment campaign, it is not possible to discern where non-recruitment represents failure to invite as

opposed to volitional non-response. The eligible sample comprises of 20,247 pregnancies. The mothers of 14,541 pregnancies (71.8%) were recruited to the study during the 1990-1992 recruitment period, and this resulted in 14,062 live born children, 13,988 of whom were alive at one year.

As part of a 'Focus at 7' follow-up assessment, attempts were made to recruit all known eligible children who fitted the new geo-coding sampling frame but were not enrolled, excluding those who had previously refused enrolment. Known as phase II of the ALSPAC recruitment, these methods recruited an additional 456 children from 452 pregnancies (2.2% of the eligible sample).

ALSPAC continues to recruit individuals who would have been eligible under the original study frame in an opportunistic fashion. During Phase III of recruitment (when the eligible children were aged 8-18 years) a further 257 children were recruited from 254 pregnancies (1.2% of the eligible sample). Therefore, the ALSPAC 'enrolled' sample' (aged from birth to 18 years) has an overall total of 15,247 pregnancies, 75.3% of the determined eligible sample. These pregnancies resulted in 14,775 live-born children of which 14,701 were alive at one year of age.

Please note that the determined 'eligible sample' remains eligible for subsequent follow-up waves, regardless of participation history or geographic location. In addition, it should be noted that study consent in ALSPAC is 'opt out', and that participants not actively declining participation will continue to be invited to participate in data collection regardless of recent participation patterns. Participants who 'opt out' can also re-enrol in the study at any follow-up phase, and 32 families re-joined this study in this way by the 18 year follow-up phase.

2.3.3 External validity

Comparisons of the ALSPAC cohort to the wider demographic profile in the United Kingdom have indicated that the ALSPAC sample may be biased towards mothers and children from higher socio-economic position than the British average. A comparison of 1991 United Kingdom census data with both mothers in the catchment area, as well as mothers enrolled in ALSPAC

(using data collected from approximately 80% of the ALSPAC mothers 8 months postnatal), indicated that some of this socio-economic bias may reflect the chosen catchment area. In 1991, mothers of infants in Avon were more likely to live in owner-occupied accommodation and to have a car available to the household, and less likely to have one or more persons per room when compared to mothers of infants in Britain as whole. The population of this area was also less ethnically diverse than other counties in Britain, with only 4.1% of the population of mothers in Avon listed as non-white when compared to the average of 7.6% in the whole of Great Britain. However, no substantial differences in the proportions of married versus unmarried mothers emerged when marriage rates were compared. Yet, indicators of socio-economic position for the ALSPAC sample when 8 months postnatal, indicated a higher socio-economic profile than both the British average and the average for Avon county, with mothers in this sample more likely to live in owner-occupied accommodation and have a car available to the household than mothers in Avon county. Only 2.2% of the mothers in the ALSPAC sample were indicated to be non-white, meaning that this group is highly ethnically homogenous when compared to the general British population from this period. However, it should be noted, mothers in ALSPAC were more likely than mothers in Avon, or the average mother in Britain, to be living in overcrowded conditions, with a higher proportion living in households with on average one person per room.

The socio-economic differences indicated at 8 months, were similarly reflected in external validity analyses of the data of children enrolled in ALSPAC at 16 years with the national average. Children who were enrolled in ALSPAC sample had a higher educational attainment at 16 than the National Pupil Database (NPD) Key Stage 4 (KS4) Government-Maintained Establishments (GME) national sample. The ALSPAC sample was also less likely to be eligible for free school meals than the national sample. As would be expected based on the 8-month postnatal data, participants were less ethnically diverse than the national sample, a continuing limitation given changing demographics in the United Kingdom, with 14% of students in the NPD KS4 GME data described as “non-white”.

These socio-economic variations are a limitation to the representativeness of the sample from a population standpoint, and must be acknowledged and considered when trying to consider how patterns in the ALSPAC data might be applicable to trends in the United Kingdom in general. Please note that due to the recruitment methods of the ALSPAC study, it is not possible to assess whether this demographic bias was due to recruitment biases, or due to volitional non-participation from mothers of a lower socio-economic position.

2.3.4 Sample follow-up

One of the strengths of the ALSPAC study has been the breadth of the data collection. There are 68 main identifiable data collection time points from birth to when the sample reached 18 years of age. Data was not only collected through mailed questionnaires for caregivers and the study participants, but also through on-site clinical assessments where questionnaire measures were, again, completed alongside a number of medical assessments and the collection of biological samples. To aid clarity, these 68 collection points have been summarised into six phases in the child's lifespan by the ALSPAC study team:

i) Infancy (≥ 4 weeks and ≤ 2 years of age)

- Four questionnaires about the child completed by the mother/main caregiver
- Subsample completed four 'Child in Focus' assessment clinics

ii) Early childhood (> 2 years and < 7 years)

- Eleven questionnaires about the child completed by the mother/main caregiver
- Six child-completed questionnaires
- Subsample completed six 'Child in Focus' assessment clinics

iii) Childhood (7 years of age)

- 'Focus at 7' clinical assessment
- One child-completed questionnaire

iv) Late childhood (>7 years and <13 years)

- Six questionnaires about the child completed by the mother/main caregiver
- Nine child-completed questionnaires
- Four “Child in Focus” assessment clinics

v) Adolescence (≥13 years and <16 years)

- Three questionnaires about the child completed by the mother/main caregiver
- Seven child-completed questionnaires
- Two ‘Child in Focus’ assessment clinics

vi) Transition to Adulthood (>16 years and ≤18 years)

- One questionnaire about the child completed by the mother/main caregiver
- Two child-completed questionnaires
- One clinical assessment visit

Additional data regarding the study child was collected through school-administered questionnaires and assessments made by the child’s class teacher during School Year 3, Year 4, Year 6, and Year 8. Recent years have also seen a focus on linking the sample data to routine health and administrative records. Currently, linkage is available to the ‘Office of National Statistics’ (ONS) deaths and cancer registration (99% coverage of the eligible sample), the National Pupil Database (approximately 82% coverage of the eligible sample depending on the time point), and the General Practice Research Database (approximately 4% coverage of the eligible sample). It should also be noted that there have been a number of independent subpopulation studies of the sample, and that the enrolled sample has also been used to select cases for inclusion in randomised control trials.

Although detailed follow-up of participants in ALSPAC has largely focused on the offspring, there were nineteen questionnaires focusing on the mothers of the ALSPAC cohort administered between early gestation and when the child turned eighteen. Data collection in this maternal sample will become more extensive in the coming years with the recent funding of the genetic and phenotypic data collection. There has also been a wealth of data collected

regarding the mother's partner both through maternal responses regarding their partner's behaviour and through partner-focused questionnaires (sixteen administered between pregnancy and when the child turned eighteen). Please note, the partner-questionnaire was not directly delivered to the partners, but rather was mailed to the primary caregiver in the household who then opted whether to pass on this questionnaire.

2.3.5 Attrition

Official records indicate participation attrition within the study has been minimal, although drop-out rates have risen steadily from late childhood onwards. Please note that withdrawals were based on active statement of wish to withdraw. Official attrition rates were as thus:

i) Pregnancy/Birth

- 53 Deaths
- 5 Untraceable
- 156 Withdrawals

ii) Infancy (≥ 4 weeks and ≤ 2 years of age)

- 24 Deaths
- 52 Untraceable
- 72 Withdrawals

iii) Early childhood (> 2 years and < 7 years)

- 10 Deaths
- 158 Untraceable
- 72 Withdrawals

iv) Childhood (7 years of age)

- 64 Untraceable
- 2 Withdrawals

v) Late childhood (>7 years and <13 years)

- 5 Deaths
- 1021 Untraceable
- 259 Withdrawals

v) Adolescence (≥13 years and <16 years)

- 3 Deaths
- 348 Untraceable
- 178 Withdrawals

vi) Transition to Adulthood (>16 years and ≤18 years)

- 5 Deaths
- 370 Untraceable
- 100 Withdrawals

One caveat regarding the published attrition rates needs to be noted. These official records do not reflect active participation levels across follow-up phases, which show selective participation patterns and decreasing consistency in the sample which responds. Analyses show this selective participation bias has been particularly high during the adolescent phase of the study, which the study team hypothesised may be due to 'study fatigue'. The average response to the 12 measures during the 'adolescence' stage of data collection was 6155, just under half (48.2%) of the 12,776 participants who were enrolled during this phase of data collection. Yet, 9600 participants (75%) responded at least once during this study phase, meaning that the responding samples between data collection points were somewhat inconsistent.

Overall, a core sub-sample of over 3000 families have responded to all 55 assessments, with 5777 responding to 75% or more of these questionnaires. However, it has been found the socio-economic bias in the ALSPAC sample increases with increasing completeness of participation in ALSPAC. When looking at the age 16 comparisons to the NPD KS4 GME sample, children who had not recently participated, or have been lost to follow-up through attrition, had a lower educational attainment than both the ALSPAC responders and the national average. Recent participants in ALSPAC at 16 years were also more likely to be female, white and less likely to be eligible for free school meals. The ALSPAC study team have acknowledged the limitations arising from the selective participation patterns, and have noted inconsistencies in sample participation across many measures. However,

although they estimate that these on-going issues may influence the external validity of results concerning prevalence, it has been argued this over-representation of higher socio-economic groups should not unduly prejudice longitudinal associations providing the features affecting bias are included. To account for these discrepancies across time-points the team has been increasingly exploring data linkage to official records. They also recommend the use of sophisticated statistical techniques such as multiple imputation to account for the missing data.

2.3.6 Strengths and limitations of the ALSPAC dataset in the context of this study

One of the main limitations highlighted in previous investigations of the mental health of child and adolescent chronic illness was the reliance on small, possibly unrepresentative samples. Therefore, the strengths of the ALSPAC sample are clear in this respect. The ALSPAC sample is a large, community sample, with recruitment covering a substantial proportion of the selected catchment area. Moreover, given the over-arching study focus on investigating childhood determinants of lifetime health, the dataset contains a wealth of extensive measures of both physical and mental health taken at multiple time-points. In addition, the measurement of lifestyle and family factors allows for an investigation of possible mediating factors in the association between chronic illness and mental illness. Therefore, the use of this dataset for secondary analyses offers an immediate advantage over previous sampling methods in this research area.

Yet, the relatively high socio-economic status of the ALSPAC sample creates limitations for the research. The literature review highlighted socio-economic gradients in the incidence of chronic illness, and there were trends among some of the non-categorical studies in the systematic review, and in studies focusing on asthma, sickle cell disease, and cystic fibrosis, which suggested that rates of emotional and behavioural symptomatology were comparatively higher amongst chronically ill children from socio-economically deprived backgrounds. From the outset it was clear there would be limited scope to explore the role of socio-economic deprivation on chronic illness

comorbidities in the ALSPAC sample given the relatively advantaged socio-economic profile of the cohort. Based on this socio-economic profile, it was also clear that the representativeness of the associations identified in this research to the larger British population could be called into question, giving the more ethnically and socially diverse characteristics of the wider population. However, it was felt that the larger advantages of the ALSPAC dataset, in terms of sample size and measurement, outweighed this limitation, especially as it was the core aim of this study to first establish that an association between chronic illness and poor mental health outcomes is identifiable, before starting to explore socio-demographic factors which may moderate this association. Therefore, it was strongly believed that the use of this dataset would provide an insight into this association, beyond that which is currently available based on previous studies in the area.

The problems relating to attrition in the dataset were highlighted as a cause for concern in the early stages of the development of this research. Although the study team have noted that it should not unduly bias the findings regarding the nature of associations, especially in the longitudinal analyses, it was highlighted that the nature of the missing data could affect the precision of estimates of prevalence of mental illness at each time-point. Although the primary focus of this research was to investigate a particular theory of the association of chronic health problems in childhood and adolescence to rates of psychiatric illness, rather than to isolate precise point estimations, missing case data might limit the sensitivity of analyses and possible obscure true associations through the impact on complete case sample size. Therefore, analytic power was a recurring consideration in the design of the primary analyses (see section 2.5.1 and 2.5.2), and methods to address any incomplete data identified on measures were also explored (see section 2.5.4). Therefore, as a consequence, it was considered that issues of data attrition should not unduly bias the investigations of this study.

2.4 Measurement

At present, the ALSPAC data is set up as a supported access resource rather than an open access resource. In order to access data from the study, a proposal outlining the plan for data analysis must be approved by the ALSPAC Executive Committee. A full description of available items in the dataset is then provided, and the researcher must select and request a concise list of items that they wish to use in their analyses. The items must be consistent with the research plan that has been approved by the Executive Committee, with the request of superfluous variables for exploratory purposes not advised. Therefore, the chosen time points and variables of interest had to be narrowed down at a very early stage in the project timescale. The selection of measures was made based on consideration of the research and theory overviewed in the literature review. This will be emphasised in the following selection which focuses on the chosen measures for the primary and secondary analyses. Please note that due to the nature of the analyses, the number of variables selected for the analyses, and the related number of measures requested, was extensive. Therefore, following the discussion of the methods of selecting the study time-points, which was pivotal in guiding the process of the data request, the discussions of the related measures used in this research will be segregated into the following sub-sections for clarity:

2.4.1 Selection of study time-points

The ALSPAC dataset contains follow-up data on the study child from birth to eighteen years, and indeed into the young adulthood period. The selection of

which time-points to specifically focus on in the analyses was complicated by the fact that within the literature review, no acute periods of risk for the development of mental health issues among children with chronic illness were particularly highlighted. Although many theoretical articles highlighted the period of adolescence as a possible area of heightened vulnerability to mental illness among this population, due to possible disruptions to normative patterns of psychosocial development (e.g. Michaud et al., 2007), there was no overwhelming evidence to support this position, apart from trends in studies focusing on the conditions of asthma and diabetes mellitus. However, as has already been emphasised, this lack of identification of age-related variations may be more reflective of methodological practices than true differences in the mental health of children and adolescents. To avoid making unsubstantiated assumptions regarding data patterns, it was clear that the measurement waves selected should be inclusive of both childhood and adolescent stages in the lifespan.

Consequently, the narrowing down of the time-frame of the research analyses was based on the availability of the primary outcome measures, that is to say the available measures of mental health at each time-wave. In previous studies, variations in outcome measures have been noted, with parents tending to provide comparatively more negative appraisals of their child's adjustments than ratings provided by other informants, such as the children themselves (e.g. Pinquart & Shen, 2011a; 2011b; 2011c). It was a determined aim of this research to overcome the limitations of perceptual biases by using a broad range of psychiatric outcome measures, inclusive of parent-report, child-report, and teacher-report, with the availability of clinician ratings a decided advantage. This would allow for the exploration of child functioning from multiple perspectives. A range of parent-rated and child-completed psychometric questionnaires are available across the waves, with teachers also completing behavioural ratings at multiple time-points, but the Development and Well-Being Assessment (DAWBA), a measure designed to combine respondent-based measures with the professional expertise of clinician ratings, was only available at when the child was aged approximately seven years, ten years, thirteen years, and fifteen years.

Although, there are measures that require clinical insight at age 16 years and beyond, it was decided to focus on the DAWBA measure for reasons of consistency. Based on the DAWBA availability, the ages of 10 years to 15 years were selected as the specific period of the analysis. Epidemiological data in the literature highlighted this period as a dynamic period in mental health, with the highest prevalence of mental disorders among children being seen among children aged nine to ten years, with levels falling through the age of twelve, and rising steadily again throughout adolescence (e.g. Costello et al., 2006). Costello, Foley and Angold (2006) have attributed this trend to a fall in rates of what could be characterised as childhood disorders (e.g. ADHD, separation anxiety disorder) by adolescence, and the gradual emergence of characteristic adult conditions (e.g. major depressive disorder) in adolescence. Therefore, focusing specifically on this period of development in the ALSPAC sample was theorised to provide a broad picture of child mental health both at the peak point of childhood psychopathology disorders and the emergence of more adult-typified illnesses.

2.4.2 Exposure measures

In the quality rating of the systematic review, an emphasis was based on the importance of using objective health indices in the measurement of child physical health. One of the advantages attributed to the ALSPAC study at the time of study design was the recorded linkage of this dataset to general practice records. Indeed, this linkage data was previously used in ALSPAC studies to examine the relationship between child socio-economic position and childhood multi-morbidity (Cornish, Boyd, Van Staa, Salisbury, & MacLeod, 2013). Although the ALSPAC executive committee approved access to the linked general practice data for this research, it subsequently became clear that the process of authorisation would delay access to the data, and it would not be feasible to use these records within the timeline of this study. It should be noted that although this was a limitation, it was not a disproportionate disadvantage. Currently linkage data is only available for approximately 4% of the eligible ALSPAC sample and it is likely that were this data supplied, the sample size would not be sufficient to power the more sophisticated analyses for this study – for example, only 342 participants had both linked medical data and completed measures of socio-economic position in Cornish and colleagues (2013) study. Therefore, the measures of both chronic illness and asthma diagnosis were selected from the main ALSPAC questionnaire set, and were cross-referenced against other health measures in order to explore patterns of consistency and, consequently, approximately assess the validity of the measures.

2.4.2.1 Measure of chronic health problems

In the 26 studies identified in the systematic review which studied the impact of chronic illness non-categorically a variety of measures were used to identify the "chronically ill" sample (see Appendix II). Just a little over-half (54%) used a pre-specified list of diagnoses which the researchers had predetermined met the criteria of a chronic illness. This use of inclusion or exclusion criteria based on diagnostic lists was also found to be the most common measure of chronic illness in paediatric cohorts in a systematic review of literature of the field by van der Lee and colleagues (2007). However, these reviewers noted that measures of exposure which focus on

consequences of the condition, in terms of duration and impairment, were the more favoured approach by official public health bodies. Van der Lee and colleagues (2007) concluded that this seemed the more logical approach, given that there was little true comparability between the conditions included, or deemed eligible a priori, between research studies, with the rationale for the conditions chosen being quite arbitrary. Similarly, although there was some overlap between conditions included across the 26 non-categorical studies of chronic illness identified in the systematic review – for example, the majority of studies included children with asthma and diabetes mellitus – there were notable variations. For example, Curtis and Luby (2008) excluded children with marked speech and language delays from their sample, as well as those with neurological or developmental disorders, or an IQ which fell below a cut-off of 70. Children with more severe chronic medical conditions (such as cystic fibrosis, cancer and even diabetes mellitus) were also excluded. Such patterns of exclusion were not noted for any other study in this cohort.

There was a lack of thorough recording of specific diagnoses within the ALSPAC, meaning that replicating the most commonly used measure of chronic illness within the research field was not a possibility. However, this was not deemed to be a substantial limitation to the scope of the research. Given the inconsistencies and arbitrary nature of these categorical diagnostic lists, it is not likely that using such an approach would guarantee consistency with other studies in the field for comparative purposes. This study instead used an overall measure of health to identify children with chronic health problems within the ALSPAC dataset. Please note that although many health bodies recommend that functional impairments and dependence on health care services should also be used as an eligibility criteria in identifying children with chronic health problems (see van der Lee et al., 2007), the mediating role of these variables and other indications of condition severity were of explicit interest to this study. Therefore, beyond the recognition of the presence of impairments of health, no other illness-related variables were used as a discriminatory tool to restrict the exposed sample.

In the 128 months/10.67 years questionnaire (taken as the baseline questionnaire due to the administration of the DAWBA at this time point), the primary caregiver was asked “how would you assess the health of your study child?” They then indicated whether their child was “very healthy, no problems”, “healthy, but a few minor problems”, “sometimes quite ill”, or “almost always unwell” over the past twelve months. 7420 primary caregivers (71.06% of the 10441 of the mothers who were sent this questionnaire) indicated the quality of their child’s health over the past twelve months in the survey responses. At the intermediate point in the time frame of the analyses – 166 months/13.83 years - 6745 primary caregivers (64.92% of the 10390 mothers who were sent this questionnaire) again provided indications of their child’s health over the past twelve months. The response breakdown to these items can be viewed in Table 2.1.

Table 2.1 Parental ratings of child health over the preceding 12 months in the 10 and 13 year child-based questionnaire

	N	Very Healthy, No Problems	Quite Healthy, But a Few Minor Problems	Sometimes Quite Unwell	Almost Always Unwell
10.67 Years	7420	4588 (61.83%)	2703 (36.43%)	114 (1.54%)	15 (0.2%)
13.83 Years	6745	4126 (61.17%)	2479 (36.75%)	109 (1.62%)	31 (0.46%)

Based on the research design, it was envisioned that the sample of children with chronic health problems would be identified based on the baseline questionnaire only. However, the rating of health of baseline was not a measure of long-term chronicity of illness, given that it only identified relative levels of illness over the past twelve months. Therefore, it became clear that the identification of the chronic illness sample for the analyses could not just be based on baseline health ratings, but must be based on a consistent identification of health-related impairments across both the 10.67 years and the 13.83 year child-based questionnaire.

5721 primary caregivers provided health ratings on both the 10 year and 13 questionnaires. Cross-tabulations of the ratings over the two time waves (see Table 2.2) indicated that 1303 children who were identified as having some degree of health impairment on the baseline questionnaire were also

identified as having some degree of illness on the 13.83 year questionnaire. However, it was clear that using severity of illness across the two waves to categorise these children would pose methodological problems, given that these ratings fluctuated substantially between these two waves (see Table 2.2). However, for the purposes of the 10 year cross-sectional analyses, 1239 (95.09%) of these children were rated as "healthy, but a few minor problems", 59 (4.53%) as "sometimes quite ill" and 5 (0.38%) as "almost always unwell", and for the age 13 cross-sectional analyses 1229 children (30.85%) were rated as "healthy, but a few minor problems", 62 (4.76%) as "sometimes quite ill" and 12 (0.92%) as "almost always unwell". Please note the relatively small number of children living with severe levels of illness is in keeping with the epidemiological literature in this area. The comparative sample for the age 10 cross-sectional analyses was the 4588 children rated as being "very healthy, no problems", and for the age 13 cross-sectional analyses it was the 4126 children who were placed in this category on the child-based questionnaire. For the longitudinal analyses, the comparative sample consisted of 2681 children who were rated as being "very healthy, no problems" on both questionnaires.

Table 2.2 Cross tabulation of parental health ratings at 10 and 13 years

		10.67 Years			
13.83 Years		**Very Healthy, No Problems**	**Quite Healthy, But a Few Minor Problems**	**Sometimes Quite Unwell**	**Almost Always Unwell**
	Very Healthy, No Problems	2681 (75.48%)	842 (40.42%)	19 (24.36%)	5 (50%)
	Quite Healthy, But a Few Minor Problems	842 (23.34%)	1177 (59.56%)	48 (61.54%)	4 (40%)
	Sometimes Quite Unwell	31 (0.87%)	55 (2.64%)	7 (8.97%)	0
	Almost Always Unwell	11 (0.31%)	7 (0.34%)	4 (5.13%)	1 (10%)

The measure of chronic health problems showed strong consistency with other indicators of physical health within the ALSPAC dataset. Children with chronic health problems missed a statistically higher number of days from school for health-related reasons than the longitudinal comparative sample on both the 10.67 year questionnaire (M Chronic Health Problems: 6.56 (SD: 7.36); M Comparative Group: 2.41 (SD: 3.03); T: -25.01 ($p<0.001$)) and 13.83 questionnaire (M Chronic Health Problems: 7.42 (SD: 9.71); M

Comparative Group: 2.91 (SD: 4.15); T: -20.31 ($p<0.001$)). It also identified 21 of the 30 children (70%) indicated to have medical conditions on the Year 6 questionnaire. However, it should be noted that a further 124 children who were indicated to have a medical condition on the Year 6 questionnaire did not have data on this measure. Similarly, although this item identified 2 of 3 children indicated to have taken medication for diabetes in the past 12 months on the 10.67 year questionnaire, and 9 of the 12 children identified as having taken such medication on the 13.83 year child-based questionnaire, a further 6 and 10 children who had been indicated to have taken medication for diabetes at each time point respectively did not have concurrent data on this measure. Such lack of consistency in responses possibly reflects the concerns regarding participation bias across questionnaires in the ALSPAC dataset.

2.4.2.2 Measurement of asthma diagnosis

This study aimed to test the applicability of patterns seen when using a non-categorical measure to patterns specific to asthma diagnosis. A measure of asthma diagnosis was used that was indicated to be both sensitive (88.5%) and specific (95.7%) in the ALSPAC validation of asthma measures administered longitudinally from 6 months to 8.5 years, which was based on 141 participants with both complete parent-reported data and linked medical records (see Cornish et al., 2014).

In the primary caregiver questionnaire at baseline (128 months/10.67 years), the primary caregiver was asked, “Has a doctor ever actually said that your child has asthma or eczema?” Of the 7810 caregivers who responded to this question (74.8% of the 10441 of the mothers who were sent this questionnaire), 1124 (14.39%) indicated that the doctor confirmed their child had asthma, while 574 (7.25%) reported that the doctor had stated that their child had both asthma and eczema. Please note that this question was also asked in the primary caregiver questionnaire at 166 months/13.83 years, where, of the 7067 participants who responded (68.02% of the 10,390 of the mothers who were sent this questionnaire)), 1129 (15.98%) indicated that the doctor had confirmed that their child had asthma, and 514 (7.27%) both asthma and eczema. Asthma diagnosis at 10 years was a perfect predictor

of reports of asthma diagnosis at 13 years, indicating that this is a reliable indicator across questionnaire waves. However, these were not identical samples. Of the 1698 children who were identified as having an asthma diagnosis at baseline, 441 (25.97%) did not participate in the 13.83 year questionnaire. In addition, 334 children with an asthma diagnosis were identified in the 13.83 year questionnaire (20.33% of the asthma cohort at this wave) who did not participate in the baseline questionnaire.

As stated in the study design, the asthma sample for the prospective longitudinal analysis was identified based on the baseline measure only (n=1698). This selection was supported by the finding that asthma diagnosis at 10 years was a perfect predictor of asthma diagnosis at 13 years within the ALSPAC dataset. However, the comparative sample was identified based on the health ratings in both the 10.67 and 13.83 year questionnaire, with only children without asthma who were rated as “very healthy, no problems” at both time points included. This was to ensure that all children in the comparative sample were relatively free from any form of health-related impairment. Please note that, of the 820 children who had concurrent data on the measure of chronic health problems, 56.7% of children with asthma at baseline were identified as having a chronic health problem. Of the 864 children who had concurrent data on the measure of chronic health problems at 13 years, 57.1% of children with asthma were identified as having a chronic health problem.

2.4.3 Primary outcome measure

A number of outcome measures were selected to give a broad perspective on child mental health over the period of study. The measures chosen were the Development and Well Being Questionnaire (DAWBA) (section 2.4.3.1), the Strengths and Difficulties Questionnaire (SDQ) (section 2.4.5.1.1), and the short Moods and Feelings Questionnaire (sMFQ) (section 2.4.5.1.2). A table which summarises the administration of these outcome measures, and the informants used at each administration, is presented in Table 2.3. However, as was suggested by the opening discussion, the DAWBA was viewed as the primary outcomes measure. This choice was partially guided by the aforementioned clinician input on this measure, but was also strongly based in the psychometric properties of this instrument, especially in the context of studying the associated mental health of children living with chronic illness. Official reports have shown that the DAWBA is a sensitive and discriminant measure of emotional disorders in the context of somatic symptomatology (e.g. Meltzer, Gatward, Corbin, Goodman, & Ford, 2003). This was a decided advantage given that the precision of many psychometric measures in the context of chronic illness was explicitly questioned in the literature review (e.g. Canning & Kelleher, 1994). In addition, the DAWBA aims to measure prevalence rates of psychiatric disorders in line with current diagnostic guidelines (section 2.4.3.1), which lays the way for easier assessment of the clinical implications of the findings. Therefore, outcomes as measured by the DAWBA were the primary focus of the analyses, and the 'Strengths and Difficulties Questionnaire' SDQ (see section 2.4.5.1.1) and the 'short Moods and Feelings Questionnaire' sMFQ (see section 2.4.5.1.2) scales were used as comparative outcome measures, in order to explore the consistency of indications across measures and informants.

Table 2.3 Administration of the outcome measures over the time-period chosen for analysis

	Version	10 Yrs	11 Yrs	12 Yrs	13 Yrs	14 Yrs	15 Yrs
DAWBA	**Parent**	✓ (n=7820)			✓ (n=7103)		
	Parent & Child						✓ (n=5395)
SDQ	**Parent**		✓ (n=7348)		✓ (n=7027)		
	Teacher	✓ (n=7574)					
sMFQ	**Parent**		✓ (n=7130)		✓ (n=6991)		
	Child	✓ (n=7363)		✓ (n=6715)	✓ (n=6019)		

2.4.3.1 The Development and Well-Being Assessment

The Development and Well-Being Assessment (DAWBA) is a package of questionnaires, interviews and rating techniques designed to generate ICD-10 and DSM-IV psychiatric diagnoses for children (Goodman, Ford, Richards, Gatward, & Meltzer, 2000). It has been specifically designed for use in epidemiological studies, such as the United Kingdom's Office of National Statistic's explorations of the prevalence of child mental health disorders in Great Britain (see Meltzer, Gatward, Corbin, Goodman, & Ford, 2003).

As outlined by Goodman, Heiervang, Collishaw, and Goodman (2011), the DAWBA consists of a semi-structured interview which can be administered through either lay interviewers, or by self-completion, to parents of children age 4-16, and to children and adolescents over the age of 11. A brief questionnaire is also available for teachers. The interview is structured and has sections covering individual emotional, behavioural and hyperactivity disorders, in addition to sections on autistic spectrum disorders, eating disorders and tics, which follows both the diagnostic criteria outlined in in the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV) (American Psychiatric Association, 1994) and the International Classification of Diseases [ICD-10] (World Health Organisation, 1993). Please note, that children are not questioned explicitly in relation to symptoms of oppositional defiant disorder or hyperactivity, and, in addition, there are no detailed questions about emotional symptomatology in the teacher questionnaire. This is based on a strong literature base which indicates that these informants often do not provide reliable indications of the presence of such

symptomatology. Each structured section of the questionnaire, focuses on the symptomatology relating to one set of disorders, and is followed by an open-ended set of questions which encourages the informant to describe the child's difficulties in more detail. Clinicians then review the accounts of all available informants, and use these to rate the presence or absence of individual diagnoses.

The original validation study of this measure by Goodman, Ford, Richards, Gatward & Meltzer (2000) established that there was substantial agreement between diagnostic categorisations based on the DAWBA and case note diagnoses in a community sample (n=491) as well as a clinical sample (n=39) from the United Kingdom. Please note that in addition to binary ratings of the absence or presence of named disorders, feedback on the DAWBA can also alternatively be scored in a dimensional fashion, where symptoms of disorders are considered on a spectrum (see Goodman et al., 2011). These dimensional scores were also available in the ALSPAC dataset for the administration periods selected. However, although these dimensional ratings, termed "DAWBA bands", indicated similar associations with mental health risk factors in a validation study with 7,912 British children and 1,364 Norwegian children, prevalence estimates based on these dimensional scores were much weaker than those using the binary ratings, and were not reliable approximations of the 'gold-standard' clinician-rated diagnoses (see Goodman et al., 2011).

The ALSPAC study administered the DAWBA in child-based questionnaires at 10.67 years (baseline) and 13.83 years. Parents and children also completed this measure at the 'Teen in Focus' clinical assessment at 15 years. Data was available for 7820 children at 10 years (representing 74.9% of respondents to 10,441 mailed questionnaires), 7103 children at 13 years (representing 68.36% of respondents to 10,390 mailed questionnaires), and 5395 children at 15 years (representing 50.36% of the families invited to participate in this clinical assessment).

In the ALSPAC, an overall summary indication of the presence of "any psychiatric disorder" is available for each study child at each of the three

administration waves. The definition of “any psychiatric disorder” is broad, and encompasses a wide range of emotional, behavioural, and hyperactivity disorders, inclusive of:

- Separation anxiety
- Specific phobia
- Social phobia
- Panic disorder/agoraphobia
- Post-traumatic stress disorder
- Obsessive compulsive disorder
- Generalised anxiety disorder
- Body dysmorphic disorder
- Disruptive mood dysregulation disorder
- Major depression
- ADHD/hyperkinesis
- Oppositional defiant disorder
- Conduct disorder
- Eating disorders, including anorexia, bulimia and binge eating
- Autism spectrum disorders
- Tic disorders, including Tourette syndrome
- Bipolar disorders

This binary indicator, therefore, encompasses a wide spectrum of different psychopathologies and is not truly insightful into the underlying characterisation of disorders. For this reason, the ALSPAC database also includes three more narrow binary indications of “any emotional disorder” (inclusive of major depressive disorder and depressive disorder not otherwise specified), “any anxiety disorder” (inclusive of separation anxiety disorder, specific phobia, social phobia, posttraumatic stress disorder, obsessive-compulsive disorder, generalised anxiety disorder, and anxiety disorder not otherwise specified), or “any behavioural disorder” (inclusive of oppositional defiant disorder and conduct disorder) based on the responses on each DAWBA administration. Please note that, for the age 15 wave, a broader measure of conduct-related disorder is available (“any externalising

disorder") which encompasses disorders such as oppositional defiant disorder, conduct disorder, and ADHD/hyperkinesis. However, to maintain consistency with the two preceding waves, only the measure of "any behavioural disorder" (a measure of conduct disorder/oppositional behavioural disorder) was requested. The frequencies of psychiatric disorders overall, and more specific prevalence rates of emotional, anxiety, and behavioural disorders, are listed in Table 2.4. Please note that as the indications of "any psychiatric disorder" require complete data across all sections of the DAWBA questionnaire, the amalgamated numbers of children identified as having "any emotional disorder", "any anxiety disorder" or "any behavioural disorder" outnumber this summary measure.

Table 2.4 Prevalence rates of psychiatric disorders in the ALSPAC (measured by the DAWBA)

	Any Psychiatric Disorder	**Any Emotional Disorder**	**Any Anxiety Disorder**	**Any Behavioural Disorder**
10 Years	468 (5.98% of 7820 respondents)	219 (2.8% of 7819 respondents)	166 (2.12% of 7819 respondents)	265 (3.42% of 7755 respondents)
13 Years	393 (5.53% of 7103 respondents)	148 (2.08% of 7103 respondents)	109 (1.53% of 7103 respondents)	258 (3.67% of 7038 respondents)
15 Years	368 (6.82% of 5395 respondents)	172 (3.21% of 5366 respondents)	107 (1.99% of 5366 respondents)	206 (3.82% of 5395 respondents)

Behavioural disorders were the most prevalent types of psychiatric disorders at all three administration waves, with the prevalence slightly rising over time. Moreover, rates of emotional disorders fell substantially from 10 to 13 years, although a slight increase was indicated at the 15 year wave. The rates of anxiety disorders remained somewhat consistent over the three waves. As can be seen, based on the frequencies on both the totalled scale, and these more condition-specific indicators, the actual prevalence of psychiatric disorders in the DAWBA was quite low. Estimates based on national representative British child and adolescent populations (e.g. Ford, Goodman, & Meltzer, 2003; Costello et al., 2003) would suggest that psychiatric disorders are prevalent amongst 10% of the child and adolescent population. These figures suggest that prevalence rates are over 40% lower in the ALSPAC sample than expected rates across all three measurement waves. Please note that these low prevalence rates may reflect selective patterns in

study drop-out. In previous analyses of ALSPAC data by Wolke, Waylen, Samara, Steer, Goodman, Ford and Lamberts (2009), albeit specifically focused on behaviour disorders, findings suggested that drop out in the study was selective, with children presenting with symptoms of conduct disorder more likely to leave the study. However, they found that although this bias resulted in lower prevalence estimates, it did not bias conclusions regarding associative relationships, with regression models only marginally affected. Therefore, it was considered unlikely that it would unduly bias the associative analyses of this study.

2.4.4 Covariates in associative analyses

2.4.4.1 Moderating variables

Psychiatric disorders have been shown to demonstrate gender profiles in childhood and adolescent groups, with behavioural disorders showing a marked male predominance, and internalising disorders being more prevalent amongst females (e.g. Zahn-Waxler, Shirtcliff, & Marceau, 2008). Many chronic illness conditions are also more prevalent in a specific gender. For example, the genetic condition of haemophilia is more common amongst boys (see Evans, Cottrell, & Shiach, 2000). Perhaps as a result, in the systematic review, gender was repeatedly identified as a moderating variable in the association between long-term conditions and mental health. Therefore, gender was also examined as a moderating covariate in the analyses for this study.

The ALSPAC dataset has a binary code for the gender of each study child. In this study males were coded as ‘0’ and females were coded as ‘1’.

2.4.4.2 Confounding variables

Two variables were explicitly identified as possible confounding variables a priori. The first of these two variables was socio-economic position. Socio-economic disparities were identified in incidence of chronic health conditions, and trends among studies eligible for the systematic review similarly suggested that children and adolescents with chronic illness from deprived backgrounds reported higher levels of emotional and behavioural difficulties than children with chronic illness from more socially advantageous

backgrounds. An ALSPAC study which examined the relationship of socio-economic position to childhood multi-morbidity using the linked medical data (Cornish et al., 2013) indicated that living in a more deprived area, as indicated by geo-coding scores, was associated with the onset of both physical and mental illness in the ALSPAC cohort. Therefore, it was hypothesised that this factor could play some confounding role in the association of interest, and that controlling for the effects of this variable could lead to a more insightful estimate of the association between chronic illness and mental health. Although these were the reasons socio-economic status was included in the analyses for the purposes of this research, it should be noted that the ALSPAC study team advised that this covariate should be included as a covariate in all associative analyses to control for the high socio-economic bias (see Boyd et al., 2012).

A further variable was identified a priori as a possible confounding variable, based on the literature regarding both childhood psychopathology and chronic illness in childhood and adolescence. There are substantial hereditary factors in childhood-onset psychiatric illness, underlined by both genetic influences and the family environment (e.g. Jaffee et al., 2002). Chronic illness in childhood has been hypothesised as an associated factor in parental mental health and related malfunctioning family dynamic - however, it should again be noted that, currently, the supporting evidence for this position is weak (e.g. Barlow & Ellard, 2006). Therefore, it is possible that the poor mental health outcomes attributable to chronic illness are reflective of this association with parental mental health across childhood, a strong predictor of childhood- and adolescent- onset psychopathology, rather than any on-going association of chronic health problems to poor psychosocial outcomes and mental health. Therefore, it was considered important to control for the possible effects of parental history of mental illness on the association between chronic health problems and rates of psychiatric illness.

The measures for these hypothesised confounding variables are described in section 2.4.4.1.1 (socio-economic status) and 2.4.4.1.2 (history of parental mental illness) below, and are summarised in Table 2.5.

2.4.4.1.1 Socio-economic status

The Townsend score used by Cornish et al (2013), which was calculated from the geo-coding of addresses of the ALSPAC cohort, was not available to researchers at the time of the data request. Therefore, the second measure of socio-economic position used in this linkage study - a scale of childhood adversity developed by the ALSPAC team - was explored as a potential measure of socio-economic position. As described by Bowen and colleagues (2005), this scale uses response patterns across questionnaires to measure a variety of different risk factors to child psychosocial well-being (specifically maternal age at birth, housing inadequacy, low educational attainment (of either mother or father), financial difficulties, partner relationships, family structure, social network, maternal affective disorder, substance abuse and crime) during three distinct phases in early childhood: pregnancy, birth to two years, and two years to four years. As researchers are advised to select items from the scale based on their research aims and objectives, initial exploratory analyses focused on the items thought to be most related to continued socio-economic deprivation from childhood into adolescence - specifically early parenthood, low educational attainment, housing inadequacy, and financial difficulties. As there were high amounts of variability in the indications of these items over the three life phases (e.g. only 37.42% of those who were indicated to be in inadequate housing during pregnancy were indicated to still indicated to be in such housing from birth to two years), a cumulative count was taken of risk over the three periods. However, this totalled scale showed poor factor loadings and inter-item correlations in both exploratory factor analysis and principal components analyses, even with the application of a varimax rotation. It also showed poor predictive associations with the available National Statistics Socio-Economic Classification (NSSEC) scores for the mother and the partner in early childhood, and with family income as reported by the child's primary caregiver at 11 years. Please note similarly poor associations were indicated when scores relating to any of the three distinct measurement periods were isolated. Therefore, it was decided that there was a strong rationale to explore alternative measures of socio-economic status.

The National Statistics Socio-Economic Classification (NSSEC) scores were available for both mothers and their partners. However, the most recent of these derived scores was based on responses from the period when the study children were aged three years and eleven months approximately. There were also significant amounts of missing data on all NSSEC classifications. For example, the most complete NSSEC score (partner proxy as measured at 8 months) only accounted for 3441 (46.37%) of the children who had parental ratings of health at the study's baseline. Moreover, the exploratory analyses indicated significant amounts of variability within ratings, which perhaps accounts for why the NSSEC scores showed poor and inconsistent relationships with family income as reported by the primary caregiver at eleven years.

Most studies which have used ALSPAC data have selected socio-economic indicators from the pregnancy and early childhood years (e.g. Culpin, Stapinski, Miles, Araya, & Joinson, 2015; Russell, Ford, & Russell, 2015), which has been attributed to the larger sample size available in these early years (Kendler et al., 2014). However, the exploratory analyses indicated high variability in socio-economic position in the early years, with no consistently deprived sample identifiable, and, most importantly, indicated that these early-life measures showed poor relationships to socio-economic indicators during the period selected for analysis. Although socio-economic indicators from the late childhood/early adolescent period had more incomplete response patterns, it was hypothesised that these more recent indicators would be more valid indicators of socio-economic position for the sample and time period of interest. Therefore, family income as measured at 11 years was selected as the primary measure of socio-economic position. Family income has been described as one of the primary structural determinants of socio-economic position, and has frequently been used as a measure of socio-economic status (see Lorant, Kunst, Huisman, Costa, & Mackenbach, 2005). However, as this item was recorded at a later period than the baseline of this study (approximately 10 years), housing tenure was used as an alternative measure of socio-economic position for the cross-sectional analyses of the age 10 questionnaire. Housing tenure has often

been used as a measure of socio-economic position in British cohorts as it is indicative of the position of all members of the population, inclusive of children and the retired (see Filakti & Fox, 1995).

Household income was coded in a binary fashion due to the high amount of individual response categories. The average weekly household income (inclusive of social benefits) was indicated by 5532 primary caregivers in a questionnaire at 134 months/11.17 years, with the frequencies for each individual category recorded as followed:

1) < £120: n=116 (2.1%)
2) £120 - £189: n=261 (4.72%)
3) £190 - £239: n=272 (4.92%)
4) £240 - £289: n=355 (6.42%)
5) £290 - £359: n=623 (11.26%)
6) £360 - £429: n=559 (10.1%)
7) £430 - £479: n=351 (6.34%)
8) £480 - £559: n=775 (14.01%)
9) £560 - £799: n=1047 (18.93%)
10) £800 or more: n=718 (12.98%)
11) Don't Know: n=455 (8.22%)

In the coding process for this study, responses in the "Don't Know" category were scored as missing data. Based on calculations of UK income distribution 2016 (see Department for Work and Pensions, 2016) households earning under £289 per week were coded as 'low income households' (n=1004; 19.78% respondents) and the remaining households were coded as 'average to high income households' (n=4073; 80.22% of respondents).

As stated, the alternative measure of socio-economic position for use in baseline analyses was housing tenure. 6313 primary caregivers indicated their home ownership status at 122 months/10.17 years. The categories and frequencies were as follows:

1) Being bought/mortgaged: n=4938 (78.22%)
2) Being bought from council: n=95 (1.5%)
3) Owned/no mortgage: n=407 (6.45%)

4) Rented from council: n=443 (7.02%)
5) Rented privately – furnished: n=26 (0.41%)
6) Rented privately – unfurnished: n=157 (2.49%)
7) Rented – housing association: n=162 (2.57%)
8) Other: 85 (1.35%)

The 85 respondents who selected other were asked to explicitly describe their home ownership status. However, as this data was text data and contained in the qualitative files, it was not requested for this research. Consequently, responses from these 85 respondents were coded as missing. The rest of the data was recoded in line with previous studies using housing tenure as a measure of socioeconomic position (see Marmot, Kogevinas, & Elston, 1987):

i) *Owner-Occupied*: n=5440 (87.35%) inclusive of those who indicated that their home was being bought/mortgaged, being bought from the council and those who owned their own home outright)

ii) *Privately Rented*: n=183 (2.94%) inclusive of those who indicated that their home was privately rented, either furnished or unfurnished

iii) *Local Authority*: n=605 (9.71%) inclusive of those who were renting their home from the council or housing association

Please note that although logistic regression models indicated that low household income was strongly associated with living in private rental accommodation and living in local authority housing, as would be hypothesised, overall there was quite low concordance between the measures. For example, 74.63% of the 268 respondents who lived in local authority housing were indicated to belong to an average to high income household. However, it should be noted that consistent responses across the two measures were only available for 2805 children in the ALSPAC dataset (18.98% of live-born children).

Therefore, the relative socio-economic homogeneity of the ALSPAC sample, especially in the adolescent years, and substantial data attrition, made it difficult to identify a sensitive measure of socio-economic status. It was considered that the measures of low household income and housing tenure were the best measures of socio-economic position in the context of this

study. Although these measures were also affected by data attrition, albeit to a lesser extent than alternative measures in the dataset such as the NSSEC, it was considered that they would be a more valid indication of socio-economic status under the period of study. Although measures of adversity during pregnancy and early childhood had more complete data, and had been used in previous studies using the ALSPAC data, these measures showed very low predictive value of socio-economic outcomes during the adolescent period. Moreover, using household income and housing tenure as a general indication of socio-economic position is supported by the frequent use of these measures among a substantial number of studies in the epidemiological literature base.

2.4.4.1.2 History of parental mental illness

Measures of maternal mental health in ALSPAC have predominantly focused on the pre- and antenatal period, in order to facilitate the investigation of the impact of post-natal emotional disorders on child health. However, for the purposes of this research, what was needed was an insight into the mother's history of mental illness at a time close to the adolescent period, to get a sense of not only genetic risk, but also possible impact on the family environment. Consequently, maternal responses on a number of questions concerning their history of mental illness in a questionnaire administered when the child was approximately 97 months/8.08 years was used to screen for a history of poor mental health in the mother. In this questionnaire, mothers were asked if they ever had any of the following mental health conditions: bulimia, drug addiction, alcoholism, schizophrenia, anorexia nervosa or any other psychiatric problem. The response categories were: "Yes, had it recently (in past year)"; "Yes, in past, not recently"; or "No, never". 6131 mothers responded to one or more of these items, and 1025 (16.72%) of these mothers indicated that they had suffered from one or more of these illness, either at a time close to the questionnaire administration or in the past. A nearly identical set of questions was used to identify a history of mental illness in the father of the study child. As completion of the partner's questionnaire was dependent on the mother's passing on of the questionnaire to their current partner, it was decided that the measure of

paternal history of mental illness should focus on the early childhood period to ensure that responses were most likely provided by the child's biological father. However, it is acknowledged that this procedure did not allow for the inclusion of father's who developed mental illness in the childhood period, and the possible impact of this illness on the family environment. In one of the first partner's questionnaires (responses were collected in the early gestation period to the four month period post-delivery dependent on the enrolment time of the mother), fathers indicated whether they had ever suffered from any of the following conditions: drug addiction, alcoholism, schizophrenia, anorexia nervosa, severe depression, or any other psychiatric problem. Similar to the maternal measure, the response categories were: "Yes, had it recently"; "Yes, in past, not now"; "No, never", and "Don't know. 8641 fathers responded to one or more of these items in a meaningful fashion, with 804 (9.3%) of these fathers indicating that they had suffered from one or more of these illness, either at the time of administration or in the past.

Concordant responses for both mothers and fathers were available for only 3260 of the ALSPAC study cohort (representing 22.06% of 14,775 live-born children). Therefore, a dependence on cases in which both parents provided their history of mental illness would most likely result in an underpowered set of analyses. Therefore, as the purpose of including this variable in the analyses was to get an approximate insight into whether a parental history of mental illness may act as a confounding variable in the association of paediatric chronic illness into poor mental health outcomes, the parental history of mental illness item was considered complete if one or other of the child's parents indicated their history of mental illness (n=11,341; 76.76% of live-born children). This item was coded as a binary category, with the classifications of "no reported history of parental mental illness" (n=9565; 84.34% of respondents) and "reported history of parental mental illness" (n=1776; 15.66%). Please note that this measure was likely biased by the lack of concordant responses.

Table 2.5 Summary of measures of confounding variables

Variable	Measure	N
Socio-Economic Status	Low Household Income as Reported by Primary Caregiver at 11 Years *Alternative Measure for Baseline Analyses:* Housing Tenure as Reported by Primary Caregiver at 10 Years	5077 6228
History of Parental Mental Illness	Mother's reports of mental health history at 8 Years *AND/OR* Partner's reports of mental health history in early gestation – early postnatal period	11,341

2.4.5 Mediating variables

One of the aims of this study was to identify mediators in the association of chronic health problems to psychiatric illness, and to examine the relative role of symptom severity and functional impairments in this association, in addition to the family and social outcomes implicated as the mediating mechanisms in the over-arching theory in this field. This sub-section of the measurement overview outlines the measurements of these variables, starting with measures of symptom severity and impairment, which are described in section 2.4.4.1.1, and then the measures of stressors to child development, which are outlined in section 2.4.4.1.2. The complete range of mediating variables explored in this research, and the related measures, are then summarised in Table 2.7. In addition, a timeline of the administration of the related measures, in relation of the exposure and primary outcome measure, is provided in Table 2.8. Both tables can be found at the conclusion of section 2.4.4.1.2.

2.4.4.1.1 Symptom severity and functional impairment

The systematic review suggested that children who were experiencing more impairment as a result of the severity of their condition were more likely to report an elevated level of emotional and behavioural symptomatology, regardless of the primary diagnosis. It was questioned whether symptom severity, or the related impairments incurred, played a key mediating role in the association of chronic health problems to poor mental health in childhood and adolescence, or whether these were some factors among many which moderated this association. Given the cross-sectional methodology of many of the studies reviewed, it was also questioned whether the presence of psychiatric illness symptomatology was more likely to lead to poor physical health outcomes. Therefore, it was crucial to examine the role of symptom severity in the associated outcomes of chronic health problems. However, one challenge was to identify proxy measures of symptom severity and impairments within the ALSPAC dataset that would be common to all conditions, especially as no formalised measure was identifiable in the existing literature using the ALSPAC dataset.

The first measure of impairment chosen was a measure of health-related school absenteeism. Weitzman (1986) argued that school absenteeism is a key measure of chronic illness health status as it gives a holistic indication of daily impairment because of both symptom activity and on-going medical intervention. A similar emphasis was put forward by Geist, Grdisa and Otley (2003) who highlighted that such absences reflect the burden of on-going medical treatment and maintenance even in periods of disease inactivity. In a follow-up to questions regarding the child's health in the 128 month (10.67 years) and 166 month (13.83 year) child-based questionnaire, 7730 mothers and 6980 mothers respectively indicated the specific number of days missed from school over the past twelve months due to:

I. Infections

10 Years: 5573 (72.1%) missed 1or more days (M:4.42 (SD:4.45); 1-60)

13 Years: 4947 (70.59%) missed 1or more days (M:4.72 (SD:5.04); 1-98)

II. Hospital investigations

10 Years: 697 (9.02%) missed 1or more days (M:3.48 (SD:5.33); 1-59)

13 Years: 776 (11.12%) missed 1or more days (M:4.01 (SD:7.16); 1-90)

III. Other Investigations

10 Years: 282 (3.65%) missed 1or more days (M:2.24 (SD:3.11); 1-35)

13 Years: 503 (7.21%) missed 1or more days (M:2.88 (SD:4.6); 1-80)

IV. Asthma

10 Years: 253 (3.27%) missed 1or more days (M:4.21 (SD:4.98); 1-50)

13 Years: 159 (2.28%) missed 1or more days (M:3.27 (SD:2.95); 1-20)

V. Eczema/Itchy Rash

10 Years: 56 (0.72%) missed 1or more days (M:3.2 (SD:4.45); 1-30)

13 Years: 42 (0.6%) missed 1or more days (M:3.14 (SD:2.76); 1-14)

VI. Hay Fever/Allergic Rhinitis

10 Years: 127 (1.64%) missed 1or more days (M:2.11 (SD:1.8); 1-12)

13 Years: 122 (1.74%) missed 1or more days (M:5.75 (SD:17.41); 1-99)

VII. Other Reason 1

10 Years: 701 (9.07%) missed 1or more days (M:3.03 (SD:3.71); 1-40)

13 Years: 834 (11.95%) missed 1or more days (M:4.52 (SD:9.05); 1-98)

VIII. Other Reason 2

10 Years: 102 (1.32%) missed 1or more days (M:2.27 (SD:2.16); 1-15)

13 Years: 136 (1.95%) missed 1or more days (M:3 (SD:3.75); 1-35)

IX. Other Reason 3

10 Years: 17 (0.22%) missed 1or more days (M:2.41 (SD:1.94); 1-7)

13 Years: 29 (0.42%) missed 1or more days (M:3.76 (SD:6.23); 1-30)

Please note that the specific details of the “other reason” are supplied in the ALSPAC qualitative dataset, which was not requested for this research. This was limiting as a substantial number of parents indicated that their children had missed schools for health-related reasons not listed across the two questionnaires.

When summing together participants who responded on any one of these nine items, and looking at the resulting scale distributions a clear demarcation was observed. At the year 10 questionnaire the number of days in total missing ranged from 0 to 79 days, but 75% of the sample missed 5 days or less. Similarly, in the age 13 questionnaire, although the summed scale ranged from 0 to 123, 75% of the sample missed 6 days or less. Therefore, there was a strong rationale for creating a binary categorisation based on responses to these items, in which a score of 6 days or more indicated a high degree of health-related school absenteeism. 1636 of the 7730 children who had absenteeism related data at 10 years (21.16%) fell into this category and 1867 of 6980 children (26.75%) fell into this classification at 13 years. Please note that this demarcation was also supported by the prevalence studies of Newacheck and Taylor (1992) which indicated that children with chronic illness miss on average 3.1 days of school per year because of their illness, and van Gent and colleagues (2008) which surmised that the average child with a chronic condition misses 5 school days per year. Therefore, these studies would suggest that the six day cut-off would represent children with chronic illness who are experiencing an above average level of absenteeism as a consequence of their condition.

As activity limitations were highlighted as the strongest insight into mental ill-health outcomes into mental ill-health outcomes in the non-categorical studies of the systematic review, it was considered important that this measure of absenteeism was supplemented by a measure of impairment that focused specifically on physical limitations and functionality. In the 166 month (13.83 years) self-completed questionnaire, children in the ALSPAC sample completed a number of questions regarding their levels of fitness and fatigue over the past three months. This scale was a novel scale designed for ALSPAC, and no previous studies which had used the scale as a measure could be identified. When the inter-item correlations were calculated for the twenty items, the resulting correlation matrix indicated quite poor correlations between the majority of the twenty items. However, two groups of questions which seemed to cluster together, due to inter-item correlations of magnitude 0.5 – 0.7. The first set of questions, overall, could be viewed as a measure of activity:

1) Degree to which child felt fit
2) Degree to which child was very active
3) Degree to which child did a lot each day
4) Degree to which child felt physically in excellent condition

The second set of scales could, in contrast, be viewed as a measure of fatigue:

1) Degree to which child felt in bad condition
2) Degree to which child didn't get much done
3) Degree to which child thought they did not do much
4) Degree to which child did not feel like doing anything

Please note that the children responded to each item on a five point Likert scale ('Exactly like me'; 'Most of the time like me'; 'Sometimes like me'; 'Not much like me'; 'Not at all like me'). The items were scored on a scale of one to five, so that five indicated a higher level of impairment. When inter-item correlations were calculated for these eight questions in isolation from the remaining items on the questionnaire, strong and significant associations were identified between all items. Subsequently, a unitary structure of the

items was supported by both exploratory factor analyses and principal components analysis (see Appendix IV for a fuller account of these analyses). Cronbach's alpha for these eight items also indicated strong internal consistency (α=0.86). Therefore, these items were isolated as a unitary scale measuring a variable conceptualised as 'Perceptions of Fatigue', with total scores ranging from five to forty. 6647 children in the ALSPAC responded all eight questions in the 13.83 year questionnaire (M: 18.59 (SD: 5.32)).

As these scales were not formalised measures of impairments, but were selected based on face validity and their consistency with the literature, it was important to establish support for the position that these measures indicated impairment to daily activity as an associated consequence of illness severity. The measures of health-related absenteeism were included in the same questionnaires as those in which parents rated their children's health. There was quite high concordance between ratings of illness severity and health related absenteeism at the two waves (e.g. at 10 years, 103 of the 128 children who were rated as "Sometimes Quite Unwell/Almost Always Unwell" fell into the grouping of high health-related absenteeism (80.47%), as did 97 of the 130 children at age 13 years (74.62%)). However, a substantial proportion of children rated as "Quite healthy, but a few minor problems" also indicated to have high levels of health-related absenteeism at 10 years (34.12%) and 13 years (41%). Therefore, it is clear that, although this measure does seem to be related to illness severity, it is an independent measure of illness-related impairment. Similar indications were made regarding the scale "Perceptions of Fatigue". Although significant differences were indicated between children with various health ratings on the age 13 child-based questionnaire ($F:27.9$, $p<0.001$), with mean scores for the "Sometimes Quite Unwell/Almost Always Unwell" group being slightly higher than those of the "Quite Healthy, but a Few Minor Problems" group (M: 21.8 (SD: 6.83) versus M: 19.2 (SD 5.3)), differences in mean scores were not excessively large and the standard deviation suggested high amounts of variability within groups. This again suggests that, although this measure is

related to illness severity, it is a unique measure of health and the impact of illness.

2.4.4.1.2 Variables signifying impairments to normative trajectories of development

Chronic health problems in childhood and adolescence are theorised to be associated with poor mental health outcomes as they present as a source of continuous stress throughout child development. To support this view, previous studies have focused on how chronic illness may lead to many disruptions to family functioning and social development. Although support for a clear association of chronic illness to these variables was mixed, it was continuously questioned whether this was a consequence of methodological artefacts among the studies overviewed. Therefore, it was important to identify measures of these variables in this study, in order to identify if strong and more consistent indications of an association were identifiable in this larger and more representative sample.

2.4.4.1.2.1 Intra-familial conflict and cohesion

Intra-familial conflict and cohesion were the two aspects of family functioning which showed the strongest associations with child outcomes in the meta-analysis of Leeman and colleagues (2016). Therefore, attempts were made to identify measures of these variables within the ALSPAC dataset. The only identifiable measure was a proxy set of questions which had not, as of the time of research design, been used as a formalised measure. These questions, relating to conflict in the parental relationship, were identified in the primary caregiver questionnaire at 110 months (9.17 years approx.) and 145 months (12.08 years approx.). Although this did not comprise a complete picture of conflict within in the family, it has been found that conflicting parental relationships often correlate with disruptions to other relationships within the family, such as that between the parent and child (e.g. Grych & Fincham, 2001). Moreover, overt expressions of hostility between parents have been linked with childhood maladjustment (e.g. Amato & Cheadle, 2005), and this is especially so when this conflict arises from issues relevant to the child in question (e.g. Shelton & Harold, 2008). Therefore, there is

some evidence to suggest that conflict in the parental relationship may be indicative of general dysfunctional familial dynamics and a lack of cohesion.

In the 110 month and 145 month "mother's" questionnaire, five conflict scenarios were listed and the mother responded "Yes, I did this"; "Yes, he did this"; "Yes, we both did this"; or "No not at all" based on their recollections of the three months preceding the questionnaire administration. These scenarios were as follows:

1. Mother/husband/partner were not speaking for more than half an hour
2. Mother/husband/partner walked out of the house
3. Mother/husband/partner shouted or called one another names
4. Mother/husband/partner hit or slapped one another
5. Mother/husband/partner threw or broke things

Any positive response to any of these scenarios was marked as '1' and scores across the five items were totalled. 5586 mothers responded to all five questions when the study child was nine years (M: 0.93 (SD: 1.06)) and 4897 mothers responded at twelve years (M: 0.87 (SD: 1.03)). However, it should be noted that, perhaps unsurprisingly given the fact that these questions were not selected from a validated measure, average inter-item covariance and scale reliability coefficients were quite low (Average inter-item covariance: 0.02; Cronbach's Alpha: 0.55 for both waves). In addition, responses on these questions were not strong predictors of the partner's response to these same set of questions at approximately the same time period. However, the proportions of parents with responses across the two questionnaires was generally quite low (e.g. n=1280 at 9 years).

2.4.4.1.2.2 Overdependence in the parent-child relationship

More recent discussions of family outcomes in the context of chronic illness have hypothesised that chronic illness may cause over-dependence in the parent-child relationship, and that this decreased level of autonomy may have detrimental mental health outcomes, in particular during the adolescent period (e.g. Surís, 2003). However, this theory was not substantially tested in the empirical research overviewed. The ALSPAC dataset contains four

scales designed by Stattin and Kerr (2000) to measure different aspects of "parental monitoring", the term that has often been used to define parental tracking and surveillance. These scales were consistently administered in the adolescent period during the clinical assessments at age 12.5 years, 13.5 years, and 15.5 years. Please note that there were some minor modifications of Stattin and Kerr's original wording to make the items more appropriate to a British context.

The first scale "parental monitoring" was designed to assess parent's knowledge of the child's daily activities. The scale consisted of nine questions:

1) How often do your carers/parents know what you do during your free time?
2) How often do your carers/parents know who your friends are outside of school?
3) How often do your parents/carers know what type of homework you have?
4) How often do your carers/parents know what you spend your money on?
5) How often do your carers/parents know you have an exam/test at school?
6) How often do your carers/parents know how you are doing in different subjects at school?
7) How often do your carers/parents know where you go when you are out with your friends at night?
8) How often do your carers/parents know where you go and what you do after school?
9) How often, during the last month, have your carers/parents been unaware of where you were at night?

The second "child disclosure", measured how often children shared information about their lives with their parents, and consisted of five questions:

1) How often do you tell your carers / parents about your friends (which friends you hang out with and what they have been talking about) without being asked?
2) How often do you want to tell your carers / parents about school (how each subject is going; your relationships with teachers)?
3) How often do you keep secrets from your carers / parents about what you do during your free time?
4) How often do you keep things from your carers / parents about what you do during nights and weekends?
5) How often do you tell your carers / parents about what you did and where you went during the evening?

The third, “Parental Solicitation”, measured how frequently parent’s initiated conversations with their children about their lives and activities, and the five questions were as follows:

1) How often do your carers / parents talk with your friends when they come over to your house?
2) How often do your carers / parents ask you about what happened during your free time?
3) How often were conversations about your spare time started by your carers / parents during the past month?
4) How often do your carers / parents take the time to listen to you when you talk about what happened during your free time?
5) How often do your carers / parents ask you to tell them what happened at school on a normal school day?

The final scale was “Parental Control”, which measured relative levels of autonomy in the parent child relationship. This scale also consisted of five questions:

1) How often do you have to have your carers / parents’ permission before you go out on weeknights?
2) How often, if you have stayed out later than allowed, do your carers / parents expect you to explain why and tell who you were with? (If you

have never stayed out late, do you think they would expect you to explain why and tell who you were with?)

3) How often do your carers / parents demand to know where you are in the evenings, who you are going to be with and what you are going to do before you go out?
4) How often do you have to ask your carers / parents before you can make plans with friends about what you will do on a Saturday night?
5) How often do your carers / parents ask you to tell them how you spend your money?

Children responded to the five questions on a five point Likert scale (Never, Hardly Ever, Sometimes, Most of the Time, Always). All responses were coded so that higher scores on all items indicated higher levels of parental monitoring across the scales. Therefore, scores on the 'Parental Monitoring Scale' ranged from 5 to 45, and ranged from 5 to 25 on the three remaining scales. The response patterns relating to these four scales, in addition to mean scores and reliability coefficients are listed in Table 2.6. Please note that the alpha coefficients mostly indicated adequate internal consistency of the scale across waves, although it did drop below the guideline cut-off of 0.7 at certain waves, with the lowest internal reliability coefficient indicated for the 'Parental Solicitation' scale at 15.5 years. However, given that the coefficients did not drop below a level of 0.6, it was considered that these drop-offs did not present as substantial risks to the analyses of this study.

Table 2.6 Properties of Statin and Kerr's (2000) measures of parental monitoring

	'Teen in Focus 1' Clinic (12.5 Years)			**'Teen in Focus 1' Clinic (13.5 Years)**			**'Teen in Focus 1' Clinic (15.5 Years)**		
	N	**M(SD)**	**α**	**N**	**M(SD)**	**α**	**N**	**M(SD)**	**α**
Parental Monitoring	5135	38.19 (5.07)	0.81	5846	35.97 (5.26)	0.82	4377	37.45 (3.82)	0.76
Child Disclosure	5106	19 (3.56)	0.69	5841	17.87 (3.52)	0.72	4161	19.42 (2.94)	0.75
Parental Solicitation	5098	18.27 (3.39)	0.7	5847	18.16 (3.05)	0.68	4533	20.12 (2.3)	0.61
Parental Control	5144	19.88 (3.9)	0.74	5861	18.56 (3.83)	0.74	4039	20.39 (3.24)	0.66

2.4.4.1.2.3 Satisfaction with peer relationships

It has been hypothesised that chronic illness disrupts normative patterns of psychosocial development, especially during adolescence, when social determinants come to be predominant predictors of psychological well-being (e.g. Michaud et al., 2007). There is some evidence to suggest that young people with chronic illness do engage in higher levels of health risk behaviours than their peers (e.g. Nylander et al., 2014), and it has been hypothesised that this arises from a desire to "fit in" with peers and gain their approval (e.g. Valencia & Cromer, 2000). Desire to be "normal" and similar to peers has also been a recurring theme in qualitative accounts from children living with chronic illness (e.g. Yates et al., 2010; Venning et al., 2008). However, a number studies have, in contrast, indicated that adolescents with chronic illness report comparable patterns of socialisation to peers (e.g. Denny et al., 2014). ALSPAC administered the 'Cambridge Hormone and Moods Project Friendship Questionnaire', a measure of the study child's relative satisfaction with their peer relationships (e.g. Singh, Winsper, Wolke, & Bryson, 2014) in the 'Focus at 10' and the 'Teen in Focus 1' clinical assessment (conducted at 10 years and 12.5 years approximately). Please note, that a modified version of this scale was also included at the 'Teen in Focus 2' clinical assessment (13.5 years approximately) but that, because of the changes in the items administered, it was not possible to apply the standard scoring guideline in a consistent fashion. The scale in the 'Focus at 10' and the 'Teen in Focus 1' assessments consisted of five items, to which the child responded on an item specific scale. The questions used were as follows:

1) Are you happy with the number of friends you have?
   *Responses: V*ery Happy, Quite Happy, Quite Unhappy, Unhappy, No Friends
2) How often do you see your friends outside of school?
   Responses: Almost Everyday, More than Once per Week, Once Per Week, Less than Once per Week, Hardly Ever, Never
3) Do you think that your friends understand you?
   Responses: Most of the Time, Sometimes, Not Often, Not at All

4) Do you talk about problems with your friends?
   Responses: Most of the Time, Sometimes, Not Often, Not at All)
5) Overall how happy are you with your friends?
   Responses: Very Happy, Quite Happy, Quite Unhappy, Unhappy

ALSPAC studies which have used this questionnaire (e.g. Bowen, Heron, Steer, & El Komy, 2008; Holme, Blair, & Emond, 2013) have used the recommended scale scoring guidelines (see, for example, Singh, et al., 2014). This results in a 15-point scale, with higher scores indicating higher levels of dissatisfaction with peer relationships. Using this scoring guideline, 7279 children responded in a meaningful fashion to all five questions at 'Focus in 10' clinical assessment (M: 2.78 (SD: 1.96)) and 6743 children responded in the 'Teen Focus 1' assessment (M: 3.05 (SD: 2.06)). Please note that, although this scale has been used in previous studies dependent on ALSPAC data, Cronbach's alpha coefficients fell well below the 0.7 cut-off guideline, raising concerns about the internal consistency and reliability of this scale (10 Year α: 0.37; 12.5 Year α: 0.48).

2.4.4.1.2.4 Peer victimisation

The meta-analysis of Sentenac and colleagues (2012) indicated that children living with chronic illness may be more at risk of experiencing peer victimisation, although this review highlighted that this risk may not be identifiable across all chronic illness conditions. The ALSPAC study used the 'Bullying and Friendship Interview Schedule' (see Wolke, Woods, Stanford, & Schulz, 2001) to measure peer victimisation among the sample. These structured questions have been validated in studies using German and British samples (Wolke et al. 2001), and have been used in assessments of peer related effects of medical interventions (e.g. Williams et al., 2006). Similar to the 'Cambridge Hormone and Moods Project Friendship Questionnaire', this interview schedule was administered as part of the 'Focus at 10' and 'Teen in Focus 1' clinical assessment (when the study child was aged 10 years and 12.5 years approximately). Children responded on a four-point frequency scale (i.e. 0=Never, 1 seldom, 2=frequently, 3=very frequently, and there was also an optional response of "don't know") on nine questions, five of which focused on overt victimisation (theft, threats or

blackmail, physical violence, nasty names, nasty tricks), and four of which focused on relational victimisation (social exclusion, spreading lies, or rumours, coercive behaviour, deliberately spoiling games). The frequencies were totalled, resulting in a total scale ranging from 0 to 27. Please note that 'Don't Know' responses were coded as missing. 7145 children responded to all nine items at the 'Focus at 10' clinic (M: 1.93 (SD: 2.71)) and 6612 children responded at the 'Teen in Focus 1' clinic (M: 1.82 (SD: 2.76)). The scale demonstrated adequate levels of internal reliability at both waves (10 Year α: 0.71; 12.5 Year α: 0.75). Previous studies have used scale scores to classify children into three categories, with those scoring 1-3 being classified as occasionally bullied and those who scored 4 or more being classified as frequently bullied (e.g. Lereya, Copeland, Costello, & Wolke, 2015). However, this classification system did not have adequate levels of discrimination in the ALSPAC sample, as just under 40% of the sample were classified as being occasionally bullied based on the 'Focus at 10' scores. Therefore, victimisation was classified in a binary fashion, with children scoring four or more on this scale being classified as victims of bullying (10 years n=1399 (19.58%); 12.5 years n=1162 (17.57%))

Table 2.7 Overview of the variables of interest for explorations of mediation, and the measures selected from the ALSPAC dataset

Variable of Interest	Measure/Measures Selected	Range	N	Mean (SD)	Alpha Coefficient
Disease Severity and Functional Impairments	**1)** Mother's Report of Above Average Health-Related School Absenteeism **2)** Eight self-completed questions measuring 'Perceptions of Fatigue'	**1)** Binary Classification ("Average"/ "High") **2)** 5-40 (higher scores indicating more perceptions of fatigue)	**1)** *10 Yrs:* 7730 *13 Yrs: 6980* **2)** 6647	**1)** *10 Yrs:* 1636 (21.16%) "high" *13 Yrs:* 1867 (26.75%) "high" **2)** 18.59 (5.32)	**1)** N/A **2)** 0.86
Inter-Familial Conflict and Cohesion	Mother's report of conflicts in the parental relationship	1-5 (higher scores) indicating more conflict)	*9 Yrs*: 5586 *12 Yrs*: 4897	*9 Yrs*: 0.93 (1.06) *12 Yrs*: 0.87 (1.03)	*9 Yrs*: 0.55 *12 Yrs*: 0.55
Overdependence in the Parent-Child Relationship	Stattin and Kerr's (2002) four self-report scales of Parental Monitoring: **1)** Parental Monitoring **2)** Child Disclosure **3)** Parental Solicitation **4)** Parental Control	**1)** 5-45 (higher scores indicating more monitoring) **2)** 5-25 (higher scores indicating more disclosures)	**1)** *12.5 Yrs*: 5135 *13.5 Yrs*: 5847 *15.5 Yrs*: 4377 **2)** *12.5 Yrs*: 5106 *13.5 Yrs*: 5841 *15.5 Yrs*: 4161	**1)** *12.5 Yrs*: 38.19 (5.07) *13.5 Yrs*: 35.97 (5.26) *15.5 Yrs*: 37.45 (3.82) **2)** *12.5 Yrs*: 19 (3.56) *13.5 Yrs*: 17.87 (3.52) *15.5 Yrs*: 19.42 (2.94)	**1)** *12.5 Yrs*: 0.81 *13.5 Yrs*: 0.82 *15.5 Yrs*: 0.76 **2)** *12.5 Yrs*: 0.69 *13.5 Yrs*: 0.72 *15.5 Yrs*: 0.75

		3) 5-25 (higher scores indicating more solicitations) **4)** 5-25 (higher scores indicating more control)	**3)** *12.5 Yrs*: 5098 *13.5 Yrs*: 5847 *15.5 Yrs*: 4533 **4)** *12.5 Yrs*: 5144 *13.5 Yrs*: 5861 *15.5 Yrs*: 4039	**3)** *12.5 Yrs*: 18.27 (3.39) *13.5 Yrs*: 18.16 (3.05) *15.5 Yrs*: 20.12 (2.3) **4)** *12.5 Yrs*: 19.88 (3.9) *13.5 Yrs*: 18.56 (3.83) *15.5 Yrs*: 20.39 (3.34)	**3)** *12.5 Yrs*: 0.7 *13.5 Yrs*: 0.68 *15.5 Yrs*: 0.61 **4)** *12.5 Yrs*: 0.74 *13.5 Yrs*: 0.74 *15.5 Yrs*: 0.66
Satisfaction with Peer Relations	The self-completed 'Cambridge Hormones and Moods Project Friendship Questionnaire	1-15 (higher scores indicating higher levels of dissatisfaction)	*10 Yrs*: 7279 *12.5 Yrs*: 6743	*10 Yrs*: 2.78 (1.96) *12.5 Yrs*: 3.05 (2.06)	*10 Yrs*: 0.37 *12.5 Yrs*: 0.48
Peer Victimisation	The self-completed 'Bullying and Friendship Interview Schedule'	Binary Classification ("Not Victims"/ "Victimised")	*10 Yrs*: 7145 *12.5 Yrs*: 6612	*10 Yrs:* 1399 (19.58%) victimised *12.5 Yrs:* 1162 (17.57%) victimised	*Underlying Scale:* *10 Yrs*: 0.71 *12.5 Yrs*: 0.75

Table 2.8 Timeline of the administration of the mediating variable measures in relation to the administration of the exposure and outcome measures

	9 Yrs	10 Yrs	11 Yrs	12 Yrs	13 Yrs	14 Yrs	15 Yrs
Exposure							
Health		✓ (n=7420)			✓ (n=7067)		
Asthma		✓ (n=7830)			✓ (n=7067)		
Outcome							
DAWBA		✓ (n=7820)			✓ (n=7103)		✓ (n=5395)
Possible Mediators							
Conflict B/N Parents	✓ (n=5586)			✓ (n=4897)			
Parental Monitoring				✓ (n=5135)	✓ (n=5846)		✓ (n=4377)
Child Disclosure				✓ (n=5106)	✓ (n=5841)		✓ (n=4161)
Parental Solicitation				✓ (n=5098)	✓ (n=5847)		✓ (n=4533)
Parental Control				✓ (n=5144)	✓ (n=5861)		✓ (n=4039)
Satisfaction with Peer Relationships		✓ (n=7279)		✓ (n=6743)			
Peer Victimisation		✓ (n=7145)		✓ (n=6612)			
Health-Related Absenteeism		✓ (n=7730)			✓ (n=6980)		
Perceptions of Fatigue					✓ (n=6657)		

2.4.5 Measures for secondary analyses

2.4.5.1 Alternative outcome measures

As stated, the Strengths and Difficulties Questionnaire (SDQ) and the short Moods and Feelings Questionnaire (sMFQ) were selected as comparative outcome measures, in order to investigate the consistency of the indications of the DAWBA, the primary outcome measure. These specific measures were chosen as alternative indications of mental ill-health for this sample due to the availability of published details of their psychometric properties, and due to frequent use of these measures in investigations of paediatric mental health. In addition, as the SDQ administration in the ALSPAC focused on parent and teacher ratings, and the sMFQ was administered in questionnaires for both primary caregivers and the children themselves, they represent a range of perspectives on the child's psychological well-being. The specific properties of these alternative outcome measures are reviewed below.

2.4.5.1.1 The Strengths and Difficulties Questionnaire (SDQ)

The 'Strengths and Difficulties' Questionnaire (SDQ) is a brief behavioural screening questionnaire for children aged 3 to 16 years which is completed by parents and teachers (see Goodman, 1997), with a self-rated version also available for adolescents aged 11 to 16 years old (see Goodman, Meltzer, & Bailey, 1998). All versions of the SDQ include 25 statements, some positive and others negative. The respondent is required to indicate whether the statement is 'Not True', 'Somewhat True', or 'Certainly True'. The items are equally divided between 5 scales:

(1) Emotional Symptoms
(2) Conduct Problems
(3) Hyperactivity/Inattention
(4) Peer Relationship Problems
(5) Prosocial Behaviour

A total score indicating the child's total level of difficulties is generated by summing scores on scales (1) to (4). Please note that scores on each of the five scales can be scaled up pro-rata if at least 3 of the items are completed.

In the ALSPAC dataset, SDQ total difficulty scores based on primary care-giver ratings were available for 7348 children at 140 months/11.66 years (inclusive of 1157 participants who had pro-rated scores) and 7027 children at 157 months/13.08 years (inclusive of 228 participants who had pro-rated scores). In addition, Year 6 teacher-ratings on the SDQ were available for 7574 children. Please note that this figure is inclusive of 70 participants who had pro-rated scores. A comparative outline of the administration of this measure versus the DAWBA assessment can be seen in Table 2.9. As can be seen, one minor limitation was that the first administration of the primary-caregiver completed SDQ fell during an interim period between DAWBA measurements. Although this may provide insight into child functioning in these intervening periods, it is possible that any inconsistencies in indications between the DAWBA and the parent-rated SDQ at this administrative wave may be due to age-related variations.

Table 2.9 SDQ administration over the time period of study, in relation to the administration of the primary outcome measure

	Version	10 Yrs	11 Yrs	12 Yrs	13 Yrs	14 Yrs	15 Yrs
DAWBA	**Parent**	✓ (n=7820)			✓ (n=7103)		
	Parent & Child						✓ (n=5395)
SDQ	**Parent**		✓ (n=7348)		✓ (n=7027)		
	Teacher	✓ (n=7574)					

Low internal consistency scores were indicated for the sub-scales of the SDQ within the ALSPAC dataset (for example, alphas ranged from 0.28 for the "peer problems" sub-scale to 0.62 for the "emotional problems" sub-scale on the parent-rated measure at 157 months), and, consequently, it was deemed that it would be unwise to make comparisons based on the indications of these sub-scales. Comparisons with the DAWBA indications were, therefore, made based on the 'Total Difficulties' score only. As the outcomes on the DAWBA were binary indicators, indicating the likely presence or absence of psychiatric illness, SDQ total difficulties scored were also classified in accordance with the recommended official cut-offs into the binary outcomes of 'Normal', and 'Abnormal' (see www.sdq.info). Specifically, 'Total Difficulties' scores of 17 or over on the parent-rated scale were

classified as ‘Abnormal’, while those of 16 or over on the teacher-scale were classified to be in this ‘Abnormal’ range. The cut-off for the ‘Abnormal’ categorisation was based on the distributions in Goodman’s (2001) large population-based UK survey from which the scale norms were also derived.

Please note that, as a screening tool for assessing emotional health and problem behaviour in children, the SDQ has been found to differentiate well between clinical and community-based samples (Goodman, 1997; Goodman & Scott, 1999; Klasen et al., 2000), with a study by Goodman, Ford, Simmons, et al. (2000) finding that these ‘abnormal’ total difficulties (based on scores at or above the 90th percentile) were predictive of a 15-fold increase in the likelihood of any independently diagnosed psychiatric disorder. The SDQ has also been shown to correlate highly with other measurement scales of child psychopathology, such as the Rutter scales (Goodman, 1997), and the Child Behaviour Checklist (Goodman & Scott, 1999; Klasen et al, 2000; Koskelainen, Sourander, & Vauras, 2001; Becker, Woerner, Hasselhorn, Banaschewski, & Rothenberger, 2004). However, these categorisations showed low concordance with the DAWBA measure in the ALSPAC dataset. Of the 4404 children with complete data on both the teacher-rated SDQ and DAWBA at 10 years, only 60 of the 248 children scored in the ‘Abnormal’ range were also identified as having a psychiatric illness by the DAWBA (24.2%). There was a much higher concordance rate on the parent-rated SDQ at 13 years (n=6172 for complete data on both SDQ and DAWBA), but still only 113 of the 280 scored in the ‘Abnormal’ range were also identified as having a psychiatric illness on the DAWBA (40.4%).

Finally, it should be noted that mean scores on this scale, based on ratings from both informants, strongly contrasted with SDQ normative means scores (see Table 2.10). The SDQ normative mean scores, or “norms”, are based on a large national survey by the Office of National Statistics of 10,438 British children and adolescents (5 – 15 years) (see Meltzer et al., 2000). When comparing the mean scores of the ALSPAC sample with the provided normative guidelines, the ALSPAC sample have both lower mean scores,

and, based on the ratings of the primary caregiver, lower standard deviation scores. Consistent with indications of the DAWBA measure, this suggests that the ALSPAC sample who responded to the ALSPAC questionnaires during the selected period of study have higher levels of mental well-being than would be expected based on population norms.

Table 2.10 SDQ mean and standard deviation scores for the ALSPAC sample and published scale norms

	Parent Questionnaire		**Teacher Questionnaire**	
	5 -10 Years	**11-15 Years**	**5 -10 Years**	**11-15 Years**
Scale Norms				
Mean (SD)	*8.6 (5.7)*	*8.2 (5.8)*	*6.7 (5.9)*	*6.3 (6.1)*
ALSPAC Scales				
Year 6 M(SD)			5.85 (6.0)	
140 Months M(SD)		6.55 (4.97)		
157 Months M(SD)		6.8 (4.99)		

2.4.5.1.2 The Short Moods and Feelings Questionnaire

The short 'Moods and Feelings' questionnaire (sMFQ) consists of a series of 13 descriptive phrases regarding how the subject has been feeling and acting in the preceding two weeks. Responses reflect whether the phrase was descriptive of the study child "Most of the time", "Sometimes", or "Not at all" during the given time period (scored on a scale from 2 to 0 respectively). The shortened version of the form was developed specifically as a quick evaluation of depressive symptomatology for epidemiological studies (Angold et al., 1995). As detailed by Angold and colleagues (1995), the initial validation study- which was based on a sample of 173 American 8 to 16 year olds comprised of both psychiatric and community paediatric controls - indicated that scoring patterns on this scale successfully discriminated clinically-referred subjects from paediatric controls. Total scale scores also discriminated DISC-diagnosed children with depressive disorder from non-depressed subjects.

The ALSPAC dataset contains self-completed sMFQ questionnaires for 7363 children at 10 years, 6715 children at 12.5 years and 6019 children at 13.5 years. Cronbach's Alpha coefficient at the three time points were 0.79, 0.84 and 0.86 respectively, indicating good internal reliability of the scale. All self-completed questionnaires were administered as part of an on-site clinical assessment. At ten years and twelve years, administration was led by a psychologist or researcher, while at thirteen the questionnaire was completed on a computer. Please note that three dummy statements were added to the questionnaire at all administration waves to balance the more negative descriptions, and make the task, overall, a more positive experience for the children.

The sMFQ was also completed by the child's primary caregiver through mailed questionnaires at 140 months/11.66 years and 157 months/13.08 years. Total scores, based on these ratings, are available for 7130 children from the 140 month administration and 6991 children at the 157 month administration. Cronbach's Alpha coefficient at the two time points were 0.85 and 0.87 respectively, indicating consistently good internal reliability of this measure across informants. Please note that an additional pro-rata scoring system was available on the 140 month questionnaire. However, as this scoring system did not follow standard guidelines for scoring the sMFQ, only the total scores based on the complete cases were used in the analyses for this research.

There has been a degree of debate over the correct procedure for using the sMFQ as an outcome measure in analyses with childhood and adolescent samples. As the sMFQ often yields a highly skewed scale, the majority of research using this scale has used a binary categorisation of the totalled scale score, which ranges from 0 to 26 (Joinson, Heron, Lewis, Croudace, & Araya, 2011). Using this scale as a binary measure also allows for easier comparison with DAWBA indications. However, there has been a lack of consensus regarding what a suitable cut-off should be. For example, a score of 8 or over was indicated to have a positive predictive value of 70% and a negative predictive value of 68% for emotional psychopathology in a

longitudinal validation study based on 1428 boys from the Pittsburgh Youth Study (Messer et al., 1995), and this cut-off was also used as the cut-off point in the 'Research with East London Adolescents: Community Health Survey' (RELACHS) study (see Stansfeld et al., 2003). In contrast, one of the original studies which investigated the psychometric properties of this scale (Angold et al., 1995), recommended a much higher cut-off point of 12. Yet, the cut-off score most frequently used with ALSPAC data has been a score of 11 (e.g. Pearson et al., 2015). The validity of this cut-off for use with ALSPAC data has received support from empirical investigations. For example, a validation study by Thapar and McGuffin (1998), based on a sample of 78 parents and 71 twins from the Cardiff Births Survey, showed that a cut-off point of 11 showed a sensitivity of 0.6 and specificity of 0.61 for ICD-10 depression, and a sensitivity of 0.75 and specificity of 0.74 for DSM-III-R depression. In order to promote consistency between empirical studies of ALSPAC data, this study also used a cut-off of 11 to categorise sMFQ scores into 'Normal' and 'Abnormal' binary categorisations.

Please note that, similar to comparisons of the SDQ and the DAWBA, there was very little consistency between "Abnormal" classifications on the sMFQ and indications of emotional disorders on the DAWBA. At 10 years, only 25 of the 338 children identified as having likely emotional psychopathology on the child-rated sMFQ were identified as having an emotional disorder on the DAWBA (7.4%; n with complete data across the two measures=6244), while at 13 years only 21 of the 456 children scoring in the 'Abnormal' range on the child-rated sMFQ were identified as having an emotional disorder on the DAWBA (4.6%; n with complete data across the two measures=5203). Concordance between the DAWBA and the parent-rated version of this scale at this age was substantially higher, albeit still quite weak overall, with 30 of the 155 children scoring in the 'Abnormal' range on the child-rated sMFQ identified as having an emotional disorder on the DAWBA (19.35%; n with complete data across the two measures=6133). Finally, it should be noted that only 36 of the 400 children identified as having likely emotional psychopathology on the age 13 child-rated measure were also identified by the parent-rated measure (8.26%; n with complete data across the two

measures=5031). Therefore, concordance across the outcome measures, even on different versions of the same scale was, overall, quite low.

A comparative outline of the administration of the sMFQ questionnaire for both parents and children versus the DAWBA assessment can be seen in Table 2.11. As can be seen, both the parent-rated sMFQ and the child-rated sMFQ were administered during the period that fell in the interim period between DAWBA assessments at 10 and 13 years, introducing possible age-related fluctuations in mental health into comparisons. However, there was a concurrent administration of the sMFQ identifiable for the DAWBA administration at both 10 and 13 years.

Table 2.11 sMFQ administration over the time period of study, in relation to the administration of the primary outcome measure

	Version	10 Yrs	11 Yrs	12 Yrs	13 Yrs	14 Yrs	15 Yrs
DAWBA	**Parent**	✓ (n=7820)			✓ (n=7103)		
	Parent & Child						✓ (n=5395)
sMFQ	**Parent**		✓ (n=7130)		✓ (n=6991)		
	Child	✓ (n=7363)		✓ (n=6715)	✓ (n=6019)		

Please note that there are no official normative mean scores available for this scale. However, analysis of two longitudinal datasets in the United States (the Great Smokey Mountains Study and the Virginia Twin Study of Adolescent Behaviour and Development) (Angold, Erkanli, Silberg, Eaves, & Costello, 2002) indicated the following age and gender corrected means on the self-completed scale: 4.2 (95% CI: 4-4.4) for 9 year olds; 3.3 (95% CI: 3.1-3.4) for 11 year olds; and 2.8 (95% CI: 2.5-3.1) for 13 years olds. In contrast, the RELACHS study, a large cross-sectional examination of child health in East London (see Stansfeld et al., 2003), indicated a much higher means of 4.96 for those in year 7 (11 years approximately) and 5.18 for those in year 9 (13 years approximately), with substantially higher mean scores found for girls (5.22 Year 7; 6.15 Year 9) than boys (4.69 Year 7; 4.13 Year 9). Self-rated scores on the sMFQ for the ALSPAC cohort ranged from a mean score of 4.04 at 10 years to 4.92 at 13 years, showing strong comparability with this representative sample of children in East London. In addition, a gender gradient also emerged in total scores for the ALSPAC

sample at 12 and 13 years, with females showing significantly higher scores (12 Years: 4.35 versus 3.57 (T: -8.36; p<0.001);13 Years: 5.71 versus 4.09 (T: -14.27; p<0.001). Please note that no gender difference was identifiable on the 10 year, child completed questionnaire. Therefore, scores on the self-rated scale show comparative patterns to the RELACHS study, suggesting that mean scores for the ALSPAC sample on this scale are comparable to those of other age-matched British cohorts.

Finally, it should be noted that one of the concerns that could be raised regarding the reliance on the sMFQ as an alternative measure of child psychological functioning is that the scale contains items measuring somatic indications of emotional psychopathology – for example "I/He/She felt so tired, I/he/she sat around and did nothing". Canning and Kelleher (1994) raised concerns about the sensitivity of such scales in the context of chronic illness, given that scores may disproportionately represent symptoms of the child's underlying health condition, such as fatigue. In fact, items measuring energy levels and concentration on the sMFQ show a lot of overlap with measures on the 'Perceptions of Fatigue' scale derived as a measure of functional impairment for the purposes of this study. Yet, it should be noted that Pinquart and Shen (2011c) found equivocal responses for somatic and non-somatic items among children with chronic illness in their meta-analysis. Therefore, a decision was made to retain this scale not only because it contains an indication of the child's emotional functioning from both the child's and parent's perspective, but also because it may provide some insight into the relative concordance of measures indicating somatic symptomatology to other psychometric measures.

2.4.5.2 Measure of active asthma symptomatology

In Delmas and colleagues (2011) study of major depressive episodes in asthma, adolescents with an asthma diagnosis, but no active symptomatology, were indistinguishable from their peers on the mental health outcome measure. Therefore, it was considered important that the role of active asthma symptomatology in the associated mental health outcomes attributed to asthma in these analyses was also explored. In the 10 year and 13 year questionnaires, in addition to indicating whether their

child had a doctor's diagnosis of asthma, mothers also indicated the frequency with which children had used the 'reliever' inhaler for their asthma in the past month. As the measure of interest was the activity of asthma symptoms, rather than the severity of these symptoms – which would require more extensive measurement of daytime and night-time asthma symptomatology and pulmonary function (see Bacharier, Strunk, Mauger, White, Lemanske Jr., & Sorkness, 2004) – all children who had used their reliever inhaler in the past month were amalgamated into one group, and the children who had not used their inhaler were amalgamated into another. At age 10, 761 children with a stated asthma diagnosis were indicated to have used their inhaler in the past month (44.82%). Please note that information about the use of reliever inhalers was not available for 214 children (12.6%) who were indicated to have a doctor's diagnosis of asthma at age 10. At age 13, a smaller proportion of the 1643 children with a stated asthma diagnosis were indicated to have used their reliever inhaler in the past month (n=604; 36.76%). Please note that information regarding inhaler usage was not available for 225 (13.69%) of the children with an asthma diagnosis at 13 years.

2.5 Statistical Analyses

The aim of building a sound, empirically strong test of the hypothesised relationship of chronic health problems to mental ill-health outcomes in childhood and adolescence has been core to the design of this study, and will again be reflected in this overview of the statistical analyses. Given the sampling issues identified in previous studies, and the identification of the potential substantial rate of attrition in the ALSPAC adolescent sample, analyses of the sample size were first conducted to ensure that the sample size was large enough to power the associative investigations that were at the core of this study. The statistical analyses section will open with an overview of these analyses and will then outline how the primary analyses were designed around these findings to fulfil the four primary study aims. The secondary analyses will then be detailed, and the section will conclude with an overview of how missing data was treated given the variations in response patterns suggested in the measurement section of this methodology chapter.

2.5.1 Sample size analyses

Sampling bias could be seen as the central methodological issue highlighted in the literature. Concerns over sample quality, and possible introduction of sampling artefacts, were highlighted not only in the meta-analyses of psychological outcomes, but also in explorations of the developmental outcomes of living with a chronic illness in childhood and adolescence. Therefore, it was one of the central aims of this study to identify a sample large enough to reliably examine the associations of chronic health problems to mental ill-health in childhood and adolescence, as well as a substantial asthma sample to use as a point of comparison. Indeed, the ALSPAC data was chosen for the analyses of this study due to the large number of active participants. Therefore, the key initial step in this study was to identify if the samples identified by the exposure measures would be large enough to sensitively detect increased rates of psychiatric illness between healthy children and those living with chronic health problems. For this reason, sample size calculations were performed to ensure that the samples were surplus to the minimal sample size requirements to detect a minimum 50%

increased rate of psychiatric illness. Although this figure was well below the increased prevalence rate seen for psychiatric disorders in the studies of asthma in the systematic review, it was also much higher than the rates indicated for children and adolescents living with diabetes mellitus type 1 (approximately 10% increased prevalence). This percentage increase was chosen after exploring actual prevalence figures of psychiatric illness in the ALSPAC, which were lower than would be expected based on population prevalence and norms. Based on these prevalence figures, a 10% increased prevalence on the baseline questionnaire would represent a rise from 5.98% prevalence to 6.58% prevalence, and would not only require an extremely large sample size for reliable detection (circa 206,183 in a sample where chronic health problems were present in 10% of the population), but such a marginal increase in prevalence might raise concerns over practical implications and the absolute level of risk posed. This is highlighted when considering prevalence rates of specific groups disorders – for example, a 10% increased prevalence of emotional disorders at baseline would reflect a rise from 2.8% to 3.08%. Therefore, a 50% minimum threshold (e.g. an increase of 5.98% to 8.97% on the baseline questionnaire) was chosen as the marker, as, within the ALSPAC, this would represent a real and unobscured risk to children with chronic illness.

Alpha levels were set at 0.05 and a power of 0.9 was selected. Please note that as analyses were conducted in the Stata © 12 software package, the correction “nocont” was used. The analyses relating to the measure of chronic illness can be found in section 2.5.1.1.1, and those relating to the comparative associative analyses, which examined the associations of asthma diagnosis to rates of psychiatric illness, can be found in section 2.5.1.1.2. Please note, that these were initial steps to ensure, in advance of the design of the primary analyses, that the sample identified by the exposure measures would allow for the reliable exploration of the rates of co-occurring psychiatric illness that is core to this study. However, issues of sample power were considered repeatedly throughout the design of the primary analyses (see section 2.5.2).

2.5.1.1.1 Analyses of the associated mental health outcomes of chronic health problems more generally

The sample size calculations were first conducted to identify if the chronic illness sample, as it was classified by the health ratings in the age 10 and age 13 questionnaire respectively, was of a sufficient size to conduct reliable comparisons to the children indicated to be "very healthy, no problems" at each cross-sectional wave. For the age 10 cross-sectional analyses, the comparative sample consisted of 4588 children. Children identified as having chronic health problems were segregated into three separate degrees of symptom severity at this wave: 1239 children were classified as "healthy, but a few minor problems"; 59 were classified as "sometimes quite ill", and 5 were classified as "Almost always unwell". In a similar fashion, the comparative sample for the age 13 cross-sectional analyses consisted of 4126 children who were classified as "very healthy, no problems". Again at this wave, the chronic illness sample was segregated into three separate degrees of severity: 1229 were classified as "healthy, but a few minor problems"; 62 were classified as "sometimes quite ill", and 12 were classified as "almost always unwell".

Given that symptom severity was of interest as a mediating factor in this study, it was hoped to retain the categorisation of the chronic illness sample into different classifications of severity for the cross-sectional analyses. However, it was very clear from the outset that the "almost always unwell" category at both waves was insubstantial, and would be too small to reliably identify variations in the rates of psychiatric illness from the comparative sample. Therefore, it was decided to test if an amalgamation of the "sometimes quite ill group" and the "almost always unwell" group would result in a sample size adequate to power the associative analyses.

The sample size calculations first aimed to identify if these groups were of adequate size to detect significant differences in the prevalence of psychiatric illness overall, before examining the ability to detect differences on the more specific indicators of emotional disorders, anxiety disorders, and behavioural disorders within these cohorts. Please note that for these analyses, the expected prevalence rates of psychiatric illness were based on

the actual frequency of such disorders in the ALSPAC at both cross-sectional waves, which were lower in prevalence than would be assumed based on population norms (see Table 2.4). The analyses (as summarised in Table 2.12) indicated that the sample size was adequate to power comparative analyses for the "quite healthy, but a few minor problems" classification to the "very healthy, no problems" comparative grouping at both cross-sectional waves. However, the size of the comparative sample and the "sometimes quite ill/almost always unwell" group was just too limited to reliably detect variations in rates of psychiatric illness between groups.

Table 2.12 Minimum sample size requirements to detect a 50% increased prevalence rate in psychiatric diagnoses among children with chronic illness on the DAWBA cross-sectionally, and the cross-sectional sample sizes in the ALSPAC

	Minimum Sample Size Required	**Sample Size in ALSPAC Dataset**
Baseline Questionnaire	***(Comparative increase from 5.98% prevalence to 8.97%)***	
Minor Health Problems versus No Health Problems (n2/n1=0.27)	Comparative: 3722 Exposed: 1005	Comparative: 4588 Exposed: 1239
Sometimes Quite Ill/Almost Always Unwell versus No Health Problems (n2/n1=0.01)	Comparative: 78101 Exposed: 782	Comparative: 4588 Exposed: 64
Age 13 Questionnaire	***(Comparative increase from 5.53% prevalence to 8.3%)***	
Minor Health Problems versus No Health Problems (n2/n1=0.3)	Comparative: 3117 Exposed: 936	Comparative: 4126 Exposed: 1229
Sometimes Quite Ill/Almost Always Unwell versus No Health Problems (n2/n1=0.02)	Comparative: 35704 Exposed: 715	Comparative: 4126 Exposed: 74

Given these indications, it seemed unlikely that these cross-sectional groupings would be of adequate size to sensitively detect comparative variations in rates of emotional disorders, anxiety disorders, and behavioural disorders, especially given that the prevalence rates of these disorders were quite low within the ALSPAC dataset. Sample size calculations confirmed that sample sizes were too limited to sensitively detect 50% increased prevalence rates of specific groups of disorders when comparing the healthy comparative sample to the different classifications of chronic illness at both cross-sectional waves (see Table 2.13). Therefore, these power size calculations raised concerns about the introduction of bias to analyses by the

retention of the “sometimes quite ill/almost always unwell” grouping, and questioned whether the cross-sectional sample size was sufficient to sensitively detect increases in more specific prevalence rates of emotional disorders, anxiety disorders, and behavioural disorders.

Table 2.13 Minimum sample size requirements to detect a 50% increased prevalence rate in emotional, anxiety, and behavioural disorders among children with chronic illness on the DAWBA cross-sectionally, and the cross-sectional sample sizes in the ALSPAC

	Any Emotional Disorder		**Any Anxiety Disorder**		**Any Behavioural Disorder**	
	Minimum Sample Size Required	**Sample Size in ALSPAC Dataset**	**Minimum Sample Size Required**	**Sample Size in ALSPAC Dataset**	**Minimum Sample Size Required**	**Sample Size in ALSPAC Dataset**
Baseline Questionnaire	***(Comparative increase from 2.8% prevalence to 4.2%)***		***(Comparative increase from 2.12% prevalence to 3.18%)***		***(Comparative increase from 3.42% prevalence to 5.13%)***	
Minor Health Problems versus No Health Problems (n2/n1=0.27)	Comparative: 8288 Exposed: 2238	Comparative: 4588 Exposed: 1239	Comparative: 11041 Exposed: 2982	Comparative: 4588 Exposed: 1239	Comparative: 6731 Exposed: 1818	Comparative: 4588 Exposed: 1239
Sometimes Quite Ill/Almost Always Unwell versus No Health Problems (n2/n1=0.01)	Comparative: 173,810 Exposed: 1739	Comparative: 4588 Exposed: 64	Comparative: 231,539 Exposed: 2316	Comparative: 4588 Exposed: 64	Comparative: 141,182 Exposed: 1412	Comparative: 4588 Exposed: 64
Age 13 Questionnaire	***(Comparative increase from 2.08% prevalence to 3.12%)***		***(Comparative increase from 1.53% prevalence to 2.3%)***		***(Comparative increase from 3.67% prevalence to 5.51%)***	
Minor Health Problems versus No Health Problems (n2/n1=0.3)	Comparative: 10,393 Exposed: 3118	Comparative: 4126 Exposed: 1229	Comparative: 14060 Exposed: 4218	Comparative: 4126 Exposed: 1229	Comparative: 5742 Exposed: 1723	Comparative: 4126 Exposed: 1229
Sometimes Quite Ill/Almost Always Unwell versus No Health Problems (n2/n1=0.02)	Comparative: 119,370 Exposed: 2388	Comparative: 4126 Exposed: 74	Comparative: 161,442 Exposed: 3229	Comparative: 4126 Exposed: 74	Comparative: 65968 Exposed: 1320	Comparative: 4126 Exposed: 74

As these power analyses suggested that the cross-sectional analyses may be biased by both the small sample size of the "sometimes quite ill/almost always quite unwell" group and the low prevalence rates on the more specific diagnostic grouping indications, it was deemed important to examine if there was a possibility of any source of analytic limitations affecting the longitudinal analyses, where the chronic illness sample would be viewed as an amalgamated group, regardless of symptom severity at any individual wave. Please note that the comparative group selected for the longitudinal analyses was a group of 2681 children who were indicated to be "very healthy, no problems" on both the 10.67 and 13.83 year child-based questionnaires. The sample size calculations again first concentrated on identifying whether the chronic illness sample and the healthy, comparative sample were of sufficient size to a detect a 50% increased prevalence of overall rates of psychiatric illness in the chronic illness sample, before looking at the ability to detect variations on the more specific indicators of emotional disorders, anxiety disorders, and behavioural disorders. These initial sample size calculations suggested that the chronic illness sample and the comparative sample were of sufficient size to sensitively detect variations in overall rates of psychiatric illness at all three DAWBA waves (see Table 2.14).

Table 2.14 Minimum sample size requirements to detect a 50% increased prevalence rate in psychiatric diagnoses among children with chronic illness on the DAWBA at each wave of administration, and the size of the longitudinal sample identified in the ALSPAC

	Minimum Sample Size Required	**Sample Size in ALSPAC Dataset**
Baseline Questionnaire	***(Comparative increase from 5.98% prevalence to 8.97%)***	
Chronic Health Problems versus No Health Problems	Comparative: 2447 Exposed: 1190	Comparative: 2681 Exposed: 1303
Age 13 Questionnaire	***(Comparative increase from 5.53% prevalence to 8.3%)***	
Chronic Health Problems versus No Health Problems	Comparative: 2653 Exposed: 1290	Comparative: 2681 Exposed: 1303
Age 15 Questionnaire	***(Comparative increase from 6.62% prevalence to 9.93%)***	
Chronic Health Problems versus No Health Problems	Comparative: 2191 Exposed: 1065	Comparative: 2681 Exposed: 1303

Given that the sample size was sufficient to detect variations in psychiatric illness at all three waves, overall, it was hoped that it would also be sufficient to detect variations in the more specific rates of emotional disorders, anxiety disorders, and behavioural disorders. However, the sample size calculations indicated that both the healthy comparative sample and the chronic illness sample were too small to sensitively detect variations in prevalence among any of the three groupings of disorders at any one wave (see Table 2.15). Therefore, while these sample sizes were sufficient to detect a minimum 50% increase in rates of psychiatric illness overall, they were not substantial enough to reliably examine variations in rates of specific types of psychiatric illness.

Table 2.15 Minimum sample size requirements to detect a 50% increased prevalence rate in emotional disorders, anxiety disorders, and behavioural disorders among children with chronic illness on the DAWBA at each wave of administration, and the size of the longitudinal sample identified in the ALSPAC

	Any Emotional Disorder		**Any Anxiety Disorder**		**Any Behavioural Disorder**	
	Minimum Sample Size Required	**Sample Size in ALSPAC Dataset**	**Minimum Sample Size Required**	**Sample Size in ALSPAC Dataset**	**Minimum Sample Size Required**	**Sample Size in ALSPAC Dataset**
Baseline Questionnaire	***(Comparative increase from 2.8% prevalence to 4.2%)***		***(Comparative increase from 2.12% prevalence to 3.18%)***		***(Comparative increase from 3.42% prevalence to 5.13%)***	
Chronic Health Problems versus No Health Problems	Comparative: 5450 Exposed: 2649	Comparative: 2681 Exposed: 1303	Comparative: 7261 Exposed: 3529	Comparative: 2681 Exposed: 1303	Comparative: 4426 Exposed: 2312	Comparative: 2681 Exposed: 1303
Age 13 Questionnaire	***(Comparative increase from 2.08% prevalence to 3.12%)***		***(Comparative increase from 1.53% prevalence to 2.3%)***		***(Comparative increase from 3.67% prevalence to 5.51%)***	
Chronic Health Problems versus No Health Problems	Comparative: 7405 Exposed: 3599	Comparative: 2681 Exposed: 1303	Comparative: 10018 Exposed: 4869	Comparative: 2681 Exposed: 1303	Comparative: 4091 Exposed: 1989	Comparative: 2681 Exposed: 1303
Age 15 Questionnaire	***(Comparative increase from 3.21% prevalence to 4.82%)***		***(Comparative increase from 1.99% prevalence to 2.99%)***		***(Comparative increase from 3.82% prevalence to 5.73%)***	
Chronic Health Problems versus No Health Problems	Comparative: 4702 Exposed: 2286	Comparative: 2681 Exposed: 1303	Comparative: 7678 Exposed: 3732	Comparative: 2681 Exposed: 1303	Comparative: 3942 Exposed: 1916	Comparative: 2681 Exposed: 1303

2.5.1.1.2 Analyses of the associated mental health outcomes of asthma diagnosis

The outcomes of asthma diagnoses were chosen as a point of comparison for the more generalised analyses in part due to the fact that this condition is so prevalent among child and adolescent groups. It was hypothesised that, as a consequence, it would be possible to identify a sufficiently large sample to avoid the introduction of sampling bias into analyses. Therefore, it was important to assess the validity of the assumption, starting with the comparative and asthma cohort identified in the cross-sectional 10.67 and 13.83 questionnaires. As in the investigations with the measure of chronic health problems, sample size calculations first examined whether the cross-sectional sample was of sufficient size to detect a comparative 50% minimum increase in rates of overall psychiatric disorders. Please note that for the cross-sectional analyses at age 10, the comparative sample was 3861 children who were indicated to be free from asthma diagnosis and were also rated as being "very healthy, no problems". Similarly, for the cross-sectional analyses at age 13, the comparative sample was 3398 children who were indicated to be free from asthma diagnosis and were also rated as being "very healthy, no problems" in the child-based questionnaire. The sample size calculations indicated that the comparative sample and the exposed asthma sample at both cross-sectional waves were of a sufficient size to sensitively detect a 50% minimum increased prevalence of psychiatric illness in the exposed samples (see Table 2.16).

Table 2.16 Minimum sample size requirements to detect a 50% increased prevalence rate in psychiatric diagnoses among children with asthma on the DAWBA cross-sectionally, and the size of the cross-sectional asthma samples identified in the ALSPAC

	Minimum Sample Size Required	**Sample Size in ALSPAC Dataset**
Baseline Questionnaire	***(Comparative increase from 5.98% prevalence to 8.97%)***	
Asthma Diagnosis versus No Health Problems (n2/n1=0.44)	Comparative: 2614 Exposed: 1151	Comparative: 3861 Exposed: 1698
Age 13 Questionnaire	***(Comparative increase from 5.53% prevalence to 8.3%)***	
Asthma Diagnosis versus No Health Problems (n2/n1=0.48)	Comparative: 2675 Exposed: 1284	Comparative: 3398 Exposed: 1643

As the cross-sectional samples were sufficient to examine variations in rates of psychiatric illness overall, it was hoped that they would also be large enough to reliably investigate variations in more specific rates of emotional, anxiety, and behavioural disorders. However, despite the samples being substantially larger than the minimum needed to examine overall prevalence rates of psychiatric illness, the power analyses indicated that the sample size was too small to sensitively detect a minimum 50% increased prevalence on the more narrowed indicators of “any emotional disorder”, “any anxiety disorder” and “any behavioural disorders” at both cross-sectional waves (see Table 2.17). Therefore, while the asthma sample and comparative sample at the cross-sectional waves were sufficient to examine overall differences in rates of psychiatric illness, examining more specific variations in rates of emotional disorders, anxiety disorders, and behavioural disorders, may open the analyses to a degree of sampling bias.

Table 2.17 Minimum sample size requirements to detect a 50% increased prevalence rate in any emotional disorder, any anxiety disorder, and any behavioural disorder among children with asthma on the DAWBA cross-sectionally, and the size of the cross-sectional asthma samples identified in the ALSPAC

	Any Emotional Disorder		**Any Anxiety Disorder**		**Any Behavioural Disorder**	
	Minimum Sample Size Required	**Sample Size in ALSPAC Dataset**	**Minimum Sample Size Required**	**Sample Size in ALSPAC Dataset**	**Minimum Sample Size Required**	**Sample Size in ALSPAC Dataset**
Baseline Questionnaire	***(Comparative increase from 2.8% prevalence to 4.2%)***		***(Comparative increase from 2.12% prevalence to 3.18%)***		***(Comparative increase from 3.42% prevalence to 5.13%)***	
Asthma Diagnosis versus No Health Problems	Comparative: 5821 Exposed: 2562	Comparative: 3861 Exposed: 1698	Comparative: 7756 Exposed: 3413	Comparative: 3861 Exposed: 1698	Comparative: 4728 Exposed: 2081	Comparative: 3861 Exposed: 1698
Age 13 Questionnaire	***(Comparative increase from 2.08% prevalence to 3.12%)***		***(Comparative increase from 1.53% prevalence to 2.3%)***		***(Comparative increase from 3.67% prevalence to 5.51%)***	
Asthma Diagnosis versus No Health Problems	Comparative: 7465 Exposed: 3584	Comparative: 3398 Exposed: 1643	Comparative: 10100 Exposed: 4848	Comparative: 3398 Exposed: 1643	Comparative: 4124 Exposed: 1980	Comparative: 3398 Exposed: 1643

Given that the longitudinal analyses were designed to be based on the sample of children identified as having an asthma diagnosis on the baseline questionnaire (n=1698), with the comparative sample being 2313 children who were indicated to be free from asthma and were also rated as "very healthy, no problems" on 10.67 and 13.83 child-based questionnaire, it was expected that, given the indications of the sample size calculations for the cross-sectional analyses, this sample size would be sufficient to sensitively detect a minimum 50% comparative increase in overall rates of psychiatric illness on the baseline questionnaire, and the two subsequent questionnaire waves. However, it was expected that the sample size would be too limited to detect variations in more specific rates of emotional, anxiety, and behavioural disorders. The sample size calculations confirmed these hypotheses. Although the sample chosen for the longitudinal analyses of the associated mental health outcomes of asthma diagnosis was of sufficient size to sensitively detect a minimum 50% increased rate of psychiatric disorders at all three waves (see Table 2.18), both the comparative and exposed samples were too small to reliably detect comparatively increased rates of emotional, anxiety, and behavioural disorders at any wave (see Table 2.19). Therefore, using more specific rates of emotional, anxiety, and behavioural disorders as the primary outcome measure may introduce a degree of sampling bias into the analyses.

Table 2.18 Minimum sample size requirements to detect a 50% increased prevalence rate in psychiatric diagnoses among children with asthma on the DAWBA at each wave of administration, and the size of the longitudinal asthma sample identified in the ALSPAC

	Minimum Sample Size Required	**Sample Size in ALSPAC Dataset**
Baseline Questionnaire	***(Comparative increase from 5.98% prevalence to 8.97%)***	
Asthma Diagnosis versus No Health Problems	Comparative: 1912 Exposed: 1296	Comparative: 2313 Exposed: 1698
Age 13 Questionnaire	***(Comparative increase from 5.53% prevalence to 8.3%)***	
Asthma Diagnosis versus No Health Problems	Comparative: 2074 Exposed: 1515	Comparative: 2313 Exposed: 1698
Age 15 Questionnaire	***(Comparative increase from 6.62% prevalence to 9.93%)***	
Asthma Diagnosis versus No Health Problems	Comparative: 1713 Exposed: 1251	Comparative: 2313 Exposed: 1698

Table 2.19 Minimum sample size requirements to detect a 50% increased prevalence rate in emotional disorders, anxiety disorders, and behavioural disorders among children with asthma on the DAWBA at each wave of administration, and the size of the longitudinal asthma sample identified in the ALSPAC

	Any Emotional Disorder		**Any Anxiety Disorder**		**Any Behavioural Disorder**	
	Minimum Sample Size Required	**Sample Size in ALSPAC Dataset**	**Minimum Sample Size Required**	**Sample Size in ALSPAC Dataset**	**Minimum Sample Size Required**	**Sample Size in ALSPAC Dataset**
Baseline Questionnaire	***(Comparative increase from 2.8% prevalence to 4.2%)***		***(Comparative increase from 2.12% prevalence to 3.18%)***		***(Comparative increase from 3.42% prevalence to 5.13%)***	
Chronic Health Problems versus No Health Problems	Comparative: 4261 Exposed: 3111	Comparative: 2313 Exposed: 1698	Comparative: 5678 Exposed: 4145	Comparative: 2313 Exposed: 1698	Comparative: 3460 Exposed: 2526	Comparative: 2313 Exposed: 1698
Age 13 Questionnaire	***(Comparative increase from 2.08% prevalence to 3.12%)***		***(Comparative increase from 1.53% prevalence to 2.3%)***		***(Comparative increase from 3.67% prevalence to 5.51%)***	
Chronic Health Problems versus No Health Problems	Comparative: 5790 Exposed: 4227	Comparative: 2313 Exposed: 1698	Comparative: 7834 Exposed: 5719	Comparative: 2313 Exposed: 1698	Comparative: 3198 Exposed: 2335	Comparative: 2313 Exposed: 1698
Age 15 Questionnaire	***(Comparative increase from 3.21% prevalence to 4.82%)***		***(Comparative increase from 1.99% prevalence to 2.99%)***		***(Comparative increase from 3.82% prevalence to 5.73%)***	
Chronic Health Problems versus No Health Problems	Comparative: 3676 Exposed: 2684	Comparative: 2313 Exposed: 1698	Comparative: 6004 Exposed: 4383	Comparative: 2313 Exposed: 1698	Comparative: 082 Exposed: 2250	Comparative: 2313 Exposed: 1698

2.5.2 Primary analyses

The primary steps in this research project were outlined thus:

V. To examine the cross-sectional and longitudinal associations of chronic health problems to rates of mental ill-health across childhood and adolescence, using data from a large, representative sample, high quality measures of mental health, and controlling for the possible influence of confounding factors.

VI. To identify mediators in the associations identified. Specifically, to explore the role of symptom severity and functional impairment in this association, and to also look at the mediating role of a number of variables indicative of impairments to normative trajectories of development.

VII. To build a model of the association of chronic health problems to mental ill-health outcomes across the childhood and adolescent period, and test this for goodness-of-fit to the data.

VIII. To examine the applicability of these findings to specific chronic conditions by comparing the indications of the cross-sectional and longitudinal associations to a similar set of analyses using asthma diagnosis as the independent variable. The mediation model will also be tested for goodness-of-fit to the mental health outcomes associated with asthma diagnosis.

The specific analyses underlining each of these steps will be outlined in the four sections that follow.

2.5.2.1 To examine the cross-sectional and longitudinal associations of chronic health problems to rates of mental ill-health across childhood and adolescence, using data from a large, representative sample, high quality measures of mental health, and controlling for the possible influence of confounding variables

The first aim of this study was to build upon the limitations identified in previous empirical investigations in order to get a more balanced view of the associated mental health outcomes of chronic health problems. However, although the ALSPAC was selected due to its large, representative nature, and a sensitive measure of mental ill-health was identified in the form of the DAWBA, the sample size calculations indicated that the sample size may pose limitations to the scope of the analyses to some degree, and issues were also identified regarding missing data on the measures of the confounding variables. This section will detail how the initial step of this research was built around these identified limitations starting first with the investigation of the cross-sectional associations of chronic health problems, followed by the longitudinal investigations.

2.5.2.1.1 Cross-sectional analyses

As stated in sample size calculations, the initial hope was that the segregation of the chronic illness sample into different classifications of severity at each of the cross-sectional waves could be retained in order to provide some insight into the comparative risk associated with more minor severity versus more severe symptomatology. As one of the big research questions to emerge from the systematic review regarded whether severity of symptomatology fully mediated the association between chronic health problems and psychiatric disorder, it was deemed important, even at this initial stage of the analyses, to investigate if any association to mental health outcomes identified was applicable across the chronic illness cohort. Yet, the sample size calculations indicated that analyses comparing the “sometimes quite ill/almost always unwell” grouping to children rated as “very healthy, no problems” would be open to a severe risk of bias, given the limited size of this grouping. Yet, a decision was made to retain this grouping, even though it was acknowledged that any comparative risk identified for this group would only be able to be taken as an indicative of a risk that may exist, rather than

a reliable insight into the cross-sectional psychiatric associations of more severe types of chronic illness. It was decided that it would be more limiting to the scope of this study to fail to examine whether a cross-sectional association of chronic illness to poor mental health could be identified for children recently experiencing both mild symptomatology and more severe symptomatology of their condition.

The sample size calculations also indicated that the cross-sectional sample sizes were too small to sensitively detect differences in more specific rates of emotional disorders, anxiety disorders, and behavioural disorders, as opposed to comparative differences in rates of psychiatric illness overall. Therefore, rates of overall psychiatric illness were chosen as the primary outcome measure. However, it was decided that variations in rates of specific disorders would be explored as part of these associative analyses to provide additional insight, with the acknowledgement that these explorations were likely underpowered. Therefore, the various steps of the cross-sectional analyses were as follows. Please note that all analyses were conducted using Stata 12© software.

2.5.2.1.1.1 Primary associative models

For both cross-sectional waves, a crude logistic regression model was first run to identify the estimated odds of “any psychiatric illness” in the “quite healthy, but a few minor problems group” and the “sometimes quite ill/almost always unwell” amalgamated group when compared to the “very healthy, no problems” group. A subsequent binary logistic model was calculated to adjust for the likely moderating role of the gender of the study child. Adjustments for the preselected confounding variables, “history of parental mental illness” and “socio-economic status” were made in a third and separate model. Please note that the measure socio-economic status in the 10 year cross-sectional analysis was housing tenure, while the measure of socio-economic status in the 13 year cross-sectional analysis was low household income. A summary of these models and the size of the samples with complete data are presented in Table 2.20.

Table 2.20 Overview of the binomial logistic regression models exploring the cross-sectional associations of chronic illness to rates of psychiatric illness

	Age 10 Cross-Sectional Analyses	Age 13 Cross-Sectional Analyses
Model 1: Crude Logistic Model (Outcome: Any Psychiatric Illness)	"Healthy no problems" n: 4577 "Healthy, minor problems" n: 1236 "Sometime quite ill/Almost always unwell" n: 44	"Healthy no problems" n: 4126 "Healthy, minor problems" n: 1229 "Sometime quite ill/Almost always unwell" n: 74
Model 2: Logistic Model Adjusted for Gender	"Healthy no problems" n: 4577 "Healthy, minor problems" n: 1236 "Sometime quite ill/Almost always unwell" n: 44	"Healthy no problems" n: 4126 "Healthy, minor problems" n: 1229 "Sometime quite ill/Almost always unwell" n: 74
Model 3: Logistic Model Adjusted for Gender, History of Parental Mental Illness and Socio-Economic Status	"Healthy no problems" n: 1580 "Healthy, minor problems" n: 439 "Sometime quite ill/Almost always unwell" n: 20	"Healthy no problems" n: 1165 "Healthy, minor problems" n: 324 "Sometime quite ill/Almost always unwell" n: 22

As may be noticed, small amounts of missing data on the DAWBA measure at 10 reduced the cross-sectional sample size in the crude and gender-adjusted model. However, the sample size for the comparison of the "quite healthy, but a few minor problems" group to the "healthy, no problems" group was still above the minimum sample size indicated as being necessary in the sample size calculations (i.e. n exposed sample: 1005; n comparative sample: 3722). However, estimates from the third model at both cross-sectional waves, were likely biased due to the substantial amounts of missing data on the measures of the confounding covariates. Steps were taken to investigate the possible imprecision of the resulting estimates due to missing data (see section 2.5.4.1). In addition, likelihood ratio testing was used to investigate if the adjustment for gender, and consequently for the confounding variables, significantly improved model fit over the crude associate model.

2.5.2.1.1.2 Tests for interaction

Likelihood ratio testing was also used to test if adding an interaction term between chronic illness and each of the three covariates in turn significantly improved the associative model fit, which would suggest an interaction between chronic health problems and the covariate in the associated rates of psychiatric illness. This was in order to fully explore the role of these covariates in the association of chronic health problems to mental ill-health.

However, it was expected that given the substantial amount of missing data on the confounding variables of “socio-economic status” and “history of parental mental analysis”, analyses of the interactive relationship of these variables with chronic illness to mental health outcomes may be open to some degree of bias.

2.5.2.1.1. 3 Explorations of comparative rates of emotional, anxiety, and behavioural disorders

A subsequent set of three logistic regression models were run to identify odds on the underlying rates of “Any Emotional Disorder”, “Any Anxiety Disorder” or “Any Behavioural Disorder”, in order to identify if the association seemed to be characterised by an increase in one particular type of psychiatric disorder. However, given the results of the sample size calculations, these were more exploratory analyses, and considered to be overviews of possible trends, rather than precise indications of disorder characteristics. Due to the limitations in analytic power, it was decided not to adjust for “socio-economic status” and “history of parental mental illness” in these models unless these variables were indicated to have a significant confounding effect on the overall association between chronic illness and psychiatric illness (as indicated by a significant result in likelihood ratio testing).

2.5.2.1.2 Longitudinal analyses

Based on the sample size calculations, it was decided, consistent with the cross-sectional analyses, to use overall rates of psychiatric illness as the primary outcome. Sample size calculations indicated that the comparative and the exposed sample were too limited to sensitively detect comparative increases in rates of emotional, anxiety and behavioural disorders. However, as in the cross-sectional analyses, differences in rates of these underlying disorders were explored to provide additional insight, with the acknowledgement that these explorations were likely open to sample bias. Therefore, the steps of the longitudinal analyses were as follows. Please note that all analyses were conducted using Stata 12© software.

2.5.2.1.2.1 Primary associative models

Initially three associative models were calculated to examine the association between chronic health problems and psychiatric illness at each of the three questionnaire waves - a crude binary logistic regression model, subsequently followed by a model adjusting for the possible moderating role of gender, and a final model adjusted for the hypothesised confounding variables: “history of parental mental illness” and “socio-economic status” (as indicated by household income). Please see Table 2.21 for a summary of the models and the related sample sizes. Please note that missing data on the DAWBA substantially reduced the sample size in the analyses of both the age 10 and the age 15 administration waves. However, although the sample size at the age 10 measurement wave was still above the minimum required to sensitively detect a 50% minimum increased rate of mental illness (i.e. n exposed sample: 1190; n comparative sample: 2447), the sample size of both the chronic illness sample and the comparative sample at the age 15 measurement fell below the minimum sample size requirements to detect variations at this wave (i.e. n exposed sample: 2190; n comparative sample: 1065). Missing data on the measures of the confounding variables, “socio-economic status” and “history of parental mental illness” also significantly impacted on sample size, and it was likely that adjustments for these variables introduced bias into the estimates at all waves. Again, steps were taken to address the issues caused by this missing data (see section 2.5.4.1). Likelihood ratio testing was again also used to test the relative contribution of adjustments for these covariates to the associative model fit.

Table 2.21 Overview of the initial longitudinal binomial logistic regression models exploring the association of chronic illness to rates of psychiatric illness at each DAWBA wave

	Age 10 Measurement	**Age 13 Measurement**	**Age 15 Measurement**
Model 1: Crude Logistic Model (Outcome: Any Psychiatric Illness)	Healthy Comparative Sample n: 2678 Chronically Ill Sample n: 1300	Healthy Comparative Sample n: 2681 Chronically Ill Sample n: 1303	Healthy Comparative Sample n: 1753 Chronically Ill Sample n: 890
Model 2: Logistic Model Adjusted for Gender	Healthy Comparative Sample n: 2678 Chronically Ill Sample n: 1300	Healthy Comparative Sample n: 2681 Chronically Ill Sample n: 1303	Healthy Comparative Sample n: 1753 Chronically Ill Sample n: 890
Model 3: Logistic Model Adjusted for Gender, History of Parental Mental Illness and Socio-Economic Status	Healthy Comparative Sample n: 779 Chronically Ill Sample n: 345	Healthy Comparative Sample n: 781 Chronically Ill Sample n: 346	Healthy Comparative Sample n: 522 Chronically Ill Sample n: 243

The longitudinal analyses were designed to give a thorough insight into the associated mental ill-health outcomes of living with chronic illness in late childhood and entry into adolescence. This included examining the continuing predictive power of chronic illness in the onset of psychiatric illness over this phase of development. Therefore, a further logistic model was calculated for the age 13 analyses, adjusting for gender and the presence of a psychiatric illness at age 10. Please note that, due to the indications of the power analyses, it was decided to adjust only for “socio-economic status” and “history of parental mental illness” if these variables were shown to be confounding variables, as hypothesised. This contingency planning was also applicable to two further logistic models which used the age 15 DAWBA measurement as the outcome measure, the first of which controlled for the presence of a mental illness at age 13 and the second for the presence of a mental illness at either age 10 or 13. Please find a summary of these models in Table 3.22.

Table 2.22 Overview of the binomial logistic regression models examining the association of chronic illness to rates of psychiatric illness, when adjusting for mental health at preceding waves

	Age 13 Measurement	Age 15 Measurement
Model 4: Logistic Model Adjusted for Gender and DAWBA Indications at the Previous Measurement Wave	Healthy Comparative Sample n: 2678 Chronically Ill Sample n: 1300	Healthy Comparative Sample n: 1754 Chronically Ill Sample n: 890
Model 5: Logistic Model Adjusted for Gender and DAWBA Indications at the Two Previous Measurement Waves		Healthy Comparative Sample n: 1753 Chronically Ill Sample n: 888

2.5.2.1.2.2 Tests for interaction

As in the cross-sectional analyses, likelihood ratio testing was also used to test if adding an interaction term between chronic illness and each of the three covariates in turn would significantly improve the associative model fit, which would suggest an interaction between chronic health problems and the covariate being tested in the associated rates of psychiatric illness. However, given that missing data on the confounding covariates of "socio-economic status" and "history of parental mental illness" was similarly identified as a limiting factor in the longitudinal analyses, it was expected that analyses of the interactive relationship of these variables with chronic illness to mental ill-health may be open to some degree of bias.

2.5.2.1.1.3 Explorations of comparative rates of emotional, anxiety, and behavioural disorders

Please note that, similar to the cross-sectional analyses, the underlying prevalence of emotional disorders, anxiety disorders, and behavioural disorders were explored at each wave, in order to identify if the associations identified seemed to be characterised by an increase in one particular type of psychiatric disorder. Again, due to the limited sample size, these analyses were considered to be exploratory only in nature. To explore longitudinal associations, for the age 13 and age 15 measurements these models were first run with adjustments made for gender, and were then re-run with adjustments made for the presence of psychiatric disorders at previous waves. Adjustments were only made for the effect of "socio-economic status" and "parental history of mental illness" if these variables were supported as

having a significant confounding effect on the overall association between chronic illness and rates of psychiatric illness.

2.5.2.2 To identify mediators in the associations identified. Specifically, to explore the role of symptom severity and functional impairment in this association, and to also look at the mediating role of a number of variables indicative of impairments to normative trajectories of development

This research aimed to test the proposal that chronic illness is associated with poor mental health outcomes in childhood and adolescence due to the continuing stress that such health problems present to normative patterns of development. However, it was not possible to isolate strong and consistent pathways from chronic illness to factors indicative of impairment to normative developmental trajectories in previous empirical investigations. Furthermore, it was suggested that symptom severity and functional impairment may play a key mediating role in the associations identified. Therefore, it was considered a vital initial step in these mediation analyses to establish what factors mediate the associated mental health outcomes of chronic illness in the ALSPAC dataset.

The initial mediation analyses followed the guidelines of mediation theorists, such as Baron and Kenny (1986) and James and Brett (1984), who suggested a four step approach to establishing mediation. This is the most commonly cited approach to establishing mediation within the literature (see Fritz & MacKinnon, 2007), and it allows for the identification of both full and partial mediation patterns. The steps are as follows:

I. Show that the causal variable is correlated with the outcome (i.e. use psychiatric illness as the criterion variable in a regression equation and chronic illness as the predictor)
II. Show that the causal variable is correlated with the mediator (i.e. use the hypothesised mediator as the criterion variable in the regression equation and chronic illness as the predictor)
III. Show that the mediator affects the outcome variable (i.e. use psychiatric illness as the criterion variable in a regression equation and chronic illness and the mediating variable as the predictors)
IV. To establish complete mediation in the relationship, the effect of the causal variable on the outcome should be zero when controlling for the mediator. If both the causal variable and mediating variable

remain significantly associated with the outcome, this suggests partial mediation

Therefore, these four steps of analysis were conducted with all the measures of functional impairments and family and social outcomes in order to identify if these variables played a full or partially mediating role in the association of chronic health problems to psychiatric illness at all three measurement waves (for an outline of these analyses and the related sample sizes please see Table 2.23). Please note that, given that most variables were measured repeatedly throughout the time period of analysis, analyses focused on concurrent, or close to concurrent, mediating associations in mental health outcomes.

Please note that based on the low prevalence rates of specific groups of psychiatric illness, and given the power considerations for mediation analyses, it was decided to retain “any psychiatric illness” as the primary outcome. It is difficult to calculate minimum sample size requirements for mediation analyses (see Fritz & MacKinnon, 2007), and debate surrounds the test for power of the indirect effect (Loeys, Moerkerke, & Vansteelandt, 2015). However, Fritz and MacKinnon (2007) indicated that mediation analyses in this form are generally underpowered, given that a sample size of at least 20,886 is necessary to achieve 0.8 power in an analysis of full mediation, where there is a small effect size of the causal variable to the mediation variable, and the mediation variable to the outcome variable. Comparing the sample sizes for this study with simulations conducted as part of Fritz and MacKinnon’s (2007) power investigation, it was suggested that although these analyses may be powered to detect full mediation and partial mediation when strong relationships are indicated between variables, the sample size may be too limited to detect significant associations between variables of a low effect size. Therefore, the sample size was much too limited to identify mediating effects for specific groupings of disorders. Although this was limiting to this research to a degree, as aetiological factors differ in various ways between different types of psychopathology, it has been argued that all types of psychopathology are underlined by a neural

susceptibility to stress (Hayden & Marsh, 2014), such as that hypothesised to be incurred throughout development as a consequence of chronic illness.

Please note that all analyses were conducted in Stata 12© software.

Table 2.23 Overview of mediation pathways that were tested

Mediation Pathway to Test	Sample with Complete Data
Chronic Illness – Conflict in the Parents Relationship at 9 – Any Psychiatric Illness at 10	Healthy Comparative Sample n: 956 Chronically Ill Sample n: 456
Chronic Illness – Conflict in the Parents Relationship at 12 – Any Psychiatric Illness at 13	Healthy Comparative Sample n: 850 Chronically Ill Sample n: 438
Chronic Illness – Parental Monitoring at 12 – Any Psychiatric Illness at 13	Healthy Comparative Sample n: 1630 Chronically Ill Sample n: 797
Chronic Illness – Parental Monitoring at 13 – Any Psychiatric Illness at 13	Healthy Comparative Sample n: 1953 Chronically Ill Sample n: 958
Chronic Illness – Parental Monitoring at 15 – Any Psychiatric Illness at 15	Healthy Comparative Sample n: 1490 Chronically Ill Sample n: 757
Chronic Illness – Child Disclosure at 12 – Any Psychiatric Illness at 13	Healthy Comparative Sample n: 1626 Chronically Ill Sample n: 797
Chronic Illness – Child Disclosure at 13 – Any Psychiatric Illness at 13	Healthy Comparative Sample n: 1953 Chronically Ill Sample n: 960
Chronic Illness – Child Disclosure at 15 – Any Psychiatric Illness at 15	Healthy Comparative Sample n: 1429 Chronically Ill Sample n: 715
Chronic Illness – Parental Solicitation at 12 – Any Psychiatric Illness at 13	Healthy Comparative Sample n: 1625 Chronically Ill Sample n: 794
Chronic Illness – Parental Solicitation at 13 – Any Psychiatric Illness at 13	Healthy Comparative Sample n: 1955 Chronically Ill Sample n: 960
Chronic Illness – Parental Solicitation at 15 – Any Psychiatric Illness at 15	Healthy Comparative Sample n: 1553 Chronically Ill Sample n: 785
Chronic Illness – Parental Control at 12 – Any Psychiatric Illness at 13	Healthy Comparative Sample n: 1631 Chronically Ill Sample n: 795
Chronic Illness – Parental Control at 13 – Any Psychiatric Illness at 13	Healthy Comparative Sample n: 1950 Chronically Ill Sample n: 965
Chronic Illness – Parental Control at 15 – Any Psychiatric Illness at 15	Healthy Comparative Sample n: 1369 Chronically Ill Sample n: 692
Chronic Illness – Satisfaction with Peer Relationships at 10 – Any Psychiatric Illness at 10	Healthy Comparative Sample n: 2210 Chronically Ill Sample n: 1082
Chronic Illness – Satisfaction with Peer Relationships at 12 – Any Psychiatric Illness at 13	Healthy Comparative Sample n: 2144 Chronically Ill Sample n: 1051
Chronic Illness – Peer Victimisation at 10 – Any Psychiatric Illness at 10	Healthy Comparative Sample n: 2180 Chronically Ill Sample n: 1060
Chronic Illness – Peer Victimisation at 12 – Any Psychiatric Illness at 13	Healthy Comparative Sample n: 2109 Chronically Ill Sample n: 1031
Chronic Illness – High Levels of Health-Related School Absenteeism at 10 – Any Psychiatric Illness at 10	Healthy Comparative Sample n: 2640 Chronically Ill Sample n: 1294
Chronic Illness – High Levels of Health-Related School Absenteeism at 13 – Any Psychiatric Illness at 13	Healthy Comparative Sample n: 2644 Chronically Ill Sample n: 1271

Chronic Illness – Perceptions of Fatigue – Any Psychiatric Illness at 13	Healthy Comparative Sample n: 2256 Chronically Ill Sample n: 1093

2.5.2.3 To build a model of the associations of chronic health problems to mental ill-health outcomes across the childhood and adolescent period

The introduction in the opening chapter highlighted that the onset of psychopathology is best understood as a dynamic process, that is not a direct result of the impact a single risk factor, or set of risk factors, but as a developmental trajectory, with the unique interplay of risk and protective factors giving rise to mental illness across different developmental milestones (e.g. Holmbeck, 2002). Therefore, it is unlikely that a simple identification of a number of mediating factors in the association of chronic problems to psychiatric illness at a given time wave could give a full sense of the interactive and complex nature of the relationship of chronic health problems to mental ill-health outcomes. For this reason, many researchers have been using different forms of structural equation models to create models of the association of risk factors to mental health outcomes (e.g. Mroczek & Spiro, 2003). These models allow for the assessment of the fit of a theoretical model to patterns in collected data, by comparing the covariance structure of the theoretical model to observed relationships in the data (see Muthén & Muthén, 2002). Therefore, in order to get a full sense of the mediation pathways in the association of chronic health problems to mental ill-health longitudinally across the childhood and adolescent period, it was an aim of this study from the very outset to create a theoretical model, based on the outcomes of the associative models and mediation analyses, and to test this for goodness of fit to the data.

The theoretical design of this model was largely built around research in the area of developmental cascades (e.g. Masten & Cicchetti, 2010). In one such study, Masten and colleagues (2005) depicted externalising problems in childhood as the primary predictive factor in a negative cascade of events across development, with externalising symptomatology feeding into adaptive functioning, and poorer adaptive functioning consequently escalating the presentation of externalising, as well as internalising, symptoms. Considering the impact of chronic illness in such a framework

would allow for an overview of the interaction of the mediating factors in the associated mental health outcomes of children and adolescents living with chronic illness over time. The cascade model view of the feedback of psychiatric illness into later child and adolescent developmental outcomes is also beneficial to understanding health outcomes in the context of the chronic illness. Much of the previous research has been based on cross-sectional data, and in the systematic review, it was questioned whether the strong association between functional impairments and mental health was due to a mediating role of illness severity, or due to the impact of psychiatric illness on child functioning. Therefore, designing a model using the cascade framework would allow for the establishment of a timeframe in the relationship of variables to mental ill-health outcomes.

One initial limitation to the design of this complex model was the lack of thorough measurement of mediating variables in the period between the 13 year and 15 year measurement. The ALSPAC team shortened their questionnaires in the adolescent years in order to prevent further sample attrition (see Boyd et al., 2012), and, as a consequence, the only measures administered in the intervening years between the 13 year and 15 year measurement were Stattin and Kerr's (2000) scales of parental monitoring. The cascade model framework argues that psychopathology can only be understood from a broad perspective through the interaction of many mediating variables (e.g. Masten & Cicchetti, 2010). Therefore, including the 15 year DAWBA administration in the cascade model, without measurement of developmental factors in the intervening period between measurements, would breach the primary hypothesis of the underlying theory. The lack of measurement at the age 15 wave also prevented the creation of a true cascades model, as such a model would require at least three time points in order to reliably establish the direction of effects (see Masten & Cicchetti, 2010). Therefore, the path model focused on the relationship of chronic illness to mental health outcomes at 10 and 13 years only. Rates of psychiatric illness overall were also retained as the primary outcome measure to promote consistency within the analyses of this research.

In the model, chronic illness was depicted as the primary causative factor, predicting all mediating factors in the model. A pathway was also placed from the mediating factors to rates of psychiatric illness within time. If the mediation analyses indicated no variable fully mediated the association between chronic health problems and mental ill-health at 10 and 13 years, a pathway was also placed directly from chronic illness to psychiatric illness at both time waves. A pathway was placed from psychiatric illness at 10 years to psychiatric illness at 13 years, and pathways were also placed between psychiatric illness at 10 years and the mediating factors in psychiatric illness outcomes at 13 years. Pathways were also placed between different administrations of the same measure. Decisions about further pathways were made based on a correlation matrix which was calculated to examine relationships between the variables over the time period of analysis. Please note that as both the measure of chronic illness and psychiatric illness was underlined by a binary measure, as indeed were many of the measures of the mediating variables, correlations were based on the non-parametric Spearman's Rho.

2.5.2.3.1 Assessing Model Fit

This pathways model was fitted to the ALSPAC data used MPlus© software, as this software uses a weighted least squares means and variance (WLSMV) estimator to adjust for the non-normal distribution of categorical data. Most modelling software is dependent on maximum likelihood estimation, and the use of this estimator in categorical data would result in misspecifications in the standard errors, and chi-square tests. As the global goodness of fit test, based on chi square, is a test of the *exact* fit of the covariance structure of the hypothesised model to that of the sample, it is often significant when models are tested with larger samples. Therefore, two additional and commonly used tests of fit were also examined – namely the Root Mean Square of Approximation (RMSEA) and the Comparative Fit Index (CFI). RMSEA values of 0.05 indicate a close fit; while values greater than 0.1 indicate a poor fit. CFI values fall between 0 and 1, with values closer to 1 indicating a good fit. Please note that Hu and Bentler (1999) suggest that a stricter cut-off value of 0.95 for CFI and 0.06 for RMSEA for

models with non-normally distributed data, such as the binary indicators that will be used in this study.

2.5.2.3.2 Sensitivity analyses

The decision to omit psychiatric illness outcomes at 15 years caused a further limitation to the understanding of the relationship of chronic illness to mental health outcomes. As outlined in the description of the exposure measure of chronic illness (section 2.4.2.1), this measure was based on reports of illness on both the age 10 and age 13 questionnaire. This is important as this study was originally envisioned as a prospective longitudinal study, where a sample of children living with chronic illness was identified at baseline, and patterns in the co-occurrence of psychiatric illness in the period from 10 to 15 years were examined. However, it could be questioned whether this model, or the longitudinal analyses of the age 10 and age 13 questionnaire in general, were truly longitudinal in nature, given that the chronic illness measure was based on two child-based questionnaires administered simultaneous to the measure of mental health. To ensure that these analyses were not just a reflection of the concurrent association of physical health to mental health, a sensitivity paths model was run with the ratings of health at 10 years and 13 years used as independent predictors of mediators and mental health outcomes within time. Please note this model included all children with health ratings at either cross-sectional wave, not just children with chronic illness symptomatology. The results of this model were compared to the primary model in order to assess if this model was likely to reflect the relationship of chronic health problems to mental health outcomes over time, rather than just concurrent associations, which would be a contrast to the model hypothesised.

2.5.2.3.3 Power considerations

There is no consensus regarding the appropriate sample size for testing covariance-based pathways models (Wang & Wang, 2012), although it is generally agreed that structural equation models can be meaningfully tested even in very limited samples (e.g. Hoyle & Kenny, 1999; Marsh & Hau, 1999). The usual rule of thumb is 100 to 150 participants minimum (e.g. Tinsley & Tinsley, 1987; Tabachnick & Fidell, 2001), a position that has been

supported by simulation studies (e.g. Muthén and Muthén, 2002). However, it should be noted that these studies assumed normally distributed indicator variables and no missing data. A simulation study by Wolf, Harrington, Clark and Miller (2013) suggested that minimum sample size requirements for pathways models ranged from 30 to 460 participants, with larger sample sizes needed when there are correlational relationships in the data and larger amounts of missing data among the variables. Please note that the size of the ALSPAC sample far exceeds the maximum sample size calculated indicated in this simulation study.

2.5.2.4 To examine the applicability of these findings to specific chronic conditions by comparing the indications of the cross-sectional and longitudinal associations to a similar set of analyses using asthma diagnosis as the independent variable. The mediation model will also be tested for goodness-of-fit to the mental health outcomes associated with asthma diagnosis.

Asthma diagnoses were chosen as a point of comparison for all analyses using the general measure of chronic health problems. This was to ensure that any patterns observed were applicable to specific chronic illness conditions. Therefore, the cross-sectional and longitudinal analyses were again carried out, using asthma diagnosis as the causal variable. The role of the variables indicating disruptions to development, and the measures of symptom severity and functional impairments, in mediating the association between asthma and mental health outcomes were also explored. Finally, the fit of the theoretical model, developed in the context of chronic health problems more generally, and confirmed as a good fit to the data, was assessed for fit to the patterns of psychiatric illness co-occurrence seen for asthma diagnosis. A more detailed outline of each of these four set of analyses can be found in section 2.5.2.4.1 to 2.5.2.4.2.

2.5.2.4.1 Cross-Sectional analyses

2.5.2.4.1.1 Primary associative models

For each cross-sectional wave, a crude model was first run to examine the associated rates of psychiatric illness in children who were indicated as having been diagnosed with asthma, relative to children who were rated as being “Very healthy, no problems” in the same questionnaire. A subsequent model adjusted for the moderating effect of gender, while a third model adjusted for gender, and the pre-selected confounding variables: “history of parental mental illness” and “socio-economic status” (as indicated by housing tenure in the age 10 analyses and low household income in the age 13 analyses) (see Table 2.24 for a summary of them models). As in the analyses with the chronic illness exposure measure, small amounts of missing cases on the DAWBA measure at 10 years had minimal impact, as the exposed sample and the comparative sample were still surplus to the

minimum requirement (i.e. n exposed sample: 1151; n comparative sample: 2614). However, adjustments for the confounding covariates drastically reduced the sample size at both waves, and introduced bias into the resulting estimates. Therefore, as in the analyses using the generalised measure of chronic illness, methods to address the limitations introduced by the missing data on the measures of the confounding covariates were explored (see section 2.5.4.1). Likelihood ratio tests were also used to identify if adjustments for gender, and subsequently for the confounding covariates, substantially improved the model fit over and above the crude associative logistic regression model.

Table 2.24 Overview of the binomial logistic regression models exploring the cross-sectional associations of asthma to rates of psychiatric illness

	Age 10 Cross-Sectional Analyses	**Age 13 Cross-Sectional Analyses**
Model 1: Crude Logistic Model (Outcome: Any Psychiatric Illness)	"Healthy no problems" n: 3852 "Asthma Diagnosis" n: 1694	"Healthy no problems" n: 3398 "Asthma Diagnosis" n: 1643
Model 2: Logistic Model Adjusted for Gender	"Healthy no problems" n: 3852 "Asthma Diagnosis" n: 1694	"Healthy no problems" n: 3398 "Asthma Diagnosis" n: 1643
Model 3: Logistic Model Adjusted for Gender, History of Parental Mental Illness and Socio-Economic Status	"Healthy no problems" n: 1349 "Asthma Diagnosis" n: 544	"Healthy no problems" n: 993 "Asthma Diagnosis" n: 416

2.5.2.4.1.2 Tests for interaction

Likelihood ratio testing was also used to test if adding an interaction term between asthma and each of the three interaction terms in turn significantly improved the associative model fit, suggesting an interaction between asthma and the covariate being tested in the associated mental health outcomes. This was in order to fully explore the role of these covariates in the association of asthma to psychiatric illness. However, it was expected, as a consequence of the substantial amount of missing data on the confounding variables of "socio-economic status" and "history of parental mental analysis", these analyses may be open to some degree of bias.

2.5.2.4.1.2 Explorations of comparative rates of emotional, anxiety, and behavioural disorders

A subsequent set of three logistic regression models were run to examine associated rates of "Any Emotional Disorder", "Any Anxiety Disorder" or "Any

Behavioural Disorder" among children with asthma, in order to identify if there was a characteristic increase in one particular type of psychiatric disorder. However, these were more exploratory analyses, and considered to be overviews of possible trends, rather than precise indications of disorder characteristics. Due to the limitations in analytic power, it was decided not to adjust for "socio-economic status" and "history of parental mental illness" unless these were indicated to have a significant confounding effect on the overall association between chronic illness and psychiatric illness (as indicated by a significant result of the likelihood ratio testing).

2.5.2.4.2 Longitudinal analyses

2.5.2.4.2.1 Primary associative models

An initial set of three binary logistic associative models were run for the age 10, age 13 and age 15 measurements in the longitudinal sample – one a crude model, the second adjusting for the moderating role of gender, and the third adjusting for gender and the confounding covariates of "History of Parental Mental Illness" and "Socio-Economic Status". Please note that household income was used as the indicator of "Socio-Economic Status" at all three measurement waves. Possible limitations regarding the resulting sample size having controlled for the hypothesised confounding variables should be noted (please see the model overview in Table 2.25). Consistent with the generalised measures of chronic health problems, missing cases on the baseline measure had minimal impact on the analyses at this wave, due to the comparative and exposed sample remaining surplus to the minimum sample size indicated to be necessary (i.e. n exposed cohort: 1296; n comparative cohort: 1912). However, a substantial proportion of the asthma sample had missing data on the age 13 DAWBA questionnaire, meaning that the sample size fell below the minimum sample size indicated to be necessary for the asthma cohort in order to detect variations at this wave (i.e. n exposed sample: 1515). Moreover, missing cases on the age 15 DAWBA measure resulted in the size of the comparative and exposed sample falling below the minimum requirements for this wave (i.e. n exposed cohort: 1251; n comparative cohort: 1713). Furthermore, adjustments for the confounding covariates drastically reduced the minimum sample size indicated as

necessary to sensitively detect a minimum 50% increased prevalence of psychiatric illness at all waves, introducing the risk of bias to the analyses. Therefore, methods for addressing this missing data were explored (see section 2.5.4). Likelihood ratio testing was also used to examine if adjustments for gender, and subsequently for the confounding covariates, substantially improved model fit over the crude logistic model.

Table 2.25 Overview of the initial binomial logistic regression models exploring the association of asthma to rates of psychiatric illness at each DAWBA wave

	Age 10 Measurement	Age 13 Measurement	Age 15 Measurement
Model 1: Crude Logistic Model (Outcome: Any Psychiatric Illness)	"Healthy no problems" n: 2313 "Asthma Diagnosis" n: 1694	"Healthy no problems" n: 2313 "Asthma Diagnosis" n: 1342	"Healthy no problems" n: 1506 "Asthma Diagnosis" n: 999
Model 2: Logistic Model Adjusted for Gender	"Healthy no problems" n: 2313 "Asthma Diagnosis" n: 1694	"Healthy no problems" n: 2313 "Asthma Diagnosis" n: 1342	"Healthy no problems" n: 1506 "Asthma Diagnosis" n: 999
Model 3: Logistic Model Adjusted for Gender, History of Parental Mental Illness and Socio-Economic Status	"Healthy no problems" n: 678 "Asthma Diagnosis" n: 442	"Healthy no problems" n: 679 "Asthma Diagnosis" n: 351	"Healthy no problems" n: 452 "Asthma Diagnosis" n: 276

In order to explore the longitudinal associations of asthma to psychiatric illness rates, a logistic model was then calculated examining the association between asthma diagnosis and rates of psychiatric illness on the age 13 DAWBA administration, after adjusting for gender and the presence of a psychiatric illness at age 10. Two further gender-adjusted models using the age 15 DAWBA administration as the outcome measure were calculated, the first of which controlled for the presence of a mental illness at age 13 and the second for the presence of a mental illness at either age 10 or 13. Please find a summary of these models in Table 2.26. Please note that it was pre-determined that adjustments in these models for the variables of "socio-economic status" and "history of parental mental illness" would be made only if these variables were indicated to play a confounding role in the association between asthma diagnosis and overall rates of psychiatric illness, based on the likelihood ratio testing.

Table 2.26 Overview of the binomial logistic regression models examining the association of chronic illness to rates of psychiatric illness, when adjusting for mental health at preceding waves

	Age 13 Measurement	Age 15 Measurement
Model 4: Logistic Model Adjusted for Gender and DAWBA Indications at the Previous Measurement Wave	"Healthy no problems" n: 2312 "Asthma Diagnosis" n: 1339	"Healthy no problems" n: 1506 "Asthma Diagnosis" n: 902
Model 5: Logistic Model Adjusted for Gender and DAWBA Indications at the Two Previous Measurement Waves		"Healthy no problems" n: 1506 "Asthma Diagnosis" n: 900

2.5.2.4.2.2 Tests for interaction

As in the cross-sectional analyses, likelihood ratio testing was also used to test if adding an interaction term between asthma and each of the three covariates in turn significantly improved the associative model fit, suggesting an interaction between asthma and the covariate being tested in the associated mental health outcomes at any given wave. However, given the substantial amount of missing data identified on the confounding covariates of "socio-economic status" and "history of parental mental illness", it was expected that these analyses may be open to some degree of bias.

2.5.2.1.1.3 Explorations of comparative rates of emotional, anxiety, and behavioural disorders

Please note that, consistent with the analyses of the generalised measure of chronic health problems, the underlying prevalence of emotional disorders, anxiety disorders, and behavioural disorders were explored at each wave, in order to identify if the associations identified seemed to be characterised by an increase in one particular type of psychiatric disorder. Again, due to the limited sample size, these analyses were considered exploratory in nature. To explore longitudinal associations for the age 13 and age 15 measurements, these models were first run with adjustments made for gender, and were then re-run with adjustments made for the presence of psychiatric disorders at previous waves. Adjustments were made for the effect of "socio-economic status" and "history of parental mental illness" only if these variables were supported as having a significant confounding effect on the overall association between chronic illness and rates of psychiatric illness.

2.5.2.4.3 Mediation analyses

Using Baron and Kenny's (1986) four step method to establishing mediation, all possible mediating variables identified in the ALSPAC dataset, were explored as mediating factors in the association of asthma to rates of psychiatric illness. A summary of the complete set of mediation analyses conducted can be found in Table 2.27. Please note that, based on Fritz & MacKinnon's (2007) simulation study, the sample size was adequate to identify moderate to large effect sizes, but comparisons suggested the cohort was too limited to identify small effect sizes.

Table 2.27 List of mediation pathways that were tested in the association of asthma diagnosis to rates of psychiatric illness

Mediation Pathway to Test	Sample with Complete Data
Asthma – Conflict in the Parents Relationship at 9 – Any Psychiatric Illness at 10	Healthy Comparative Sample n: 826 Asthma Sample n: 601
Asthma – Conflict in the Parents Relationship at 12 – Any Psychiatric Illness at 13	Healthy Comparative Sample n: 734 Asthma Sample n: 554
Asthma – Parental Monitoring at 12 – Any Psychiatric Illness at 13	Healthy Comparative Sample n: 1399 Asthma Sample n: 933
Asthma – Parental Monitoring at 13 – Any Psychiatric Illness at 13	Healthy Comparative Sample n: 1682 Asthma Sample n: 1066
Asthma – Parental Monitoring at 15 – Any Psychiatric Illness at 15	Healthy Comparative Sample n: 1267 Asthma Sample n: 844
Asthma – Child Disclosure at 12 – Any Psychiatric Illness at 13	Healthy Comparative Sample n: 1394 Asthma Sample n: 936
Asthma – Child Disclosure at 13 – Any Psychiatric Illness at 13	Healthy Comparative Sample n: 1684 Asthma Sample n: 1062
Asthma – Child Disclosure at 15 – Any Psychiatric Illness at 15	Healthy Comparative Sample n: 1215 Asthma Sample n: 789
Asthma – Parental Solicitation at 12 – Any Psychiatric Illness at 13	Healthy Comparative Sample n: 1392 Asthma Sample n: 935
Asthma – Parental Solicitation at 13 – Any Psychiatric Illness at 13	Healthy Comparative Sample n: 1683 Asthma Sample n: 1072
Asthma – Parental Solicitation at 15 – Any Psychiatric Illness at 15	Healthy Comparative Sample n: 1323 Asthma Sample n: 871
Asthma – Parental Control at 12 – Any Psychiatric Illness at 13	Healthy Comparative Sample n: 1401 Asthma Sample n: 931
Asthma – Parental Control at 13 – Any Psychiatric Illness at 13	Healthy Comparative Sample n: 1678 Asthma Sample n: 1074
Asthma – Parental Control at 15 – Any Psychiatric Illness at 15	Healthy Comparative Sample n: 1170 Asthma Sample n: 760
Asthma – Satisfaction with Peer Relationships at 10 – Any Psychiatric Illness at 10	Healthy Comparative Sample n: 1910 Asthma Sample n: 1347
Asthma – Satisfaction with Peer Relationships at 12 – Any Psychiatric Illness at 13	Healthy Comparative Sample n: 1842 Asthma Sample n: 1230
Asthma – Peer Victimisation at 10 – Any Psychiatric Illness at 10	Healthy Comparative Sample n: 1882 Asthma Sample n: 1334
Asthma – Peer Victimisation at 12 – Any Psychiatric Illness at 13	Healthy Comparative Sample n: 1818 Asthma Sample n: 1201
Asthma – High Levels of Health-Related School Absenteeism at 10 – Any Psychiatric Illness at 10	Healthy Comparative Sample n: 2277 Asthma Sample n: 1679
Asthma – High Levels of Health-Related School Absenteeism at 13 – Any Psychiatric Illness at 13	Healthy Comparative Sample n: 2282 Asthma Sample n: 1315

Asthma – Perceptions of Fatigue – Any Psychiatric Illness at 13	Healthy Comparative Sample n: 1945 Asthma Sample n: 1197

2.5.2.4.4 Assessing model fit

The path model, which was fitted to the patterns of co-occurring psychiatric illness observed when using the generalised measure of chronic illness, was also tested using baseline asthma diagnosis as the primary causative factor. To test the adequacy of this model in explaining the pattern of co-occurrence of psychiatric illness demonstrated in children living with asthma diagnoses over this age range, it was pivotal that the chosen fit indices were within the acceptable ranges – i.e. that CFI values were above 0.95 and RMSEA values were below 0.06. The fit of this model to the ALSPAC data was also assessed using MPlus© software, with the weighted least squares means and variance (WLSMV) estimator used to correct for the non-normally distributed data.

2.5.3 Secondary analyses

Two sets of secondary analyses provided insight into remaining questions arising from the study design and the literature review. Please note that the findings of Chen and colleagues (2014b), concerning the association between behavioural comorbidities in asthma and the onset of subsequent emotional symptomatology, could be seen as requiring a unique line of inquiry. However, as the longitudinal analyses controlled for the effects of pre-established psychiatric illness on subsequent mental health outcomes, it was determined that these elements of the primary analyses already allowed for adequate exploration of the replicability of this finding within the ALSPAC data. Please note that the secondary analyses were planned with the aim of ensuring that all primary analyses reflect valid and reliable reflections of patterns in the ALSPAC data.

2.5.3.1 Comparisons of the indications of the primary outcome measure with those of the alternative outcome measures

The literature review suggested that a range of psychometric measures may be required to assess the functioning of children with chronic illness, as indications may be biased due to on-going somatic symptomatology and parental perceptions. The primary outcome measure was selected due to its ability to sensitively detect psychiatric comorbidities in the context of somatic symptomatology, and the input of clinician expertise. However, it was deemed important to examine the consistency of these indications with alternative measures of the child's mental health as well as to explore the child's mental health from a range of perspectives. Please note that these analyses will focus on the indications of these alternative outcome measures longitudinally. However, indications of the available alternative outcome measures at the 10 and 13 year cross-sectional wave are compared to those of the primary outcome measure in Appendix V.

The analyses examined the associated outcomes for children with chronic illness and asthma diagnosis on three alternative measures longitudinally over the period of study. Please note that these measures were:

1. The parent-rated 'Strengths and Difficulties Questionnaire' (SDQ) [Measured at 11 and 13 years]

2. The parent-rated ‘short Moods and Feelings Questionnaire’ (sMFQ) [Measured at 11 and 13 Years]
3. The child-rated ‘short Moods and Feelings Questionnaire’ (sMFQ) [Measured at 10, 12 and 13 Years]

Please note that, consistent with the primary analyses, these longitudinal analyses controlled for the presence of likely psychopathology at previous waves as indicated by the outcome measure under examination. These models were run subsequent to a set of three models which explored the association between the exposure measure and the alternative outcome measure under analysis at each time wave, inclusive of the crude association, the association when controlling for the moderating effect of gender of the study child, and the association when controlling for the hypothesised confounding effects of “socio-economic status” and “history of parental mental illness”. To get a full sense of the relationship of these covariates to the associated outcomes on these measures, likelihood ratio testing was used to explore if adjustment for these covariates substantially improved model fit, and to identify interactions between each of the covariates with chronic health problems. However, it was expected that the sensitivity of these analyses would be affected by the high amount of missing data on the measures of the confounding covariates.

2.5.3.2 Concurrent asthma symptomatology and co-occurring psychiatric illness

In the systematic review, the studies which looked at psychiatric illness associations in the context of asthma used quite strict eligibility criteria for asthma diagnoses, which was inclusive of active patterns of symptomatology. This is significant as the analyses of Delmas and colleagues (2007) suggested that adolescents who had been diagnosed with asthma, but were not experiencing active symptomatology at the time of measurement, were indistinguishable from their healthy peers on the outcome measure. However, this study only looked specifically at associations with measures of major depressive episodes. Therefore, it was important to examine if any mental ill-health outcomes identified for asthma diagnosis in the primary analyses were applicable across children in the

ALSPAC living with an asthma diagnosis, or whether they were reflective of an acute risk associated with on-going patterns of asthma symptomatology.

The gender-adjusted cross-sectional association between asthma diagnosis and mental health outcomes on the DAWBA on the 10 and 13 year questionnaire were again explored in these secondary analyses, and compared to the estimates calculated after adjustments were made for the child's use of reliever medication for asthma in the past month. Please note, due to issues of power, it was pre-determined that adjustments would only be made for the confounding covariates of "socio-economic status" and "history of parental mental illness" if these variables were indicated to improve the associative model fit in the primary analyses. The gender-adjusted cross-sectional association with rates of emotional disorders were also explored before and after adjusting for the child's use of reliever medication for asthma in the past month. However, it was acknowledged that these analyses may be limited by a lack of analytic power.

2.5.4 Addressing issues related to missing data

2.5.4.1 Cross-sectional and longitudinal associative analyses

The central aim of this study was to provide a more balanced insight into the associated mental health of children and adolescents living with chronic health problems, and a vital element of this aim was to control for the influence of possible confounding variables. Socio-economic status and history of parental mental illness were identified as two possible confounding variables in the association of chronic health problems to mental ill-health outcomes, given that socio-economic deprivation and poor parental mental health are associated both with the incidence of childhood and adolescent chronic illness, and are consistently identified as aetiological factors in youth-onset psychopathology. However, there were substantial difficulties in finding strong measures of these variables within the ALSPAC dataset that had been completed by a large proportion of the sample, and this, in particular, extended to the measures of socio-economic position. This had significant implications for the analyses in this research. As described in the outline of the primary analyses, when adjustments for these variables were introduced into the associative models, the sample size was reduced to such a degree that both the exposed and comparative sample sizes fell below the minimum threshold indicated in the sample size calculations (see Table 2.28 for a summary of the prevalence of missing data across the cross-sectional and longitudinal analyses). Not only did this have significant implications for the sensitivity of the resulting estimates, but it could also raise concerns about the ability of these analyses to accurately discriminate any confounding role these variables may play in the association of interest.

The significant amount of missing case data identified on the DAWBA measure at 15 years overall, and at 13 years for children with an asthma diagnosis at baseline, raised similar concerns about the possible impact on the sensitivity of resulting estimates. There was such a high proportion of missing cases on these measures that the sample size in the crude logistic regression model fell below the minimum threshold requirements to sensitively detect a 50% increased rate of psychiatric illness. Therefore,

these estimates were already at risk of some degree of bias even before adjusting the confounding covariates.

This study aimed to build upon the limitations of previous investigations by providing a more methodologically balanced insight into the associated mental health outcomes of chronic health problems. However, the high amounts of missing data on these variables, which were central to the cross-sectional and longitudinal associative analyses, could jeopardise this core aim. Therefore, it was clear that there had to be some exploration into how this missing data may have affected the precision of the resulting estimates. For this purpose, it was decided to use the statistical technique of multiple imputation.

Table 2.28 Summary of the missing data across variables used in the cross-sectional and longitudinal associative analyses

	Variables with missing data in the analyses of the associated outcomes of chronic health problems	**Variables with missing data in the analyses of the associated outcomes of asthma diagnosis**
Cross-Sectional Analyses Age 10	*DAWBA Measure*: 14 / 5891 (0.24%) *Parental History of Parental Mental Illness*: 1020 / 5891 (17.31%) *Socio-Economic Status (Housing Tenure)*: 3515 / 5891 (59.67%)	*DAWBA Measure*: 13 / 5559 (0.23%) *Parental History of Parental Mental Illness*: 1005 / 5559 (18.08%) *Socio-Economic Status (Housing Tenure)*: 3326 / 5559 (59.83%)
Cross-Sectional Analyses Age 13	*Parental History of Parental Mental Illness*: 956 / 5429 (17.61%) *Socio-Economic Status (Low Household Income)*: 3662 / 5429 (67.45%)	*Parental History of Parental Mental Illness*: 907 / 5041 (17.99%) *Socio-Economic Status (Low Household Income)*: 3375 / 5041 (66.95%)
Longitudinal Analyses	*DAWBA Measure 10 Years*: 6 / 3984 (0.15%) *DAWBA Measure 15 Years*: 1341 / 3984 (33.66%) *Parental History of Parental Mental Illness*: 637 / 3984 (15.99%) *Socio-Economic Status (Low Household Income)*: 2691 / 3984 (67.5%)	*DAWBA Measure 10 Years*: 5 / 4011 (0.12%) *DAWBA Measure 13 Years*: 356 / 4011 (8.88%) *DAWBA Measure 15 Years*: 1506 / 4011 (37.55%) *Parental History of Parental Mental Illness*: 693 / 4011 (17.28%) *Socio-Economic Status (Low Household Income)*: 2689 / 4011 (67.04%)

Multiple imputation is the statistical practice recommended by the ALSPAC study team to account for missing data when undertaking associative analyses (e.g. Boyd et al., 2012), and has been frequently used in previous empirical investigations using the ALSPAC data (e.g. Bowes, Joinson,

Wolke, & Lewis, 2015; Kidger, Heron, Lewis, Evans, & Gunnell, 2012). Multiple imputation involves the creation of a number of datasets in which missing values are replaced by imputed values (see Carpenter & Kenward, 2012). These imputed values are sampled from a posterior predictive distribution which has been estimated from the patterns in the partially observed data (see Carpenter & Kenward, 2012). The imputation strategy for this study was strongly guided by the steps of Spratt, Carpenter, Sterne, Carlin, Heron, Henderson and Tilling (2010), who focused on imputation techniques for the ALSPAC dataset. This study created imputed datasets based on chained equations. When using chained equations, each imputation cycle produces an imputed value for each variable with missing data based on the predictive distribution derived from a regression of all remaining variables in the equation. At the end of each ten cycles, 1 imputed dataset is created. Please note that this technique results in the creation of imputed values for all variables with missing data in the chain, regardless of whether these variables are the variables of interest in the subsequent analyses.

Spratt and colleagues (2010) recommended the use of careful preliminary analyses to identify the variables to be included in these chained equations. Given that the primary assumption of multiple imputation is that the data is missing at random, given the variables included in the chained equation (see Carpenter & Kenward, 2012), preliminary analyses were first conducted to identify variables associated with 'missingness' in the associative model variables, regardless of whether these variables were to be included in the associative models. Please note that in addition to explorations of the relationship of the covariates, the exposure measure, and the primary outcome measure to missing data in the model, the predictive role of the variables isolated as potential mediating variables in the association between chronic health problems and poor mental health outcomes were also explored. The predictive value of a derived adversity index, based on responses from the primary caregiver in three separate developmental periods (pregnancy, 0-2 years, 2-4 years), was also explored, as this was one of the primary scales used in the ALSPAC imputation conducted by

Spratt and colleagues (2010). Please note that, as the samples used in the cross-sectional and longitudinal analyses differed slightly in kind – for example, different comparative samples were used in the analyses with the chronic health measure, and different cross-sectional samples were identified with the asthma exposure measure – these explorations were conducted for six individual samples (i.e. the two cross-sectional samples and the longitudinal sample for both exposure measures used in this study). Once variables associated with missing data across the samples were identified, meaning that the 'Missing Not At Random' assumption of multiple imputation was not breached, these analyses were re-run, using the variables examined as predictors of 'missingness' as predictors of values in the variables with missing data instead. Spratt and colleagues (2010) study found that the inclusion of strong predictor variables in the chained equation may be more important in producing valid imputed datasets than including variables which predict "missingness".

A full overview of the outcomes of these guiding analyses can be found in Appendix VI. In brief, the totalled adversity scale scores had very little association with the variables of interest, either in terms of the prediction of "missingness", or the prediction of the variable values. Some individual items on these scales showed significant associations with either "missingness" or the value of certain variables, although no consistent pattern of association could be identified across the samples. Surprisingly, although these items have been used in previous imputation models using ALSPAC datasets because of the high amounts of complete data on these variables (e.g. Spratt et al. 2010), there were substantial amounts of missing data on these scales for the six samples studied in these analyses. This would suggest that many respondents from the samples selected for this research were recruited during latter attempts to bolster the ALSPAC sample. The items of 'low educational attainment' (pertaining to either the mother or the father) and 'early parenthood' from the adversity scale were retained in the imputation model as general markers of adversity for consistency with previous imputation strategies in the ALSPAC.

The variables which showed the strongest and most consistent associations with both patterns of missing data, and the values of variables with missing data, across the samples were the binary indications of health-related absenteeism at 10 and 13 years, the binary indications of victimisation at 10 and 13 years, and the four scales of parental monitoring at 10, 13 and 15 years. Moreover, the variables included in the associative models, such as health ratings, asthma diagnosis, chronic illness status, and DAWBA outcomes, were also associated in a statistically significant fashion with the missing data and values in the confounding variables.

All imputation analyses were conducted in Stata© 12 software. Attempts were first made to impute datasets for each of the studies based on the variables to be used in the logistic models, the binary indications of health-related absenteeism, peer victimisation, low educational attainment and early parenthood, and ratings on the four parental monitoring scales at the three administration periods. However, given that the multiple imputation was dependent on chained equations, the sample size with complete data on all measures was too limited to create the imputed datasets. As the scales of parental monitoring were highly correlated across the three measurement periods, it was decided to retain scores from the wave at which most complete responses were collected. Therefore, totalled scale scores on the age 13 measure of 'parental monitoring' were included in the chained equations as a proxy indication of scores across the three administration waves.

A summary of the variables used in the chained equation for each of the six samples is summarised in Table 2.29, alongside details of the number of datasets which were imputed. As there is no official consensus on how many datasets should be created for imputation analyses, this study followed Bodner's (2008) general rule of thumb of imputing as many datasets as the percentage of missing data. As the highest amounts of missing data across the six samples were indicated for the measures of "socio-economic status" (both housing tenure and household income –see Table 2.28), the number of datasets imputed was based on the percentage of data missing on these variables. However, due to processing limitations, this percentage was

rounded down to the nearest whole number for the age 10 cross-sectional analyses and longitudinal analyses.

Table 2.29 Summary of variables included in each imputation chain and the number of datasets imputed

	Variables with missing data in the analyses of the associated outcomes of health problems	**Variables with missing data in the analyses of the associated outcomes of asthma diagnosis**
Cross-Sectional Analyses Age 10	*Variables in Chain:* Severity of chronic health problem at 10 Health ratings at 13 Gender of study child Parental history of mental illness DAWBA Indications at 10, 13 and 15 Years Binary indications of health-related absenteeism at 10 and 13 years Binary indications of peer victimisation at 10 and 12.5 years Housing Tenure 10 Years Low Household Income 11 Years Parental Monitoring 13 Years Child Disclosure 13 Years Parental Solicitations 13 Years Parental Control 13 Years Early Parenthood Low Educational Attainment *Number of Imputed Datasets:* 59	*Variables in Chain:* Asthma Diagnosis at 10 Gender of study child Parental history of mental illness DAWBA Indications at 10, 13 and 15 Years Binary indications of health-related absenteeism at 10 and 13 years Binary indications of peer victimisation at 10 and 12.5 years Housing Tenure 10 Years Low Household Income 11 Years Parental Monitoring 13 Years Child Disclosure 13 Years Parental Solicitations 13 Years Parental Control 13 Years Early Parenthood Low Educational Attainment *Number of Imputed Datasets:* 59
Cross-Sectional Analyses Age 13	*Variables in Chain:* Health ratings at 10 (Binary Coding) Health ratings at 13 Gender of study child Parental history of mental illness DAWBA Indications at 10, 13 and 15 Years Binary indications of health-related absenteeism at 10 and 13 years Binary indications of peer victimisation at 10 and 12.5 years Low Household Income 11 Years Parental Monitoring 13 Years Child Disclosure 13 Years Parental Solicitations 13 Years Parental Control 13 Years Early Parenthood Low Educational Attainment *Number of Imputed Datasets:* 67	*Variables in Chain:* Asthma Diagnosis at 13 Gender of study child Parental history of mental illness DAWBA Indications at 10, 13 and 15 Years Binary indications of health-related absenteeism at 10 and 13 years Binary indications of peer victimisation at 10 and 12.5 years Housing Tenure 10 Years Low Household Income 11 Years Parental Monitoring 13 Years Child Disclosure 13 Years Parental Solicitations 13 Years Parental Control 13 Years Early Parenthood Low Educational Attainment *Number of Imputed Datasets:* 67

Longitudinal Analyses	*Variables in Chain:* Longitudinal measure of chronic health problems Gender of study child Parental history of mental illness DAWBA Indications at 10, 13 and 15 Years Binary indications of health-related absenteeism at 10 and 13 years Binary indications of peer victimisation at 10 and 12.5 years Low Household Income 11 Years Parental Monitoring 13 Years Child Disclosure 13 Years Parental Solicitations 13 Years Parental Control 13 Years Early Parenthood Low Educational Attainment *Number of Imputed Datasets:* 67	*Variables in Chain:* Longitudinal measure of asthma diagnosis Gender of study child Parental history of mental illness DAWBA Indications at 10, 13 and 15 Years Binary indications of health-related absenteeism at 10 and 13 years Binary indications of peer victimisation at 10 and 12.5 years Low Household Income 11 Years Parental Monitoring 13 Years Child Disclosure 13 Years Parental Solicitations 13 Years Parental Control 13 Years Early Parenthood Low Educational Attainment *Number of Imputed Datasets:* 67

Follow-up explorations of the resulting imputed datasets provided confidence that the imputation strategy was a success. Monte Carlo error estimates were of acceptable value for variables with missing data in the imputed associative models. Graphs of the iterative sequences also indicated successful convergence of the ICE algorithm (full details of these errors estimates and copies of these iterative sequence graphs can be viewed in Appendix VII). Therefore, it was hoped that the resulting estimates from these imputed datasets should provide a relatively unbiased insight into how the missing data may have obscured associations with the age 15 DAWBA measurement, and the possible confounding effects of the variables of "socio-economic status" and "history of parental mental illness". Consequently, analyses relating to the imputed datasets will be placed in a section entitled "sensitivity analyses" which will follow-on from the main associative models in the cross-sectional and longitudinal analyses.

It should be noted that one of the additional concerns raised about the significant amounts of missing data on the measures of "socio-economic status" and "history of parental mental illness" regarded the impact this may have on the ability to detect interactions between these variables and chronic health problems in mental health. However, it was not feasible within the

constraints of this study to examine the possible obscuring of interaction effects using multiple imputation strategies. Interaction relationships must be specifically imputed in the chained equation, and there must be a strong rationale for believing that an interactive relationship will be found (see Carpenter & Kenward, 2012). As there was no strong evidence of interactions between any of the covariates and chronic health problems in the literature review, it was decided that there was not a strong enough rationale to impute interaction terms.

2.5.4.2 Mediation analyses

There were varying degrees of missing data across the variables isolated as potential mediators in the association between chronic health problems and mental ill-health outcomes. However, based on the simulations of Fritz and MacKinnon (2007), it was clear that even though analyses with imputed datasets may provide more precise estimates of the associations identified, it would not address the significant limitation affecting these mediation analyses: the ability to detect associative relationships of a small effect size. This could only be addressed by identifying larger sample sizes. Therefore, for the mediation analyses, the substantial amount of exploration required to perform imputation would not be offset by the benefits to this research in terms of insight into the role of these variables in the association between chronic health problems and mental ill-health outcomes.

2.5.4.3 Path models

The path models were fitted using MPlus© software. This software includes an imputation package based on Bayesian mathematics to improve the precision of the estimates of predictive pathways between variables in the models. Although the use of this imputation software is often considered to be a standard procedure when using MPlus© (see Wang & Wang, 2012), it was not used in the calculation of the path models designed for the purposes of this study. The reasons for this decision were numerous, and based on both the study aims, and the remits of this imputation technique. Although, as Wang and Wang (2012) describe, imputation in MPlus© is often run as standard practice in analyses using this software package, the creators of the package argue that preliminary checks need to be conducted to ensure that

statistical assumptions are not being breached, inclusive of assumptions regarding the patterns of 'missingness' within the variables (Muthén & Muthén, 2010). As the path models in this study were envisioned to include a broad range of variables, preliminary checks would be onerous, and not balanced with the benefits to the study. It should be kept in mind that sample sizes for the models using both the chronic illness and the asthma exposure measure were well in excess of the minimum sample size indicated in simulation studies (Wolf et al., 2013). Therefore, imputation techniques would not be necessary to provide power to the assessment of model fit. It is possible that imputation may provide more precise estimates of the relationships between variables in the model. However, providing specific estimates of relationships between individual variables in the model was not the primary aim in the calculation of these models, but rather to get an overview of the relationship of all variables in the association of chronic illness to mental ill-health outcomes over the period of study. As previous empirical research has highlighted that missing data is unlikely to change the nature of associations when conducting associative analyses (see Wolke et al., 2009), it would, therefore, provide limited benefit to impute missing case data. In conclusion, for the purposes of this study, using imputation techniques in the calculation of the path models would have been cumbersome, and would not have been balanced with the relative advantages to insight gained by the use of such techniques.

2.6 Conclusion to the Methodology Chapter

It is hoped that this chapter conveyed how much consideration was put into the design of the research, in order to limit the introduction of methodological bias into the analyses. Sample size and the provision of analytic power was identified throughout as a priority, and the primary outcome measure was selected due to its discriminatory ability in the context of chronic illness symptomatology. Moreover, all indications were tested against alternative outcome measures, and examined for general applicability against the analyses of asthma diagnosis. Moreover, the study was designed around methods to address the missing data on the confounding covariates, which was identified as a source of possible risk to the reliability and sensitivity of analyses.

However, there were some limitations to this methodology that were beyond the remit of this research to control. The low prevalence rates of psychiatric illness within the ALSPAC limited the scope of the analyses, given that it was not possible to use rates of specific categories of psychiatric illness as the primary outcome. Moreover, although the measures of health-related impairment had adequate face validity, they were not formalised measures of this construct. The lack of thorough measurement of developmental variables between the age 13 and age 15 administrations of the DAWBA also substantially limited the scope of the path model as it was originally envisioned. However, overall, it is strongly argued that this research provides a substantial improvement on previous investigations in the area, given its longitudinal methodology, and balanced consideration of the nature of the association of chronic health problems to mental ill-health outcomes in a large and representative sample. Moreover, the breadth of measures still allows for a thorough investigation of the association of chronic health problems to mental health outcomes in the early adolescent years, inclusive of what factors may mediate this association. The substantial prevalence of asthma in the ALSPAC dataset also allows for confidence in the reliability and insight provided by comparative analyses. Therefore, it is believed that the methodology of this study has a greater degree of identifiable strengths relative to any methodological limitations.

CHAPTER 3

Results

3.1 Chapter Overview

The results chapter presents the findings from the primary analyses and secondary analyses, which were outlined in the methodology chapter. These results will be as presented as follows.

Relating to the primary analyses (Section 3.2) -

3.2.1 Cross-sectional associations of chronic health problems to prevalence rates of psychiatric illness

This section of the results will be divided into two sub-sections, one focusing on the analyses of the age 10 child-based questionnaire (3.2.1.1), and the other on the analyses of the age 13 child-based questionnaire (3.2.1.2). Please note that each sub-section will contain the following elements:

I. Descriptive overview of the breakdown of all variables by chronic illness status
II. An overview of the estimates from the primary associative models, and the results of likelihood ratio testing of models
III. Results of tests for interactions
IV. Explorations of comparative rates of emotional, anxiety, and behavioural disorders
V. Findings of the sensitivity analyses, which were conducted with the imputed datasets

A summary of the findings regarding the cross-sectional associations of mental ill-health and chronic illness will be provided at the conclusion of this section.

3.2.2 Longitudinal associations of chronic health problems to prevalence rates of psychiatric illness

The results of these analyses will be divided up as follows:

I. Descriptive overview of the breakdown of all variables by chronic illness status
II. An overview of the estimates from the primary associative models regarding the association of chronic health problems to rates of psychiatric illness as measured at 10, 13 and 15 years, and the results of likelihood ratio testing of models

III. Longitudinal associations of chronic health problems to rates of psychiatric illness at 13 and 15 years
IV. Results of tests for interaction
V. Explorations of comparative rates of emotional, anxiety, and behavioural disorders at 10, 13, 15 years, and longitudinal associations of chronic health problems to prevalence rates
VI. Findings of the sensitivity analyses, which were conducted with the imputed datasets

A summary of the findings regarding the associated longitudinal mental health outcomes of chronic illness will be provided at the conclusion of this section.

3.2.3 Mediation analyses

The outcomes of the four steps of the mediation analyses will be presented in an overview table (Table 3.19) for clarity. A short paragraph will summarise the main findings of these analyses.

3.2.4 Creation of the path model

This section will outline the process of designing and fitting the path model, a theoretical model outlining the mechanisms of the association of chronic health problems to mental health outcomes at 10 and 13 years. This outline will be divided into to the following sections:

I. Initial design of the path model
II. Subsequent design of the path model following correlation analyses
III. Assessment of goodness-of-fit to the ALSPAC data
IV. Sensitivity analyses

A summary of the findings will be presented at the conclusion of the section.

3.2.5 Comparative analyses of the associated mental health outcomes of asthma diagnosis

This section will contain the analyses of the associated mental health outcomes of asthma diagnosis, which will be used as a point of comparison for the analyses using the generalised measure of chronic health problems. These analyses will be broken into the following sub-sections:

I. Cross-sectional associations of asthma diagnosis to prevalence rates of psychiatric illness
II. Longitudinal associations of asthma diagnosis to prevalence rates of psychiatric illness
III. Mediation analyses
IV. Goodness-of-fit of the path model to the mental health outcomes associated with asthma

Each sub-section will contain a summary comparison of findings against those using the generalised measure of chronic health problems.

The secondary analyses (section 3.3) will be outlined as thus -

3.3.1 Indications of the alternative outcome measures

This overview of the indications of the associative analyses using the alternative outcome measures – namely the the parent-rated Strengths and Difficulties Questionnaire' (SDQ) (measured at 11 and 13 years approximately); the parent-rated 'short Moods and Feelings Questionnaire' (sMFQ) (measured at 11 and 13 years approximately); and the child-rated 'short Moods and Feelings Questionnaire' (sMFQ) (measured at 10, 12 and 13 years approximately) - will be divided into three sub-sections, each relating to the analyses of one of the measures:

I. The parent-rated 'Strengths and Difficulties Questionnaire' (SDQ) (measured at 11 and 13 years approximately)
II. The parent-rated 'short Moods and Feelings Questionnaire' (sMFQ) (measured at 11 and 13 years approximately)
III. The child-rated 'short Moods and Feelings Questionnaire' (sMFQ) (measured at 10, 12 and 13 years approximately)

The section will conclude with a summary table overviewing the findings of these analyses with those using the primary outcome measure.

3.3.2 The role of active asthma symptoms in the association of asthma diagnosis to prevalence rates of psychiatric illness

Section 3.3.2 will present the findings from the age 10 and age 13 cross-sectional models examining the associated mental health outcomes of

asthma diagnosis before and after controlling for the child's use of a reliever inhaler in the past twelve months.

Please note that as all the findings will be overviewed and discussed in depth in the chapter that follows (i.e. Chapter 4 – Discussion), there will be no conclusion section to this results chapter.

3.2 Primary Analyses

3.2.1 Cross-sectional associations of chronic health problems to prevalence rates of psychiatric illness

3.2.1.1 The age 10 child-based questionnaire

3.2.1.1.1 Descriptive analyses

Table 3.1 outlines the breakdown of all variables used in the associative models in the age 10 cross-sectional sample by chronic illness status, as well as examining prevalence rates of emotional, anxiety, and behavioural disorders. There was a slightly higher prevalence of females experiencing chronic health problems, especially in the "sometimes quite ill/almost quite unwell" group. In contrast, males were slightly overrepresented in the healthy comparative sample. There was also a slightly higher prevalence of children who had a parent with a history of mental illness in the "quite healthy, but minor problems" group ($p<0.05$). Significantly higher prevalence rates of psychiatric illness were identified in children living with chronic health problems, inclusive of underlying prevalence rates of emotional, anxiety, and behavioural disorders. Moreover, it should be noted rates of psychiatric illness were consistently higher in prevalence among children rated as "sometimes quite ill" or "always quite unwell" when compared to children rated as "quite healthy, but a few minor problems". No statistically significant differences were detected between children rated as "very healthy, no problems" and chronically ill children on the measure of socio-economic status at this cross-sectional wave (i.e. 'housing tenure').

Table 3.1 Breakdown of all measures used in the age 10 cross-sectional binomial logistic regression models by chronic illness status, and comparative statistics

	Very Healthy, No Problems (n=4588)	**Children with Chronic Health Problems (n=1303)**		**Group Comparative Tests**
		Quite Healthy, but a Few Minor Problems (n=1239)	**Sometimes Quite Ill/Almost Always Unwell (n=64)**	
Gender, N(%)				
Male	2387 (52.03%)	590 (47.62%)	25 (39.06%)	*Chi²:*11.25
Female	2201 (47.97%)	649 (52.38%)	39 (60.94%)	(p<0.01)
Missing	-	-	-	
Socio-Economic Status (i.e. Housing Tenure), N(%)				
Owned/Mortgaged	1620 (35.31%)	456 (36.8%)	19 (26.69%)	
Rented Privately	46 (1%)	19 (1.53%)	0 (0%)	
Council/Housing Association	168 (3.66%)	46 (3.71%)	2 (3.13%)	*Fisher's Exact P:*
Missing Data	2543 (60.03%)	718 (57.95%)	43 (67.19%)	0.665 (ns)
History of Parental Mental Illness, N(%)				
No Reported History of Parental Mental Illness	3246 (70.75%)	835 (67.39%)	46 (71.88%)	
History of Parental Mental Illness	553 (12.05%)	183 (14.77%)	8 (12.5%)	*Chi²*:7.27
Missing Data	789 (17.2%)	221 (17.84%)	10 (15.63%)	(p<0.05)
Any Psychiatric Disorder DAWBA, N(%)				
No	4367 (95.18%)	1145 (92.41%)	53 (82.81%)	*Chi²*:33.06
Yes	210 (4.58%)	91 (7.34%)	11 (17.19%)	(p<0.001)
Missing	11 (0.24%)	3 (0.24%)	0	
Any Emotional Disorder DAWBA, N(%)				
No	4490 (97.86%)	1189 (95.96%)	55 (85.94%)	*Chi²*: 51.69
Yes	87 (1.9%)	47 (3.79%)	9 (14.06%)	(p<0.001)
Missing	11 (0.24%)	3 (0.24%)	0	

Any Anxiety Disorder DAWBA, N(%)				
No	4509 (98.28%)	1197 (96.61%)	61 (95.31%)	
Yes	68 (1.48%)	39 (3.15%)	3 (4.69%)	Chi^2:17.56 (p<0.001)
Missing	11 (0.24%)	3 (0.24%)	0	
Any Behavioural Disorder DAWBA, N(%)				
No	4419 (96.32%)	1179 (95.16%)	60 (93.75%)	
Yes	124 (2.7%)	48 (3.87%)	4 (6.5%)	Chi^2:6.92 (p<0.05)
Missing	45 (0.98%)	12 (0.97%)	0	

3.2.1.1.2 Primary associative models

The resulting odds ratio estimates of the three binomial logistic regression models are presented in Table 3.2. In the unadjusted model, children who were rated as "quite healthy, but a few minor problems" were approximately 65% more likely to present with a psychiatric disorder than their healthy peers, while children who were rated as either "sometimes quite unwell" or "almost always unwell" were nearly four times as likely to present with a disorder (although the imprecision of this estimate as indicated by the confidence intervals should be noted) (both p<0.001). These associations were consistently identifiable, and even slightly strengthened, when adjustments were made for gender in the second model. In the third model, which adjusted for all three pre-selected covariates, the model size was greatly reduced. Although the magnitude of the estimated relationship between minor health problems and psychiatric illness fell only marginally for the minor health problems group to 51% (95% CI: 0.98 – 2.33), and remained quite substantial in the sometimes quite ill/almost always unwell group at 2.26 times higher than the healthy, comparative group (95% CI: 0.51 – 10.13), the significance level for both estimates fell above the threshold for statistical significance. As the likelihood ratio tests indicated the addition of the covariates 'socio-economic status' and 'history of parental mental illness' did not substantially improve model fit over the gender-adjusted model (LR chi^2: 6.8, ns), and the confidence intervals also indicated a degree of imprecision, it was hypothesised that this inconsistency in the final model was due to the loss of analytic power. Adjusting for the

moderating effect of gender, substantially improved the associative model fit (LR chi^2: 17.92, p<0.001), given the strong and significant association between male gender of the study child and an increased rate of psychiatric illness at this wave.

Table 3.2 Odds ratios and 95% confidence intervals for the cross-sectional association of chronic illness to rates of psychiatric illness at 10 years

	Model N	Quite healthy, but a few minor problems		Sometimes Quite Ill/Almost Always Unwell	
		N	Odds Ratio (95% Confidence Interval)	N	Odds Ratio (95% Confidence Interval)
Model 1: Basic Model	5877	1236	1.65 (1.28 – 2.13)	64	4.32 (2.22 – 8.38)
Model 2: Model with adjustment for gender of the study child	5877	1236	1.69 (1.31 – 2.19)	64	4.65 (2.38 – 9.06)
Model 3: Model with adjustment for gender, history of parental mental illness and socio-economic status	2039	439	1.51 (0.98 – 2.32)	20	2.26 (0.51 – 10.13)

3.2.1.1.3 Tests for interaction

The likelihood ratio tests indicated that there was no significant interaction between gender of the study child and chronic health problems with mental health outcomes on the baseline questionnaire (LR: 0.14, p>0.05). Furthermore, there was no evidence of an interaction between chronic health problems and parental history of mental illness on rates of psychiatric illness at this cross-sectional wave (LR: 0.26, p>05). The final test for interaction was substantially impacted by the missing data on the measure of socio-economic status. Due to a lack of cases, the interaction terms between being rated as “sometimes quite ill/almost always unwell” and living in private rental accommodation, and that of being rated as “sometimes quite ill/almost

always unwell" and living in council/housing association accommodation, were dropped in the logistic regression models. Therefore, it was not possible to compare the model with the interaction terms to the model without interaction terms in likelihood ratio testing. However, it seemed unlikely that a significant improvement on model fit would be identified giving that the interaction term between being rated as "quite healthy, but a few minor problems" and living in private rental accommodation, and the interaction term between being rated as "quite healthy, but a few minor problems" and living in council/housing association accommodation, were both statistically non-significant.

3.2.1.1.4 Explorations of comparative rates of emotional, anxiety and behavioural disorders

The resulting estimates of the models examining the associated rates of emotional, anxiety and behavioural disorders in chronically ill children rated as "quite healthy, but a few minor problems" and "sometimes quite ill/almost always unwell" relative to children rated as "very healthy, no problems" on the baseline child-based questionnaire are summarised in Table 3.3. The associative models were adjusted for gender only, given that this was the only covariate indicated to improve the overall model fit (LR chi^2: 26.78, $p<0.001$). A substantially increased prevalence of all three types of disorders was indicated among both sub-samples in comparison to the healthy, comparative group.

All associations reached the level of statistical significance for the "quite healthy, but a few minor problems group". The strongest association identified for children with minor health problems was with the prevalence of anxiety disorders (aOR: 2.16 (95% CI: 1.45-3.23), $p<0.001$) although the magnitude of the association with emotional disorders was only slightly lower (aOR: 2.04 (95% CI: 1.43 – 2.93), $p<0.001$). The rate of behavioural disorders on the age 10 questionnaire was also approximately 50% higher in this group relative to healthy peers (aOR: 1.51 (95% CI: 1.07 -2.12), $p<0.001$). There was quite a large amount of imprecision indicated by the confidence intervals for the estimates for the "sometimes quite ill/almost always unwell" group, most likely because of the small sample size of this

group (n=64). The only significant association identified for this group was with an increased rates of emotional disorders (aOR: 8.5; 95% CI: 4.07 – 17.78; p<0.001), although the association with an increased rate of anxiety disorders was just on the threshold of statistical significance (aOR: 3.27; 95% CI: 1.9 – 10.71; p=0.05). As the magnitude of the odds for the rate of behavioural disorders was also substantial in this group, although statistically non-significant (aOR: 2.69; 95% CI: 0.96 – 7.59), it is likely that these non-significant results are an artefact of the lack of analytic power.

Table 3.3 Odds ratios and 95% confidence intervals for the cross-sectional association of chronic illness to rates of emotional, anxiety, and behavioural disorders at 10 years

	Model N	Quite healthy, but a few minor problems		Sometimes Quite Ill/Almost Always Unwell	
		N	Adjusted Odds Ratio (95% Confidence Interval)	N	Adjusted Odds Ratio (95% Confidence Interval)
Model 1: "Any Emotional Disorder" Adjusted for gender	5877	1236	2.04 (1.43 – 2.93)	64	8.5 (4.07 – 17.78)
Model 2: "Any Anxiety Disorder" Adjusted for gender	5877	1236	2.16 (1.45 – 3.23)	64	3.27 (1.0 – 10.71)
Model 3: "Any Behavioural Disorder" Adjusted for gender	5834	1227	1.51 (1.07 – 2.12)	64	2.69 (0.96 – 7.59)

3.2.1.1.5 Sensitivity analyses

It was hypothesised that the inconsistencies in the model which adjusted for all three preselected covariates was due to data attrition. To assess the support for this hypothesis, the more fully adjusted model (i.e. the associative model controlling for gender of the study child, socio-economic status, and history of parental mental illness) was calculated with the imputed datasets.

The estimated odds ratios in the imputed dataset are compared to those of the complete case analysis in Table 3.4. Based on the imputed datasets, estimates for both the “quite healthy, but a few minor problems” group and the “sometimes quite ill/almost always unwell” group were statistically significant (both $p<0.001$), and of a similar magnitude to those seen in the gender adjusted model based on complete cases (i.e. aOR “quite healthy, but a few minor problems”: 1.69 (95% CI: 1.31 – 2.19); aOR “sometimes quite ill/almost always unwell”: 4.65 (95% CI: 2.38 – 9.06). Consistent with the likelihood ratio testing of the primary associative models, these sensitivity analyses further suggest that the covariates of “socio-economic status” and “parental history of mental illness” do not account for the significant associations identified between chronic health problems and associated rates of mental illness at this cross-sectional wave.

Table 3.4 Odds ratios and 95% confidence intervals for the cross-sectional association of chronic illness to rates of psychiatric illness at 10 years based on complete case analysis, and based on analysis with imputed data

	Model N	Quite healthy, but a few minor problems		Sometimes Quite Ill/Almost Always Unwell	
		N	Odds Ratio (95% Confidence Interval)	N	Odds Ratio (95% Confidence Interval)
Complete Case Analysis	2039	439	1.51 (0.98 – 2.32)	2.26	2.26 (0.51 – 10.13)
Analysis with the Imputed Dataset	5891	1239	1.68 (1.3 – 2.17)	64	4.58 (2.32 – 9.01)

3.2.1.2 The age 13 child-based questionnaire

3.2.1.2.1 Descriptive analyses

Table 3.5 outlines the breakdown of all variables used in the associative models in the age 13 cross-sectional sample by chronic illness status, as well as examining prevalence rates of emotional, anxiety, and behavioural disorders. As would be expected based on the age 10 cross-sectional descriptive statistics, a higher prevalence of females and parents with a history of mental illness was indicated amongst children living with chronic health problems when compared to the healthy, comparative sample. No significant variation in the measure of socio-economic status (i.e. low household income) was indicated when comparing the prevalence rates of low household incomes amongst children classified as healthy to children classified as "quite healthy, but a few minor problems" and children classified as "sometimes quite ill/almost always unwell". A significant increase was seen in overall rates of psychiatric illness in children with chronic health problems when compared to children rated as "very healthy, no problems", with analyses of the underlying groups of disorders suggesting that this rise was due to a significantly increased rate of emotional and anxiety disorders, but not behavioural disorders. It should be noted rates of psychiatric illness were consistently higher in prevalence among children rated as "sometimes quite ill" or "always quite unwell" when compared to children rated as "quite healthy, but a few minor problems".

Table 3.5 Breakdown of all measures used in the age 13 cross-sectional binomial logistic regression models by chronic illness status, and comparative statistics

	Very Healthy, No Problems (n=4126)	**Children with Chronic Health Problems (n=1303)**		**Group Comparative Tests**
		Quite Healthy, but a Few Minor Problems (n=1229)	**Sometimes Quite Ill/Almost Always Unwell (n=74)**	
Gender, N(%)				
Male	2162 (52.4%)	587 (47.76%)	28 (37.84%)	
Female	1964 (47.6%)	642 (52.24%)	46 (62.16%)	Chi^2:13.47
Missing	-	-	-	(p<0.001)
Socio-Economic Status (i.e. Low Household Income), N(%)				
Average/High Income	1113 (26.98%)	313 (25.47%)	19 (25.68%)	Chi^2: 2.48
Low Income	254 (6.16%)	61 (4.96%)	7 (9.46%)	*(ns)*
Missing Data	2759 (66.87%)	855 (69.57%)	48 (64.86%)	
History of Parental Mental Illness, N(%)				
No Reported History of Parental Mental Illness	2927 (70.94%)	834 (67.86%)	47 (63.51%)	
History of Parental Mental Illness	474 (11.49%)	177 (14.4%)	14 (18.92%)	Chi^2:11.04
Missing Data	725 (17.57%)	218 (17.74%)	13 (17.57%)	(p<0.01)
Any Psychiatric Disorder DAWBA, N(%)				
No	3951 (95.76%)	1152 (93.73%)	65 (87.84%)	Chi^2: 17.34
Yes	175 (4.24%)	77 (6.27%)	9 (12.16%)	(p<0.001)
Missing	-	-	-	
Any Emotional Disorder DAWBA, N(%)				
No	4077 (98.81%)	1198 (97.48%)	66 (89.19%)	Chi^2: 50.31
Yes	49 (1.19%)	31 (2.52%)	8 (10.81%)	(p<0.001)
Missing	-	-	-	

Any Anxiety Disorder DAWBA, N(%)				
No	4093 (99.2%)	1207 (98.21%)	67 (90.54%)	
Yes	33 (0.8%)	22 (1.79%)	7 (9.46%)	Chi^2: 54.2 (p<0.001)
Missing	-	-	-	
Any Behavioural Disorder DAWBA, N(%)				
No	3968 (96.17%)	1176 (95.69%)	68 (91.89%)	
Yes	120 (2.91%)	46 (3.74%)	5 (6.76%)	Chi^2: 5.35 (ns)
Missing	38 (0.92%)	7 (0.57%)	1 (1.35%)	

3.2.1.2.2 Primary associative models

The resulting odds ratio estimates of the three binomial logistic regression models are presented in Table 3.6. As in the age 10 cross-sectional analyses, the "very healthy, no problems" group was used as the comparative sample. In the unadjusted model, children who were classified as "quite healthy, but a few minor problems" were approximately 51% more likely to present with a psychiatric illness than their healthy peers, and children who were classified as "sometimes quite unwell/almost always unwell" were over three times as likely to present with a mental health disorder (although the imprecision in this estimate, as indicated by the confidence intervals, should be noted) (both p<0.01). Similar to the age 10 cross-sectional analyses, an adjustment for gender slightly strengthened the magnitude of these estimated associations. In the third, and more fully adjusted, model, a substantial difference was seen in the resulting estimates. There was no longer any associated increased rate of psychiatric illness identified in the "quite healthy, but a few minor problems" group (aOR: 0.97 (95% CI: 0.53 – 1.78), although a strong association between being rated as "sometimes quite ill/almost always unwell" and an increased rate of psychiatric illness remained identifiable (aOR: 4.56 (95% CI: 1.47 – 14.16). However, given the wide confidence intervals, and indications that the adjustments in this model did not add any significant improvement to the fit over the gender-adjusted model (LR chi^2: 0.95, p>0.05), it seemed that the inconsistencies in the more fully adjusted model at this wave were also due

to a loss of analytic power, rather than a confounding impact of these variables on the association identified. However, adjustments for gender of the study child did improve the fit of the associative model at this cross-sectional wave (LR chi^2: 13.89; $p<0.01$), due to the strong association between male gender of the study child and an increased rate of psychiatric illness.

Table 3.6 Odds ratios and 95% confidence intervals for the cross-sectional association of chronic illness to rates of psychiatric illness at 13 years

	Model N	Quite healthy, but a few minor problems		Sometimes Quite Ill/Almost Always Unwell	
		N	Odds Ratio (95% Confidence Interval)	N	Odds Ratio (95% Confidence Interval)
Model 1: Basic Model	5429	1229	1.51 (1.15 – 1.99)	74	3.14 (1.53 – 6.38)
Model 2: Model with adjustment for gender of the study child	5429	1229	1.54 (1.17 – 2.04)	74	3.37 (1.65 – 6.9)
Model 3: Model with adjustment for gender, history of parental mental illness and socio-economic status	1511	324	0.97 (0.53 – 1.78)	22	4.56 (1.47 – 14.15)

3.2.1.2.3 Tests for interaction

The likelihood ratio testing indicated that there was no significant interaction between chronic health problems and gender of the study child with mental health outcomes at this cross-sectional wave (LR chi^2: 1.07; $p>0.05$). Furthermore, there was no evidence of an interaction between chronic health problems and parental history of mental illness in the associated rates of psychiatric illness (LR chi^2: 2.79; $p>0.05$). Due to a lack of cases, the interaction term between being rated as “sometimes quite ill/almost always unwell” and living in a low income household was dropped in the logistic

regression models. Therefore, it was not possible to compare the model with the interaction terms to the model without interaction terms in likelihood ratio testing. However, it seemed unlikely that a significant improvement on model fit would be identified giving that the interaction term between being rated as "quite healthy, but a few minor problems" and living in a low income household was statistically non-significant.

3.2.1.2.4 Explorations of comparative rates of emotional, anxiety and behavioural disorders

The resulting estimates of the models examining the associated rates of emotional, anxiety and behavioural disorders in chronically ill children rated as "quite healthy, but a few minor problems" and "sometimes quite ill/almost always unwell" relative to children rated as "very healthy, no problems on the baseline" are summarised in Table 3.7. The associative models were adjusted for gender only, given that this was the only covariate indicated to improve the overall model fit (LR chi^2: 13.89, $p<0.001$). A significantly increased rate of all three types of disorders was indicated for the "sometimes quite ill/almost always unwell" group (all $p<0.05$), while a significantly increased rate of emotional and anxiety disorders was indicated for children classified as "quite healthy, but a few minor problems". For both groups the strongest association was with increased rates of anxiety disorders, however the association with an increased rate of emotional disorders was also quite strong. The imprecision in the estimates for the "sometimes quite ill/almost always unwell" amalgamated group, likely as a result of the limited size of this sub-sample, should be noted.

Table 3.7 Odds ratios and 95% confidence intervals for the cross-sectional association of chronic illness to rates of emotional, anxiety, and behavioural disorders at 13 years

	Model N	Quite healthy, but a few minor problems		Sometimes Quite Ill/Almost Always Unwell	
		N	Odds Ratio (95% Confidence Interval)	N	Odds Ratio (95% Confidence Interval)
Model 1: "Any Emotional Disorder" Adjusted for gender	5429	1229	2.16 (1.37 – 3.41)	74	10.26 (4.66 – 22.58)
Model 2: "Any Anxiety Disorder" Adjusted for gender	5429	1229	2.26 (1.31 – 3.9)	74	13.03 (5.55 – 30.6)
Model 3: "Any Behavioural Disorder" Adjusted for gender	5383	1222	1.32 (0.94 – 1.87)	73	2.62 (1.03 – 6.6)

3.2.1.2.5 Sensitivity analyses

In the third binomial logistic regression model, vast differences were seen in estimates when compared to those of the gender-adjusted model. However, it was hypothesised that this effect was most likely the result of data attrition rather than a true confounding effect, due to the non-significant results of likelihood ratio testing. In order to investigate the support for this hypothesis, the more fully adjusted model (which controls for 'gender', 'socio-economic status', and 'history of parental mental illness') was calculated based on the imputed datasets in order to explore the consistency of the model findings. The estimated odds ratios in the imputed dataset are compared to those of the complete case analysis in Table 3.8. In the associative model calculated based on the imputed datasets, estimates for both the "quite healthy, but a few minor problems" group and the "sometimes quite ill/almost always unwell" group were statistically significant (both $p<0.01$), and of a similar magnitude to those seen in the gender adjusted model based on complete

cases (i.e. aOR “quite healthy, but a few minor problems”: 1.54 (95% CI: 1.17 – 2.04); aOR “sometimes quite ill/almost always unwell”: 3.37 (95% CI: 1.65 – 6.9). Therefore, consistent with the likelihood ratio testing of the primary associative models, these sensitivity analyses further suggest that the covariates of “socio-economic status” and “parental history of mental illness” do not account for the significant associations identified between chronic health problems and associated rates of mental illness at this cross-sectional wave.

Table 3.8 Odds ratios and 95% confidence intervals for the cross-sectional association of chronic illness to rates of psychiatric illness at 13 years based on complete case analysis, and based on analysis with imputed data

	Model N	Quite healthy, but a few minor problems		Sometimes Quite Ill/Almost Always Unwell	
		N	Odds Ratio (95% Confidence Interval)	N	Odds Ratio (95% Confidence Interval)
Complete Case Analysis	1511	324	0.97 (0.53 – 1.78)	22	4.56 (1.47 – 14.15)
Analysis with the Imputed Dataset	5429	1229	1.53 (1.16 – 2.02)	74	3.38 (1.65 – 6.96)

3.2.1.3 Summary of the findings of the cross-sectional analyses

The findings of the cross-sectional analyses are summarised in Table 3.9.

Table 3.9 Summary Table: Cross-Sectional associations of chronic health problems to prevalence rates of psychiatric illness

	Findings of Associative Analyses	**Analyses of More Specific Groupings of Disorders**	**Sensitivity of Estimations**
Age 10	Children with chronic health problems rated as "quite healthy, but a few minor problems" were approximately 69% more likely to present with a mental health disorder than those rated as "very healthy, no problems" (gender-adjusted OR: 1.69 (95% CI: 1.31 – 2.19)) Children with chronic health problems rated as being "sometimes quite ill" or "almost always unwell" were approximately 4 times more likely to present with a mental health disorder than those rated as "very healthy, no problems" (gender-adjusted OR: 4.65 (95% CI: 2.38 – 9.06)) No interaction effects were detected in the prediction of mental health outcomes.	Associations were detected between chronic health problems (both minor and more severe) and an increased rate of emotional, anxiety and behavioural disorders. However, the associations with rates of behavioural disorders were weaker than those indicated for anxiety and emotional disorders, and was not statistically significant for the "sometimes quite ill/almost always unwell" group	Associations of a lower magnitude were identified in the model which adjusted for the effects of all three preselected covariates. Analyses with the imputed datasets suggested that this weakening effect was due to data attrition, rather than a confounding effect of these variables on the associations identified.
Age 13	Children with chronic health problems rated as "quite healthy, but a few minor problems" were approximately 54% more likely to present with a mental health disorder than those rated as "very healthy, no problems" (gender-adjusted OR: 1.54 (95% CI: 1.17 – 2.04)) Children with chronic health problems rated as being	Associations were identified between both ratings of ill health and an increased prevalence of all three groupings of disorders (i.e. emotional disorders, anxiety disorders, and behavioural disorders) at this wave. However, the associations with rates of behavioural disorders were weaker than those indicated for anxiety and	Associations of a lower magnitude were identified in the model which adjusted for the effects of all three preselected covariates. Analyses with the imputed datasets suggested that this weakening effect was due to data attrition, rather than a confounding effect of these variables on the associations identified.

	"sometimes quite ill" or "almost always unwell" were approximately 3 times more likely to present with a mental health disorder than those rated as "very healthy, no problems" (gender-adjusted OR: 3.37 (95% CI: 1.65 – 6.9)) No interaction effects were detected in the prediction of mental health outcomes.	emotional disorders, and was not statistically significant for the "quite healthy, but a few minor problems" group	

3.2.2 Longitudinal analyses

3.2.2.1 Descriptive analyses

Table 3.10 outlines the breakdown of all variables used in the associative models in the longitudinal cohort by chronic illness status, as well as examining prevalence rates of emotional, anxiety, and behavioural disorders at each wave. The longitudinal cohort consisted of children who were identified as having some degree of illness on both the 10.67 and 13.83 year child-based questionnaire, as well as the control sample of children who were identified as being "Very healthy, no problems" on both questionnaires. As would be expected based on the cross-sectional descriptive analyses, males were slightly more prevalent in the comparative sample while females were slightly over represented in the chronic illness sample. In addition, there was a higher prevalence of parents reporting a history of mental illness in the chronically ill sample ($p<0.01$). However, no difference was detected between the healthy comparative sample and children with chronic illness on the measure of 'socio-economic status' (i.e. low household income). Mental health disorders were more prevalent in the chronic illness sub-sample at all three measurement waves, and this was reflected in underlying rates of emotional, anxiety and behavioural disorders. However, it should be noted that variations in the prevalence rates of anxiety and behavioural disorders at the age 15 measurement wave did not reach the threshold of statistical significance. As noted in the methodology chapter, this measurement wave had higher rates of participant attrition than the two preceding waves. It should also be noted that there was a slightly higher percentage of missing data on the variables 'socio-economic status' and 'history of parental mental illness' among the sample with chronic health problems.

Table 3.10 Breakdown of all measures used in the longitudinal binomial logistic regression models by chronic illness status, and comparative statistics

	Healthy Comparative Sample (n=2681)	**Chronically Ill Sample (n=1303)**	**Group Comparative Tests**
Gender, N(%)			
Male	1424 (53.11%)	615 (47.2%)	
Female	1257 (46.89%)	688 (52.8%)	Chi^2:12.28
Missing	-	-	(p<0.001)
Socio-Economic Status (i.e. Low Household Income), N(%)			
Average/High Income	727 (27.12%)	332 (25.28%)	
Low Income	166 (6.19%)	68 (5.22%)	Chi^2:0.47 (ns)
Missing Data	1788 (66.69%)	903 (69.3%)	
History of Parental Mental Illness, N(%)			
No Reported History of Parental Mental Illness	1958 (73.03%)	881 (67.61%)	
History of Parental Mental Illness	317 (11.82%)	191 (14.66%)	Chi^2: 8.53 (p<0.01)
Missing Data	406 (15.14%)	231 (17.73%)	
Any Psychiatric Disorder DAWBA 10 Years, N(%)			
No	2658 (95.79%)	1198 (91.94%)	
Yes	110 (4.1%)	102 (7.83%)	Chi^2: 24.25
Missing	3 (0.11%)	3 (0.23%)	(p<0.001)
Any Emotional Disorder DAWBA 10 Years, N(%)			
No	2642 (98.55%)	1244 (95.47%)	
Yes	36 (1.34%)	56 (4.3%)	Chi^2: 34.02
Missing	3 (0.11%)	3 (0.23%)	(p<0.001)
Any Anxiety Disorder DAWBA 10 Years, N(%)			
No	2651 (98.88%)	1258 (96.55%)	
Yes	27 (1.01%)	42 (3.22%)	Chi^2: 25.36
Missing	3 (0.11%)	3 (0.23%)	(p<0.001)

Any Behavioural Disorder DAWBA 10 Years, N(%)			
No	2600 (95.98%)	1239 (95.09%)	
Yes	66 (2.46%)	52 (3.99%)	Chi^2: 7.24
Missing	15 (0.56%)	12 (0.92%)	(p<0.01)
Any Psychiatric Disorder DAWBA 13 Years, N(%)			
No	2592 (96.68%)	1217 (93.4%)	
Yes	89 (3.32%)	86 (6.6%)	Chi^2: 22.47
Missing	-	-	(p<0.001)
Any Emotional Disorder DAWBA 13 Years, N(%)			
No	2656 (99.07%)	1264 (97.01%)	
Yes	25 (0.93%)	39 (2.99%)	Chi^2: 23.56
Missing	-	-	(p<0.001)
Any Anxiety Disorder DAWBA 13 Years, N(%)			
No	2663 (99.3%)	1274 (97.77%)	
Yes	18 (0.67%)	29 (2.34%)	Chi^2: 18.17
Missing	-	-	(p<0.001)
Any Behavioural Disorder DAWBA 13 Years, N(%)			
No	2602 (97.05%)	1244 (95.47%)	
Yes	60 (2.24%)	51 (3.91%)	Chi^2: 9.06
Missing	19 (0.71%)	8 (0.61%)	(p<0.01)
Any Psychiatric Disorder DAWBA 15 Years, N(%)			
No	1668 (62.22%)	882 (63.09%)	
Yes	85 (3.17%)	68 (5.22%)	Chi^2: 8.44
Missing	928 (34.61%)	413 (31.7%)	(p<0.01)
Any Emotional Disorder DAWBA 15 Years, N(%)			
No	1714 (63.93%)	849 (65.16%)	
Yes	32 (1.19%)	34 (2.61%)	Chi^2: 9.76
Missing	935 (34.88%)	420 (32.23%)	(p<0.01)

Any Anxiety Disorder DAWBA 15 Years, N(%)			
No	1725 (64.34%)	867 (66.54%)	
Yes	21 (0.78%)	16 (1.23%)	Chi^2: 1.57
Missing	935 (34.88%)	420 (32.23%)	(ns)
Any Behavioural Disorder DAWBA 15 Years, N(%)			
No	1697 (63.3%)	857 (65.77%)	
Yes	56 (2.09%)	33 (2.53%)	Chi^2: 0.48
Missing	928 (34.61%)	413 (31.7%)	(ns)

3.2.2.2 Primary associative models

Initially three binomial logistic regression models were run for each measurement wave in turn, one examining the unadjusted association between chronic health problems and psychiatric illness, the next with adjustments for gender and the final model controlling for the effects of 'gender', 'socio-economic status' and 'history of parental mental illness'. The resulting odds ratio estimates from these models are presented in Table 3.11. The unadjusted models indicated a statistically significant increase in the prevalence of mental health disorders amongst the chronically ill sub-sample at all three time waves. The magnitude of these associations were comparable for the 10 year and 13 year measurement wave (OR: 1.99 (95% CI: 1.51 – 2.64), p<0.001; 13 Year OR: 2.06 (95% CI: 1.52 – 2.79), p<0.001), while a weaker association was identified at 15 years, with children with chronic illness 1.62 times more likely to meet the threshold for mental illness at this time wave than their healthy peers (95% CI: 1.17 – 2.26; p<0.01). However, sample size calculations indicated that the estimates for the age 15 wave may be biased by the substantial amount of data attrition on this measure. Adjustments for gender slightly strengthened the magnitude of these associations for the 10 and 13 years measurement wave, but had a slight weakening effect for the age 15 years association. All associations identified were reduced to levels of statistical non-significance when adjusting for the covariates of 'socio-economic status' and 'history of parental mental illness', with very little consistency in the magnitude of the odds ratios when compared to the preceding models. As the likelihood ratio tests

indicated that the addition of the variables of ‘parental history of mental illness’ and ‘socio-economic status’ did not substantially improve model fit at any of the three measurement waves (LR chi^2 10 Years: 3.3; LR chi^2 13 Years: 4.34; LR chi^2: 4.32; all $p>0.05$), it is likely that, as in the cross-sectional analyses, this weakening effect was a consequence of data attrition. Although adjusting for gender significantly improved the associative model fit at the baseline and 13 year wave due to a strong association between male gender of the study of the child and an increased rate of psychiatric illness (LR chi^2 10 Years: 7.66; LR chi^2 13 Years: 7.14; both $p<0.01$), this adjustment did not improve the associative model fit for the 15 year wave (LR chi^2 15 Years: 2.68; $p>0.05$).

Table 3.11 Odds ratios and 95% confidence intervals for the association of chronic illness to rates of psychiatric illness at each DAWBA wave

	Model 1: Basic Model			**Model 2:** Model with adjustment for gender of the study child			**Model 3:** Model with adjustment for gender, history of parental mental illness and socio-economic status		
	Model N	**Chronically Ill Sample**		**Model N**	**Chronically Ill Sample**		**Model N**	**Chronically Ill Sample**	
		N	**Odds Ratio (95% Confidence Interval)**		**N**	**Odds Ratio (95% Confidence Interval)**		**N**	**Odds Ratio (95% Confidence Interval)**
Age 10 Measurement	3978	1300	1.99 (1.51 – 2.62)	3978	1300	2.04 (1.54 – 2.69)	1124	345	1.45 (0.81 – 2.57)
Age 13 Measurement	3984	1303	2.06 (1.52 – 2.79)	3984	1300	2.11 (1.56 – 2.87)	1127	346	1.83 (0.97 – 3.44)
Age 15 Measurement	2643	890	1.62 (1.17 – 2.26)	2643	890	1.6 (1.15 – 2.22)	765	243	0.93 (0.46 – 1.88)

Three further binomial logistic models were calculated in order to identify the associations between chronic health problems and mental ill-health longitudinally when adjusting for the presence of psychiatric illness at previous waves. ‘Socio-economic status’ and ‘history of parental mental illness’ were not adjusted for in these models due to sample size concerns, and the indications from likelihood ratio testing. The estimated odds ratios indicated from the calculation of these two models are presented in Table 3.12. Having adjusted for the presence of psychiatric illness at age 10, chronic health problems continued to be associated with an increased prevalence of psychiatric illness at age 13 ($p<0.01$). An association between chronic health problems and an approximate 30% increased prevalence of psychiatric illness at the age 15 measurement wave was indicated when controlling for the presence of psychiatric illness at the previous DAWBA measurement waves. However, these associations did not reach the threshold of statistical significance ($p>0.05$).

Table 3.12 Odds ratios and 95% confidence intervals for the association of chronic illness to rates of psychiatric illness at 13 and 15 years, after adjusting for mental health outcomes at preceding waves

	Age 13 Measurement			Age 15 Measurement		
	Model N	Chronically Ill Sample		Model N	Chronically Ill Sample	
		N	Odds Ratio (95% Confidence Interval)		N	Odds Ratio (95% Confidence Interval)
Model 4: Logistic Model Adjusted for Gender and DAWBA Indications at the Previous Measurement Wave	3978	1300	1.73 (1.25 – 2.4)	2643	890	1.34 (0.95 – 1.9)
Model 5: Logistic Model Adjusted for Gender and DAWBA Indications at the Two Previous Measurement Waves				2641	888	1.27 (0.89 – 1.81)

3.2.2.3 Tests for interaction

There was no evidence of an interaction effect between chronic health problems and gender of the study child on mental health outcomes at any of the three administration waves (LR chi^2 10 Years: 0.03; LR chi^2 13 Years: 0.39; LR chi^2: 0.29; all $p>0.05$). Similarly, no interaction effect was suggested between chronic health problems and history of parental mental illness in the associated rates of psychiatric illness across the time period of analysis (LR chi^2 10 Years: 0.05; LR chi^2 13 Years: 1.34; LR chi^2: 1.86; all $p>0.05$). Finally, the test for interaction between chronic health problems and socio-economic status was not significant at any of the three measurement waves (LR chi^2 10 Years: 0.38; LR chi^2 13 Years: 1.81; LR chi^2: 0.48; all $p>0.05$).

3.2.2.4 Explorations of comparative rates of emotional, anxiety and behavioural disorders

The resulting estimates of the models examining the associated rates of emotional, anxiety and behavioural disorders in chronically ill children relative to the healthy, comparative groups at the three measurement waves are summarised in Table 3.13. The associative models were adjusted for gender only, given that this was the only covariate indicated to improve the overall model fit, specifically at the 10 and 13 year wave. At the age ten and thirteen year measurements, a significant association was identified between chronic health problems and an increase in all three types of disorders. As would be expected based on the cross-sectional analyses, the association between emotional and anxiety disorders and chronic health problems at both waves was of a similar magnitude, and substantially stronger than the association identified between chronic health problems and behavioural disorders at these waves. Although an increase in all three types of disorder was identifiable amongst adolescents with chronic health problems at age 15 years, the only association to reach the level of statistical significance was that between chronic health problems and an increased prevalence of emotional disorders (aOR: 2.04 (95% CI: 1.24 – 3.33), $p<0.01$).

Table 3.13 Odds ratios and 95% confidence intervals for the association of chronic illness to rates of emotional, anxiety, and behavioural disorders at each DAWBA measurement wave

	Model 1: "Any Emotional Disorder" Adjusted for gender			**Model 2:** "Any Anxiety Disorder" Adjusted for gender			**Model 3:** "Any Behavioural Disorder" Adjusted for gender		
	Model N	**Chronic Illness Sample**		**Model N**	**Chronic Illness Sample**		**Model N**	**Chronic Illness Sample**	
		N	**Odds Ratio (95% Confidence Interval)**		**N**	**Odds Ratio (95% Confidence Interval)**		**N**	**Odds Ratio (95% Confidence Interval)**
Age 10 Measurement	3978	1300	3.23 (2.11 – 4.94)	3978	1300	3.2 (1.96 – 5.21)	3957	1291	1.75 (1.21 – 2.54)
Age 13 Measurement	3984	1303	3.28 (1.97 – 5.45)	3984	1302	3.36 (1.86 – 6.08)	3957	1295	1.83 (1.25 – 2.68)
Age 15 Measurement	2629	883	2.04 (1.24 – 3.33)	2629	883	1.42 (0.74 – 2.74)	2643	890	1.17 (0.77 – 1.82)

Three further binomial logistic models were calculated in order to identify the associations between chronic health problems and rates of specific groups of psychiatric disorders longitudinally when adjusting for the presence of psychiatric illness at previous waves. The resulting odds ratios estimates from these analyses can be seen in Table 3.14. When adjusting for the presence of mental illness at age 10 years, chronic health problems were no longer significantly associated with an increase in behavioural disorders, but remained a significant predictor of the presence of emotional and anxiety disorders at thirteen years. The association between chronic health problems and an increased rate of emotional disorders at 15 years remained identifiable even after adjusting for the presence of mental illness at 13 years, and consequently for the presence of mental illness at either of the earlier waves (both $p<0.05$). The magnitude of the association between chronic illness and an increased prevalence of anxiety disorders remained consistent even after adjustments were made for the prevalence of mental illness at previous waves. However, this association was not statistically significant. It is possible that this lack of significance, in spite of the constancy of the estimates, may be due to underpowered analyses as a consequence of the high rate of data attrition at this wave.

Table 3.14 Odds ratios and 95% confidence intervals for the association of chronic illness to rates of emotional, anxiety, and behavioural disorders at 13 and 15 years, after adjusting for mental health outcomes at previous waves

	Model 1: "Any Emotional Disorder" Adjusted for gender			**Model 2:** "Any Anxiety Disorder" Adjusted for gender			**Model 3:** "Any Behavioural Disorder" Adjusted for gender		
	Model	**Chronic Illness Sample**		**Model**	**Chronic Illness Sample**		**Model**	**Chronic Illness Sample**	
	N	**N**	**Odds Ratio (95% Confidence Interval)**	**N**	**N**	**Odds Ratio (95% Confidence Interval)**	**N**	**N**	**Odds Ratio (95% Confidence Interval)**
Age 13 Measurement (Adjusted for Presence of Mental Illness at 10 Years)	3978	1300	2.77 (1.65 – 4.64)	3978	1300	2.76 (1.51 – 5.05)	3952	1293	1.39 (0.93 – 2.09)
Age 15 Measurement (Adjusted for Presence of Mental Illness at 13 Years)	2629	883	1.96 (1.19 – 3.21)	2629	883	1.4 (0.72 – 2.71)	2643	890	0.86 (0.53 – 1.38)
Age 15 Measurement (Adjusted for Presence of Mental Illness at 10 or 13 Years)	2627	881	1.88 (1.14 – 3.1)	2627	881	1.4 (0.72 – 2.71)	2641	888	0.82 (0.51 – 1.33)

3.2.2.5 Sensitivity analyses

As in the cross-sectional analyses, weakening effects in the models adjusting for 'socio-economic status' and 'history of parental mental illness' at 10 and 13 years were hypothesised to be a consequence of data attrition, rather than a consequence of confounding. This hypothesis seemed supported in the sensitivity analyses with the imputed datasets (see Table 3.15). The associations between chronic health problems and psychiatric illness were stronger in the analyses with the imputed datasets, and were comparable with the estimates of the complete case unadjusted and gender adjusted model at both measurement waves (i.e. gender-adjusted OR 10 years: 2.04 (95% CI: 1.54 – 2.69); gender-adjusted OR 13 years: 2.11 (95% CI: 1.56 – 2.87)). The associations for both waves reached the threshold of statistical significance based on the imputed datasets ($p<0.001$). Therefore, consistent with the likelihood ratio testing of the primary associative models, these sensitivity analyses further suggest that the covariates of "socio-economic status" and "parental history of mental illness" do not account for the associations identified between chronic health problems and mental health outcomes on the 10 and 13 year questionnaires.

Table 3.15 Odds ratios and 95% confidence intervals for the association of chronic illness to rates of psychiatric illness at 10 and 13 years in the longitudinal complete case analyses, and analyses based on imputed data

	10 Year Measurement			13 Year Measurement		
		Chronic Illness Sample			Chronic Illness Sample	
	Model N	N	Odds Ratio (95% Confidence Interval)	Model N	N	Odds Ratio (95% Confidence Interval)
Complete Case Analysis	1124	345	1.45 (0.81 – 2.57)	1127	346	1.83 (0.97 – 3.44)
Analysis with the Imputed Datasets	3984	1303	2.03 (1.53 – 2.69)	3984	1303	2.08 (1.53 – 2.83)

Due to the high amount of attrition on the age 15 DAWBA measurement, all analyses with this outcome measure were repeated using data from the

imputed datasets. The odds ratio estimates from the initial three binomial logistic regression models are compared to those of the complete case analyses in Table 3.16. In spite of the substantial amount of missing data on the age 15 wave, the estimates of the crude model and gender-adjusted model based on the imputed datasets were highly consistent with the complete case analysis. Children with chronic health problems were approximately 60% more likely to present with a mental illness than their healthy peers across these models. Moreover, the magnitude of this association was consistent when adjustments were made for 'history of parental mental illness' and 'socio-economic status' in the imputed datasets, suggesting that there was no substantial confounding effect of these variables on the associations identified. Based on the analyses with the imputed datasets, the associations between chronic health problems and psychiatric illness at age 15 reached the threshold of statistical significance in all three models ($p<0.01$).

Table 3.16 Odds ratios and 95% confidence intervals for the association of chronic illness to rates of psychiatric illness at 15 years in the longitudinal complete case analyses, and analyses based on imputed data

	Model 1: Crude Model			**Model 2:** Model with adjustment for gender of the study child			**Model 3:** Model with adjustment for gender, history of parental mental illness and socio-economic status		
	Model N	**Chronically Ill Sample**		**Model N**	**Chronically Ill Sample**		**Model N**	**Chronically Ill Sample**	
		N	**Odds Ratio (95% Confidence Interval)**		**N**	**Odds Ratio (95% Confidence Interval)**		**N**	**Odds Ratio (95% Confidence Interval)**
Complete Case Analysis	2643	890	1.62 (1.17 – 2.26)	2643	890	1.6 (1.15 – 2.22)	765	243	0.93 (0.46 – 1.88)
Analysis with the Imputed Datasets	3984	1303	1.64 (1.17 – 2.23)	3984	1303	1.62 (1.15 – 2.26)	3984	1303	1.6 (1.14 – 2.25)

In the complete case analyses, the association between chronic health problems and an increased rate of psychiatric illness at 15 years was no longer statistically significant after controlling for the initial presence of psychiatric illness. Even when missing data was accounted for in re-calculations of these models based on the imputed datasets, this association remained statistically non-significant, although a slightly increased associated prevalence remained (approximately 30%) (see Table 3.17). Gender was the only covariate adjusted for in these models to maintain consistency with the complete case analysis.

Table 3.17 Odds ratios and 95% confidence intervals for the association of chronic illness to rates of psychiatric illness at 15 years, after controlling for mental health outcomes at preceding waves, in the longitudinal complete case analyses, and analyses based on imputed data

	Logistic Model Adjusted for Gender and DAWBA Indications at the 13 Year Measurement Wave			**Logistic Model Adjusted for Gender and DAWBA Indications at the 10 and 13 Year Measurement Wave**		
	Model N	**Chronic Illness Sample**		**Model N**	**Chronic Illness Sample**	
		N	**Odds Ratio (95% Confidence Interval)**		**N**	**Odds Ratio (95% Confidence Interval)**
Complete Case Analysis	1124	345	1.45 (0.81 – 2.57)	2641	888	1.27 (0.89 – 1.81)
Analysis with the Imputed Datasets	3984	1303	1.37 (0.95 – 1.97)	3984	1303	1.3 (0.9 – 1.89)

3.2.2.6 Summary of the Longitudinal Analyses

The findings of the longitudinal analyses are summarised in Table 3.18.

Table 3.18 Summary Table: Longitudinal associations of chronic health problems to prevalence rates of psychiatric illness

Findings of Associative Analyses	Analyses of More Specific Groupings of Disorders	Sensitivity of Estimations
At 10 years and 13 years, children with chronic health problems were approximately twice as likely to present with a mental health disorder than the comparative group (gender-adjusted 10 year OR: 2.04 (95% CI: 1.54-2.69); gender-adjusted 13 year OR: 2.11 (95% CI: 1.56-2.87)). At 15 years, these children were 60% more likely to present with such disorders (gender-adjusted OR: 1.6 (95% CI: 1.15-2.22). When controlling for the presence of mental illness at previous waves, chronic illness continued to be associated with a rise in the prevalence of mental health disorders at age 13 and age 15 (aOR 13 Years: 1.73 (95% CI: 1.25 – 2.4); aOR 15 Years: 1.27 (95% CI: 0.89 – 1.81)). However, the associated increase at age 15 did not reach the level of statistical significance. No interaction effects were detected in the prediction of mental health outcomes at any wave.	Significant associations were identified between chronic health problems and an increased prevalence of all three types of disorders (i.e. emotional disorders, anxiety disorders, and behavioural disorders) at ten and thirteen years. At fifteen years, although an increased prevalence of all three types of disorders was indicated, only the association with emotional disorders reached the level of statistical significance. When controlling for the presence of mental illness at previous measurement waves, chronic illness continued to be associated with a statistically significant increased prevalence of emotional and anxiety disorders at age 13 years. At fifteen years, chronic health problems were associated with a significant increase in rates of emotional disorders only.	There were high rates of attrition in the DAWBA measurement for the 15 year measurement wave. However, estimates resulting from analyses with imputed datasets were highly consistent with the outcomes of complete case analyses. Associations of a lower magnitude were identified in the models adjusting for all three pre-selected covariates at all three measurement waves. Analyses with the imputed datasets suggested that this weakening effect was due to data attrition, rather than a confounding effect of these variables on the associations identified.

3.2.3 Mediation analyses

The outcomes of the four steps of the mediation analyses are presented in an overview table (Table 3.19) for clarity. The variables extracted as measures of symptom severity and functional impairments – high levels of health-related school absenteeism and perceptions of fatigue – were both indicated to have a mediating role in the association between chronic health problems and rates of psychiatric illness at 10 and 13 years. However, neither of these factors was indicated to play a fully mediating role in this association at either wave. The associations at 10 and 13 years also seemed to be mediated by the high levels of peer victimisation identified among children living with chronic health problems on both the 10 year and 12.5 year measurement. It was found that children with chronic health problems also indicated significantly higher levels of dissatisfaction with friendships on the 'Cambridge Hormone and Moods Project Friendship Questionnaire' ($p<0.05$) at age 12. However, these friendship satisfaction scores did not predict mental health outcomes at age 13. Finally, despite being the most consistently measured variables among the identified mediating variables, parental monitoring, child disclosures, and parental solicitations mediated the association between chronic illness and rates of psychiatric illness at age 15 years only. This finding is consistent with the literature in suggesting that the aetiological factors in childhood and adolescent-psychopathology vary in significance over development. The fourth variable measured in these scales, parental control, did not mediate the association between chronic health problems and mental health outcomes at any wave. Significantly, in contrast to the hypothesised associations, chronic health problems were associated with a lower prevalence of these aspects of parental monitoring at 15 years, and these aspects of parental monitoring were, in turn, associated with a lower prevalence of psychiatric illness.

Table 3.19 Outcomes of the mediation analyses based on the four-step approach to establishing mediation (e.g. Baron and Kenny, 1986)

Mediation Pathway to Test	***Step 1:* Confirm causal variable is associated with outcome**	***Step 2:* Confirm causal variable is associated with mediator**	***Step 3:* Show the mediator effects the association with the outcome variable**	***Step 4:* Identify if it is partial/full mediation**
Chronic Illness – High Levels of Health-Related School Absenteeism at 10 – Any Psychiatric Illness at 10	✓ OR: 1.99 (95% CI: 1.51 – 2.62)	✓ Significant association with high-levels of absenteeism (OR: 6.11 (95% CI: 5.14 – 7.26), p<0.001)	✓	**Partial** A significant association is still identified between chronic illness and psychiatric illness at age 10 (p<0.01)
Chronic Illness – High Levels of Health-Related School Absenteeism at 13 – Any Psychiatric Illness at 13	✓ OR: 2.06 (95% CI: 1.52 – 2.79)	✓ Significant association with high-levels of absenteeism (OR: 4.29 (95% CI: 3.76 – 5.13), p<0.001)	✓	**Partial** A significant association is still identified between chronic illness and psychiatric illness at age 13 (p<0.01)
Chronic Illness – Perceptions of Fatigue – Any Psychiatric Illness at 13	✓ OR: 2.06 (95% CI: 1.52 – 2.79)	✓ Significant association with perceptions of fatigue (Coeff: 1.8 (95% CI: 1.42 – 2.18), p<0.001)	✓	**Partial** A significant association is still identified between chronic illness and psychiatric illness at age 13 (p<0.01)

Chronic Illness – Conflict in the Parents Relationship at 9 – Any Psychiatric Illness at 10	✓ OR: 1.99 (95% CI: 1.51 – 2.62)	**X** Regression coefficient is not significant (p=0.91)		
Chronic Illness – Conflict in the Parents Relationship at 12 – Any Psychiatric Illness at 13	✓ OR: 2.06 (95% CI: 1.52 – 2.79)	**X** Regression coefficient is not significant (p=0.56)		
Chronic Illness – Parental Monitoring at 12 – Any Psychiatric Illness at 13	✓ OR: 2.06 (95% CI: 1.52 – 2.79)	**X** Regression coefficient is not significant (p=0.97)		
Chronic Illness – Parental Monitoring at 13 – Any Psychiatric Illness at 13	✓ OR: 2.06 (95% CI: 1.52 – 2.79)	**X** Regression coefficient is not significant (p=0.5)		
Chronic Illness – Parental Monitoring at 15 – Any Psychiatric Illness at 15	✓ OR: 1.62 (95% CI: 1.17 – 2.26)	✓ Borderline association with lower levels of monitoring (Coefficient: -0.32 (95% CI: -0.65 – 0.01), p=0.054)	✓	**Partial** A significant association is still identified between chronic illness and psychiatric illness at age 15 ($p<0.05$)
Chronic Illness – Child Disclosures at 12 – Any Psychiatric Illness at 13	✓ OR: 2.06 (95% CI: 1.52 – 2.79)	**X** Regression coefficient is not significant (p=0.28)		

Chronic Illness – Child Disclosures at 13 – Any Psychiatric Illness at 13	✓ OR: 2.06 (95% CI: 1.52 – 2.79)	**X** Regression coefficient is not significant (p=0.93)		
Chronic Illness – Child Disclosures at 15 – Any Psychiatric Illness at 15	✓ OR: 1.62 (95% CI: 1.17 – 2.26)	✓ Significant association with lower levels of disclosures (Coefficient: -0.36, (95% CI: -0.63 – -0.1), p<0.01)	✓	**Partial** A significant association is still identified between chronic illness and psychiatric illness at age 15 (p<0.05)
Chronic Illness – Parental Solicitation at 12 – Any Psychiatric Illness at 13	✓ OR: 2.06 (95% CI: 1.52 – 2.79)	**X** Regression coefficient is not significant (p=0.55)		
Chronic Illness – Parental Solicitation at 13 – Any Psychiatric Illness at 13	✓ OR: 2.06 (95% CI: 1.52 – 2.79)	**X** Regression coefficient is not significant (p=0.37)		
Chronic Illness – Parental Solicitation at 15 – Any Psychiatric Illness at 15	✓ OR: 1.62 (95% CI: 1.17 – 2.26)	✓ Significant association with lower levels of disclosures (Coefficient: -0.28 (95% CI: -0.48 – -0.08, p<0.01)	✓	**Partial** A significant association is still identified between chronic illness and psychiatric illness at age 15 (p<0.05)

Chronic Illness – Parental Control at 12 – Any Psychiatric Illness at 13	✓ OR: 2.06 (95% CI: 1.52 – 2.79)	**X** Regression coefficient is not significant (p=0.13)		
Chronic Illness – Parental Control at 13 – Any Psychiatric Illness at 13	✓ OR: 2.06 (95% CI: 1.52 – 2.79)	**X** Regression coefficient is not significant (p=0.15)		
Chronic Illness – Parental Control at 15 – Any Psychiatric Illness at 15	✓ OR: 1.62 (95% CI: 1.17 – 2.26)	**X** Regression coefficient is not significant (p=0.97)		
Chronic Illness – Satisfaction with Peer Relationships at 10 – Any Psychiatric Illness at 10	✓ OR: 1.99 (95% CI: 1.51 – 2.62)	**X** Regression coefficient is not significant (p=0.22)		
Chronic Illness – Satisfaction with Peer Relationships at 12 – Any Psychiatric Illness at 13	✓ OR: 2.06 (95% CI: 1.52 – 2.79)	✓ Significant association with higher level of dissatisfaction (Coefficient: 0.16, $p<0.05$)	**X** Friendship dissatisfaction scores are not significantly associated with the prevalence of mental health disorders at 13 years (p=0.57)	

Chronic Illness – Peer Victimisation at 10 – Any Psychiatric Illness at 10	✓ OR: 1.99 (95% CI: 1.51 – 2.62)	✓ Significant association with victimisation (OR: 1.32 (95% CI: 1.1 – 1.59), p<0.01)	✓	**Partial** A significant association is still identified between chronic illness and psychiatric illness at age 10 (p<0.001)
Chronic Illness – Peer Victimisation at 12 – Any Psychiatric Illness at 13	✓ OR: 2.06 (95% CI: 1.52 – 2.79)	✓ Significant association with victimisation (OR: 1.58 (95% CI: 1.31 – 1.92), p<0.01)	✓	**Partial** A significant association is still identified between chronic illness and psychiatric illness at age 10 (p<0.001)

3.2.4 Creation of the path model

3.2.4.1 Initial design of the path model

As outlined in the methodology chapter, in the initial design of the path model, a pathway was proposed from chronic illness (the exposure measure of interest) to the mediating factors in mental health outcomes at 10 years (i.e. peer victimisation and high levels of health-related absenteeism) and 13 years (i.e. peer victimisation, high levels of health-related absenteeism, and perceptions of fatigue). To complete the mediation pathway, a pathway was placed from each mediating variable to the concurrent measurement of mental health outcomes. As all factors were partially mediating variables, and it was unclear if they would accumulatively mediate the association identified between chronic health problems and increased rates of psychiatric illness, a direct pathway was also placed between chronic illness and psychiatric illness at both 10 and 13 years. A direct pathway was also placed from psychiatric illness at 10 years to psychiatric illness at 13 years, and psychiatric illness at 10 years was depicted as predicting the mediating variables underlying mental health outcomes at age 13 (i.e. peer victimisation at 12.5 years approximately, high levels of health-related absenteeism at 13 years, and scores on the perceptions of fatigue scale at 13 years old). A pathway was also placed from peer victimisation at 10 years to peer victimisation at 12.5 years, and similarly a pathway was placed from high levels of health-related absenteeism at 10 years to high levels of health-related absenteeism at 13 years. The resulting model is illustrated in Figure 3.1.

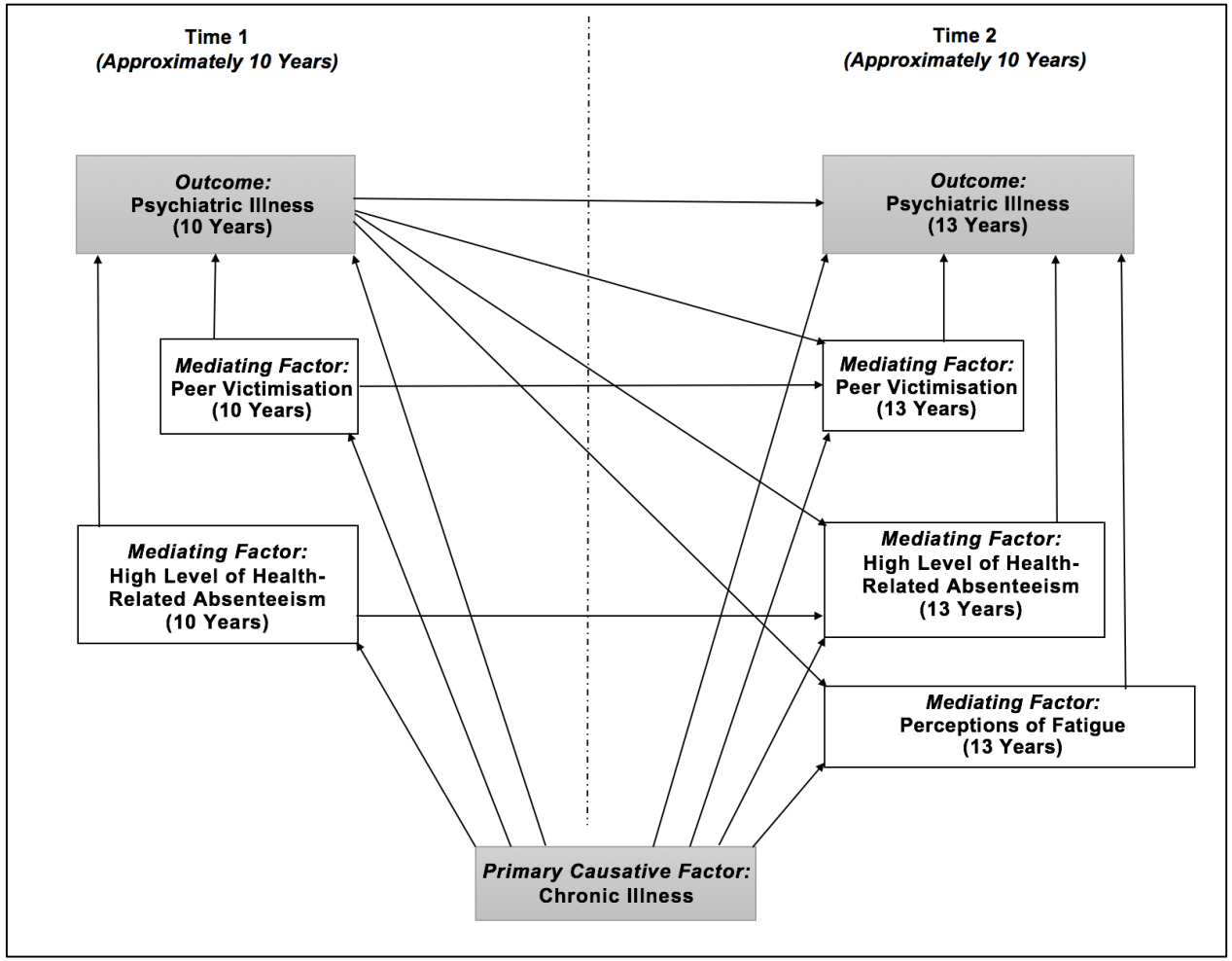


Figure 3.1 Initial design of the path model

3.2.4.2 Subsequent modification of the path model following correlational analyses

Support for the design of the path model was initially examined using a correlational matrix, based on the non-parametric spearman's rho (see Table 3.20). These analyses were also used to identify significant relationships between the model variables that were not accounted for in the initial design. Please note the correlation matrix was calculated based on a sample of 2484 children with complete data across all eight measures.

Table 3.20 Correlation matrix of all variables included in the initial design of the path model

	Chronic Illness	DAWBA 10	DAWBA 13	Health-Related Absenteeism 10	Health-Related Absenteeism 13	Victimisation 10	Victimisation 12	Perceptions of Fatigue
Chronic Illness	1.0							
DAWBA 10	0.08***	1.0						
DAWBA 13	0.08***	0.31***	1					
Health-Related Absenteeism 10	0.34***	0.09***	0.05*	1				
Health-Related Absenteeism 13	0.31***	0.05**	0.09***	0.29***	1			
Victimisation 10	0.06**	0.09***	0.11***	0.01	0.04*	1		
Victimisation 12	0.1***	0.08***	0.06**	0.06**	0.04*	0.27***	1	
Perceptions of Fatigue	0.15***	0.05*	0.03	0.11***	0.13***	0.02	0.09***	1

*p<0.05
**p<0.01
***p<0.001

These correlational analyses strongly supported most of the initial pathways placed in the model. Chronic health problems were significantly associated with all other variables. In addition, outcomes on the DAWBA measurement at age 10 were correlated with an increased prevalence of peer victimisation, high levels of health-related absenteeism, and perceptions of fatigue in the period between the 10 year and 13 year measurement wave.

One initial concern noted was that, in this correlation matrix, scores on the 'Perceptions of Fatigue' scale were not correlated with mental health outcomes at the concurrent wave, and were only weakly correlated with mental health outcomes at the preceding wave. As this contrasted with the initial mediation analyses, this mediation pathway was isolated and tested for goodness of fit using MPlus© software. In this mediation model, chronic illness predicted scores on the 'Perceptions of Fatigue' scale as well as mental health outcomes at 10 and 13 years. Mental health outcomes at 10 years predicted 'Perceptions of Fatigue' scores, which, in turn, predicted mental health outcomes at 13 years. Fit indices indicated that this mediation pathway was a very poor fit to patterns seen in the ALSPAC data. The chi square test was significant, and the two alternative indicators of fit, the RMSEA and the CFI were also well above recommended guidelines (RMSEA guideline: 0.06 or under; RMSEA for mediation pathway: 0.28 (90% CI: 0.26 – 0.3); CFI guideline: 0.95 or over; CFI for mediation pathway: 0.35). Overall, these indications seemed to suggest that scores on the 'Perceptions of Fatigue' scale are associated with chronic illness and mental health outcomes at 13 years, and may be predicted by the presence of psychiatric illness at 10 years, but do not play a substantial mediating role in the association between chronic illness and mental health outcomes, in and of themselves. Therefore, given these indications, scores on the 'Perceptions of Fatigue' scale were removed as a mediating variable in the design of the path model.

Some additional longitudinal pathways were put in place based on the indications of these correlational analyses. The mediators of mental health outcomes at 10 years were also significantly correlated with mental health outcomes at 13 years. Therefore, these variables were also depicted as

mediators of mental health outcomes at this later wave. High levels of health-related absenteeism at 10 years were not correlated with peer victimisation during this initial measurement period. However, high levels of health-related absenteeism at 13 years were correlated with peer victimisation at 12.5 years approximately, albeit weakly. Therefore, a pathway was placed in the path model from peer victimisation at 12.5 years to high levels of health-related absenteeism at 13 years. A pathway was also placed from peer victimisation at 10 years to high levels of health absenteeism at 13 years, given that these two variables were also significantly correlated in these analyses ($p<0.05$). A final pathway was placed from high levels of health-related absenteeism at 10 years to peer victimisation at 12.5 years, also based on the significance of this association in the correlation matrix. The final design of the path model, based on support from the indications of both the initial mediation analyses and the correlation matrix can be seen in Figure 3.2.

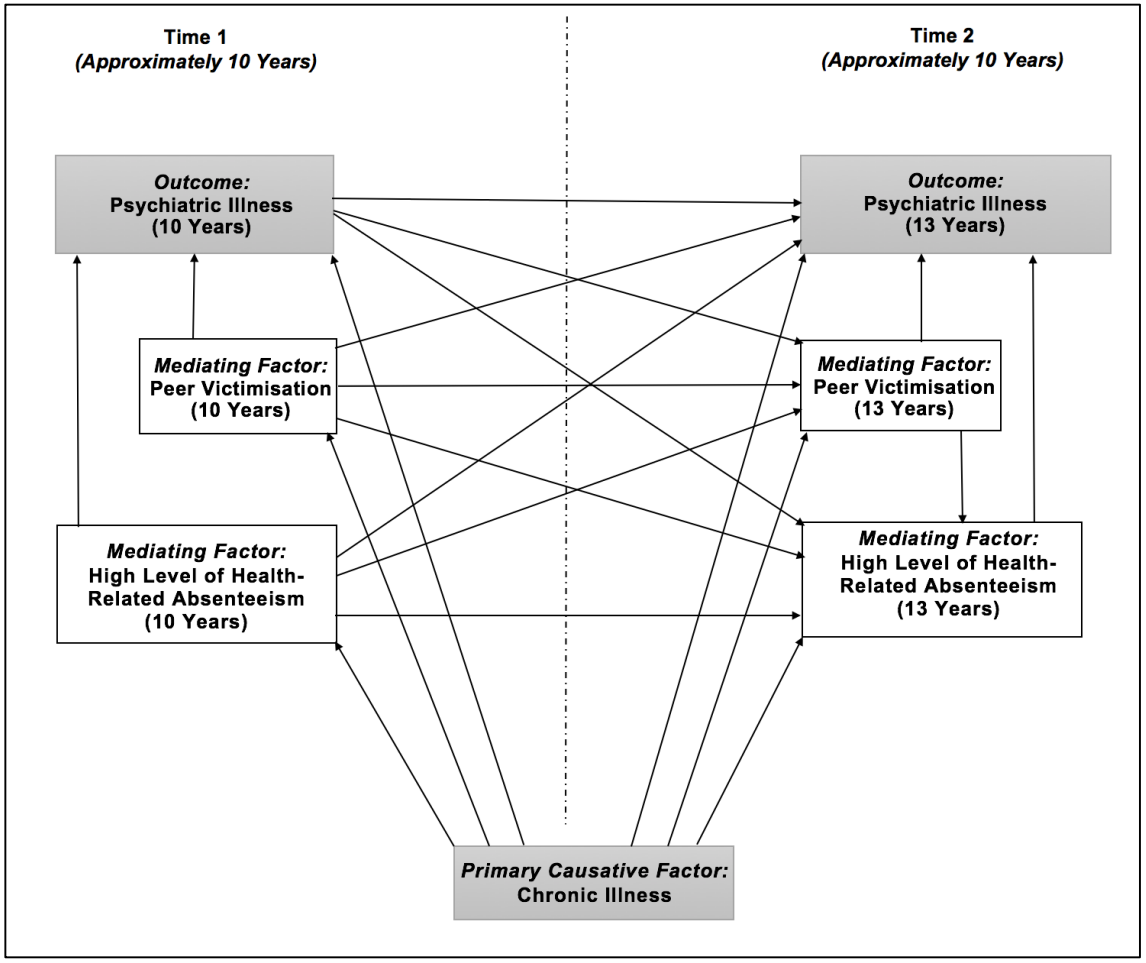


Figure 3.2 Final design of the path model tested for goodness-of-fit to the ALSPAC data using MPlus©

3.2.4.3 Assessment of goodness-of-fit to the ALSPAC data

The model was tested for goodness of fit to the ALSPAC data using MPlus© software. This model was fitted based on 3984 observations, 2842 (71.34%) of whom had complete data across all measures. All fit indices were in acceptable ranges, indicating a good fit of the model to the data. Specifically, the chi-square test of model fit was non-significant, despite the large sample size. The RMSEA value was optimal at 0, and the confidence interval range was also well below the recommended cut-off of value of 0.06 (90% CI: 0.00 – 0.025). In addition, a CFI of 1.0 was obtained, indicating very strong model fit. Therefore, the path model was supported as an adequate model of mental health outcomes at 10 and 13 years in the context of chronic health problems.

Despite the strong support for the structure of the model from the fit indices, the majority of the pathways in the fitted model were statistically non-significant. A summary of the model results can be seen in Table 3.21, and these results are also illustrated in Figure 3.3 for clarity. The first of these non-significant pathways were the direct pathways from chronic health problems to mental health outcomes at 10 years and 13 years, which suggested that the associations with psychiatric illness identified at these waves were fully mediated by the model variables. However, it should be noted that within this model, when controlling for all other variables, chronic illness was no longer associated with the mediating variable of peer victimisation at 12.5 years, with this pathway just over the threshold of significance (p=0.083). In fact, this model would suggest that while peer victimisation was the strongest mediating factor in the association between chronic illness and mental health outcomes at age 10 years, when controlling for this association, and the relationship of measures of peer victimisation and mental health outcomes across the two time waves, peer victimisation at 12.5 years did not independently predict mental health outcomes at 13 years in and of itself. However, high levels of health-related absenteeism were a consistent predictor of mental health outcomes over the two time-waves. Not only did high-levels of health related absenteeism predict higher levels of health-related absenteeism within time at both 10 and 13 years, but it

appeared that high levels of health-related absenteeism at 10 years were associated with mental health outcomes at 13 years, both indirectly through the predictive pathway of high levels of health-related absenteeism at 13 years to psychiatric illness at 13 years, and directly, by leading to a slight reduction in rates of psychiatric illness at this wave. Finally, it should be noted that psychiatric illness at 10 years did not predict health-related absenteeism and peer victimisation at subsequent measurement waves.

Table 3.21 Results of the path model tested in MPlus© software

	Beta Estimate	Standard Error	Est/Standard Error	Two-Tailed P Value
Psychiatric Illness 10 Years on				
Chronic Illness	0.13	0.09	1.45	0.146
Health-Related Absenteeism 10 Years	0.17	0.05	3.16	0.002
Peer Victimisation 10 Years	0.27	0.06	4.75	0.000
Psychiatric Illness 13 Years on				
Chronic Illness	0.12	0.11	1.04	0.297
Psychiatric Illness 10 Years	0.9	0.09	9.69	0.000
Health-Related Absenteeism 13 Years	0.23	0.08	2.86	0.004
Peer Victimisation 12.5 Years	0.04	0.09	0.44	0.659
Health-Related Absenteeism 10 Years	-0.19	0.1	-2.03	0.04
Peer Victimisation 12.5 Years	0.04	0.1	0.44	0.66
Health-Related Absenteeism 10 Years on				
Chronic Illness	1.03	0.05	21.0	0.000
Health-Related Absenteeism 13 Years on				
Chronic Illness	0.5	0.06	8.76	0.000
Health-Related Absenteeism 10 Years	0.43	0.04	10.97	0.000
Psychiatric Illness 10 Years	0.017	0.055	0.307	0.759
Peer Victimisation 12.5 Years	-0.006	0.048	-1.118	0.906
Peer Victimisation 10 Years	0.019	0.055	0.345	0.730

Peer Victimisation 10 Years on Chronic Illness	0.16	0.05	2.95	0.003
Peer Victimisation 12.5 Years				
Chronic Illness	0.13	0.08	1.73	0.083
Peer Victimisation 10 Years	0.51	0.05	10.27	0.000
Psychiatric Illness 10 Years	0.04	0.05	1.35	0.18
Health-Related Absenteeism 10 Years	0.06	0.05	1.35	0.18

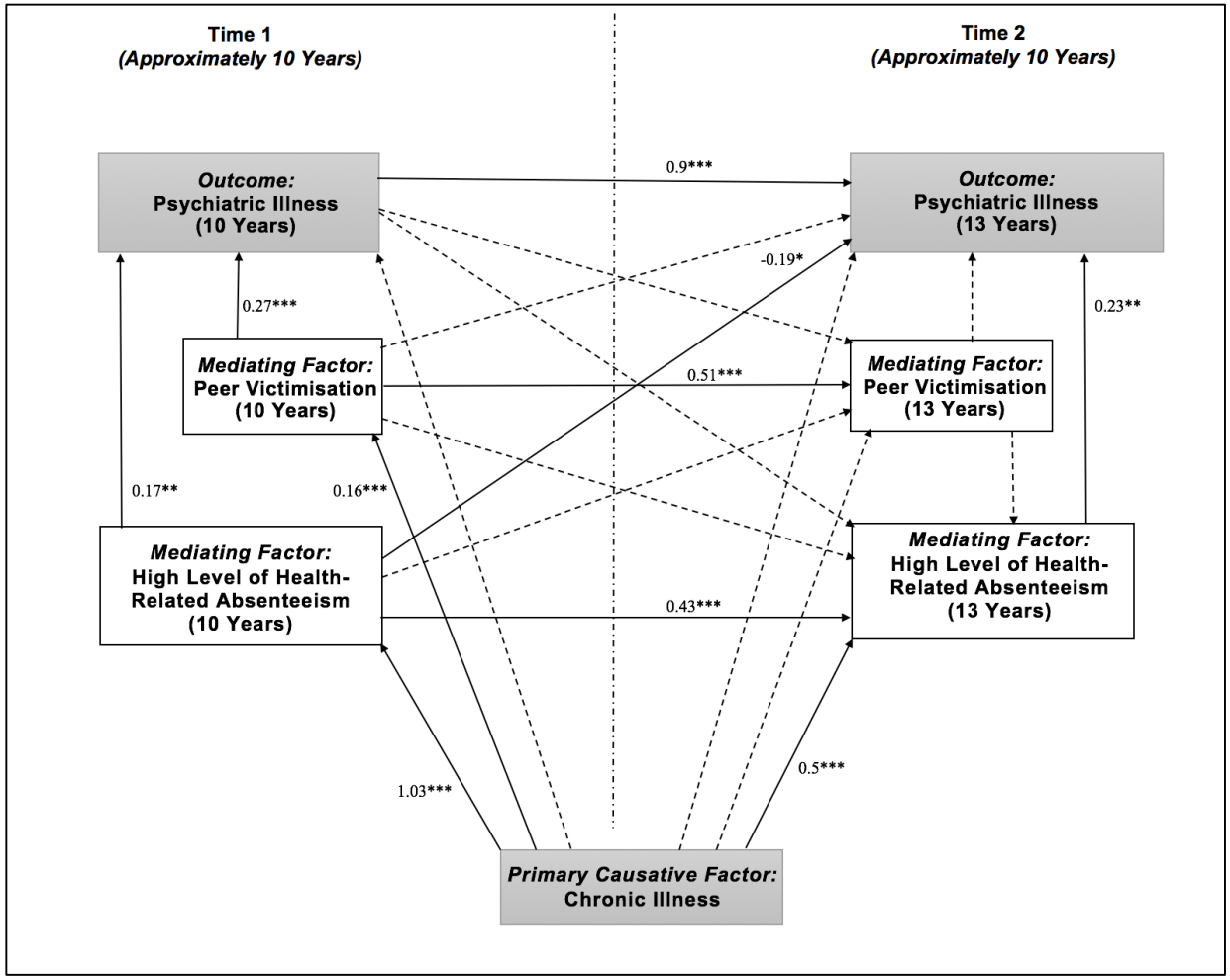


Figure 3.3 Illustrated results of the path model tested in MPlus© software (*p<0.05; **p<0.01; ***p<0.001; significant pathways: bold; non-significant pathways: dashes)

3.2.4.4 Sensitivity analyses

The model was re-designed using health ratings at 10 years and health ratings at 13 years as two independent variables in the prediction of the mediating variables and mental health outcomes, as opposed to a primary causative factor of chronic illness as in the primary model. This was to ensure that the longitudinal analyses were not merely a reflection of concurrent associations of health to mental health outcomes. An illustration of this model can be seen in Figure 3.4. Even though the measure of peer victimisation at 12.5 years preceded the assignation of the health ratings in the age 13 questionnaire, this was depicted as a concurrent measure in the path model given that the mediating role of this variable within time was the variable of interest.

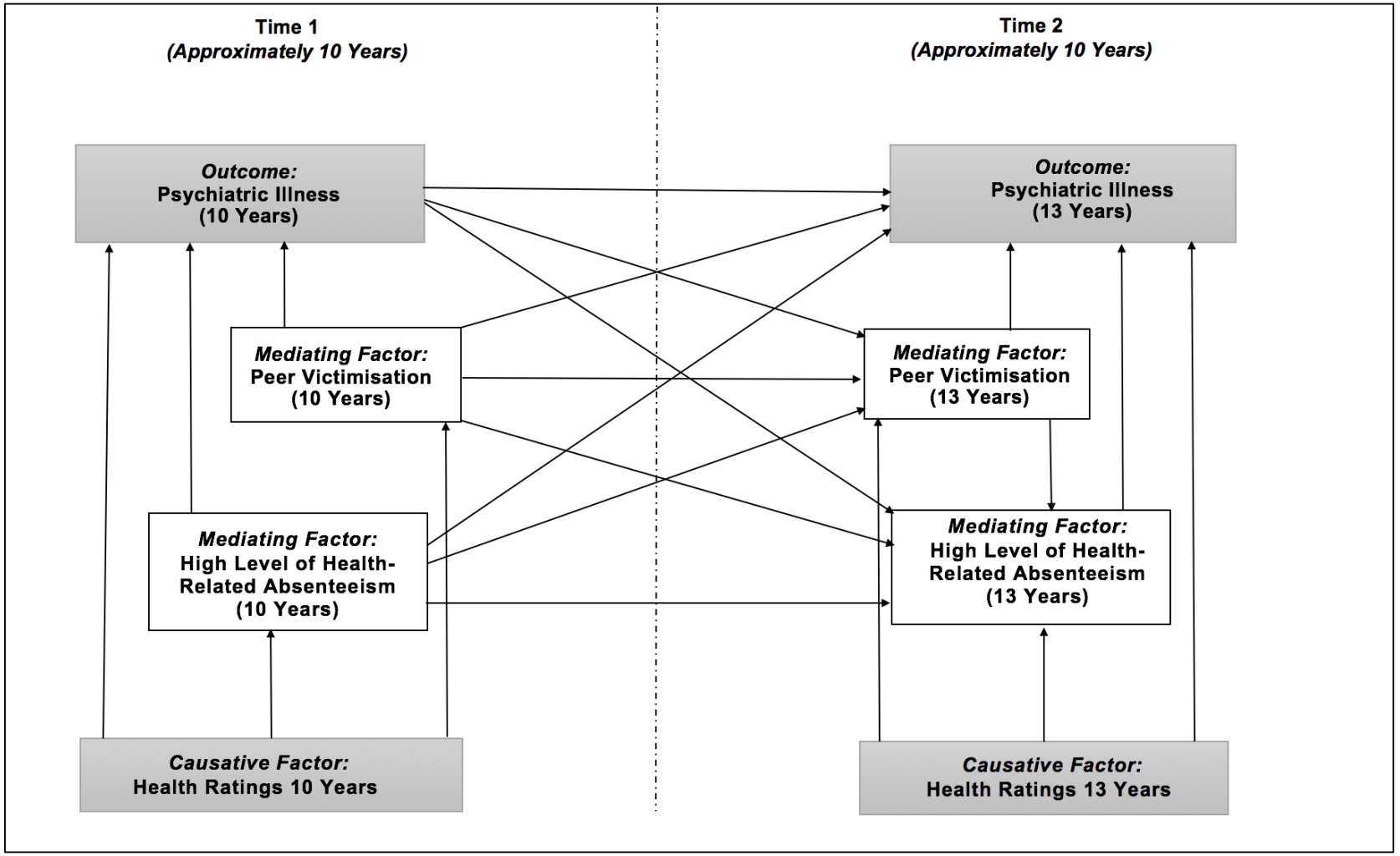


Figure 3.4 Design of the path model used in the sensitivity analyses

This model was also tested for goodness of fit to the ALSPAC data using MPlus© software, based on 5721 observations, 4101 (71.68%) of whom had complete data across all model variables. The chi-square test was significant ($p<0.001$), but the alternative fit indices were just within the guidelines of acceptable ranges (RMSEA guideline: 0.06 or under, RMSEA for model: 0.04 (90% CI: 0.032 – 0.049); CFI guideline: 0.95 or over: CFI for model: 0.968).

A summary of the model results can be seen in Table 3.22. These results are also illustrated in Figure 3.5 for clarity, with statistically significant pathways depicted in bold and non-significant pathways depicted in dashes. Many of the indications of the model results contrast with that of the primary model. In this model, peer victimisation did not play a mediating role in the mental health outcomes associated with health ratings at 10 years, but rather this association was fully mediated by high levels of health-related absenteeism. Moreover, it should be noted that peer victimisation at 12.5 years was associated with health ratings at 13 years, which is a contrast to the non-significant associations between peer victimisation at 12.5 years and chronic health problems in the primary model. However, consistent with this primary model, peer victimisation at 12.5 years did not lead to higher rates of psychiatric illness at 13 years in a statistically significant fashion. It should be noted that the association between health ratings and mental health outcomes at 13 years were not fully mediated by the variables in the model. However, consistent with the primary path model, high levels of health-related absenteeism was the most consistent mediator of the association between health ratings and mental health outcomes over time, mediating this association both within time and across time.

Table 3.22 Summary of results of the model used for sensitivity analyses

	Beta Estimate	Standard Error	Est/Standard Error	Two-Tailed P Value
Psychiatric Illness 10 Years on				
Health Ratings 10 Years	0.1	0.06	1.55	0.120
Health-Related Absenteeism 10 Years	0.14	0.04	3.28	0.002
Peer Victimisation 10 Years	0.25	0.05	5.37	0.000
Psychiatric Illness 13 Years on				
Health Ratings 13 Years	0.25	0.08	2.93	0.003
Psychiatric Illness 10 Years	0.92	0.08	11.94	0.000
Health-Related Absenteeism 13 Years	0.2	0.06	3.12	0.002
Peer Victimisation 12.5 Years	-0.002	0.07	-0.03	0.976
Health-Related Absenteeism 10 Years	-0.18	0.07	-2.75	0.006
Peer Victimisation 12.5 Years	-0.004	0.082	-0.054	0.957
Health-Related Absenteeism 10 Years on				
Health Ratings 10 Years	0.71	0.04	18.05	0.000
Health-Related Absenteeism 13 Years on				
Health Ratings 13 Years	0.74	0.04	18.55	0.000
Health-Related Absenteeism 10 Years	0.39	0.03	13.84	0.000
Psychiatric Illness 10 Years	0.02	0.04	0.4	0.688
Peer Victimisation 12.5 Years	0.03	0.04	0.7	0.486

Peer Victimisation 10 Years	-0.01	0.05	-0.24	0.814
Peer Victimisation 10 Years on Health Ratings 10 Years	0.03	0.04	0.71	0.48
Peer Victimisation 12.5 Years Health Ratings 13 Years	0.23	0.05	4.46	0.000
Peer Victimisation 10 Years	0.56	0.04	13.24	0.000
Psychiatric Illness 10 Years	0.08	0.05	1.59	0.112
Health-Related Absenteeism 10 Years	0.03	0.04	0.86	0.392

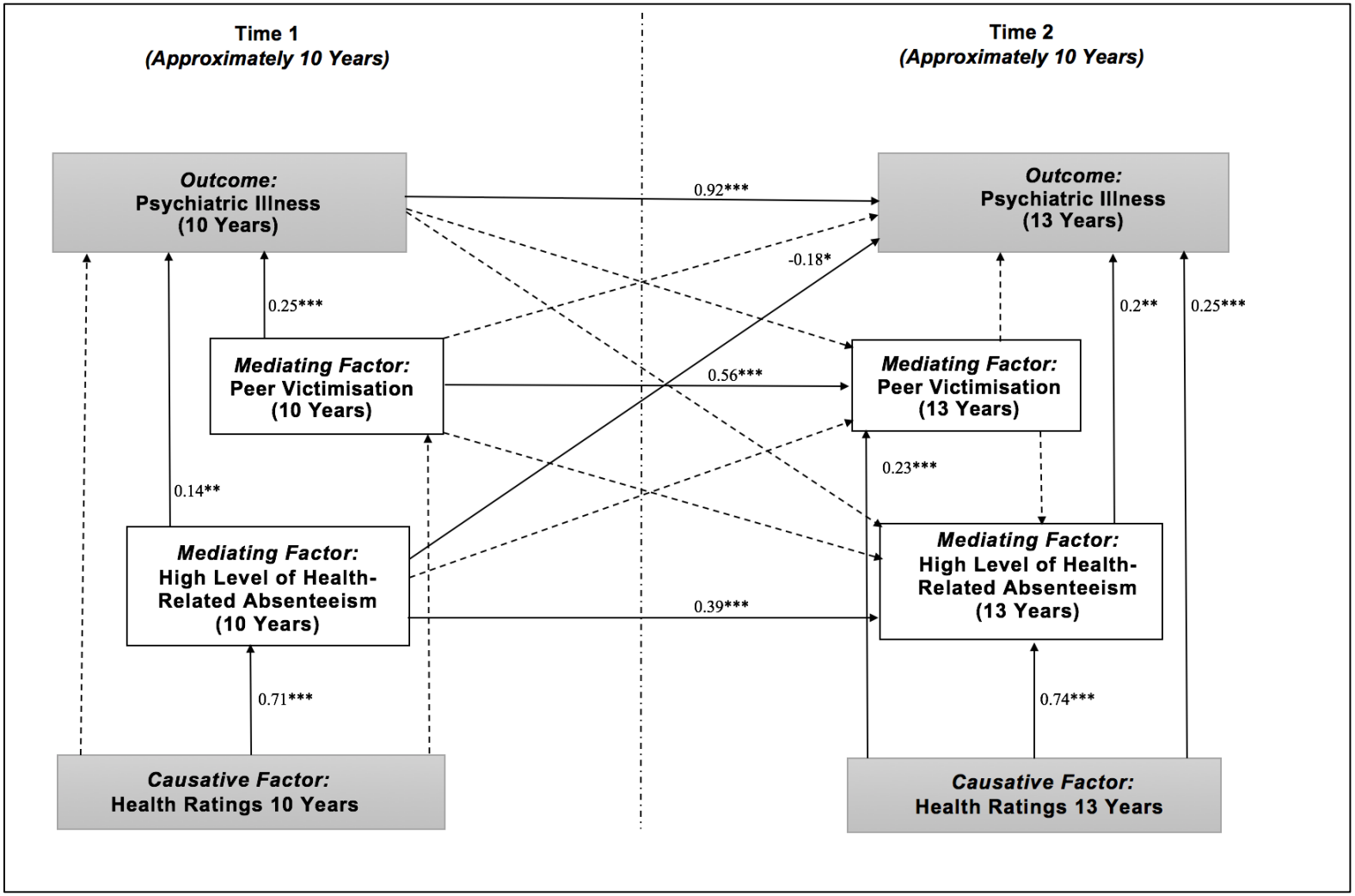


Figure 3.5 Illustrated results of the path model used in sensitivity analyses (*p<0.05; **p<0.01; ***p<0.001 significant pathways: bold; non-significant pathways: dashes)

3.2.4.5 Summary of findings

These analyses indicated that the association between chronic health problems and mental health outcomes at 10 and 13 years was fully mediated by high levels of health-related school absenteeism and peer victimisation. However, when controlling for the strong mediating association of peer victimisation to poor mental health outcomes at age 10, peer victimisation did not continue to independently predict mental health outcomes at 13 years. Instead, a high level of health-related school absenteeism was the most consistent predictor of mental health outcomes both within time and across time. It should be noted that, in contrast to the underlying cascade theory on which the design was based, mental health outcomes at 10 years showed no association with the mediating variables of the mental health outcomes at 13 years, meaning that a negative cascade could not be identified in the association of chronic health problems to rates of psychiatric illness.

Sensitivity analyses supported the view that the longitudinal analyses were reflecting unique associations of chronic health problems to psychiatric illness over time, rather than just concurrent associations of physical health to mental health outcomes. In the sensitivity model, which used health ratings at 10 and 13 years as the primary independent variables, significant differences in the association of health to rates of psychiatric illness were observed. Peer victimisation did not play a strong mediating role in mental health outcomes at 10 years, but was associated with health ratings at 13 years. Moreover, the variables in the model did not fully mediate the association between health ratings and rates of psychiatric illness at 13 years. However, as in the primary path model, a high-level of health-related absenteeism was the most consistent predictor of mental health outcomes both within time and across time.

3.2.5 Comparative analyses of the associated mental health outcomes of asthma diagnosis

3.2.5.1 Cross-Sectional associations of asthma diagnosis to prevalence rates of psychiatric illness

3.2.5.1.1 The age 10 child-based questionnaire

3.2.5.1.1.1 Descriptive analyses

Table 3.23 outlines the breakdown of all variables used in the associative models in the age 10 cross-sectional sample by asthma status, as well as examining prevalence rates of emotional, anxiety, and behavioural disorders. While a more equivalent gender distribution was indicated in the comparative group, males were slightly more over-represented in the asthma sample. In addition, parents of children with a reported asthma diagnosis were more likely to report a history of mental illness ($p<0.01$). Significantly higher prevalence rates of psychiatric illness were identified in children living with asthma, and this was reflected in underlying rates of emotional and anxiety disorders. However, no differences in the rates of behavioural disorders were indicated between the healthy comparative sample and children diagnosed with asthma. Finally, there was no difference detected between the healthy, comparative sample and children with asthma on the measure of 'socio-economic status' (i.e. housing tenure) at this cross-sectional wave.

Table 3.23 Breakdown of all measures used in the age 10 cross-sectional binomial logistic regression models by asthma status, and comparative statistics

	Healthy Comparative Sample (n=3861)	**Asthma Sample (n=1698)**	**Group Comparative Tests**
Gender, N(%)			
Male	1960 (50.76%)	972 (57.24%)	
Female	1901 (49.24%)	726 (42.76%)	Chi^2:19.87
Missing	-	-	(p<0.01)
Socio-Economic Status (i.e. Housing Tenure), N(%)			
Owned/Mortgaged	1385 (35.87%)	587 (34.57%)	
Rented Privately	40 (1.04%)	18 (1.06%)	
Council/Housing Association	146 (3.78%)	57 (3.36%)	Chi^2:0.31
Missing Data	2290 (59.31%)	1036 (61.01%)	(ns)
History of Parental Mental Illness, N(%)			
No Reported History of Parental Mental Illness	2740 (70.97%)	1118 (65.84%)	
History of Parental Mental Illness	458 (11.86%)	238 (14.02%)	Chi^2: 7.67
Missing Data	663 (17.17%)	342 (20.14%)	(p<0.01)
Any Psychiatric Disorder DAWBA, N(%)			
No	3673 (95.13%)	1583 (93.23%)	
Yes	179 (4.64%)	111 (6.54%)	Chi^2: 8.62
Missing	9 (0.23%)	4 (0.24%)	(p<0.01)
Any Emotional Disorder DAWBA, N(%)			
No	3778 (97.85%)	1643 (96.76%)	
Yes	74 (1.92%)	51 (3%)	Chi^2: 6.34
Missing	9 (0.23%)	4 (0.24%)	(p<0.05)
Any Anxiety Disorder DAWBA, N(%)			
No	3795 (98.29%)	1655 (97.47%)	
Yes	57 (1.48%)	39 (2.3%)	Chi^2: 4.68
Missing	9 (0.23%)	4 (0.24%)	(p<0.05)

Any Behavioural Disorder DAWBA, N(%)			
No	3714 (96.19%)	1621 (95.47%)	
Yes	109 (2.82%)	57 (3.36%)	*Chi*^{2}: 1.19
Missing	38 (0.98%)	20 (1.18%)	(ns)

3.2.5.1.1.2 Primary associative models

The resulting odds ratio estimates of the three binomial logistic regression models are presented in Table 3.24. In the unadjusted model, asthma diagnosis was associated with a 40% increased rate in the odds of mental illness, an association which reached the threshold of statistical significance ($p<0.01$). Although the magnitude of this association was consistent across the two adjusted models, the association in the more fully adjusted model, which included all three preselected covariates, was not statistically significant. As the likelihood ratio tests indicated that the addition of the variables of 'socio-economic status' and 'history of parental mental illness' did not improve the fit of the model (LR chi^2: 6.37, $p>0.05$), it is likely that this inconsistent finding can be attributed to the loss of analytic power resulting from the reduced model size. However, adjustments for gender did significantly improve the fit of the associative model due to the strong association between male gender of the study child and an increased rate of psychiatric illness at this wave (LR chi^2: 6.37, $p<0.001$).

Table 3.24 Odds ratios and 95% confidence intervals for the cross-sectional association of asthma to rates of psychiatric illness at 10 years

	Model N	**Asthma Diagnosis**	
		N	**Odds Ratio (95% Confidence Interval)**
Model 1: Basic Model	5546	1694	1.44 (1.13 – 1.84)
Model 2: Model with adjustment for gender of the study child	5546	1694	1.39 (1.09 – 1.78)
Model 3: Model with adjustment for gender, history of parental mental illness and socio-economic status	1893	544	1.41 (0.94 – 2.13)

3.2.5.1.1.3 Tests for interaction

The likelihood ratio tests indicated that there was no significant interaction between gender of the study child and asthma diagnosis in mental health outcomes (LR: 0.44, p>0.05). Furthermore, there was no evidence of an interaction between asthma diagnosis and parental history of mental illness on rates of psychiatric illness at this cross-sectional wave (LR: 0.01, p>05). The test for interaction with socio-economic status was substantially impacted by the missing data on the socio-economic measure. Due to a lack of cases, the interaction term between asthma diagnosis and living in private rental accommodation was dropped in the logistic regression models. Therefore, it was not possible to compare the model with the interaction terms to the model without interaction terms in likelihood ratio testing. However, it seemed unlikely that a significant improvement on model fit would be identified given that the interaction term between asthma diagnosis and living in council/housing association accommodation was statistically non-significant.

3.2.5.1.1.4 Explorations of comparative rates of emotional, anxiety and behavioural disorders

The resulting estimates of the models examining the associated rates of emotional, anxiety and behavioural disorders in children with an asthma diagnosis relative to the healthy comparison group at this cross-sectional wave are summarised in Table 3.25. The associative models were adjusted for gender only, given that this was the only covariate indicated to improve the overall model fit (LR chi^2: 6.37, p<0.001). Consistent with the indications of the descriptive analyses, a significant association was identified between asthma diagnosis and an increased prevalence of emotional disorders (aOR: 1.57 (95% OR: 1.09 – 2.25), p<0.05) and anxiety disorders (aOR: 1.54 (95% OR: 1.02 – 2.33), p<0.05) only. Although rates of behavioural disorders were approximately 14% higher in the asthma sample relative to the healthy comparative group, this association was not statistically significant.

Table 3.25 Odds ratios and 95% confidences intervals for the cross-sectional association of asthma to rates of emotional, anxiety, and behavioural disorders at 10 years

	Model N	Asthma Diagnosis	
		N	Odds Ratio (95% Confidence Interval)
Model 1: "Any Emotional Disorder" Adjusted for gender	5546	1694	1.57 (1.09 – 2.25)
Model 2: "Any Anxiety Disorder" Adjusted for gender	5546	1694	1.54 (1.02 – 2.33)
Model 3: "Any Behavioural Disorder" Adjusted for gender	5501	1678	1.14 (0.82 – 1.58)

3.2.5.1.1.5 Sensitivity analyses

Although the magnitude of the estimated relationship between asthma diagnosis and psychiatric illness was consistent in the more fully adjusted model, which adjusted for the effects of all three preselected covariates, this association did not reach the level of statistical significance. Due to the indications of the likelihood ratio tests, it seemed likely that this non-significant association was a consequence of the reduced sample size in the more fully adjusted model. This hypothesis was supported by analyses with the imputed datasets (see Table 3.26). Significantly, the magnitude of the estimated odds ratio was comparable across the two analyses. However, the association in the larger imputed samples met the threshold for statistical significance ($p<0.01$).

Table 3.26 Odds ratios and 95% confidence intervals for the cross-sectional association of asthma to rates of psychiatric illness at 10 years based on complete case analysis, and based on analysis with imputed data

	Model N	Asthma Diagnosis	
		N	Odds Ratio (95% Confidence Interval)
Complete Case Analysis	1893	544	1.41 (0.94 – 2.13)
Analysis with the Imputed Datasets	5559	1698	1.39 (1.09 – 1.78)

3.2.5.1.2 The age 13 child-based questionnaire

3.2.5.1.2.1 Descriptive analyses

Table 3.27 outlines the breakdown of all variables used in the associative models in the age 13 cross-sectional sample by asthma status, as well as examining prevalence rates of emotional, anxiety, and behavioural disorders. A significant group variation was observed on the variable of 'parental history of mental illness', with parents of children with an asthma diagnosis more likely to report a history of mental illness. Borderline significant variations were indicated on the variables of gender and overall rates of psychiatric disorders, with there being a higher percentage of males amongst children with an asthma diagnosis, and a higher percentage of children presenting with a psychiatric disorder. However, a significantly higher prevalence of anxiety disorders was indicated among children with an asthma diagnosis at this cross-sectional wave. There was no identifiable sample difference on the variable of 'socio-economic status' (i.e. low household income).

Table 3.27 Breakdown of all measures used in the age 13 cross-sectional binomial logistic regression models by asthma status, and comparative statistics

	Healthy Comparative Sample (n=3398)	**Asthma Sample (n=1643)**	**Group Comparative Tests**
Gender, N(%)			
Male	1757 (51.71%)	897 (54.6%)	
Female	1642 (48.29%)	746 (45.4%)	Chi^2:3.76
Missing	-	-	(p=0.054)
Socio-Economic Status (i.e. Low Household Income), N(%)			
Average/High Income	935 (27.52%)	413 (25.14%)	
Low Income	224 (6.59%)	94 (5.72%)	Chi^2:0.14
Missing Data	2239 (65.89%)	1136 (69.14%)	(ns)
History of Parental Mental Illness, N(%)			
No Reported History of Parental Mental Illness	2430 (71.51%)	1092 (66.46%)	
History of Parental Mental Illness	385 (11.33%)	227 (13.82%)	Chi^2: 8.89
Missing Data	583 (17.16%)	324 (19.72%)	(p<0.01)
Any Psychiatric Disorder DAWBA, N(%)			
No	3259 (95.91%)	1556 (94.7%)	
Yes	139 (4.09%)	87 (5.3%)	Chi^2: 3.75
Missing	-	-	(p=0.053)
Any Emotional Disorder DAWBA, N(%)			
No	3357 (98.79%)	1614 (98.23%)	
Yes	41 (1.21%)	29 (1.77%)	Chi^2: 2.52
Missing	-	-	(ns)
Any Anxiety Disorder DAWBA, N(%)			
No	3372 (99.23%)	1620 (98.6%)	
Yes	26 (0.77%)	23 (1.4%)	Chi^2: 4.64
Missing	-	-	(p<0.05)

Any Behavioural Disorder DAWBA, N(%)			
No	3274 (96.35%)	1567 (95.37%)	
Yes	97 (2.85%)	61 (3.71%)	*Chi*^{2}: 2.71
Missing	27 (0.79%)	15 (0.91%)	(ns)

3.2.5.1.2.2 Primary associative models

The resulting odds ratio estimates of the three binomial logistic regression models are presented in Table 3.28. Although an association was identified between asthma diagnosis and an increased rate of psychiatric illness in the unadjusted model, this association was just above the threshold of statistical significance (p=0.053). The magnitude of this association was slightly weakened when adjustments were made for the effects of gender of the study child, although it was again strengthened in the more fully adjusted model which controlled for the effects of 'socio-economic status' and 'history of parental mental illness' in addition to 'gender'. The imprecision indicated in the confidence intervals, and the non-significant values of the likelihood ratio tests (LR chi^2: 0.45, p>0.05) suggests that this strengthening effect may be due to imprecision in the estimates as a consequence of the loss of analytic power. In contrast, the adjustment for gender significantly improved the fit of the associative model due to strong association between male gender of the study child and an increased rate of psychiatric illness at this cross-sectional wave (LR chi^2: 13.44, p>0.001).

Table 3.28 Odds ratios and 95% confidence intervals for the cross-sectional association of asthma to rates of psychiatric illness at 13 years

	Model N	**Asthma Diagnosis**	
		N	**Odds Ratio (95% Confidence Interval)**
Model 1: Basic Model	5041	1643	1.31 (1.0 – 1.73)
Model 2: Model with adjustment for gender of the study child	5041	1643	1.29 (0.98 – 1.7)
Model 3: Model with adjustment for gender, history of parental mental illness and socio-economic status	1409	416	1.43 (0.86 – 2.39)

3.2.5.1.2.3 Tests for interaction

The likelihood ratio testing indicated that there was no significant interaction between asthma diagnosis and gender of the study child in mental health outcomes at this cross-sectional wave (LR chi^2: 2.6; $p>0.05$). Furthermore, there was no evidence of an interaction between asthma diagnosis and parental history of mental illness in the associated rates of psychiatric illness (LR chi^2: 3.09; $p>0.05$). Finally, no interaction effect was indicated between asthma diagnosis and socio-economic status in the mental health outcomes at this cross-sectional wave (LR chi^2: 0.18, $p>0.05$).

3.2.5.1.2.4 Explorations of comparative rates of emotional, anxiety and behavioural disorders

The resulting estimates of the models examining the associated rates of emotional, anxiety and behavioural disorders in chronically ill children rated as “quite healthy, but a few minor problems” and “sometimes quite ill/almost always unwell” relative to children rated as “very healthy, no problems on the baseline” are summarised in Table 3.29. The associative models were adjusted for gender only, given that this was the only covariate indicated to improve the overall associative model fit (LR chi^2: 13.44, $p<0.001$). Although asthma diagnosis was associated with a rise in the prevalence in all three types of disorder at this wave, the only association to reach the level of statistical significance was that between asthma diagnosis and the prevalence of anxiety disorders at 13 years ($p<0.05$).

Table 3.29 Odds ratios and 95% confidence intervals for the cross-sectional association of asthma to rates of emotional, anxiety, and behavioural disorders at 13 years

	Model N	Asthma Diagnosis	
		N	Odds Ratio (95% Confidence Interval)
Model 1: "Any Emotional Disorder" Adjusted for gender	5041	1643	1.46 (0.9 – 2.36)
Model 2: "Any Anxiety Disorder" Adjusted for gender	5041	1643	1.84 (1.04 – 3.23)
Model 3: "Any Behavioural Disorder" Adjusted for gender	4999	1628	1.3 (0.94 – 1.8)

3.2.2.1.2.5 Sensitivity analyses

The imprecision in the estimates in the more fully adjusted model examining the association of asthma diagnosis to mental health outcomes at age 13 was high, and indicated a stronger association between asthma diagnosis and rates of psychiatric illness than that seen in the crude and gender-adjusted model. Explorations of model fit using likelihood ratio testing suggested that this strengthening effect was due to data attrition, rather than a true confounding impact of the covariates of 'parental history of mental illness' and 'socio-economic status' on the association between asthma and rates of psychiatric illness. The analyses with the imputed dataset supported this hypothesis (see Table 3.30), with the magnitude of the odds ratio being much lower in the imputed model, and consistent with the gender-adjusted model based on complete cases (i.e. 1.29 (95% CI: 0.98 – 1.7)).

Table 3.30 Odds ratios and 95% confidence intervals for the cross-sectional association of asthma to rates of psychiatric illness at 13 years based on complete case analysis, and based on analysis with imputed data

	Model N	Asthma Diagnosis	
		N	Odds Ratio (95% Confidence Interval)
Complete Case Analysis	1409	416	1.43 (0.86 – 2.39)
Analysis with the Imputed Datasets	5041	1643	1.29 (0.98 – 1.7)

3.2.5.1.3 Summary of the comparative cross-sectional analyses

Table 3.31 summarises the findings from the cross-sectional analyses using the generalised measure of chronic health problems and compares them to the analyses using asthma diagnoses as the independent variable.

Table 3.31 Summary table comparing the indications of the cross-sectional analyses using the generalised chronic illness measure to those using asthma diagnoses as the independent variable

	Findings of Associative Analyses	**Analyses of More Specific Groupings of Disorders**	**Sensitivity of Estimations**
	Age 10		
Primary	Children with chronic health problems rated as "quite healthy, but a few minor problems" were approximately 69% more likely to present with a mental health disorder than those rated as "very healthy, no problems" (gender-adjusted OR: 1.69 (95% CI: 1.31 – 2.19)) Children with chronic health problems rated as being "sometimes quite ill" or "almost always unwell" were approximately 4 times more likely to present with a mental health disorder than those rated as "very healthy, no problems" (gender-adjusted OR: 4.65 (95% CI: 2.38 – 9.06)) No interaction effects were detected in the prediction of mental health outcomes.	Associations were detected between chronic health problems (both minor and more severe) and an increased rate of emotional, anxiety and behavioural disorders. However, the associations with rates of behavioural disorders were weaker than those indicated for anxiety and emotional disorders, and was not statistically significant for the "sometimes quite ill/almost always unwell" group	Associations of a lower magnitude were identified in the model which adjusted for the effects of all three preselected covariates. Analyses with the imputed datasets suggested that this weakening effect was due to data attrition, rather than a confounding effect of these variables on the associations identified.
Asthma	Children with an asthma diagnosis were approximately 40% more likely to present with a	Associations were identified between asthma diagnosis and an increased prevalence of all three types of underlying disorders (i.e.	The association between asthma diagnosis and psychiatric illness did not reach the threshold of statistical

	mental health disorder than children rated as "very healthy, no problems" (gender-adjusted OR: 1.39 (95% CI: 1.09 – 1.78)). No interaction effects were detected in the prediction of mental health outcomes.	emotional disorders, anxiety disorders, and behavioural disorders) at this wave. However, only the associations with an increased prevalence of emotional and anxiety disorders met the threshold of statistical significance ($p<0.05$).	significance in the model which adjusted for the effects of all three preselected covariates. Analyses with the imputed datasets suggested that this weakening effect was due to data attrition, rather than a confounding effect of these variables on the association identified.
	Age 13		
Primary	Children with chronic health problems rated as "quite healthy, but a few minor problems" were approximately 54% more likely to present with a mental health disorder than those rated as "very healthy, no problems" (gender-adjusted OR: 1.54 (95% CI: 1.17 – 2.04)) Children with chronic health problems rated as being "sometimes quite ill" or "almost always unwell" were approximately 3 times more likely to present with a mental health disorder than those rated as "very healthy, no problems" (gender-adjusted OR: 3.37 (95% CI: 1.65 – 6.9)) No interaction effects were detected in the prediction of mental health outcomes.	Associations were identified between both ratings of ill health and an increased prevalence of all three groupings of disorders (i.e. emotional disorders, anxiety disorders, and behavioural disorders) at this wave. However, the associations with rates of behavioural disorders were weaker than those indicated for anxiety and emotional disorders, and was not statistically significant for the "quite healthy, but a few minor problems" group	Associations of a lower magnitude were identified in the model which adjusted for the effects of all three preselected covariates. Analyses with the imputed datasets suggested that this weakening effect was due to data attrition, rather than a confounding effect of these variables on the associations identified.
Asthma	Children with an asthma diagnosis were approximately 30% more likely to present with a	An increased prevalence of all types groups of disorders was indicated among children with asthma, with the association with	The association between asthma diagnosis and psychiatric illness was of a higher magnitude in the model

	mental health disorder than children rated as "very healthy, no problems" (gender-adjusted OR: 1.29 (95% CI: 0.98 – 1.7)). This association did not reach the threshold of statistical significance ($p>0.05$). No interaction effects were detected in the prediction of mental health outcomes.	an increased prevalence of anxiety disorders reaching the level of statistical significance ($p<0.05$).	which adjusted for the effects of all three preselected covariates. Analyses with the imputed datasets suggested that this effect was due to data attrition, rather than a confounding effect of these variables on the association between asthma diagnoses and rates of psychiatric illness.

3.2.5.2 Longitudinal analyses

3.2.5.2.1 Descriptive analyses

Table 3.32 outlines the breakdown of all variables used in the associative models in the longitudinal cohort by asthma status, as well as examining prevalence rates of emotional, anxiety, and behavioural disorders at each wave. There was a significantly higher prevalence of psychiatric illness indicated among children with an asthma diagnosis when compared with the comparison group across all three measurement waves (all $p<0.05$). However, asthma diagnoses showed more inconsistent associations with rates of the more narrowed groupings of emotional, anxiety, and behavioural disorders over the three measurement waves. Please also note that children with asthma diagnoses had a higher percentage of missing data on the DAWBA than the comparative group at the age 13 measurement wave. As was expected based on the cross-sectional analyses of the age 10 child-based questionnaire, the parents of children with an asthma diagnosis were more likely to report a history of mental illness, and there was an over-representation of males among this group. However, there was no significant difference identified between children with asthma and the healthy comparative sample on the measure of 'socio-economic status' (i.e. low household income).

Table 3.32 Breakdown of all measures used in the longitudinal binomial logistic regression models by asthma status, and comparative statistics

	Healthy Comparative Sample (n=2313)	**Asthma Sample (n=1698)**	**Group Comparative Tests**
Gender, N(%)			
Male	1211 (52.36%)	972 (57.24%)	
Female	1102 (47.64%)	726 (42.76%)	Chi^2: 9.43
Missing	-	-	(p<0.01)
Socio-economic status (i.e. Low Household Income), N(%)			
Average/High Income	632 (27.32%)	436 (25.68%)	
Low Income	149 (6.44%)	105 (6.18%)	Chi^2: 0.02 (ns)
Missing Data	1532 (66.23%)	1157 (68.14%)	
Parental Mental Illness, N(%)			
No Reported History of Parental Mental Illness	1699 (73.45%)	1118 (65.84%)	
History of Parental Mental Illness	263 (11.37%)	238 (14.02%)	Chi^2: 10.76 (p<0.01)
Missing Data	351 (15.18%)	342 (20.14%)	
Any Psychiatric Disorder DAWBA 10 Years, N(%)			
No	2215 (95.76%)	1583 (93.23%)	
Yes	97 (4.19%)	111 (6.54%)	Chi^2: 11.03
Missing	1 (0.04%)	4 (0.24%)	(p<0.01)
Any Emotional Disorder DAWBA 10 Years, N(%)			
No	2228 (98.66%)	1643 (96.76%)	
Yes	30 (1.3%)	51 (3%)	Chi^2: 14.48
Missing	1 (0.04%)	4 (0.24%)	(p<0.001)
Any Anxiety Disorder DAWBA 10 Years, N(%)			
No	2291 (99.05%)	1655 (97.47%)	
Yes	21 (0.91%)	39 (2.3%)	Chi^2: 12.88
Missing	1 (0.04%)	4 (0.24%)	(p<0.001)

Any Behavioural Disorder DAWBA 10 Years, N(%)			
No	2240 (96.84%)	1621 (95.47%)	
Yes	61 (2.64%)	57 (3.36%)	Chi^2: 1.88
Missing	12 (0.52%)	20 (1.18%)	(ns)
Any Psychiatric Disorder DAWBA 13 Years, N(%)			
No	2241 (96.89%)	1269 (74.73%)	
Yes	72 (3.11%)	73 (4.3%)	Chi^2: 5.04
Missing	-	356 (20.97%)	($p<0.05$)
Any Emotional Disorder DAWBA 13 Years, N(%)			
No	2291 (99.05%)	1321 (77.8%)	
Yes	22 (0.95%)	21 (1.24%)	Chi^2: 2.75
Missing	-	356 (20.97%)	(ns)
Any Anxiety Disorder DAWBA 13 Years, N(%)			
No	2297 (99.31%)	1328 (78.21%)	
Yes	16 (0.69%)	14 (0.82%)	Chi^2: 1.29
Missing	-	356 (20.97%)	(ns)
Any Behavioural Disorder DAWBA 13 Years, N(%)			
No	2248 (97.19%)	1271 (74.85%)	
Yes	49 (2.12%)	56 (3.3%)	Chi^2: 13.02
Missing	16 (0.69%)	371 (21.85%)	($p<0.001$)
Any Psychiatric Disorder DAWBA 15 Years, N(%)			
No	1438 (62.17%)	922 (54.3%)	
Yes	68 (2.94%)	77 (4.53%)	Chi^2: 11.22
Missing	807 (34.89%)	699 (41.17%)	($p<0.01$)
Any Emotional Disorder DAWBA 15 Years, N(%)			
No	1474 (63.73%)	957 (56.36%)	
Yes	25 (1.08%)	37 (2.18%)	Chi^2: 10.4
Missing	814 (35.19%)	704 (41.46%)	($p<0.01$)

Any Anxiety Disorder DAWBA 15 Years, N(%)			
No	1483 (64.12%)	976 (57.48%)	
Yes	16 (0.69%)	18 (1.06%)	*Chi*^{2}: 2.46
Missing	814 (35.19%)	704 (41.46%)	(ns)
Any Behavioural Disorder DAWBA 15 Years, N(%)			
No	1461 (63.16%)	957 (56.36%)	
Yes	45 (1.95%)	42 (2.47%)	*Chi*^{2}: 2.65
Missing	807 (34.89%)	699 (41.17%)	(ns)

3.2.5.2.2 Primary associative models

Initially three binomial logistic regression models were calculated for each measurement wave in turn, one examining the unadjusted association between asthma diagnosis and psychiatric illness, the next with adjustments for gender and the final model controlling for the effects of 'gender', 'socio-economic status' and 'parental history of mental illness'. The resulting odds ratios from these binomial logistic regression models are presented in Table 3.33. The reduction of sample size in the crude logistic model at the 13 and 15 year wave is due to missing data on the outcome measure. The unadjusted models indicated an increase in the prevalence of mental health disorders amongst children with an asthma diagnosis at all three time waves. Moreover, the magnitude of this association was comparable at all waves, and remained somewhat consistent when adjustments were made for the hypothesised confounding variables. However, it should be noted that in the more fully adjusted models, these associations did not reach the threshold of statistical significance at any time wave ($p>0.05$). As the likelihood ratio tests indicated that the addition of the variables of 'parental history of mental illness' and 'socio-economic status' did not substantially improve model fit at any of the three measurement waves (LR chi^2 10 Years: 3.41; LR chi^2 13 Years: 2.24; LR chi^2: 1.89; all $p>0.05$), it is likely that, as in the cross-sectional analyses, this weakening effect was a consequence of data attrition. Although adjusting for gender significantly improved the associative model fit at the baseline and 13 year wave due to a strong association between male gender of the study child and an increased rate of psychiatric

illness (LR chi^2 10 Years: 8.13; LR chi^2 13 Years: 7.14; both $p<0.05$), this adjustment did not improve the associative model fit for the 15 year wave (LR chi^2 15 Years: 2.92; $p>0.05$).

Table 3.33 Odds ratios and 95% confidence intervals for the association of asthma to rates of psychiatric illness at each DAWBA wave

	Model 1: Basic Model			**Model 2:** Model with adjustment for gender of the study child			**Model 3:** Model with adjustment for gender, history of parental mental illness and socio-economic status		
	Model N	**Asthma Diagnosis**		**Model N**	**Asthma Diagnosis**		**Model N**	**Asthma Diagnosis**	
		N	**Odds Ratio (95% Confidence Interval)**		**N**	**Odds Ratio (95% Confidence Interval)**		**N**	**Odds Ratio (95% Confidence Interval)**
Age 10 Measurement	4006	1694	1.6 (1.21 – 2.12)	4006	1694	1.57 (1.19 – 2.08)	1120	442	1.67 (0.99 – 2.82)
Age 13 Measurement	3655	1342	1.79 (1.28 – 2.5)	3655	1342	1.76 (1.26 – 2.45)	1030	351	1.88 (0.99 – 3.55)
Age 15 Measurement	2505	999	1.77 (1.26 – 2.47)	2505	999	1.79 (1.28 – 2.51)	728	276	1.72 (0.91 – 3.27)

Three further binomial logistic models were calculated in order to explore the associations between asthma diagnosis and rates of psychiatric illness longitudinally, when controlling for the presence of psychiatric illness at previous waves. ‘Socio-economic status’ and ‘history of parental mental illness’ were not adjusted for in these models due to the indications from likelihood ratio testing which suggested that these covariates did not significantly improve the associative model fit at any wave. The odds ratios indicated from these two models are presented in Table 3.34. These analyses indicated that a diagnosis of asthma remained significantly associated with an increase in psychiatric illness at 13 and 15 years, even after controlling for the presence of psychiatric illness at previous waves.

Table 3.34 Odds ratios and 95% confidence intervals for the association of asthma to rates of psychiatric illness at 13 and 15 years, after adjusting for mental health outcomes at preceding waves

	Age 13 Measurement			Age 15 Measurement		
	Model N	Asthma Diagnosis		Model N	Asthma Diagnosis	
		N	Odds Ratio (95% Confidence Interval)		N	Odds Ratio (95% Confidence Interval)
Model 4: Logistic Model Adjusted for Gender and DAWBA Indications at the Previous Measurement Wave	3651	1339	1.62 (1.13 – 2.3)	2408	140	1.73 (1.21 – 2.48)
Model 5: Logistic Model Adjusted for Gender and DAWBA Indications at the Two Previous Measurement Waves				2406	139	1.69 (1.18 – 2.43)

3.2.5.2.3 Tests for interaction

There was no strong evidence of an interaction effect of asthma diagnosis and gender of the study child on mental health outcomes at any of the three administration waves (LR chi^2 10 Years: 0.01; LR chi^2 13 Years: 2.75; LR chi^2: 0.15; all $p>0.05$). Similarly, no interaction effect was suggested between asthma diagnosis and history of parental mental illness in the associated rates of psychiatric illness across the time period of analysis (LR chi^2 10 Years: 0.01; LR chi^2 13 Years: 1.6; LR chi^2: 0.52; all $p>0.05$). Finally, the test for interaction between asthma diagnosis and socio-economic status was not significant at any of the three measurement waves (LR chi^2 10 Years: 2.98; LR chi^2 13 Years: 0.65; LR chi^2: 0.2; all $p>0.05$).

3.2.5.2.4 Explorations of comparative rates of emotional, anxiety and behavioural disorders

The resulting estimates of the models examining the associated rates of emotional, anxiety and behavioural disorders in children with asthma relative to the healthy, comparative groups at the three measurement waves are summarised in Table 3.35. The associative models were adjusted for gender only, given that this was the only covariate indicated to improve the overall fit of the associative models, specifically at the 10 and 13 year wave. There was high variability identified in the associations with specific groupings of disorders across the waves. Similar to the former analyses of the age 10 questionnaire, although associations between asthma and an increased prevalence of all three types of disorders was indicated, only the associations between asthma diagnosis and emotional and anxiety disorders reached the level of statistical significance ($p<0.001$). In contrast, in the 13 year wave, although associated increases in all disorders were again identified, only the association with an increased rate of behavioural disorders was statistically significant ($p<0.01$). At fifteen years, the only statistically significant association identifiable was between asthma diagnosis and an increased prevalence of emotional disorders ($p<0.01$), although, as at the other waves, an increased rate of all types of disorders was indicated. It should be kept in mind that not only were the analyses possibly biased due to the low prevalence rates of these specific groups of disorders within

ALSPAC, but that analyses were further compromised by data attrition on the age 13 and age 15 measure.

Table 3.35 Odds ratios and 95% confidence intervals for the association of asthma to rates of emotional, anxiety, and behavioural disorders at each DAWBA measurement wave

	Model 1: "Any Emotional Disorder" Adjusted for gender			**Model 2:** "Any Anxiety Disorder" Adjusted for gender			**Model 3:** "Any Behavioural Disorder" Adjusted for gender		
	Model N	**Asthma Diagnosis**		**Model N**	**Asthma Diagnosis**		**Model N**	**Asthma Diagnosis**	
		N	**Odds Ratio (95% Confidence Interval)**		**N**	**Odds Ratio (95% Confidence Interval)**		**N**	**Odds Ratio (95% Confidence Interval)**
Age 10 Measurement	4006	1694	2.38 (1.51 – 3.75)	4006	1694	2.57 (1.51 – 4.39)	3979	1678	1.25 (0.86 – 1.8)
Age 13 Measurement	3655	1342	1.62 (0.88 – 2.95)	3655	1342	1.49 (0.72 – 3.05)	3624	1327	1.99 (1.35 – 2.94)
Age 15 Measurement	2493	994	2.37 (1.42 – 3.97)	2493	994	1.78 (0.9 – 3.52)	2505	999	1.42 (0.92 – 2.18)

Three further binomial logistic models were calculated to identify the associations between asthma and rates of specific groups of psychiatric disorders longitudinally when adjusting for the presence of psychiatric illness at previous waves. The resulting odds ratios estimates from these analyses can be seen in Table 3.36. When controlling for pre-existing psychiatric disorders, asthma diagnosis was independently associated with a statistically significant increased prevalence of behavioural disorders at 13 years ($p<0.01$), and a statistically significant increased prevalence of emotional disorders at 15 years ($p<0.01$). However, it should be noted that asthma was independently associated with an increased prevalence of all types of disorders at the 13 and 15 year waves, although these associations were not significantly significant.

Table 3.36 Odds ratios and 95% confidence intervals for the association of chronic illness to rates of emotional, anxiety, and behavioural disorders at 13 and 15 years, after adjusting for mental health outcomes at previous waves

	Model 1: "Any Emotional Disorder" Adjusted for gender			**Model 2:** "Any Anxiety Disorder" Adjusted for gender			**Model 3:** "Any Behavioural Disorder" Adjusted for gender		
	Model N	**Asthma Diagnosis**		**Model N**	**Asthma Diagnosis**		**Model N**	**Asthma Diagnosis**	
		N	**Odds Ratio (95% Confidence Interval)**		**N**	**Odds Ratio (95% Confidence Interval)**		**N**	**Odds Ratio (95% Confidence Interval)**
Age 13 Measurement (Adjusted for Presence of Mental Illness at 10 Years)	3651	1339	1.42 (0.77 – 2.64)	3651	1339	1.29 (0.62 – 2.69)	3621	1325	1.81 (1.2 – 2.73)
Age 15 Measurement (Adjusted for Presence of Mental Illness at 13 Years)	2396	897	2.51 (1.49 – 4.23)	2396	897	1.98 (1.0 – 3.92)	2408	902	1.21 (0.75 – 1.94)
Age 15 Measurement (Adjusted for Presence of Mental Illness at 10 or 13 Years)	2394	895	2.44 (1.45 – 4.13)	2394	895	2.0 (1.01 – 3.96)	2406	900	1.21 (0.75 – 1.95)

3.2.5.2.5 Sensitivity analyses

A weakening effect was recorded in the model adjusting for 'gender', 'socio-economic status', and 'history of the parental mental illness' at the age 10 wave. Consistent with the evidence, it was hypothesised that this effect was due to the reduced sample size rather than a confounding effect of the covariates. Sensitivity analyses with the imputed datasets seemed to support this hypothesis (see Table 3.37). The estimates from the imputed model were of a similar magnitude to the gender-adjusted model in the complete case analysis, with the association between asthma diagnosis and an increased prevalence of psychiatric illness reaching the threshold of statistical significance ($p<0.01$).

Table 3.37 Odds ratios and 95% confidence intervals for the association of asthma to rates of psychiatric illness at 10 years in the longitudinal complete case analyses, and analyses based on imputed data

	Model N	Asthma Diagnosis	
		N	Odds Ratio (95% Confidence Interval)
Complete Case Analysis	1120	442	1.67 (0.99 – 2.82)
Analysis with the Imputed Datasets	4011	1698	1.56 (1.17 – 2.06)

As high rates of attrition in the DAWBA measurement were noted at the age 13 and 15 waves, all associative binomial logistic regression models were re-calculated in the imputed datasets to explore the consistencies of the associations. The estimated odds ratios for the associations of asthma to psychiatric illness at age 13 in these analyses are compared to those of the complete case analyses in Table 3.38 and Table 3.39. The magnitude of the odds ratios in the unadjusted and gender-adjusted model were of a slightly higher magnitude in the analyses with the imputed datasets when compared to the complete case analysis. In contrast, the magnitude of the odds ratio for the model adjusting for all three preselected covariates was lower in analyses with the imputed datasets, but reached the threshold of statistical significance in this model and the former models ($p<0.01$). Finally, the independent association between asthma and mental health outcomes at

age 13, after controlling for the presence of psychiatric illness at age 10, was highly consistent between the analysis with the imputed dataset and the complete case analysis (see Table 3.39).

Table 3.38 Odds ratios and 95% confidence intervals for the association of asthma to rates of psychiatric illness at 13 years in the longitudinal complete case analyses, and analyses based on imputed data

	Model 1: Basic Model			**Model 2:** Model with adjustment for gender of the study child			**Model 3:** Model with adjustment for gender, history of parental mental illness and socio-economic status		
	Model N	**Asthma Diagnosis**		**Model N**	**Asthma Diagnosis**		**Model N**	**Asthma Diagnosis**	
		N	**Odds Ratio (95% Confidence Interval)**		**N**	**Odds Ratio (95% Confidence Interval)**		**N**	**Odds Ratio (95% Confidence Interval)**
Complete Case Analysis	3655	1342	1.79 (1.28 – 2.12)	3655	1342	1.76 (1.26 – 2.45)	1030	351	1.88 (0.99 – 3.55)
Analysis with the Imputed Datasets	4011	1698	1.85 (1.22 – 2.57)	4011	1698	1.81 (1.3 – 2.52)	4011	1698	1.79 (1.28 – 2.49)

Table 3.39 Odds ratios and 95% confidence intervals for the association of chronic illness to rates of psychiatric illness at 13 years, after controlling for mental health outcomes at 10 years, in the longitudinal complete case analysis, and analysis based on imputed data

	Logistic Model Adjusted for Gender and DAWBA Indications at the 10 Year Measurement Wave		
	Model N	Asthma Diagnosis	
		N	Odds Ratio (95% Confidence Interval)
Complete Case Analysis	3651	1339	1.62 (1.13 – 2.3)
Analysis with the Imputed Datasets	4011	1698	1.63 (1.14 – 2.32)

The estimated odds ratios for the initial three binomial logistic models examining the mental ill-health associations for asthma on the age 15 measurement wave in the imputed datasets are compared to the complete case analyses estimates in Table 3.40, and are subsequently followed by a comparison of the models controlling for pre-existing mental illness in Table 3.41. In a similar pattern to the analyses with imputed data for the age 13 measurement wave, associations between asthma diagnoses and psychiatric illness rates were slightly stronger in the analyses with the imputed longitudinal dataset when compared to the complete case analysis. The magnitude of the odds ratio in the more fully adjusted model was also higher overall in the analyses with the imputed datasets, and reached the threshold of statistical significance (all $p<0.001$). In addition, the independent association between asthma and rates of psychiatric illness, after controlling for the presence of psychopathology at previous waves, was slightly stronger based on the imputed data.

Table 3.40 Odds ratios and 95% confidence intervals for the association of asthma to rates of psychiatric illness at 15 years in the longitudinal complete case analyses, and analyses based on imputed data

	Model 1: Crude Model			**Model 2:** Model with adjustment for gender of the study child			**Model 3:** Model with adjustment for gender, history of parental mental illness and socio-economic status		
	Model N	**Asthma Diagnosis**		**Model N**	**Asthma Diagnosis**		**Model N**	**Asthma Diagnosis**	
		N	**Odds Ratio (95% Confidence Interval)**		**N**	**Odds Ratio (95% Confidence Interval)**		**N**	**Odds Ratio (95% Confidence Interval)**
Complete Case Analysis	2505	999	1.77 (1.26 – 2.47)	2505	999	1.79 (1.28 – 2.51)	728	276	1.72 (0.91 – 3.27)
Analysis with the Imputed Datasets	4011	1698	1.85 (1.33 – 2.59)	4011	1698	1.88 (1.35 – 2.63)	4011	1698	1.85 (1.32 – 2.58)

Table 3.41 Odds ratios and 95% confidence intervals for the association of asthma to rates of psychiatric illness at 15 years, after controlling for mental health outcomes at preceding waves, in the longitudinal complete case analyses, and analyses based on imputed data

	Logistic Model Adjusted for Gender and DAWBA Indications at the 13 Year Measurement Wave			**Logistic Model Adjusted for Gender and DAWBA Indications at the 10 and 13 Year Measurement Wave**		
	Model N	**Asthma Diagnosis**		**Model N**	**Asthma Diagnosis**	
		N	**Odds Ratio (95% Confidence Interval)**		**N**	**Odds Ratio (95% Confidence Interval)**
Complete Case Analysis	2408	140	1.73 (1.21 – 2.48)	2406	139	1.69 (1.18 – 2.43)
Analysis with the Imputed Datasets	3984	1303	1.76 (1.22 – 2.53)	3984	1303	1.77 (1.22 – 2.54)

3.2.5.2.6 Summary of the comparative longitudinal analyses

Table 3.42 summarises the findings from the longitudinal analyses using the generalised measure of chronic health problems and compares them to the analyses using asthma diagnoses as the independent variable.

Table 3.42 Summary table comparing the indications of the longitudinal analyses using the generalised chronic illness measure to those using asthma diagnoses as the independent variable

Findings of Associative Analyses	Analyses of More Specific Groupings of Disorders	Sensitivity of Estimations
Primary		
At 10 years and 13 years, children with chronic health problems were approximately twice as likely to present with a mental health disorder than the comparative group (gender-adjusted 10 year OR: 2.04 (95% CI: 1.54-2.69); gender-adjusted 13 year OR: 2.11 (95% CI: 1.56-2.87)). At 15 years, these children were 60% more likely to present with such disorders (gender-adjusted OR: 1.6 (95% CI: 1.15-2.22). When controlling for the presence of mental illness at previous waves, chronic illness continued to be associated with a rise in the prevalence of mental health disorders at age 13 and age 15 (aOR 13 Years: 1.73 (95% CI: 1.25 – 2.4); aOR 15 Years: 1.27 (95% CI: 0.89 – 1.81)). However, the associated increase at age 15 did not reach the level of statistical significance. No interaction effects were detected in the prediction of mental health outcomes at any wave.	Significant associations were identified between chronic health problems and an increased prevalence of all three types of disorders (i.e. emotional disorders, anxiety disorders, and behavioural disorders) at ten and thirteen years. At fifteen years, although an increased prevalence of all three types of disorders was indicated, only the association with emotional disorders reached the level of statistical significance. When controlling for the presence of mental illness at previous measurement waves, chronic illness continued to be associated with a statistically significant increased prevalence of emotional and anxiety disorders at age 13 years. At fifteen years, chronic health problems were associated with a significant increase in rates of emotional disorders only.	There were high rates of attrition in the DAWBA measurement for the 15 year measurement wave. However, estimates resulting from analyses with imputed datasets were highly consistent with the outcomes of complete case analyses. Associations of a lower magnitude were identified in the models adjusting for all three pre-selected covariates at all three measurement waves. Analyses with the imputed datasets suggested that this weakening effect was due to data attrition, rather than a confounding effect of these variables on the associations identified.
Asthma		
At 10 years, children with asthma diagnosis were approximately 57% more likely to present with a mental health disorder than the comparative group (gender-adjusted OR: 1.57 (95% CI: 1.19 – 2.08)). At 13 and 15 years, these children were 76% to 79% more likely to present with such	Although asthma diagnosis was associated with an increased prevalence of all three types of disorders at the three measurement waves, at age 10 statistically significant associations were identified with increased prevalence of emotional	Data attrition was detected on the DAWBA measurement at the 13 and 15 year measurement waves. Analyses with the imputed datasets indicated slightly stronger associations between asthma diagnosis and

disorders (gender-adjusted 13 year OR: 1.76 (95% CI: 1.26 – 2.45); gender-adjusted 15 year OR: 1.79 (95% CI: 1.28 – 2.51)). When controlling for the presence of mental illness at previous waves, asthma diagnoses continued to be associated with a statistically significant rise in the prevalence of mental health disorders at age 13 and age 15. No interaction effects were detected in the prediction of mental health outcomes at any wave.	and anxiety disorders only. At 13 years, only the association with an increased prevalence of behavioural disorders was statistically significant, and remained so after adjustments were made for the presence of psychiatric illness at ten years. At 15 years, in contrast, significant associations with emotional disorders only were indicated, and again, this strong association was consistently identifiable following adjustments for the presence of psychiatric illness at previous waves.	psychiatric illness at these waves than were found in the complete case analysis. Associations of a lower magnitude were identified in the models adjusting for all three pre-selected covariates at all three measurement waves, although overall magnitudes were high. Analyses with the imputed datasets suggested that these effects were due to data attrition, rather than a confounding effect of these variables on the associations identified.

3.2.5.3 Mediation analyses

The outcomes of the four steps of the mediation analyses are presented in an overview table (Table 3.43) for clarity. Similar to the analyses with the generalised measure of chronic health problems, high levels of health-related school absenteeism were indicated to partially mediate the association between asthma diagnosis and mental health outcomes at 10 and 13 years. However, although the second indicator of symptom severity and functional impairments– scores on the 'Perceptions of Fatigue' scale – were significantly associated with asthma diagnosis, it did not mediate mental health outcomes at the 13 year wave. Similar to the primary longitudinal analyses, asthma diagnosis was significantly associated with higher levels of peer victimisation at 10 and 12.5 years, and this was indicated to partially mediate mental health outcomes at 10 and 13 years. However, children with asthma diagnoses were not more likely to report dissatisfaction with friendships, nor was asthma diagnosis statistically associated with any aspect of parental monitoring at any measurement wave.

Table 3.43 Outcomes of the comparative mediation analyses based on the four-step approach to establishing mediation (e.g. Baron and Kenny, 1986)

Mediation Pathway to Test	***Step 1:* Confirm causal variable is associated with outcome**	***Step 2:* Confirm causal variable is associated with mediator**	***Step 3:* Show the mediator effects the association with the outcome variable**	***Step 4:* Identify if it is partial/full mediation**
Asthma Diagnosis – High Levels of Health-Related School Absenteeism at 10 – Any Psychiatric Illness at 10	✓ OR: 1.6 (95% CI: 1.21 – 2.12)	✓ Significant association with high-levels of absenteeism (OR: 4.77 (95% CI: 3.97 – 5.71), p<0.001)	✓	**Partial** A significant association is still identified between Asthma Diagnosis and psychiatric illness at age 10 (p<0.01)
Asthma Diagnosis – High Levels of Health-Related School Absenteeism at 13 – Any Psychiatric Illness at 13	✓ OR: 1.79 (95% CI: 1.28 – 2.5)	✓ Significant association with high-levels of absenteeism (OR: 3.05 (95% CI: 2.59 – 3.6), p<0.001)	✓	**Partial** A significant association is still identified between Asthma Diagnosis and psychiatric illness at age 13 (p<0.01) *(Please note that the association between absenteeism and psychiatric illness is borderline significant (p=0.057)*
Asthma Diagnosis – Perceptions of Fatigue – Any Psychiatric Illness at 13	✓ OR: 2.06 (95% CI: 1.52 – 2.79)	✓ Significant association with perceptions of fatigue (Coeff: 0.93 (95% CI: 0.55 – 1.3), p<0.001)	**X** Perceptions of fatigues are not associated with the prevalence of psychiatric illness (p=0.3)	

Asthma Diagnosis – Conflict in the Parents Relationship at 9 – Any Psychiatric Illness at 10	✓ OR: 1.6 (95% CI: 1.21 – 2.12)	**X** Regression coefficient is not significant (p=0.08)		
Asthma Diagnosis – Conflict in the Parents Relationship at 12 – Any Psychiatric Illness at 13	✓ OR: 1.79 (95% CI: 1.28 – 2.5)	**X** Regression coefficient is not significant (p=0.56)		
Asthma Diagnosis – Parental Monitoring at 12 – Any Psychiatric Illness at 13	✓ OR: 1.79 (95% CI: 1.28 – 2.5)	**X** Regression coefficient is not significant (p=0.37)		
Asthma Diagnosis – Parental Monitoring at 13 – Any Psychiatric Illness at 13	✓ OR: 1.79 (95% CI: 1.28 – 2.5)	**X** Regression coefficient is not significant (p=0.71)		
Asthma Diagnosis – Parental Monitoring at 15 – Any Psychiatric Illness at 15	✓ OR: 1.77 (95% CI: 1.26 – 2.47)	**X** Regression coefficient is not significant (p=0.61)		
Asthma Diagnosis – Child Disclosures at 12 – Any Psychiatric Illness at 13	✓ OR: 1.79 (95% CI: 1.28 – 2.5)	**X** Regression coefficient is not significant (p=0.53)		
Asthma Diagnosis – Child Disclosures at 13 – Any Psychiatric Illness at 13	✓ OR: 1.79 (95% CI: 1.28 – 2.5)	**X** Regression coefficient is not significant (p=0.39)		

Asthma Diagnosis – Child Disclosures at 15 – Any Psychiatric Illness at 15	✓ OR: 1.77 (95% CI: 1.26 – 2.47)	**X** Regression coefficient is not significant (p=0.17)		
Asthma Diagnosis – Parental Solicitation at 12 – Any Psychiatric Illness at 13	✓ OR: 1.79 (95% CI: 1.28 – 2.5)	**X** Regression coefficient is not significant (p=0.1)		
Asthma Diagnosis – Parental Solicitation at 13 – Any Psychiatric Illness at 13	✓ OR: 1.79 (95% CI: 1.28 – 2.5)	**X** Regression coefficient is not significant (p=0.88)		
Asthma Diagnosis – Parental Solicitation at 15 – Any Psychiatric Illness at 15	✓ OR: 1.77 (95% CI: 1.26 – 2.47)	**X** Regression coefficient is not significant (p=0.23)		
Asthma Diagnosis – Parental Control at 12 – Any Psychiatric Illness at 13	✓ OR: 1.79 (95% CI: 1.28 – 2.5)	**X** Regression coefficient is not significant (p=0.93)		
Asthma Diagnosis – Parental Control at 13 – Any Psychiatric Illness at 13	✓ OR: 1.79 (95% CI: 1.28 – 2.5)	**X** Regression coefficient is not significant (p=0.33)		
Asthma Diagnosis – Parental Control at 15 – Any Psychiatric Illness at 15	✓ OR: 1.77 (95% CI: 1.26 – 2.47)	**X** Regression coefficient is not significant (p=0.69)		

Asthma Diagnosis – Satisfaction with Peer Relationships at 10 – Any Psychiatric Illness at 10	✓ OR: 1.6 (95% CI: 1.21 – 2.12)	**X** Regression coefficient is not significant (p=0.09)		
Asthma Diagnosis – Satisfaction with Peer Relationships at 12 – Any Psychiatric Illness at 13	✓ OR: 1.79 (95% CI: 1.28 – 2.5)	**X** Regression coefficient is not significant (p=0.16)		
Asthma Diagnosis – Peer Victimisation at 10 – Any Psychiatric Illness at 10	✓ OR: 1.6 (95% CI: 1.21 – 2.12)	✓ Significant association with victimisation (OR: 1.38 (95% CI: 1.16 – 1.65), p<0.001)	✓	**Partial** A significant association is still identified between Asthma Diagnosis and psychiatric illness at age 10 (p<0.05)
Asthma Diagnosis – Peer Victimisation at 12 – Any Psychiatric Illness at 13	✓ OR: 1.79 (95% CI: 1.28 – 2.5)	✓ Significant association with victimisation (OR: 1.42 (95% CI: 1.17 – 1.72), p<0.001)	✓	**Partial** A significant association is still identified between Asthma Diagnosis and psychiatric illness at age 10 (p<0.01)

3.2.5.4 Goodness-of-fit of the path model to the mental health outcomes associated with asthma

The path model was calculated in MPlus© software using asthma, rather than chronic health problems, as the primary causative variable. This model was fitted based on 4010 observations, 2606 of whom had complete data across all measures. All fit indices were in acceptable ranges, indicating a good fit of the model to the data. Specifically, the chi-square test of model fit was non-significant, despite the large sample size. The RMSEA value was optimal at

0, and the confidence interval range was also well below the recommended cut-off of value of 0.06 (90% CI: 0.00 – 0.035). In addition, a CFI of 1.0 was obtained, indicating very strong model fit. Therefore, the path model was supported as an adequate model of mental health outcomes at 10 and 13 years in the context of both chronic health problems and asthma diagnosis.

A summary of the model results can be seen in Table 3.44, and these results are also illustrated in Figure 3.6 for clarity. The resulting pathways showed high consistency with those of the primary path model. The association between asthma and higher rates of psychiatric illness was fully mediated by the variables in the model. Peer victimisation was the strongest mediator of the mental health outcomes associated with asthma at 10 years, but when controlling for this association, asthma did not independently predict peer victimisation at 12.5 years, and peer victimisation at 12.5 years in turn did not independently predict mental health outcomes at 13 years. As in the primary model, high levels of school absenteeism was the most consistent predictor of mental health outcomes both within time and across time, although it should be noted that the direct pathway from high levels of school absenteeism at 10 years to mental health outcomes at 13 years was over the threshold of statistical significance (p=0.07).

Table 3.44 Results of the comparative path model tested in MPlus© software

	Beta Estimate	Standard Error	Est/Standard Error	Two-Tailed P Value
Psychiatric Illness 10 Years on				
Asthma Diagnosis	0.05	0.08	0.61	0.543
Health-Related Absenteeism 10 Years	0.15	0.053	2.79	0.005
Peer Victimisation 10 Years	0.29	0.06	5.13	0.000
Psychiatric Illness 13 Years on				
Asthma Diagnosis	0.18	0.12	1.58	0.115
Psychiatric Illness 10 Years	0.9	0.10	8.92	0.000
Health-Related Absenteeism 13 Years	0.17	0.09	2.0	0.046
Peer Victimisation 12.5 Years	0.03	0.09	0.35	0.727
Health-Related Absenteeism 10 Years	-0.2	0.11	-1.81	0.070
Peer Victimisation 12.5 Years	0.004	0.11	0.04	0.970
Health-Related Absenteeism 10 Years on				
Chronic Illness	0.87	0.05	17.45	0.000
Health-Related Absenteeism 13 Years on				
Asthma Diagnosis	0.3	0.06	5.06	0.000
Health-Related Absenteeism 10 Years	0.48	0.04	11.06	0.000
Psychiatric Illness 10 Years	-0.04	0.06	-0.59	0.554
Peer Victimisation 12.5 Years	0.03	0.05	0.5	0.615
Peer Victimisation 10 Years	0.009	0.062	0.147	0.883

Peer Victimisation 10 Years on Asthma Diagnosis	0.183	0.05	3.54	0.000
Peer Victimisation 12.5 Years				
Asthma Diagnosis	0.06	0.08	0.86	0.391
Peer Victimisation 10 Years	0.55	0.05	10.41	0.000
Psychiatric Illness 10 Years	0.08	0.07	1.17	0.24
Health-Related Absenteeism 10 Years	0.05	0.05	0.95	0.34

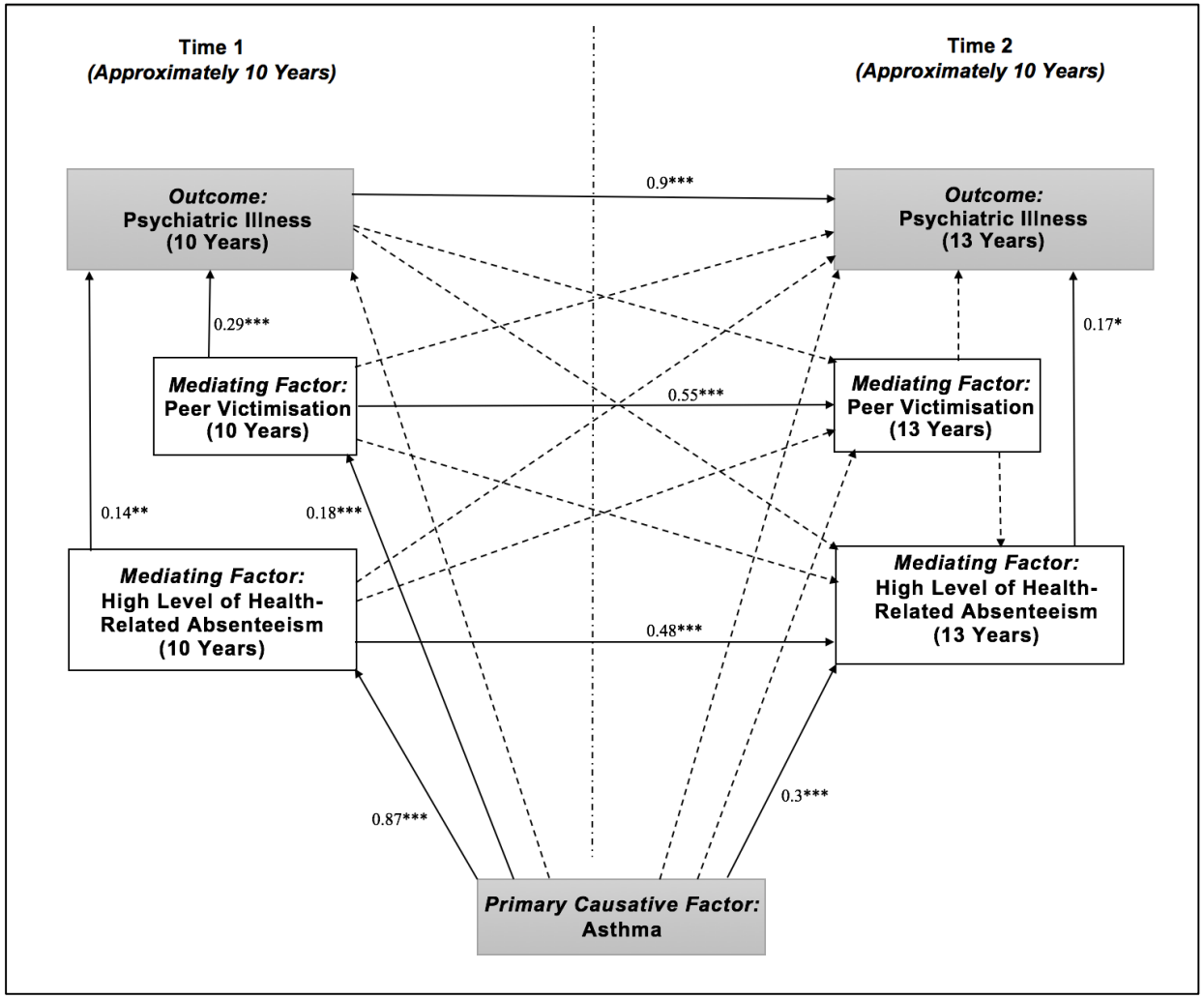


Figure 3.6 Illustrated results of the comparative path model tested in MPlus© software (*p<0.05; **p<0.01; ***p<0.001; significant pathways: bold; non-significant pathways: dashes)

3.3 Secondary Analyses

3.3.1 Indication of the alternative outcome measures

Please note as no alternative outcome measure was administered past the age of 13 years, comparison between the DAWBA and the alternative outcome measures in the longitudinal analyses will focus on the period from 10 to 13 years. At 10 and 13 years, children with chronic health problems were approximately twice as likely to present with a mental health disorder when compared with the healthy, comparative sample. This increase seemed to be underlined by an increase in all three types of disorders – emotional, behavioural and anxiety. When controlling for the presence of psychiatric illness at age 10, the association between chronic health problems and an increased rate of psychiatric illness remained identifiable. However, this association seemed to be underlined by an increased prevalence of emotional and anxiety disorders only. Children with an asthma diagnosis were also more likely to present with a mental health disorder than their healthy peers at the DAWBA measurement at 10 and 13 years. At ten years, there was an approximate 60% increase in psychiatric disorders amongst this group, which seemed primarily driven by an increased rate of emotional and anxiety disorders. At 13 years, overall, there was approximately a 75% increased incidence of mental health disorders amongst this group, but the association at this age seemed largely underlined by an increased prevalence of behavioural disorders. This characteristic association remained identifiable even after controlling for the presence of psychiatric illness at previous waves.

Three alternative outcome measures were administered at more than one time-point over these three years. One was a parent-rated measure, the 'Strengths and Difficulties Questionnaire' (SDQ) (administered at 11 and 13 years), which is an accumulative measure of total psychological difficulties. The two remaining measures were different versions of the same scale, specifically the 'Short Moods and Feelings Questionnaire' (sMFQ), a measure of depressive symptomatology. One was the parent-rated version of this measure (administered at 11 and 13 years) and the other a child-rated

version (administered at 10, 12 and 13 years). Binary ratings on these scales were used in the binomial regression models, with scores of '1' (i.e. scores in the range above the scale cut-offs) representing likely psychopathology. However, the mean scores on these scales are presented in the descriptive statistics in Table 3.45 for the chronic illness sample, and Table 3.46 for the asthma sample.

Table 3.45 Breakdown of the alternative outcome measures across waves by chronic illness status, and comparative statistics

	Healthy Comparative Sample (n=2681)	**Chronically Ill Sample (n=1303)**	**Group Comparative Tests**
Parent-Rated SDQ 11 Years			
M(SD)	5.56 (4.34)	7.51 (5.1)	*T:* -12.03 (p<0.001)
Distributions of Score Around Scale Cut-Off N(%)			
Below Cut-Off	2407 (89.78%)	1125 (86.34%)	Chi^2: 22.09 (p<0.001)
Above Cut-Off	70 (2.61%)	72 (5.53%)	
Missing	204 (7.61%)	106 (8.41%)	
Parent-Rated SDQ 13 Years			
M(SD)	5.71 (4.33)	7.83 (5.03)	*T:* -13.11 (p<0.001)
Distributions of Score Around Scale Cut-Off N(%)			
Below Cut-Off	2349 (87.62%)	1124 (86.26%)	Chi^2: 21.58 (p<0.001)
Above Cut-Off	66 (2.46%)	70 (5.37%)	
Missing	266 (9.92%)	109 (8.37%)	
Parent-Rated sMFQ 11 Years			
M(SD)	1.77 (2.66)	2.9 (3.53)	*T:* -10.65 (p<0.001)
Distributions of Score Around Scale Cut-Off N(%)			
Below Cut-Off	2391 (89.18%)	1123 (86.19%)	Chi^2: 9.35 (p<0.01)
Above Cut-Off	32 (1.19%)	32 (2.46%)	
Missing	258 (9.62%)	148 (11.38%)	

Parent-Rated sMFQ 13 Years M(SD) *Distributions of Score Around Scale Cut-Off N(%)* Below Cut-Off Above Cut-Off Missing	1.68 (2.56) 2379 (88.74%) 35 (1.31%) 267 (9.96%)	2.98 (3.62) 1139 (87.41%) 40 (3.07%) 124 (9.52%)	*T:* -12.41 (p<0.001) *Chi²:* 14.63 (p<0.001)
Child-Rated sMFQ 10 Years M(SD) *Distributions of Score Around Scale Cut-Off N(%)* Below Cut-Off Above Cut-Off Missing	3.62 (3.15) 2143 (79.93%) 90 (3.36%) 448 (16.71%)	4.46 (3.68) 1025 (78.66%) 77 (5.91%) 201 (15.43%)	*T:* -6.87 (p<0.001) *Chi²:* 13.56 (p<0.001)
Child-Rated sMFQ 12 Years M(SD) *Distributions of Score Around Scale Cut-Off N(%)* Below Cut-Off Above Cut-Off Missing	3.43 (3.43) 2063 (76.95%) 73 (2.72%) 545 (20.33%)	4.61 (4.08) 973 (74.67%) 75 (5.76%) 255 (19.57%)	*T:* -8.52 (p<0.001) *Chi²:* 22.17 (p<0.001)
Child-Rated sMFQ 13 Years M(SD) *Distributions of Score Around Scale Cut-Off N(%)* Below Cut-Off Above Cut-Off Missing	4.39 (4.18) 1853 (69.12%) 140 (5.22%) 688 (25.66%)	5.54 (4.73) 878 (67.38%) 115 (8.83%) 310 (23.79%)	*T:* -6.75 (p<0.001) *Chi²:* 17.62 (p<0.001)

Table 3.46 Breakdown of the alternative outcome measures across waves by asthma status, and comparative statistics

	Healthy Comparative Sample (n=2313)	**Asthma Sample (n=1698)**	**Group Comparative Tests**
Parent-Rated SDQ 11 Years			
M(SD)	5.47 (4.31)	7.0 (5.17)	*T:* -9.53 (p<0.001)
Distributions of Score Around Scale Cut-Off N(%)			
Below Cut-Off	2080 (89.93%)	1319 (77.68%)	
Above Cut-Off	59 (2.55%)	82 (4.83%)	Chi^2: 21.2 (p<0.001)
Missing	174 (7.52%)	297 (17.49%)	
Parent-Rated SDQ 13 Years			
M(SD)	5.65 (4.32)	7.21 (5.08)	*T:* -9.62 (p<0.001)
Distributions of Score Around Scale Cut-Off N(%)			
Below Cut-Off	2034 (87.94%)	1254 (73.85%)	Chi^2: 21.77 (p<0.001)
Above Cut-Off	55 (2.38%)	77 (4.53%)	
Missing	224 (9.68%)	367 (21.61%)	
Parent-Rated sMFQ 11 Years			
M(SD)	1.74 (2.62)	2.45 (3.29)	*T:* -7.09 (p<0.001)
Distributions of Score Around Scale Cut-Off N(%)			
Below Cut-Off	2061 (89.11%)	1131 (78.39%)	Chi^2: 4.9 (p<0.05)
Above Cut-Off	28 (1.21%)	32 (1.88%)	
Missing	224 (9.68%)	335 (19.73%)	
Parent-Rated sMFQ 13 Years			
M(SD)	1.65 (2.52)	2.53 (3.42)	*T:* -8.69 (p<0.001)
Distributions of Score Around Scale Cut-Off N(%)			
Below Cut-Off	2056 (88.89%)	1297 (76.38%)	Chi^2: 13.1 (p<0.001)
Above Cut-Off	29 (1.25%)	43 (2.53%)	
Missing	228 (9.86%)	358 (21.08%)	

Child-Rated sMFQ 10 Years			
M(SD)	3.6 (3.11)	4.26 (3.62)	*T:* -5.58 (p<0.001)
Distributions of Score Around Scale Cut-Off N(%)			
Below Cut-Off	1848 (79.9%)	1277 (75.21%)	Chi^2: 13.21
Above Cut-Off	75 (3.24%)	92 (5.42%)	(p<0.001)
Missing	390 (16.86%)	329 (19.38%)	
Child-Rated sMFQ 12 Years			
M(SD)	3.43 (3.44)	4.02 (3.8)	*T:* -4.46 (p<0.001)
Distributions of Score Around Scale Cut-Off N(%)			
Below Cut-Off	1773 (76.65%)	1162 (68.43%)	Chi^2: 5.45
Above Cut-Off	63 (2.72%)	63 (3.71%)	(p<0.05)
Missing	477 (20.62%)	473 (27.86%)	
Child-Rated sMFQ 13 Years			
M(SD)	4.34 (4.15)	5.11 (4.73)	*T:* -4.53 (p<0.001)
Distributions of Score Around Scale Cut-Off N(%)			
Below Cut-Off	1593 (68.87%)	991 (58.36%)	Chi^2: 8.7
Above Cut-Off	119 (5.14%)	111 (6.54%)	(p<0.01)
Missing	601 (25.98%)	596 (35.1%)	

3.3.1.1 The parent-rated 'Strengths and Difficulties Questionnaire' (SDQ)

3.3.1.1.1 Analyses of chronic illness outcomes more generally

Based on the analyses with the primary outcome measure, it appears that children with chronic health problems would present with a higher level of psychopathology on this scale across both time waves.

Initially, three binomial logistic regression models were calculated for both the 11 year and 13 year administration wave to examine the association between chronic health problems and likely psychopathology as indicated by this measure. The resulting odds ratio estimates are presented in Table 3.47.

The magnitude of the odds ratio for the two administration waves were of a similar magnitude to that of the DAWBA measurement across all models, indicating that children with chronic health problems were over twice as likely to present with psychopathology than their healthy peers. All associations identified in the models were of statistical significance, with the exception of the estimate for the age 11 measure in the model that adjusted for all three preselected covariates. As additional adjustments for history of parental mental illness and socio-economic status substantially improved the model fit on the age 11 wave (LR chi^2: 6.76, $p<0.05$), although not the age 13 wave (LR chi^2: 2.32, $p>0.05$), it is unclear if this weakening effect is a consequence of controlling for these variables, or the reduced sample size. Adjustments for gender improved the associative model fit at both waves (11 Year LR chi^2: 7.64, 13 Year LR chi^2: 8.05; both $p>0.05$). There was no interaction effect indicated between the covariates of gender (11 Year LR chi^2: 0.2, 13 Year LR chi^2: 0.12; both $p>0.05$), history of parental mental illness (11 Year LR chi^2: 0.64, 13 Year LR chi^2: 0.02; both $p>0.05$), and socio-economic status (11 Year LR chi^2: 0.35, 13 Year LR chi^2: 1.79; both $p>0.05$) and chronic health problems in outcomes on this measure at either wave.

Table 3.47 Odds ratios and 95% confidence intervals for the association of chronic illness to rates of psychiatric illness at 11 and 13 years, as measured by the parent-rated SDQ

	Model 1: Basic Model			**Model 2:** Model with adjustment for gender of the study child			**Model 3:** Model with adjustment for gender, history of parental mental illness and socio-economic status		
	Model N	**Chronically Ill Sample**		**Model N**	**Chronically Ill Sample**		**Model N**	**Chronically Ill Sample**	
		N	**Odds Ratio (95% Confidence Interval)**		**N**	**Odds Ratio (95% Confidence Interval)**		**N**	**Odds Ratio (95% Confidence Interval)**
Age 11 Measurement	3674	1197	2.2 (1.57 – 3.08)	3674	1197	2.28 (1.62 – 3.19)	1029	315	1.96 (0.99 – 3.88)
Age 13 Measurement	3609	1194	2.06 (1.52 – 2.79)	3609	1194	2.06 (1.63 – 3.26)	1020	319	2.3 (1.21 – 4.35)

A subsequent binomial logistic regression model was calculated for the age 13 measurement wave, controlling for indications of psychopathology on the age 11 measurement. This model was adjusted for the gender of the study child only given that this was the only covariate indicated to improve the overall associative model fit at this wave (LR chi^2: 13.76, $p<0.001$). Chronic health problems remained associated with an increased rate of likely psychopathology in this model, and this association remained statistically significant (aOR: 1.62 (95% CI: 1.08 – 2.43), $p<0.05$).

3.3.1.1.2 Analyses of asthma diagnosis outcomes

Based on the analysis with the primary outcome measure, it would be expected that asthma diagnoses would show a significant association with psychopathology as indicated by this scale, although the association would be of a lower magnitude than that indicated for chronic health problems.

To explore the associations between asthma diagnosis and indications of likely psychopathology on the parent-rated SDQ, three initial binomial logistic regression models were calculated for both administration waves. The resulting odds ratios are presented in Table 3.48. Consistent with the DAWBA, asthma diagnoses were associated with increased rates of likely psychopathology at both waves. However, the increased prevalence of psychopathology among children with asthma diagnoses was indicated to be much higher on this measure, standing at over twice that of rates seen in the healthy, comparative group at both measurement waves. All associations across the models were of statistical significance, with the exception of the association between asthma diagnosis and likely psychopathology in the more fully adjusted model at age 13. As the likelihood ratio tests indicated that additional adjustments for the covariates of 'socio-economic status' and 'history of parental mental illness' did not significantly improve the fit of the associative models at either wave (age 11 LR chi^2: 3.67, $p>0.05$; age 13 LR chi^2: 2.52, $p>0.05$), it is likely that this weakening effect was a consequence of the reduced sample size. In contrast, adjustments for gender improved the associative model fit at both waves (11 Year LR chi^2: 7.64, 13 Year LR chi^2: 8.05; both $p>0.05$). There was no interaction effect indicated between the

covariates of gender (11 Year LR chi^2: 0.77, 13 Year LR chi^2: 0.04; both p>0.05), history of parental mental illness (11 Year LR chi^2: 0.01, 13 Year LR chi^2: 0.03; both p>0.05), and socio-economic status (11 Year LR chi^2: 0.2, 13 Year LR chi^2: 1.89; both p>0.05) and asthma diagnosis in outcomes on this measure at either wave.

Table 3.48 Odds ratios and 95% confidence intervals for the association of asthma to rates of psychiatric illness at 11 and 13 years, as measured by the parent-rated SDQ

	Model 1: Basic Model			**Model 2:** Model with adjustment for gender of the study child			**Model 3:** Model with adjustment for gender, history of parental mental illness and socio-economic status		
	Model N	**Asthma Diagnosis**		**Model N**	**Asthma Diagnosis**		**Model N**	**Asthma Diagnosis**	
		N	**Odds Ratio (95% Confidence Interval)**		**N**	**Odds Ratio (95% Confidence Interval)**		**N**	**Odds Ratio (95% Confidence Interval)**
Age 11 Measurement	3540	1401	2.19 (1.56 – 3.08)	3540	1401	2.15 (1.53 – 3.03)	989	365	2.34 (1.18 –4.66)
Age 13 Measurement	3420	1331	2.27 (1.6 – 3.23)	3420	1331	2.23 (1.56 – 3.17)	959	346	1.44 (0.71 – 2.92)

Consistent with the analyses with chronic health problems, a subsequent binomial logistic regression model was calculated for the age 13 measurement wave, controlling for indications of likely psychopathology on the age 11 measurement. This model was adjusted for the gender of the study child only, given that this was the only covariate indicated to improve the overall model fit (LR chi^2: 8.05, $p<0.01$). In this model asthma diagnoses remained associated with a rise in likely psychopathology at age 13, and this association remained statistically significant (aOR: 1.68 (95% CI: 1.11 – 2.56)).

3.3.1.2 The parent-rated 'Short Moods and Feelings Questionnaire' (sMFQ)

3.3.1.2.1 Analyses of chronic illness outcomes more generally

Based on the indications of the analyses with the primary outcome measure, it would be expected that an association between chronic health problems and an increased rate of psychopathology would be indicated on this scale at both waves, and that this association would remain identifiable at age 13 after adjusting for the presence of emotional psychopathology at age 11.

Three initial binomial logistic regression models were calculated for both the 11 year and 13 year administration wave to examine the association between chronic health problems and likely emotional psychopathology as indicated by the parent-rated sMFQ. The resulting odds ratio estimates are presented in Table 3.49. Chronic health problems were associated with an increase in likely emotional psychopathology at both the age 11 and the age 13 measurement waves, and this increase was over two times that of the healthy comparative group at both waves. There was a weakening effect identified when the covariates of 'history of parental mental illness' and 'socio-economic status' were included in the associative models at both waves. However, as the inclusion of these variables into the associative models did not substantially improve the model fit at either wave (age 11 LR chi^2: 0.41; age 13 LR chi^2: 1.28, $p>0.05$), it is likely that this weakening effect was due to data attrition. Adjustments for gender also did not significantly improve the associative model fit at either wave (age 11 LR chi^2: 1.02, $p>0.05$; age 13 LR chi^2: 0.16, both $p>0.05$). Furthermore, there was no

interaction effect indicated between the covariates of gender (11 Year LR chi^2: 0.18, 13 Year LR chi^2: 0.12; both $p>0.05$), history of parental mental illness (11 Year LR chi^2: 0.18, 13 Year LR chi^2: 0.04; both $p>0.05$), and socio-economic status (11 Year LR chi^2: 0.59, 13 Year LR chi^2: 0.55; both $p>0.05$) and chronic health problems in outcomes on this measure at either wave.

Table 3.49 Odds ratios and 95% confidence intervals for the association of chronic illness to rates of emotional psychopathology at 11 and 13 years, as measured by the parent-rated sMFQ

	Model 1: Basic Model			**Model 2:** Model with adjustment for gender of the study child			**Model 3:** Model with adjustment for gender, history of parental mental illness and socio-economic status		
	Model N	**Chronically Ill Sample**		**Model N**	**Chronically Ill Sample**		**Model N**	**Chronically Ill Sample**	
		N	**Odds Ratio (95% Confidence Interval)**		**N**	**Odds Ratio (95% Confidence Interval)**		**N**	**Odds Ratio (95% Confidence Interval)**
Age 11 Measurement	3578	1155	2.13 (1.3 – 3.49)	3578	1155	2.1 (1.28 – 3.45)	1011	304	1.61 (0.61 – 4.29)
Age 13 Measurement	3593	1179	2.39 (1.51 – 3.78)	3593	1179	2.4 (1.52 – 3.8)	1009	312	1.83 (0.78 – 4.29)

A subsequent binomial logistic regression model was calculated for the age 13 measurement wave, controlling for the presence of likely emotional psychopathology on the age 11 measurement. This model was adjusted for 'gender' only due to sample size concerns. After having made this adjustment, chronic health problems remained associated with an increase in emotional psychopathology at 13 years on this measure, and this association did reach the threshold of statistical significance (aOR: 1.8 (95% CI: 1.08 – 3.0).

3.3.1.2.2 Analyses of asthma diagnosis outcomes

Based on the indications of the analyses with the primary outcome measure, it would be expected that associations between asthma diagnosis and emotional psychopathology at 13 years would be weak, and attenuated by adjustments for the presence of emotional psychopathology at age 11.

Three initial binomial logistic regression models were calculated for both administration waves to examine the association between asthma diagnosis and likely emotional psychopathology on this scale. The resulting odds ratios are presented in Table 3.50. Asthma diagnoses were associated with an increased rate of likely emotional psychopathology at both measurement waves. In contrast to the indications of the DAWBA measure, which largely signalled that the psychiatric associations of asthma diagnoses at age 13 were behavioural in nature, the association between asthma diagnosis and emotional psychopathology was stronger in the age 13 models than in the age 11 models (unadjusted OR 11 years: 1.8 (95% CI: 1.06 – 2.95); unadjusted OR 13 years: 2.35 (95% CI: 1.46 – 3.78)). Additional adjustments for 'history of parental mental illness' and 'socio-economic status' reduced the magnitude of the odds ratios at both waves, and associations in these models were not of statistical significance. However, as in previous analyses, the likelihood ratio tests indicated that the addition of these covariates to the models did not substantially improve the model fit (age 11 LR chi^2: 0.19; age 13 LR chi^2: 3.19, $p>0.05$), suggesting that this weakening effect was due to loss in analytic power. Adjustments for gender also did not significantly improve the associative model fit at either wave (age 11 LR chi^2: 0.88; age

13 LR chi^2: 0.12, both p>0.05). Furthermore, there was no interaction effect indicated between the covariates of gender (11 Year LR chi^2: 0.18, 13 Year LR chi^2: 0.53; both p>0.05), history of parental mental illness (11 Year LR chi^2: 1.69; 13 Year LR chi^2: 0.22; both p>0.05), and socio-economic status (11 Year LR chi^2: 0.73; 13 Year LR chi^2: 3.41; both p>0.05) and asthma diagnosis in outcomes on this measure at either wave.

Table 3.50 Odds ratios and 95% confidence intervals for the association of asthma to rates of emotional psychopathology at 11 and 13 years, as measured by the parent-rated sMFQ

	Model 1: Basic Model			**Model 2:** Model with adjustment for gender of the study child			**Model 3:** Model with adjustment for gender, history of parental mental illness and socio-economic status		
	Model N	**Asthma Diagnosis**		**Model N**	**Asthma Diagnosis**		**Model N**	**Asthma Diagnosis**	
		N	**Odds Ratio (95% Confidence Interval)**		**N**	**Odds Ratio (95% Confidence Interval)**		**N**	**Odds Ratio (95% Confidence Interval)**
Age 11 Measurement	3452	1363	1.8 (1.06 – 2.95)	3452	1363	1.79 (1.07 – 2.99)	974	357	0.88 (0.3 – 2.62)
Age 13 Measurement	3425	1340	2.35 (1.46 – 3.78)	3425	1340	2.36 (1.46 – 3.8)	956	347	1.7 (0.68 – 4.26)

As for the analyses with chronic health problems, a subsequent binomial logistic regression model was calculated for the age 13 measurement wave, controlling for the presence of likely psychopathology as indicated by the age 11 measurement. Due to sample size concerns, and because of the likelihood ratio testing, this model was adjusted for the gender of the study child only. In this model asthma diagnoses remained associated with a rise in likely emotional psychopathology at age 13, and this association remained statistically significant (aOR: 1.84 (95% CI: 1.08 – 3.13), p<0.05).

3.3.1.3 The child-rated 'Short Moods and Feelings Questionnaire' (sMFQ)

3.3.1.3.1 Analyses of chronic illness outcomes more generally

As with the parent-rated version of this scale, based on the analyses with the primary outcome measure it was expected that consistently strong associations would be identifiable between chronic illness and likely psychopathology on this measure.

Three initial binomial logistic regression models examined the association between chronic health problems and each of the individual waves of the child-rated 'Short Moods and Feelings Questionnaire' (sMFQ). The resulting odds ratios are presented in Table 3.51. Chronic health problems were associated with a rise in likely emotional psychopathology at all three measurement waves in the unadjusted and gender adjusted models, and these associations were statistically significant (all p<0.01). In the unadjusted models, the strongest association was shown at age 12, children with chronic health problems over twice as likely to present with psychopathology as their healthy peers, but they were also 70% to 80% more likely to present with such psychopathologies at ten and thirteen years. Controlling for 'gender' weakened the association identified on the 10 and 13 year wave. However, while adjustments for this variable substantially improved the model fit at 12 and 13 years (age 12 LR chi^2: 13.77; age 13 LR chi^2: 52.55, both p<0.001), it did not add to the associative model fit at 10 years (LR chi^2: 0.99, p>0.05). Furthermore, in the three models that adjusted for the covariates of 'history of parental mental illness' and 'socio-economic status' the magnitude of the odds ratios were inconsistent from the two proceeding models at all waves,

with the age 12 association falling below the level of statistical significance. However, it is likely that these effects are due to the reduced sample size, rather than confounding effects, as the likelihood ratio tests indicated that the addition of these covariates did not substantially improve the model fit at any wave (age 10 LR chi^2: 0.66, $p>0.05$; age 12 LR chi^2: 0.02, $p>0.05$ age 13 LR chi^2: 3, $p>0.05$). Moreover, there was no interaction effect indicated between the covariates of gender (10 Year LR chi^2: 0.59; 12 Year chi^2: 0.34; 13 Year LR chi^2: 1.19; all $p>0.05$), history of parental mental illness (10 Year LR chi^2: 0.14; 12 Year chi^2: 0.89; 13 Year LR chi^2: 0.11; all $p>0.05$), and socio-economic status (10 Year LR chi^2: 0.22; 12 Year chi^2: 0.87; 13 Year LR chi^2: 0.15; all $p>0.05$) and chronic health problems in outcomes on this measure at any wave.

Table 3.51 Odds ratios and 95% confidence intervals for the association of chronic illness to rates of emotional psychopathology at 10, 12, and 13 years, as measured by the child-rated sMFQ

	Model 1: Basic Model			**Model 2:** Model with adjustment for gender of the study child			**Model 3:** Model with adjustment for gender, history of parental mental illness and socio-economic status		
	Model N	**Chronically Ill Sample**		**Model N**	**Chronically Ill Sample**		**Model N**	**Chronically Ill Sample**	
		N	**Odds Ratio (95% Confidence Interval)**		**N**	**Odds Ratio (95% Confidence Interval)**		**N**	**Odds Ratio (95% Confidence Interval)**
Age 10 Measurement	3335	1102	1.79 (1.31 – 2.45)	3335	1102	1.81 (1.32 – 2.47)	950	298	2.68 (1.47 – 4.91)
Age 12 Measurement	3184	1048	2.18 (1.56 – 3.03)	3184	1048	2.09 (1.5 – 2.92)	901	279	1.66 (0.88 – 3.11)
Age 13 Measurement	2986	993	1.73 (1.34 – 1.63)	2986	993	1.63 (1.25 – 2.12)	852	273	1.66 (1.03 – 2.68)

Consequently, three further binomial logistic models were calculated to identify the associations between chronic health problems and emotional psychopathology longitudinally, when controlling for the presence of emotional psychopathology at previous waves. Due to the indications of likelihood ratio testing, gender of the study child was the only covariate included in these models. The estimated odds ratios indicated from the calculation of these two models are presented in Table 3.52. A significant association remained identifiable between chronic health problems and likely emotional psychopathology across all three models (all $p<0.05$).

Table 3.52 Odds ratios and 95% confidence intervals for the association of chronic illness to rates of emotional psychopathology at 12 and 13 years, as measured by the child-rated sMFQ, after adjusting for emotional mental health outcomes at previous waves

	Age 12 Measurement			Age 13 Measurement		
	Model N	Chronically Ill Sample		Model N	Chronically Ill Sample	
		N	Odds Ratio (95% Confidence Interval)		N	Odds Ratio (95% Confidence Interval)
Model 4: Logistic Model Adjusted for Gender and Child-rated sMFQ Indications at the Previous Measurement Wave	3013	1002	2.01 (1.42 – 2.85)	2835	946	1.44 (1.08 – 1.91)
Model 5: Logistic Model Adjusted for Gender and Child-rated sMFQ Indication at the Two Previous Measurement Waves				2709	911	1.47 (1.1 – 1.97)

3.3.1.3.3.2 Analyses of asthma diagnosis outcomes

As with the parent-rated version of this scale, based on the analyses with the primary outcome measure it was expected that the association between asthma and emotional psychopathology would be strong at the age 10 wave, but weaken at the latter waves.

Three initial binomial logistic regression models were also calculated for the three waves of the child-rated sMFQ using asthma diagnosis as the primary predictive factor. The resulting odds ratios are presented in Table 3.53. Asthma diagnoses were associated with a rise in likely emotional psychopathology at all three waves in the unadjusted and gender adjusted models, and these associations were statistically significant (all $p<0.01$). The strongest association was seen at the age 10 wave, with children with an asthma diagnosis approximately 75% more likely to present with emotional psychopathology than their healthy peers. At the twelve and thirteen year measurement, emotional psychopathologies were approximately 50% more prevalent than in the healthy, comparative group. Adjustments for gender had a slightly strengthening impact on the associations identified at the age 12 and age 13 measurement, perhaps due to the slight predominance of males among the asthma sample. Moreover, adjustments for this variable substantially improved the model fit at 12 and 13 years (age 12 LR chi^2: 7.49; age 13 LR chi^2: 43.35, both $p<0.01$), though not at the 10 year wave (LR chi^2: 1.8, $p>0.05$). As in the analyses with the chronic illness sample, the magnitude of the odds ratios among three models that adjusted for the covariates of 'history of parental mental illness' and 'socio-economic status' were inconsistent with the unadjusted and gender-adjusted models, with the association falling below the threshold of significance at the age 12 wave. Again, as in previous analyses, it is likely that these effects are due to the reduced sample size, rather than confounding effects, as the likelihood ratio tests indicated that the addition of these covariates did not substantially improve the model fit at any wave (age 10 LR chi^2: 0.78, $p>0.05$; age 12 LR chi^2: 0.67, $p>0.05$ age 13 LR chi^2: 1.05, $p>0.05$). Finally, there was no interaction effect indicated between the covariates of gender (10 Year LR chi^2: 0.31; 12 Year chi^2: 0.13; 13 Year LR chi^2: 0.27; all $p>0.05$), history of

parental mental illness (10 Year LR chi^2: 1.8; 12 Year chi^2: 0.89; 13 Year LR chi^2: 2.37; all $p>0.05$), and socio-economic status (10 Year LR chi^2: 2.2; 12 Year chi^2: 0.03; 13 Year LR chi^2: 0.93; all $p>0.05$) and asthma diagnosis in outcomes on this measure at any wave.

Table 3.53 Odds ratios and 95% confidence intervals for the association of asthma to rates of emotional psychopathology at 10, 12, and 13 years, as measured by the child-rated sMFQ

	Model 1: Basic Model			**Model 2:** Model with adjustment for gender of the study child			**Model 3:** Model with adjustment for gender, history of parental mental illness and socio-economic status		
	Model N	**Asthma Diagnosis**		**Model N**	**Asthma Diagnosis**		**Model N**	**Asthma Diagnosis**	
		N	**Odds Ratio (95% Confidence Interval)**		**N**	**Odds Ratio (95% Confidence Interval)**		**N**	**Odds Ratio (95% Confidence Interval)**
Age 10 Measurement	3292	1369	1.78 (1.3 – 2.43)	3292	1369	1.75 (1.28 – 2.4)	919	355	2.57 (1.36 – 4.87)
Age 12 Measurement	3061	1225	1.53 (1.07 – 2.18)	3061	1225	1.56 (1.09 – 2.24)	856	320	1.62 (0.84 – 3.12)
Age 13 Measurement	2814	1102	1.5 (1.14 – 1.97)	2814	1102	1.56 (1.18 – 2.04)	797	300	1.83 (1.11 – 3.02)

Three further binomial logistic models were calculated to identify the associations between asthma diagnoses and likely emotional psychopathologies longitudinally, when controlling for the presence of emotional psychopathology at previous waves. Consistent with the indications of the likelihood ratio tests, these models were adjusted for gender only. The resulting odds ratios are presented in Table 3.54. When adjustments were made for the presence of likely emotional psychopathologies at age 10, asthma diagnoses were no longer associated with an increased rate of emotional psychopathologies at age 12 in a statistically significant fashion. However, associations remained identifiable on the age 13 wave, even in the more stringent model adjusting for the presence of emotional psychopathologies at both age 10 and 12 (both $p<0.01$)

Table 3.54 Odds ratios and 95% confidence intervals for the association of asthma to rates of emotional psychopathology at 12 and 13 years, as measured by the child-rated sMFQ, after adjusting for emotional mental health outcomes at previous waves

	Age 12 Measurement			Age 13 Measurement		
	Model N	Asthma Diagnosis		Model N	Asthma Diagnosis	
		N	Odds Ratio (95% Confidence Interval)		N	Odds Ratio (95% Confidence Interval)
Model 4: Logistic Model Adjusted for Gender and Child-rated sMFQ Indications at the Previous Measurement Wave	2884	1154	1.4 (0.96 – 2.04)	2663	1004	1.51 (1.12 – 2.02)
Model 5: Logistic Model Adjusted for Gender and Child-rated sMFQ Indication at the Two Previous Measurement Waves				2536	994	1.54 (1.14 – 2.08)

Table 3.55 presents an overview of the primary findings of these analyses in comparison to those using the primary outcome measure.

Table 3.55 Summary table: Indications of the alternative outcome measures in comparison to the primary outcome measure

	Associations of Chronic Health Problems	Associations of Asthma Diagnosis
DAWBA	At 10 and 13 years children with chronic health problems were approximately twice as likely to present with mental health disorders as their healthy peers (gender-adjusted 10 year OR: 2.04 (95% CI: 1.54-2.69); gender-adjusted 13 year OR: 2.11 (95% CI: 1.56-2.87)), with this association remaining identifiable at age 13 after controlling for the presence of psychiatric illness at ten years (aOR: 1.73 (95% CI: 1.25-2.4). Although increased rates of all underlying disorders were identifiable at both waves, only associations with emotional and anxiety disorders were statistically significant at 13 years when controlling for the presence of psychiatric illness at ten years.	***:*** Children with asthma diagnoses were approximately 60% more likely to present with a mental health disorder than their healthy peers at age 10 (gender-adjusted OR: 1.57 (95% CI: 1.19-2.08)), with this increase largely typified by an increase in emotional and anxiety disorders. At the age 13 wave, these children were 75% more likely to present with these disorders than their healthy peers (gender-adjusted OR: 1.76 (95% CI: 1.26-2.45)), but the increase at this wave seemed characterised by a rise in behavioural disorders. This association remained identifiable after controlling for the presence of psychiatric illness at 10 years (aOR: 1.62 (95% CI: 1.13-2.3)).
SDQ	Children with chronic health problems were over twice as likely to present with psychopathology as their healthy peers at both the age 11 and age 13 waves (gender-adjusted 11 year OR: 2.2 (95% CI: 1.57-3.08); gender-adjusted 13 year OR: 2.06 (95% CI: 1.52-2.79)). The association between chronic illness and psychopathologies at age 13 remained identifiable after controlling for the presence of psychopathologies at 11 years (aOR: 1.62 (95% CI: 1.08-2.43).	Children with asthma diagnoses were over twice as likely to present with psychopathology as their healthy peers at both the age 11 and age 13 waves (gender-adjusted 11 year OR: 2.15 (95% CI: 1.53-3.03); gender-adjusted 13 year OR: 2.23 (95% CI: 1.56-3.17)). The association between asthma diagnoses and psychopathologies at age 13 remained identifiable after controlling for the presence of psychopathologies at 11 years (aOR: 1.68 (95% CI: 1.11-2.56)).
sMFQ (Parent)	Children with chronic health problems were over twice as likely to present with emotional psychopathology as their healthy peers at both the age 11 and age 13 waves (gender-adjusted 11 year OR: 2.1 (95% CI: 1.28-3.45); gender-adjusted 13 year OR: 2.4 (95% CI: 1.52-3.8)). The association between chronic illness and emotional psychopathologies at age 13 remained identifiable after controlling for the presence of emotional psychopathologies at 11 years (aOR: 1.8 (95% CI: 1.08 – 3.0)).	Children with asthma diagnoses were approximately 80% more likely to present with emotional psychopathologies at 10 years, and 3.3 times more likely to present with these diagnoses at age 13 in comparison to their healthy peers (gender-adjusted 11 year OR: 1.79 (95% CI: 1.07-2.99); gender-adjusted 13 year OR: 2.36 (95% CI: 1.46-3.8)). The association between chronic illness and emotional psychopathologies at age 13 remained identifiable after controlling for the presence of emotional psychopathologies at 11 years (aOR: 1.84 (95% CI: 1.08-3.13)).
sMFQ (Child)	Children with chronic health problems were over twice as likely to present with emotional	Children with asthma diagnoses were approximately 75% as likely to present with

	psychopathology as their healthy peers at 12 years (gender-adjusted OR: 2.09 (95% CI: 1.5 – 2.09)), and an 80% increased prevalence was also identifiable at 10 (gender-adjusted 10 year OR: 1.81 (95% CI: 1.32-2.47)) and a lower prevalence of 60% at 13 years (gender-adjusted 13 year OR: 1.63 (95% CI: 1.25-2.12)). The association between chronic illness and psychopathologies at age 12 and 13 remained identifiable after controlling for the presence of emotional psychopathologies at the previous waves (aOR 12 Years: 1.44 (95% CI: 1.08-1.91); aOR 13 Years: 1.47 (95% 1.1 – 1.97).	emotional psychopathology as their healthy peers at 10 years (gender-adjusted OR: 1.75 (95% CI: 1.28-2.4), and approximately 50% more likely to present with these psychopathologies at 12 (gender-adjusted OR: 1.56 (95% CI: 1.09-2.24)) and 13 years (gender-adjusted OR: 1.56 (95% CI: 1.18-2.04)). The association between asthma diagnoses and emotional psychopathologies at 13 years remained identifiable after controlling for the presence of emotional psychopathologies at the previous waves (aOR: 1.54 (95% CI: 1.14-2.08)), but the association with emotional psychopathologies at 12 years fell below the levels of statistical significance (aOR: 1.4 (95% CI: 0.96-2.04)).

3.3.2 Concurrent asthma symptomatology and co-occurring psychiatric illness

The odds ratio for the cross-sectional associations between asthma diagnosis and psychiatric illness, and with more specific rates of emotional disorders are presented in Table 3.66 both before and after adjusting for use of reliever medication in the past month. Due to the indications of likelihood ratio testing, these models were adjusted for gender only. For the cross-sectional association at age 10, controlling for the use of reliever medication in the past month did not negate the significant association identified between asthma diagnosis and an increased rate of psychiatric illness at this wave. In fact, controlling for the use of reliever medication in the past slightly strengthened the magnitude of the association identified at this wave for both psychiatric disorders overall (aOR: 1.41 (95% CI: 1.02 – 1.96) versus unadjusted OR: 1.31 (95% CI: 1.01 – 1.71)), and emotional disorders more specifically (1.76 (95% CI: 1.11 – 2.82) versus unadjusted OR: 1.5 (95% CI: 1.01 – 2.21)). In the age 13 cross-sectional wave, the initial association identified between asthma diagnosis and an increased rate of psychiatric illness was weak, and controlling for the use of reliever medication in the past month attenuated this association further. Yet, it slightly strengthened the odds ratio indicated for the association between asthma diagnosis and the prevalence of emotional disorders at this cross-sectional wave, although it should be noted that this association was also statistically non-significant. It should be noted that the additional control for this covariate in the associative model did not substantially contribute to the fit of the models at the age 13 cross-sectional wave (LR 'any psychiatric illness' chi^2=0.06, p>0.05; LR 'any emotional disorder' chi^2=0.01, p>0.05), or indeed at the baseline cross-sectional wave (LR 'any psychiatric illness chi^2=0.048; p>0.05; LR 'any emotional disorder' chi^2=1.41; p>0.05), despite the variations in magnitude of the estimates.

Table 3.56 Odds ratios and 95% confidence intervals for the cross-sectional associations between asthma and rates of psychiatric illness, before and after controlling for use of reliever medication in the past month

	Adjustment for Gender Only			Adjustment for Gender and Use of Reliever Medication in Past Month		
	Model N	Asthma Diagnosis		Model N	Asthma Diagnosis	
		N	Odds Ratio (95% Confidence Interval)		N	Odds Ratio (95% Confidence Interval)
Age 10 Cross-Sectional Analysis: ***Any Psychiatric Illness***	4641	1483	1.31 (1.01 – 1.71)	4641	1483	1.41 (1.02 – 1.96)
Age 10 Cross-Sectional Analysis: ***Any Emotional Disorder***	4641	1483	1.5 (1.01 – 2.21)	4641	1483	1.76 (1.11 – 2.82)
Age 13 Cross-Sectional Analysis: ***Any Psychiatric Illness***	4135	1418	1.28 (0.95 – 1.72)	4135	1418	1.25 (0.87 – 1.78)
Age 13 Cross-Sectional Analysis: ***Any Emotional Disorder***	4135	1418	1.45 (0.87 – 2.43)	4135	1418	1.48 (0.81 – 2.71)

CHAPTER 4

Discussion

4.1 Chapter Overview

This research aimed to provide a more balanced insight into the mental health outcomes associated with chronic health problems in childhood and adolescence, and, more specifically, to test the hypothesis that chronic health problems in childhood and adolescence are associated with poor mental health. To test this hypothesis, the primary analyses were built around three main investigative steps, with the aim of identifying the applicability of each set of findings to the mental health outcomes associated with asthma diagnosis. Therefore, this discussion chapter will open with a thorough overview of how each step of the research helped to achieve further insight into the associated mental health outcomes of chronic health problems in the late childhood and early adolescent years.

The chapter will then focus on the findings of the secondary analyses. The secondary analyses were designed to provide a greater confidence with regards to the validity and reliability of the indications of the primary analyses. Specifically, these analyses examined the consistency of the findings across outcome measures, and examined whether the psychiatric associations attributed to asthma diagnoses were applicable to all children with an asthma diagnosis, regardless of the recent activity of symptoms**.**

Throughout this discussion chapter, limitations to the analyses will be highlighted, and emphasised. This will help to identify the most substantial limitations to the scope of this research, which will be outlined thoroughly in section 4.5.

In consideration of these limitations, the final section of the chapter, and the thesis, will define the major learning points from this research. Most importantly it will draw on the crucial learning points from the thesis overall to consider what are the next steps going forward in understanding, and supporting, the mental health of children and adolescents living with chronic illness.

4.2 The Cross-Sectional and Longitudinal Associations of Chronic Health Problems to Rates of Psychiatric Illness

The aim of this research was to provide a more robust test of the theory that chronic health problems in childhood and adolescence are associated with poor mental health outcomes, through the stress these health issues place on normative patterns of development. Therefore, an important initial step was to establish whether chronic health problems had an identifiable association with increased rates of psychopathology in the younger age groups examined as part of the ALSPAC study. It should be kept in mind that while previous research indicated that there may be a relatively higher prevalence of mental health symptomatology among children and adolescents living with chronic health problems, this was of a small to moderate effect size, with many authors questioning whether this increase reflected a rise of clinical significance (e.g. Bennet, 1994). Moreover, although many authors indicated that adolescence may be a particular period of acute psychiatric risk for children with chronic health problems, this remained largely unsubstantiated by the research evidence.

Previous analyses suggested that the generally low magnitude of the associations identified between chronic illness and poor mental health outcomes in childhood and adolescence may reflect methodological artefacts, such as dependence on small samples (e.g. Lavigne & Faier-Routman, 1992) and poor measures of mental health (e.g. Canning & Kelleher, 1994). This study aimed to identify if using a larger sample, with high quality measures of mental health, would aid in the identification of stronger and more consistent associations of chronic health problems in childhood and adolescence to psychiatric illness. Initial indications suggested that this may be the case. Within this study, chronic health problems were found to be strongly and significantly associated with relatively increased rates of psychiatric illness at 10, 13 and 15 years when associations were examined both cross-sectionally and longitudinally. Moreover, although this association was moderated by gender, likelihood ratio testing and sensitivity analyses suggested that the socio-economic status of the child's family, or a history of parental mental illness, did not account for the associations

identified (although limitations to these measures are discussed in section 4.6.2). Some findings of note from these analyses will now be discussed.

4.2.1 The role of illness severity

The ratings of illness severity were retained in the cross-sectional analyses, despite the limited analytic power indicated, as the literature review consistently highlighted that severity and impairment may play a key role in the mental health outcomes attributable to chronic illness. For example, the studies of Delmas and colleagues (2011) and Katon and colleagues (2007), which achieved the quality criteria of the systematic review, suggested that poor physical health, and active patterns of asthma symptomatology, were key mediating factors in the mental health outcomes attributable to asthma. The findings of the systematic review raise a question of whether children with more mild and unobtrusive symptomatology – which evidence suggests comprises most of the child and adolescent population with chronic health conditions (e.g. Newacheck & Taylor, 1992; Barlow & Ellard. 2006) – were at risk of experiencing poor mental health outcomes. Therefore, a key point of interest in the initial cross-sectional analyses, regarded whether children with chronic illness rated by parents as “quite healthy, but a few minor problems” would be equally at risk of experiencing poor mental health outcomes to children rated as “sometimes quite unwell” or “almost always unwell”.

It is firstly important to note that ratings of illness severity amongst children with chronic illness did show a degree of fluctuation between time-points. Although, in keeping with the epidemiological literature, only a small minority of children with chronic health problems were identified as experiencing more severe levels of illness at each cross-sectional wave, the sample of children rated as being ““sometimes quite unwell” or “almost always unwell” was not equivocal. This finding highlights that many chronic health problems may show variations in activity over time, and this may be an important consideration when identifying children at risk of experiencing poor mental health outcomes, especially as illness severity did seem to play an important role in these outcomes. The degree of illness severity in the preceding year showed significant associations with rates of psychiatric illness at both cross-

sectional waves. Although severity of illness did not fully mediate the mental health outcomes identified – children who were identified as having experienced mild symptoms in the past year still indicated a minimum 50% rise in rates of psychiatric illness relative to their healthy peers at both cross-sectional waves (both $p<0.01$) – children who were experiencing more severe symptomatology showed exponentially higher increases in overall rates of psychiatric illness relative to both their healthy peers and children experiencing milder symptomatology. This is illustrated by the fact that, in spite of limited analytic power, statistically significant increases in rates of psychiatric illness were indicated at both cross-sectional waves. However, imprecision in the confidence intervals were wide due to the small sample size. It is also important to note that these analyses were cross-sectional and based on parent's recollections of illness severity over the past year. Therefore, it is not possible to delineate directionality on the basis of these findings, as there is an equal possibility that children experiencing higher levels of mental illness were perceived to be more ill by their parents. Yet, these cross-sectional indications were significant as they stood as initial insight into the role illness severity may play a role in poor mental health outcomes observed among children with chronic illness.

4.2.2 Longitudinal associations between chronic illness and mental health outcomes

The longitudinal analyses indicated that children with chronic health problems were, at baseline, over twice as likely to be identified as having a psychiatric illness as their healthy peers. At 13 years, they were again twice as likely to present with a psychiatric illness relative to the comparative group. Significantly, chronic health problems remained independently associated with a 73% rise in the prevalence of psychiatric illness at this wave, after having controlled for the baseline association between chronic illness and psychiatric illness. Yet, in contrast to initial hypotheses, the association between chronic illness and the prevalence of psychiatric illness was weakest at the 15 year measurement wave. Please note that this was also the only wave at which both parents and their children were informants on the DAWBA measure. Although adolescents with chronic illness were still

indicated to experience a 60% increase in rates of psychiatric illness at this wave, this association did not remain statistically significant after adjusting for the presence of psychiatric illness at 13 years. It was initially hypothesised that the weakening association of chronic health problems to rates of psychiatric illness at 15 years could be an artefact of the substantial amount of missing case data on the DAWBA measure at this wave. However, analyses with the imputed dataset showed high consistency with the complete case analysis. It should be noted that an independent association between chronic illness and a statistical significant increase in rates of emotional disorders at 15 years was identified, which suggests there may not be an overall increase in rates of psychiatric illness amongst children with psychiatric illness at this wave, a more nuanced relationship exists. Please note that the association between chronic illness and psychopathology in adult samples is largely characterised by emotional psychopathology (Academy of Royal Colleges, 2009). Further adjustment for the presence of psychiatric illness at 10 years had no further discernible impact on the association between chronic illness and mental health at 15 years, which suggests a possibility that the longitudinal associative models were over-adjusted. Yet, it was considered important to ensure that the association at age 15 represented the unique association of chronic illness with psychiatric illness rates at this specific time-point.

Overall the findings do suggest that although the age of 13 was the acute period of psychopathology-onset for children living with chronic health problems within the ALSPAC study sample, this risk was attenuated slightly at age 15 years. However, an increased rate of emotional disorders among adolescents with chronic illness may still be observed. Therefore, in contrast to the views of the theorists in the literature review of adolescence as a period of increasing risk for poor mental health in children with chronic illness (e.g. Sawyer et al., 2007; Michaud et al., 2007), based on these observations, chronic health problems in the ALSPAC dataset would seem to be associated with a late childhood and early adolescent critical period of risk. However, comparisons of these findings with the associated outcomes of asthma diagnosis showed a degree of divergence.

4.2.3 Comparisons with analyses of asthma diagnoses

The analyses with the associated outcomes of asthma diagnosis were insightful in many ways. First of all, the cross-sectional and longitudinal indications of an increased rate of psychiatric illness among children with asthma supported the theory of chronic illness as a risk factor to child and adolescent mental health. However, given the relatively lower magnitude of the odds ratios, it suggests that the association with psychiatric illness may vary in degree between different conditions. It should be noted that the cross-sectional association of asthma diagnosis to increased rates of psychiatric illness at 13 years was just above the threshold of statistical significance, despite an identified 30% increase in overall rates of psychiatric illness among children with asthma at this wave. However, the lack of statistical significance for the association at this cross-sectional wave may simply reflect a lack of sensitivity within the analyses to increases below the rate of 50% .

As previously suggested, one of the most interesting insights was in terms of the applicability of the early adolescent risk identified in the analyses of children with chronic illness. The analyses of children identified as having an asthma diagnosis at 10 years suggested that not only was there an independent association of asthma diagnosis to rates of psychiatric illness at 13 years, but that there was also an independent association of asthma with rates of psychiatric illness at 15 years. Moreover, the association of asthma to rates of psychiatric illness at 15 years when controlling for pre-established psychiatric illness was slightly stronger than that of the 13 year association, and this magnitude was reflected in the analyses using the imputed datasets. Yet, it should be noted that similar to the analyses of children with chronic health problems more generally, the association between asthma and rates of psychiatric illness at 15 years seemed to be driven by an increased rate of emotional disorders. There are many possible reasons why this stronger association with psychiatric illness at this wave may have been observed. In the opening literature review it was suggested that asthma may have a stronger association with mental health outcomes in adolescence; however, this trend was identified based on studies that did not achieve the quality

criteria set for the systematic review. An alternative hypothesis, based on the variations in the analyses between the cross-sectional and longitudinal asthma samples, suggests that there is some unique characteristic of the children identified as having an asthma diagnosis at 10 years in the ALSPAC dataset that places them at an increased risk of developing psychiatric illness at subsequent waves. Although the samples for both the age 13 cross-sectional analyses and the longitudinal analyses were indicated to be large enough to power comparative analyses, and increased rates of psychiatric illness among children with asthma were identified in both samples, the magnitude of the association between asthma and rates of psychiatric illness at 13 years was exponentially higher in the longitudinal analyses than the cross-sectional analyses (gender-adjusted OR: 1.76 (95% CI: 1.26 – 2.45) versus gender-adjusted OR: 1.29 (95% CI: 0.98 – 1.7)). Some of this variation could be due to the more homogenous nature of the comparative sample in the longitudinal analyses. The longitudinal comparison group was identified based on health ratings on both the age 10 and age 13 questionnaires, and it is known that socio-economic gradients within the ALSPAC dataset tend to increase with increasing completeness of participation in ALSPAC (Boyd et al., 2012). To illustrate, the gender-adjusted odds ratio for the baseline asthma association to psychiatric illness increased from 39% (95% CI: 1.09 – 1.78) to 57% (95% CI: 1.19 – 2.08) when the longitudinal comparative sample was used as the point of comparison, rather than the age 10 comparative cross-sectional sample. However, the dramatic nature of the increased strength of this association suggests that, in addition to methodological artefacts, there must be some form of variation between the characteristics of the baseline and age 13 sample that are implicit to the increased mental health risk identified. For example, given that the cross-sectional analyses of chronic illness suggested that illness severity moderates the associated rates of chronic illness, it may be possible that children with asthma at baseline had a higher prevalence of chronic, persistent forms of the condition.

The possibility that these findings were due to the poor validity of the chronic illness measure were explored. This measure was based on parental health

ratings at 10 and 13 years, meaning there was a possibility that the longitudinal associations may reflect concurrent associations of health to mental health, rather than longitudinal outcomes. However, the sensitivity model (see 3.2.3.4) indicated very different patterns in the association of concurrent health ratings to mental health outcomes at 10 and 13 years, which provides a degree of confidence that this divergence is not a methodological artefact. Instead it appears that this divergence at the 15 year measurement is due to a unique characteristic of the baseline asthma sample, either in terms of a unique association of asthma to mental health at 15 years, relative to other chronic illness conditions, or in terms of a unique psychiatric risk attributable to this specific sample.

4.2.4 Explorations of comparative rates of emotional, anxiety and behavioural disorders

The explorations of the comparative rates of emotional, anxiety, and behavioural were considered exploratory in nature. The findings regarding the associations of asthma diagnosis highlighted the reasons for this caution. Based on the cross-sectional analyses of the age 13 questionnaire, it would be inferred that the association with psychiatric illness at this wave is strongly driven by an observed increase in rates of anxiety disorders among the asthma sample. Yet, based on the longitudinal analyses, it would be surmised that the association at this wave was strongly associated with a rise in behavioural disorders that was observed among children with asthma at this wave. The reason for these inconsistencies is most likely underlined by the low prevalence rates of such disorders overall, which cause extremely small differences in prevalence rates of the disorders relative to the comparative groups to be exaggerated. For illustrative purposes, it should be noted that the prevalence of anxiety disorders was actually higher among the longitudinal asthma cohort than the cross-sectional cohort (2.3% versus 1.44%), whilst behavioural disorders were actually slightly more prevalent in the longitudinal sample than in the cross-sectional sample (3.71% versus 3.6%). Yet, when looking at the trends across observations as a whole, the finding that chronic illness seems to be associated with a rise in both behavioural, emotional and anxiety disorders - although the relationship with

emotional and anxiety disorders seems to be stronger and more consistent - is extremely important. This finding underscores the unique nature of the mental health associations for chronic illness in this younger age group, given that the comorbidities seen in adult populations are seen to be driven largely by increased rates of major depressive disorder (see Academy of Royal Colleges, 2009). This is further substantive evidence against the commonly held view in healthcare discourse of children and adolescents living with chronic illness as “small adults” (e.g. Grey & Sullivan-Bolyai, 1999).

4.2.5 Comparisons with the opening literature review

It is hard to compare the findings concerning the cross-sectional and longitudinal associations of chronic illness to rates of psychiatric illness given that the opening literature review specifically highlighted a lack of prevalence studies. On the surface, these analyses showed a lot of consistency with studies which examined the mental health outcomes of chronic illness in the literature review. As in previous meta-analyses (e.g. Lavigne and Faier-Routman, 1992; Pinquart & Shen, 2011a; 2011b; 2011c), chronic health problems in general were associated with increased rates of emotional and anxiety typified psychopathology, and to a lesser degree, behavioural symptomatology. Moreover, severity of the illness was indicated to play some form of role in the mental health outcomes observed across many studies in the literature, and was also suggested to play some form of role in the associated mental health outcomes in the cross-sectional analyses of this research. Moreover, trends amongst the studies suggested that although associations may be more strongly characterised by a rise in emotional and anxiety disorders, a rise in behavioural disorders was also identifiable. However, where the indications between this study and previous studies diverge is in terms of the magnitude of the association indicated. While these analyses suggest that chronic illness shows strong and significant associations with rates of psychiatric illness, previous studies, such as the meta-analysis of Bennett (1994) suggested that children with chronic illness may not be at an acute clinical risk. This suggests that sample size may play a substantial role in obscuring the psychiatric illness associations of

childhood and adolescent chronic illness. However, it should be noted that actual prevalence rates of psychiatric illness among children with chronic illness in the ALSPAC sample fell below 10% at all waves. Yet, this may reflect the selective drop-out bias of children with higher levels of mental health symptomatology within the ALSPAC, an artefact which is observed across most cohort studies (see Wolke et al. 2009). Finally, these findings diverged with previous research by indicating that socio-economic status may not play a substantive role in the mental health associations identified. Although there is an empirically-based rationale for why this research did not find such an association (see section 4.6.3), it must be acknowledged that it may also represent the lack of sensitivity of analyses with ALSPAC data to socio-economic gradients. It was acknowledged at the outset of this study that the ALSPAC would be limited in its ability to provide insight into the nature of socio-economic variations in psychiatric illness prevalence rates, given the relatively affluent nature of this sample (e.g. Boyd et al., 2012). However, as stated in the methodology, it was considered that it was more important to establish if an association with psychiatric illness may be observed in a large and locally-representative cohort, before exploring possible variations by socio-economic status.

When comparing the outcomes specifically related to asthma to studies in the systematic review, difficulties again occur given the lower prevalence rates of anxiety and emotional disorders in the ALSPAC, which limited the power of the analyses. Limitations are also imposed by the cross-sectional nature of previous investigations, and the broad age range of the samples used. However, the indications of a 70% increased rate of depressive disorders in Delmas and colleagues (2007) study, and Katon and colleagues (2007) finding of a 1.83 odds ratio for the comparative increase in rates of anxiety and depressive disorders among adolescents with asthma, are not very different than the comparative risks indicated in this study for the mid-adolescent period (e.g. gender-adjusted OR emotional disorders 15 years: 2.37 (95% CI (1.42-3.97)); gender-adjusted OR emotional disorders 15 years: 1.78 (95% CI (0.9-3.52)); in spite of the stricter criteria of asthma diagnosis used in the former studies. This could perhaps be seen as an

indication that the asthma sample identified at baseline may have stronger patterns of symptomatology than would be expected based on population norms, where children with mild persistent asthma are found to be in the majority (e.g. Van Gent et al., 2008). Moreover, as stated, the age-related gradient in rates of psychiatric illness that was observed amongst children with asthma in the longitudinal analyses was also consistent with trends in studies that did not achieve the quality criteria. Finally, it should be noted that in contrast to the findings of Chen and colleagues (2014b), asthma remained associated with increased rates of psychiatric illness, inclusive of emotional disorders, following adjustment for pre-established psychiatric disorders.

4.2.6 The importance of examining mediating and moderating factors in the association of chronic illness to mental ill-health

These analyses underscored the importance of examining the mechanisms by which chronic illness is associated with poor mental health. Symptom severity was associated with increased rates of psychiatric illness in children with chronic illness, and it is important to understand whether this moderating role was due to physical illness or a related impairment on daily activity. Indeed, there is also a possibility that these severity ratings were an outcome of co-occurring psychiatric illness in the context of chronic health problems. Furthermore, it is important to understand why children with less obtrusive symptomatology in the ALSPAC dataset were also at an increased risk, relative to their peers, of experiencing mental illness. Moreover, it is important to understand why the indications of the analyses examining the outcomes of chronic health problems more generally, diverged from the analyses of children with asthma at 15 years, and whether this reason was underlined by factors non-specific to any illness, such as symptom severity, or whether it reflected a risk specific to asthma diagnoses. Therefore, the next stage of the discussion will look at what this study suggested regarding the mechanisms of the association of chronic health problems to psychiatric illness.

4.3 The Mechanisms by which Chronic Illness leads to Poor Mental Health Outcomes

The literature review indicated that chronic illness is viewed as a stressor in the lives of children and adolescents, disrupting the normative patterns of development, and leading to poor mental health outcomes in this group (e.g. Wallander & Varni, 1998; Michaud et al., 2007). However, investigations of supporting evidence questioned whether there was conclusive evidence of generalised impairments to the development of children and adolescents with chronic illness relative to their healthy peers. Moreover, the evidence suggested that any forms of disruption to normative patterns of development may be contingent on diagnosis or degree of illness severity and impairment. The initial associative analyses also emphasised the importance of looking at the mechanisms underlying the association of chronic illness to poor mental health in order to understand diverging patterns in children with asthma, and the role of symptom severity in moderating mental health outcomes. Although the cross-sectional analyses were important key signifiers that symptom severity may play some role in the psychiatric illness associations observed, it was also important to build on these analyses by looking at different measures of severity and impairment, and to explore directionality. This section of the discussion chapter will more fully explore the findings of the mediation analyses and learning points from the creation and fitting of the path model in order to identify the mechanisms by which chronic illness in the ALSPAC was associated with mental ill-health outcomes at 10 and 13 years.

4.3.1 Consistency in the findings of the mediating mechanisms in asthma diagnoses

One of the key findings in the mediation analyses and the fitting of the path models was the high degree of consistency in the factors predictive of mental health outcomes in asthma more particularly, and in chronic illness more generally. In fact, when comparing the pathways in the two separate path models, the only point of divergence was that the direct association between health-related absenteeism at 10 years old and rates of psychiatric illness at

13 years was slightly over the threshold of significance. This would suggest that factors non-specific to any one condition may be the best insight into the mental health outcomes associated with chronic health problems. This would be consistent with assertions of theorists in the field that the residual outcomes common to all chronic illness are the best insight into associated mental health outcomes, even in life-threatening conditions such as cancers (e.g. Stein & Jessop, 1982; Eiser, 1993; Wallander & Varni, 1998). However, although the consistency of the models and pathways between the two sets of analyses in a substantive finding, it must be balanced with the caveat that the vast majority of the mediation analyses in this study focused on the early adolescent period.

Although the mediating factors in mental health outcomes at 10 and 13 years were highly consistent, the initial mediation analyses pointed to some degree of divergence in psychosocial outcomes. This indicates that although the factors predicting mental health outcomes in chronic illness may be applicable across conditions, the lived experience and general psychosocial outcomes of different conditions may differ. In contrast to the findings of the associations of chronic illness more generally, asthma diagnosis at baseline did not predict higher levels of dissatisfaction with friendships at 12 years. This finding regarding the comparable peer satisfaction scores was consistent with a meta-analysis by Martinez et al. (2011), which found that children with asthma had comparable social competence scores to peers across studies. One other point of divergence in the initial mediation analyses should be noted. A seemingly developmental trend emerged in the mental health outcomes associated with chronic illness. The age 15 DAWBA measurement was the only wave at which the factors of parental monitoring, parental solicitation and child disclosures were indicated to mediate mental health outcomes, despite the fact that these measures were also completed by children in the ALSPAC in the early adolescent period. However, it should be noted that this mediation trend was in the opposite direction to that hypothesised, with chronic health problems predicting significantly lower levels of parental monitoring, parental solicitation and child disclosures at this wave. Yet, given that these factors were associated with a lower prevalence

of psychiatric illness across waves, it could be argued that, based on face validity, these scales seemed to be a stronger indicator of familial cohesion than the measure extracted for this study – that of inter-parental conflict. This may reflect that parental monitoring becomes a more pivotal factor in the mental health of children with chronic illness as adolescence progresses, consistent with the theories put forward by researchers in the field (e.g. Suris, 2003). However, asthma diagnosis at baseline showed no significant association with any aspect of parental monitoring at 15 years. This finding again raises questions about whether the consistency found in the factors predictive of mental health outcomes at earlier waves would be demonstrated at later years of adolescence, given the divergence indicated in the associative analyses at this wave.

4.3.2 Mediating variables in the association of chronic illness to rates of psychiatric illness

The emergence of peer victimisation and school absenteeism as the key mediating variables in the association of chronic health to poor mental health outcomes at 10 and 13 years was again in many ways a surprising finding. As the methodology chapter implied, the derivation of the 'Perceptions of Fatigue' scale as a measure of impairment was to supplement the more holistic measure of health-related impairment - school absenteeism – as it was largely hypothesised that it would be these physical limitations that would provide the best insight into the mental health outcomes observed. This hypothesis was based on the recurring identification of symptom severity as a moderating variable in the systematic review, and, indeed, condition severity was also suggested to play a role in the mental health outcomes associated with chronic illness in the cross-sectional analyses. Yet, although chronic illness, and asthma diagnosis, was associated with higher scores on the 'perceptions of fatigue' scale, and these scores emerged in the initial mediation analyses as an independent predictor of mental health outcomes of chronic illness, follow-up analyses indicated that scores on this scale were not strong enough predictors of the association of chronic health problems to psychiatric illness in their own right. Rather, a basic model suggested that scores regarding physical limitations may be a

related outcome in this association, rather than playing a primary or causative role. Perhaps, this contrasting finding from studies using a non-categorical methodology in the systematic review (e.g. Schmidt, Petersen, & Bullinger, 2003; McDougall et al., 2004) reflects the use of a longitudinal methodology, and indicates that for the ALSPAC perceptions of activity limitations are a related outcome of mental health symptomatology in the context of chronic illness.

Given that the 'Perceptions of Fatigue' scale was not indicated to play a mediating role in the association of chronic health problems to mental ill-health outcomes, the indications that school-related absenteeism played a consistent mediating role in mental health outcomes for children with chronic illness both within-time and across time is an extremely notable finding. This finding is especially important given that similar patterns emerged for children with asthma. Significantly, this is a chronic illness outcome that is unique to this younger age group, standing as a further suggestion that attempts to infer the mental health associations of chronic illness in children and adolescents from adult populations may ultimately be deficient. Moreover, given that health-related absenteeism was correlated with parental ratings of illness severity, this may be the mechanism by which illness ratings moderate associated mental health outcomes. Overall, the findings would suggest that school absenteeism rates may be a means to identify children with chronic illness who are at risk of developing poor mental health in late childhood and early adolescence, regardless of the presence of activity limitations. However, the more nuanced understanding of why health-related absenteeism may play such a key role in the outcomes observed is not as easy to isolate.

Weitzman (1986) argued that although school-related absenteeism is a key measure of chronic illness status, researchers must recognise that it is a non-specific factor, and, therefore, interpret the role of this factor in light of controls for other variables. Indeed school-related absenteeism as a consequence of chronic illness has been discussed as an indicator of disease activity and symptom control (Kearney, 2008; Hsu, Qin, Beavers, & Mirabelli, 2004), an early marker of anxiety and depressive disorders

(Michaud et al., 2007; Kearney, 2008), psychosomatic symptomatology (Kearney, 2008), as well as a signifier of disruptions to social development and academic attainment (Eiser, 2003). In these analyses, the association of health-related absenteeism to poor mental health outcomes was not supported as being contingent on the functional limitations identified by the 'Perceptions of Fatigue' scale, which suggests that this relationship reflects more than a relationship of disease activity, or psychosomatic symptoms, to mental health outcomes. Moreover, psychiatric illness at 10 years was not associated with health-related absenteeism at 13 years. However, it should be noted that this may reflect the nature of measurement in this scale. Health-related absenteeism was coded as a binary variable, and there was strong consistency in the children identified as demonstrating high levels of health-related absenteeism across the two measurement waves. Therefore, perhaps a stronger association would have been identifiable if scalar measures were used rather than binary categorisations.

Based on the literature review a theory of school absenteeism affecting mental health as a consequence of social disruption would be the most consistent. In qualitative interviews conducted with children with illness-related disruptions to schooling, Yates and colleagues (2010) indicated that a strong concern to emerge in the accounts of both children and their parents regarded how these disruptions may affect peer relationships. Indeed, concerns regarding the impact of chronic illness on friendships emerged as the strongest theme in Taylor, Gibson and Franck's (2008) review of the qualitative literature. However, although dissatisfaction with peer relationships may be symptomatic of the wider negative impact chronic illness has on the lives of children and adolescents, it may not be a full account of the mechanisms underlying the high rates of mental illness symptomatology observed among this population. In this study, although children with chronic illness reported higher levels of dissatisfaction with friendships at 12 years, these scores were not independently predictive of mental health outcomes at 13 years. Moreover, although absenteeism plays an equally important role in the mental health outcomes attributed to asthma at 10 and 13 years, children with asthma were not indicated to report

increased levels of dissatisfaction with friendships relative to their health peers. Furthermore, although Yates and colleagues (2010) qualitative accounts indicate that bullying in children with chronic illness is attributed by the child and their parents to the way in which absenteeism makes children seem different from their peers, the path model indicated that bullying and health-related absenteeism were independent predictors of mental health outcomes in children with chronic illness in the ALSPAC. Moreover, although the over-arching discursive focus in these studies returns consistently to peer relationships, it is clear from the related discourses that health-related absenteeism and increased contact with healthcare services makes the child more internally focused and aware of the possibility of their own limitations (see Yates et al., 2010; Taylor et al, 2008; Lambert & Keogh, 2005). It is important to note that self-focused internal attention and feelings of loss of control have also been independently associated with mental illness (e.g. Lindsay, Kingsnorth, & Hamdani, 2011). Moreover, the stresses associated with keeping up with school work, in spite of any on-going physical symptomatology, can also not be discounted (e.g. Geist et al., 2003). Therefore, although school-related absenteeism emerged as a consistent indication of risk for developing psychiatric illness in the context of chronic illness within the ALSPAC study, it is not possible based on these findings, or indeed based on previous investigations, to conclude why this factor plays such a key role in mental health outcomes. More nuanced measures, such as measures of locus of control and academic stressors, would be required to illuminate the specific reasons why this variable has such a strong association with the associated mental health outcomes.

As stated, the other key mediating variable to emerge in both analyses of chronic illness more generally, and asthma more specifically, was peer victimisation. This was especially surprising given that the systematic review of Sentenac and colleagues (2012) specifically highlighted asthma as a condition in which higher levels of peer victimisation might not be indicated, relative to other chronic illness conditions. Yet, although peer victimisation has been identified as one of the strongest predictors of youth-onset psychopathology (e.g. Lereya et al., 2015), peer victimisation was not a

consistent predictor of mental health outcomes among children with chronic health problems in the ALSPAC dataset across waves. Although peer victimisation was the strongest mediating factor in mental health outcomes at 10 years, having controlled for this association, and controlling for the strong association of psychiatric illness at 10 years to psychiatric illness at 13 years, peer victimisation at 12.5 years did not continue to independently predict new onset psychopathology. However, it should be noted that there was a great deal of consistency in the children identified as experiencing peer victimisation across the two measurement waves, meaning that this lack of continuing predictive power of peer victimisation to mental health outcomes may reflect a sample artefact. In conclusion, within the remits of this study, peer victimisation was a within time predictor of the associated mental health outcomes of chronic illness, and was indirectly associated with subsequent mental health outcomes due to the pervasiveness of mental health disorders over time. However, peer victimisation did not provide insight into why chronic illness continued to be associated with increased rates of psychiatric illness at 13 years. In contrast, high levels of health-related school absenteeism were associated with concurrent mental health outcomes within time and also across time, emphasising that for the ALSPAC sample at this developmental phase, this variable seemed key to identifying children at risk of developing mental illness in late childhood to early adolescence.

It was originally questioned what it would mean for the theory under examination if impairments, rather than poor developmental outcomes, were indicated to be the strongest mediators of mental health outcomes. Previous research indicated that health-related impairments are not highly prevalent amongst children with chronic health problems (e.g. Barlow & Ellard, 2006), and it was questioned whether this would suggest that only a minority of children with chronic illness were at an increased risk of developing psychopathology. However, it is clear that, within this study, the finding that health-related absenteeism was the strongest and most consistent mediator of the mental ill-health outcomes associated with chronic illness in no way contradicts the underlying theory that chronic health problems generally pose a risk to childhood and adolescent mental health. Initial exploratory analyses

indicated that health-related absenteeism was by no means a proxy measure of symptom severity, although these variables were correlated. In fact, a substantial proportion of children with more minor health problems also fell into the grouping at the two cross-sectional waves (possible limitations in this finding are discussed in 4.4.1). Yet, school-related absenteeism in the context of chronic illness has been viewed as a marker of so many variables which would introduce stress into the lives of young people (e.g. disease activity (Kearney, 2008); disruptions to social development and academic achievement (Eiser, 2003)). Therefore, it could be argued that high levels of health-related absenteeism are a proxy measure of the type of stressors that have previously been implicated in the mental health outcomes attributable to chronic illness in childhood and adolescence. Yet, the mediating role of peer victimisation in the associated mental health outcomes at age 10 years was independent of that of health-related absenteeism, highlighting that reports of peer victimisation were not contingent on children reporting some degree of health-related impairment as a consequence of their chronic illness. Above all, the finding that school-absenteeism and peer victimisation emerged as key mediators of mental health outcomes in children with chronic illness, rather than a measure of activity limitations, underscores the importance of examining the mental health associations of chronic illness in an age-specific framework.

4.3.2 Limitations to the use of the cascade model framework in the context of this study

As stated, the model tested for this research was built on the premises of cascade model theory, which hypothesises that not only do identifiable risk factors lead to poor mental health outcomes, but that poor mental health outcomes result in subsequently poor developmental outcomes, and that this in turn exacerbates the expression of psychiatric illness (i.e. the risk factors lead to a negative cascade of consequent outcomes) (see Masten & Cicchetti, 2010). Although the literature review did not identify an existing study using the cascade model framework which focused explicitly on child physical health, it was theorised at an early stage of this research that this framework would be insightful into the mental health associations of

childhood and adolescent chronic illness. This reasoning was based in previous discussions of the interactive nature of psychiatric illness comorbidities and symptom severity, with the expression of mental illness exacerbating symptom severity in turn, and this severity further leading to poor mental health outcomes (see Academy of Medical Royal Colleges, 2009). Although it was not possible to create a cascade model that was truly fitting to the literature, due to a lack of repeated measures at the 15-year wave (see Masten & Cicchetti 2010), it was hypothesised that an interactive association between mental health and the mediating variables would be shown over the two-time waves studies. However, in contrast to initial hypotheses, a true negative trend of mental illness leading to stronger expression of the mediators of mental health outcomes at subsequent time-points was not identifiable in the path models which were indicated to be a good fit to the data in this study. Even though high levels of health-related absenteeism were strongly correlated with severity ratings, and this variable was the most consistent mediator of mental health outcomes at 10 years and 13 years, both within time and across time, psychiatric illness at 10 years did not predict high levels of health-related absenteeism at 13 years. However, this may be more of a reflection of the way in which health-related absenteeism was measured in this study, rather than reflecting a true lack of relationship. As stated, absenteeism was coded as a binary variable, and there was strong consistency in the children identified as demonstrating high levels of health-related absenteeism across the two measurement waves. The same was true of children experiencing peer victimisation. Therefore, perhaps a negative trend would have been identifiable if scalar measures had been used rather than binary categorisations. It should be noted that, although scores on the ‘Perceptions of Fatigue’ scale were not a mediating factor in the mental health outcomes identified, higher scores on this scale were predicted to a small degree by the presence of psychiatric illness at 10 years in the analyses of this mediation pathway. This would suggest that some form of body-mind interaction in outcomes over time may be found if using more dimensional measures.

Please note, that based on the opening discussions of the epidemiological literature, it was a surprising finding that only two variables emerged as key mediating variables in the association of chronic illness to mental health outcomes at 10 and 13 years. As stated in the opening overview chapters, psychopathology onset in childhood and adolescence is known to be a consequence of the interaction of numerous factors (e.g. Holmbeck, 2002). Yet, peer victimisation has been identified as one of the strongest, independent risk factors to child and adolescent mental health (see Sentenac et al., 2012; Wolke et al., 2001; Lereya et al., 2015). Moreover, as previously discussed, health-related absenteeism is underlined by numerous risk factors to child and adolescent well-being, such as increased health care contact and disruptions to everyday functioning. Therefore, perhaps the emergence of these factors as the strongest mediating mechanisms in the mental health associations identified may reflect the fact that they are strong indicators of a number of stresses to everyday quality of life and development, and underlined by multiple risk factors to child and adolescent mental health. Consequently, although it may be a possibility that these mediating factors may not be a complete account of the specific mechanistic pathways underlining the associations with mental health identified, they are still likely to provide most insight into the underlying factors in these associations.

Indications of points of possible divergence at 15 years emphasise the reason why a dynamic interpretation of mental health outcomes was chosen. The age 15 DAWBA measurement was the only wave at which the factors of parental monitoring, parental solicitation and child disclosures were indicated to mediate the mental health outcomes associated with chronic illness, despite of these measures being the most consistently administered among those selected for the mediation analyses. The fact that this age-dependent trend emerged adds further confidence for the validity of the measure of chronic health problems as a sensitive measure of longitudinal outcomes. Moreover, the fact that the associative analyses showed an age-related increasing gradient in rates of the associated psychiatric illness with asthma, underscores that understanding mental health outcomes needs to be

underlined by considerations of possible age-related variations. It should also be kept in mind that parental-ratings of illness severity fluctuated between waves, and this also supports a dynamic conceptualisation of the lived experience of chronic illness and the associated mental health outcomes. Therefore, although a developmental and dynamic cascade did not emerge in the models for this study, this is more likely to be a consequence of the limited period of analysis chosen for the analyses, as well as reflecting the measures chosen, rather than an indication of general stability in mental health outcomes across childhood and adolescence, and in the related factors predicting these outcomes.

4.4 Insight Gained from the Secondary Analyses

The secondary analyses were designed to provide concurrent support that the primary analyses were the most reliable and valid signifiers of patterns within the ALSPAC data as were possible to isolate. Therefore, given that the sensitivity of psychiatric outcome measures in the context of paediatric chronic illness was questioned in previous empirical investigations, it was deemed important to examine the consistency of the findings of the primary outcome measure, the DAWBA, against alternative measures of mental health contained in the ALSPAC dataset, and to examine the children's mental health from a range of perspectives. In addition, given that previous investigations suggested that asthma diagnoses without the presence of on-going symptomatology were not associated with increased rates of psychiatric illness, it was important to examine if the mental health outcomes attributed to asthma diagnoses in the primary analyses were applicable across children living with asthma diagnoses. The outcomes of these analyses will be discussed in section 4.5.1 and 4.5.2 that follow.

4.4.1 Indications of the alternative outcome measures

Analyses with the alternative outcome measures reflected the results of the primary analyses by unanimously indicating strong and significant associations between chronic health problems and increased rates of psychopathology, with the exception of analyses of the teacher-rated SDQ. This finding was also applicable to children with asthma, with strong associations identified in both the cross-sectional and longitudinal analyses. Although underlying prevalence rates suggested an increased rate of psychopathology in children with chronic illness rated as being "sometimes quite ill/almost always unwell" when compared to children rated as "quite healthy, but a few minor problems" at both cross-sectional waves, this group was not consistently identified as having a significantly increased rate of psychopathology on the alternative measures. However, this is a likely consequence of the higher prevalence of missing data on these measures, relative to the primary outcome measure. This contrasts with evidence from previous meta-analyses drawing on scales of emotional and behavioural symptomatology (e.g. Lavigne & Faier-Routman, 1992; Bennett, 1994),

which indicated that the rise in mental illness symptomatology amongst children with chronic illness may not represent an acute clinical risk. This comparative difference again emphasises the greater deal of insight that can be gained by examining larger and more heterogeneous community-based samples, such as the ALSPAC data. It also contrasts with the findings of previous meta-analyses in which parent- and child-reported measures were found to differ significantly in their indications regarding the presence of mental health symptomatology (e.g. Pinquart & Shen 2011a; 2011b; 2011c). The findings of these analyses suggested that the poor mental health outcomes indicated are not contingent on the perspective of the informant used. The consistency in findings is especially interesting given that initial exploratory analyses suggested that there was very low concordance between the children identified as having a psychiatric illness on each of these measures overall. Comparison of the standard deviation scores for the chronic illness sample and asthma sample to normative guidelines also suggested a lack of disproportionate variation in mental health symptomatology scores among the samples, which may suggest that the consistency of findings is due to the leveling out of intra-individual variability in chronic illness cohorts in the larger sample. This variation was highlighted as a possible rationale for the findings of high intra-disease variation in mental health outcomes in previous investigations (e.g. Lavigne & Faier-Routman, 1992). Yet some caution should be taken, as this lack of variability may also reflect the selective drop-out bias identified in the ALPAC cohort (see section 4.6.4).

The lack of consistency in findings when using the teacher-rated SDQ is quite interesting (see Appendix V). Evidence would seem to suggest that, while teacher's ratings are very sensitive to detecting externalising symptomatology, their ratings are not very reliable indicators of internalising symptoms (e.g. Loades & Mastroyannopoulou, 2010). Given that both the analyses with the generalised chronic illness measure and the measure of asthma diagnoses seemed to indicate that the association with psychiatric illness at this wave was more strongly underlined by a rise in emotional and anxiety symptomatology, it is interesting to find that teacher ratings, which

are strong indicators of behavioural disorders, suggest a weak association between the exposure measures and likely psychopathology, and that this contrasts with indications of all other outcome measures examined. However, it should be kept in mind that associations with increased rates of likely psychopathology, although not statistically significant, were still indicated, and that high amounts of missing data on this measure (over 40% across samples) may have also limited analytic power to detect comparative variations in outcomes on this scale. These measures also suggested that chronic illness may be associated with an increase in overall psychopathology, as well as emotional psychopathology more specifically, consistently across the early adolescent period. Results of the analyses with the primary measures suggested that asthma diagnoses were inconsistently associated with rates of emotional disorders, with the magnitude of this association differing across time-points. However, analyses of the secondary measures suggested strong and significant associations between chronic illness and emotional psychopathology at all waves, inclusive of independent associations when controlling for outcomes at previous waves, and that this was also applicable to the analyses of the outcomes of asthma diagnosis. This may suggest that the inconstancies in the magnitude of the association between asthma and emotional disorders in the primary analyses is due to low analytic power.

It should be noted that although all outcome measures, with the exception of the teacher-rated SDQ, indicated strong and statistically significant associations between chronic health problems and increased rates of psychopathology across waves, this does not mean that the identified underlying prevalence rates of disorders among the sample were comparable. Emotional psychopathology was identified as being more highly prevalent in the ALSPAC sample when children's ratings on the sMFQ were used compared to both parent-ratings on this measure and ratings on the primary outcome measure. Moreover, although previous meta-analyses have indicated that parents generally provide more negative appraisals of their child's adjustment (Pinquart & Shen, 2011a; 2011b; 2011c), and indeed estimates for the association between chronic health problems and

increased rates of psychopathology in this study were of a slightly larger magnitude on parent-rated measures, underlying examinations of prevalence rates suggest that parent-rated measures provide more conservative estimates of psychiatric illness rates than child- and teacher-rated measures, and the primary outcome measure. However, the exception was that parents indicated a higher prevalence of emotional psychopathology among children with asthma on the age 13 sMFQ than would be expected based on the prevalence rates on the primary outcome measure for both the baseline sample and the age 13 cross-sectional sample. Therefore, although the overall indications of a significant association between chronic health problems and increased rates of psychiatric illness were consistent across measures, the magnitude of the associations identified differed.

The concordance of the sMFQ with the SDQ and the DAWBA was particularly of interest to this study, given that this scale is reliant on items measuring somatic symptomatology as an indication of depressive symptomatology. In contrast to the findings of Canning and Kelleher (1994), the odds ratios indicating the relative increase in emotional psychopathology in children with chronic illness were slightly lower when the sMFQ (both child-rated and parent-rated) was used as the outcome measure rather than the DAWBA. Furthermore, the magnitudes of the odds ratios indicating the relative increase in emotional psychopathology for children with asthma were highly similar when the child-rated sMFQ was used as the outcome measure as opposed to the DAWBA. However, the magnitude of odds ratio on the parent-rated measure for the age 13 cross-sectional wave was slightly higher (OR parent-rated sMFQ: 1.74 (95% CI: 1.15 – 2.62); OR DAWBA emotional disorders: 1.46 (95% CI: 0.9-2.36), but this reflects a generally higher magnitude in odds ratios across measures using parents as informants. This high degree of concordance between the sMFQ and the other measures of mental health was a surprising finding, but perhaps is an artefact of the use of the scale as a binary measure, where the use of a scale cut-off possibly prevents a disproportionate representation of somatic as opposed to non-somatic items. It may also reflect Pinquart and Shen's (2011b) finding of equivalence of responses in children with chronic illness across somatic and

non-somatic items on psychometric scales. However, it should be noted that comparisons with the DAWBA were limited by the likely lack of sensitivity on this measure to increases in emotional psychopathology among children with chronic illness.

One further point of variation in the analyses with the alternative outcome measures should be noted. Adjustments for the hypothesised confounding covariates 'history of parental mental illness' and 'socio-economic status' were indicated to significantly improve the associative model fit for the age 10 cross-sectional analyses of the psychiatric associations of asthma, based on the teacher rating of the SDQ, and the age 11 longitudinal analysis of the psychiatric associations of chronic health problems, based on the parent-rated SDQ. This would suggest that although these covariates may not play a statistically significant role in the associations identified on the primary outcome measure, substantial confounding effects may be found on other psychometric scales. It should be noted, however, that there was no evidence of an interaction effect between these covariates and outcomes on any given scale, consistent with the findings of the analyses with the primary outcome measure. However, this may have been due to the substantially high prevalence of missing case data on these measures. Finally, it should also be highlighted that none of these alternative outcome measures were administered past the age of 13 years, meaning that it is not possible to examine the consistency of the estimates resulting from the analyses with the primary outcome measure at age 15.

In conclusion, these analyses suggested that findings regarding the association between chronic health problems and an increased rate of psychiatric illness at 10 and 13 years were consistently reflected across the alternative outcome measures administered during this developmental phase in the ALSPAC study. This suggests the findings of poor mental health outcomes are not dependent on the perspective of any one group of informants. However, these findings should be balanced with the caveat that these alternative measures were only administered to the ALSPAC sample during the period of 10 to 13 years, meaning that it was not possible to compare the consistency of indications at 15 years. It should be highlighted

that this was the wave at which divergence in the mental health outcomes of asthma, when compared to chronic illness more generally, was observed in the primary analyses.

4.4.2 Concurrent asthma symptomatology and co-occurring psychiatric illness

In the systematic review, the inclusion criteria for asthma diagnosis among the studies found to be at a low risk for methodological bias were quite rigorous. In one of the studies, that of Delmas and colleagues (2011) which examined the prevalence of major depressive episodes in a cross-sectional study of 7000 French 9th grade students (M=15.1 years), it was suggested that adolescents with asthma diagnosis who were not experiencing on-going asthma symptomatology were not at a heightened risk of experiencing major depressive disorders when compared to their healthy peers. For this reason, secondary analyses explored whether controls for dependence on reliever medication in the past month affected the consistency of associations indicated between asthma diagnoses and the prevalence of psychiatric illness in the cross-sectional analyses at age 10 and age 13. The cross-sectional models suggested that reliance on reliever medication did not seem to play a substantial role in the associated mental health outcomes. In these analyses, adjustments for the use of reliever medication within the past month had a minimal impact on the indications of the associative models, and likelihood ratio testing indicated that adjustments for this variable did not substantially improve the fit of the associative model at either cross-sectional wave. This is surprising given that health-related absenteeism, which would seem to be indicative of some level of disease-related activity, and was also shown to be correlated with chronic illness severity in the previous twelve months, was found to be the most consistent mediator of the mental health outcomes associated with asthma. However, it is possible that the measure selected as an indicator of asthma symptomatology - use of reliever medication within the past month, was not a sensitive enough measure to detect variations in the relationship of asthma symptomatology to rates of psychiatric illness. For example, Delmas and colleagues (2011) used both feedback on a questionnaire of asthma symptomatology and a medical

examination to identify adolescents with on-going symptoms of asthma. Yet, it should be noted that given that associated rates of psychiatric illness within this study were so highly comparable with Delmas and colleagues (2011) despite the more general measure of asthma diagnosis used, it may reflect the fact that children recognised as having asthma at baseline in this study were more likely to have active symptoms of asthma, and that, therefore, further adjustment for dependence on reliever medication had no discernible effect. Therefore, these analyses as a whole suggest that although recent use of reliever medication may not particularly illuminate the mechanisms underlying the mental health outcomes associated with asthma, it would be expected that disease activity would be a factor in the associated mental health outcomes given that health-related impairments, and specifically health-related absenteeism, played such a key role in the mental health outcomes observed for asthma diagnosis at 10 and 13 years.

Finally, it should be noted that these analyses again suggested there may be some unique feature of the baseline asthma sample which placed them at an increased risk of poor mental health outcomes. It should be noted that the baseline asthma sample was slightly more likely to report dependence on reliever medication in the past month than the children who were identified as having an asthma diagnosis in the age 13 questionnaire (44.82% versus 36.76%). This may suggest that the increased levels of psychiatric illness indicated among the baseline sample as opposed to the age 13 cross-sectional sample were moderated by symptom activity, but, the lack of consistent measurement of health variables means that this is just a speculative hypothesis (see section 4.4.1).

4.5 Research Limitations

This study was designed to explore the mental health associations of chronic illness that was not available based on the current empirical body of research. Indeed in many ways it did serve this purpose by indicating a stronger and more consistent association between chronic illness and rates of mental ill-health than has been previously found, and by identifying mediating variables in this association. It has also explored the wider applicability of these trends by examining the mental health associations of asthma. However, there were a number of limitations to the scope of the study and the relative insight provided. These limitations can be divided into five major categories: (i) Limitations in the measures of health; (ii) Limitations in the measurement of confounding variables; (iii) The relatively advantaged profile of the ALSPAC sample; (iv) The low prevalence of psychiatric illness within the ALSPAC sample; (v) The lack of thorough measurement of psychosocial development within ALSPAC in the adolescent years; and (vi) issues of multiple comparisons. Each of these groups of limitations, and their possible impact on the thoroughness and the conclusiveness of the study findings will be discussed in turn.

4.5.1 Limitations in the measures of health

As a consequence of the lack of comprehensive measurement of specific chronic illness conditions within ALSPAC, this study could not replicate the most common methodology of defining chronic illness in the field, and instead had to identify a measure of chronic health problems that was based on health-ratings on the age 10 and age 13 child-based questionnaires. Although this measurement practice was consistent with the recommendations of public health bodies (see Van der Lee et al., 2007), and some would argue that measures of chronic illness based on diagnostic lists have their own shortcomings (e.g. Davis & Brosco, 2007), it was limiting that there was no possibility to explore just what forms of chronic illness symptomatology this measure was sensitive to. It was also a substantial limitation that there was not the possibility to examine whether the sample identified as having a chronic illness in this study were still identified at 15 years, a wave in which a degree of divergence in associative patterns of

mental illness was observed between the primary analyses and the analyses of children with asthma. Moreover, due to the failure to secure access to the linked medical data within the study timeline, it was not possible to explore the associations of this measure with these objective indicators. Although exploratory analyses would suggest that this measure of chronic illness at 10 and 13 years did identify the majority of children with an asthma diagnosis within the ALSPAC, as well as those who had taken insulin for diabetes on the 10.67 and 13.83 year questionnaire and those identified as having a medical condition on the Year 6 teacher's questionnaire, it is not known why a minority of these children were not identified as having some degree of illness by their parents. Although the sensitivity model and mediation analyses provided some confidence that analyses with this measure were doing more than just reflecting concurrent associations of health to mental health outcomes, it could be a concern that this measure was identifying children who were in some way noticeably affected by their condition. Indeed, the measures of chronic illness and asthma diagnosis strongly predicted higher scores on the 'Perceptions of Fatigue' scale, and, in addition, a substantial amount of children across the chronic sample, regardless of illness severity ratings, indicated a high degree of health-related school absenteeism – although, it should be noted, that as in studies of prevalence, school absenteeism rates vary substantially across studies. For example, although the cut-off of six days was supported by Newacheck & Taylor (1992) and van Gent and colleagues (2008), Shaw and McCabe (2008) indicated that the average numbers of school days missed by children with chronic illness annually is 16 days. The possibility of the sample being more impaired by their illness than a representative sample is of concern as it would suggest that some of the findings of the mediation analyses – for example, indications that activity limitations did not play a role in the associated mental health outcomes and that there were high amounts of peer victimisation among children with chronic illness – may reflect the baseline level of impairment and disease activity amongst this group.

Please note that these concerns could especially be extended towards the analyses of the baseline sample of children with asthma. Rates of psychiatric

illness among these children were highly similar to rates found in Delmas and colleagues (2011) study, despite this cross-sectional study having a much stricter definition of asthma activity. Therefore, this would suggest that the sample would have a higher prevalence of children with chronic persistent asthma than children with asthma in the general population (e.g. van Gent et al., 2008), and that the related indications of the role of functional impairments are not cross-applicable. It also raises questions about the factors underlying the high levels of psychiatric illness identified for this sample at the 15 year wave, and raises concerns about the degree to which this reflects sample bias.

It is unclear how much of a limitation this lack of a comparative health measure overall poses for the explanatory value of this study's findings. The findings of increased rates of psychopathology in the analyses using the primary exposure measure were supported by more specific examinations of asthma diagnoses, and the analyses, as a whole, suggested that disease-related factors were moderating factors in the associated mental health outcomes, rather than causative factors. Moreover, epidemiological data would suggest that although these samples may show a greater disease activity than an average sample, given that disease severity and impairment as a consequence of chronic illness is so low in prevalence in the actual population (e.g. Barlow & Ellard, 2006), and the samples in this study were larger than average, it is unlikely that it subjected the analyses to a disproportionate amount of bias. It is, above all, important to emphasise, that the ALSPAC dataset was chosen to ensure that the risk of sample bias, as a consequence of small sample size, would be reduced, and the initial sample size calculations supported this rationale. However, a slight concern exists, as stated, that perhaps a more substantial mediating role of activity limitations would have been indicated if children with more mild impairments had been included. Therefore, in consideration of the study findings as a whole, perhaps the most balanced conclusion to draw is that findings regarding the nature of association to psychiatric illness are robust, given the caveat that the magnitude of the actual association may vary depending on symptom severity. However, it must also be noted that the burden of disease

was not explicitly examined as part of this study. Previous meta-analyses (e.g. Lavigne & Faier-Routman, 1992) highlighted that there seemed to be some protective mechanism for mental well-being in more serious chronic health conditions, although it was noted that these findings may be due to methodological artefacts. Yet, it has been noted that qualitative analyses of the lived experience of chronic debilitating illness find that an illness identity sometimes emerges which can foster a sense of resilience and community (e.g. Solomon, 2012). Therefore, it is possible that although severity of symptoms may be a risk factor for mental well-being in the context of more prevalent and moderate forms of chronic illness, different risk and protective factors may impact on mental well-being in more burdensome disease presentations.

Finally, it should be noted that the exposure measures in this study could be criticised for not controlling for the possible impact of comorbid physical illness, consistent with the majority of studies included in the systematic review. In fact, based on the measure of asthma diagnosis chosen, it is a certainty that a proportion of the children affected by asthma diagnosis had a comorbid diagnosis of eczema. However, given the limited measures of specific diagnoses within the ALSPAC, any attempts to control for physical comorbidity would inevitably be incomplete. Moreover, this lack of adjustment would only be a limitation if the findings suggested that there were illness-specific factors that were causal in mental health outcomes. However, overall, this study suggested that factors non-specific to any illness were the strongest insight into the association between chronic health problems and mental health outcomes during the period studied, and this was reflected in the study of the associated mental health outcomes of asthma diagnosis. In addition, although the opening literature suggested that conditions with a neurological aetiology may have a unique association with psychopathology, meaning that it may have been important to control for the mental health outcomes of these conditions above others, neurological conditions are quite low in prevalence in the general population (e.g. epilepsy, the most prevalent neurological condition, affects between 4 and 10 per 1000 people (de Boer, Mula, & Sander, 2008)) so it was unlikely to have

played a significant confounding role in the study findings. Therefore, it is unlikely that the lack of adjustment for comorbid physical illness has had a substantial impact on the validity of the study findings.

4.5.2 Limitations in the measurement of confounding variables

The methodology chapter outlined the significant challenges in selecting the variables that were considered to be possible confounding factors when examining the relationship between chronic health problems and associated mental health outcomes. Even though, as outlined, every attempt was made to find reliable and valid measures with a high response rate, it is clear that these measures were open to some degree of bias. It was acknowledged at the outset that the measure of parental history of mental illness was limited by the lack of concordant parent responses. However, it should be noted that despite this limitation, the parents of children with chronic health problems were significantly more likely to report a history of mental illness, and this pattern was also shown in children identified as having an asthma diagnosis. In contrast, although the measures of 'socio-economic status' (i.e. housing tenure and low household income) were chosen due to their common usage in empirical investigations, no significant socio-economic variations were identified in the chronic illness cohort, in spite of the a previous ALSPAC investigation, which used linked medical data, confirming that children with chronic health problems within the ALSPAC were significantly more likely to reside in socio-demographically deprived areas (see Cornish et al., 2013). However, it is likely that the high amount of missing data on these measures reduced the sensitivity of measurement.

It should be noted that in spite of the likely over-representation of children from low socio-economic groups and children with parents with a history of mental illness in the chronic illness sample, and concerns over the sensitivity of the chosen measures to represent these characteristics, thorough likelihood ratio testing and exploratory analyses indicated that there was no evidence to suggest that these variables played any form of substantial confounding role in the associated mental health outcomes, with the exception of a limited effect on the outcomes of the alternative measures.

Perhaps this is not surprising given that a “social equalisation” hypothesis of adolescent health has been put forward, based on evidence that known socio-economic inequalities in physical and mental health have limited applicability to patterns seen in late childhood and adolescence (e.g. West & Sweeting, 2004). Moreover, while Spencer (2006) indicated that this attenuation effect may not apply to youths with chronic illness conditions, it was argued that any sustained inequality was limited to children from households marked by extreme patterns of deprivation. Furthermore, a Danish study by Hammer-Helmich and colleagues (2016), which used socioeconomic indicators from national registers, indicated that the mental health burdens of atopic conditions were independent of those of socio-economic position. Yet, as socio-economic status and reported histories of parental mental illness were associated with a disproportionate rise in psychiatric illness throughout the associative models, perhaps the poor nature of the measures of confounding variables most impacted on the tests of interactions. Although no interaction effects were indicated in this study between chronic illness status and socio-economic position, or history of parental mental illness, in the associated mental health outcomes, it is likely that these tests were underpowered and may not reflect the actual nature of the association between these variables in mental health outcomes.

In conclusion, there were significant limitations surrounding the measures of the confounding covariates. However, the fact that these measures were not indicated to account in a significant way for the association of interest in the analyses with imputed data suggest that the impact on study findings may have been limited. Therefore, it is unlikely that the conclusions made based on the analyses are in any way unsubstantiated. However, missing data perhaps obscured interaction effects between these covariates and chronic health problems in predicting mental health outcomes. Yet, without support from empirical data, this hypothesis is only speculative.

4.5.3 The relatively advantaged profile of the ALSPAC sample

Before socio-economic variables were even considered for the role they may play in the association of chronic health problems to poor mental health,

limitations to the study of socio-economic gradients within the ALSPAC sample were already identified. The ALSPAC sample is acknowledged to be not only more socio-economically advantaged than would be expected based on British population norms, but also more ethnically homogeneous, and it has been highlighted that this is an important consideration when speculating on how trends in the ALSPAC data might be applicable to the United Kingdom in general (see Boyd et al., 2012). Even though the equalisation hypothesis states that socio-economic inequalities in health may attenuate somewhat in adolescence (e.g. West & Sweeting, 2004), and there was no evidence of a confounding effect of socio-economic status in this study, it is possible that this dataset is just too advantaged in the first instance, with too little variability in socioeconomic position, to truly explore the association of socio-economic gradients to chronic health outcomes. Moreover, although there was no evidence within the opening literature to suggest that ethnic variations in the associated outcomes of chronic health problems would be found, it cannot be fully concluded that the patterns seen in the ALSPAC data would be applicable across different ethnic populations in the United Kingdom. As the ALSPAC study team (Boyd et al., 2012) have argued that socio-economic gradients are unlikely to change the nature of associations, it is important to keep in mind that the association identified between chronic health problems and increased rates of psychiatric illness may be robust, especially as evidence based on adult populations would suggest that this association would only strengthen in more deprived populations. However, as stated in the methodology chapter, it does emphasise that the prevalence of psychiatric illness identified in children with chronic health problems within the ALSPAC dataset cannot be taken as point prevalence estimates of the prevalence of psychiatric illness among British children with chronic health problems. This could only be established using a more nationally representative dataset. Moreover, although peer victimisation and high levels of health-related absenteeism play the most substantial mediating role in mental health outcomes for the ALSPAC sample, it is possible that different, or additional, outcomes of chronic health problems may be identified as playing a more pivotal mediating role in more heterogeneous population groups. It should also be noted that baseline peer victimisation rates in the

ALSPAC dataset were highlighted to be substantially high – for example, it was not possible to create a category for children who were “occasionally bullied” given the substantial proportion of children who fell into this group (just under 40% on the age 10 questionnaire). Moreover, findings that children with asthma were more likely to be victimised contrasts with an earlier systematic review (see Sentenac and colleagues, 2012). This raises concerns about how applicable the role of peer victimisation in the associated mental health outcomes of chronic illness may be to other population groups.

In conclusion, although the association between chronic health problems and increased rates of psychiatric illness may be applicable to child and adolescent groups in the general population, it is most likely that the magnitude of the association identified in the ALSPAC is not truly representative of the magnitude of this association in the general British population. Moreover, it is possible that mediating factors in the association between chronic health problems and mental health outcomes could change in nature across different population groups.

4.5.4 The low prevalence of psychiatric illness within the ALSPAC sample

Complicit with the issues regarding external validity of the ALSPAC sample, were the limitations imposed by the low prevalence of psychiatric illness within the ALSPAC sample. Based on national population estimates (e.g. Ford et al., 2003; Costello et al., 2003), it would be expected that psychiatric disorders would be prevalent at a rate of approximately 10% of the ALSPAC sample. However, the actual prevalence of mental health disorders in this dataset, based on the indications of the primary outcome measure, was substantially lower. For example, at 15 years - the DAWBA wave at which the highest prevalence of psychiatric illness was observed - 6.82% of the respondents were identified as having a psychiatric illness. This low prevalence is likely to be a consequence of two factors. The relatively advantaged profile of the ALSPAC sample means that it is probably not sensitive to existing childhood inequalities in mental health (e.g. Wickrama,

Noh, & Elder, 2009). Moreover, a study of ALSPAC data by Wolke and colleagues (2009) suggested that drop-out may have been biased towards children presenting with mental illness symptomatology. This has significant implications for the robustness of findings within this study. It confirms that the prevalence estimates on psychometric measures in this study cannot be taken in any way as being representative of the true prevalence of such disorders among children and adolescents with chronic health problems in the United Kingdom. To illustrate the limitations posed, if relative risks were not examined, and this low prevalence of psychiatric illness was not examined and considered, it would have been concluded that children with chronic health problems had lower rates of psychiatric illness than would be expected based on population norms. Moreover, it raises concerns that although children with chronic illness may be at a comparatively higher risk of experiencing mental illness within this study, this risk may vary in more heterogeneous samples. This highlights, in line with the discussions of socio-economic characteristics, that the ALSPAC dataset is limited in providing insight into what are likely to be nationally representative characteristics in the association of chronic health problems to increased rates of psychiatric illness in childhood and adolescence.

The low prevalence rates of psychiatric illness also gave an additional limitation to the scope of this study. Due to power limitations, rates of psychiatric illness more generally were taken as the primary outcome. This was limiting to the mediation analyses, as, although all psychiatric illness can be understood to some degree as a consequence of neural reactions to stress, aetiological factors in different disorders do show some heterogeneity (Henje Blom et al., 2016). Moreover, it should be noted that health-related school absenteeism, which emerged as the most consistent predictor of mental health outcomes in this study, has been associated with the onset of both emotional and behavioural symptomatology (Kearney, 2008). This raises the possibility that the emergence of this factor as a mediating variable in the analyses is a function of the more general outcome measure chosen.

As stated analyses were not powered to examine the association with rates of specific disorder categories, and they were also indicated to be limited in

detected mediating relationships of a smaller effect size. This may be the reason why only two factors emerged as key mediating variables in this study. Perhaps there were more nuanced relationships between chronic illness outcomes and specific types of symptomatology, such as between peer satisfaction scores and functional limitations and emotional symptomatology, that the analyses were just not powered to identify.

Therefore, the low prevalence rates of psychiatric illness within ALSPAC limited the insight that could be gained into the nature of the association between chronic health problems and increased rates of psychiatric illness, and also placed a further limitation on the likely representativeness of point prevalence estimates.

4.5.5 The lack of thorough measurement of psychosocial development within ALSPAC in the adolescent years

One of the most substantial limitations to the scope of this study was the lack of thorough and consistent measurement instruments within the ALSPAC dataset. The impact of this lack of consistent measurement was most clear for the age 15 wave, when it was not possible to examine mediating factors in the associations, or even compare findings on the primary outcome measure against alternative outcome measures. This was a substantial limitation, given the divergence in the magnitude of the associated relationship to mental health outcomes in the analyses using the generalised chronic illness measure relative to the measure of asthma diagnosis. It is possible that some particular psychiatric risk factor mediated this strong association in the baseline asthma sample. However, because of the lack of measurement of health and developmental outcomes surrounding the age 15 measurement wave, there was no possibility of exploring what this mediating factor, or mediating factors, may be, and if, like the mediators of the associated mental health outcomes at age 10 and 13 years, they were also non-specific to asthma.

There were also subtle impacts of measurement limitations in the analyses of the age 10 and age 13 wave. No formalised measure of many variables, including family cohesion or activity limitations, could be identified, and as

some of the measures chosen as a consequence were novel, or had low reliability coefficients, it could be questioned how reliable they were in indicating the associations with the underlying constructs. Although structural equation modelling indicates the fit of a theoretical model to data, it requires that the researcher gives due consideration to the specificity of findings (e.g. Chin, 1998) – for example, the consideration that high levels of health-related absenteeism may mediate mental health outcomes through a number of underlying, although closely related mental health risk factors. Therefore, a more nuanced model, designed on the basis of more thorough and specific measures of impairment and psychosocial developmental outcomes, might have given a clearer insight into specific pathways of the association of chronic health problems to mental health outcomes within the ALSPAC dataset. Therefore, the lack of thorough measure within ALSPAC limited the insight that could be gained into the nature of the association of chronic health problems to mental health outcomes overall, but particularly extends to the period surrounding the age 15 DAWBA wave.

A more nuanced understanding of the associated mental health outcomes of chronic illness at 10 and 13 years may have also been achieved by forgoing initial mediating analyses, and progressing straight to the design of the pathways model. The mediation analyses used were based on isolated analyses of specific variables, and comparing multiple statistical inferences is ill advised due to the risk of making erroneous conclusions. This was clearly illustrated by the analyses in this study, given that these analyses erroneously led to the conclusion that scores on the ‘Perceptions of Fatigue’ scale played a mediating role in the mental health outcomes associated with chronic illness. In the initial mediation analyses, peer victimisation, peer dissatisfaction and high levels of school related absenteeism were individually indicated to be associated with chronic illness, and it was very tempting to hypothesise that these variables were in some way related, given that the literature review had implicated disruptions to social development as a key factor in the mental ill-health outcomes attributable to chronic illness. However, the path model indicated that although school absenteeism and peer victimisation were both mediating factors in mental health outcomes at

10 and 13 years, they were not interrelated. Therefore, creating a larger path model may not have provided any further insight into mediation of mental health outcomes, but it may have provided clearer insight into the inter-relationships between the variables identified as possible mediators. Yet, this was a limitation that could only be identified in retrospect based on the study findings, and would not have been strongly relevant to the primary aims of this research.

A further criticism of this study that could be made, given the strong associations identified between chronic illness and mental health outcomes at baseline, and the more thorough and complete range of measures available in ALSPAC during the childhood years, is that the timeline of this study could have been more extensive. Specifically, it could suggest that the study should have examined the association of chronic health problems to the DAWBA at 7 years. After all, independent of health-related impairments, these children were more likely to be victimised by peers at 10 years, and it would have been insightful to identify early signs and associated variables in this relationship. However, this study was designed around the indications of the opening literature review. It should be kept in mind that, based on this review, it was uncertain whether an association between chronic health problems and increased rates of psychiatric illness would even be indicated in this research. As several theoretical articles suggested that adolescence would be the period when the strongest association with mental health outcomes would be shown (e.g. Sawyer et al., 2007; Michaud et al., 2007), it was hypothesised that the period of 10 to 15 years would be a developmental period where the most complex and dynamic changes in the association of chronic illness to mental health outcomes would be seen. Therefore, it was envisioned that the study timeline would allow the analyses to capture this late childhood pattern and allow for the analysis of the changes during the subsequent period of development. There was nothing to suggest that the period of mid- to late childhood should be a particularly important period for research focus. Therefore, although studying the association of chronic health problems to mental health at 7 years may have

been insightful, this limitation could again only be identified in retrospect, based on insight accrued from the research analyses.

4.5.6 Issues of multiple comparisons

Comparing multiple statistical inferences is ill advised as it is known that the more inferences are made, the more likely erroneous inferences are to occur by chance (e.g. Miller, 1981; Benjamini & Hochberg, 1995). Please note that the limitations of the comparison of many statistical inferences simultaneously could be thought to apply to this thesis more generally. This thesis drew together learning from a large set of statistical analyses inclusive of cross-sectional and longitudinal associative models, mediation tests and structural equation models. Therefore, although all attempts were made to assess findings from each set of tests on their own merit, it is possible that erroneous conclusions were made given that conclusions seemed consistent with another set of analyses. For example, the role of symptom severity and functional impairments was explored from a variety of proxy measures in different forms of analyses (e.g. cross-sectional, mediation, statistical modelling) and, perhaps, therefore multiple comparison bias was introduced. Moreover, given the indications of the associative models as a whole, it was concluded that the non-significant nature of association between asthma diagnosis and an increased rate of psychiatric illness in the age 13 cross-sectional analyses was most likely the outcome of reduced sample power. However, it is possible that this finding may reflect a true non-significant association between asthma and rates of psychiatric illness at this wave, as a consequence of the characteristics of the age 13 cross-sectional sample. In conclusion, there is a risk that biases associated with multiple comparisons were introduced to the findings, and this is an important consideration when examining pathways for future research.

4.6 Conclusions and Implications for Public Health and Future Research

The discussion chapter has thoroughly reviewed each separate stage of analysis in this study, and how it has provided insight into the nature of associated mental health outcomes. The reliability of these findings have also been examined through the process of the secondary analyses, and any limitations to the scope of these analyses have been identified, and balanced with how they may have impacted on the validity and explanatory value of the findings. This section will subsequently draw on these discussions as a whole in order to define the study conclusions and outline the related implications for public health and future research.

As stated in the opening to this thesis, the major question posed by this research was regarding whether the lack of high quality epidemiological data in the field is obscuring a true psychiatric risk associated with chronic illness in childhood and adolescence, or whether, in contrast, the theory of chronic health problems as being a particular risk factor to child and adolescent health was based on false premises. This research concludes that there is a strong and significant association identifiable between chronic health problems and an increased presence of psychiatric illness, relative to healthy age-matched peers, across the late childhood and early adolescent when using larger samples, such as that seen in the ALSPAC sample. Moreover, as this association was reflected consistently across outcome measures, it suggests that the low to moderate effect sizes indicated in previous research may not be an artefact of the psychiatric measures selected, but rather a reflection of sampling bias. The findings also suggested that this association was identifiable beyond the influence of covariates identified as possible confounding factors, but may vary in strength depending on condition severity. Finally, the analyses also provided a degree of confidence that this association was not an over-inflation of an acute risk association only identifiable for a small number of conditions, given that these outcomes seemed to be mediated by factors non-specific to any one condition, and all patterns were applicable to the outcomes seen for asthma diagnosis. Although, it was not possible to explore the association between chronic

health problems and mental ill-health outcomes in a thorough fashion in the mid-adolescent period, a period depicted as an acute period of risk in the theoretical literature (e.g. Michaud et al., 2007; Sawyer et al., 2007), this research provided important insight into factors which may strongly mediate this association in early adolescence. Based on the observations in the ALSPAC data, it was concluded that although peer victimisation is the strongest predictor of the mental ill-health outcomes associated with chronic illness within time, high levels of school related absenteeism were the most consistent mediators of these outcomes across time. Although it was recognised that future research would need to build a on these findings, specifically in order to get a more nuanced understanding of the aspects of school absenteeism that are most pivotal to child and adolescent health, the finding that these factors emerged as the mediating factors across these time-points is especially significant. The literature review highlighted a call for more age-focused research in the area of chronic illness looking at child and adolescent population, and looking at the impact of such illness on child development (e.g. Sawyer et al., 2007; Michaud et al., 2007). The findings of the mediation analyses in a large way supported this call, indicating that chronic illness may negatively impact on the lives of children and adolescence, and that this impact can be understood when using an age-specific framework.

The literature review also highlighted a number of identified methodological limitations in research which has taken this age-specific focus. One of the strongest aspect of this research was its dependence on a large sample, which was adequate to power the comparative analyses examining prevalence rates of psychiatric illness across the late childhood to mid-adolescent period. Use of this large sample reduced the possible introduction of intra-disease variability, which was highlighted as a possible source of confounding in previous investigations of the associated mental health outcomes of chronic illness in childhood and adolescence. Therefore, it is important to note that the findings of an associated increase in rates of psychiatric illness amongst children with chronic illness were found consistently across the psychometric measures explored in this study.

Moreover, all available data would suggest that this association is likely to be robust, although magnitude may vary given the characteristics of the particular population under study. These findings suggest that the arguments of previous research inquiries, such as Lavigne and Faier-Routman (1992), that methodological artefacts are unduly biasing empirical investigations, and are having a negative impact on our understanding of the associated mental health impact of chronic health problems in childhood and adolescence, are very much valid.

This research has been insightful into the ways to study the associated outcomes of chronic illness in childhood and adolescence, and has also highlighted the ways in which researchers may be challenged. Although use of a cohort study, such as the much larger ALSPAC dataset, allowed for more analytic power, which was crucial to the aims of this research inquiry, the nature of measuring such a large number of variables across such a vast sample meant that there was a degree of selective drop-out bias and inconsistency in measurement. This, in particular, extended to measures of physical health outcomes. This has implications for research studies going forward. This thesis overall has highlighted the importance of sample size, and how an understanding of the associated mental health outcomes of chronic illness in childhood and adolescence can only be reliably gained from large datasets, given the generally low prevalence of such conditions in the general population. For example, even when considering the substantial size of the ALSPAC dataset relative to samples seen in the opening systematic review, the sample was still too small to power analyses of the associations between chronic illness and more specific rates of emotional, anxiety, and behavioural disorders. Yet, it is important to balance sample size concerns with considerations of measurement consistency. Therefore, although this study has highlighted that the use of large cohort studies may present some limitations to the exploration of the mental health outcomes associated with mental illness, based on the indications of this thesis as whole, it is strongly argued that reliance on these large datasets is the only way in which methodological sampling bias will be avoided and age-related variations can be explored. However, selection of datasets with strong participant retention,

and constancy of measurement, should be a priority for researchers choosing this observational mode of study. This consistency also extends to the measures of physical health, such as those of symptom severity. This study attempted to examine the role of such severity on a number of different measures from different sets of analyses, and it was highlighted that such practices introduce a risk of multiple comparison bias. At the time of the design of this research, the 'Millennium Cohort Study' presented as a strong pathway for future investigations into more nationally representative patterns of mental health outcomes for children with chronic illness into the adolescent period, given the stated aims of the study team to combine survey data with official records and linked medical data (e.g. Hockley et al., 2008). Therefore, learning from the substantive findings in this thesis, it is strongly recommended that future research studies forego the over-arching methods of examining small and possible homogenous samples, and look to larger cohort studies with good measurement consistency.

This research also highlighted areas to build upon in future research. As stated, it was considered to be an important initial step to establish whether an association between chronic illness and mental ill-health might be established in larger samples with more reliable measures of mental health, and this was why ALSPAC data was chosen. However, it is important to build upon these findings and look at how the magnitude of this association may vary in different population groups. It is also highly important to build on the findings of the mediation analyses and to look more into the impact of chronic illness on child and adolescent development, and, in particular, the experience of schooling. Finally, given that there were some trends which suggested that there may be a high prevalence of children with active symptomatology in the samples studied, the magnitude of the role of symptom severity in the mental health associations of chronic illness also remains to be defined. To summarise, the areas highlighted as a priority for future research are as follows:

- Identification of the prevalence of mental illness of children in more recent nationally representative samples

- Identification of age-related variations in the mental health outcomes associated with chronic illness across mid- to late- adolescence, with the early childhood years also a focus of investigation
- Explorations of the applicability of findings exploring chronic illness more generally to specific diagnoses
- Explorations of the mediating factors underlying the mental ill-health associations related to chronic illness in childhood and adolescence, with a specific focus on how chronic illness may impact on the experience of schooling
- Isolating the role of disease severity and impairment in the associated mental health outcomes of chronic illness

The findings of this study also have significant implications for public health and for the provision of healthcare resources to the substantial number of children and adolescents living with chronic illness in the United Kingdom. The findings strongly supported the repeated hypothesis in this field that chronic illness negatively impacts on child and adolescent development, and results in poor mental health outcomes for these children. It should be emphasised that it was never questioned that there was some form of negative mental health association of chronic illness in younger populations. After all, previous explorations consistently highlighted a comparatively higher level of mental illness symptomatology among children and adolescents living with chronic health conditions. However, as was consistently highlighted in the opening literature review, these studies were in many ways limited by their reliance on small samples and use of cross-sectional methodology. Not only did the systematic review of this research emphasise that no strong conclusions could be made based on this existing research, but such arguments were made in reviews focusing on the impact of chronic illness on child and adolescent development (e.g. Barlow & Ellard, 2006; McClellan & Cohen, 2007). Although it has been argued that these quality issues are a consequence of the low prevalence of chronic illness conditions in the juvenile population (e.g. Wallander & Varni, 1998), the over-arching focus in the field of public health on adult populations has also caused the impact of chronic illness in these younger age groups to become

neglected (Sawyer et al., 2007; Michaud et al., 2007). This study aimed to provide a more balanced insight into the mental health associations of chronic illness in these younger age groups, and in many ways highlighted why this view of children and adolescents with chronic illness as "small adults" (see Grey & Sullivan-Bolyai, 1999) is highly deficient. The findings highlighted that previous studies may have underestimated the degree to which psychiatric illness is prevalent among this population group, and supports the arguments of previous authors (e.g. Michaud et al., 2007) that younger age groups living with chronic illness are greatly deserving of a more thorough and targeted healthcare support. Even more significantly the findings of this study have supported the argument that chronic illness in these younger age groups are independently associated with poor mental health outcomes, for reasons that can in no way be seen as approximations of the patterns seen in older age groups. The mechanisms identified in this study as mediating mental health outcomes – namely high levels of school absenteeism and peer victimisation – are age-dependent variables, and can only be identified and understood by an isolated focus on child and adolescent groups. Therefore, this implies that supporting the mental health of children and adolescents living with chronic illness needs to become a priority in the field of public healthcare, and that mental ill-health in this population needs to be seen as a health issue seperate from the high rates of psychiatric comorbidities seen in adult populations. Therefore, based on the findings of this study as a whole, significant implications are identified for public health, which can be classified into implications for the context of service provision and implications for future intervention.

4.6.1 Implications for the Context of Service Provision

As was repeatedly emphasised in the opening literature review, the growing prevalence of chronic diseases across age groups has led to what has been termed an 'epidemiological transition' in the field of medicine (Michaud et al., 2007), and this transition could be viewed as not only a challenge to the way population health has been previously characterised, but also to the very way in which medical practitioners view and treat disease (e.g. Lyons & Chamberlain, 2006). The focus on biological and chemical bases for disease allowed for the objectification of the body (e.g. Jewson, 1976), therefore reducing the relevance of social and behavioural

factors to diagnosis (see Engel, 1977; Lyons & Chamberlain, 2006). Although this may have been appropriate to the course of acute and infectious disease, it limits the understanding of disease with chronic symptomatology (Lyons & Chamberlain, 2006). These conditions are multiply determined, with lifestyle and socio-demographic factors being crucial to the onset and course of many conditions (Wilkinson, 1997; Lyons & Chamberlain, 2006). Most importantly, as has been emphasised throughout this study, the health and well-being of adolescents with chronic illness cannot be understood without a proper acknowledgement of the developmental tasks and social context of these transitional years. The opening literature review highlighted that empirical evidence has indicated that self-management and adherence behaviours during the adolescent period cannot be understood without an understanding of the developmental changes that occur during adolescence, specifically increased social awareness and experimentation with adult behaviours (see Michaud et al., 2007). This study has further built on these studies to emphasise that the mental health of adolescents living with chronic illness cannot be understood without an understanding of how chronic illness presents as a stressor to the normative trajectory of development during these years. Therefore, it is heavily emphasised, in the context of planning for service provision, that adolescent development, well-being and physical health are linked by reciprocal processes, and these interactive processes must be considered when creating both physical and mental health supports.

In the Department of Health (2012) report outlining policy planning for the treatment of people with chronic illness in England Wales, children and adolescents are given relatively limited focus when compared to their adult counterparts. However, it was highlighted that a priority within the health services in the United Kingdom at this time was to ensure a more substantial presence of Child and Adolescent Mental Health Services (CAMHS) in paediatric chronic illness teams. In a more contemporary planning document, Naylor and colleagues (2016) acknowledge that this policy plan has since only been realised in a minority of healthcare teams across England and Wales. Although this study has supported the view that mental health provisions are urgently needed in the context of children and adolescents with chronic illness, it is still believed that these stated policy plans are short sighted. The CAMHS service is designed to intervene on cases of moderate to severe psychopathology in children and adolescents, providing intense treatment interventions mostly within healthcare settings (see NHS England, 2014). This study has suggested that the disruptions to daily lifestyles as a consequence of chronic

illness, such as higher than normative levels of school absenteeism, may be amongst the factors leading to mental ill-health among these adolescents. Moreover, prescribing psychoactive drugs for these young people may result in the low adherence that has already been recognised for physical health regimens (see Gray & Wood, 2017). Therefore, increasing healthcare contact for these children and adolescents may be more counterproductive than helpful. Although CAMHS services could be beneficial for these patients – for example, it was found that psychological therapies increased well-being and reduced hospital bed days for people with severe asthma (Hope & Niven, 2017) – it is known that there is a recognised issue in adolescents refusing to engage with CAMHS services internationally (Hawker, 2007; Neufeld, Jones, & Goodyer, 2017). Moreover, Thorley (2016) has highlighted a disproportionately high increase in CAMHS referrals over the past decade. Therefore, proceeding to provide services in this manner might not only run the risk of introducing a further stressor into the lives of young people with chronic illness, resulting in them failing to engage with the treatment provided, but may also place strain on a service that has already been identified as being resource strained.

The importance of screening for symptoms of mental ill health in children and adolescents with chronic illness, and providing appropriate and efficient treatments, cannot be underestimated. Given that mental illness in the context of chronic illness not only has an independent burden on health and quality of life, but limits the long-term prognosis for individual functioning and health (Academy of Medical Royal Colleges, 2009), it is important that any impact to the mental health of children and adolescents as a consequence of their illness is addressed at an early stage. However, as Christie and Viner (2005) highlight, when treating adolescents one must consider the social and psychological growth factors that interact with their illness symptoms and their response to treatment, and design medical interventions with these systemic factors in mind. In 2008, a NHS national report acknowledged that the health service needed to move out of traditional healthcare models in order to fully address public healthcare needs and this innovation may especially be needed to address the mental health needs of children and adolescents with chronic illness. For example, as part of an ambulatory initiative at New York Langone Medical Centre, an intervention programme targeting illness burden and emotional distress that was co-designed with clients and their families showed significant benefits for young people with chronic illness (see Lois, 2017). However, based on

the findings of this study, interventions supplementary to those in traditional healthcare settings are suggested.

4.6.2 Potential Interventions

The 2008 NHS report which highlighted a need for more innovation in healthcare models specifically emphasised schools as an untapped resource where frontline early intervention health programmes could be provided. The possible benefits of embedding mental healthcare in schools was also highlighted in papers by Thorley (2016), Fazel and colleagues (Fazel, Hoagwood, Stephen, & Ford, 2014) and Neufeld and colleagues (Neufeld, Jones, & Goodyer, 2017), with Fazel and colleagues (2014) arguing that such policies might also have the additional benefit of improving educational attainment among adolescents with mental health issues. However, introducing mental health supports in schools may have particular benefits for children and adolescents with chronic illness.

The findings of this study suggest that one way in which to identify children with chronic illness at risk of experiencing mental health symptomatology is to look at health-related school absenteeism rates. It has been previously argued that public health bodies need to pay more attention to school absenteeism rates to identify children at risk of experiencing greater disease activity and limitations (e.g. Hsu et al., 2016; Weitzman, 1986), which perhaps indicates that school absenteeism rates are a key factor in identifying children at risk of experiencing a variety of negative outcomes overall as a consequence of chronic illness. However, this study would go further as to argue that the two mediators identified in this study – school absenteeism and peer victimisation – suggest that the experience of schooling is integral to the child and adolescent well-being in the context of chronic illness. Although this finding needs further external validation in more heterogeneous samples, and, in particular, older adolescent populations, it is important to highlight that it shows many parallels with qualitative accounts of the lived experience of chronic illness (e.g. Taylor, Gibson, & Franck, 2008), where being respected and treated like peers within the school context is a highlighted desire of young people living with chronic illness. This suggests that another important avenue in order to support the mental well-being of children and adolescents with chronic illness may be to work with health care teams and teaching staff within schools, in order to identify ways in which schools can support the needs of children living with these long-term conditions, especially after prolonged absences. As children with chronic health problems within the ALSPAC were indicated to be particularly at risk of experiencing peer victimisation, consistent with the meta-analysis of Sentenac and

colleagues (2012), it should perhaps also be a priority to work with schools to increase awareness of the vulnerability of this population group, and to identify means of targeting and reducing rates of peer victimisation. Therefore, based on the findings of this study, it is suggested that working with schools may be a key target for improving the mental well-being of children and adolescents living with chronic illness, especially in the late childhood and early adolescent period.

Although it is argued that some tailoring of the programmes might be important to address both physical and mental health issues in young people with chronic illness, Sawyer and colleagues (2007) highlight that generic peer support programmes and school well-being programmes have also been shown to have efficacy in treating mental ill-health symptoms in teenagers' with chronic health problems. It is important to highlight that the embedding of the mental health resources within school seems to be a crucial factor, as a review of online peer support programmes found that such programmes are not always beneficial to teenagers mental well-being (see Easton et al., 2017). This is important to consider given that the introduction of technological resources has been considered by the health service as one way of addressing the resource challenge of chronic illness (e.g. Liddell, Adshead, & Burgess, 2008).

Eccleston, Palermo, Fisher, and Low (2012) have highlighted that treatments to support the well-being of parents of children with chronic illness and to educate them about their child's illness may also benefit their children's well-being. It is possible, in acknowledgement of the developmental changes in the childhood and adolescent period, that such interventions may have less efficacy in the adolescent years, given that this period is dominated by increased independence from parents (e.g. Michaud et al., 2007). However, as the analyses of the study suggested that parental monitoring did take on a protective role in mental health outcomes for adolescents with chronic health problems in the ALSPAC at 15 years, it is possible that an age-specific parenting intervention may also be protective at this age. Therefore, there are many directions for possible intervention among young people with chronic illness, but the most important factor to consider, for policy planning, is the appropriateness of the intervention to the young person's stage in the lifespan. In conclusion, it is argued that biopsychosocial factors must be a key consideration when working with children and adolescents with chronic illness, regardless of whether supports are being provided for their physical or mental well-being.

4.6.3 Conclusions

This thesis has highlighted how little is understood about the associated mental health of children and adolescents living with chronic illness. As the opening literature review highlighted, a theory of chronic health problems in childhood and adolescence as having a negative impact on mental health in these age groups, regardless of primary diagnosis or symptom severity, underlies the majority of research in this field. Yet, due to the difficulties in studying this population group, this position was not fully substantiated by existing empirical research. The considered nature of this study allowed an insight into the psychiatric associations of chronic health problems, beyond that which was previously available, and suggested that chronic illness may be a strong risk factor to the mental well-being of child and adolescent groups across time and across outcome measures when larger and more robust sample sizes are analysed. It has highlighted that the impact of chronic illness on the quality of life of this age group needs more isolated attention within the research, and that screening for mental health issues within these younger age groups needs to be prioritised within the public healthcare sector. However, it is also clear that further research is needed in order to fully clarify prevalence rates of mental illness, and to understand mediating factors in this association. Therefore, it is hoped that this study will stand as an important stepping stone in the understanding of the associated mental health outcomes of child and adolescent chronic illness, and will consequently lead to better support and treatments for the growing number of young patients living with long-term conditions internationally.

References

Abdul-Rasoul, M., Hajiyya, J., Alshawaf, F., Abdal, Y., Al-Azmni, A., & Al-Mahdi, M. (2010). Psychological status of children with Type 1 diabetes in Kuwait. *Kuwait Medical Journal, 42*(2), 139-145.

Academy of Medical Royal Colleges. (2009). *No health without mental health ALERT report: The supporting evidence*. Retrieved from http://www.rcpsych.ac.uk/pdf/No%20Health%20-%20%20the%20evidence%20revised%20May%2010.pdf

Acosta-Pérez, E., Canino, G., Ramírez, R., Prelip, M., Martin, M., & Ortega, A. N. (2012). Do Puerto Rican youth with asthma and obesity have higher odds for mental health disorders? *Psychosomatics: Journal of Consultation and Liaison Psychiatry, 53*(2), 162-171. doi:10.1016/j.psym.2011.07.011

Aina, O. F., Fadaka, K., Temiye, E., & Renner, J. K. (2010). Sexual maturation and psychiatric morbidity among persons with sickle cell anaemia in a Nigerian teaching hospital. *International Journal of Psychiatry in Medicine, 40*(1), 31-43. doi:10.2190/PM.40.1.c

Akbas, S., Karabekiroglu, K., Ozgen, T., Tasdemir, G., Karakurt, M., Senses, A., Boke, O., & Aydin, M. (2009). Association between emotional and behavioral problems and metabolic control in children and adolescents with Type 1 diabetes. *Journal of Endocrinological Investigation*, 32(4), 325-329. doi:10.1007/BF03345721

Akcakaya, N., Aydogan, M., Hassanzadeh, A., Camcioglu, Y., & Cokugras, H. (2003). Psychological problems in Turkish asthmatic children and their families. *Allergologia et Immunopathologia, 31*(5), 282-287.

Alvim, C. G., Ricas, J., Camargos, P. A., Lasmar, L. M., Andrade, C. R., & Ibiapina Cda, C. (2008). Prevalence of emotional and behavioral disorders in adolescents with asthma. *Jornal Brasileiro de Pneumologia, 34*(4), 196-204.

Amato, P. R., & Cheadle, J. (2005). The long reach of divorce: Divorce and child well-being across three generations. *Journal of Marriage and Family, 67*(1), 191-206. doi:10.1111/j.0022-2445.2005.00014.x

American Psychiatric Association. (1994). *Diagnostic and Statistical Manual of Mental Disorders (*4th ed.). Virginia: American Psychiatric Association.

Amr, M., Amin, T., & Hablas, H. (2010). Psychiatric Disorders in a Sample of Saudi Arabian Adolescents with Sickle Cell Disease. *Child & Youth Care Forum, 39*(3), 151-166. doi:10.1007/s10566-009-9091-9

Amr, M., Bakr, A., & El-Gilany, A. H. (2008). Corporate assessment of behaviour adjustment in children with chronic renal failure. *Paediatrics ME, 13*(1), 4-10.

Amr, M., El-Gilany, A. H., Bakr, A., & El Sheshtawy, E. (2007). Assessment of cognition, behaviour and quality of life of children with chronic renal failure. *Paediatrics ME, 12*(3), 60-66.

Angold, A., Costello, E. J., Messer, S. C., Pickles, A., Winder, F., & Silver, D. (1995). Development of a short questionnaire for use in epidemiological studies of depression in children and adolescents. *International Journal of Methods in Psychiatric Research, 5,* 237-249.

Angold, A., Erkanli, A., Silberg, J., Eaves, L., & Costello, E. J. (2002). Depression scale scores in 8–17-year-olds: effects of age and gender. *Journal of Child Psychology and Psychiatry, 43*(8), 1052-1063.

Annesi-Maesano, I., Zhou, C., Baiz, N., Banerjee, S., Andre Charpin, D., Caillaud, D., de Blay, F., Raherison, C., & Lavaud, F. (2013). Externalizing and internalizing behavioural problems related to asthma in school children. *Allergy, 68*(11), 1471-1474.

Arabiat, D. H., Al Jabery, M., & Wardam, L. (2013). Screening for anxiety symptoms and social desirability in children and adolescents living with chronic illnesses in Jordan. *Journal of Child Health Care, 17*(1), 62-71. Doi:10.1177/1367493512450623

Arif, A. A. (2010). The association between symptomatic asthma and neurobehavioral comorbidities among children. *Journal of Asthma, 47*(7), 792-796. doi:10.3109/02770903.2010.491148

Asmundson, G. J., Noel, M., Petter, M., & Parkerson, H. A. (2012). Pediatric fear-avoidance model of chronic pain: Foundation, application and future directions. *Pain Research Management, 17*(6), 397-405.

Austin, J. K., Dunn, D. W., Caffrey, H. M., Perkins, S. M., Harezlak, J., & Rose, D. F. (2002). Recurrent seizures and behavior problems in children with first recognized seizures: a prospective study. *Epilepsia, 43*(12), 1564-1573.

Austin, J. K., Harezlak, J., Dunn, D. W., Huster, G. A., Rose, D. F., & Ambrosius, W. T. (2001). Behavior problems in children before first recognized seizures. *Pediatrics, 107*(1), 115-122.

Austin, J. K., Perkins, S. M., Johnson, C. S., Fastenau, P. S., Byars, A. W., & Dunn, D. W. (2011). Behavior problems in children at time of first recognized seizure and changes over the following 3 years. *Epilepsy & Behavior, 21*(4), 373-381. doi:10.1016/j.yebeh.2011.05.028

Bacharier, L. B., Strunk, R. C., Mauger, D., White, D., Lemanske, R. F., Jr., & Sorkness, C. A. (2004). Classifying asthma severity in children: mismatch between symptoms, medication use, and lung function. *American Journal of Respiratory and Critical Care Medicine, 170*(4), 426-432. doi:10.1164/rccm.200308-1178OC

Bahreinian, S., Ball, G. D., Colman, I., Becker, A. B., & Kozyrskyj, A. L. (2011). Depression is more common in girls with nonatopic asthma. *Chest, 140*(5), 1138-1145. doi:10.1378/chest.11-0219

Bakare, M. O., Omigbodun, O. O., Kuteyi, O. B., Meremikwu, M. M., & Agomoh, A. O. (2008). Psychological complications of childhood chronic physical illness in Nigerian children and their mothers: The implication for developing pediatric liaison services. *Child and Adolescent Psychiatry and Mental Health, 2*(1), 34. doi:10.1186/1753-2000-2-34

Barlow, J. H., & Ellard, D. R. (2006). The psychosocial well-being of children with chronic disease, their parents and siblings: an overview of the research evidence base. *Child: Care, Health and Development, 32*(1), 19-31. doi:10.1111/j.1365-2214.2006.00591.x

Barnett, K., Mercer, S. W., Norbury, M., Watt, G., Wyke, S., & Guthrie, B. (2012). Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study. *The Lancet, 380*(9836), 37-43. doi:10.1016/S0140-6736(12)60240-2

Baron, R. M., & Kenny, D. A. (1986). The moderator–mediator variable distinction in social psychological research: Conceptual, strategic, and statistical considerations. *Journal of Personality and Social Psychology, 51*(6), 1173.

Becker, A., Woerner, W., Hasselhorn, M., Banaschewski, T., & Rothenberger, A. (2004). Validation of the parent and teacher SDQ in a clinical sample. *European Child & Adolescent Psychiatry, 13*, ii11-ii16. doi:10.1007/s00787-004-2003-5

Bender Berz, J., Murdock, K. K., & Koinis Mitchell, D. (2005). Children's asthma, internalizing problems, and social functioning: an urban perspective. *Journal of Child and Adolescent Psychiatric Nursing, 18*(4), 181-197.

Bender, B. G. (2007). Depression symptoms and substance abuse in adolescents with asthma. *Annals of Allergy Asthma, & Immunology, 99*(4), 319-324. doi:10.1016/S1081-1206(10)60547-9

Bender, B. G., Annett, R. D., Ikle, D., DuHamel, T. R., Rand, C., & Strunk, R. C. (2000). Relationship between disease and psychological adaptation in children in the Childhood Asthma Management Program and their families. CAMP Research Group. *Archives of Pediatrics and Adolescent Medicine Journal, 154*(7), 706-713.

Benjamini, Y., & Hochberg, Y. (1995). Controlling the false discovery rate: a practical and powerful approach to multiple testing. *Journal of the Royal Statistical Society. Series B (Methodological), 57*(1), 289-300.

Bennett, D. S. (1994). Depression among children with chronic medical problems: a meta-analysis. *Journal of Pediatric Psychology, 19*(2), 149-169. doi:10.1093/jpepsy/19.2.149

Berntsson, L., & Köhler, L. (2001). Long-term illness and psychosomatic complaints in children aged 2–17 years in the five Nordic countries. *The European Journal of Public Health, 11*(1), 35-42.

Bilfield, S., Wildman, B. G., & Karazsia, B. T. (2006). Brief report: The relationship between chronic illness and identification and management of psychosocial problems in pediatric primary care. *Journal of Pediatric Psychology, 31*(8), 813-817. doi:10.1093/jpepsy/jsj092

Blackman, J. A., & Conaway, M. R. (2012). Changes over time in reducing developmental and behavioral comorbidities of asthma in children. *Journal of Developmental and Behavioral Pediatrics, 33*(1), 24-31. doi:10.1097/DBP.0b013e3182396895

Blackman, J. A., & Conaway, M. R. (2013). Developmental, emotional and behavioral co-morbidities across the chronic health condition spectrum. *Journal of Pediatric Rehabilitation Medicine, 6*(2), 63-71. doi:10.3233/PRM-130240

Blackman, J. A., & Gurka, M. J. (2007). Developmental and behavioral comorbidities of asthma in children. *Journal of Developmental and Behavioral Pediatrics, 28*(2), 92-99. doi:10.1097/01.DBP.0000267557.80834.e5

Blackman, J. A., Gurka, M. J., Gurka, K. K., & Oliver, M. N. (2011). Emotional, developmental and behavioural co-morbidities of children with chronic health conditions. *Journal of Paediatrics and Child Health, 47*(10), 742-747. doi:10.1111/j.1440-1754.2011.02044.x

Blakemore, S. J. (2008). The social brain in adolescence. *Nature Reviews: Neuroscience, 9*(4), 267-277.

Bleil, M. E., Ramesh, S., Miller, B. D., & Wood, B. L. (2000). The influence of parent-child relatedness on depressive symptoms in children with asthma: Tests of moderator and mediator models. *Journal of Pediatric Psychology, 25*(7), 481-491.

Bodner, T. E. (2008). What improves with increased missing data imputations? *Structural Equation Modeling: A Multidisciplinary Journal, 15*(4), 651-675. doi:10.1080/10705510802339072

Boekaerts, M., & Roder, I. (1999). Stress, coping, and adjustment in children with a chronic disease: a review of the literature. *Disability and Rehabilitation, 21*(7), 311-337.

Borus, J. S. & Laffel, L. (2010). Adherence challenges in the management of type 1 diabetes in adolescents: Prevention and intervention. Current Opinion in Pediatrics, 22(4), 405-411. doi: 10.1097/MOP.0b013e32833a46a7

Bowen, E., Heron, J., Steer, C., & El Komy, M. (2008). *Anti-social and other problem behaviours among young children: findings from the Avon*

Longitudinal Study of Parents and Children. Retrieved from: http://dera.ioe.ac.uk/9122/1/rdsolr0208.pdf.

Bowen, E., Heron, J., Waylen, A., & Wolke, D. (2005). Domestic violence risk during and after pregnancy: findings from a British longitudinal study. *BJOG: An International Journal of Obstetrics & Gynaecology, 112*(8), 1083-1089. doi:10.1111/j.1471-0528.2005.00653.x

Bowes, L., Joinson, C., Wolke, D., & Lewis, G. (2015). Peer victimisation during adolescence and its impact on depression in early adulthood: prospective cohort study in the United Kingdom. *BMJ: British Medical Journal, 350*. doi:10.1136/bmj.h2469

Boyd, A., Golding, J., Macleod, J., Lawlor, D. A., Fraser, A., Henderson, J., Molloy, L., Ness, A., Ring, S., & Smith, G. D. (2012). Cohort profile: the 'children of the 90s'—the index offspring of the Avon Longitudinal Study of Parents and Children. *International Journal of Epidemiology, 42*(1), 111-127. doi: 10.1093/ije/dys064

Brace, M. J., Smith, M. S., McCauley, E., & Sherry, D. D. (2000). Family reinforcement of illness behavior: A comparison of adolescents with chronic fatigue syndrome, juvenile arthritis, and healthy controls. *Journal of Developmental and Behavioral Pediatrics, 21*(5), 332-339.

Bregnballe, V., Thastum, M., & O Schiotz, P. (2007). Psychosocial problems in children with cystic fibrosis. *Acta Paediatrica, 96*(1), 58-61. doi:10.1111/j.1651-2227.2006.00014.x

Bruzzese, J.-M., Fisher, P. H., Lemp, N., & Warner, C. M. (2009). Asthma and social anxiety in adolescents. *The Journal of Pediatrics, 155*(3), 398-403. doi:10.1016/j.jpeds.2009.04.004

Bynum, B. (2015). A history of chronic diseases. *The Lancet, 385*(9963), 105-106. doi:10.1016/S0140-6736(15)60007-1

Caffrey-Craig, B. (2005). Childhood asthma: A stress-related illness? More myth than fact. *The Irish Journal of Psychology, 26*(3-4), 149-159. doi:10.1080/03033910.2005.10446217

Cakaloz, B., Cakaloz, I., Polat, A., Inan, M., & Oguzhanoglu, N. K. (2009). Psychopathology in thalassemia major. *Pediatrics International, 51*(6), 825-828. doi:10.1111/j.1442-200X.2009.02865.x

Canning, E. H., & Kelleher, K. (1994). Performance of screening tools for mental health problems in chronically ill children. *Archives of Pediatrics & Adolescent Medicine, 148*(3), 272-278. doi:10.1001/archpedi.1994.02170030042008

Carotenuto, M., Esposito, M., Di Pasquale, F., De Stefano, S., & Santamaria, F. (2013). Psychological, cognitive and maternal stress assessment in children with primary ciliary dyskinesia*. World Journal of Pediatrics, 9*(4), 312-317. doi:10.1007/s12519-013-0441-1

Carpenter, J., & Kenward, M. (2012). *Multiple imputation and its application*. Hoboken: John Wiley & Sons.

Caruso, N. C., Radovanovic, B., Kennedy, J. D., Couper, J., Kohler, M., Kavanagh, P. S., Martin, A. J., & Lushington, K. (2014). Sleep, executive functioning and behaviour in children and adolescents with type 1 diabetes. *Sleep Medicine, 15*(12), 1490-1499. doi:10.1016/j.sleep.2014.08.011

Castro, D., Tubiana-Rufi, N., Moret, L., & Fombonne, E. (2000). Psychological adjustment in a French cohort of type 1 diabetic children. PEDIAB Collaborative Group. *Diabetes & Metabolism, 26*(1), 29-34.

Cato, M. A., Mauras, N., Ambrosino, J., Bondurant, A., Conrad, A. L., Kollman, C., Cheng, P., Beck, R. W., Ruedy, K. J., Aye, T., Reiss, A. L., White, N. H., & Hershey, T. (2014). Cognitive functioning in young children with type 1 diabetes. *Journal of the International Neuropsychological Society, 20*(2), 238-247. doi:10.1017/S1355617713001434

Chang, H. Y., Seo, J. H., Kim, H. Y., Kwon, J. W., Kim, B. J., Kim, H. B., Lee, S. Y., Jang, G. C., Song, D. J., Kim, W. K., Shim, J. Y., Kim, H. J., Park, J. W., Cho, S. H., Lee, J. S., Shin, Y. J., & Hong, S. J. (2013). Allergic diseases in preschoolers are associated with psychological and behavioural problems. *Allergy, Asthma and Immunology Research, 5*(5), 315-321. doi:10.4168/aair.2013.5.5.315

Charmaz, K. (1995). The body, identity, and self. *Sociological Quarterly, 36*(4), 657-680. doi:10.1111/j.1533-8525.1995.tb00459.x

Chen, J. H. (2014). Asthma and child behavioral skills: Does family socioeconomic status matter? *Social science & medicine,115*, 38-48. doi:10.1016/j.socscimed.2014.05.048

Chen, M. H., Su, T. P., Chen, Y. S., Hsu, J. W., Huang, K. L., Chang, W. H., Chen, T. J., & Bai, Y. M. (2014a). Higher risk of developing major depression and bipolar disorder in later life among adolescents with asthma: a nationwide prospective study. *Journal of Psychiatric Research*, *49*, 25-30. doi:10.1016/j.jpsychires.2013.10.015

Chen, M. H., Su, T. P., Chen, Y. S., Hsu, J. W., Huang, K. L., Chang, W. H., Chen, T. J., & Bai, Y. M. (2014b). Higher risk of mood disorders among adolescents with ADHD and asthma: A nationwide prospective study. *Journal of Affective Disorders, 156*, 232-235. doi:10.1016/j.jpsychires.2013.10.015

Chin, W. W. (1998). Commentary: Issues and Opinion on Structural Equation Modeling. *MIS Quarterly, 22*(1), vii-xvi.

Christie, D. & Viner, R. (2005). Adolescent development. *British Medical Journal, 330*, 301. doi: 10.1136/bmj.330.7486.301.

Churchill, R. (2010). No health without mental health: A role for the cochrane collaboration. *Cochrane Database of Systematic Reviews 2010, 10*, ED000012.

Cicchetti, D., & Walker, E. F. (2001). Stress and development: biological and psychological consequences. *Development and Psychopathology, 13*(3), 413-418.

Collins, J. E., Gill, T. K., Chittleborough, C. R., Martin, A. J., Taylor, A. W., & Winefield, H. (2008). Mental, emotional, and social problems among school children with asthma. *Journal of Asthma, 45*(6), 489-493. doi:10.1080/02770900802074802

Compas, B. E., Jaser, S. S., Dunn, M. J., & Rodriguez, E. M. (2012). Coping with chronic illness in childhood and adolescence*. Annual Review of Clinical Psychology, 8*, 455. doi:10.1146/annurev-clinpsy-032511-143108

Cornish, R. P., Boyd, A., Van Staa, T., Salisbury, C., & Macleod, J. (2013). Socio-economic position and childhood multimorbidity: a study using linkage between the Avon Longitudinal study of parents and children

and the general practice research database. *International Journal of Equity in Health, 12*, 66. doi:10.1186/1475-9276-12-66

Cornish, R. P., Henderson, J., Boyd, A. W., Granell, R., Van Staa, T., & Macleod, J. (2014). Validating childhood asthma in an epidemiological study using linked electronic patient records. *British Medical Journal Open, 4*(4), e005345. doi:10.1136/bmjopen-2014-005345

Cortina, S., McGraw, K., deAlarcon, A., Ahrens, A., Rothenberg, M. E., & Drotar, D. (2010). Psychological functioning of children and adolescents with eosinophil-associated gastrointestinal disorders. *Children's Health Care, 39*(4), 266-278. doi:10.1080/02739615.2010.515927

Costello, E. J., Foley, D. L., & Angold, A. (2006). 10-year research update review: the epidemiology of child and adolescent psychiatric disorders: II. Developmental epidemiology. *Journal of the American Academy of Child & Adolescent Psychiatry, 45*(1), 8-25. doi:10.1097/01.chi.0000184929.41423.c0

Costello, E. J., Mustillo, S., Erkanli, A., Keeler, G., & Angold, A. (2003). Prevalence and development of psychiatric disorders in childhood and adolescence. *Archives of General Psychiatry, 60*(8), 837-844. doi:10.1001/archpsyc.60.8.837

Cousins, L. A., Kalapurakkel, S., Cohen, L. L., & Simons, L. E. (2015). Topical review: Resilience resources and mechanisms in pediatric chronic pain. Journal of Pediatric Psychology, 40(9), 840-845. doi: 10.1093/jpepsy/jsv037.

Crombez, G., Eccleston, C., Van Damme, S., Vlaeyen, J. W., Karoly, P. (2012). Fear-avoidance model of chronic pain: The next generation. *Clinical Journal of Pain, 28*(6), 475-483. Doi: 10.1097/AJP.0b013e3182385392.

Culpin, I., Stapinski, L., Miles, Ö. B., Araya, R., & Joinson, C. (2015). Exposure to socioeconomic adversity in early life and risk of depression at 18 years: The mediating role of locus of control. *Journal of Affective Disorders, 183*, 269-278. doi:10.1016/j.jad.2015.05.030

Curtis, C. E., & Luby, J. L. (2008). Depression and social functioning in preschool children with chronic medical conditions. *The Journal of Pediatrics, 153*(3), 408-413. doi:10.1016/j.jpeds.2008.03.035

Cutuli, J. J., Herbers, J. E., Lafavor, T. L., Ahumada, S. M., Masten, A. S., & Oberg, C. N. (2014). Asthma and Adaptive Functioning among Homeless Kindergarten-Aged Children in Emergency Housing. *Journal of Health Care for the Poor and Underserved, 25*(2), 717-730. doi:10.1353/hpu.2014.0099

Dabelea, D., Mayer-Davis, E. J., Saydah, S., Imperatore, G., Linder, B., Divers, J., Bell, R., Badaru, A., Talton, J. W., Crume, T., Liese, A. D., Merchant, A.T., Lawrence, J. M., Reynolds, K., Dolan, L., Liu, L. L., & Hamman, R. F. (2014). Prevalence of Type 1 and Type 2 Diabetes Among Children and Adolescents From 2001 to 2009. JAMA, 311(17), 1778–1786. doi: 10.1001/jama.2014.3201

Davis, M. M., & Brosco, J. P. (2007). Being specific about being special: defining children's conditions and special health care needs. *Archives of Pediatrics & Adolescent Medicine, 161*(10), 1003-1005. doi:10.1001/archpedi.161.10.1003

Dayte, K. A., Moore, D. J., Russell, W. E., & Jaser, S. S. (2015). A review of adolescent adherence in type 1 diabetes and the untapped potential of diabetes providers to improve outcomes. Current Diabetes Reports, 15(8), 51. Doi: 10.1007/s11892-015-0621-6

de Boer, H. M., Mula, M., & Sander, J. W. (2008). The global burden and stigma of epilepsy. *Epilepsy & Behavior, 12*(4), 540-546. doi:10.1016/j.yebeh.2007.12.019

de Vries, P. J., Hunt, A., & Bolton, P. F. (2007). The psychopathologies of children and adolescents with tuberous sclerosis complex (TSC): A postal survey of UK families. *European Child & Adolescent Psychiatry, 16*(1), 16-24. doi:10.1007/s00787-006-0570-3

Deeks, J. J., Dinnes, J., D'Amico, R., Sowden, A. J., Sakarovitch, C., Song, F., Petticrew, M., & Altman, D. G. (2003). Evaluating non-randomised intervention studies. *Health Technology Assessment, 7*(27), iii-x, 1-173.

Delmas, M.-C., Guignon, N., Chan Chee, C., Fuhrman, C., Herbet, J.-B., & Gonzalez, L. (2011). Asthma and major depressive episode in adolescents in France. *Journal of Asthma, 48*(6), 640-646. doi:10.3109/02770903.2011.585410

Denny, S., de Silva, M., Fleming, T., Clark, T., Merry, S., Ameratunga, S., Milfont, T., Farrant, B., & Fortune, S. A. (2014). The prevalence of chronic health conditions impacting on daily functioning and the association with emotional well-being among a national sample of high school students. *Journal of Adolescent Health, 54*(4), 410-415. doi:10.1016/j.jadohealth.2013.09.010

Department for Work and Pensions. (2016). *Households below average income: an analysis of the income distribution 1994/95 to 2014/15*. Retrieved from: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/532416/households-below-average-income-1994-1995-2014-2015.pdf.

Department of Health. (2011). *No health without mental health: A cross-government mental health outcomes strategy for people of all ages*. Retrieved from: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/213761/dh_124058.pdf.

Department of Health. (2012). Long Term Conditions Compendium of Information (3rd ed.). Retrieved from: https://www.gov.uk /government/uploads/system/uploads/attachment_data/file/216528/dh_134486.pdf

Department of Health. (2015). 2010 to 2015 government policy: long term health conditions. Retrieved from: https://www.gov. uk /government/publications/2010-to-2015-government-policy-long-term-health-conditions/2010-to-2015-government-policy-long-term-health-conditions.

Didsbury, M. S., Kim, S., Medway, M. M., Tong, A., McTaggart, S. J., Walker, A. M., White, S., Mackie, F. E., Kara, T., Craig, J. C., & Wong, G. (2016). Socio-economic status and quality of life in children with

chronic disease: A systematic review. *Journal of Paediatrics and Child Health*, 52(12), 1062-1069. doi:10.1111/jpc.13407

Eapen, V., Mabrouk, A. A., Sabri, S., & Bin-Othman, S. (2006). A controlled study of psychosocial factors in young people with diabetes in the United Arab Emirates. *Annals of the New York Academy of Sciences, 1084*(1), 325-328. doi:10.1196/annals.1372.020

Easton, K., Diggle, J., Ruethi-Davis, M., Holmes, M., Byron-Parker, D., Nuttall, J., & Blackmore, C. (2017). Qualitative exploration of the potential for adverse events when using an online peer support network for mental health: Cross-Sectional survey. *JMIR Mental Health, 4*(4), e49. doi: 10.2196/mental.8168

Eccleson, C., Fisher, E., Law, E., Bartlett, J., & Palermo, T.M. (2015). Psychological interventions for parents of children and adolescents with chronic illness. *The Cochrane Database of Systematic Reviews, 15*(4), CD009660. doi: 10.1002/14651858.CD009660.pub3

Eiser, C. (1990). Psychological effects of chronic disease. *Journal of Child Psychology and Psychiatry, 31*(1), 85-98. doi:10.1111/j.1469-7610.1990.tb02274.x

Eiser, C. (1993). *Growing up with a chronic disease: The impact on children and their families.* London: Jessica Kingsley Publishers.

Ekinci, O., Celik, T., Unal, S., & Ozer, C. (2012). Psychiatric problems in children and adolescents with sickle cell disease, based on parent and teacher reports. *Turkish Journal of Hematology, 29*(3), 259-264. doi:10.5505/tjh.2012.15986

El-Sayed, Z. F., & Barakat, A. H. A. (2013). The psychological problems among children suffering from chronic diseases. *Life Science Journal-Acta Zhengzhou University Overseas Edition, 10*(1), 1676-1683.

Engel, G.L. (1977). The need for a new medical model: a challenge for biomedicine. *Science, 196*(4286), 129-136

Erickson, J. D., Patterson, J. M., Wall, M., & Neumark-Sztainer, D. (2005). Risk behaviors and emotional well-being in youth with chronic health conditions. *Children's Health Care, 34*(3), 181-192. doi:10.1207/s15326888chc3403_2

Evans, M., Cottrell, D., & Shiach, C. (2000). Emotional and behavioural problems and family functioning in children with haemophilia: a cross-sectional survey. *Haemophilia, 6*(6), 682-687.

Faugli, A., Bjornland, K., Emblem, R., Novik, T. S., & Diseth, T. H. (2009). Mental health and psychosocial functioning in adolescents with esophageal atresia. *Journal of Pediatric Surgery, 44*(4), 729-737. doi:10.1016/j.jpedsurg.2008.09.027

Fazel, M., Hoagwood, K., Stephan, S., & Ford, T. (2014). Mental health interventions in schools: Mental health interventions in schools in high-income countries. *Lancet Psychiatry, 1*(5), 377-387. doi: 10.1016/S2215-0366(14)70312-8.

Feitosa, C. A., Santos, D. N., Barreto do Carmo, M. B., Santos, L. M., Teles, C. A. S., Rodrigues, L. C., & Barreto, M. L. (2011). Behavior problems and prevalence of asthma symptoms among Brazilian children. *Journal of Psychosomatic Research, 71*(3), 160-165. doi:10.1016/j.jpsychores.2011.02.004

Feldman, J. M., Ortega, A. N., McQuaid, E. L., & Canino, G. (2006). Comorbidity between asthma attacks and internalizing disorders among Puerto Rican children at one-year follow-up. *Psychosomatics: Journal of Consultation and Liaison Psychiatry, 47*(4), 333-339. doi:10.1176/appi.psy.47.4.333

Feldmann, R., Weglage, J., & Frosch, M. (2012). Cognitive function in patients with epidermolysis bullosa: Social adjustment and emotional problems. *Klinische Padiatrie, 224*(1), 22-25. doi: 10.1055/s-0031-1295437

Ferguson, P., & Walker, H. (2014). 'Getting on with life': Resilience and normalcy in adolescents living with chronic illness. *International Journal of Inclusive Education, 18*(3), 227-240. doi:10.1080/13603116.2012.676082

Filakti, H., & Fox, J. (1995). Differences in mortality by housing tenure and by car access from the OPCS Longitudinal Study. *Population Trends,* (81), 27-30.

Ford, T., Goodman, R., & Meltzer, H. (2003). The British Child and Adolescent Mental Health Survey 1999: the prevalence of DSM-IV

disorders. *Journal of the American Academy of Child and Adolescent Psychiatry, 42*(10), 1203-1211. doi:10.1097/00004583-200310000-00011

Fox, N. A., Zeanah, C. H., & Nelson, C. A. (2012). Introduction to the special issue on the effects of early experience and stress on brain and behavioral development. *International Journal of Behavioral Development, 36*(1), 1-1. doi:doi:10.1177/0165025411407149

Fraser, A., Macdonald-Wallis, C., Tilling, K., Boyd, A., Golding, J., Smith, G. D., Henderson, J., Macleod, J., Molloy, L., & Ness, A. (2013). Cohort profile: The Avon Longitudinal Study of Parents and Children: ALSPAC mothers cohort. *International Journal of Epidemiology, 42*(1), 97-110. doi:10.1093/ije/dys066

Fritz, M. S., & MacKinnon, D. P. (2007). Required sample size to detect the mediated effect. *Psychological Science, 18*(3), 233-239. doi:10.1111/j.1467-9280.2007.01882.x

Fuhr, D. C., & De Silva, M. J. (2008). Physical long-term health problems and mental comorbidity: evidence from Vietnam. *Archives of Disease in Childhood, 93*(8), 686-689. doi:10.1136/adc.2007.116731

Ganz, M. L., & Tendulkar, S. A. (2006). Mental health care services for children with special health care needs and their family members: Prevalence and correlates of unmet needs. *Pediatrics, 117*(6), 2138-2148. doi:10.1542/peds.2005-1531

Geist, R., Grdisa, V., & Otley, A. (2003). Psychosocial issues in the child with chronic conditions. *Best Practice & Research Clinical Gastroenterology, 17*(2), 141-152. doi:10.1016/S1521-6918(02)00142-7

Giuffre, R. M., Gupta, S., Crawford, S. G., & Leung, A. K. C. (2008). Fears and anxiety in children with long-QT syndrome compared to children with asthma. *Journal of the National Medical Association, 100*(4), 420-424. doi:10.1016/S0027-9684(15)31275-X

Glazebrook, C., McPherson, A. C., Macdonald, I. A., Swift, J. A., Ramsay, C., Newbould, R., & Smyth, A. (2006). Asthma as a barrier to children's physical activity: implications for body mass index and

mental health. *Pediatrics, 118*(6), 2443-2449. doi:10.1542/peds.2006-1846

Goldbeck, L., Holling, I., Schlack, R., West, C., & Besier, T. (2011). The impact of an inpatient family-oriented rehabilitation program on parent-reported psychological symptoms of chronically ill children. *Klinische Padiatrie, 223*(2), 79-84. doi:10.1055/s-0030-1262831

Goldbeck, L., Koffmane, K., Lecheler, J., Thiessen, K., & Fegert, J. M. (2007). Disease severity, mental health, and quality of life of children and adolescents with asthma. *Pediatric Pulmonology, 42*(1), 15-22. doi:10.1002/ppul.20509

Goodman, A., Heiervang, E., Collishaw, S., & Goodman, R. (2011). The 'DAWBA bands' as an ordered-categorical measure of child mental health: description and validation in British and Norwegian samples. *Social Psychiatry and Psychiatric Epidemiology, 46*(6), 521-532. doi:10.1007/s00127-010-0219-x

Goodman, R. (1997). The Strengths and Difficulties Questionnaire: a research note. *Journal of Child Psychology and Psychiatry, 38*(5), 581-586. doi:10.1111/j.1469-7610.1997.tb01545.x

Goodman, R. (2001). Psychometric properties of the strengths and difficulties questionnaire. *Journal of the American Academy of Child & Adolescent Psychiatry, 40*(11), 1337-1345. doi:10.1097/00004583-200111000-00015

Goodman, R., Ford, T., Richards, H., Gatward, R., & Meltzer, H. (2000). The Development and Well-Being Assessment: description and initial validation of an integrated assessment of child and adolescent psychopathology. *Journal of Child Psychology and Psychiatry, 41*(5), 645-655. doi:10.1111/j.1469-7610.2000.tb02345.x

Goodman, R., Ford, T., Simmons, H., Gatward, R., & Meltzer, H. (2000). Using the Strengths and Difficulties Questionnaire (SDQ) to screen for child psychiatric disorders in a community sample. *The British Journal of Psychiatry, 177*(6), 534-539. doi:10.1192/bjp.177.6.534

Goodman, R., Meltzer, H., & Bailey, V. (1998). The Strengths and Difficulties Questionnaire: A pilot study on the validity of the self-report version.

European Child & Adolescent Psychiatry, 7(3), 125-130. doi:10.1007/s007870050057

Goodman, R., & Scott, S. (1999). Comparing the Strengths and Difficulties Questionnaire and the Child Behavior Checklist: is small beautiful? *Journal of Abnormal Child Psychology, 27*(1), 17-24. doi:10.1023/A:1022658222914

Goodwin, R. D., Robinson, M., Sly, P. D., McKeague, I. W., Susser, E. S., Zubrick, S. R., Stanley, F. J., & Mattes, E. (2013). Severity and persistence of asthma and mental health: A birth cohort study. *Psychological Medicine, 43*(6), 1313-1322. doi:10.1017/S0033291712001754

Graue, M., Wentzel-Larsen, T., Hanestad, B. R., Batsvik, B., & Sovik, O. (2003). Measuring self-reported, health-related, quality of life in adolescents with type 1 diabetes using both generic and disease-specific instruments. *Acta Paediatrica, 92*(10), 1190-1196. doi:10.1111/j.1651-2227.2003.tb02483.x/

Gray, N.J., & Wood, D.M. (2017). The Role of Medication in Supporting Emotional Wellbeing in Young People with Long-Term Needs. *Healthcare, 5*(4), E84. doi: 10.3390/healthcare5040084

Grey, M., & Sullivan-Bolyai, S. (1999). Key issues in chronic illness research: lessons from the study of children with diabetes. *Journal of Pediatric Nursing, 14*(6), 351-358. doi:10.1016/s0882-5963(99)80064-5

Grych, J. H., & Fincham, F. D. (2001). Interparental conflict and child adjustment: An overview. In J. H. Grych & F. D. Fincham (Eds.), *Interparental conflict and child adjustment: Theory, research and applications* (pp. 1-6). New York: Cambridge University Press.

Guion, K., & Mrug, S. (2012). The role of parental and adolescent attributions in adjustment of adolescents with chronic illness*. Journal of Clinical Psychology in Medical Settings, 19*(3), 262-269. doi:10.1007/s10880-011-9288-6

Gupta, S., Mitchell, I., Giuffre, R. M., & Crawford, S. (2001). Covert fears and anxiety in asthma and congenital heart disease. *Child: Care, Health and Development, 27*(4), 335-348. doi: 10.1007/s12646-011-0137-3

Gupta, V., Singh, A., Upadhyay, S. K., & Bhatia, B. (2012). Psychopathology in children with thalassemia major. *Psychological Studies, 57*(1), 55-57. doi: 10.1007/s12646-011-0137-3

Hagell, A., Coleman, J., & Brooks, F. (2015). *Key data on adolescence 2015*. London: Association for Young People's Health.

Halfon, N., & Newacheck, P. W. (2010). Evolving notions of childhood chronic illness. *JAMA: The Journal of the American Medical Association, 303*(7), 665-666. doi:10.1001/jama.2010.130

Halterman, J. S., Conn, K. M., Forbes-Jones, E., Fagnano, M., Hightower, A. D., & Szilagyi, P. G. (2006). Behavior problems among inner-city children with asthma: Findings from a community-based sample. *Pediatrics, 117*(2), E192-E199. doi:10.1542/peds.2005-1140

Hammer-Helmich, L., Linneberg, A., Obel, C., Thomsen, S. F., Møllehave, L. T., Glümer, C. (2016). Mental health associations with eczema, asthma and hay fever in children: A cross-sectional survey. *British Medical Journal Open, 6,* e012637. doi:10.1136/bmjopen-2016-012637

Hawker, D.S.J. (2007). Increasing initial attendance at mental health out-patient clinics: opt-in systems and other interventions. *Psychiatric Bulletin, 31*, 179-182. doi: 10.1192/pb.bp.105.007377.

Hayden, E., & Mash, E. (2014). Child psychopathology: A developmental-systems perspective. In E. J. Marsh & R. A. Barkley (Eds.), *Child Psychopathology* (pp. 3-72). New York: The Guildford Press.

Helgeson, V. S., Snyder, P. R., Escobar, O., Siminerio, L., & Becker, D. (2007). Comparison of adolescents with and without diabetes on indices of psychosocial functioning for three years. *Journal of Pediatric Psychology, 32*(7), 794-806. doi:10.1093/jpepsy/jsm020

Henje Blom, E., Ho, T. C., Connolly, C. G., LeWinn, K. Z., Sacchet, M. D., Tymofiyeva, O., Weng, H. Y., & Yang, T. T. (2016). The neuroscience and context of adolescent depression. *Acta Paediatrica, 105*(4), 358-365. doi:10.1111/apa.13299

Herzer, M., & Hood, K. K. (2010). Anxiety symptoms in adolescents with type 1 diabetes: Association with blood glucose monitoring and glycemic

control. *Journal of Pediatric Psychology, 35*(4), 415-425. doi:10.1093/jpepsy/jsp063

Hijmans, C. T., Grootenhuis, M. A., Oosterlaan, J., Last, B. F., Heijboer, H., Peters, M., & Fijnvandraat, K. (2009). Behavioral and emotional problems in children with sickle cell disease and healthy siblings: Multiple informants, multiple measures. *Pediatric Blood & Cancer, 53*(7), 1277-1283. doi:10.1002/pbc.22257

Hilliard, M. E., Monaghan, M., Cogen, F. R., & Streisand, R. (2011). Parent stress and child behaviour among young children with type 1 diabetes. *Child: Care, Health and Development, 37*(2), 224-232. doi:10.1111/j.1365-2214.2010.01162.x

Hockley, C., Quigley, M. A., Hughes, G., Calderwood, L., Joshi, H., & Davidson, L. L. (2008). Linking Millennium Cohort data to birth registration and hospital episode records. *Paediatric and Perinatal Epidemiology, 22*(1), 99-109. doi: 10.1111/j.1365-3016.2007.00902.x

Holmbeck, G. N. (2002). A developmental perspective on adolescent health and illness: An introduction to the special issues. *Journal of Pediatric Psychology, 27*(5), 409-416. doi:10.1093/jpepsy/27.5.409

Holme, A. R., Blair, P. S., & Emond, A. M. (2013). Psychosocial and educational outcomes of weight faltering in infancy in ALSPAC. *British Medical Journal Open, 3*(7), e002863. doi:10.1136/bmjopen-2013-002863

Hooper, S. R., Duquette, P. J., Icard, P., Wetherington, C. E., Harrell, W., & Gipson, D. S. (2009). Social-behavioural functioning in paediatric chronic kidney disease*. Child: Care, Health and Development, 35*(6), 832-840. doi:10.1111/j.1365-2214.2009.00992.x

Hope, H. & Niven, R. (2017). The role of clinical psychology and the number of hospital bed days required by severe asthma patients. *Thorax, 72*, A243-A245. doi: 10.1136/thoraxjnl-2017-210983.435

Hopkins, L., Green, J., Henry, J., Edwards, B., & Wong, S. (2014). Staying engaged: the role of teachers and schools in keeping young people with health conditions engaged in education. *The Australian Educational Researcher, 41*(1), 25-41. doi:10.1007/s13384-013-0096-x

Horton, D., Berg, C. A., Butner, J., & Wiebe, D. J. (2009). The role of parental monitoring in metabolic control: Effect on adherence and externalizing behaviors during adolescence. *Journal of Pediatric Psychology, 34*(9), 1008-1018. doi:10.1093/jpepsy/jsp022

Hoyle, R. H. (1999). Sample size, reliability, and tests of statistical meditation. In R. H. Hoyle (Ed.), *Statistical strategies for small sample research* (pp. 195-222). Thousand Oaks: Sage.

Hsu, J., Qin, X., Beavers, S. F., & Mirabelli, M. C. (2016). Asthma-related school absenteeism, morbidity, and modifiable factors. *American Journal of Preventive Medicine, 51*(1), 23-32. doi:10.1016/j.amepre.2015.12.012

Hsu, Y.-Y. A., Dorn, L. D., & Sereika, S. M. (2010). Comparison of puberty and psychosocial adjustment between Taiwanese adolescent females with and without diabetes. *Journal of Clinical Nursing, 19*(19-20), 2704-2712. doi:10.1111/j.1365-2702.2010.03272.x

Hu, L. t., & Bentler, P. M. (1999). Cutoff criteria for fit indexes in covariance structure analysis: Conventional criteria versus new alternatives. *Structural Equation Modeling: A Multidisciplinary Journal, 6*(1), 1-55. doi:10.1080/10705519909540118

Huygen, A. C. J., Kuis, W., & Sinnema, G. (2000). Psychological, behavioural, and social adjustment in children and adolescents with juvenile chronic arthritis. *Annals of the Rheumatic Diseases, 59*(4), 276-282. doi:10.1136/ard.59.4.276

Hysing, M., Elgen, I., Gillberg, C., Lie, S. A., & Lundervold, A. J. (2007). Chronic physical illness and mental health in children: Results from a large-scale population study. *Journal of Child Psychology and Psychiatry, 48*(8), 785-792. doi:10.1111/j.1469-7610.2007.01755.x

Hysing, M., Elgen, I., Gillberg, C., & Lundervold, A. J. (2009). Emotional and behavioural problems in subgroups of children with chronic illness: Results from a large-scale population study. *Child: Care, Health and Development, 35*(4), 527-533. doi: 10.1111/j.1365-2214.2009.00967.x

Hysing, M., Sivertsen, B., Stormark, K. M., Elgen, I., & Lundervold, A. J. (2009). Sleep in children with chronic illness, and the relation to emotional and behavioral problems—A population-based study.

Journal of Pediatric Psychology, 34(6), 665-670. doi:10.1093/jpepsy/jsn095

Jaffee, S. R., Moffitt, T. E., Caspi, A., Fombonne, E., Poulton, R., & Martin, J. (2002). Differences in early childhood risk factors for juvenile-onset and adult-onset depression. *Archives of General Psychiatry, 59*(3), 215-222. doi:10.1001/archpsyc.59.3.215

James, L. R., & Brett, J. M. (1984). Mediators, moderators, and tests for mediation. *Journal of Applied Psychology, 69*(2), 307. doi:10.1037/0021-9010.69

Janicke, D. M., Harman, J. S., Kelleher, K. J., & Zhang, J. (2008). Psychiatric diagnosis in children and adolescents with obesity-related health conditions. *Journal of Developmental and Behavioral Pediatrics, 29*(4), 276-284. doi:10.1097/DBP.0b013e31817102f8

Jayanath, S., Lee, W. S., Chinna, K., & Boey, C. C. M. (2014). Depressive symptoms in children with chronic gastrointestinal disorders. *Pediatrics International, 56(*4), 583-587. doi:10.1111/ped.12335

Jewson, N. D. (1976). The Disappearance of the Sick-Man from Medical Cosmology, 1770-1870. *Sociology, 10*(2), 225-244.

Joinson, C., Heron, J., Lewis, G., Croudace, T., & Araya, R. (2011). Timing of menarche and depressive symptoms in adolescent girls from a UK cohort. *British Journal of Psychiatry, 198*(1), 17-23, sup 11-12. doi:10.1192/bjp.bp.110.080861

Jones, J. E., Watson, R., Sheth, R., Caplan, R., Koehn, M., Seidenberg, M., & Hermann, B. (2007). Psychiatric comorbidity in children with new onset epilepsy. *Developmental Medicine & Child Neurology, 49*(7), 493-497. doi:10.1111/j.1469-8749.2007.00493.x

Jones, S. E., & Lollar, D. J. (2008). Relationship between physical disabilities or long-term health problems and health risk behaviors or conditions among US high school students. *Journal of School Health, 78*(5), 252-257. doi:10.1111/j.1746-1561.2008.00297.x

Katon, W., Lozano, P., Russo, J., McCauley, E., Richardson, L., & Bush, T. (2007). The prevalence of DSM-IV anxiety and depressive disorders in youth with asthma compared with controls. *Journal of Adolescent Health, 41*(5), 455-463. doi:10.1016/j.jadohealth.2007.05.023

Kaufman, J., Martin, A., King, R. A., & Charney, D. (2001). Are child-, adolescent-, and adult-onset depression one and the same disorder? *Biological Psychiatry, 49*(12), 980-1001. doi:10.1016/S0006-3223(01)01127-1

Kean, E. M., Kelsay, K., Wamboldt, F., & Wamboldt, M. Z. (2006). Posttraumatic stress in adolescents with asthma and their parents. *Journal of the American Academy of Child & Adolescent Psychiatry, 45*(1), 78-86. doi:10.1097/01.chi.0000186400.67346.02

Kearney, C.A. (2008). School absenteeism and school refusal behavior in youth: A contemporary review. *Clinical Psychology Review, 28*(3), 451-471. doi:10.1016/j.cpr.2007.07.012

Kendler, K. S., Gardner, C. O., Hickman, M., Heron, J., Macleod, J., Lewis, G., & Dick, D. M. (2014). Socioeconomic Status and Alcohol-Related Behaviors in Mid- to Late Adolescence in the Avon Longitudinal Study of Parents and Children. *Journal of Studies on Alcohol and Drugs, 75*(4), 541-545. doi: 10.15288/jsad.2014.75.541

Kerkar, N., D'Urso, C., Van Nostrand, K., Kochin, I., Gault, A., Suchy, F., Miloh, T., Arnon, R., Chu, J., & Annunziato, R. (2013). Psychosocial outcomes for children with nonalcoholic fatty liver disease over time and compared with obese controls. *Journal of Pediatric Gastroenterology and Nutrition, 56*(1), 77-82. doi:10.1097/MPG.0b013e31826f2b8c

Key, J. D., Brown, R. T., Marsh, L. D., Spratt, E. G., & Recknor, J. C. (2001). Depressive symptoms in adolescents with a chronic illness. *Children's Health Care, 30*(4), 283-292. doi:10.1207/S15326888CHC3004_03

Kidger, J., Heron, J., Lewis, G., Evans, J., & Gunnell, D. (2012). Adolescent self-harm and suicidal thoughts in the ALSPAC cohort: a self-report survey in England. *BMC Psychiatry, 12*(1), 69. doi:10.1186/1471-244x-12-69

Klasen, H., Woerner, W., Wolke, D., Meyer, R., Overmeyer, S., Kaschnitz, W., Rothenberger, A., & Goodman, R. (2000). Comparing the German versions of the strengths and difficulties questionnaire (SDQ-Deu) and the child behavior checklist. *European Child & Adolescent Psychiatry, 9*(4), 271-276. doi:10.1007/s007870070030

Klinnert, M. D., McQuaid, E. L., McCormick, D., Adinoff, A. D., & Bryant, N. E. (2000). A multimethod assessment of behavioral and emotional adjustment in children with asthma. *Journal of Pediatric Psychology, 25*(1), 35-46. doi:10.1093/jpepsy/25.1.35

Kobayashi, K., Endoh, F., Ogino, T., Oka, M., Morooka, T., Yoshinaga, H., & Ohtsuka, Y. (2013). Questionnaire-based assessment of behavioral problems in Japanese children with epilepsy. *Epilepsy & Behavior, 27*(1), 238-242. doi:10.1016/j.yebeh.2013.01.020

Kohlboeck, G., Koletzko, S., Bauer, C. P., von Berg, A., Berdel, D., Kramer, U., Schaaf, B., Lehmann, I., Herbarth, O., & Heinrich, J. (2013). Association of atopic and non-atopic asthma with emotional symptoms in school children. *Pediatric Allergy and Immunology, 24*(3), 230-236. doi:10.1111/pai.12056

Koskelainen, M., Sourander, A., & Vauras, M. (2001). Self-reported strengths and difficulties in a community sample of Finnish adolescents. *European Child & Adolescent Psychiatry, 10*(3), 180-185. doi:10.1007/s007870170024

Kristensen, L. J., Birkebaek, N. H., Mose, A. H., Hohwu, L., & Thastum, M. (2014). Symptoms of emotional, behavioral, and social difficulties in the Danish population of children and adolescents with type 1 diabetes - Results of a national survey. *PLoS ONE, 9*(5), e97543. doi:10.1371/journal.pone.0097543

La Greca, A. M. (1992). Peer influences in pediatric chronic illness: An update. *Journal of Pediatric Psychology, 17*(6), 775-784.

La Greca, A. M., & Varni, J. W. (1993). Interventions in pediatric psychology: a look toward the future. *Journal of Pediatric Psychology, 18*(6), 667-679.

Lahaye, M., Luminet, O., Van Broeck, N., & Bodart, E. (2012). Psychological, social and school implications of asthma: a comparison of Belgian French-speaking children having asthma with healthy children. *Acta Clinica Belgica, 67*(1), 25-29. doi:10.2143/ACB.67.1.2062622

Lambert, V., & Keogh, D. (2015). Striving to live a normal life: A review of children and young people's experience of feeling different when living

with a long term condition. *Journal of Pediatric Nursing, 30*(1), 63-77. doi:10.1016/j.pedn.2014.09.016

Langer, S. L., Romano, J. M., Levy, R. L., Walker, L. S., & Whitehead, W. E. (2009). Catastrophizing and parental response to child symptom complaints. *Child Health Care, 38*(3), 169-184. doi: 10.1080/02739610903038750

Langer, S. L., Romano, J. M., Liu, Q., Levy, R. L., Nielson, H., & Brown, J. D. (2016). Pain catastrophizing predicts verbal expression among children with chronic pain and their mothers. *Health Psychology Open, 3*(1), 2055102916632667. doi: 10.1177/2055102916632667.

Lavigne, J. V., & Faier-Routman, J. (1992). Psychological adjustment to pediatric physical disorders: A meta-analytic review. *Journal of Pediatric Psychology, 17*(2), 133-157. doi:10.1093/jpepsy/17.2.133

Law, G. U. (2002). Dissimilarity in adolescent and maternal representations of Type 1 diabetes: exploration of relations to adolescent well-being. *Child: Care, Health and Development, 28*(5), 369-378. doi:10.1046/j.1365-2214.2002.00286.x

Leeman, J., Crandell, J. L., Lee, A., Bai, J., Sandelowski, M., & Knafl, K. (2016). Family Functioning and the Well-Being of Children With Chronic Conditions: A Meta-Analysis. *Research in Nursing & Health, 39*(4), 229-243. doi:10.1002/nur.21725

Lereya, S. T., Copeland, W. E., Costello, E. J., & Wolke, D. (2015). Adult mental health consequences of peer bullying and maltreatment in childhood: two cohorts in two countries. *The Lancet Psychiatry, 2*(6), 524-531. doi:10.1016/S2215-0366(15)00165-0

Lerner, R. M., Theokas, C., & Bobek, D. L. (2005) Concepts and theories of human development: Historical and contemporary dimensions. In M.H. Bornstein & M.E. Lamb (Eds.), *Developmental Science: An Advanced Textbook* (5th Edition) (pp.3-44). Mahwah, NJ: Lawrence Erlbaum Associates Inc., 3-44.

Letitre, S. L., de Groot, E. P., Draaisma, E., & Brand, P. L. P. (2014). Anxiety, depression and self-esteem in children with well-controlled asthma: case-control study. *Archives of Disease in Childhood, 99*(8), 744-748. doi:10.1136/archdischild-2013-305396

Leung, L. (2012). Pain catastrophizing: An updated review. *Indian Journal of Psychological Medicine, 34*(3), 204-217. doi: 10.4103/0253-7176.106012

Liakopoulou, M., Alifieraki, T., Katideniou, A., Peppa, M., Maniati, M., Tzikas, D., Hibbs, E. D., & Dacou-Voutetakis, C. (2001). Maternal expressed emotion and metabolic control of children and adolescents with diabetes mellitus. *Psychotherapy and Psychosomatics, 70*(2), 78-85. doi:10.1159/000056230

Liberati, A., Altman, D. G., Tetzlaff, J., Mulrow, C., Gøtzsche, P. C., Ioannidis, J. P. A., Clarke, M., Devereaux, P. J., Kleijnen, J., & Moher, D. (2009). The PRISMA Statement for Reporting Systematic Reviews and Meta-Analyses of Studies That Evaluate Health Care Interventions: Explanation and Elaboration. *PLOS Medicine, 6*(7), e1000100. doi:10.1371/journal.pmed.1000100

Lidell, A., Adshead, S., & Burgess, E. (2008). *Technology in the NHS: Transforming the patient's experience of care.* Retrieved from: https://www.kingsfund.org.uk/sites/default/files/Technology-in-the-NHS-Transforming-patients-experience-of-care-Liddell-Adshead-and-Burgess-Kings-Fund-October-2008_0.pdf

Lien, L., Green, K., Thoresen, M., & Bjertness, E. (2010). Atopic conditions and mental health problems: A 3-year follow-up study. *European Child & Adolescent Psychiatry, 19*(9), 705-713. doi:10.1007/s00787-010-0106-8

Lindsay, S., Kingsnorth, S., Hamdani, Y. (2011). Barriers and facilitators of chronic illness self-management among adolescents: A review and future directions. *Journal of Nursing and Healthcare of Chronic Illness, 3*(3), 186-208. doi:10.1111/j.1752-9824.2011.01090.x

Liu, A. H., Zeiger, R., Sorkness, C., Mahr, T., Ostrom, N., Burgess, S., Rosenzweig, J. C., & Manjunath, R. (2007). Development and cross-sectional validation of the Childhood Asthma Control Test. *Journal of Allergy and Clinical Immunology, 119*(4), 817-825. doi:10.1016/j.jaci.2006.12.662

Loades, M. E., & Mastroyannopoulou, K. (2010). Teachers' Recognition of Children's Mental Health Problems. *Child and Adolescent Mental Health, 15*(3), 150-156. doi:10.1111/j.1475-3588.2009.00551.x

Loeys, T., Moerkerke, B., & Vansteelandt, S. (2015). A cautionary note on the power of the test for the indirect effect in mediation analysis. *Frontiers in Psychology, 5*(1549). doi:10.3389/fpsyg.2014.01549

Lidell, A., Adshead, S., & Burgess, E. (2008). *Technology in the NHS: Transforming the patient's experience of care.* Retrieved from: https://www.kingsfund.org.uk/sites/default/files/Technology-in-the-NHS-Transforming-patients-experience-of-care-Liddell-Adshead-and-Burgess-Kings-Fund-October-2008_0.pdf

Looijmans-van den Akker, I., van Luijn, K., & Verheij, T. (2016). Overdiagnosis of asthma in children in primary care: a retrospective analysis. *British Journal of General Practice, 66*(644), e152-e157. doi:10.3399/bjgp16X683965

Lorant, V., Kunst, A. E., Huisman, M., Costa, G., & Mackenbach, J. (2005). Socio-economic inequalities in suicide: a European comparative study. *The British Journal of Psychiatry, 187*(1), 49-54. doi:10.1192/bjp.187.1.49

Louthrenoo, O., Krairojananan, J., Chartapisak, W., & Opastirakul, S. (2012). Psychosocial functioning of children with systemic lupus erythematosus. *Journal of Paediatrics and Child Health, 48*(12), 1091-1094. doi:10.1111/j.1440-1754.2012.02499.x

Lu, Y., Ho, R., Lim, T. K., Kuan, W. S., Goh, D. Y. T., Mahadevan, M., Sim, T. B., Ng, T.-P., & van Bever, H. P. S. (2014). Psychiatric comorbidities in Asian adolescent asthma patients and the contributions of neuroticism and perceived stress. *Journal of Adolescent Health, 55*(2), 267-275. doi:10.1016/j.jadohealth.2014.01.007

Lyons, A. & Chamberlain, K. (2006). *Health psychology: A critical introduction.* Cambridge: Cambridge University Press.

Maas-van Schaaijk, N. M., Roeleveld-Versteegh, A. B. C., & van Baar, A. L. (2013). The interrelationships among paternal and maternal parenting stress, metabolic control, and depressive symptoms in adolescents

with type 1 diabetes mellitus. *Journal of Pediatric Psychology, 38*(1), 30-40. doi:10.1093/jpepsy/jss096

Mackner, L. M., & Crandall, W. V. (2006). Brief Report: Psychosocial adjustment in adolescents with inflammatory bowel disease. *Journal of Pediatric Psychology, 31*(3), 281-285. doi:10.1093/jpepsy/jsj023

Makay, B., Emiroglu, N., & Uensal, E. (2010). Depression and anxiety in children and adolescents with familial Mediterranean fever. *Clinical Rheumatology, 29*(4), 375-379. doi:10.1007/s10067-009-1330-9

Marcus, S. B., Strople, J. A., Neighbors, K., Weissberg-Benchell, J., Nelson, S. P., Limbers, C., Varni, J. W., & Alonso, E. M. (2009). Fatigue and health-related quality of life in pediatric inflammatory bowel disease. *Clinical Gastroenterology and Hepatology, 7*(5), 554-561. doi:10.1016/S0016-5085(08)60878-1

Markson, S., & Fiese, B. H. (2000). Family rituals as a protective factor for children with asthma. *Journal of Pediatric Psychology, 25*(7), 471-479. doi:10.1093/jpepsy/25.7.471

Marmot, M. G., Kogevinas, M., & Elston, M. A. (1987). Social-economic status and disease. *Annual Review of Public Health, 8*, 111-135. doi:10.1146/annurev.pu.08.050187.000551

Marsh, H. W., & Hau, K.-T. (1999). Confirmatory factor analysis: Strategies for small sample sizes. In R. H. Hoyle (Ed.), *Statistical strategies for small sample size* (pp. 251-306). Thousand Oaks: Sage.

Martinez, W., Carter, J. S., & Legato, L. J. (2011). Social competence in children with chronic illness: A meta-analytic review. *Journal of Pediatric Psychology, 36*(8), 878-890. doi:10.1093/jpepsy/jsr035

Masten, A. S., & Cicchetti, D. (2010). Developmental cascades. *Development and Psychopathology, 22*(3), 491-495. doi:10.1017/s0954579410000222

Masten, A. S., Roisman, G. I., Long, J. D., Burt, K. B., Obradovic, J., Riley, J. R., Boelcke-Stennes, K., & Tellegen, A. (2005). Developmental cascades: linking academic achievement and externalizing and internalizing symptoms over 20 years. *Developmental Psychology*, 41(5), 733-746. doi:10.1037/0012-1649.41.5.733

Mazzone, L., Postorino, V., De Peppo, L., Della Corte, C., Lofino, G., Vassena, L., Fatta, L., Armando, M., Bedogni, G., Vicari, S., & Nobili, V. (2013). Paediatric Non-Alcoholic Fatty Liver Disease: Impact on Patients and Mothers' Quality of Life. *Hepatitis Monthly, 13*(3), e7871. doi:10.5812/hepatmon.7871

McCarroll, E. M., Lindsey, E. W., MacKinnon-Lewis, C., Chambers, J. C., & Frabutt, J. M. (2009). Health status and peer relationships in early adolescence: The role of peer contact, self-esteem, and social anxiety. *Journal of Child and Family Studies, 18(*4), 473-485. doi:10.1007/s10826-008-9251-9

McCarthy, A. M., Lindgren, S., Mengeling, M. A., Tsalikian, E., & Engvall, J. C. (2002). Effects of diabetes on learning in children. *Pediatrics, 109*(1), E9. doi:10.1542/peds.109.1.e9

McClellan, C. B., & Cohen, L. L. (2007). Family functioning in children with chronic illness compared with healthy controls: a critical review. *The Journal of Pediatrics, 150*(3), 221-223, 223.e221-222. doi:10.1016/j.jpeds.2006.11.063

McCorkle, R., Ercolano, E., Lazenby, M., Schulman-Green, D., Schilling, L. S., Lorig, K., & Wagner, E. H. (2011). Self-Management: Enabling and empowering patients living with cancer as a chronic illness. *CA: A Cancer Journal for Clinicians, 61*(1), 50-62. doi:10.3322/caac.20093

McCormack, A., Norrish, S., Parker, L., & Frampton, I. (2010). Consulting with young people about healthcare. Part 2: experience of long-term health conditions. *Pediatric Health, 4*(2), 167-175. doi:10.2217/phe.10.13

McDougall, J., King, G., De Wit, D., Miller, L., Hong, S., Offord, D., Laporta, J., & Meyer, K. (2004). Chronic physical health conditions and disability among Canadian school-aged children: a national profile. *Disability and Rehabilitation, 26*(1), 35-45. doi:10.1080/09638280410001645076

Meijer, S. A., Sinnema, G., Bijstra, J. O., Mellenbergh, G. J., & Wolters, W. H. G. (2000a). Peer interaction in adolescents with a chronic illness. *Personality and Individual Differences, 29*(5), 799-813. doi:10.1016/S0191-8869(99)00233-0

Meijer, S. A., Sinnema, G., Bijstra, J. O., Mellenbergh, G. J., & Wolters, W. H. G. (2000b). Social functioning in children with a chronic illness. *Journal of Child Psychology and Psychiatry, 41*(3), 309-317. doi:10.1111/1469-7610.00615

Meltzer, H., Gatward, R., Corbin, T., Goodman, R., & Ford, T. (2003*). Persistence, onset, risk factors and outcomes of childhood mental disorders*. London: The Stationary Office.

Meltzer, H., Gatward, R., Goodman, R., & Ford, T. (2000). *The mental health of children and adolescents in Great Britain.* London: The Stationery Office.

Mental Health Network/NHS Confederation. (2012). *Investing in emotional and psychological wellbeing for patients with long-term conditions*. Retrieved from: http://www.nhsconfed.org/~/media/Confederation/Files/Publications/Documents/Investing%20in%20emotional%20and%20psychological%20wellbeing%20for%20patients%20with%20long-term%20condtions%2016%20April%20final%20for%20website.pdf.

Merikangas, K. R., & He, J. (2014). Epidemiology of mental disorders in children and adolescents. *From Research to Practice in Child and Adolescent Mental Health, 19*.

Messer, S. C., Angold, A., Costello, E. J., Loeber, R., Van Kammen, W., & Stouthamer-Loeber, M. (1995). Development of a short questionnaire for use in epidemiological studies of depression in children and adolescents: Factor composition and structure across development*. International Journal of Methods in Psychiatric Research, 5*, 252-262.

Michaud, P.-A., Surís, J.-C., & Viner, R. (2007). *The adolescent with a chronic condition: epidemiology, developmental issues and health care provision*. Geneva: World Health Organization.

Miller, R. G. (1982). *Simultaneous Statistical Inference* (2nd Edition). New York: Springer Verlag.

Missotten, L. C., Luyckx, K., & Seiffge-Krenke, I. (2013). Family climate of adolescents with and without type 1 diabetes: Longitudinal associations with psychosocial adaptation. *Journal of Child and Family Studies, 22*(3), 344-354. doi:10.1007/s10826-012-9585-1

Mitchell, D. K., Murdock, K. K., & Berz, J. B. (2004). Developmental, gender, and health-related variations in self-competence and depressed mood among school-aged urban children with asthma: A pilot study. *Journal of Clinical Psychology in Medical Settings, 11*(4), 343-355. doi:10.1023/B:JOCS.0000045354.93521.9b

Moreira, H., Carona, C., Silva, N., Frontini, R., Bullinger, M., & Canavarro, M. C. (2013). Psychological and quality of life outcomes in pediatric populations: A parent-child perspective. *The Journal of Pediatrics, 163*(5), 1471-1478. doi:10.1016/j.jpeds.2013.06.028

Moussa, M. A. A., Alsacid, M., Abdella, N., Refai, T. M. K., Al-Sheikh, N., & Gomez, J. E. (2005). Social and psychological characteristics of Kuwaiti children and adolescents with type 1 diabetes. *Social Science & Medicine, 60*(8), 1835-1844. doi:10.1016/j.socscimed.2004.08.018

Mroczek, D. K., & Spiro, A. (2003). Modeling intraindividual change in personality traits: Findings from the Normative Aging Study. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences, 58*(3), P153-P165.

Mubarak, A., Fadel, W., Said, S., & Hammar, M. A. (2010). Profile of behavior and IQ in anemic children. *CNS Spectrums, 15*(12), 631-638. doi:10.1017/S1092852912000089

Mujica-Mota, R. E., Roberts, M., Abel, G., Elliott, M., Lyratzopoulos, G., Roland, M., & Campbell, J. (2015). Common patterns of morbidity and multi-morbidity and their impact on health-related quality of life: evidence from a national survey. *Quality of Life Research, 24*(4), 909-918. doi:10.1007/s11136-014-0820-7

Muthén, L. K., & Muthén, B. O. (2002). How to use a Monte Carlo study to decide on sample size and determine power. *Structural Equation Modeling, 9*(4), 599-620. doi:10.1207/S15328007SEM0904_8

Muthén, L. K., & Muthén, B. O. (2010). *MPlus user's guide: Statistical analysis with latent variables* (6th ed.). Los Angeles, CA: Muthén & Muthén.

Nardi, L., Zucchini, S., D'Alberton, F., Salardi, S., Maltoni, G., Bisacchi, N., Elleri, D., & Cicognani, A. (2008). Quality of life, psychological adjustment and metabolic control in youths with type 1 diabetes: a

study with self- and parent-report questionnaires. *Pediatric Diabetes, 9*(5), 496-503. doi:10.1111/j.1399-5448.2008.00414.x

Naylor, C., Das, P., Ross, S., Honeyman, M., Thompson, J., & Gilburt, H. (2016). *Bringing together physical and mental health: A new frontier for integrated care*. Retrieved from: https://www.kingsfund.org.uk/sites/files/kf/field /field_publication_file/Bringing-together-Kings-Fund-March-2016_1.pdf.

Naylor, C., Parsonage, M., McDaid, D., Knapp, M., Fossey, M., & Galea, A. (2012). *Long-term conditions and mental health: the cost of co-morbidities*. Retrieved from: https://www.kingsfund.org.uk/sites/files/kf/field/field_publication_file /long-term-conditions-mental-health-cost-comorbidities-naylor-feb12.pdf.

Nelson, E. E., Leibenluft, E., McClure, E. B., & Pine, D. S. (2005). The social re-orientation of adolescence: a neuroscience perspective on the process and its relation to psychopathology. *Psychological Medicine, 35*(2), 163-174. doi: 10.1017/S0033291704003915

Neufeld, S. A. S., Jones, P. B., & Goodyer, I. M. (2017). Child and adolescent mental health services: longitudinal data sheds light on current policy for psychological interventions in the community. *Journal of Public Mental Health, 16*(3), 96-99. doi: 10.1108/JPMH-03-2017-0013

Newacheck, P. W., & Halfon, N. (1998). Prevalence and impact of disabling chronic conditions in childhood. *American Journal of Public Health, 88*(4), 610-617. doi:10.2105/AJPH.88.4.610

Newacheck, P. W., & Taylor, W. R. (1992). Childhood chronic illness: prevalence, severity, and impact. *American Journal of Public Health, 82*(3), 364-371. doi:10.2105/AJPH.82.3.364

NHS England (2014). *Model Child and Adolescent Mental Health Specification for Targeted and Specialist Services (Tiers 2 and 3).* Retrieved from: https://www.england.nhs.uk/wp-content/uploads/2015/01/mod-camhs-tier-2-3-spec.pdf

Noll, R. B., Kozlowski, K., Gerhardt, C., Vannatta, K., Taylor, J., & Passo, M. (2000). Social, emotional, and behavioral functioning of children with juvenile rheumatoid arthritis. *Arthritis Rheumatology, 43*(6), 1387-1396. doi:10.1002/1529-0131(200006)43:6<1387::AID-ANR24>3.0.CO;2-C

Nylander, C., Seidel, C., & Tindberg, Y. (2014). The triply troubled teenager–chronic conditions associated with fewer protective factors and clustered risk behaviours. *Acta Paediatrica, 103*(2), 194-200. doi:10.1111/apa.12461

Ohmann, S., Popow, C., Rami, B., König, M., Blaas, S., Fliri, C., & Schober, E. (2010). Cognitive functions and glycemic control in children and adolescents with type 1 diabetes. *Psychological medicine, 40*(1), 95-103. doi:10.1017/S0033291709005777

Opolski, M., & Wilson, I. (2005). Asthma and depression: a pragmatic review of the literature and recommendations for future research. *Clinical Practice & Epidemiology in Mental Health, 1*, 18. doi:10.1186/1745-0179-1-18

Ortega, A. N., Huertas, S. E., Canino, G., Ramirez, R., & Rubio-Stipec, M. (2002). Childhood asthma, chronic illness, and psychiatric disorders. *Journal of Nervous and Mental Disease, 190*(5), 275-281. doi: 10.1097/00005053-200205000-00001

Otten, R., Van de Ven, M. O. M., Engels, R. C. M. E., & Van den Eijnden, R. J. J. M. (2009). Depressive mood and smoking onset: A comparison of adolescents with and without asthma. *Psychology & Health, 24*(3), 287-300. doi:10.1080/08870440701710038

Parry-Langdon, N. (2008). *Three years on: survey of the development and emotional well-being of children and young people*. London: Office for National Statistics.

Patel, V., Flisher, A. J., Hetrick, S., & McGorry, P. (2007). Mental health of young people: a global public-health challenge. *The Lancet, 369*(9569), 1302-1313. doi:10.1016/S0140-6736(07)60368-7

Patten, S. B. (1999). Long-term medical conditions and major depression in the Canadian population. *Canadian Journal of Psychiatry, 44*, 151-157. doi:10.1177/070674370505000402

Patton, G. C., Sawyer, S. M., Santelli, J. S., Ross, D. A., Afifi, R., Allen, N. B., Arora, M., Azzopardi, P., Baldwin, W., Bonell, C., Kakuma, R., Kennedy, E., Mahon, J., McGovern, T., Mokdad, A., Patel, V., Petroni, S., Reavley, N., Taiwo, K., Waldfogel, J., Wickremarathne, D., Barroso, C., Bhutta, Z., Fatusi, A. O., Mattoo, A., Diers, J., Ferguson, J., Ssewamala, F., & Viner, R. M. (2016). Our future: A Lancet commission on adolescent future health and wellbeing. *The Lancet Commissions, 387*(10036), 2423-2478. doi: 10.1016/S0140-6736(16)00579-1

Patton, G.C. & Viner, R. (2007). Pubertal transitions in health. *The Lancet, 369*(9567), 1130-1139. Doi: 10.1016/S0140-6736(07)60366-3

Pearson, R. M., Heron, J., Button, K., Bentall, R. P., Fernyhough, C., Mahedy, L., Bowes, L., & Lewis, G. (2015). Cognitive styles and future depressed mood in early adulthood: the importance of global attributions. *Journal of Affective Disorders, 171*, 60-67. doi:10.1016/j.jad.2014.08.057

Perrin, E. C., Stein, R. E., & Drotar, D. (1991). Cautions in using the Child Behavior Checklist: observations based on research about children with a chronic illness. *Journal of Pediatric Psychology, 16*(4), 411-421. doi:10.1093/jpepsy/16.4.411

Perrin, J. M., Bloom, S. R., & Gortmaker, S. L. (2007). The increase of childhood chronic conditions in the United States. *JAMA: The Journal of the American Medical Association, 297*(24), 2755-2759. doi:10.1001/jama.297.24.2755

Phipps, S., & Steele, R. (2002). Repressive adaptive style in children with chronic illness*. Psychosomatic Medicine, 64*(1), 34-42.

Pinquart, M., & Shen, Y. (2011a). Anxiety in children and adolescents with chronic physical illnesses: a meta-analysis. *Acta Paediatrica, 100*(8), 1069-1076. doi:10.1093/jpepsy/jsq104

Pinquart, M., & Shen, Y. (2011b). Behavior problems in children and adolescents with chronic physical illness: a meta-analysis. *Journal of Pediatric Psychology, 36*(9), 1003-1016. doi:10.1093/jpepsy/jsr042

Pinquart, M., & Shen, Y. (2011c). Depressive symptoms in children and adolescents with chronic physical illness: an updated meta-analysis.

Journal of Pediatric Psychology, 36(4), 375-384. doi:10.1111/j.1651-2227.2011.02223.x

Pless, I. B., & Pinkerton, P. (1976). *Chronic childhood disorder: Promoting patterns of adjustment*. London: Henry Kimpton Publishers.

Pop-Jordanova, N., Fustic, S., & Zorcec, T. (2008). Chronic diseases in children and adolescents - Some psychological characteristics. *Paediatria Croatica, 52*(2), 71-76.

Price, J. H., Khubchandani, J., McKinney, M., & Braun, R. (2013). Racial/ethnic disparities in chronic diseases of youths and access to health care in the United States. *BioMed research international, 2013*. doi:10.1155/2013/787616

Quittner, A. L., Goldbeck, L., Abbott, J., Duff, A., Lambrecht, P., Sole, A., Tibosch, M. M., Bergsten Brucefors, A., Yuksel, H., Catastini, P., Blackwell, L., & Barker, D. (2014). Prevalence of depression and anxiety in patients with cystic fibrosis and parent caregivers: results of The International Depression Epidemiological Study across nine countries. *Thorax, 69*(12), 1090-1097. doi:10.1136/thoraxjnl-2014-205983

Rajesh, T. V., Krishnakumar, P., & Mathews, L. (2008). Temperamental traits and psychological problems of children with bronchial asthma. *Indian Pediatrics, 45*(9), 772-774.

Reed, C. E. (2006). The natural history of asthma. *Journal of Allergy and Clinical Immunology, 118*(3), 543-548. doi:10.1016/j.jaci.2006.06.020

Remington, P. L., & Brownson, R. C. (2011). Fifty years of progress in chronic disease epidemiology and control. *Morbidity and Mortality Weekly Report Surveillance Summary, 60*(Suppl 4), 70-77.

Reynolds, K. A., & Helgeson, V. S. (2011). Children with diabetes compared to peers: Depressed? Distressed? *Annals of Behavioral Medicine, 42*(1), 29-41. doi:10.1007/s12160-011-9262-4

Rietveld, S., van Beest, I., & Prins, P. J. (2005). The relationship between specific anxiety syndromes and somatic symptoms in adolescents with asthma and other chronic diseases. *Journal of Asthma, 42*(9), 725-730. doi:10.1080/02770900500306472

Ringlever, L., Hiemstra, M., Engels, R. C. M. E., van Schayck, O. C. P., & Otten, R. (2013). The link between asthma and smoking explained by depressive feelings and self-efficacy. *Journal of Psychosomatic Research, 74*(6), 505-510. doi:10.1016/j.jpsychores.2013.03.002

Ringlever, L., Otten, R., Van Schayck, O. C. P., & Engels, R. C. M. E. (2012). Early smoking in school-aged children with and without a diagnosis of asthma. *European Journal of Public Health, 22*(3), 394-398. doi:10.1093/eurpub/ckr085

Röder, I., Kroonenberg, P. M., & Boekaerts, M. (2003). Psychosocial Functioning and Stress-Processing of Children with Asthma in the School Context: Differences and Similarities with Children without Asthma. *Journal of Asthma, 40*(7), 777-787. doi:10.1081/JAS-120023505

Russell, A. E., Ford, T., & Russell, G. (2015). Socioeconomic Associations with ADHD: Findings from a Mediation Analysis. *PLoS ONE, 10*(6), e0128248. doi:10.1371/journal.pone.0128248

Ryland, H. K., Lundervold, A. J., Elgen, I., & Hysing, M. (2010). Is there a protective effect of normal to high intellectual function on mental health in children with chronic illness. *Child and Adolescent Psychiatry and Mental Health*, *4,* 3. doi:10.1186/1753-2000-4-3

Sartain, S. A., Clarke, C. L., & Heyman, R. (2000). Hearing the voices of children with chronic illness. *Journal of Advanced Nursing, 32*(4), 913-921.

Sawyer, S. M., Drew, S., Yeo, M. S., & Britto, M. T. (2007). Adolescents with a chronic condition: challenges living, challenges treating. *The Lancet, 369*(9571), 1481-1489. doi:10.1016/S0140-6736(07)60370-5

Schmidt, S., Petersen, C., & Bullinger, M. (2003). Coping with chronic disease from the perspective of children and adolescents–a conceptual framework and its implications for participation. *Child: Care, Health and Development, 29*(1), 63-75. doi:10.1046/j.1365-2214.2003.00309.x

Sein, E. (2001). Chronic illness: the child and the family. *Current Paediatrics, 11*(1), 46-50. doi:10.1054/cupe.2000.0141

Sentenac, M., Arnaud, C., Gavin, A., Molcho, M., Gabhainn, S. N., & Godeau, E. (2012). Peer victimization among school-aged children with chronic conditions. *Epidemiologic Reviews, 34*, 120-128. doi:10.1093/epirev/mxr024

Shaw, S. R., & McCabe, P. C. (2008). Hospital-to-school transition for children with chronic illness: Meeting the new challenges of an evolving health care system. *Psychology in the Schools, 45*(1), 74-87. doi:10.1002/pits.20280

Shelton, K. H., & Harold, G. T. (2008). Interparental conflict, negative parenting, and children's adjustment: bridging links between parents' depression and children's psychological distress. *Journal of Family Psychology, 22*(5), 712-724. doi:10.1037/a0013515

Silver, E. J., Westbrook, L. E., & Stein, R. E. (1998). Relationship of parental psychological distress to consequences of chronic health conditions in children. *Journal of Pediatric Psychology, 23*(1), 5-15.

Simon, K., Barakat, L. P., Patterson, C. A., & Dampier, C. (2009). Symptoms of Depression and Anxiety in Adolescents with Sickle Cell Disease: The Role of Intrapersonal Characteristics and Stress Processing Variables. *Child Psychiatry & Human Development, 40*(2), 317-330. doi:10.1007/s10578-009-0129-x

Singh, S. P., Winsper, C., Wolke, D., & Bryson, A. (2014). School Mobility and Prospective Pathways to Psychotic-like Symptoms in Early Adolescence: A Prospective Birth Cohort Study. *Journal of the American Academy of Child & Adolescent Psychiatry, 53*(5), 518-527.e511. doi:10.1016/j.jaac.2014.01.016

Sinnamon, G. C. B., Caltabiano, M., & Baune, B. T. (2013). Differentiating disordered affect in children and adolescents with type 1 diabetes. *Journal of Affective Disorders, 147(*1-3), 51-58. doi:10.1016/j.jad.2012.10.006

Sint Nicolaas, S. M., Shchepers, S. A., van den Bergh, E. M. M, Evers, A. W. M., Hoogerbrugge, P. M., Grootenhuis, M. A., Verhaak, C. M. (2016). Illness cognitions and family adjustment: Psychometric properties of the Illness Cognition Questionnaire for parents of a child with cancer.

Supportive Care in Cancer, 24(2), 529-537. doi: 10.1007/s00520-015-2795-5.

Sivertsen, B., Petrie, K. J., Wilhelmsen-Langeland, A., & Hysing, M. (2014). Mental health in adolescents with Type 1 diabetes: Results from a large population-based study. *BMC Endocrine Disorders, 14*(1). doi:10.1186/1472-6823-14-83

Solomon, A. (2012). *Far from the Tree: Parents, Children and the Search for Identity*. New York: Scribner

Spencer, N. J. (2006). Social equalization in youth: evidence from a cross-sectional British survey. *The European Journal of Public Health, 16*(4), 368-375. doi:10.1093/eurpub/cki222

Spratt, M., Carpenter, J., Sterne, J. A., Carlin, J. B., Heron, J., Henderson, J., & Tilling, K. (2010). Strategies for multiple imputation in longitudinal studies. *American Journal of Epidemiology, 172*(4), 478-487. doi:10.1093/aje/kwq137

Stahl-Pehe, A., Lange, K., Bächle, C., Castillo, K., Holl, R. W., & Rosenbauer, J. (2014). Mental health problems among adolescents with early-onset and long-duration type 1 diabetes and their association with quality of life: A population-based survey*. PLoS ONE, 9*(3). e92473. doi:10.1371/journal.pone.0092473

Stam, H., Hartman, E. E., Deurloo, J. A., Groothoff, J., & Grootenhuis, M. A. (2006). Young adult patients with a history of pediatric disease: impact on course of life and transition into adulthood. *Journal of Adolescent Health, 39*(1), 4-13. doi:10.1016/j.jadohealth.2005.03.011

Stansfeld, S., Haines, M., Booy, R., Taylor, S., Viner, R. M., Head, J., Bhui, K., Hilier, S., Isenwater, W., Choudry-Dormer, S., Brentall, S., Klineberg, E., & Ahmed, G. (2003). *Health of young people in East London: the RELACHS study 2001*. London: The Stationary Office.

Stattin, H., & Kerr, M. (2000). Parental monitoring: A reinterpretation*. Child Development, 71*(4), 1072-1085. doi:10.1111/1467-8624.00210

Stein, R. E., & Jessop, D. J. (1982). A noncategorical approach to chronic childhood illness. *Public Health Reports, 97*(4), 354.

Stein, R. E., & Jessop, D. J. (1989). What diagnosis does not tell: the case for a noncategorical approach to chronic illness in childhood. *Social*

Science & Medicine, 29(6), 769-778. doi:10.1016/0277-9536(89)90157-3

Stewart, S. M., Simmons, A., & White, P. C. (2011). Somatic items in the assessment of depressive symptoms in pediatric patients with diabetes. *Journal of Behavioral Medicine, 34*(2), 112-119. doi:10.1007/s10865-010-9289-1

Stuber, M. L. (1996). Psychiatric sequelae in seriously ill children and their families. *Psychiatric Clinics of North America, 19*(3), 481-493. doi:10.1016/S0193-953X(05)70302-6

Surís, J.-C. (2003). Chronic conditions and adolescence. *Journal of Pediatric Endocrinology & Metabolism: JPEM, 16*, 247-251.

Tabachnick, B. G., & Fidell, L. S. (2001). *Using multivariate statistics*. Boston: Pearson.

Taylor, R. M., Gibson, F., & Franck, L. S. (2008). The experience of living with a chronic illness during adolescence: a critical review of the literature. *Journal of Clinical Nursing, 17(*23), 3082-3091. doi: 10.1111/j.1365-2702.2008.02629.x

Teng, Y. K., Chiang, L. C., Lue, K. H., Chang, S. W., Wang, L., Lee, S. P., Ting, H., & Lee, S. D. (2014). Poor sleep quality measured by polysomnography in non-obese asthmatic children with or without moderate to severe obstructive sleep apnea. *Sleep Medicine, 15*(9), 1062-1067. doi:10.1016/j.sleep.2014.04.017

Thapar, A., Collishaw, S., Pine, D. S., & Thapar, A. K. (2012). Depression in adolescence. *The Lancet, 379*(9820), 1056-1067. doi:10.1016/S0140-6736(11)60871-4

Thapar, A., & McGuffin, P. (1998). Validity of the shortened Mood and Feelings Questionnaire in a community sample of children and adolescents: a preliminary research note. *Psychiatry Research, 81*(2), 259-268. doi:10.1016/S0165-1781(98)00073-0

Thorley, C. (2016). *Education, education, mental health: Supporting secondary schools to play a central role in early intervention mental health services.* Retrieved from: https://www.ippr.org/publications/education-education-mental-health

Tinsley, H. E., & Tinsley, D. J. (1987). Uses of factor analysis in counseling psychology research. *Journal of Counseling Psychology, 34*(4), 414. doi:10.1037/0022-0167.34.4.414

Torsheim, T., Valimaa, R., & Danielson, M. (2004). Health and well-being. In C. Currie, C. Roberts, W. Settertobulte, A. Morgan, R. Smith, O. Samdal, & V. Barnekow Rasmussen (Eds.), *Young people's health in context : Health Behaviour in School-aged Children (HBSC) study: International report from the 2001/2002 survey* (pp. 55-62). Copenhagen: World Health Organisation.

Trzepacz, A. M., Vannatta, K., Davies, W. H., Stehbens, J. A., & Noll, R. B. (2003). Social, emotional, and behavioral functioning of children with hemophilia. *Journal of Developmental and Behavioral Pediatrics, 24*(4), 225-232. doi:10.1097/00004703-200308000-00002

Trzepacz, A. M., Vannatta, K., Gerhardt, C. A., Ramey, C., & Noll, R. B. (2004). Emotional, social, and behavioral functioning of children with sickle cell disease and comparison peers. *Journal of Pediatric Hematology Oncology, 26*(10), 642-648. doi:10.1097/01.mph.0000139456.12036.8d

Turkel, S., & Pao, M. (2007). Late Consequences of Pediatric Chronic Illness. *Psychiatric Clinics of North America, 30*(4), 819-835. doi:10.1016/j.psc.2007.07.009

Turner, D. C. (1996). The role of culture in chronic illness. *American Behavioral Scientist, 39*(6), 717-728. doi:10.1177/0002764296039006008

Vaisto, T., Aronen, E. T., Simola, P., Ashorn, M., & Kolho, K. L. (2010). Psychosocial Symptoms and Competence Among Adolescents with Inflammatory Bowel Disease and Their Peers. *Inflammatory Bowel Diseases, 16*(1), 27-35. doi:10.1002/ibd.21002

Valencia, L. S., & Cromer, B. A. (2000). Sexual activity and other high-risk behaviors in adolescents with chronic illness: a review. *Journal of Pediatric and Adolescent Gynecology, 13*(2), 53-64. doi:10.1016/S1083-3188(00)00004-8

van der Lee, J. H., Mokkink, L. B., Grootenhuis, M. A., Heymans, H. S., & Offringa, M. (2007). Definitions and measurement of chronic health

conditions in childhood: a systematic review. *JAMA: The Journal of the American Medical Association, 297*(24), 2741-2751. doi:10.1001/jama.297.24.2741

van Gent, R., van Essen-Zandvliet, E. E., Klijn, P., Brackel, H. J., Kimpen, J. L., van Der Ent, C. K. (2008). Participation in daily life of children with asthma. *Journal of Asthma, 45*(9), 807-813. doi: 10.1080/02770900802311477

Venning, A., Eliott, J., Wilson, A., & Kettler, L. (2008). Understanding young peoples' experience of chronic illness: a systematic review. *International Journal of Evidence-Based Healthcare, 6*(3), 321-336. doi:10.1111/j.1744-1609.2008.00107.x

Verhoof, E. J. A., Maurice-Stam, H., Heymans, H. S. A., Evers, A. W. M., & Grootenhuis, M. A. (2014). Psychosocial well-being in young adults with chronic illness since childhood: the role of illness cognitions. *Child & Adolescent Psychiatry & Mental Health, 8*, 12. doi: 10.1186/1753-2000-8-12

Verkleij, M., van de Griendt, E. J., Kaptein, A. A., van Essen-Zandvliet, L., Duiverman, E., & Geenen, R. (2011). Behavioral problems in children and adolescents with difficult-to-treat asthma. *Journal of Asthma, 48*(1), 18-24. doi:10.3109/02770903.2010.528497

Vila, G., Nollet-Clemençon, C., de Blic, J., Mouren-Siméoni, M. C., & Scheinmann, P. (2000). Prevalence of DSM IV anxiety and affective disorders in a pediatric population of asthmatic children and adolescents. *Journal of Affective Disorders, 58*(3), 223-231. doi:10.1016/S0165-0327(99)00110-X

Viner, R., & Davies, S. (2012). Life stage: Adolescence*. Annual Report of the Chief Medical Officer,* 1-11.

Wallander, J. L., & Varni, J. W. (1998). Effects of pediatric chronic physical disorders on child and family adjustment. *Journal of Child Psychology and Psychiatry, 39*(1), 29-46. doi:10.1111/1469-7610.00302

Wandell, P., Ljunggren, G., Wahlstrom, L., & Carlsson, A. C. (2014). Diabetes and psychiatric illness in the total population of Stockholm. *Journal of Psychosomatic Research, 77*(3), 169-173. doi:10.1016/j.jpsychores.2014.06.012

Wang, J., & Wang, X. (2012). Sample Size for Structural Equation Modeling. In J. Wang & X. Wang (Eds.), *Structural equation modeling* (pp. 391-427). Hoboken: John Wiley & Sons, Ltd.

Weglage, J., Grenzebach, M., Pietsch, M., Feldmann, R., Linnenbank, R., Denecke, J., & Koch, H. G. (2000). Behavioural and emotional problems in early-treated adolescents with phenylketonuria in comparison with diabetic patients and healthy controls. *Journal of Inherited Metabolic Disease, 23*(5), 487-496. doi:10.1023/A:1005664231017

Weisz, G. (2014). *Chronic Disease in the twentieth century: A history*. Baltimore: John Hopkins University Press.

Weitzman, M. (1986). School absence rates as outcome measures in studies of children with chronic illness. *Journal of Chronic Diseases, 39*(10), 799-808. doi:10.1016/0021-9681(86)90082-2

Wells, G., Shea, B., Peterson, J., Welch, V., Losos, M., & Tugwell, P. (2014). *The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses.* Ottawa: Ottawa Health Research Institute.

West, P., & Sweeting, H. (2004). Evidence on equalisation in health in youth from the West of Scotland. *Social Science & Medicine, 59*(1), 13-27. doi:10.1016/j.socscimed.2003.12.004

Wickrama, K. A., Noh, S., & Elder, G. H. (2009). An investigation of family SES-based inequalities in depressive symptoms from early adolescence to emerging adulthood. *Advances in Life Course Research, 14*(3), 147-161. doi:10.1016/j.alcr.2010.04.001

Wilkinson, R.G. (1997). Socioeconomic determinants of health. Health inequalities: relative or absolute material standards? British Medical Journal, 314(7080), 591-595.

Williams, C., Horwood, J., Northstone, K., Herrick, D., Waylen, A., & Wolke, D. (2006). The timing of patching treatment and a child's wellbeing. *British Journal of Ophthalmology, 90*(6), 670-671. doi:10.1136/bjo.2006.091082

Williams, P. G., Holmbeck, G. N., & Greenley, R. N. (2002). Adolescent health psychology. *Journal of Consulting and Clinical Psychology, 70*(3), 828. doi:10.1037/0022-006X.70.3.828

Wolf, E. J., Harrington, K. M., Clark, S. L., & Miller, M. W. (2013). Sample Size Requirements for Structural Equation Models: An Evaluation of Power, Bias, and Solution Propriety. *Education and Psychological Measurement, 76*(6), 913-934. doi:10.1177/0013164413495237

Wolke, D., Waylen, A., Samara, M., Steer, C., Goodman, R., Ford, T., & Lamberts, K. (2009). Selective drop-out in longitudinal studies and non-biased prediction of behaviour disorders. *British Journal of Psychiatry*, 195(3), 249-256. doi:10.1192/bjp.bp.108.053751

Wolke, D., Woods, S., Stanford, K., & Schulz, H. (2001). Bullying and victimization of primary school children in England and Germany: Prevalence and school factors. *British Journal of Psychology, 92*(4), 673-696. doi:10.1348/000712601162419

Wood, B. L. (1999). Relationship Matters. *Families, Systems, & Health, 17*(2), 145-147.

Woods, S. B., Farineau, H. M., & McWey, L. M. (2013). Physical health, mental health, and behaviour problems among early adolescents in foster care. *Child: Care, Health and Development, 39*(2), 220-227. doi:10.1111/j.1365-2214.2011.01357.x

World Health Organisation. (1993). *International Classification of Diseases Tenth Revision*. Geneva: World Health Organisation.

World Health Organisation (2015). *Global standards for the quality health-care services for adolescents: A guide to implement a standards-driven approach to improve the quality of health-care services for adolescents. Volume 1: Standards and Criteria.* Retrieved from: http://apps.who.int/iris/bitstream/10665/183935/1 /9789241549332_vol1_eng.pdf?ua=1

Yahia, S., El-Hadidy, M. A., El-Gilany, A. H., Anwar, R., Darwish, A., & Mansour, A. K. (2013). Predictors of anxiety and depression in Egyptian thalassemic patients: a single center study. *International Journal of Hematology, 97*(5), 604-609. doi:10.1007/s12185-013-1322-z

Yates, L., Bond, L., Dixon, M., Drew, S., Ferguson, P., Hay, T., Moss, J., St Leger, P., Walker, H., & White, J. (2010). *Keeping Connected: Identity, social connection and education for young people living with chronic illness.* Retrieved from http://vuir.vu.edu.au/21834/1/KC2010_Final_Report.pdf:

Zahn-Waxler, C., Shirtcliff, E. A., & Marceau, K. (2008). Disorders of childhood and adolescence: Gender and psychopathology*. Annual Review of Clinical Psychology, 4*, 275-303. doi: 10.1146/annurev.clinpsy.3.022806.091358

Zashikhina, A., & Hagglof, B. (2007). Mental health in adolescents with chronic physical illness versus controls in Northern Russia. *Acta Paediatrica, 96*(6), 890-896. doi:10.1111/j.1651-2227.2007.00277.x

Zehnder, D., Prchal, A., Vollrath, M., & Landolt, M. A. (2006). Prospective study of the effectiveness of coping in pediatric patients. *Child Psychiatry and Human Development, 36(3)*, 351-368. doi:10.1007/s10578-005-0007-0

Zheng, X. P., & Chen, S. H. (2013). Psycho-behavioral changes in children with type 1 diabetes mellitus. *World Journal of Pediatrics, 9*(3), 261-265. doi:10.1007/s12519-013-0428-y

Appendices

Appendix I Data extraction form

Table Key for Newcastle-Ottawa Quality Assessment Scale for Cohort Studies (NOQAS-CS):

Sel = Selection (Representativeness of the exposed cohort/selection of the non-exposed cohort/ascertainment of exposure/demonstration that outcome of interest was not present at start of study)

Comp = Comparability (Comparability of cohorts on the basis of the design or analysis)

Out = Outcome (Assessment of outcomes/Was follow-up long enough for outcomes to occur/Adequacy of follow-up cohorts)

Author and Date	Date of Data Collection	Study Design	Sample Size (n)	Description of Sample	Response Rate	Adjustment for Confounding Factors	Measure of Chronic Illness	Mental Health Outcome Under Investigation and Measure	Summary of Results	Conclusions	NOQAS - CS		
											Sel	Comp	Out

Appendix II Definitions of chronic illness used in studies eligible for the systematic review

Study Authors	Definition of Chronic Illness
Arabiat et al. (2012)	A health condition that lasts longer than 3 to 6 months
Bilfield et al. (2006)	Caregiver report of child being in fair/poor health, and report of any kind of limitation because of health over the previous 6 months
Blackman & Conaway (2013)	Asthma; Diabetes; Tourette's Syndrome; Epilepsy; Hearing Impairments; Visual Impairments; Bone/Joint/Muscle Disorders; Brain Injuries
Blackman, et al. (2011)	Allergies; Asthma; Diabetes; Heart Problems; Blood Problems; Cystic Fibrosis; Arthritis/Joint Problems; Migraines Note: To be considered chronic, the condition must have lasted longer than 12 months Note: Those with neurological conditions (e.g. cerebral palsy, epilepsy) and development delays were considered ineligible for the study
Curtis & Luby (2008)	Parent-reports of paediatric medical conditions including repeated, persistent ear infections; repeated, persistent respiratory infections; asthma; bowel diseases; repeated, persistent urinary infections; blood disease; chronic/recurrent lung disease; eczema; birth defect; congenital heart disease; hepatitis A Note: Individuals with marked speech and language delays; neurological or developmental disorders, or an IQ <70 were excluded. Children with severe chronic medical conditions, such as cystic fibrosis, diabetes mellitus, HIV/AIDS, or cancer were also excluded.
Denny et al. (2014)	Presence of health problems lasting 6 months or more
Erikson et al. (2005)	Adolescent positive response to item: "Do you have a physical or health condition that makes it hard for you to do some things other kids your age do (e.g. concentrating in school, doing sports, or eating like other teenagers)?"

Fuhr & De Silva (2008)	Long-term physical illnesses were differentiated in contrast to acute physical illnesses and aimed to include a range of enduring illness occurring in children living in resource-poor settings, including physical disability, migraine, HIV/AIDS, asthma, epilepsy, skin problems, anaemia, congenital malformations, and any other non-specified chronic illness
Ganz et al. (2006)	A child with a condition that lasted or was expected to last at least 1 year, and matched at least 1 of 5 criteria: (1) using or needing more medical care, mental health services, or educational services than are provided for other children of the same age; (2) using or needing prescription medication; (3) having a limitation in the ability to do things most children of the same age do; (4) using or needing special therapy; or (5) using or needing EDB treatment or counselling
Goldbeck et al. (2011)	A non-specific definition of chronic illness was used, where it was assumed that the all diagnoses among the study group - namely cancer, cystic fibrosis, and congenital heart disease – would have a common impact on the young person
Guion & Mrug (2012)	A non-specific definition of chronic illness was used whereby it was assumed that there would be no differences in attributional styles or adjustment based on disease – therefore, two specific disease populations (Type 1 Diabetes and Cystic Fibrosis) were used in order to recruit a large sample size, increased power, and greater generalisability
Hysing, Elgen, et al. (2007)	Any physical disorder reported by parents including asthma; epilepsy; diabetes; skeletal disorders; gastro-intestinal disorders; neurological disorders; cardiovascular disorders; endocrine disorders; kidney disease; haemophilia; rheumatoid arthritis; sensory impairment; eczema; allergy
Hysing, Elgen, et al. (2009)	Any physical disorder reported by parents, categorised into neurological disorders, asthma, and 'other' Note: Those with allergy/eczema were excluded from the 'other' subgroup due to the overlap with the asthma group

Hysing, Siversten, et al. (2008)	Any somatic-based disorder reported by parents
Key, et al. (2001)	Disease sub-samples were selected due to their high prevalence and associated morbidities. These included: sickle cell disease; cystic fibrosis; diabetes mellitus; spina bifida; and asthma
McCarroll et al. (2009)	Mother's positive response to whether their child had a chronic illness, including obesity
McDougall et al. (2004)	Physical disorder lasting longer than six months
Meijer et al. (2000a)	Diagnosis of 1 year with any of the following conditions: cystic fibrosis, diabetes mellitus; juvenile chronic arthritis, osteogenesis imperfect, constitutional eczema, or asthma. Note: 3 children that had a diagnosis that differed from the target diagnosis as they were highly motivated to participate
Meijer et al. (2000b)	Diagnosis of 1 year with any of the following conditions: cystic fibrosis, diabetes mellitus; juvenile chronic arthritis, osteogenesis imperfect, constitutional eczema, or asthma. Note: 4 adolescents that had a diagnosis that differed from the target diagnosis as they were highly motivated to participate
Ortega, et al. (2002)	Diagnosis of cardiac problems, sickle cell anaemia, diabetes, leukaemia, or tumour
Phibbs & Steele (2002)	Diagnosis of diabetes mellitus, cystic fibrosis or juvenile rheumatoid disorders, that occurred at least one month before data collection

Rietveld, et al. (2005)	A non-specific definition of chronic illness was used and diagnoses of the study cohort included asthma, congenital heart disease, gastrointestinal dysfunction, chronic migraine, and epilepsy Note: Children with asthma were separated from the general chronic illness sample as literature suggested these patients may be more vulnerable to anxiety problems
Ryland et al. (2010)	Any physical disorder reported by parents in the first stage of the study and confirmed by parents in the third stage
Woods et al. (2012)	Any reported recurring health problem including asthma, respiratory problems, low birth weight, dental problems, severe allergies, persistent bowel problems, physical deformities, anaemia, arthritis/joint problems, diabetes, skin disease, and epilepsy
Zashikhina & Hagglof (2007)	Diagnosis with one of the following conditions: diabetes, epilepsy, or asthma.
Zehnder et al. (2006)	A non-specific definition of chronic illness was used and diagnoses of the study cohort included diabetes, cancer, and epilepsy

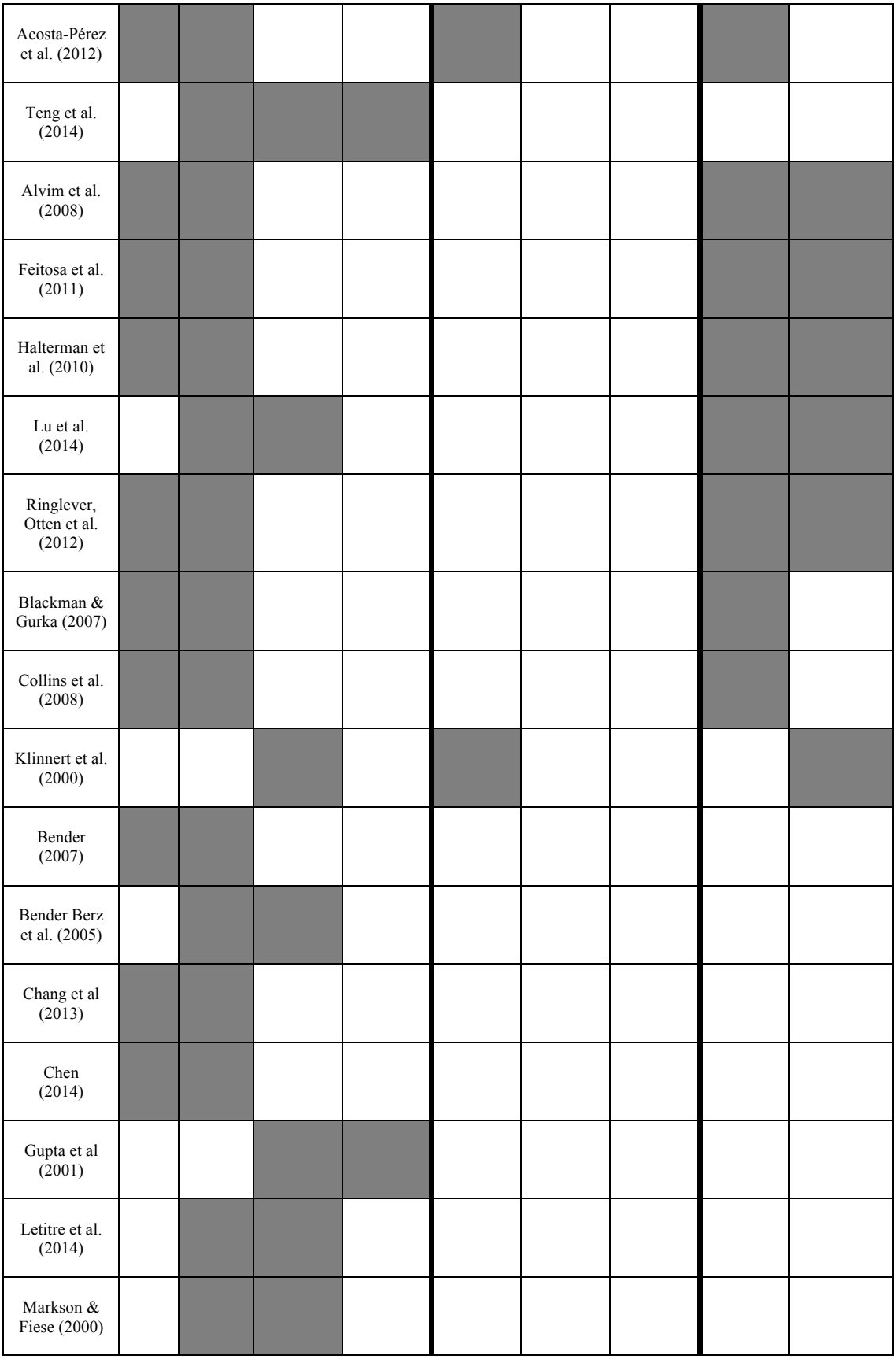
Appendix III Full overview of trends in studies that did not achieve the quality criteria set for the systematic review

Asthma

Despite having the largest research body of the conditions studied, all studies were indicated to be at risk to some degree of research bias. A substantial number of the studies did not examine representative samples or utilise high quality measures. Moreover, the failure of these studies to control for confounding variables means that these studies could introduce an additional risk of bias in across-study comparisons. A full breakdown of the quality ratings can be seen in Table 1.

Table 1. Quality ratings of asthma studies

	Risk of Bias Within Studies							Risk of Bias Across Studies	
	Selection				Outcome				
	Cohort	Control Sample	Asthma Measure	Baseline Mental Health	Psych. Measure	Adequate Follow-Up Period	Adequacy of Follow-Up Rate	Control: Demog.	Control: Additional Factor
Feldman et al. (2006)									
Ringlever, Hiemstra et al. (2013)									
Lien et al. (2010)									
Mitchell et al. (2004)									
Otten et al. (2009)									
Annesi-Maesano et al. (2013)									
Bahreinian et al. (2011)									
Blackman & Conaway (2012)									
Goodwin et al. (2013)									


Acosta-Pérez et al. (2012)
Teng et al. (2014)
Alvim et al. (2008)
Feitosa et al. (2011)
Halterman et al. (2010)
Lu et al. (2014)
Ringlever, Otten et al. (2012)
Blackman & Gurka (2007)
Collins et al. (2008)
Klinnert et al. (2000)
Bender (2007)
Bender Berz et al. (2005)
Chang et al (2013)
Chen (2014)
Gupta et al (2001)
Letitre et al. (2014)
Markson & Fiese (2000)

Rajesh et al. (2008)			■	■					
Verkleij et al (2011)			■		■				
Vila et al. (2000)		■	■						
Arif (2010)		■						■	■
Kohlboeck et al. (2013)		■						■	■
Bruzzese et al. (2009)		■						■	■
Goldbeck et al. (2007)			■					■	
Akcakaya et al. (2003)			■						
Bender et al. (2000)			■						
Bleil et al. (2000)			■						
Caffrey-Craig (2005)			■						
Cutuli et al. (2014)		■							
Glazebrook et al. (2006)			■						
Kean et al. (2006)			■						
Lahaye et al. (2012)			■						
Röder et al. (2003)			■						

Note – A grey square indicates the fulfilment of that quality criterion

In general, the trends in the findings of the studies that did not achieve the quality criteria reflected those of the main review. They suggest that children and adolescents with asthma are at a significant risk of poorer psychological adjustment than peers, with higher rates of mental health symptomatology,

both internalising and externalising, found consistently among youths with asthma relative to healthy controls. This increased prevalence was indicated even in studies that excluded those with comorbid medical illnesses, suggesting that there is an independent association of asthma symptomatology with mental health outcomes, regardless of asthma status. The clearest relationship seemed to be for depression and anxiety, where the relatively higher quality studies consistently found a clear effect of asthma diagnosis which placed youths with asthma at a 50% to 70% increased risk. Significantly, these findings were also reflected in investigations into emotional symptomatology. The findings for mental health problems and diagnoses that could be viewed as conduct-related were more varied. However, overall, the studies suggest that there is a trend towards higher levels of conduct problems among children with asthma, but the risk posed is only marginally significant (about 20% higher than that of their healthy peers).

The high quality studies among the cohort were predominantly reliant on adolescent samples. However, the remaining studies examined samples of a wide age range. Some age effects were indicated, with the associations with mental health symptomatology in adolescence of a stronger magnitude, However, it should be noted that significant associations were still indicated in younger age groups and that the studies conducted with young children tended to be of the lowest quality. Asthma severity and functional morbidity were consistently identified across studies as important moderating factors in psychological adjustment. However, it was hard to establish the primacy of these variables in their relationship with mental distress, as there were findings to suggest that those with higher levels of mental distress perceived themselves to be more functionally impaired by their asthma condition. The studies also seemed to suggest that those who were already at a high risk of developing mental illness did not experience an exacerbating effect of asthma diagnosis on mental health.

Diabetes Mellitus

Similar to the asthma studies, many of the studies indicated a risk of methodological bias. A substantial number of the studies did not examine representative samples, instead relying on convenience samples recruited from single hospital clinics. In addition, these studies also failed to subsequently control for confounding factors. A full breakdown of the quality ratings can be seen in Table 2.

Table 2. Quality ratings of diabetes studies

	Risk of Bias Within Studies							Risk of Bias Across Studies	
	Selection				Outcome				
	Cohort	Control Sample	Diab. Measure	Baseline Mental Health	Psych. Measure	Adequate Follow-Up Period	Adequacy of Follow-Up Rate	Control: Demog.	Control: Additional Factor
Missotten et al. (2013)									
Cato et al. (2014)									
Helgeson et al. (2007)									
Stahl-Pehe et al. (2014)									
Sinnammon et al. (2013)									
Siversten et al. (2014)									
Eapen et al. (2006)									
Maas-van Schaaijk et al. (2013)									
Moussa et al. (2005)									
Caruso et al. (2014)									
Abdul-Rasoul et al. (2010)									

Herzer & Hood (2010)			■	■					
Hsu et al. (2010)		■	■						
Law (2002)			■	■					
Liakopoulou et al. (2001)			■		■				
McCarthy et al. (2002)		■	■						
Nardi et al. (2008)		■	■						
Akbas et al. (2009)			■						
Castro et al. (2000)			■						
Grau et al. (2003)			■						
Hilliard et al. (2010)			■						
Horton et al. (2009)			■						
Kristensen et al (2014)			■						
Ohmann et al. (2010)			■						
Stewart et al. (2011)			■						
Zheng et al. (2013)			■						

Note – A grey square indicates the fulfilment of that quality criterion

In general, the remaining studies indicated a significant effect of diabetes on psychological adjustment, with only a minority of the studies not indicating a significant group difference in terms of mental health outcomes. Furthermore, studies finding a significant effect of diabetes on mental health indicated that this risk extended to both emotional and behavioural symptomatology. Interestingly, many studies indicated an age effect, with older adolescents

with diabetes showing relatively higher levels of mental health difficulties than lower age cohorts. Again, it should be noted that all studies focused on youths with Type 1 diabetes, raising concerns about the generalisability of results to young people living with the Type 2 condition.

Many variables were examined among these as potential moderators of the relationship between diabetes and mental health outcomes. No effects of the duration of the illness were found. In terms of condition-related factors, the studies were almost evenly divided into studies which found no association between psychological adjustment and glycaemic control, and those that did find an association, mostly through the moderating effect of the additional factor of adherence. These conflicting findings may be explained by the methods of studying the role of glycaemic control. Zheng and Chen (2013) found that there was an increase in mental distress among young people with diabetes in general, but that those with poor glycaemic control showed a significantly higher level of externalising symptomatology in comparison those with well-controlled diabetes. However, this amplifying role may not be identified in certain analyses, such as general comparative analyses. It is also important to note that, given the cross-sectional methodology of many of these studies, such a finding is just as likely to indicate that externalising problems lead to poor glycaemic control, as it is to indicate that poor glycaemic control moderates the development of externalising problems.

There were also some suggestions that adjustment was a function of daily functional comorbidity with sleep quality (Caruso et al., 2014) and self-rated physical competence in addition to self-perceived physical appearance implicated (Eapen et al., 2006). The roles of familial factors were also examined, with associations found between psychological adjustment in youth and parental stress (Hilliard et al., 2010; Maas-van Schaaijk et al., 2013). In addition, although Missotten and colleagues (2013) found no difference in psychological adjustment among their sample, they found that family climate had a significant influence of psychological adjustment in their cohort. However, youths with diabetes in their sample tended to come from families with more supportive family climates than controls.

It should be noted that, in a reflection of findings from the high quality studies of asthmatic youths, Stahl-Pehe's (2014) study of two national German surveys indicated that youths with diabetes who were rated as having higher levels of internalising symptomatology than controls were also given higher scores on the hyperactivity-inattention measure. However, this was the only study among the cohort to examine the specific co-morbidity between emotional and externalising symptomatology.

Sickle Cell Disease

As with the previous conditions reviewed, no single study fulfilled the full quality criteria. However, there was a significant issue identified regarding the representativeness of the samples across the study cohort. All the samples were recruited from one hospital unit. Therefore, concerns could be raised regarding the generalisability of the results to other samples, especially given that the study samples were relatively small in size ($n \leq 312$). When applying the quality criteria, none of the six articles was of a high enough quality to be included in the main review. Therefore, only trends among these studies will be outlined. A full breakdown of the quality ratings can be seen in Table 3.

Table 3. Quality ratings of sickle cell disease studies

	Risk of Bias Within Studies							Risk of Bias Across Studies	
	Selection				Outcome				
	Cohort	Control Sample	SCD Measure	Baseline Mental Health	Psych. Measure	Adequate Follow-Up Period	Adequacy of Follow-Up Rate	Control: Demog.	Control: Additional Factor
Simon et al. (2009)		■	■					■	■
Hijmans et al. (2009)		■	■						■
Trzpacz et al. (2004)		■	■						
Amr et al. (2010)			■		■				
Aina et al. (2014)			■						
Ekinci et al. (2013)			■						

Note – A grey square indicates the fulfilment of that quality criterion

There were conflicting trends in the studies due to variations between informants on the psychiatric measures. For example, although, based on primary caregiver reports, a higher proportion of children with sickle cell disease met the clinical threshold for conduct problems relative to controls, this trend was not identifiable based on secondary caregiver reports. However, it should be noted failure to find a significant trend based on the ratings of secondary caregivers could be accounted for by a lack of power in analyses. Yet, this may not fully account for the variations found. For example, although mothers were more likely to rate children with sickle cell disease as having a higher level of both emotional and conduct problems than control mothers in the study of Ekinci et al. (2013), teachers rated the same children as having a higher level of conduct problems only. Although, as discussed in chapter one, it has been established that teachers and parents often have discordant ratings on emotional symptoms scales relative to externalising symptom scales, with suggested reasons being that externalising symptoms are more recognisable within a classroom setting (e.g. Verhulst & Akkerhuis, 1989), the adolescents in the study of Simon et al. (2009) rated themselves as having similar levels of behavioural and

emotional functioning as peers. The high levels of discordance among these ratings emphasise the importance of using multiple measures in the assessment of mental well-being among younger age groups.

In the only study that used a structured psychiatric interview (Amr et al. 2010), adolescents with sickle cell disease were found to have significantly lower levels of disorders than the comparative group, with the exception of a slight yet significantly higher prevalence of adjustment and anxiety disorders. However, the comparison group in this study consisted of a variety of adolescents who were either attending other outpatient clinics or accompanying other patients in the general hospital from which the sample was recruited. Therefore, there was no overwhelming evidence that young people living with sickle cell disease were at a disproportionate risk of developing mental health disorders, but this may be accounted for by a lack of insightful research within this area, rather than reflective of the actual mental health risk posed to this population.

The study of Amr and colleagues (2010) highlighted contributory roles of gender, low family income and the experience of frequent painful crises in moderating the association between sickle cell disease and psychiatric disorder. Ekinci et al. (2013) also found that mothers of children with more severe sickle cell disease genotypes were more likely to rate their children as having a high number of behavioural and emotional symptoms. Yet, it should be noted that it was not possible to distinguish these children from other children with sickle cell disease in terms of mental health symptomatology on the basis of teacher ratings.

Thalassemia

Similar to the studies examining sickle cell disease, there were not only issues identified with the representativeness of the thalassemia cohorts among these studies, but concerns were also raised regarding the comparability of the control samples. All comparative samples were convenience samples, and questions regarding the true comparability between cohorts could be raised. For example, in the case of Gupta et al. (2012) the sample did not even consist of healthy peers, as the sample was

recruited among other children in the same hospital who were suffering from bronchial asthma. Moreover, none of the studies put in place any controls for the confounding effects of the demographic variables, with only one study controlling for an additional confounding factor. This means there could be a high risk of bias when comparing findings across studies. Unsurprisingly, none of these studies fulfilled the quality criteria for the main review. A full breakdown of the quality ratings can be seen in Table 4.

Table 4. Quality ratings of thalassemia studies

	Risk of Bias Within Studies							Risk of Bias Across Studies	
	Selection				Outcome				
	Cohort	Control Sample	Thal. Measure	Baseline Mental Health	Psych. Measure	Adequate Follow-Up Period	Adequacy of Follow-Up Rate	Control: Demog.	Control: Additional Factor
Yahia et al. (2013)			■		■				■
Cakaloz et al. (2009)			■		■				
Gupta et al. (2012)			■						

Note – A grey square indicates the fulfilment of that quality criterion

All studies indicated a higher prevalence of mental health symptomatology among children with thalassemia, with this risk extending to both emotional and behavioural symptomatology that was in the clinical ranges. In the case of the study of Gupta et al. (2012) children with thalassemia showed higher levels of mental health difficulties than the comparative sample of children with bronchial asthma, with externalising behaviour problems and somatisation problems being especially more prevalent among children with thalassemia.

In terms of moderating factors in the relationship between thalassemia and psychological adjustment, no relationship was found between mental distress levels and age (Yahia et al., 2013), or socio-economic variables (Gupta et al., 2012). When considering condition-related factors alone, Cakoloz et al. (2009) indicated that there was no correlation between mental distress scores and ferritin levels among their sample. However, Yahia and colleagues (2013) found that anxiety and depressive diagnoses were more

prevalent among those with more severe symptoms of thalassemia, such as mongoloid facies, co-morbid diabetes, heart failure, bronzed skin, short stature, use of chelating agents, previous hospitalisations, and splenectomy.

In summary, higher levels of mental distress were indicated among children with thalassemia, with this risk extending to both emotional and behavioural symptomatology. Similar to trends in studies examining the associated mental health outcomes of other chronic illness conditions, findings in one of the studies reviewed suggest that those with more severe symptoms of thalassemia experience more mental health difficulties.

Juvenile Arthritis

As in the studies on psychological adjustment in thalassemia, such significant risks were identified both regarding the risk of bias within-studies and also across-studies that it would not be advisable to make any conclusions regarding psychological adjustment in juvenile arthritis based on the findings of these studies. As in previous study cohorts, convenience samples were mostly used, with an absence of matched control groups and control for demographic factors. None of the studies achieved the quality criteria for the main review, so only an outline will be provided of trends across the studies. For a breakdown of quality ratings see Table 5.

Table 5. Quality ratings of juvenile arthritis studies

	Risk of Bias Within Studies							Risk of Bias Across Studies	
	Selection				Outcome				
	Cohort	Control Sample	JA Measure	Baseline Mental Health	Psych. Measure	Adequate Follow-Up Period	Adequacy of Follow-Up Rate	Control: Demog.	Control: Additional Factor
Noll et al. (2000)		■	■						
Huygen et al. (2000)			■					■	
Brace et al. (2000)			■						

Note – A grey square indicates the fulfilment of that quality criterion

In contrast to the previous reviews, trends among two of the three studies failed to establish any difference in mental well-being between their samples

of youth living with juvenile arthritis and healthy peers. The studies of Huygen and colleagues (2000) and Noll and colleagues (2000) did not find any difference between their arthritis cohort and comparative sample on any measure of emotional or behavioural symptomatology. Both studies had samples of approximately one hundred participants, with Noll and colleagues (2000) notably matching their comparative sample, recruited from the samples classmates, to the exposed cohort. In addition, Huygen and colleagues (2000) controlled for the confounding effects of demographic variables. Although, in contrast, Brace and colleagues (2000) did find that their arthritis cohort reported higher levels of emotional symptomatology than healthy peers, as well as being similarly identified on the basis of parental reports, the conclusions that can be drawn are extremely limited due to methodological limitations of this study. Only sixteen teens living with arthritis were recruited for this study, and they were recruited from a regional rheumatology centre in the United States and selected based on their resemblance to a sample of youths living with chronic fatigue syndrome who were also examined as part of this study. In addition, the comparative group consisted of fourteen teenagers who were either volunteers at this centre, or were attending paediatric continuity clinics. As the study authors reported that scores for these scales were below borderline clinical levels, and that many relationships failed to showed significance in post-hoc analyses, the findings cannot be taken as insightful indicators of the psychological functioning of adolescents living with juvenile arthritis.

In addition to the mainly non-significant trends in mental health outcomes indicated, no significant associations were found between psychological adjustment and arthritis sub-type (Huygen et al., 2000) and disease severity (Noll et al., 2000). However, Noll and colleagues (2000) did find that those with active symptoms, as defined by the presence of synovitis (indicated by swelling or painful loss of motion), had higher levels of mental distress than those whose condition was in full or partial remission at the time of the data collection.

In conclusion, trends among the studies, when taken overall, did not indicate a significant association between juvenile arthritis in children and

adolescents and psychological adjustment. In addition, no association was found between mental health outcomes and more severe sub-types of arthritis, with only the active status of arthritis symptoms having a relationship with psychological adjustment. However, these findings may be artefacts of quality issues within the studies.

Inflammatory Bowel Disease

Vaisto et al. (2010) identified their sample from the files of the Social Insurance Institution of Finland. All patients aged 10 to 18 years diagnosed with inflammatory bowel disease during 1994 to 2006 in the five university hospitals in Finland were contacted by post, with a successful response rate of 95.67%.The database of the Finish population register centre was used to find control participants matched for age, gender, and place of residence. However the remaining two studies were dependent on convenience samples. Overall, there were outstanding issues in the methodology of all three studies, including a lack of independent psychiatric measures. Therefore, none of the studies met the quality criteria for the main review. A full breakdown of quality ratings can be seen in Table 6.

Table 6. Quality ratings of inflammatory bowel disease studies

	Risk of Bias Within Studies							Risk of Bias Across Studies	
	Selection				Outcome				
	Cohort	Control Sample	IBD Measure	Baseline Mental Health	Psych. Measure	Adequate Follow-Up Period	Adequacy of Follow-Up Rate	Control: Demog.	Control: Additional Factor
Vaisto et al. (2010)	■	■	■						
Mackner & Crandall (2006)			■						
Marcus et al. (2009)			■						

Note – A grey square indicates the fulfilment of that quality criterion

The issues implicit in relying solely on self- or parent-report measures were strongly reflected in the study of Vaisto and colleagues (2010). Although parents rated adolescents with inflammatory bowel disease as having significantly higher levels of mental distress, and, in particular, emotional

symptoms, than healthy peers, the adolescents themselves did not report an increased prevalence of mental health symptomatology. It should be noted that, although the mean parent-rating scores were below clinical cut-offs for the exposed cohort, there was a higher prevalence of youths indicated as meeting clinical levels when compared to the control group. However, as these were not reflected in self-ratings, it is unclear which set of ratings should be taken as the most accurate depiction of the adolescent samples well-being. In the remaining studies no associations were found between the presence of inflammatory bowel disease and behavioural and emotional difficulties, with the exception of Mackner & Crandall's (2006) finding that adolescents with inflammatory bowel disease were rated as having higher levels of social problems and anxious/depressed symptoms by parents.

In the study of Vaisto and colleagues (2010) it was found that more severe symptoms of inflammatory bowel disease were associated with higher levels of both self-reported and parental-indicated emotional difficulties. Moreover, in a further reflection of the findings of previous reviews, no association was found between inflammatory disease sub-types and adjustment, and no effect was found for duration of the condition. It should be kept in mind that this study did not control for the effects of demographic factors, and although no associations were found between socio-economic variables and psychological adjustment, a higher prevalence of emotional symptoms were reported among females in general. There were also suggestions of an impact of condition duration on mental health outcomes, with Mackner & Crandall (2006) finding a higher level of somatic complaints in adolescents with an inflammatory bowel disease onset in adolescence, in comparison to those with childhood-onset.

Therefore, the only clear trends among these studies were between emotional symptoms and inflammatory bowel disease characterised by more severe symptoms. However, it was not indicated whether this elevated level of emotional symptomatology was clinically significant. Similar to reviews of the studies focusing on sickle cell disease and juvenile arthritis, no differences were identified in mental health outcomes between sub-types of the main condition. In addition, no associations were found between

outcomes and duration of condition, with the exception that Mackner and Crandell (2006) did indicate higher levels of somatisation symptoms among adolescents with condition onset during the adolescent years. Therefore, again, based only on study trends, there are no strong indications that children and adolescents living with inflammatory bowel disease are at a disproportionate mental health risk. An elevated risk was identified for those living with more severe symptoms of inflammatory bowel disease over peers living with more mild symptomatology, although the magnitude of this risk was not assessed.

Haemophilia

Due to the strong risk of bias both within- and across-studies, only trends among these two studies of the psychiatric outcomes of haemophilia will be outlined. A full breakdown of quality ratings can be seen in Table 7.

Table 7. Quality ratings of haemophilia studies

	Risk of Bias Within Studies							Risk of Bias Across Studies	
	Selection				Outcome				
	Cohort	Control Sample	Haem. Measure	Baseline Mental Health	Psych. Measure	Adequate Follow-Up Period	Adequacy of Follow-Up Rate	Control: Demog.	Control: Additional Factor
Evans et al. (2000)		■	■						
Trzepacz et al. (2003)		■	■						

Note – A grey square indicates the fulfilment of that quality criterion

Both studies examined male-only samples due to the predominance of haemophilia among males. Evans and colleagues (2000) did not find any significant group differences between boys with haemophilia and their classmates, however, they emphasise that this may have been due to a lack of analytic power as a consequence of the small sample size (36 participants in total, 24 of whom had haemophilia). In a larger sample of 80 participants, 40 of whom had been diagnosed with haemophilia, Trzepacz and colleagues (2003) indicated that boys with haemophilia self-reported higher levels of depressive symptoms than classmates, and were also rated by parents of having higher levels of emotional symptoms. Yet, significantly, all scores were within the normal functioning range. Boys with moderate to severe

haemophilia, reported significantly more depressive symptoms than those with mild haemophilia, but again the mean value of these scores remained below clinically significant values. No significant group differences were founds for behavioural difficulties.

In conclusion, the trends suggest that those with haemophilia show elevated levels of emotional symptomatology in comparison to peers. The patterns of results also suggest that with those with more severe haemophilia symptoms could show an increased mental health risk over those with more mild symptoms. However, significantly, none of these elevated levels of symptomatology reached clinical levels of significance.

Chronic Kidney Disease

As in the vast majority of the previous reviews, such significant risks were identified both regarding the risk of bias within-studies and also across-studies that it would not be advisable to make any conclusions regarding psychological adjustment in chronic kidney disease based on the findings of these studies. Therefore, only general trends found among these studies will be noted. A full breakdown of quality ratings can be seen in Table 8.

Table 8. Quality ratings of chronic kidney disease studies

	Risk of Bias Within Studies							Risk of Bias Across Studies	
	Selection				Outcome				
	Cohort	Control Sample	CKD Measure	Baseline Mental Health	Psych. Measure	Adequate Follow-Up Period	Adequacy of Follow-Up Rate	Control: Demog.	Control: Additional Factor
Amr, Bakr, et al. (2008)			■		■				
Amr, El-Gilany, et al. (2007)			■						
Hooper et al. (2009)			■						

Note – A grey square indicates the fulfilment of that quality criterion

Overall, no outstanding trends were indicated towards higher levels of mental distress among children with chronic kidney disease. In the studies of Amr and colleagues (2007, 2008) the only difference found between young people living with chronic kidney disease and the comparative group was

that children and adolescents on dialysis were found to have comparatively higher levels of emotional symptoms than the control group. However, the comparison group in both studies was patients from other clinics in the same hospital suffering from conditions such as respiratory illness, and the confounding effects of this selection process are reflected in the finding that there was a trend overall towards higher levels of self-reported difficulties in the comparative group (Amr, Bakr, et al., 2008). Hooper et al (2008) found that parents reported higher levels of emotional symptoms among children suffering from chronic kidney disease, but that these mean scores were all within normative ranges, well below clinical thresholds.

In terms of moderating factors between this condition and mental health outcomes, as noted, the necessity of dialysis has been indicated among these studies as being associated with higher levels of emotional symptomatology. However, no other condition-related factors were implicated in mental health outcomes, including condition severity, disease duration, or even efficacy of the dialysis. In addition, Hooper and colleagues (2009) indicated that there were no significant differences in adjustment among young people in early- versus late- stages of the disease (for example end stage renal disease versus chronic renal insufficiency). It should also be noted that Amr and colleagues (2007, 2008) did not find any effects relating to demographic variables and IQ on psychological adjustment among their samples.

In conclusion, no outstanding trends were indicated for higher levels of psychological adjustment difficulties among young people living with chronic disease among these studies. However, it does appear that being on dialysis is associated with higher levels of emotional symptomatology. Apart from dialysis-related factors, no other disease-related factors were implicated in psychological adjustment. Moreover, no associations with demographic variables were found.

Non-Alcoholic Fatty Liver Disease

As in the majority of the previous study clusters, neither of the two studies focusing on non-alcoholic fatty liver disease (NAFLD) were of a high enough

quality to warrant an in-depth review. Therefore, only general trends across these studies will be outlined. A full breakdown of quality ratings can be seen in Table 9.

Table 9. Quality ratings of non-alcoholic fatty liver disease (NAFLD) studies

	Risk of Bias Within Studies							Risk of Bias Across Studies	
	Selection				Outcome				
	Cohort	Control Sample	NAFLD Measure	Baseline Mental Health	Psych. Measure	Adequate Follow-Up Period	Adequacy of Follow-Up Rate	Control: Demog.	Control: Additional Factor
Kerkar et al. (2013)			■			■		■	
Mazzone et al. (2013)			■						

Note – A grey square indicates the fulfilment of that quality criterion

Kerkar and colleagues (2013) compared their cohorts of youths with non-alcoholic fatty liver disease (NAFLD) to a comparative group of obese control participants. They found significantly higher levels of depressive symptoms among their NAFLD cohort, but indicated that these levels decreased over the six-month period, with those whose BMI increased showing the most significant improvements. However, this is likely to be an artefact of the study as there was a high attrition rate in this follow-up period, with those who dropped out from the study more likely to have higher depression scores and lower body-esteem at baseline. Mazzone et al. (2013) found that youths with NAFLD in their sample were rated as having higher levels of emotional difficulties than the healthy comparison group based on both youth- and parent-reports, and that this association was significant for both genders. Indications of the clinical significance of these scores were not provided in either study.

In terms of moderating variables between NAFLD and psychological adjustment, Kerkar et al. (2013) found that BMI was significantly associated with depressive levels in their NAFLD cohort. In contrast, in the linear correlation analyses of Mazzone and colleagues (2013), no relationship was found between psychological adjustment and any condition-related variable, including BMI.

In conclusion, the trends in these studies indicate an association between NAFLD and emotional difficulties, although the clinical implications of these trends are unknown. It is unclear to what extent BMI moderates the association between NAFLD and emotional difficulties as one study found a significant effect of BMI, with the other finding no effect. This lack of clarity may represent the limitations caused by the bias in the methodologies of these studies.

Note: For seven remaining conditions, there was only a single study identified as eligible for the comparison of mental health outcomes for children and adolescents living with this condition relative to their healthy peers. Although, it would be inadvisable to make any conclusions regarding psychological adjustment within these conditions on the basis of one individual study, especially in consideration of the methodology limitations pertaining to each of these studies in turn, they can still contribute to the systematic review as a comparative resource in order to compare and contrast findings across the review as a whole. Therefore, each of these studies will be outlined in turn.

Cystic Fibrosis

Table 10. Quality rating of cystic fibrosis study

	Risk of Bias Within Study							Risk of Bias Across Studies	
	Selection				Outcome				
	Cohort	Control Sample	CF Measure	Baseline Mental Health	Psych. Measure	Adequate Follow-Up Period	Adequacy of Follow-Up Rate	Control: Demog.	Control: Additional Factor
Bregnballe et al. (2007)			■						

Note – A grey square indicates the fulfilment of that quality criterion

Cystic fibrosis is a significantly limiting condition, characterised by a build-up of a thick, sticky mucus in the organs, especially in the lungs, pancreas, and sweat glands. The condition is associated with respiratory problems, incomplete digestion and excessive salt loss from sweat glands and life expectancy is severely curtailed. Yet, in this study, the 43 children, 7 to 14 years who were recruited from the Danish Cystic Fibrosis Centre, were identified as having comparative levels of psychosocial functioning to the normative scores on the measure of psychological functioning, the Beck

Youth Inventories (BYI) of Emotional and Social Impairment. The only exception was that young boys with cystic fibrosis (7-10 years) had significantly higher anxiety scores than controls. However, this study did not control for the confounding effects of demographic variables, and it was found that socio-economic factors were significantly associated with anxiety scores meaning this finding may reflect an artefact of the sampling process. There were no associations found between disease-related variables and BYI scores, except with regard to a significant inverse correlation between the anxiety scale and FEV_{1AV} for patients aged 11-14 years ($r = -.53$, $p<.01$).

In conclusion, the trends in this study did not indicate a significant association between cystic fibrosis and mental health outcomes in young people. However, limitations in the study methodology – such as small sample size and lack of control for confounding factors –may have been a factor in the non-significant findings. Socio-economic factors were significantly associated with anxiety scores. Overall, there were no associations found between disease-related variables and scores for psychological adjustment. This is a contrast to trends regarding other conditions.

Epidermolysis Bullosa

Table 11. Quality rating of epidermolysis bullosa study

	Risk of Bias Within Study							Risk of Bias Across Studies	
	Selection				Outcome				
	Cohort	Control Sample	EB Measure	Baseline Mental Health	Psych. Measure	Adequate Follow-Up Period	Adequacy of Follow-Up Rate	Control: Demog.	Control: Additional Factor
Feldmann et al. (2012)			■						

Note – A grey square indicates the fulfilment of that quality criterion

Epidermolysis bullosa is characterized by fragile skin which is easily injured, causing blisters to form. In extreme cases, the individual can also develop blisters internally. The twenty children with epidermolysis bullosa examined in this study were rated by parents as having significantly more emotional difficulties and overall mental health difficulties than the twenty-four children in the comparative group. However, no significant group effect was found for conduct problems and all psychometric scores were within the normal, non-

clinical range. Furthermore, no significant effect of the severity of epidermolysis bullosa was found on the scores of social and emotional problems.

In conclusion, the trends in this study did indicate significantly higher levels of mental health difficulties in children with epidermolysis bullosa in comparison to peers, with these difficulties tending towards emotional symptoms in nature, rather than behavioural symptomatology. However, although a significant difference was indicated, mean scores for the children with epidermolysis bullosa remained in the non-clinical range. No moderating factors were identified, with a non-significant relationship indicated between the severity of epidermolysis bullosa and social and emotional problems.

Oesophageal Atresia

Table 12. Quality rating of oesophageal atresia study

	Risk of Bias Within Study							Risk of Bias Across Studies	
	Selection				Outcome				
	Cohort	Control Sample	EB Measure	Baseline Mental Health	Psych. Measure	Adequate Follow-Up Period	Adequacy of Follow-Up Rate	Control: Demo.	Control: Additional Factor
Faugli et al. (2009)			■		■			■	

Note – A grey square indicates the fulfilment of that quality criterion

Oesophageal atresia is a rare anomaly present at birth, characterised by a failure of the oesophagus to develop normally and connect to the stomach. Although this is usually surgically remedied at an early age, there are still long-term health issues associated with this condition, such as feeding problems and gastro-oesophageal reflux. The sample included in this study of adjustment in oesophageal atresia was quite small. Twenty-one adolescents aged twelve to seventeen years were recruited from a treatment centre at the Rikshospitalet University Hospital, Norway, while the thirty-six youths in the comparative group (thirteen to fifteen years) were a convenience subsample drawn from a Norwegian epidemiologic study of mental health. It should be noted that six of these control participants had been hospitalised for various medical conditions during their childhood and two adolescents had chronic illness/eczema and epilepsy. There was no significant difference found between groups on any both self- and parent-

reports of psychological adjustment, with the adolescents with oesophageal atresia even indicating significantly higher levels of self-perceived competence in various life domains than the comparative group. There was also no difference in the prevalence of psychiatric disorders between the groups.

In conclusion, from these findings, it would not appear that adolescents with oesophageal atresia are at a significant mental health risk. However the issues of representativeness within the sample raise doubts regarding the generalisability of these results.

Familial Mediterranean Fever

Table 13. Quality rating of familial Mediterranean fever study

	Risk of Bias Within Study							Risk of Bias Across Studies	
	Selection				Outcome				
	Cohort	Control Sample	FMF Measure	Baseline Mental Health	Psych. Measure	Adequate Follow-Up Period	Adequacy of Follow-Up Rate	Control: Demog.	Control: Additional Factor
Makay et al. (2010)		■	■					■	

Note – A grey square indicates the fulfilment of that quality criterion

Familial Mediterranean Fever is an inherited genetic disease which affects a gene involved in regulating inflammation, giving rise to episodic bouts of fever, abdominal pain, chest pain, joint pain, and rashes. The forty-three Turkish participants with Familial Mediterranean Fever in this sample, aged seven to eighteen years, were compared to fifty-three healthy children matched for age, sex, economic status, parental education, and family structure. The depression scores of patients with Familial Mediterranean Fever were significantly higher than their healthy peers (p=.001). 11.6% of the study group and 5.6% of the control group had clinically significant depression scores. However, there were no significant difference between patients with Familial Mediterranean Fever and control group in terms of scores on the anxiety measure (p=.78). Age or gender did not show significant associations with anxiety and depression scores. Depression and anxiety scores were significantly correlated with number of attacks and number of hospitalisations for the young people with Familial Mediterranean Fever, with severity of the condition and compliance also being associated

with depression scores. However, disease duration and Familial Mediterranean Fever genotype was not associated with depression and anxiety scores.

In conclusion, an association was indicated between Familial Mediterranean Fever and depressive symptoms, but not anxiety. The implication of condition severity, but not condition duration or genotype, as a moderating factor in the relationship between adjustment and Familial Mediterranean Fever reflects the trends regarding adjustment in other conditions.

Systemic Lupus Erythematosus

Table 14. Quality rating of lupus study

	Risk of Bias Within Study							Risk of Bias Across Studies	
	Selection				Outcome				
	Cohort	Control Sample	Lupus Measure	Baseline Mental Health	Psych. Measure	Adequate Follow-Up Period	Adequacy of Follow-Up Rate	Control: Demog.	Control: Additional Factor
Louthrenoo et al. (2012)			■						

Note – A grey square indicates the fulfilment of that quality criterion

Lupus, or Systemic Lupus Erythematosus, is an episodic autoimmune disease, which gives rise to infrequent bouts of inflammation, pain and damage. The depression and anxiety scores of forty Thai children with Systematic Lupus Erythematosus in this sample were no different to those of the forty participants in the control group who were recruited from paediatric health clinics. Furthermore, the emotional, behavioural and total difficulties scores showed no significant group effect, with the exception that the social competence score was significantly lower in the lupus cohort (p=.03).

In conclusion, no significant trends towards lower levels of psychological adjustment were found among this cohort of children and adolescents with lupus. However, there were many quality issues possibly impacting on the validity of the resulting findings. For example, the highly biased comparative group, who are only sparingly described, means that findings cannot be taken as indicative of the psychological functioning of these children relative

to the healthy general population. Therefore, this study provides negligible insight into the impact of lupus on child mental health.

Primary Ciliary Dyskinesia

Table 15. Quality rating of primary ciliary dyskinesia study

	Risk of Bias Within Study							Risk of Bias Across Studies	
	Selection				Outcome				
	Cohort	Control Sample	PCD Measure	Baseline Mental Health	Psych. Measure	Adequate Follow-Up Period	Adequacy of Follow-Up Rate	Control: Demog.	Control: Additional Factor
Carotenuto et al. (2013)			■	■					

Note – A grey square indicates the fulfilment of that quality criterion

Primary ciliary dyskinesia is a rare genetic disease that results in abnormalities in the ciliary structure and function. As a result of these abnormalities, there is impaired mucociliary clearance, which gives rise to respiratory symptoms, such as wheezing and coughing, sinusitis and frequent ear infections. The ten subjects with Primary Ciliary Dyskinesia showed significantly higher scores on the parent-rated 'Child Behaviour Checklist' overall when compared to the thirty-four controls sample in the convenience comparative sample (p=.002). Examination of the scales revealed these differences mainly pertained to higher levels of emotional symptomatology among the sample of children with primary ciliary dyskinesia. Scores for both groups of children were not in the clinical range. However, for the children with primary ciliary dyskinesia, scores for emotional difficulties, as well as difficulties in total, were in the borderline clinical range for approximately half of the sample. This proportion was significantly higher than that found for the control group.

In conclusion, although the small cohort size should be taken into consideration, a trend toward higher levels of emotional difficulties, mainly in the borderline clinical range, were found among children with primary ciliary dyskinesia, with this trend veering in particular towards higher levels of emotional symptomatology.

Eosinophil-Associated Gastrointestinal Disorders (EGID)

Table 16. Quality rating of eosinophil-associated gastrointestinal disorders (EGID) study

	Risk of Bias Within Study							Risk of Bias Across Studies	
	Selection				Outcome				
	Cohort	Control Sample	EGID Measure	Baseline Mental Health	Psych. Measure	Adequate Follow-Up Period	Adequacy of Follow-Up Rate	Control: Demog.	Control: Additional Factor
Cortina et al. (2010)			■					■	

Note – A grey square indicates the fulfilment of that quality criterion

Eosinophilic-Associated Gastrointestinal Disorders (EGID) occur when eosinophils, a white blood cell, accumulate in the gastrointestinal tract, given rise to inflammation and tissue damage, and symptoms such as feeding difficulties, nausea, and stomach pain. The primary source of recruitment for children aged two to eighteen years with eosinophil-associated gastrointestinal disorders (EGID) (inclusive of EE, EC, Eosinophilic Enteritis, EG, Eosinophilic Duodenitis, and Eosinophilic Gastroenteritis) was the Cincinnati Centre for Eosinophilic Disorders within the Cincinnati Children's Hospital Medical Centre in the United States. The 53 children with EGID who took part in the study were predominantly Caucasian and male. The scores for these children on three questionnaires – one of which was parent-and teacher rated (Behaviour Assessment System for Children – Parent and Teacher Report Scales) and two of which were self-rated (Children's Depression Inventory (CDI) and the Multidimensional Anxiety Scale for Children (MASC)) – were compared to the scores of children recruited from a clinical trials database in the medical centre which lists children whose families volunteered to have their name listed to be involved with future research. The control group was matched for gender and age. Parents and teachers rated young people with EGID as having higher levels of emotional and behavioural difficulties than the healthy comparison group, while children rated themselves as having higher levels of depressive symptoms and, although anxiety ratings did not show a group effect overall, children with EGID indicated more physical symptoms of anxiety and autonomic arousal than peers. Parent ratings placed a significantly higher proportion of children living with EGID in the clinical range for emotional difficulties, while teachers placed these children in the clinical range for somatisation disorders.

In conclusion, a higher level of psychological difficulties, both emotional and behavioural, were indicated in children with EGID across raters, however evidence that these difficulties reach the level of clinical significance is weak.

Non-Categorical Examination of Chronic Illness

Twenty-six of studies that examined the psychiatric outcomes of chronic illness non-categorically were identified during the search process. The types of conditions included in each study are overviewed in Appendix II. In summary, there were no consistent links between the definitions used and the conditions included, with some definitions even extending to include physical impairments that would not traditionally be considered a chronic illness, such as brain injuries (Blackman & Conaway, 2013) and dental problems (Ryland et al., 2010). This lack of a common linkage even extends to studies which used a definition based on duration of symptoms, with set criteria ranging from three months (Arabiat et al., 2012) to one year (e.g. Meijer et al, 2000a; 2000b). It should also be noted that on the basis of many of these definitions, psychiatric symptoms would themselves be categorised as chronic illness conditions. The quality ratings of these studies are listed in the Table 17 in descending order of quality. A certain amount of bias was expected among these studies due to the limitations in generalisability presented by the inconsistent definitions of chronic illness. However, the external validity of findings among this study cohort was further compromised by a lack of a lack of objective physical health indicators and independent psychiatric measures. When applying the quality criteria, none of the studies met the eligibility standard for an in-depth synthesis. Therefore, only the general trends founds across the studies will be outlined.

Table 17. Quality ratings of non-categorical studies

	Risk of Bias Within Studies							Risk of Bias Across Studies	
	Selection				Outcome				
	Cohort	Control Sample	Health Measure	Baseline Mental Health	Psych. Measure	Adequate Follow-Up Period	Adequacy of Follow-Up Rate	Control: Demog.	Control: Additional Factor
McCarroll et al. (2009)									
Ortega et al. (2002)									
Hysing et al. (2007)									
Ryland et al. (2010)									
Blackman & Conaway (2013)									
Fuhr & De Silva (2008)									
Hysing, Siversten et al. (2009)									
Denny et al. (2014)									
Erikson et al. (2005)									
Hysing Elgen, et al. (2009)									
McDougall et al. (2004)									
Meijer et al. (2000b)									
Blackman et al. (2011)									
Curtis & Luby (2008)									
Key et al. (2001)									
Meijer et al. (2000a)									

Phipps & Steele (2002)			■					■	
Rietveld et al. (2005)		■						■	
Arabiat et al. (2012)				■					
Bilfield et al. (2006)		■							
Ganz et al. (2006)	■								
Goldbeck et al. (2011)			■						
Guion & Mrug (2012)			■						
Woods et al. (2013)		■							
Zashikhina & Hagglof (2007)			■						
Zehnder, et al. (2006)			■						

Note – A grey square indicates the fulfilment of that quality criterion

An increased mental health risk was identified across the exposed cohorts in the studies examined, extending to both emotional and behavioural symptomatology. This was consistently demonstrated across the range of psychological adjustment measures used, which it should be noted showed significant variations in quality and validity. Most studies were dependent on parent's ratings of adjustment. Consistent with previous reviews, it was found that the magnitude of this risk varied depending on the condition sub-type, with studies such as those of Hysing and colleagues (2007; 2008; 2009) indicating that children living with neurological conditions were particularly at risk. Previous discussions (e.g. Geist, Valerie, & Otley, 2003), and indeed the findings of this systematic review, have highlighted that neurological conditions seem to have a very unique relationship with psychiatric comorbidities, with patterns of psychopathology relating to the organic bases

of these conditions (e.g. Austin, Harezlak, Dunn, Huster, Rose, & Ambrosius, 2001).

The results overall did not indicate a significant association between condition severity and psychological adjustment. Yet, it may be possible that this non-significant association is reflective of the challenges implicit in trying to study severity levels across a combination of many different conditions. Perrin and colleagues (Perrin, Newacheck, Pless, Drotar, Gortmaker, Leventhal, Perrin, Stein, Walker, Weitzman, 1993) note that studies using a non-categorical framework often employ definitions that would result in their chronic illness sample experiencing at least some level of daily impact as a result of their condition. The importance of the measure of severity was highlighted across studies. Key et al (2001) found a significant association between patient's own ratings of the severity of their condition, although no association was found for parents- and even clinician-ratings. This could be indicative that the young person's own perceptions of the severity of their symptoms are more insightful of mental health outcomes, however, it could also be reflective of the influential role of mental health symptomatology on perceptions of illness severity. A longitudinal examination would be needed in order to achieve any insight.

Although the studies did not, overall, indicate a significant moderating role of symptom severity, the studies did suggest a significant association between functional impairments resulting from the condition and mental health. For example, McDougall and colleagues (2004) found that mental health difficulties were more prevalent among those with activity-limiting conditions or impairments. Such findings are consistent with the arguments of theorists in the field, who theorise that the consequences of the illness on daily functioning are the most salient factors in the prediction of psychosocial adjustment (Schmidt, Petersen, & Bullinger, 2003). These findings are also consistent with the trends in the studies which examined the outcomes associated with specific conditions, which implicated current patterns of symptomatology and more severe impairments in mental health outcomes.

Notably, trends among the studies indicated a large impact of socio-economic factors, with children and adolescents from a lower socio-economic group rating themselves as being more functionally impaired by their condition (e.g. Ganz et al., 2006; Denny et al., 2014). In the opening chapter, socio-economic factors were largely implicated in the prevalence of chronic illness and the prevalence of co-morbidities. This could suggest that similar socio-economic disparities can be seen in paediatric forms of such conditions.

The studies also suggested a possible exacerbating role of poor social development in mental health outcomes, but it is unclear whether this association extended to conditions that were not neurologically-based (see Hysing, Elgen et al.; 2009). Indeed, it could be that mental health difficulties could pre-meditate poor social development. Again, the cross-sectional methodology on which the field is highly reliant limits insight into the possible directionality of such relationships.

Studies that Cross-Referenced Mental Health Outcomes Between Disorders

i. Juvenile Diabetes Mellitus, Sickle Cell Disease

Table 18. Quality rating of Bakare et al. (2005)

	Risk of Bias Within Study							Risk of Bias Across Studies	
	Selection				Outcome				
	Cohort	Control Sample	Health Measure	Baseline Mental Health	Psych. Measure	Adequate Follow-Up Period	Adequacy of Follow-Up Rate	Control: Demog.	Control: Additional Factor
Bakare et al. (2005)			■		■			■	■

Note – A grey square indicates the fulfilment of that quality criterion

Bakare and colleagues (2008) chose to study the mental health outcomes of diabetes and sickle cell disease as these are the most common juvenile chronic conditions in Nigeria. They selected 90 participants, aged 9 to 17 years, among the patients attending the outpatient clinic of the University of Calabar Teaching Hospital. Half of the sample had been diagnosed with Type 1 diabetes, and the other half with sickle cell disease, a diagnosis confirmed by haemoglobin electrophoresis. These patients were compared

to a sample of healthy children selected from a nearby public primary and secondary school who were of the same age as the chronic illness cohort. Prevalence rates of emotional disorders among all groups were assessed using a structured psychiatric interview, namely the National Institute of Mental Health Computerised Diagnostic Interview Schedule for Children Version 4.

4.4% of the sickle cell disease (SCD) patients and 20% of the diabetes (JDM) patients met the criteria for one or more DSM-IV diagnoses of emotional disorder, in comparison to 2.2% of the healthy controls. The findings suggest a nine-fold increase in the incidence of mental health disorders among youth living with diabetes, which clearly contrasts with the two-fold population-based estimate of Wandell et al. (2014). The findings also contrast with the weak evidence of increased levels of mental health symptomatology among children with sickle cell disease in this review. Although both groups of children with chronic illness had higher rates of emotional disorders than healthy controls, children with diabetes were more likely to both meet the criteria for one or more emotional disorders and present at threshold diagnostic levels than children with sickle cell disease. However, in contrast, rates of suicidal ideation were higher among the young people living with sickle cell disease: 20% of the sickle cell disease patients and 11.1% of diabetes patients had suicidal ideation in the past year while none of the healthy subjects expressed any such ideation. There was a significant difference in the prevalence of suicidal ideation among the three groups with patients with SCD and JDM showing more suicidal ideation than the healthy group ($p = 0.001$). Therefore, in conclusion, the findings suggest that although Nigerian young people suffering with juvenile diabetes and sickle cell disease are both at risk of suffering higher levels of psychological difficulties than healthy peers, with emotional disorders being more prevalent among children with diabetes and suicidal ideation being more prevalent in children with sickle cell disease.

ii. Asthma, Heart Disease, Renal Failure, Diabetes, Epilepsy, Malignancy

Table 19. Quality rating of El-Sayed and Barakat (2013)

	Risk of Bias Within Study							Risk of Bias Across Studies	
	Selection				Outcome				
	Cohort	Control Sample	Health Measure	Baseline Mental Health	Psych. Measure	Adequate Follow-Up Period	Adequacy of Follow-Up Rate	Control: Demog.	Control: Additional Factor
El-Sayed & Barakat (2013)			■						

Note – A grey square indicates the fulfilment of that quality criterion

El-Sayad and Barakat (2013) examined the prevalence of clinically-relevant depression and anxiety scores in three hundred and ten patients aged six to eighteen years who were being treated at various inpatient and outpatient treatment clinics at the Paediatric Hospital Affiliated to Ain Shams University Hospital in Egypt. The sample was almost equally divided in terms of those diagnosed with asthma (17%), heart diseases (17%), renal failure (17%), diabetes (17%), epilepsy (16%), and malignancy (16%). However, the authors supplied no further information about the sample, which is a significant limitation when considering that the findings indicated an extremely high prevalence of severe levels of both depression and anxiety among all patients the sample, as indicated by the guidelines of the 'Child Depression Inventory' (CDI) And 'Children Manifest Anxiety Scale' (CMAS). The prevalence of severe anxiety scores among the sample was as follows: malignancy 92%, renal failure 84.3%, heart diseases 80%, epilepsy 80%, diabetes 70%, and asthma 60%. There was a slightly lower prevalence rate of severe depression scores: malignancy 80%, renal failure 72%, heart diseases 62%, epilepsy 62%, diabetes 58% and asthma 50%. Therefore, over half of all children in all condition sub-groups suffered from both severe depression and severe anxiety, with the finding suggesting that the rates are particularly high for malignancy with nearly all children being identified as having severe levels of mental health difficulties. However, as no demographic information was supplied for the sample, and indeed there was no control group of healthy children for comparative purposes, it cannot be concluded that such findings are an accurate reflection of prevalence rates of

depression and anxiety symptoms among young people living with chronic illness.

iii. Asthma, Long QT Syndrome

Table 20. Quality rating of Giuffre et al. (2008)

	Risk of Bias Within Study							Risk of Bias Across Studies	
	Selection				Outcome				
	Cohort	Control Sample	Health Measure	Baseline Mental Health	Psych. Measure	Adequate Follow-Up Period	Adequacy of Follow-Up Rate	Control: Demog.	Control: Additional Factor
Giuffre et al. (2008)			■						

Note – A grey square indicates the fulfilment of that quality criterion

There were significant issues relating to the quality of the sample in this study. The sample consisted of forty-seven children, forty of whom had asthma. These children, who were attending an asthma clinic at Alberta Children's Hospital, were not examined directly, but had rather supplied their data during their participation in a previous study. Their data was chosen for convenience in order to contextualise the adjustment scores of seven children suffering with Long QT Syndrome – a syndrome characterised by irregular electrical cardiac activity – who were recruited from the Alberta Children's Hospital Cardiology clinic. The small sample size is further confounded by the fact that there were two sibling pairs among the seven children. Scores on the 'Revised Children's Manifest Anxiety Scale' (R-CMAS) did not indicate a significant group effect, with the exception that children with Long QT syndrome had significantly higher scores on the lie subscale. However, on the 'Child Behaviour Checklist' (CBCL), children with long QT syndrome were indicated to have a higher prevalence of emotional difficulties (42.9% versus 10%; p=.021). Moreover when they were compared only to children with severe types of asthma symptomatology, children with long QT syndrome were indicated to have higher scores for emotional difficulties (p=.042) and there was a trend towards significantly higher levels of scores for behavioural difficulties (p=.062) and total adjustment scores (p=.072). Correlation analyses indicated that these higher levels of emotional difficulties may be in part moderated by maternal anxiety scores, but in consideration of the particularly small sample size and lack of control for

confounding factors, no significant weight can be given to these findings, or indeed the findings regarding prevalence rates overall.

iv. Obesity Related Chronic Illness, Other Chronic Illness

Table 21. Quality rating of Janicke et al. (2013)

	Risk of Bias Within Study							Risk of Bias Across Studies	
	Selection				Outcome				
	Cohort	Control Sample	Health Measure	Baseline Mental Health	Psych. Measure	Adequate Follow-Up Period	Adequacy of Follow-Up Rate	Control: Demog.	Control: Additional Factor
Janicke et al. (2008)		■	■		■				

Note – A grey square indicates the fulfilment of that quality criterion

Janicke and colleagues (2008) conducted a retrospective study of Medicaid claims data from the state of Florida in the years 2001-2005 to compare relative rates of psychiatric diagnoses among children and adolescents aged five to eighteen years suffering with either an obesity-related chronic illness (namely Type 2 diabetes; metabolic syndrome, dyslipidemia, or obesity/morbid obesity) or any one of the following four chronic health conditions: asthma, cystic fibrosis, juvenile rheumatoid arthritis, or sickle cell disease. Overall, the prevalence rates of any psychiatric disorder were as follows: metabolic syndrome 36.9%, dyslipidemia 34.1%, Type 2 diabetes 35.6%, obesity 34%, asthma 32.6%, juvenile rheumatoid arthritis 29.5%, cystic fibrosis 27.7%, and sickle cell disease 22.3%. It should be noted that further inspection of the claims data did not indicate that these diagnoses were biased in either way towards emotional or behavioural diagnoses for any condition. Although there was a high prevalence of psychiatric disorders in all conditions, rates were slightly higher in those suffering from obesity related chronic illness. Among the other chronic illness group, it is interesting to note that the highest prevalence rate of psychiatric disorders is among children suffering from asthma. However, no figures were supplied to indicate if any of the trends identified were statistically significant. Furthermore, it was found that demographic factors played a significant moderating role in the likelihood of psychiatric diagnosis among the obesity-related condition cohort, with females tending to receive emotional disorder diagnosis, males behavioural disorder diagnosis, and African American and

Hispanic children at a lower odds of being diagnosed with behavioural disorders than non-Hispanic white youths. As no adjustments were made to account for the confounding role of demographic factors, it is unclear how generalisable the results relating to this sample are.

v. Chronic Gastrointestinal Disorders

Table 22. Quality rating of Jayanath et al. (2014)

	Risk of Bias Within Study							Risk of Bias Across Studies	
	Selection				Outcome				
	Cohort	Control Sample	Health Measure	Baseline Mental Health	Psych. Measure	Adequate Follow-Up Period	Adequacy of Follow-Up Rate	Control: Demog.	Control: Additional Factor
Jayanath et al. (2014)			■					■	■

Note – A grey square indicates the fulfilment of that quality criterion

The study participants, who were aged seven to seventeen years, were consecutive patients attending the paediatric gastroenterology follow-up outpatient clinic at University of Malaya Medical Centre in Kuala Lumpur, a tertiary referral centre for children with gastrointestinal and liver disease in Malaysia. 22 of the 100 patients in the total sample had Functional Abdominal Pain (FAP); 26 had Inflammatory Bowel Disease; 17 had Biliary Atresia; and 45 suffered from an otherwise unspecified gastrointestinal disorder. When examining depression scores overall as indicated by a Malay language version of the Children's Depression Inventory (CDI) the prevalence of clinically-relevant symptoms was 27%, moderate symptoms was 43%, and low scores was 30%. However, it was not found that the prevalence rates of depressive symptoms were affected by the specific type of condition. In addition, no gender or age differences were indicated. Interestingly, no correlation was identified between proposed depression risk factors, such as psychiatric illness in the family of origin, and depression scores. In addition, no relationship was found between functional morbidity and depression scores, however the examination of functional morbidity was limited to examinations of impact on physical activity. Therefore, the findings would seem to suggest that prevalence rates of depression are stable across all chronic gastrointestinal disorders, with no age or gender effects indicated.

However, the lack of a comparative group makes it difficult to contextualise these prevalence scores and the role of moderating factors.

vi. Asthma; Diabetes; Obesity; Epilepsy; Cerebral Palsy

Table 23. Quality rating of Moreira et al. (2013)

	Risk of Bias Within Study							Risk of Bias Across Studies	
	Selection				Outcome				
	Cohort	Control Sample	Health Measure	Baseline Mental Health	Psych. Measure	Adequate Follow-Up Period	Adequacy of Follow-Up Rate	Control: Demog.	Control: Additional Factor
Moreira et al. (2013)			■					■	

Note – A grey square indicates the fulfilment of that quality criterion

85 children with diabetes, 308 children with asthma, 68 children with epilepsy and 110 obese children were recruited at the paediatric departments of three public and urban hospitals in central Portugal, with 94 children with cerebral palsy also being recruited from ten Portuguese Cerebral Palsy associations. The psychological adjustments scores of these children, as measured by a Portuguese version of the 'Strengths and Difficulties Questionnaire' (SDQ), were compared to a convenience, community sample of 299 healthy and normal-weight children recruited in two Portuguese public schools. The MANCOVA for psychological adjustment revealed a significant multivariate effect of condition and a significant multivariate interaction. There was a higher prevalence of both emotional and behavioural difficulties among children with epilepsy and obesity than there were among the other illness groups and the healthy controls. It should be noted that these difficulties had a significant association with child-rated quality of life. Furthermore, an age effect was indicated, with older adolescents with diabetes and cerebral palsy indicating less emotional difficulties than younger children living with these conditions, a clear departure from the trends in the studies focusing solely on diabetes which indicated an age-related increase in emotional symptomatology. Therefore, findings indicate that, for this Portuguese sample, rates of emotional and behavioural difficulties are higher amongst children who are obese, or those suffering from epilepsy, and that there is a moderating effect of age on psychological adjustment within cerebral palsy and diabetes, with children indicating better mental health scores with time.

vii. Iron Deficiency Anaemia, Thalassemia

Table 24. Quality rating of Mubarek et al. (2010)

	Risk of Bias Within Study							Risk of Bias Across Studies	
	Selection				Outcome				
	Cohort	Control Sample	Health Measure	Baseline Mental Health	Psych. Measure	Adequate Follow-Up Period	Adequacy of Follow-Up Rate	Control: Demog.	Control: Additional Factor
Mubarak et al. (2010)		■	■					■	

Note – A grey square indicates the fulfilment of that quality criterion

Twenty-two patients with iron deficiency anaemia and twenty patients with β-thalassemia major aged 6 to 12 years were recruited from the outpatient clinic of the Haematology Unit at the Tanta University Hospital in Egypt. Their mental health scores, as measured by the Revised Behaviour Problem Checklist (RBPCL), were compared to the scores of sixteen healthy children identified from among the relatives and companions of the sick children who matched on the basis of age, gender, and cultural background. Both children with iron deficiency anaemia and thalassemia showed higher rates of mental health symptomatology than the healthy control group. However, children with thalassemia were indicated to higher levels of conduct disorders, socialised aggression, and anxiety withdrawal than children with iron deficiency anaemia, with, in turn, children with iron deficiency anaemia indicated to have higher levels of attention problems and excessive motor activity'. Moreover, it appeared that there were different moderating factors for the two groups, with blood parameters predicting attention problems and motor excess in the iron deficiency anaemia sample but not for the thalassemia cohort. This could suggest that fatigue, a predominant physical outcome of anaemia (e.g. Sobrero, Puglisi, Guglielmi, Belvedere, Aprile, Ramello, & Grossi, 2001), may underline the identified concentration difficulties in this sample. Therefore, these findings would suggest that psychological adjustment is not stable across all sub-types of anaemia, and that there are even variances in moderating factors in the association between the condition and psychological adjustment depending on the specific condition type.

viii. Cystic Fibrosis, Cancer, Juvenile Rheumatoid Arthritis, Diabetes Mellitus

Table 25. Quality rating of Pop-Jordanova et al. (2008)

	Risk of Bias Within Study							Risk of Bias Across Studies	
	Selection				Outcome				
	Cohort	Control Sample	Health Measure	Baseline Mental Health	Psych. Measure	Adequate Follow-Up Period	Adequacy of Follow-Up Rate	Control: Demog.	Control: Additional Factor
Pop-Jordanova et al. (2008)									

Note – A grey square indicates the fulfilment of that quality criterion

There were significant quality issues pertaining to the Pop-Jordanova and colleagues (2008) study of the psychological characteristics of children living with chronic illness in Macedonia. The sample consisted of 69 children with chronic illness – 25 with Cystic Fibrosis, 20 with Cancer; 15 with Juvenile Rheumatoid Arthritis; and 9 with Diabetes Mellitus – and they were compared to 25 healthy control children, as well as 25 children who had been diagnosed with neuroticism. Beyond this, no information was provided about the sample, a substantial limitation when considering that no controls were put into place for confounding variables. In addition, the methods of verifying medical diagnoses were not stated. The psychological measures used to measure mental health also varied depending on the child's age, with the 'Child Behaviour Checklist' (CBCL) completed for children twelve years or younger, the 'General Anxiety Scale' (GAS) completed for children ten years or over, and the 'Beck Depression Inventory' (BDI) completed by adolescents in the sample only. Therefore, it is not only unclear how generalisable the results are to other populations, but it is also questionable whether scores can be consistently compared across age groups within the sample. It should be noted that the findings were extremely inconsistent with previous reviews. No group effect was indicated on the CBCL, or on the BDI, although scores were elevated among cancer patients. Furthermore, children with juvenile rheumatoid arthritis had higher anxiety scores than other groups, with the exception of the sub-sample of young people with diagnosable neuroticism.

ix. Classical Phenylketonuria, Diabetes Mellitus Type 1

Table 26. Quality rating of Weglage et al. (2000)

	Risk of Bias Within Study							Risk of Bias Across Studies	
	Selection				Outcome				
	Cohort	Control Sample	Health Measure	Baseline Mental Health	Psych. Measure	Adequate Follow-Up Period	Adequacy of Follow-Up Rate	Control: Demog.	Control: Additional Factor
Weglage et al. (2000)									

Note – A grey square indicates the fulfilment of that quality criterion

Weglage and colleagues (2000) examined forty-two early-treated German patients with classical phenylketonuria aged 10-18 years and compared their scores on the 'Child Behaviour Checklist' with forty-two patients with diabetes mellitus Type 1 who were matched for age, sex, and socio-economic status. Although both samples had higher levels of emotional and behavioural difficulties when compared to the normative population data, with mean scores in the clinically significant range, the phenylketonuria group and the diabetes group did not differ significantly from each other. Furthermore, no moderating effects were found for demographic factors and biochemical control. However, the lack of sample description coupled with the lack of control for confounding factors, raises questions regarding the generalisability of the results, especially in consideration of the significantly high levels of emotional and behavioural difficulties identified across the two groups.

Conclusions of Review of Inter-Disease Variations

There were severe quality issues with the nine studies among this cohort, to the extent that the generalisability and explanatory value of results in at least five of the studies could be viewed as extremely compromised. Perhaps, this is why that, although these studies supported an overall association between chronic illness and psychological adjustment, with variations in adjustment across conditions, many of the patterns in findings contradicted those in the studies of the two previous reviews. For example, the findings of Moreira et al. (2013) did confirm an age effect in diabetes. However, this trend was in the opposite direction to the studies in the previous review of adjustment within diabetes, with children indicating better adjustment over time. There

was also no consistency in the conditions that were compared, meaning that the insight that could be gained from these studies was limited.

Therefore, these studies, due to quality and consistency issues, did not add much to the review as a whole. However, they stand as further evidence that there are inter-disease differences in mental health outcomes, with the study of Janicke et al. (2008) confirming patterns in the first part of the review by placing children with cystic fibrosis and juvenile arthritis at a relatively lower mental health risk than children suffering with asthma. A moderating role of BMI was also suggested, with the studies of Janicke et al. (2008) and Moreira et al. (2013) emphasising that interactions between obesity and chronic illness place obese children at an elevated mental health risk.

Appendix IV Derivation of the 'Perceptions of Fatigue' Scale

A scale was identified in the ALSPAC dataset which was entitled: 'All About Fitness and Fatigue', and focused on activities and activity limitations. It contained 20 questions, but in initial factor analyses indicated that there was not a unitary structure underlining the questions, and correlations amongst many of the items were quite poor. Therefore, two groups of questions, which seemed to cluster together due to inter-item correlations of magnitude 0.5 to 0.7 were isolated, and examined to identify if these made two valid measures of impairment.

Item Group 1 (Face Validity: Fitness)

- **CCP150:** Degree to which child felt fit
- **CCP152:** Degree to which child was very active
- **CCP157:** Degree to which child did a lot each day
- **CCP166:** Degree to which child felt physically in excellent condition

	ccp150	ccp152	ccp157	ccp166
ccp150	1.0000			
ccp152	0.6649 0.0000	1.0000		
ccp157	0.5074 0.0000	0.5866 0.0000	1.0000	
ccp166	0.6785 0.0000	0.6331 0.0000	0.5082 0.0000	1.0000

Item Group 2 (Face Validity: Fatigue)

- **CCP161:** Degree to which child felt in bad condition
- **CCP162:** Degree to which child didn't get much done
- **CCP167:** Degree to which child thought they did not do much
- **CCP168:** Degree to which child did not feel like doing anything

	ccp161	ccp162	ccp167	ccp168
ccp161	1.0000			
ccp162	0.5193 0.0000	1.0000		
ccp167	0.3835 0.0000	0.5066 0.0000	1.0000	
ccp168	0.3869 0.0000	0.4804 0.0000	0.5581 0.0000	1.0000

Subsequent correlation analyses of all 8 items indicated that all items were significantly correlated.

	ccp150	ccp152	ccp157	ccp166	ccp161	ccp162	ccp167	ccp168
ccp150	1.0000							
ccp152	0.6629	1.0000						
	0.0000							
ccp157	0.5047	0.5857	1.0000					
	0.0000	0.0000						
ccp166	0.6802	0.6338	0.5088	1.0000				
	0.0000	0.0000	0.0000					
ccp161	-0.3933	-0.3489	-0.3046	-0.4741	1.0000			
	0.0000	0.0000	0.0000	0.0000				
ccp162	-0.4145	-0.4488	-0.4533	-0.4458	0.5194	1.0000		
	0.0000	0.0000	0.0000	0.0000	0.0000			
ccp167	-0.2767	-0.2988	-0.3372	-0.3102	0.3825	0.5056	1.0000	
	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000		
ccp168	-0.3105	-0.3334	-0.3429	-0.3520	0.3860	0.4807	0.5578	1.0000
	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	

Various forms of factor analysis were then performed to examine support for a unidimensional scale.

FA Principal Factors

Factor analysis/correlation — Number of obs = 6647
Method: principal factors — Retained factors = 1
Rotation: (unrotated) — Number of params = 8

Factor	Eigenvalue	Difference	Proportion	Cumulative
Factor1	3.54492	2.86996	0.9455	0.9455
Factor2	0.67496	0.54616	0.1800	1.1255
Factor3	0.12880	0.13602	0.0344	1.1599
Factor4	-0.00723	0.09817	-0.0019	1.1579
Factor5	-0.10539	0.02907	-0.0281	1.1298
Factor6	-0.13446	0.03928	-0.0359	1.0940
Factor7	-0.17374	0.00484	-0.0463	1.0476
Factor8	-0.17858	.	-0.0476	1.0000

LR test: independent vs. saturated: chi2(28) = 2.3e+04 Prob>chi2 = 0.0000

Factor loadings (pattern matrix) and unique variances

Variable	Factor1	Uniqueness
ccp150	0.7248	0.4747
ccp152	0.7349	0.4600
ccp157	0.6527	0.5740
ccp166	0.7512	0.4357
ccp161	-0.5947	0.6463
ccp167	-0.5670	0.6785
ccp162	-0.6875	0.5273
ccp168	-0.5844	0.6585

FA Principal Component Factors

Factor analysis/correlation — Number of obs = 6647
Method: principal-component factors — Retained factors = 2
Rotation: (unrotated) — Number of params = 15

Factor	Eigenvalue	Difference	Proportion	Cumulative
Factor1	4.06373	2.85663	0.5080	0.5080
Factor2	1.20710	0.48882	0.1509	0.6589
Factor3	0.71828	0.18075	0.0898	0.7486
Factor4	0.53753	0.11765	0.0672	0.8158
Factor5	0.41988	0.00929	0.0525	0.8683
Factor6	0.41059	0.07678	0.0513	0.9196
Factor7	0.33381	0.02474	0.0417	0.9614
Factor8	0.30907	.	0.0386	1.0000

LR test: independent vs. saturated: chi2(28) = 2.3e+04 Prob>chi2 = 0.0000

Factor loadings (pattern matrix) and unique variances

Variable	Factor1	Factor2	Uniqueness
ccp150	0.7565	0.4148	0.2556
ccp152	0.7675	0.3925	0.2569
ccp157	0.7097	0.2278	0.4445
ccp166	0.7829	0.3364	0.2739
ccp161	-0.6580	0.2120	0.5221
ccp167	-0.6233	0.5709	0.2856
ccp162	-0.7422	0.2928	0.3634
ccp168	-0.6431	0.5092	0.3271

Principal Components Analysis

Principal components/correlation — Number of obs = 6647
Number of comp. = 2
Trace = 8
Rotation: (unrotated = principal) — Rho = 0.6589

Component	Eigenvalue	Difference	Proportion	Cumulative
Comp1	4.06373	2.85663	0.5080	0.5080
Comp2	1.2071	.488822	0.1509	0.6589
Comp3	.71828	.180751	0.0898	0.7486
Comp4	.537529	.117651	0.0672	0.8158
Comp5	.419878	.00928772	0.0525	0.8683
Comp6	.41059	.0767759	0.0513	0.9196
Comp7	.333815	.0247412	0.0417	0.9614
Comp8	.309073	.	0.0386	1.0000

Principal components (eigenvectors)

Variable	Comp1	Comp2	Unexplained
ccp150	0.3753	0.3776	.2556
ccp152	0.3807	0.3573	.2569
ccp157	0.3520	0.2073	.4445
ccp166	0.3883	0.3062	.2739
ccp161	-0.3264	0.1930	.5221
ccp167	-0.3092	0.5196	.2856
ccp162	-0.3682	0.2665	.3634
ccp168	-0.3190	0.4635	.3271

Therefore, these items were supported as a unitary scale measuring an isolated variable, which on, the basis of face validity, was termed ‘Perceptions of Fatigue’.

Appendix V Indications of the alternative outcome measures at the age 10 and age 13 cross-sectional waves

Age 10 Cross-Sectional Analyses

1.1 Analyses of chronic illness outcomes more generally

The age 10 cross-sectional analyses with the primary outcome measure suggested that both children rated as “quite healthy, but a few minor problems” and children rated as “sometimes quite ill/almost always unwell” were significantly more likely to present with psychiatric illness than children rated as “very healthy, no problems” (OR “quite healthy, but a few minor problems”: 1.8 (95% CI: 1.48 – 2.19); OR “sometimes quite unwell/almost always unwell”: 3.82 (95% CI: 2.32 – 6.27)). An increased prevalence of emotional, anxiety and behavioural disorders was identified amongst both groups.

The two alternative outcome measures which were administered at 10 years were the teacher-rated ‘Strengths and Difficulties Questionnaire’ (SDQ) and the child-rated ‘Short Moods and Feelings Questionnaire’ (sMFQ). Please note that the ‘Strengths and Difficulties Questionnaire’ was a measure of total psychological difficulties, underlined by measures of both internalising and externalising symptomatology. In contrast, the ‘Short Moods and Feelings Questionnaire’ was a measure of depressive symptomatology. As stated in the methodology, for the purposes of the associative models, scores were coded in a binary fashion, with scores above the cut-off on both scales, representing ‘abnormal’ scores or likely psychopathology, coded as ‘1’. However, mean scores on these scales are also reported in the descriptive statistics relating to these measures in Table 1.

Table 1 Breakdown of the alternative outcome measures at the age 10 cross-sectional wave by chronic illness status, and comparative statistics

	Very Healthy, No Problems (n=4588)	**Quite Healthy, but a Few Minor Problems (n=1239)**	**Sometimes Quite Unwell/Almost Always Unwell (n=64)**	**Group Comparative Tests**
Teacher-Rated SDQ				*F*: 2.99
M(SD)	4.71 (5.24)	5.21 (5.4)	5.68 (4.76)	(p=0.051)
Distributions of Score Around Scale Cut-Off N(%)				
Below Cut-Off	2478 (54.01%)	658 (53.11%)	29 (45.31%)	Chi^2:1.02
Above Cut-Off	139 (3.03%)	44 (3.55%)	2 (3.31%)	(ns)
Missing	1971 (42.96%)	547 (43.34%)	33 (51.56%)	
Child-Rated sMFQ				
M(SD)	3.74 (3.23)	4.43 (3.68)	5.23 (3.68)	*F*: 21.15
Distributions of Score Around Scale Cut-Off N(%)				(p<0.001)
Below Cut-Off	3492 (76.11%)	982 (79.26%)	43 (67.19%)	
Above Cut-Off	163 (3.55%)	73 (5.89%)	4 (6.25%)	Chi^2:14.89
Missing	933 (20.34%)	184 (14.85%)	17 (25.26%)	(p<0.01)

The associations between chronic health problems and abnormal scores on the SDQ and sMFQ at age 10 are presented in Table 2. The indications of the DAWBA measure received mixed support from the two primary outcome measures. Although an association was identified between chronic health problems and a slight increased prevalence of likely psychopathology on the teacher-rated SDQ measure, with a stronger association identified for the "sometimes quite unwell/almost always unwell" group, these associations did not reach the threshold of statistical significance among any of the three binomial logistic models calculated. Please note that in the third logistic model, the "sometimes quite unwell/almost always unwell" group was dropped due to a lack of cases. On the child-rated sMFQ, although associations were again indicated between health problems and increased rates of likely emotional psychopathology, with estimates of a higher magnitude for the "sometimes quite ill/almost always unwell group", a statistically significant association was identifiable only for children with minor

health problems (unadjusted OR: 1.59 (95% CI: 1.2 – 2.12), p<0.01). However, it should be noted that the “sometimes quite ill/almost always unwell” grouping was substantially reduced by the high amount of missing data on this measure, and this may have biased estimates. Please note that the association between minor chronic health problems and this increased prevalence of likely psychopathology remained statistically significant across all three binomial logistic regression models, inclusive of the model that adjusted for the effects of all three covariates.

The binomial logistic models that adjusted for all three covariates were significantly impacted by data attrition, and the confidence intervals indicated a lack of precision in the estimates on both measures. As the likelihood ratio tests that the addition of these covariates did not improve the fit of the associative model for either measure (SDQ LR chi^2: 5.49; sMFQ LR chi^2: 0.57, both p>0.05), it is likely that, similar to analyses with the primary outcome measure, any inconsistencies from the gender-adjusted models were due to loss of analytic power. In addition, please note that there was no evidence of interaction effects between chronic health problems and either gender on either measure (SDQ LR chi^2: 0.49; sMFQ LR chi^2: 0.15; both p>0.05), and that although it was not possible to test for interaction effects with the covariates of ‘socio-economic status’ and ‘history of parental mental illness’, due to a lack of cases in the “sometimes quite ill/almost always unwell” group, it seemed unlikely that an interaction effect would be detected due to the statistical non-significance of the remaining interaction terms.

Table 2 Odds ratios and 95% confidence intervals for the association between chronic illness and psychiatric illness based on the alternative outcome measures at age 10

	Model N	Quite healthy, but a few minor problems		Sometimes Quite Ill/Almost Always Unwell	
		N	Odds Ratio (95% Confidence Interval)	N	Odds Ratio (95% Confidence Interval)
Teacher-Rated SDQ					
Model 1: Basic Model	3350	702	1.19 (0.84 – 1.69)	31	1.23 (0.29 – 5.21)
Model 2: Model with adjustment for gender of the study child	3350	702	1.27 (0.89 – 1.81)	31	1.48 (0.34 – 6.42)
Model 3: Model with adjustment for gender, history of parental mental illness and socio-economic status	954	234	1.51 (0.83 – 2.72)	5	Dropped due to lack of cases
Child-Rated sMFQ					
Model 1: Basic Model	4757	1055	1.59 (1.2 – 2.12)	47	1.99 (0.71 – 5.62)
Model 2: Model with adjustment for gender of the study child	4747	1055	1.6 (1.2 – 2.12)	47	2.0 (0.71 – 5.64)
Model 3: Model with adjustment for gender, history of parental mental illness and socio-economic status	1670	382	2.19 (1.35 – 3.54)	16	1.75 (0.23 – 13.59)

1.2 Analyses of asthma diagnosis outcomes

In the analyses with the primary outcome measure, children with an asthma diagnosis were also significantly more likely to present with a mental illness at the baseline cross-sectional wave than their healthy peers (OR: 1.44 (95% CI: 1.13 – 1.84). This increase seemed to be largely associated with a rise in the prevalence of emotional and anxiety disorders. The descriptive analyses for the asthma cross-sectional sample on the alternative measures of mental health outcomes at this wave, inclusive of mean scores, are presented in Table 2

Table 3 Breakdown of the alternative outcome measures at the age 10 cross-sectional wave by asthma status, and comparative statistics

	Healthy Comparative Sample (n=3861)	**Asthma Diagnosis Sample (n=1698)**	**Group Comparative Tests**
Teacher-Rated SDQ			
M(SD)	4.56 (5.18)	5.55 (5.53)	*T:* -4.84 (p<0.001)
Distributions of Score Around Scale Cut-Off N(%)			
Below Cut-Off	2101 (54.42%)	882 (51.94%)	
Above Cut-Off	111 (2.87%)	64 (3.77%)	*Chi^2: 3.86* (p<0.05)
Missing	1649 (42.71%)	752 (44.29%)	
Child-Rated sMFQ			
M(SD)	3.7 (3.18)	4.26 (3.62)	*T:* -5.14 (p<0.001)
Distributions of Score Around Scale Cut-Off N(%)			
Below Cut-Off	2931 (75.91%)	1277 (75.21%)	
Above Cut-Off	132 (3.42%)	92 (5.42%)	*Chi^2:* 11.46 (p<0.01)
Missing	798 (20.67%)	329 (19.38%)	

The associations between asthma diagnosis and abnormal scores on the teacher-rated SDQ and child-rated sMFQ at age 10 are presented in Table 4. The indications of the DAWBA were mostly supported by the two alternative outcome measures, as associations were indicated between asthma diagnosis both with overall internalising and behavioural symptoms (as measured by the SDQ), and with depressive symptomatology (as measured

by the sMFQ). In the crude model, teachers were 37% more likely to place children with asthma in the abnormal range of difficulties (95% CI: 1.0 – 1.89), an increase which was just on the borderline of statistical significance (p=0.05). However, it should be noted that this significant association could be largely explained by the predominance of males among the asthma sample, as when an adjustment was made for gender of the study child, although an association remained identifiable, it was no longer statistically significant (aOR: 1.26 (0.91 – 1.74)). Both adjustments for gender (LR chi^2: 64.55, $p<0.05$), and consequently for history of parental mental illness and socio-economic status substantially improved the associative model fit on the teacher-rated SDQ (LR chi^2: 7.98, $p<0.05$), so therefore it is unclear if the larger magnitude of the odds ratio in the more fully adjusted model is a consequence of controlling for these variables, or the reduced sample size. There was no evidence of an interaction effect between asthma diagnosis and the variables of gender (LR chi^2: 0.08, $p>0.05$) and parental history of mental illness (LR chi^2: 0.98, $p>0.05$) on outcomes the teacher-rated SDQ. Moreover, although it was not possible to use likelihood ratio testing to test for an interaction between asthma diagnosis and socio-economic status on this outcome measure, due to a lack of children with asthma living in private rental accommodation, the interaction term between asthma and living in council/housing association accommodation was not statistically significant.

On the child-rated sMFQ, significant associations were indicated between asthma diagnosis and scores indicative of likely emotional psychopathology across all three models (unadjusted OR: 1.6 (95% CI: 1.22 – 2.1); $p<0.01$). Although an odds ratio of a slightly larger magnitude was also indicated in the fully adjusted model on this measure ($p<0.05$), it is likely this reflects bias due to data attrition as the addition of these covariates did not significantly improve the model fit (LR chi^2: 0.69, $p>0.05$). The adjustment for gender also did not substantially improve the associative model fit (LR chi^2: 1.29), $p>0.05$), perhaps as gender of the study child was not significantly associated with outcomes on this measure. There was no evidence of an interaction between asthma diagnosis and the variables of gender (LR chi^2: 0.02, $p>0.05$) and parental history of mental illness (LR chi^2: 0.13, $p>0.05$) on

outcomes on the child-rated measure. Moreover, although it was not possible to use likelihood ratio testing to test for an interaction between asthma diagnosis and socio-economic status on the child-rated sMFQ, again due to a lack of children with asthma living in private rental accommodation, the interaction term between asthma and living in council/housing association accommodation was not statistically significant.

Table 4 Odds ratios and 95% confidence intervals for the association between asthma and psychiatric illness based on the alternative outcome measures at age 10

	Model N	Asthma Diagnosis	
		N	Odds Ratio (95% Confidence Interval)
Teacher-Rated SDQ			
Model 1: Basic Model	3158	946	1.37 (0.99 – 1.89)
Model 2: Model with adjustment for gender of the study child	3158	946	1.26 (0.91 – 1.74)
Model 3: Model with adjustment for gender, history of parental mental illness and socio-economic status	1083	316	1.35 (0.78 – 2.35)
Child-Rated sMFQ			
Model 1: Basic Model	4432	1369	1.6 (1.22 – 2.1)
Model 2: Model with adjustment for gender of the study child	4432	1369	1.58 (1.2 – 2.08)

Model 3: Model with adjustment for gender, history of parental mental illness and socio-economic status	1530	447	1.71 (1.06 – 2.77)

Age 13 Cross-Sectional Analyses

2.1 Analyses of chronic illness outcomes more generally

The age 13 cross-sectional analyses with the DAWBA measure suggested that both children rated as "quite healthy, but a few minor problems" and children rated as "sometimes quite ill/almost always unwell" were significantly more likely to present with psychiatric illness than children rated as "very healthy, no problems" (OR "quite healthy, but a few minor problems": 1.7 (95% CI: 1.38 – 2.13); OR "sometimes quite unwell/almost always unwell": 3.33 (95% CI: 1.99 – 5.59)). An increased prevalence of emotional, anxiety and behavioural disorders was identified amongst both groups.

The three alternative outcome measures which were administered at 13 years were the parent-rated 'Strengths and Difficulties Questionnaire' (SDQ) and 'Short Moods and Feelings Questionnaire' (sMFQ). A child-rated version of the sMFQ was also administered at this wave. Consistent with the cross-sectional analyses of the age 10 questionnaires, the scales were scored in a binary fashion, with evidence to support that scores of '1' (representing scores above the scale cut-off) are indicative of likely psychopathology. Please note that means scores are reported in addition to the distributions of these binary ratings in Tables 5.

Table 5 Breakdown of the alternative outcome measures at the age 13 cross-sectional wave by chronic illness status, and comparative statistics

	Very Healthy, No Problems (n=4126)	**Quite Healthy, but a Few Minor Problems (n=1229)**	**Sometimes Quite Unwell/Almost Always Unwell (n=74)**	**Group Comparative Tests**
Parent-Rated SDQ				
M(SD)	5.96 (4.59)	7.76 (4.98)	8.96 (5.69)	*F*: 73.44 (p<0.001)
Distributions of Score Around Scale Cut-Off N(%)				
Below Cut-Off	3467 (84.03%)	1065 (86.66%)	59 (79.73%)	
Above Cut-Off	129 (3.13%)	60 (4.88%)	10 (13.51%)	Chi^2:25.35
Missing	530 (12.85%)	104 (8.46%)	5 (6.76%)	(p<0.001)
Parent-Rated sMFQ				
M(SD)	1.85 (2.82)	2.89 (3.53)	4.5 (4.62)	*F*: 70.93 (p<0.001)
Distributions of Score Around Scale Cut-Off N(%)				
Below Cut-Off	3525 (85.43%)	1076 (87.55%)	63 (85.14%)	
Above Cut-Off	66 (1.6%)	35 (2.85%)	5 (6.76%)	Chi^2:15.08
Missing	535 (12.97%)	118 (9.6%)	6 (8.11%)	(p<0.01)
Child-Rated sMFQ				
M(SD)	4.5 (4.22)	5.4 (4.62)	7.88 (5.82)	*F*: 29.84 (p<0.001)
Distributions of Score Around Scale Cut-Off N(%)				
Below Cut-Off	2792 (67.67%)	837 (68.1%)	41 (55.41%)	
Above Cut-Off	216 (5.24%)	100 (8.14%)	15 (20.27%)	Chi^2:37.13
Missing	1118 (27.1%)	292 (23.76%)	18 (28.32%)	(p<0.001)

The associations between ratings of ill health and scores above cut-off on the three alternative outcome measures administered at 13 years are presented in Table 6. The indications of the DAWBA measure received strong support from these analyses. Not only were significant associations identified between chronic health problems and likely psychopathology on the overall measure of internalising and externalising difficulties, but significant associations between health problems and likely psychopathology was also identified on the scales of emotional symptomatology, on both the child-rated and parent-rated measures. Stronger associations were indicated

for the “sometimes quite unwell/almost always unwell” group than for the “quite healthy, but a few minor problems” group across the measures, consistent with the DAWBA indications. In comparison to their healthy peers, the “quite healthy, but a few minor problems” group had over a 50% increased prevalence of psychopathology in the unadjusted and gender-adjusted models on the parent-rated SDQ (gender-adjusted OR: 1.56 (95% CI: 1.14 – 2.13); p<0.01), and were approximately 75% more likely to present with emotional psychopathology based on parent-ratings on the sMFQ (gender-adjusted OR: 1.73 (95% CI: 1.14 – 2.63); p<0.01), although their own ratings placed them at a slightly lower risk (gender-adjusted OR: 1.48 (95% CI: 1.15 – 1.9); p<0.01). The ‘Sometimes Quite Unwell/Almost Always Unwell’ group were over five times as likely to present with psychopathology after adjustment for gender on the parent-rated SDQ (gender-adjusted OR: 5.05 (95% CI: 2.51 – 10.17); p<0.001), and over four times more likely to present with emotional psychopathology on the parent-rated sMFQ (gender-adjusted OR: 4.22 (95% CI: 1.64 – 10.85); p<0.01), with odds ratios comparable on child-rated version of this scale (gender-adjusted OR: 4.29 (95% CI: 2.32 – 7.95)). However, the imprecision in the estimates for this group indicated by odds ratios should be noted. Inconsistencies in odd ratios were also identified in the models which additionally adjusted for ‘history of parental mental illness’ and ‘socio-economic status’ across all three measures. However, as the LR tests indicated that the addition of these covariates did not significantly improve the fit of the associative models for any of the three measures (parent-rated SDQ LR chi^2: 0.76, p>0.05; parent-rated sMFQ LR chi^2: 0.02, p>0.05; child-rated sMFQ LR chi^2: 0.68, p>0.05), it is likely that these effects can attributed to data attrition. Please note that there was no evidence for an interaction between gender (parent-rated SDQ LR chi^2: 1.97, p>0.05; parent-rated sMFQ LR chi^2: 1.11, p>0.05; child-rated sMFQ LR chi^2: 2.45, p>0.05), or history of parental mental illness (parent-rated SDQ LR chi^2: 1.44, p>0.05; parent-rated sMFQ LR chi^2: 0.07, p>0.05; child-rated sMFQ LR chi^2: 3.37, p>0.05) and chronic health problems on outcomes on any of the three alternative measures at this wave. In addition, there was no evidence of an interaction between socio-economic status and chronic health problems on outcomes on the parent-rated SDQ (LR chi^2:

1.95, p>0.05) or the child-rated sMFQ (LR chi^2: 0.71, p>0.05). Moreover, although it was not possible to use likelihood ratio testing to detect differences on the parent-rated sMFQ, due to a lack of low income households among children who were rated as “sometimes quite ill/almost always unwell”, the interaction term between being “quite healthy, but a few minor problems” and living in a low income household was statistically non-significant.

Table 6 Odds ratios and 95% confidence intervals for the association between chronic illness and psychiatric illness based on the alternative outcome measures at age 13

	Model N	Quite healthy, but a few minor problems		Sometimes Quite Unwell/Almost Always Unwell	
		N	Odds Ratio (95% Confidence Interval)	N	Odds Ratio (95% Confidence Interval)
Parent-Rated SDQ					
Model 1: Basic Model	3596	1125	1.51 (1.11 – 2.07)	69	4.56 (2.28 – 9.11)
Model 2: Model with adjustment for gender of the study child	3596	1125	1.56 (1.14 – 2.13)	69	5.05 (2.51 – 10.17)
Model 3: Model with adjustment for gender, history of parental mental illness and socio-economic status	1339	299	1.58 (0.87 – 2.85)	20	4.34 (1.2 – 15.66)
Parent-Rated sMFQ					
Model 1: Basic Model	4770	1111	1.74 (1.15 – 2.63)	68	4.24 (1.65 – 10.88)
Model 2: Model with adjustment for gender of the study child	4770	1111	1.73 (1.14 – 2.63)	68	4.22 (1.64 – 10.85)
Model 3: Model with adjustment for gender, history of parental mental illness and socio-economic status	1329	293	1.22 (0.56 – 2.64)	19	2.14 (0.27 – 16.92)

Child-Rated sMFQ					
Model 1: Basic Model	4001	937	1.54 (1.2 – 1.98)	56	4.73 (2.58 – 8.68)
Model 2: Model with adjustment for gender of the study child	4001	937	1.48 (1.15 – 1.9)	56	4.29 (2.32 – 7.95)
Model 3: Model with adjustment for gender, history of parental mental illness and socio-economic status	1135	254	1.42 (0.88 – 2.3)	19	7.16 (2.66 – 19.23)

2.2 Analyses of asthma diagnosis outcomes

In the analyses with the primary outcome measure, although asthma diagnosis was associated with an increased prevalence of psychiatric illness (OR: 1.31 (95% CI: 1.0 – 1.73)), this increase did reach the threshold of statistical significance. However, the analyses of rates of underlying disorders did suggest an acute association between asthma diagnosis and an increased prevalence of anxiety disorders at this wave. The descriptive statistics relating to the alternative outcome measures at this cross-sectional wave are presented in Table 7.

Table 7 Breakdown of the alternative outcome measures at the age 13 cross-sectional wave by asthma status, and comparative statistics

	Healthy Comparative Sample (n=3398)	**Asthma Diagnosis Sample (n=1643)**	**Group Comparative Tests**
Parent-Rated SDQ			
M(SD)	5.89 (4.57)	7.1 (5.01)	*T:* -7.94 (p<0.001)
Distributions of Score Around Scale Cut-Off N(%)			
Below Cut-Off	2876 (84.64%)	1326 (80.71%)	
Above Cut-Off	99 (2.91%)	74 (4.5%)	Chi^2*:* 9.61 (p<0.01)
Missing	423 (12.45%)	243 (14.79%)	
Parent-Rated sMFQ			
M(SD)	1.85 (2.82)	2.47 (3.4)	*T:* -6.39 (p<0.001)
Distributions of Score Around Scale Cut-Off N(%)			
Below Cut-Off	2913 (85.73%)	1357 (82.59%)	Chi^2*:* 7.03
Above Cut-Off	52 (1.53%)	42 (2.56%)	(p<0.01)
Missing	433 (12.74%)	244 (14.85%)	
Child-Rated sMFQ			
M(SD)	4.45 (4.22)	5.14 (4.62)	*T:* -4.47 (p<0.001)
Distributions of Score Around Scale Cut-Off N(%)			
Below Cut-Off	2300 (67.69%)	1072 (65.25%)	
Above Cut-Off	174 (5.12%)	121 (7.36%)	Chi^2*:* 10.52
Missing	924 (27.19%)	450 (27.39%)	(p<0.01)

The associations between asthma diagnosis and scores on the three alternative outcome measures at age 13 years are presented in Table 8. The indications of the alternative outcome measures were much stronger than the weak associations indicated on the DAWBA measure. Significant associations between asthma diagnosis and likely psychopathology at 13 years were indicated consistently across all three of the alternative outcome measures (gender adjusted OR parent-rated SDQ: 1.59 (95% CI: 1.17 – 2.16), p<0.01; gender adjusted OR parent-rated sMFQ: 1.74 (95% CI: 1.15 – 2.62), p<0.01; gender adjusted OR child-rated sMFQ: 1.52 (95% CI: 1.19 – 1.95), p<0.01). Any inconsistencies in the more fully adjusted models, which

controlled for the effects of ‘gender’, ‘socio-economic status’ and ‘history of parental mental illness’ were most likely a consequence of data attrition, as the likelihood ratio tests of the fully adjusted models were non-significant across all measures (parent-rated SDQ LR chi^2: 2.14, $p>0.05$; parent-rated sMFQ LR chi^2: 0.62, $p>0.05$; child-rated sMFQ LR chi^2: 1.12, $p>0.05$). Moreover, although adjustments for gender substantially improved the associative model fit for the parent-rated SDQ (LR chi^2: 16.32, $p<0.001$) and the child-rated sMFQ (LR chi^2: 47.58, $p>0.001$), it did not add to the associative model for the parent-rated sMFQ (LR chi^2: 0.01, $p>0.05$). Finally, there was no evidence for an interaction between gender (parent-rated SDQ LR chi^2: 0.86, parent-rated sMFQ LR chi^2: 0.91; child-rated sMFQ LR chi^2: 0.84; all $p>0.05$), history of parental mental illness (parent-rated SDQ LR chi^2: 0.26; parent-rated sMFQ LR chi^2: 0.07; child-rated sMFQ LR chi^2: 0.52; all $p>0.05$), or socio-economic status (parent-rated SDQ LR chi^2: 0.03; parent-rated sMFQ LR chi^2: 0.2; child-rated sMFQ LR chi^2: 0.65; all $p>0.05$) and asthma diagnosis on any of the three alternative outcome measures at this wave.

Table 8 Odds ratios and 95% confidence intervals for the association between asthma and psychiatric illness based on the alternative outcome measures at age 13

	Model N	Asthma Diagnosis	
		N	Odds Ratio (95% Confidence Interval)
Parent-Rated SDQ			
Model 1: Basic Model	4375	1400	1.62 (1.19 – 2.21)
Model 2: Model with adjustment for gender of the study child	4375	1400	1.59 (1.17 – 2.16)
Model 3: Model with adjustment for gender, history of parental mental illness and socio-economic status	1229	356	0.98 (0.52 – 1.85)
Parent-Rated sMFQ			
Model 1: Basic Model	4364	1399	1.73 (1.15 – 2.62)
Model 2: Model with adjustment for gender of the study child	4364	1399	1.74 (1.15 – 2.62)
Model 3: Model with adjustment for gender, history of parental mental illness and socio-economic status	1222	353	1.35 (0.64 – 2.84)
Child-Rated sMFQ			
Model 1: Basic Model	3667	1193	1.49 (1.17 – 1.9)

Model 2: Model with adjustment for gender of the study child	3667	1193	1.52 (1.19 – 1.95)
Model 3: Model with adjustment for gender, history of parental mental illness and socio-economic status	1045	316	1.64 (1.03 – 2.59)

Appendix VI Identification of predictors of missing data, and item values

Analyses Using the Chronic Illness Measure

i. Cross-sectional analyses at age 10 (*p<0.05; **p<0.01; ***p<0.001)

	DAWBA 10		Parental History of Mental Illness		Housing Tenure	
	Missingness (OR)	Complete Case Data (OR)	Missingness (OR)	Complete Case Data (OR)	Missingness (OR)	Complete Case Data (β Coeff.)
Chronic Illness Age 10	0.91	1.78***	1.03	1.23**	0.96	*Rental:* 0.26 *Council/HA:* -0.22
Gender	1.87	0.63***	0.96	0.96	1.02	*Rental:* 0.53* *Council/HA:* -0.05
DAWBA 10	N/A	N/A	1.07	1.24	0.93	*Rental:* 0.44 *Council/HA:* 0.65*
Parental History of Mental Illness	1.23	1.24	N/A	N/A	0.86	*Rental:*- 0.54 *Council/HA:* 0.002
Socio-Economic Status	1.34	1.39**	0.96	0.97	N/A	N/A
Illness Ratings Age 13	1.38	1.56	1.18*	1.25**	0.86**	*Rental:*- 0.03 *Council/HA:* -0.1
Low Household Income	0.74	1.78*	1.43*	1.06	0.97	*Rental:*-0.79 *Council/HA:* 0.3
DAWBA 13	No Cases	16.52***	1.53**	1.29	1.35*	*Rental:*- 0.24 *Council/HA:* -0.08
DAWBA 15	10.31*	7.38***	2.01***	1.11	1.1	*Rental:* 0.17 *Council/HA:* 0.22
High Levels of Health Related Absenteeism 10 Years	1.17	1.97***	0.97	1.15	0.88	*Rental:* 0.33 *Council/HA:* 0.14
High Levels of Health Related Absenteeism 13 Years	2.8	1.54**	1.14	1.21	1.03	*Rental:* -0.44 *Council/HA:* 0.03
Perceptions of Fatigue	0.97	1.03*	0.99	1.01	0.99	*Rental:* 0.01 *Council/HA:* -0.01
Inter-Parental Conflict 9 Years	1.54	0.98	0.98	1.07	0.94	*Rental:* -0.24 *Council/HA:* 0.02
Inter-Parental Conflict 12 Years	No Cases	0.94	1.06	0.89	1.1*	*Rental:* -0.07 *Council/HA:* 0.04

Parental Monitoring 12 Years	1.09	0.95**	1.0	0.98	1.0	*Rental:* 0.06 *Council/HA:* 0.04*
Parental Monitoring 13 Years	1.15	0.97*	0.99	1.0	1.0	*Rental:* -0.06 *Council/HA:* 0.01
Parental Monitoring 15 Years	1.05	0.91***	1.0	1.01	1.0	*Rental:* 0.03 *Council/HA:* 0.02
Child Disclosures 12 Years	0.97	0.97	1.01	0.98	1.0	*Rental:* 0.05 *Council/HA:* 0.07*
Child Disclosures 13 Years	1.12	0.97	0.99	1.0	0.99	*Rental:* 0.03 *Council/HA:* 0.01
Child Disclosures 15 Years	1.44	0.91**	1.01	0.99	1.01	*Rental:* 0.04 *Council/HA:* -0.01
Parental Solicitation 12 Years	1.15	0.94**	0.99	0.98	0.99	*Rental:* 0.07 *Council/HA:* 0.02
Parental Solicitation 13 Years	1.21	0.95	0.99	0.97	0.99	*Rental:* 0.05 *Council/HA:* -0.001
Parental Solicitation 15 Years	0.86	0.92*	0.98	1.01	1.01	*Rental:* -0.13* *Council/HA:* -0.11**
Parental Control 12 Years	1.01	0.96	0.99	0.97	1.0	*Rental:* 0.1* *Council/HA:* 0.04
Parental Control 13 Years	1.23	0.95*	1.02	0.99	0.98	*Rental:* 0.01 *Council/HA:* -0.02
Parental Control 15 Years	1.63	0.93**	0.98	0.98	1.0	*Rental:* 0.09 *Council/HA:* 0.004
Satisfaction with Peer Relationships 10 Years	0.93	1.16***	0.98	1.06*	0.99	*Rental:* -0.045 *Council/HA:* 0.06
Satisfaction with Peer Relationships 12 Years	1.28	1.09**	1.01	1.01	1.0	*Rental:* -0.07 *Council/HA:* 0.02
Peer Vicimisation 10 Years	1.45	2.24***	1.13	1.08	0.89	*Rental:*-0.01 *Council/HA:* -0.01
Peer Vicimisation 12 Years	4.81	2.26***	0.77	1.11	0.95	*Rental:* -0.12 *Council/HA:* -0.03
Early Parenthood	3.16	1.04	1.07	1.01	0.82	*Rental:* -0.05 *Council/HA:* 0.01
Housing Adequacy	1.32	0.88	0.97	1.04	1.06	*Rental:* 0.57 *Council/HA:* 0.18
Housing Basic Living	No Cases	0.81	0.61	1.25	1.32	*Rental:*-0.31 *Council/HA:* 0.03

Housing Defects	0.78	1.49*	0.97	1.02	0.94	*Rental:* 0.17 *Council/HA:* 0.19
Low Educational Attainment	2.4	0.87	1.1	1.29*	0.93	*Rental:* -0.3 *Council/HA:* 0.13
Financial Difficulties	No Cases	1.04	0.88	1.03	1.47	*Rental:* 0.26 *Council/HA:* 0.14
Single Parenthood	No Cases	1.85	1.38	1.23	1.27	*Rental:* -13.36 *Council/HA:* -0.08
Partner Affection	No Cases	0.67	1.15	1.08	0.98	*Rental:* -0.29 *Council/HA:* 0.08
Partner Cruelty	2.36	0.54	0.91	0.65	1.06	*Rental:* -0.45 *Council/HA:* -0.11
Family Size	No Cases	0.28	0.91	0.93	0.85	*Rental:* 0.01 *Council/HA:* -1.29
Family Major Problems	No Cases	1.39	1.17	0.79	0.97	*Rental:* -14.61 *Council/HA:* -0.07
Psychopathology	0.96	1.17	1.07	0.97	1.13	*Rental:* -0.45 *Council/HA:* -0.02
Substance Abuse	2.12	1.67*	0.88	0.67	0.89	*Rental:* -13.74 *Council/HA:* 0.21
Trouble with Police	No Cases	0.6	1.15	0.8	0.93	*Rental:* -0.68 *Council/HA:* -0.07
Crime Convictions	No Cases	No Cases	0.63	No Cases	0.64	*Rental:* -10.27 *Council/HA:* 0.46
Social Network Emotional	No Cases	0.87	1.06	1.11	1.17	*Rental:* 0.43 *Council/HA:* -0.08
Social Network Practical	1.63	0.69	0.96	1.24	0.99	*Rental:* 1.24 *Council/HA:* 0.07
Pregnancy Short Adversity Index	0.93	1.03	1.01	1.0	1.02	*Rental:* -0.1 *Council/HA:* 0.04
Pregnancy Long Adversity Index	0.94	1.0	1.01	1.01	1.02	*Rental:* -0.01 *Council/HA:* 0.03
Housing Adequacy	No Cases	1.12	0.9	0.84	1.19	*Rental:* 0.29 *Council/HA:* -0.48
Housing Basic Living	3.32	0.76	0.92	0.63	1.02	*Rental:* -14.26 *Council/HA:* -0.17

Housing Defects	1.99	0.83	0.85	1.03	1.19	*Rental:* 0.18 *Council/HA:* 0.25
Financial Difficulties	3.95	1.22	0.79	0.97	1.14	*Rental:* 0.01 *Council/HA:* -0.41
Single Parenthood	No Cases	1.41	1.28	0.82	1.14	*Rental:* 0.37 *Council/HA:* 0.17
Partner Affection	2.73	0.91	1.0	1.12	1.12	*Rental:* -1.36 *Council/HA:* -0.19
Partner Cruelty	0.85	0.66	1.08	0.77	1.08	*Rental:* -0.45 *Council/HA:* 0.08
Family Size	2.12	0.66	1.19	0.88	1.17	*Rental:*-0.41 *Council/HA:* 0.39
Family Major Problems	No Cases	0.38	1.07	0.82	0.66	*Rental:* -12.62 *Council/HA:* -0.4
Psychopathology	0.52	1.25	1.1	0.78	1.2	*Rental:* -0.35 *Council/HA:* 0.07
Substance Abuse	0.95	0.79	0.88	0.75	0.95	*Rental:*-0.66 *Council/HA:* -0.18
Trouble with Police	No Cases	0.8	1.56*	0.58	1.07	*Rental:* 0.32 *Council/HA:* 0.07
Crime Convictions	No Cases	1.98	0.99	0.64	0.84	*Rental:* 0.77 *Council/HA:* -0.46
Partner Support	3.14	0.86	0.98	1.1	1.04	*Rental:* 0.35 *Council/HA:* 0.2
Social Network Emotional	0.88	1.03	1.07	0.93	1.08	*Rental:*-0.16 *Council/HA:* 0.23
Social Network Practical	1.05	0.98	0.79	1.15	1.05	*Rental:* 0.46 *Council/HA:* 0.08
0-2 Years Short Adversity Index	1.06	1.0	1.01	0.96	1.05*	*Rental:* -0.06 *Council/HA:* -0.0003
0-2 Years Long Adversity Index	1.05	1.0	1.0	0.98	1.04*	*Rental:* -0.01 *Council/HA:* 0.02
Housing Adequacy	No Cases	0.86	0.77	0.92	1.18	*Rental:* -0.62 *Council/HA:* -0.06
Housing Basic Living	No Cases	0.45	1.38	0.88	1.18	*Rental:* -12.37 *Council/HA:* -0.2

Housing Defects	2.27	1.11	1.08	1.15	1.01	*Rental:* 1.19*** *Council/HA:* 0.32
Financial Difficulties	3.26	1.02	0.92	0.81	1.24	*Rental:* -0.14 *Council/HA:* 0.19
Single Parenthood	1.77	1.0	1.06	1.07	1.03	*Rental:* 0.22 *Council/HA:* 0.38
Partner Affection	No Cases	1.14	1.07	0.86	1.09	*Rental:* 0.42 *Council/HA:* -0.23
Partner Cruelty	No Cases	0.9	1.24	0.9	1.02	*Rental:* 0.06 *Council/HA:* -0.13
Family Size	2.17	0.65	1.25	0.81	1.19	*Rental:* 0.23 *Council/HA:* 0.17
Family Major Problems	No Cases	0.7	1.12	1.04	0.52*	*Rental:* -12.84 *Council/HA:* -0.15
Psychopathology	2.21	1.19	1.02	0.9	1.09	*Rental:* -0.04 *Council/HA:* 0.28
Substance Abuse	0.92	0.89	1.11	0.67*	0.94	*Rental:* -0.55 *Council/HA:* -0.14
Trouble with Police	4.32	0.98	0.52	0.97	1.53*	*Rental:* 1.05 *Council/HA:* -0.37
Crime Convictions	No Cases	3.57*	0.37	0.63	0.56	*Rental:* 1.06 *Council/HA:* -0.03
2-4 Years Short Adversity Index	1.29	0.99	1.02	0.96	1.02	*Rental:* 0.07 *Council/HA:* 0.05

ii. Cross-sectional analyses at age 13 (*p<0.05; **p<0.01; ***p<0.001)

	Parental History of Mental Illness		Low Household Income	
	Missingness (OR)	**Complete Case Data (OR)**	**Missingness (OR)**	**Complete Case Data (OR)**
Chronic Illness Age 13	1.01	1.32**	1.09	0.95
Gender	0.98	0.92	0.95	0.91
DAWBA 13	1.26	1.13	1.06	0.92
Parental History of Mental Illness	N/A	N/A	0.87	1.04
Socio-Economic Status	1.27	1.04	N/A	N/A
Illness Ratings Age 10	1.01	1.32**	1.09	0.95
DAWBA 10	1.06	1.36	1.08	1.66*
DAWBA 15	1.75**	1.52*	1.06	1.15
High Levels of Health Related Absenteeism 10 Years	0.95	1.05	1.04	1.22
High Levels of Health Related Absenteeism 13 Years	1.06	1.33**	0.99	0.99
Perceptions of Fatigue	0.98*	1.02*	1.0	1.02
Inter-Parental Conflict 9 Years	0.95	1.05	0.95	1.03
Inter-Parental Conflict 12 Years	0.99	0.91	1.05	0.89
Parental Monitoring 12 Years	0.99	0.99	1.01	0.99
Parental Monitoring 13 Years	0.99	0.99	1.0	0.98
Parental Monitoring 15 Years	0.99	1.0	0.99	0.94
Child Disclosures 12 Years	1.0	0.99	1.0	1.01

Child Disclosures 13 Years	0.99	0.98	0.99	0.97
Child Disclosures 15 Years	0.99	0.98	1.02	0.95
Parental Solicitation 12 Years	0.98	0.99	1.0	1.0
Parental Solicitation 13 Years	0.99	0.97	0.99	0.99
Parental Solicitation 15 Years	0.99	1.02	1.0	0.9**
Parental Control 12 Years	0.99	0.99	1.0	1.01
Parental Control 13 Years	1.02	0.99	1.0	0.98
Parental Control 15 Years	0.98	0.96*	0.98	1.01
Satisfaction with Peer Relationships 10 Years	0.98	1.05*	1.02	1.0
Satisfaction with Peer Relationships 12 Years	0.97	1.0	1.01	1.05
Peer Vicimisation 10 Years	1.0	1.0	0.85*	1.16
Peer Vicimisation 12 Years	0.77*	1.12	0.96	0.81
Early Parenthood	1.08	0.98	0.89	0.7
Housing Adequacy	0.88	1.2	0.98	1.15
Housing Basic Living	1.0	1.25	0.95	0.89
Housing Defects	1.11	1.22	0.94	1.06
Low Educational Attainment	1.13	1.35*	0.94	1.15
Financial Difficulties	0.8	0.91	1.35	0.9
Single Parenthood	1.06	1.37	0.94	1.1
Partner Affection	0.95	0.99	0.86	0.59*

Partner Cruelty	0.73	0.68	0.91	0.63
Family Size	1.36	0.94	1.13	0.97
Family Major Problems	0.79	0.86	1.02	1.06
Psychopathology	0.82	0.96	1.16	0.73
Substance Abuse	0.86	0.59*	1.02	1.64*
Trouble with Police	0.71	0.61	0.99	0.5
Crime Convictions	0.42	No Cases	1.56	2.96
Social Network Emotional	0.93	1.26	0.91	1.01
Social Network Practical	0.91	1.1	1.34*	0.97
Pregnancy Short Adversity Index	0.96	0.99	1.01	0.96
Pregnancy Long Adversity Index	0.98	1.01	1.01	0.97
Housing Adequacy	0.9	0.91	1.13	1.07
Housing Basic Living	1.15	0.68	1.09	1.06
Housing Defects	1.03	1.33*	1.05	1.13
Financial Difficulties	0.98	0.89	1.33**	0.96
Single Parenthood	0.95	0.69	1.02	0.93
Partner Affection	0.86	1.02	1.21	0.93
Partner Cruelty	0.74	0.75	1.13	1.01
Family Size	1.36	0.95	0.88	0.79

Family Major Problems	0.6	0.57	0.84	0.47
Psychopathology	0.98	0.89	1.07	1.0
Substance Abuse	0.84	0.84	0.96	1.23
Trouble with Police	1.08	0.68	1.02	1.15
Crime Convictions	1.09	1.14	0.9	1.1
Partner Support	0.98	1.01	1.09	0.72
Social Network Emotional	0.94	1.04	1.33	1.08
Social Network Practical	0.77	1.23	1.35	1.01
0-2 Years Short Adversity Index	0.99	0.96	1.03	1.02
0-2 Years Long Adversity Index	0.98	0.98	1.04*	1.0
Housing Adequacy	0.85	0.82	1.56**	1.43
Housing Basic Living	1.39	0.74	0.71	1.25
Housing Defects	1.34*	1.43*	0.92	1.76**
Financial Difficulties	0.86	0.75	1.15	1.27
Single Parenthood	0.72	1.2	1.1	1.1
Partner Affection	0.79	0.87	0.95	0.98
Partner Cruelty	0.86	0.95	1.12	1.22
Family Size	1.29	0.85	0.9	1.11
Family Major Problems	1.49	0.88	0.93	0.2

Psychopathology	0.82	0.9	0.92	1.39
Substance Abuse	1.18	0.7*	0.99	1.23
Trouble with Police	0.54	0.85	1.24	2.28*
Crime Convictions	0.78	No Cases	1.41	No Cases
2-4 Years Short Adversity Index	0.99	0.97	1.0	1.13**

iii. Longitudinal analyses (*p<0.05; **p<0.01; ***p<0.001)

	DAWBA 10		DAWBA 15		Parental History of Mental Illness		Low Household Income	
	Missingness (OR)	Complete Case Data (OR)	Missingness (OR)	Complete Case Data (OR)	Missingness (OR)	Complete Case Data (OR)	Missingness (OR)	Complete Case Data (OR)
Chronic Illness	2.06	1.99***	0.87	1.62**	1.22*	1.33**	1.12	0.89
Gender	1.05	0.7*	0.83	1.25	1.0	0.92	0.88	0.86
DAWBA 10	N/A	N?A	1.52**	6.47***	1.24	1.4	1.17	1.77*
DAWBA 13	No Cases	18.29***	1.5**	14.34***	1.43	1.45	1.28	0.9
DAWBA 15	16.38*	6.48***	N/A	N/A	2.24***	1.43	1.14	1.53
Parental History of Mental Illness	1.4	1.4	1.13	1.43	N/A	N/A	0.86	1.17
Socio-Economic Status	2.27	1.77	1.15	1.53	1.41	1.17	N/A	N/A
High Levels of Health Related Absenteeism 10 Years	4.31	2.26***	1.1	0.95	0.91	1.16	1.03	1.24

High Levels of Health Related Absenteeism 13 Years	3.25	1.69***	1.28***	1.37	1.0	1.29*	1.03	0.96
Perceptions of Fatigue	1.0	1.03*	1.01	1.08	0.98*	1.01	1.0	1.02
Inter-Parental Conflict 9 Years	No Cases	1.0	1.02	1.04	1.0	1.06	0.97	1.13
Inter-Parental Conflict 12 Years	No Cases	0.84	1.07	1.08	1.07	0.89	1.08	0.91
Parental Monitoring 12 Years	1.18	0.95**	0.99	0.91***	1.0	0.99	0.99	0.96*
Parental Monitoring 13 Years	1.06	0.96*	0.99	0.92***	0.98	0.99	0.99	0.96*
Parental Monitoring 15 Years	1.13	0.9	No Cases	0.84***	1.0	1.01	0.99	0.94*
Child Disclosures 12 Years	0.92	0.97	0.99	0.92**	1.01	0.99	1.0	1.01
Child Disclosures 13 Years	0.86	0.96	0.98	0.86***	0.99	0.99	0.99	0.94**
Child Disclosures 15 Years	1.58	0.9**	No Cases	0.8***	0.99	0.98	1.02	0.95
Parental Solicitation 12 Years	1.47	0.94*	0.97*	0.93**	0.99	0.98	0.99	1.03
Parental Solicitation 13 Years	1.1	0.95	0.98	0.92**	0.99	0.96	0.98	0.8

Parental Solicitation 15 Years	1.36	0.91*	No Cases	0.88**	0.97	1.01	1.0	0.92*
Parental Control 12 Years	1.15	0.96	0.99	0.94**	1.0	0.97	0.99	1.01
Parental Control 13 Years	1.3	0.94**	0.97**	0.98	1.02	0.98	0.99	0.97
Parental Control 15 Years	2.1	0.92*	No Cases	0.92**	0.98	0.96	0.98	1.05
Satisfaction with Peer Relationships 10 Years	1.14	1.15***	0.97	1.15**	0.99	1.05	1.01	0.98
Satisfaction with Peer Relationships 12 Years	0.9	1.06	0.97	1.09	1.0	1.0	1.0	1.03
Peer Vicimisation 10 Years	1.16	1.16***	1.05**	1.17***	1.0	1.03	0.97	1.03
Peer Vicimisation 12 Years	0.99	1.09***	0.98	1.13***	0.97	1.02	0.98	0.97
Early Parenthood	3.66	1.16	0.85	1.01	0.97	1.15	0.9	0.61
Housing Adequacy	No Cases	0.86	1.12	1.01	0.85	1.18	1.08	1.31
Housing Basic Living	No Cases	0.65	0.93	0.28	0.62	1.65	0.8	0.9
Housing Defects	2.54	1.27	1.09	1.35	1.04	1.11	0.89	0.99

Low Educational Attainment	2.93	1.06	0.96	1.47	1.13	1.37*	0.82	1.17
Financial Difficulties	No Cases	1.26	1.2	1.85	0.89	0.98	1.28	1.09
Single Parenthood	No Cases	1.77	0.89	1.13	0.94	1.55	1.08	1.21
Partner Affection	No Cases	0.98	1.2	0.94	1.07	0.97	0.76*	0.52*
Partner Cruelty	5.36	0.8	1.14	1.92	0.66	0.68	0.95	0.98
Family Size	No Cases	0.45	1.58	1.56	1.21	0.83	1.31	1.11
Family Major Problems	No Cases	0.9	0.78	1.61	0.85	0.81	1.05	0.57
Psychopathology	2.9	1.09	1.2	1.15	0.94	0.95	1.08	0.81
Substance Abuse	5.51	1.52	1.27	0.95	1.07	0.49*	0.98	1.3
Trouble with Police	No Cases	0.67	0.83	0.28	1.03	0.65	0.91	0.51
Crime Convictions	No Cases	No Cases	0.26	2.39	0.85	No Cases	2.71	4.43

Social Network Emotional	No Cases	0.63	1.5*	2.24*	1.07	1.28*	0.78	0.89
Social Network Practical	No Cases	0.62	1.09	1.34	0.79	1.3	1.38	1.02
Pregnancy Shor Adversity Index	1.35	1.06	1.04	1.07	0.98	1.0	0.98	0.94
Pregnancy Long Adversity Index	1.17	1.02	1.04	1.08	0.99	1.01	0.99	0.95
Housing Adequacy	No Cases	0.86	0.89	0.74	0.89	0.78	1.05	0.99
Housing Basic Living	No Cases	0.91	1.09	0.42	1.37	0.75	1.17	1.17
Housing Defects	No Cases	0.79	0.99	1.06	0.96	1.31	0.98	1.22
Financial Difficulties	2.71	1.17	1.05	1.04	0.94	0.9	1.35**	0.91
Single Parenthood	No Cases	1.36	0.91	1.14	1.07	0.68	1.11	0.63
Partner Affection	5.3	1.04	1.07	1.0	0.94	1.04	1.06	0.85

Partner Cruelty	2.99	0.76	0.96	1.36	0.9	0.61**	1.08	1.01
Family Size	7.48	0.49	1.08	1.84	1.52	0.91	0.84	0.81
Family Major Problems	No Cases	0.5	0.64	0.62	0.84	0.32	0.8	0.57
Psychopathology	1.85	1.43	1.15	1.46	1.0	0.83	0.98	0.94
Substance Abuse	3.3	0.98	1.08	0.81	0.79	0.79	0.89	1.4
Trouble with Police	No Cases	1.26	1.11	0.76	1.23	0.55	0.78	1.2
Crime Convictions	No Cases	1.79	1.39	No Cases	1.1	0.96	0.62	0.88
Partner Support	4.09	1.14	1.0	1.2	1.01	1.0	1.03	0.77
Social Network Emotional	No Cases	0.96	1.21	1.73*	1.07	0.87	1.27*	0.99
Social Network Practical	No Cases	0.89	1.14	1.07	0.81	1.26	1.19	1.14
0-2 Years Short Adversity Index	1.23	1.03	1.01	1.04	1.0	0.95	1.01	1.01

0-2 Years Long Adversity Index	1.12	1.02	1.01	1.04	1.0	0.97	1.02	1.0
Housing Adequacy	No Cases	0.5	1.06	0.58	0.58	0.79	1.35	1.17
Housing Basic Living	No Cases	0.32	1.53	No Cases	1.36	0.51	0.74	0.99
Housing Defects	No Cases	0.99	0.99	1.84*	1.27	1.47*	0.92	1.74*
Financial Difficulties	4.24	1.08	1.03	1.64	1.12	1.32	0.88	0.74
Single Parenthood	No Cases	0.96	1.17	1.13	0.88	1.26	1.05	0.95
Partner Affection	No Cases	1.34	1.09	0.89	0.83	0.88	0.87	0.81
Partner Cruelty	No Cases	1.25	1.0	0.81	1.07	0.9	0.98	1.39
Family Size	6.37	0.58	1.33	1.87	1.28	0.84	0.93	1.17
Family Major Problems	No Cases	0.5	0.55	0.59	1.35	0.34	0.9	No Cases
Psychopathology	No Cases	1.37	1.04	0.7	0.9	0.85	0.83	1.52
Substance Abuse	2.75	0.97	1.12	0.37*	1.19	0.63*	0.96	1.16

Trouble with Police	12.22*	0.89	1.21	0.31	0.25*	0.92	1.02	1.79
Crime Convictions	No Cases	3.5	0.39	No Cases	0.61	No Cases	1.06	No Cases
2-4 Years Short Adversity Index	1.28	1.03	1.03	0.98	0.99	0.96	0.97	1.11*

Analyses Using the Measure of Asthma Diagnosis

i. Cross-sectional analyses at age 10 (*p<0.05; **p<0.01; ***p<0.001)

	DAWBA 10		Parental History of Mental Illness		Housing Tenure	
	Missingness (OR)	**Complete Case Data (OR)**	**Missingness (OR)**	**Complete Case Data (OR)**	**Missingness (OR)**	**Complete Case Data (β Coeff.)**
Asthma Age 10	1.01	1.41**	1.22**	1.27**	1.07	*Rental:* 0.05 *Council/HA:* -0.08
Gender	1.79	0.58***	0.99	1.03	1.03	*Rental:* 0.27 *Council/HA:* -0.03
DAWBA 10	N/A	N/A	0.92	1.29	0.85	*Rental:* -0.03 *Council/HA:* 0.61
Parental History of Mental Illness	1.39	1.29	N/A	N/A	0.8**	*Rental:*- 0.38 *Council/HA:* 0.12
Socio-Economic Status	1.51	1.34*	1.03	1.04	N/A	N/A
Low Household Income	0.87	1.57*	1.34	1.08	0.96	*Rental:* 0.62 *Council/HA:* 0.2
DAWBA 13	No Cases	17.01***	1.28	1.21	1.44*	*Rental:*- 0.69 *Council/HA:* -0.45
DAWBA 15	10.27*	7.31***	1.7**	1.3	0.96	*Rental:* 0.48 *Council/HA:* -0.05
High Levels of Health Related Absenteeism 10 Years	1.25	1.89***	1.07	1.1	0.81**	*Rental:* -1.13* *Council/HA:* 0.13
High Levels of Health Related Absenteeism 13 Years	1.6	1.3	1.26*	1.14	1.03	*Rental:* -0.68 *Council/HA:* -0.05
Perceptions of Fatigue	0.99	1.03	0.99	1.02	0.99	*Rental:*- 0.01 *Council/HA:* -0.004
Inter-Parental Conflict 9 Years	1.51	1.05	0.98	1.08	0.98	*Rental:* -0.35 *Council/HA:* 0.05
Inter-Parental Conflict 12 Years	No Cases	1.04	1.07	0.91	1.06	*Rental:* -0.07 *Council/HA:* -0.03
Parental Monitoring 12 Years	1.09	0.94***	0.99	0.98	1.01	*Rental:* 0.06 *Council/HA:* 0.03
Parental Monitoring 13 Years	1.15	0.95**	1.0	0.99	1.0	*Rental:* 0.02 *Council/HA:* -0.001
Parental Monitoring 15 Years	1.04	0.88***	1.0	No Cases	1.0	*Rental:* 0.02 *Council/HA:* -0.004

Child Disclosures 12 Years	0.97	0.96	1.0	0.98	1.0	*Rental:* 0.04 *Council/HA:* 0.06
Child Disclosures 13 Years	1.12	0.94*	1.0	0.99	0.99	*Rental:* 0.04 *Council/HA:* -0.0004
Child Disclosures 15 Years	1.42	0.88***	1.02	0.99	1.01	*Rental:* 0.06 *Council/HA:* -0.02
Parental Solicitation 12 Years	1.14	0.95	0.99	0.97	1.01	*Rental:* 0.09 *Council/HA:* -0.0008
Parental Solicitation 13 Years	1.21	0.95	1.01	0.98	0.99	*Rental:* 0.04 *Council/HA:* -0.007
Parental Solicitation 15 Years	0.85	0.91*	1.01	1.02	0.99	*Rental:* -0.09 *Council/HA:* -0.09*
Parental Control 12 Years	1.01	0.98	0.99	0.98	1.0	*Rental:* 0.06 *Council/HA:* 0.04
Parental Control 13 Years	1.23	0.95*	1.91	0.98	0.98*	*Rental:* 0.03 *Council/HA:* -0.01
Parental Control 15 Years	1.6	0.93*	0.99	0.97	1.0	*Rental:* 0.05 *Council/HA:* -0.02
Satisfaction with Peer Relationships 10 Years	0.93	1.13***	0.97	1.05*	0.98	*Rental:* -0.09 *Council/HA:* 0.04
Satisfaction with Peer Relationships 12 Years	1.3	1.13***	1.01	1.02	0.99	*Rental:* -0.08 *Council/HA:* 0.002
Peer Vicimisation 10 Years	1.06	1.16***	1.0	1.02	1.0	*Rental:*-0.48 *Council/HA:* -0.01
Peer Vicimisation 12 Years	1.13	1.14***	0.98	1.03	1.0	*Rental:* -0.62 *Council/HA:* -0.12
Early Parenthood	6.66*	1.11	0.99	0.92	0.89	*Rental:* 0.15 *Council/HA:* 0.1
Housing Adequacy	1.53	0.83	1.0	1.03	0.86	*Rental:* 0.48 *Council/HA:* 0.14
Housing Basic Living	No Cases	0.7	0.7	0.99	1.23	*Rental:*-0.24 *Council/HA:* -0.17
Housing Defects	No Cases	1.69**	0.92	0.95	0.96	*Rental:* 0.29 *Council/HA:* 0.14
Low Educational Attainment	3.03	0.94	1.0	1.33*	0.94	*Rental:* -0.1 *Council/HA:* 0.03
Financial Difficulties	No Cases	1.24	0.85	0.97	1.38**	*Rental:* 0.31 *Council/HA:* 0.17
Single Parenthood	No Cases	1.71	1.07	1.21	1.25	*Rental:* -12.55 *Council/HA:* -0.8

Partner Affection	No Cases	0.71	1.02	1.1	0.92	*Rental:* -0.49 *Council/HA:* -0.07
Partner Cruelty	No Cases	0.66	0.86	0.83	1.02	*Rental:* -1.14 *Council/HA:* -0.25
Family Size	No Cases	0.66	0.93	1.15	0.85	*Rental:* 0.87 *Council/HA:* -1.19
Family Major Problems	No Cases	1.53	0.88	0.74	0.92	*Rental:* -12.72 *Council/HA:* 0.001
Psychopathology	1.13	1.45*	1.17	1.36	1.04	*Rental:* -0.12 *Council/HA:* -0.01
Substance Abuse	2.36	1.53	0.82	0.75	0.94	*Rental:* -13.72 *Council/HA:* 0.26
Trouble with Police	No Cases	0.86	0.97	0.88	1.0	*Rental:* -12.61 *Council/HA:* -0.15
Crime Convictions	No Cases	No Cases	0.49	No Cases	0.5	*Rental:* -10.31 *Council/HA:* 0.17
Social Network Emotional	No Cases	0.83	0.8	0.97	1.03	*Rental:* 0.46 *Council/HA:* -0.21
Social Network Practical	1.93	0.93	0.98	1.26	0.95	*Rental:* 1.05** *Council/HA:* -0.07
Pregnancy Short Adversity Index	0.92	1.08	0.97	1.0	1.0	*Rental:* -0.06 *Council/HA:* 0.02
Pregnancy Long Adversity Index	0.94	1.04	0.98	1.01	1.0	*Rental:* 0.01 *Council/HA:* 0.01
Housing Adequacy	No Cases	1.16	0.86	0.75	1.25	*Rental:* 0.43 *Council/HA:* -0.61
Housing Basic Living	4.22	0.47	0.86	0.56*	0.89	*Rental:* -14.05 *Council/HA:* -0.72
Housing Defects	2.46	0.87	0.94	1.02	1.15	*Rental:* 0.48 *Council/HA:* 0.23
Financial Difficulties	2.61	1.29	0.83	1.05	1.03	*Rental:* 0.03 *Council/HA:* -0.38
Single Parenthood	No Cases	1.3	1.18	0.88	1.19	*Rental:* -0.19 *Council/HA:* 0.12
Partner Affection	2.86	0.96	0.95	1.08	1.05	*Rental:* -1.3 *Council/HA:* -0.21

Partner Cruelty	0.98	0.54*	1.2	0.88	1.04	*Rental:* -0.001 *Council/HA:* 0.04
Family Size	2.5	0.52	1.06	0.92	1.11	*Rental:*0.06 *Council/HA:* 0.27
Family Major Problems	No Cases	0.44	1.0	1.17	0.56	*Rental:* -12.35 *Council/HA:* -0.29
Psychopathology	0.6	1.3	1.12	0.77*	1.12	*Rental:* -0.31 *Council/HA:* 0.04
Substance Abuse	1.08	0.81	0.92	0.75	0.95	*Rental:*-0.94 *Council/HA:* -0.41
Trouble with Police	No Cases	0.73	1.32	0.5*	1.04	*Rental:* -0.03 *Council/HA:* 0.12
Crime Convictions	No Cases	1.42	0.75	0.95	0.88	*Rental:* 0.94 *Council/HA:* -0.31
Partner Support	3.15	0.89	1.05	1.05	0.99	*Rental:* 0.65* *Council/HA:* 0.15
Social Network Emotional	1.01	1.18	1.02	0.94	0.99	*Rental:*-0.14 *Council/HA:* 0.19
Social Network Practical	1.2	1.03	0.72*	1.1	0.96	*Rental:* 0.35 *Council/HA:* 0.13
0-2 Years Short Adversity Index	1.11	1.0	1.0	0.97	1.03	*Rental:* -0.02 *Council/HA:* -0.03
0-2 Years Long Adversity Index	1.09	1.0	1.0	0.99	1.02	*Rental:* 0.03 *Council/HA:* -0.003
Housing Adequacy	No Cases	1.03	0.8	0.88	1.35*	*Rental:* -1.15 *Council/HA:* -0.7
Housing Basic Living	No Cases	1.01	1.4	0.95	1.13	*Rental:* -12.41 *Council/HA:* -0.57
Housing Defects	2.84	1.12	0.98	1.1	1.05	*Rental: 1.55*** *Council/HA:* 0.34
Financial Difficulties	1.59	0.9	0.84	0.76	1.21	*Rental:* -0.01 *Council/HA:* 0.24
Single Parenthood	2.05	1.39	0.87	0.91	0.98	*Rental:* 0.56 *Council/HA:* 0.4
Partner Affection	No Cases	1.33	1.24	0.73	1.11	*Rental:* 0.43 *Council/HA:* 0.15

Partner Cruelty	1.13	0.78	1.12	0.91	1.04	*Rental:* 0.12 *Council/HA:* 0.03
Family Size	No Cases	0.48	1.18	1.02	1.14	*Rental:* 0.28 *Council/HA:* -0.1
Family Major Problems	No Cases	0.93	1.05	1.21	0.38**	*Rental:* -12.64 *Council/HA:* -0.53
Psychopathology	5.47*	1.16	0.95	0.86	1.08	*Rental:* 0.13 *Council/HA:* 0.29
Substance Abuse	1.11	0.97	1.17	0.72*	0.99	*Rental:* -0.9 *Council/HA:* -0.04
Trouble with Police	5.31	1.27	0.53	1.13	1.62*	*Rental:* 0.96 *Council/HA:* -0.27
Crime Convictions	No Cases	2.77	No Cases	0.72	0.55	*Rental:* 1.39 *Council/HA:* 0.2
2-4 Years Short Adversity Index	1.44	1.02	1.0	0.95	1.03	*Rental:* 0.11 *Council/HA:* 0.06

ii. Cross-sectional analyses at age 13 (*p<0.05; **p<0.01; ***p<0.001)

	Parental History of Mental Illness		Low Household Income	
	Missingness (OR)	**Complete Case Data (OR)**	**Missingness (OR)**	**Complete Case Data (OR)**
Asthma Age 13	1.19*	1.31**	1.16*	0.95
Gender	1.0	1.02	0.97	0.98
DAWBA 13	1.14	1.1	0.95	1.03
Parental History of Mental Illness	N/A	N/A	0.84*	0.97
Socio-Economic Status	1.22	0.97	N/A	N/A
DAWBA 10	0.99	1.36	0.85	1.57
DAWBA 15	1.7**	1.62*	0.97	0.93
High Levels of Health Related Absenteeism 10 Years	0.94	0.91	1.1	1.1
High Levels of Health Related Absenteeism 13 Years	1.11	1.25*	0.93	1.05
Perceptions of Fatigue	0.99	1.02	1.0	1.03
Inter-Parental Conflict 9 Years	0.96	1.01	0.93	1.02
Inter-Parental Conflict 12 Years	1.04	0.97	0.99	0.88
Parental Monitoring 12 Years	0.99	0.99	1.01	1.0
Parental Monitoring 13 Years	1.0	0.99	1.0	0.99
Parental Monitoring 15 Years	1.0	0.99	1.0	0.93**
Child Disclosures 12 Years	1.0	0.99	1.0	1.02
Child Disclosures 13 Years	1.0	0.98	1.0	0.98
Child Disclosures 15 Years	0.99	1.0	1.03	0.95

Parental Solicitation 12 Years	0.98	0.99	0.99	1.02
Parental Solicitation 13 Years	1.01	0.98	1.0	0.98
Parental Solicitation 15 Years	1.01	1.01	1.01	0.89**
Parental Control 12 Years	0.99	1.0	1.0	1.02
Parental Control 13 Years	1.02	0.99	1.0	0.98
Parental Control 15 Years	0.99	0.96	0.99	1.01
Satisfaction with Peer Relationships 10 Years	0.98	1.06*	1.03	1.03
Satisfaction with Peer Relationships 12 Years	0.99	1.03	1.02	1.02
Peer Vicimisation 10 Years	1.02	0.96	0.78**	1.15
Peer Vicimisation 12 Years	0.88	1.17	0.98	0.87
Early Parenthood	0.97	1.03	0.91	0.77
Housing Adequacy	0.86	1.16	0.99	1.24
Housing Basic Living	1.31	1.11	0.96	0.8
Housing Defects	0.98	1.19	1.05	1.01
Low Educational Attainment	1.07	1.38*	1.03	1.13
Financial Difficulties	0.77	0.86	1.41**	0.97
Single Parenthood	1.02	1.39	1.05	1.21
Partner Affection	0.82	1.01	0.87	0.7
Partner Cruelty	0.89	0.82	0.97	0.72

Family Size	0.85	1.05	1.04	0.73
Family Major Problems	0.81	0.82	1.23	1.43
Psychopathology	0.77	0.87	1.18*	0.82
Substance Abuse	0.74	0.65	0.96	1.75*
Trouble with Police	0.74	0.81	1.15	0.56
Crime Convictions	0.4	No Cases	1.6	2.81
Social Network Emotional	0.87	1.23	1.0	1.08
Social Network Practical	0.94	1.32	1.39	0.79
Pregnancy Short Adversity Index	0.94	0.99	1.03	0.99
Pregnancy Long Adversity Index	0.95	1.0	1.03	0.99
Housing Adequacy	0.96	0.75	1.15	1.05
Housing Basic Living	1.08	0.66	0.99	0.88
Housing Defects	1.07	1.28	1.08	0.99
Financial Difficulties	0.99	0.9	1.37**	0.81
Single Parenthood	0.78	0.71	0.97	1.07
Partner Affection	0.87	0.99	1.19	0.91
Partner Cruelty	0.76	0.81	1.19	0.91
Family Size	1.13	0.94	1.02	0.61
Family Major Problems	0.65	0.82	0.86	0.5

Psychopathology	0.99	0.82	1.05	1.08
Substance Abuse	0.85	0.84	0.99	1.27
Trouble with Police	1.01	0.54*	1.06	1.24
Crime Convictions	0.91	1.22	1.02	1.24
Partner Support	1.01	0.98	1.1	0.65*
Social Network Emotional	0.89	1.09	1.33**	1.12
Social Network Practical	0.72	1.21	1.38**	1.16
0-2 Years Short Adversity Index	0.97	0.96	1.04	1.0
0-2 Years Long Adversity Index	0.97	0.98	1.04*	1.0
Housing Adequacy	0.93	0.7	1.64**	1.44
Housing Basic Living	1.26	0.69	0.73	1.42
Housing Defects	1.18	1.44*	0.84	1.64*
Financial Difficulties	0.82	0.65	1.34	1.26
Single Parenthood	0.58*	1.1	1.2	1.37
Partner Affection	0.88	0.73	1.04	1.2
Partner Cruelty	0.74	1.03	1.12	1.13
Family Size	1.12	0.96	0.9	0.83
Family Major Problems	1.43	1.64	0.65	0.37
Psychopathology	0.78	0.87	0.94	1.54

Substance Abuse	1.07	0.68*	1.0	1.07
Trouble with Police	0.69	0.8	1.33	2.53**
Crime Convictions	0.4	No Cases	1.58	No Cases
2-4 Years Short Adversity Index	0.95	0.96	1.02	1.12*

iii. Longitudinal analyses (*p<0.05; **p<0.01; ***p<0.001)

	DAWBA 10		DAWBA 13		DAWBA 15		Parental History of Mental Illness		Low Household Income	
	Missingness (OR)	Complete Case Data (OR)	Missingness (OR)	Complete Case Data (OR)	Missingness (OR)	Complete Case Data (OR)	Missingness (OR)	Complete Case Data (OR)	Missingness (OR)	Complete Case Data (OR)
Asthma Diagnosis	5.45	1.6**	No Cases	1.79**	1.31***	1.77**	1.41***	1.38**	1.09	1.02
Gender	0.8	0.64	0.73**	0.54**	0.82**	1.31	1.05	1.03	0.95	0.94
DAWBA 10	N/A	N/A	1.73**	18.65***	1.55**	6.41***	1.04	1.37	0.79	1.47
DAWBA 13	No Cases	18.65***	N/A	N/A	1.55*	15.16***	1.15	1.3	1.1	1.22
DAWBA 15	16.38*	6.41***	0.88	15.16***	N/A	N/A	1.88**	1.62*	0.95	1.09
Parental History of Mental Illness	1.88	1.37	0.96	1.3	1.14	1.62*	N/A	N/A	0.86	1.1
Socio-Economic Status	4.21	1.47	1.11	1.22	1.09	1.09	1.4	1.1	N/A	N/A
High Levels of Health Related Absenteeism 10 Years	4.68	1.94***	2.61***	1.3	1.34**	1.53*	1.06	1.08	1.07	0.88
High Levels of Health Related Absenteeism 13 Years	1.25	1.28	No Cases	1.64**	1.21*	1.53*	1.21	1.26	0.98	1.09
Perceptions of Fatigue	1.05	1.03	1.03	1.03	1.01	1.09***	0.99	1.03*	1.0	1.03*

Inter-Parental Conflict 9 Years	No Cases	1.08	1.13	1.0	1.05	0.98	0.99	1.09	0.98	1.07
Inter-Parental Conflict 12 Years	No Cases	1.0	1.04	0.97	1.07	1.2	1.09	0.95	1.03	0.97
Parental Monitoring 12 Years	1.17	0.95**	0.97	0.92***	0.99	0.91	0.99	0.98	1.01	1.0
Parental Monitoring 13 Years	1.06	0.94***	0.97	0.9***	0.99	0.9***	1.0	0.99	1.0	0.97*
Parental Monitoring 15 Years	1.12	0.88***	1.01	0.78***	No Cases	0.84***	1.0	0.99	1.0	0.91***
Child Disclosures 12 Years	1.15	0.98	0.97	0.92**	0.99	0.91***	0.99	0.97*	0.99	1.0
Child Disclosures 13 Years	1.31	0.94**	0.96	0.87***	0.96**	0.96	1.02	0.97*	1.0	0.97
Child Disclosures 15 Years	2.0	0.93	0.96	0.85***	No Cases	0.93**	0.99	0.96	1.0	1.01
Satisfaction with Peer Relationships 10 Years	1.14	1.08	0.97	1.03	0.98	1.1*	0.96	1.04	1.02	0.99
Satisfaction with Peer Relationships 12 Years	0.9	1.1*	0.99	1.02	0.99	1.04	1.0	1.02	1.01	1.0
Peer Vicimisation 10 Years	2.17	2.85***	1.63**	2.23***	1.42***	2.53***	0.98	1.14	0.79*	1.13
Peer Vicimisation 12 Years	2.55	2.23***	1.55*	2.0**	0.87	2.59***	0.76*	1.17	0.91	0.93

Early Parenthood	23.24*	1.32	0.61	1.58	0.71*	0.87	0.73	1.15	1.04	0.63
Housing Adequacy	No Cases	0.78	0.75	1.26	0.98	1.17	0.93	1.21	1.11	1.25
Housing Basic Living	No Cases	0.67	0.52	1.05	0.92	No Cases	0.86	1.31	0.74	0.96
Housing Defects	No Cases	1.53	1.11	1.87*	1.06	1.3	0.9	1.05	1.04	0.96
Low Educational Attainment	5.88	1.09	1.13	1.27	1.11	0.95	1.02	1.49**	0.9	1.25
Financial Difficulties	No Cases	1.49	1.17	2.4**	1.29	2.37**	0.86	0.95	1.22	1.13
Single Parenthood	No Cases	1.43	0.8	1.34	0.8	1.99	0.6	1.6	0.99	1.03
Partner Affection	No Cases	0.96	0.94	1.08	1.05	1.09	0.93	1.03	0.78*	0.57*
Partner Cruelty	No Cases	0.91	1.31	1.74	0.89	1.45	0.67	0.91	1.06	0.42*
Family Size	No Cases	0.94	0.82	0.72	1.25	1.51	1.33	1.1	1.18	0.95

Family Major Problems	No Cases	1.31	0.17	1.91	0.67	1.23	0.69	0.73	1.26	0.89
Psychopathology	5.67	1.55*	1.05	1.3	1.08	1.28	0.9	0.8	1.05	0.84
Substance Abuse	7.85	1.44	1.0	0.86	1.18	1.3	0.9	0.57	0.94	1.35
Trouble with Police	No Cases	0.99	1.29	1.15	0.97	0.64	0.98	0.88	1.04	0.54
Crime Convictions	No Cases	No Cases	No Cases	No Cases	0.17	1.72	0.6	No Cases	2.15	8.34
Social Network Emotional	No Cases	0.5	0.99	1.08	1.23	1.28	0.66	1.12	0.87	0.85
Social Network Practical	No Cases	0.89	0.82	0.88	1.18	0.84	0.82	1.42	1.22	0.69
Pregnancy Short Adversity Index	1.46	1.13*	1.0	1.2**	1.01	1.11	0.94	1.01	1.0	0.96
Pregnancy Long Adversity Index	1.25	1.08	1.0	1.14*	1.02	1.09	0.95	1.01	1.0	0.96
Housing Adequacy	No Cases	0.97	1.03	1.17	0.8	0.96	0.87	0.68	1.09	1.16

Housing Basic Living	No Cases	0.47	0.74	0.99	1.04	0.44	1.16	0.58	1.07	0.83

Housing Defects	No Cases	0.82	1.22	1.16	0.92	0.99	0.99	1.23	1.05	0.98
Financial Difficulties	No Cases	1.21	0.85	1.08	1.04	1.3	0.92	1.05	1.45**	0.79
Single Parenthood	No Cases	1.06	1.29	0.8	0.99	1.2	0.86	0.82	1.06	0.78
Partner Affection	5.82	1.12	0.92	1.2	1.08	0.99	0.88	0.94	1.08	0.73
Partner Cruelty	5.95	0.52*	1.15	1.2	1.05	1.06	1.07	0.76	1.21	0.85
Family Size	15.02	0.34	1.2	1.71	1.2	2.16*	1.26	0.98	1.17	0.89
Family Major Problems	No Cases	0.53	0.96	1.73	0.89	1.56	1.04	0.99	1.04	0.65
Psychopathology	3.62	1.43	0.71	1.49	1.03	1.43	1.02	0.8	0.95	0.89
Substance Abuse	6.22	0.97	1.48*	0.57	0.99	0.9	0.85	0.79	0.95	1.52*
Trouble with Police	No Cases	1.08	1.04	0.54	0.87	0.96	0.95	0.4*	0.85	1.17
Crime Convictions	No Cases	0.85	1.56	No Cases	1.69	No Cases	0.62	1.25	0.78	1.56
Partner Support	4.14	1.13	1.12	0.86	0.97	0.95	1.16	0.93	0.97	0.74

Social Network Emotional	No Cases	1.06	1.0	1.41	1.05	1.48	1.0	0.88	1.17	0.89
Social Network Practical	No Cases	0.98	1.03	1.44	1.05	0.96	0.72	1.2	1.18	1.11
0-2 Years Short Adversity Index	1.42	1.01	1.03	1.07	1.0	1.05	0.99	0.96	1.03	0.99
0-2 Years Long Adversity Index	1.25	1.02	1.03	1.06	1.0	1.04	0.99	0.98	1.02	0.99
Housing Adequacy	No Cases	0.84	1.33	1.83	0.87	0.52	0.76	0.7	1.41*	1.58
Housing Basic Living	No Cases	1.0	1.26	0.58	2.11	No Cases	1.37	0.5	0.72	0.89
Housing Defects	No Cases	0.97	1.06	1.37	0.98	1.72	1.09	1.32	0.85	1.69
Financial Difficulties	No Cases	0.83	1.41	0.59	0.94	1.64	0.76	0.65	1.36	1.04
Single Parenthood	No Cases	1.35	1.26	2.08	1.23	1.17	0.56*	0.98	1.16	0.9

Partner Affection	No Cases	1.51	0.89	1.14	0.97	0.81	1.16	0.66	0.98	0.88

Partner Cruelty	5.7	0.94	1.01	0.88	0.95	0.66	0.91	0.92	1.0	1.18
Family Size	No Cases	0.42	1.39	2.48**	1.23	2.05*	1.17	1.13	0.97	1.06
Family Major Problems	No Cases	0.57	0.66	0.86	0.3	0.6	1.39	0.62	0.65	No Cases
Psychopathology	5.54	1.28	0.65	1.3	0.95	0.73	0.88	0.8	0.87	1.49
Substance Abuse	5.33	1.08	1.39	1.21	1.15	0.5	1.21	0.64*	0.93	1.13
Trouble with Police	24.53*	1.41	0.9	1.13	1.1	0.94	0.29*	1.0	1.03	1.62
Crime Convictions	No Cases	1.76	0.99	No Cases	0.62	No Cases	No Cases	No Cases	1.38	No Cases
2-4 Years Short Adversity Index	1.68	1.05	1.03	1.12	1.01	0.97	0.96	0.94	1.0	1.09

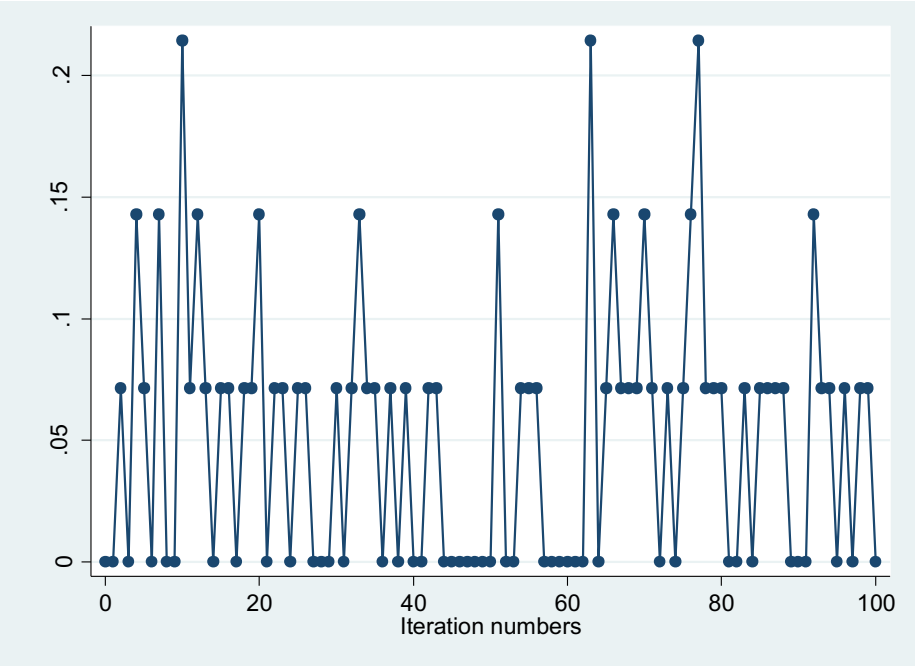
Appendix VII Convergence graphs and Monte Carlo error terms in the associative models using imputed data

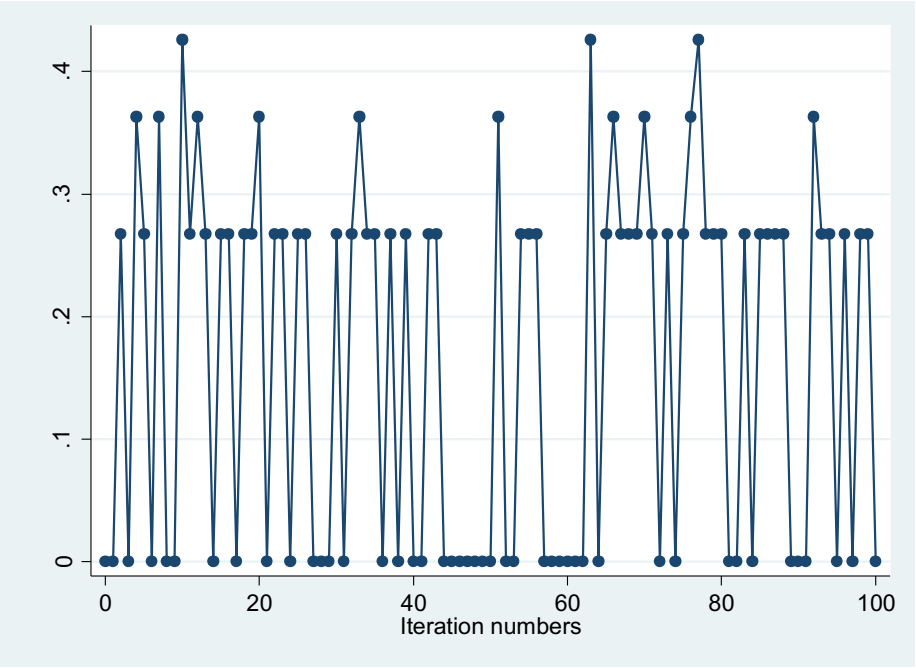
Note: If imputation models are working well, the mean values, as well as the standard deviations, from imputations at successive iterations should move about randomly in convergence graphs, and Monte Carlo error terms should be as close to 0 as possible.

Analyses Using the Chronic Illness Measure

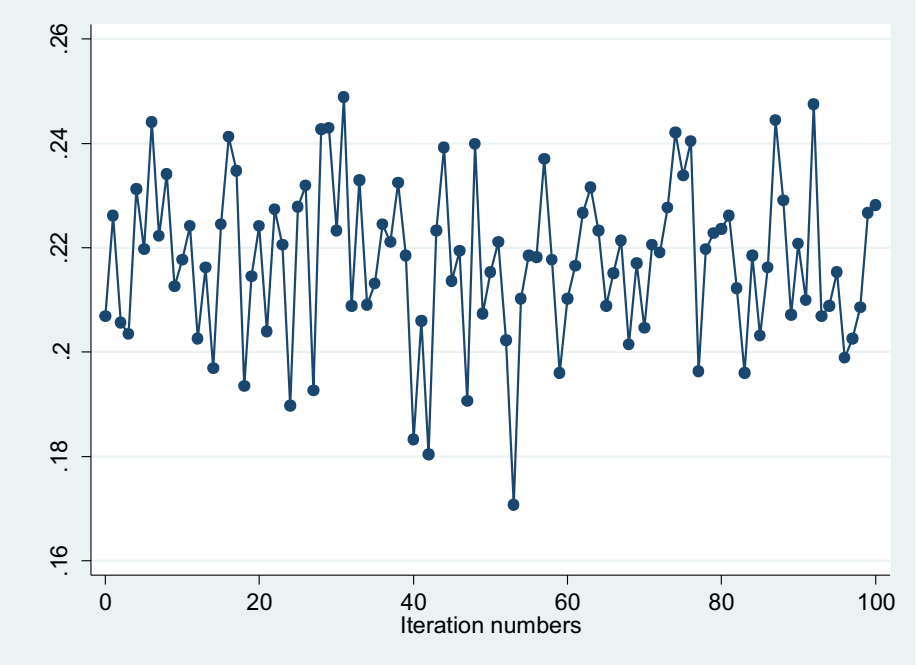
i. Cross-Sectional Analyses at Age 10

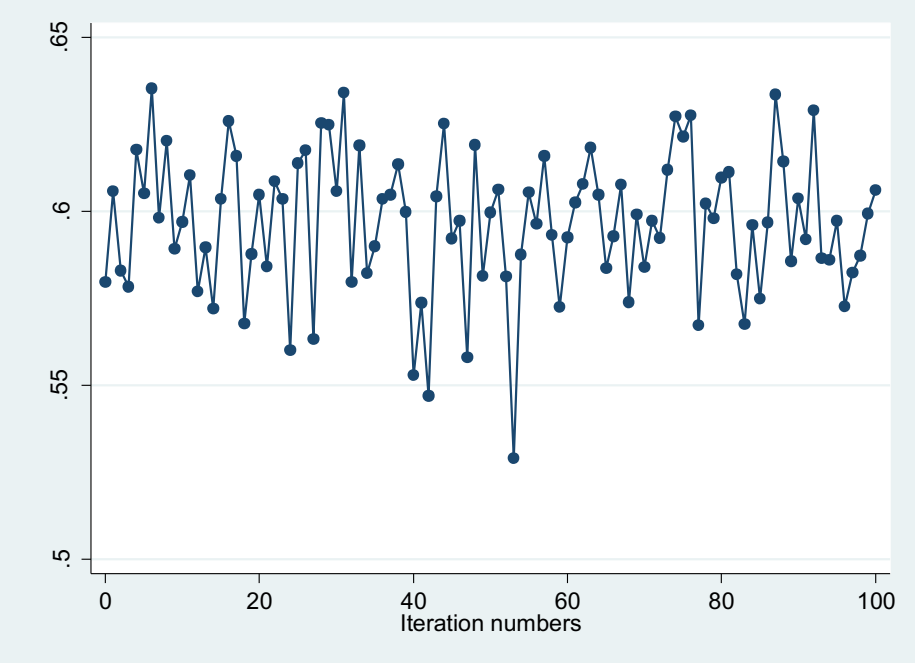
DAWBA 10



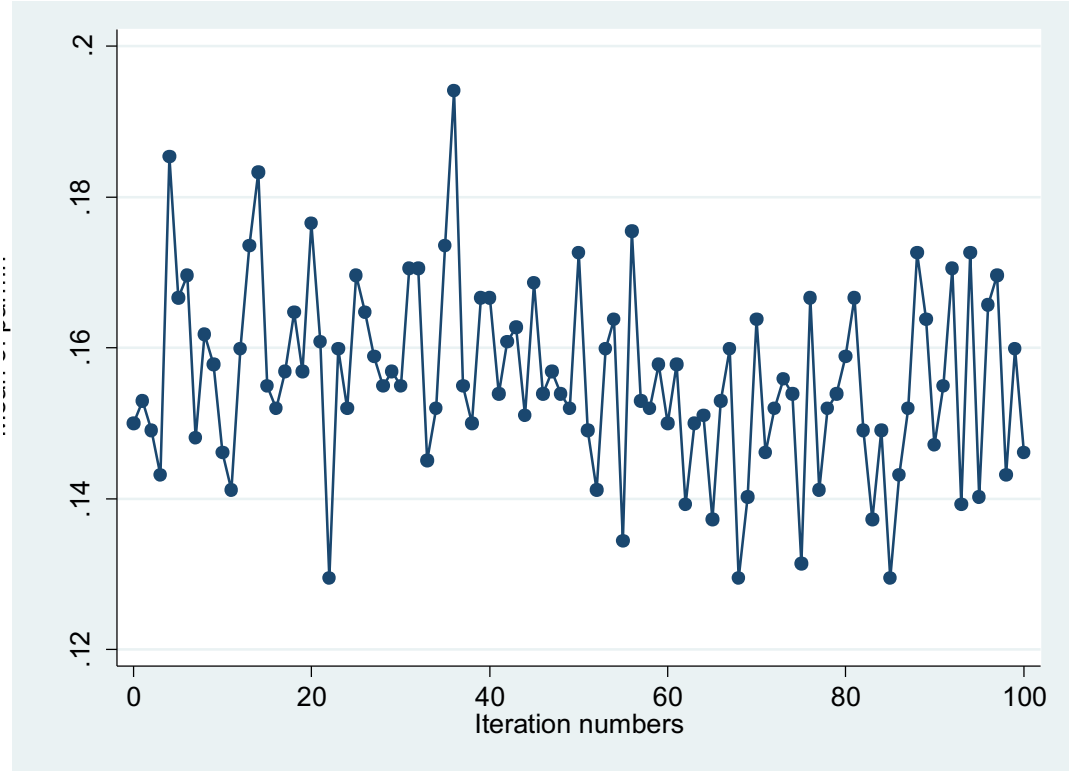

0
.1
.2
.3
.4
0
20
40
60
80
100
Iteration numbers

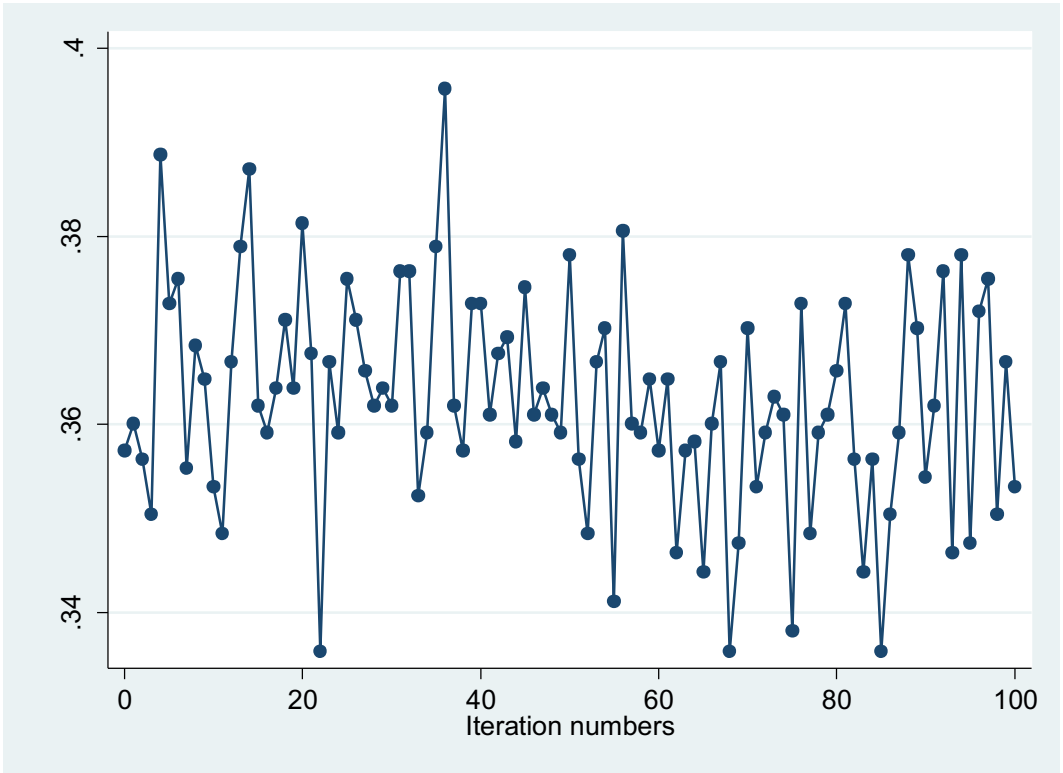
Housing Tenure





History of Parental Mental Illness





Monte Carlo Error Terms

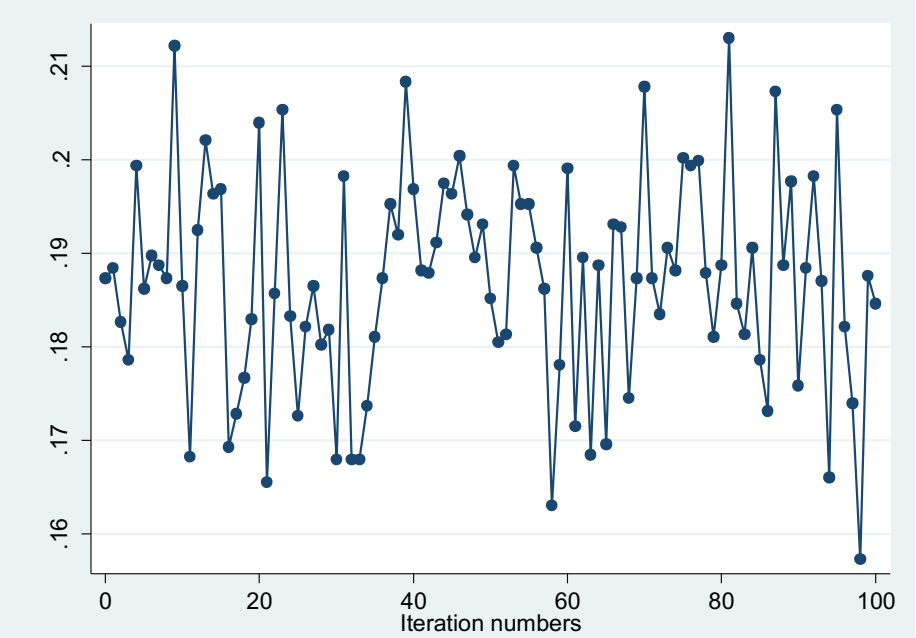
```
. mi estimate, mcerror: logistic pany01_10 i.nbaseill sex i.baseho parmh

Multiple-imputation estimates                     Imputations     =         59
Logistic regression                               Number of obs   =       5891
                                                  Average RVI     =     0.4939
                                                  Largest FMI     =     0.6443
DF adjustment:   Large sample                     DF:     min     =     141.89
                                                          avg     =  168696.98
                                                          max     =  579163.02
Model F test:       Equal FMI                     F(   6, 2571.1) =       6.71
Within VCE type:          OIM                     Prob > F        =     0.0000
```

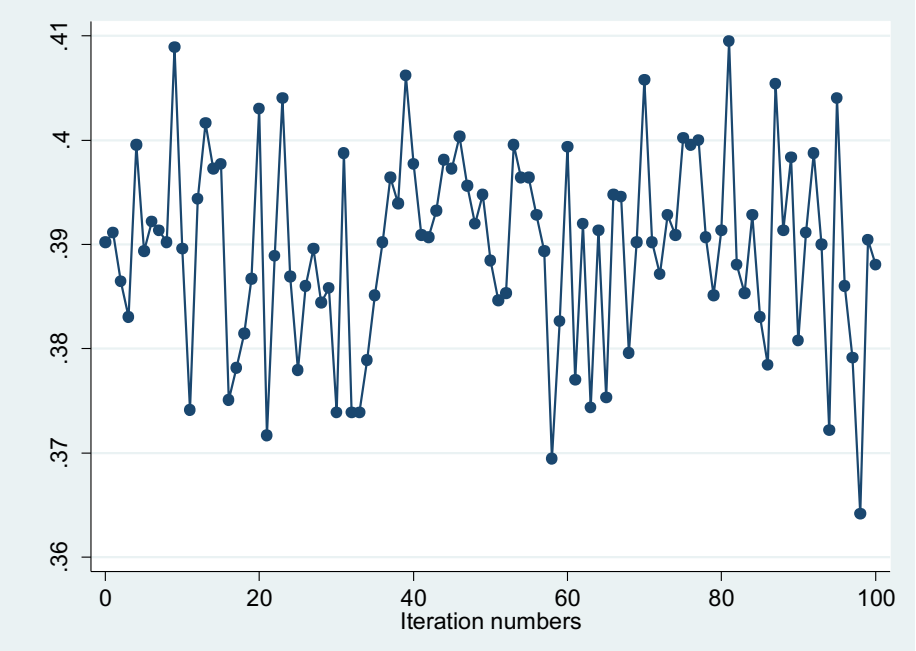
pany01_10	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
nbaseill						
2	.5184154	.1313138	3.95	0.000	.2610445	.7757863
	.0017987	.0001281	0.01	0.000	.0017519	.0018782
3	1.521894	.3450909	4.41	0.000	.8455265	2.198261
	.0044567	.0004624	0.02	0.000	.0047235	.0043655
sex	-.5086178	.1218859	-4.17	0.000	-.7475119	-.2697236
	.0022484	.0002819	0.02	0.000	.0024224	.0022034
baseho						
1	.4694078	.5218679	0.90	0.370	-.5622333	1.501049
	.0538707	.0280325	0.12	0.064	.0836741	.0716314
2	.6115991	.2553512	2.40	0.018	.1077005	1.115498
	.0248946	.0126981	0.16	0.007	.0359277	.0354641
parmh	.2044599	.1736786	1.18	0.239	-.1363196	.5452395
	.0107498	.0040393	0.08	0.030	.0151807	.0113951
_cons	-2.945372	.0985423	-29.89	0.000	-3.138579	-2.752165
	.0045766	.0011847	0.34	0.000	.0062416	.0037303

Note: values displayed beneath estimates are Monte Carlo error estimates.

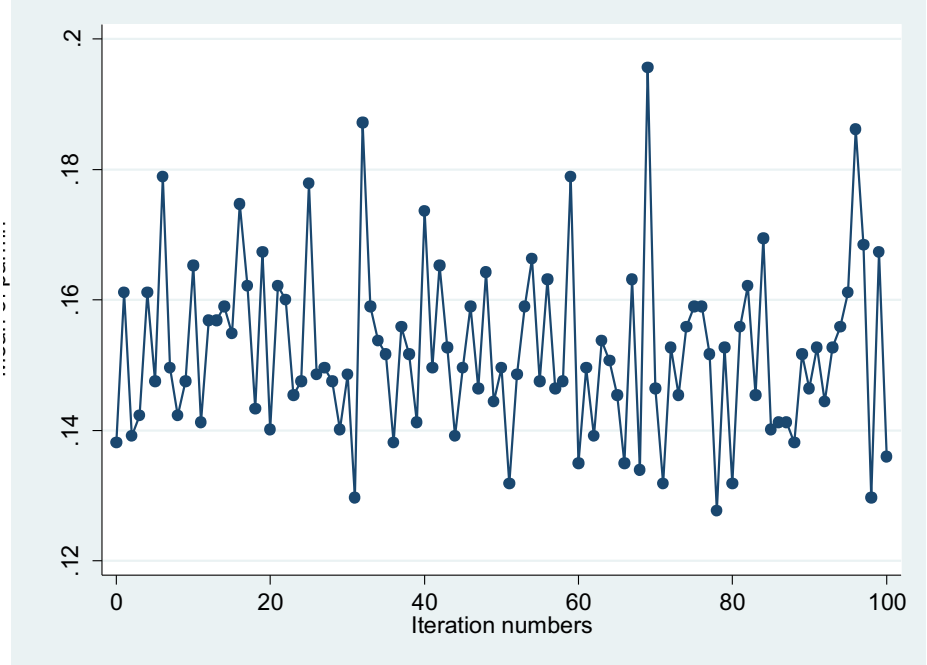
ii. Cross-Sectional Analyses at Age 13

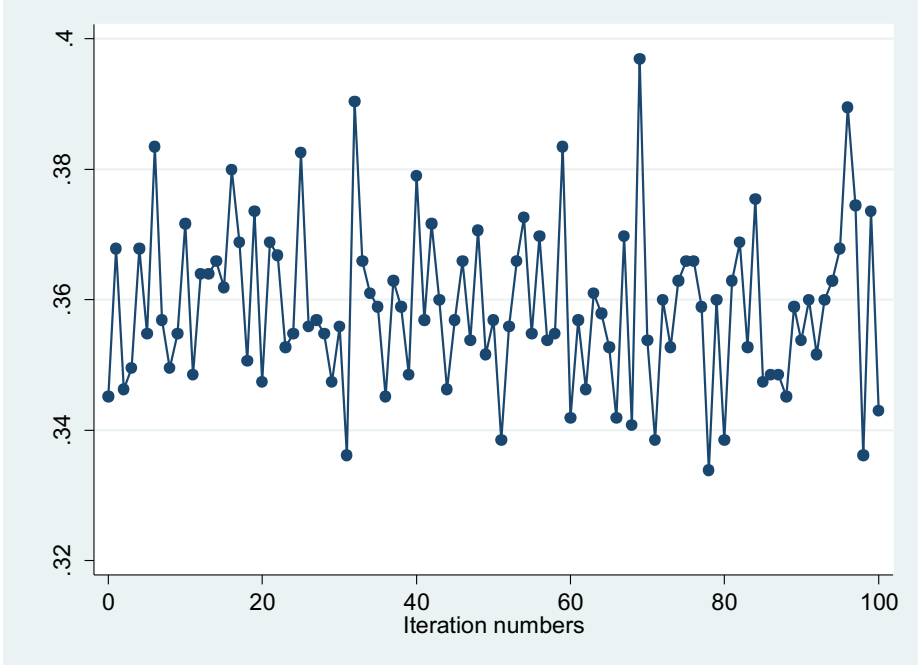
Low Household Income





History of Parental Mental Illness





Monte Carlo Error Terms

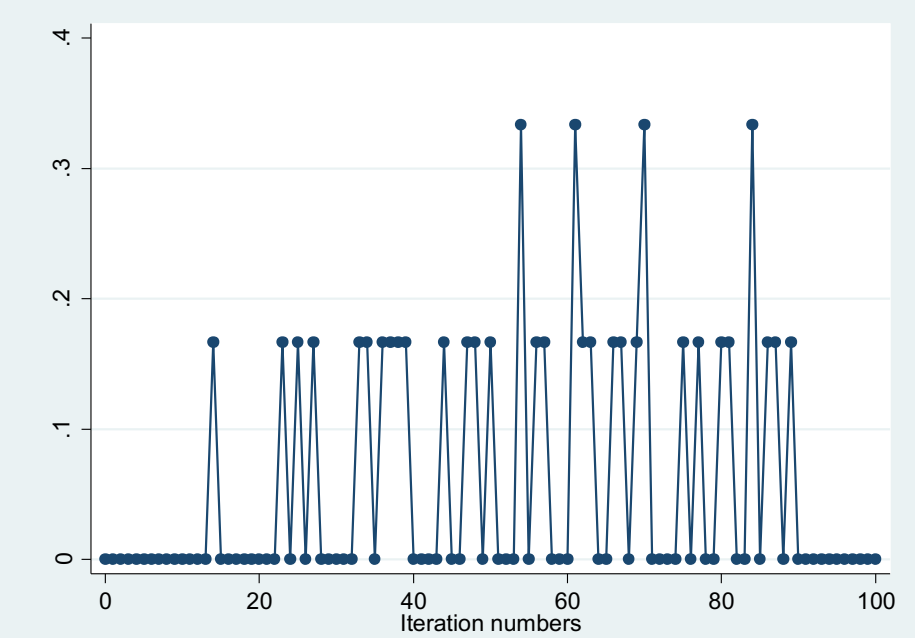
```
. mi estimate, mcerror: logistic pany01_13 i.nill13 sex fincomebin parmh

Multiple-imputation estimates                     Imputations     =         67
Logistic regression                               Number of obs   =       5429
                                                  Average RVI     =     0.3511
                                                  Largest FMI     =     0.6539
DF adjustment:   Large sample                     DF:     min     =     156.47
                                                          avg     = 8452784.04
                                                          max     =   3.07e+07
Model F test:       Equal FMI                     F(   5, 3696.0) =       4.32
Within VCE type:          OIM                     Prob > F        =     0.0006
```

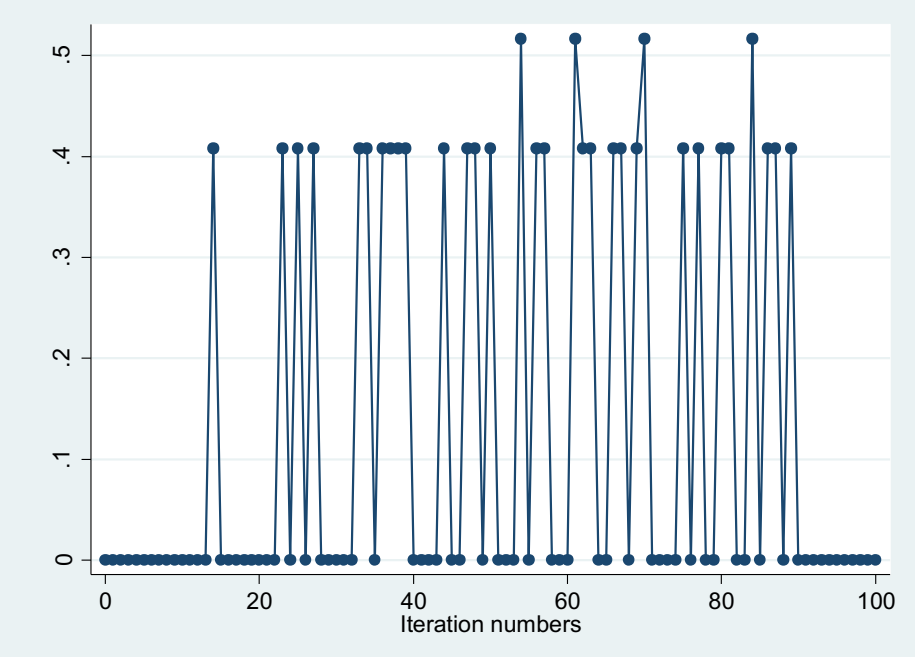
pany01_13	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
nill13						
2	.4280832	.1415295	3.02	0.002	.1506905	.7054759
	.0006569	.0000227	0.00	0.000	.0006592	.0006577
3	1.219287	.3680854	3.31	0.001	.4978526	1.940722
	.003603	.0002791	0.01	0.000	.0033651	.0039037
sex	-.4827204	.1311326	-3.68	0.000	-.7397355	-.2257052
	.0006919	.0000271	0.01	0.000	.000708	.0006797
fincomebin	-.1365428	.2901715	-0.47	0.639	-.7097015	.436616
	.0283584	.0139908	0.10	0.073	.0387483	.0410707
parmh	.0967911	.1913975	0.51	0.613	-.2786037	.4721858
	.0102562	.0034987	0.06	0.041	.0150671	.0089154
_cons	-2.906782	.1103883	-26.33	0.000	-3.12327	-2.690294
	.0057066	.0016198	0.37	0.000	.0073679	.0056087

```
Note: values displayed beneath estimates are Monte Carlo error estimates.
```

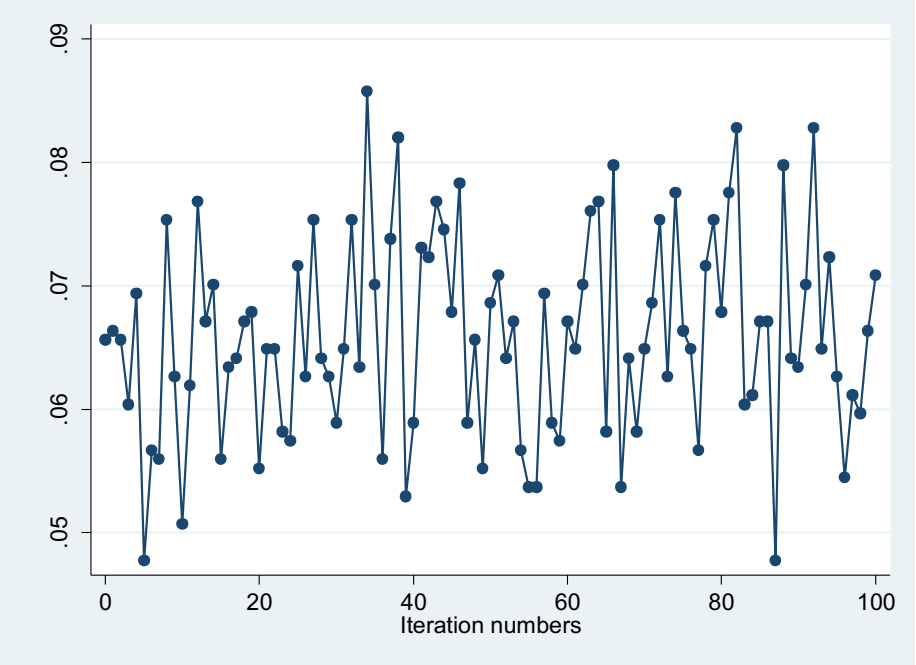
iii. Longitudinal Analyses

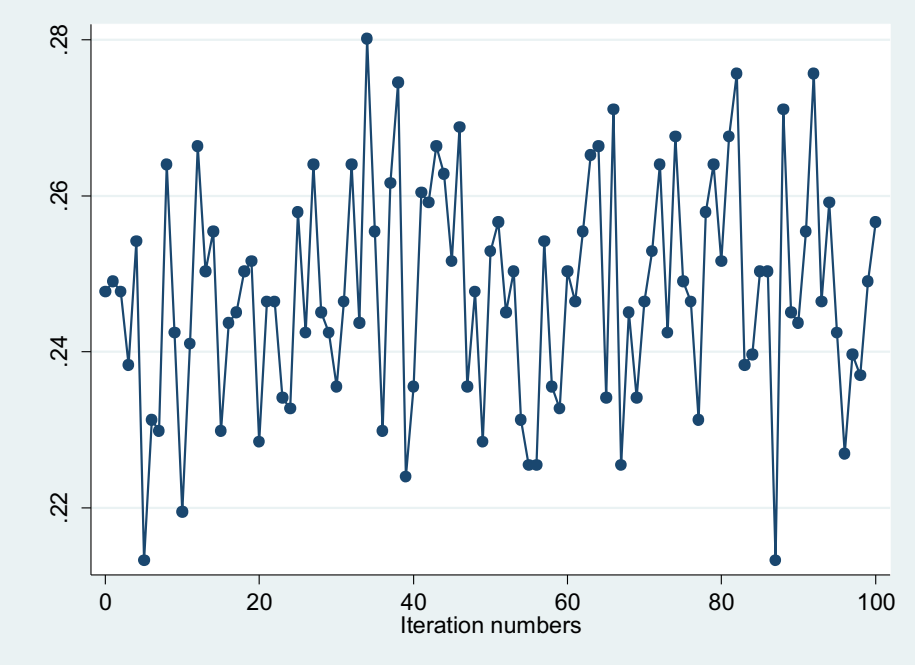
DAWBA 10 Years



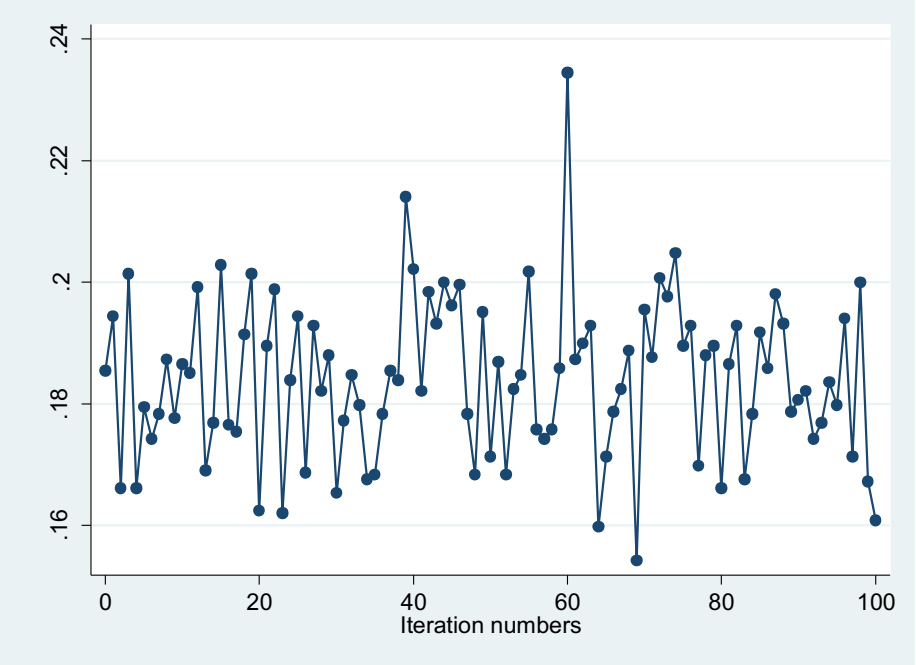


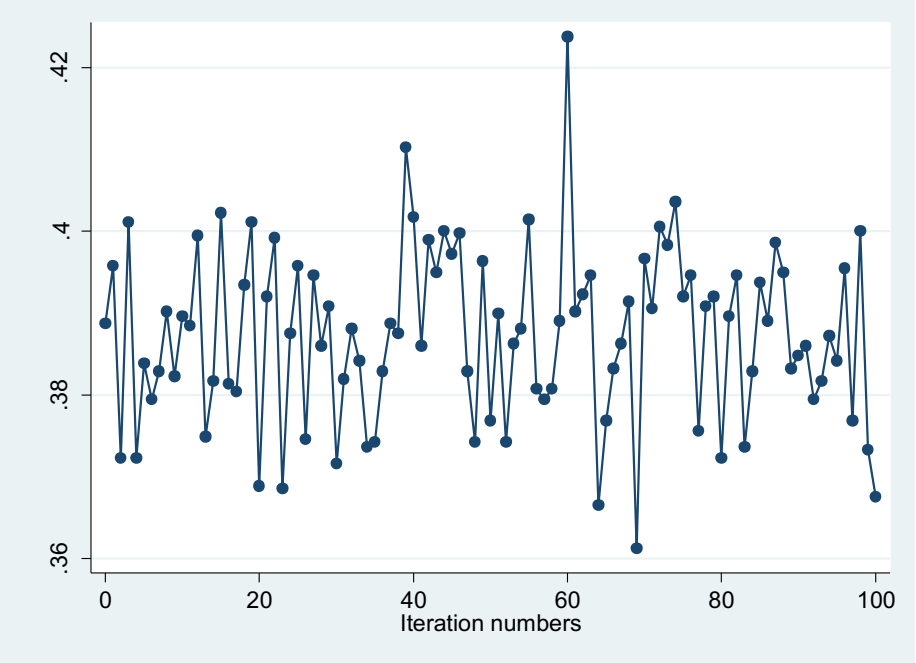
DAWBA 15 Years



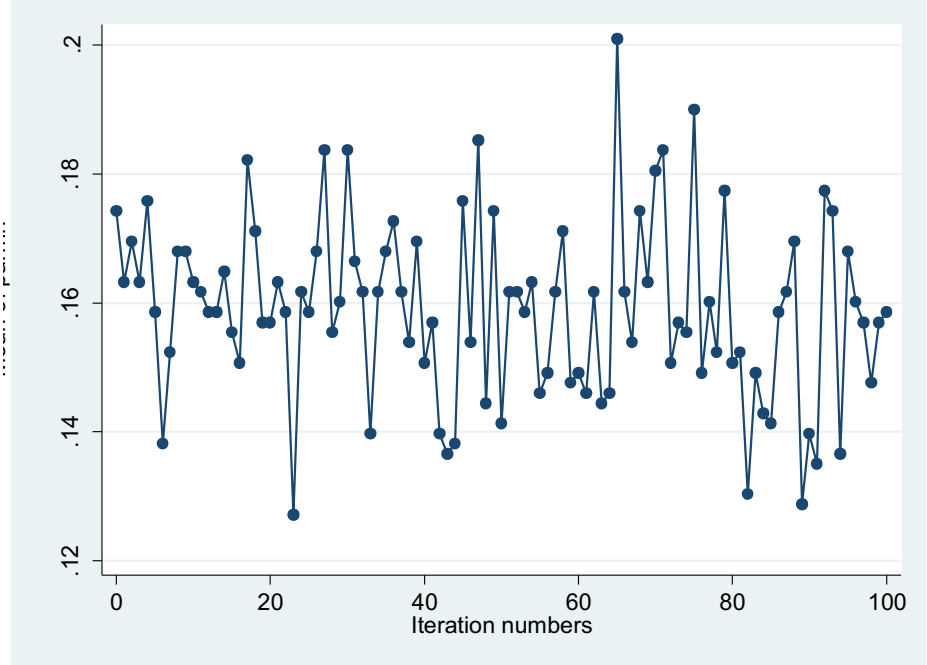


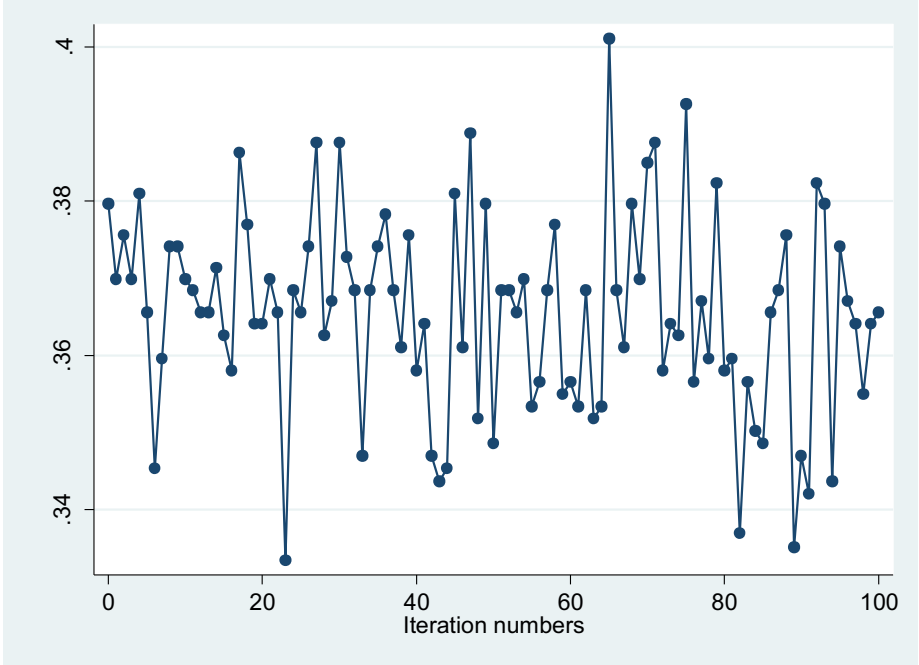
Low Household Income





History of Parental Mental Illness





Monte Carlo Error Terms

```
. mi estimate, mcerror: logistic pany01_10 longill sex fincomebin parmh

Multiple-imputation estimates                     Imputations     =         67
Logistic regression                               Number of obs   =       3984
                                                  Average RVI     =     0.4098
                                                  Largest FMI     =     0.6316
DF adjustment:   Large sample                     DF:     min     =     167.74
                                                          avg     =  141196.10
                                                          max     =  464832.76
Model F test:       Equal FMI                     F(   4, 2271.6) =       7.55
Within VCE type:          OIM                     Prob > F        =     0.0000

------------------------------------------------------------------------------
   pany01_10 |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
     longill |   .7055795   .1440855     4.90   0.000     .4231755    .9879834
             |   .0022712   .0003171     0.02   0.000     .0021539    .0025401
             |
         sex |  -.3742107   .1456231    -2.57   0.010    -.6596273    -.088794
             |   .0019277   .0001785     0.01   0.000     .0018219    .0020875
             |
  fincomebin |   .5654809   .2641906     2.14   0.034     .0439138    1.087048
             |   .0253741   .0153576     0.16   0.013     .0399434    .0399378
             |
       parmh |   .2774744   .2068055     1.34   0.180    -.1283073     .683256
             |    .012439   .0041779     0.07   0.022     .0151266    .0147881
             |
       _cons |  -3.874707   .2433505   -15.92   0.000    -4.351732   -3.397683
             |   .0087093   .0025824     0.16   0.000       .01206    .0076189
------------------------------------------------------------------------------
Note: values displayed beneath estimates are Monte Carlo error estimates.
```

```
. mi estimate, mcerror: logistic any01_15 longill sex fincomebin parmh

Multiple-imputation estimates                     Imputations     =         67
Logistic regression                               Number of obs   =       3984
                                                  Average RVI     =     1.3372
                                                  Largest FMI     =     0.8243
DF adjustment:   Large sample                     DF:     min     =      97.97
                                                          avg     =     375.97
                                                          max     =     537.16
Model F test:       Equal FMI                     F(   4,   693.5) =       2.76
Within VCE type:          OIM                     Prob > F        =     0.0268
```

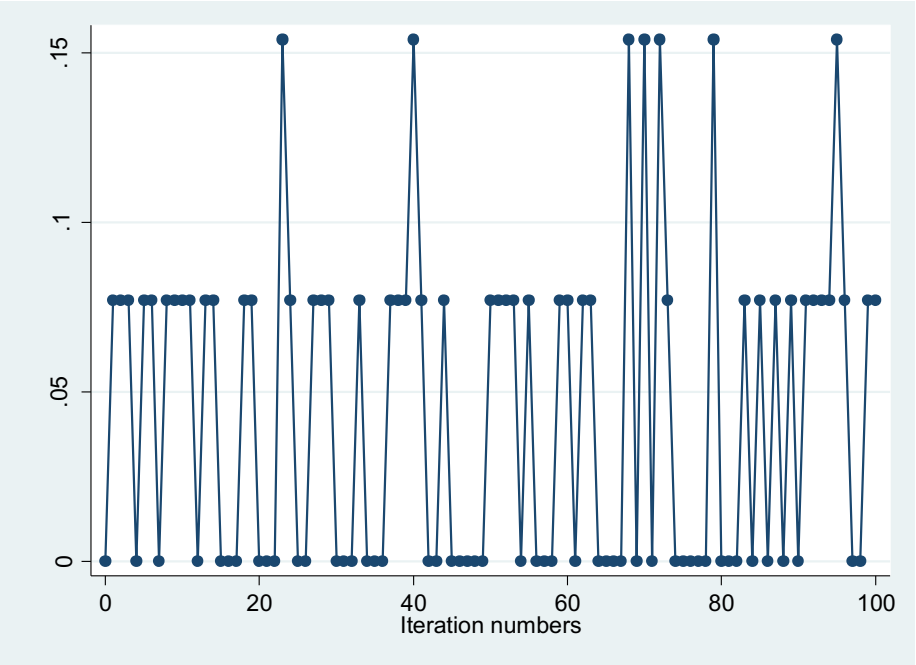
any01_15	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
longill	.4708571	.1732627	2.72	0.007	.1303352	.811379
	.0130639	.005808	0.12	0.002	.0170144	.0179344
sex	.2939611	.1674527	1.76	0.080	-.0349813	.6229036
	.0120226	.0058527	0.09	0.015	.01537	.0180581
fincomebin	.4104626	.3757485	1.09	0.277	-.3352008	1.156126
	.0412813	.0228579	0.13	0.056	.0619866	.0614183
parmh	.3483375	.2137242	1.63	0.104	-.071683	.7683581
	.0160361	.0079273	0.11	0.023	.0262186	.01812
_cons	-3.704395	.2929066	-12.65	0.000	-4.280458	-3.128332
	.0233614	.0107414	0.46	0.000	.0341736	.0291285

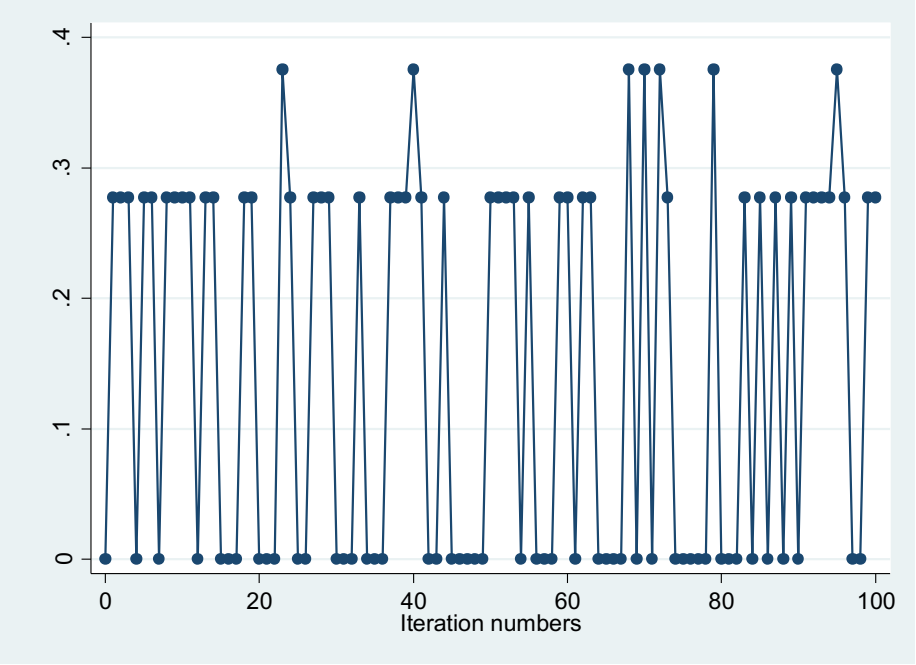
Note: values displayed beneath estimates are Monte Carlo error estimates.

Analyses Using the Measure of Asthma Diagnosis

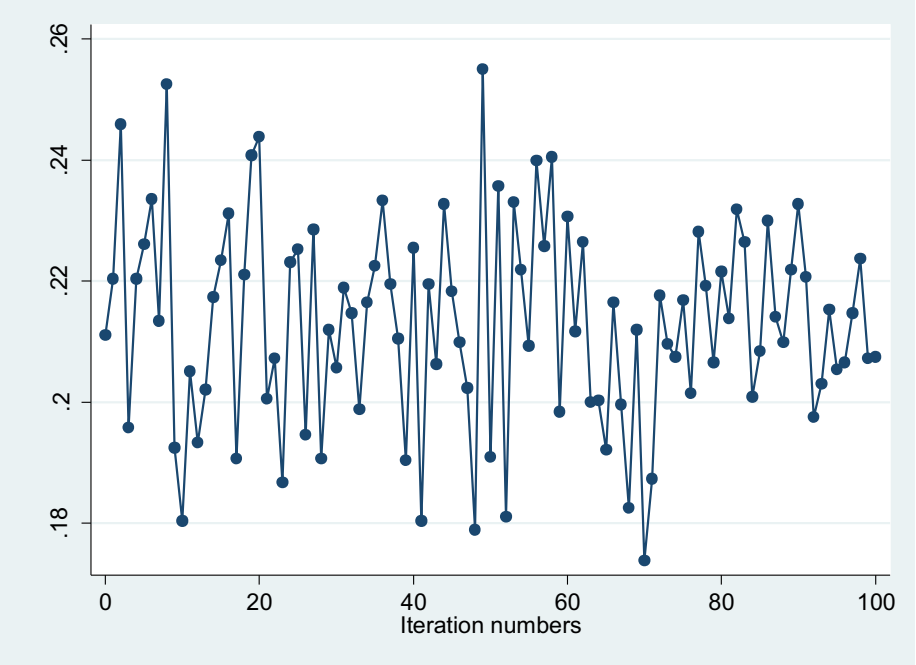
i. Cross-Sectional Analyses at Age 10

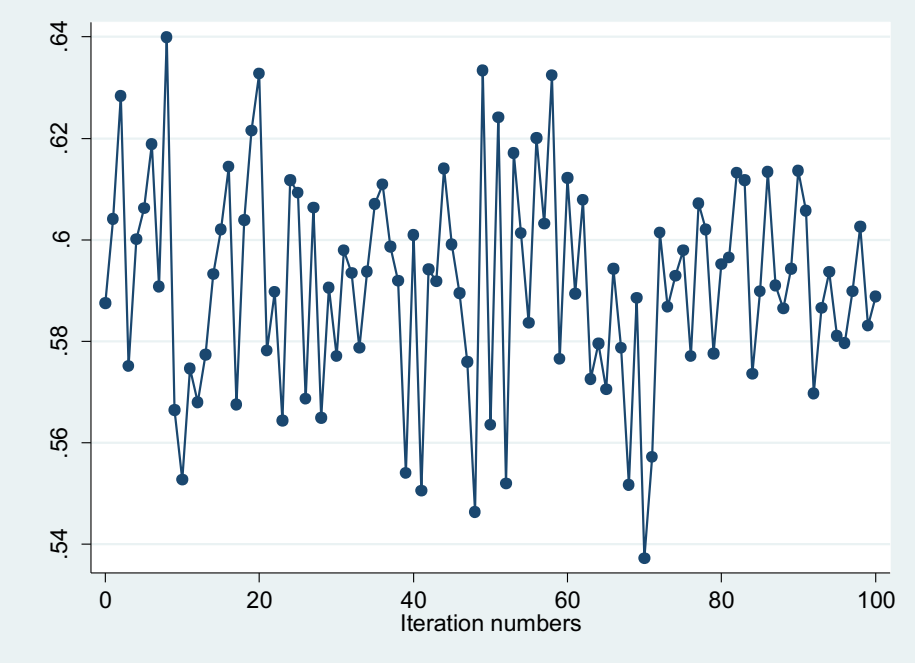
DAWBA 10 Years



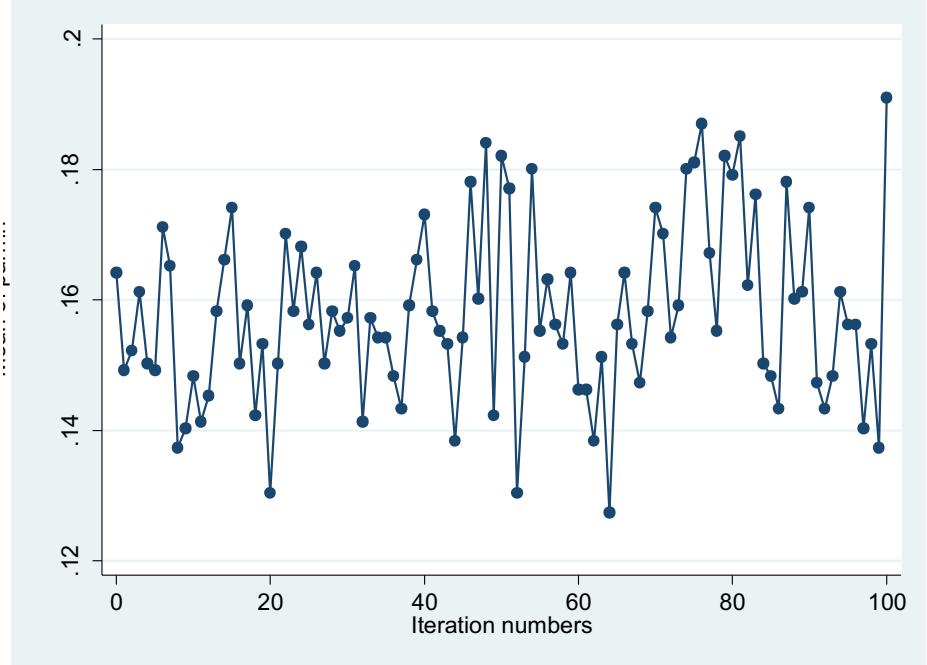


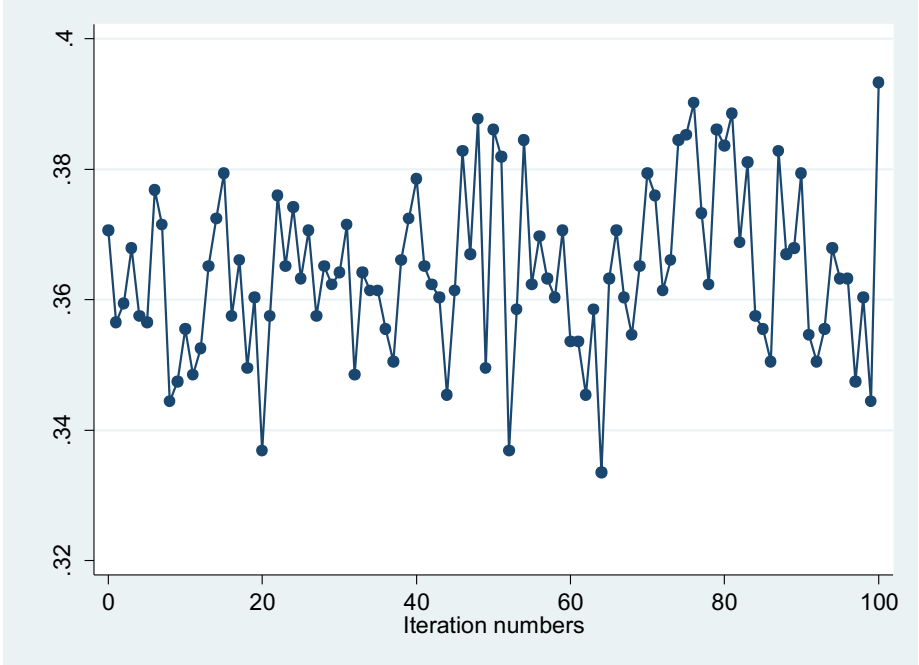
Housing Tenure





History of Parental Mental Illness





Monte Carlo Error Terms

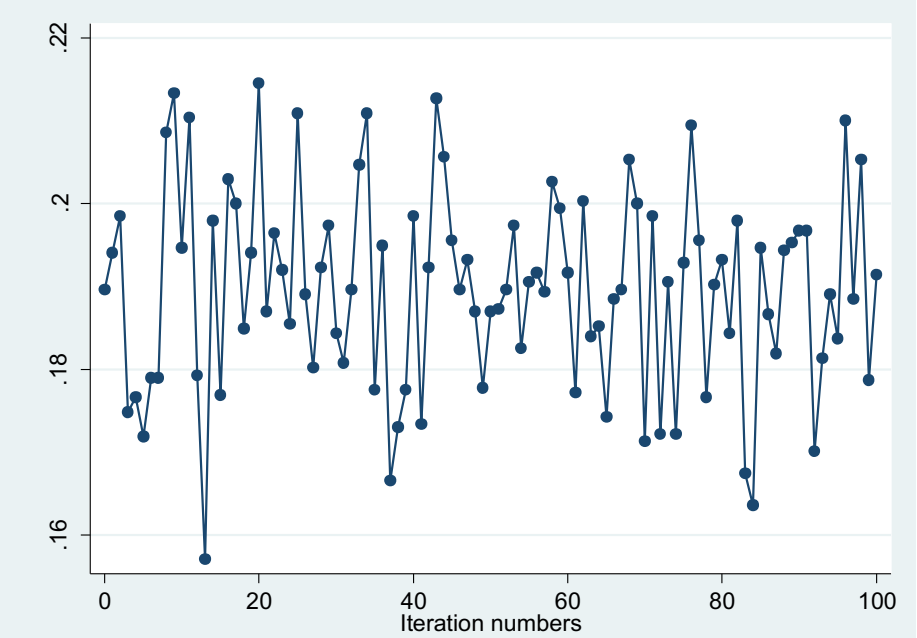
```
Multivariate imputation                      Imputations =       59
Chained equations                                added =       59
Imputed: m=1 through m=59                        updated =       0

Initialization: monotone                     Iterations =     5900
                                                burn-in =      100

             parmh: logistic regression
        fincomebin: logistic regression
         pany01_10: logistic regression
         pany01_13: logistic regression
          any01_15: logistic regression
    schoolabs10bin: logistic regression
    schoolabs13bin: logistic regression
    earlyparenth~d: logistic regression
         loweduatt: logistic regression
            baseho: multinomial logistic regression
          parmon13: linear regression
           cdisc13: linear regression
          parsol13: linear regression
         parcont13: linear regression
```

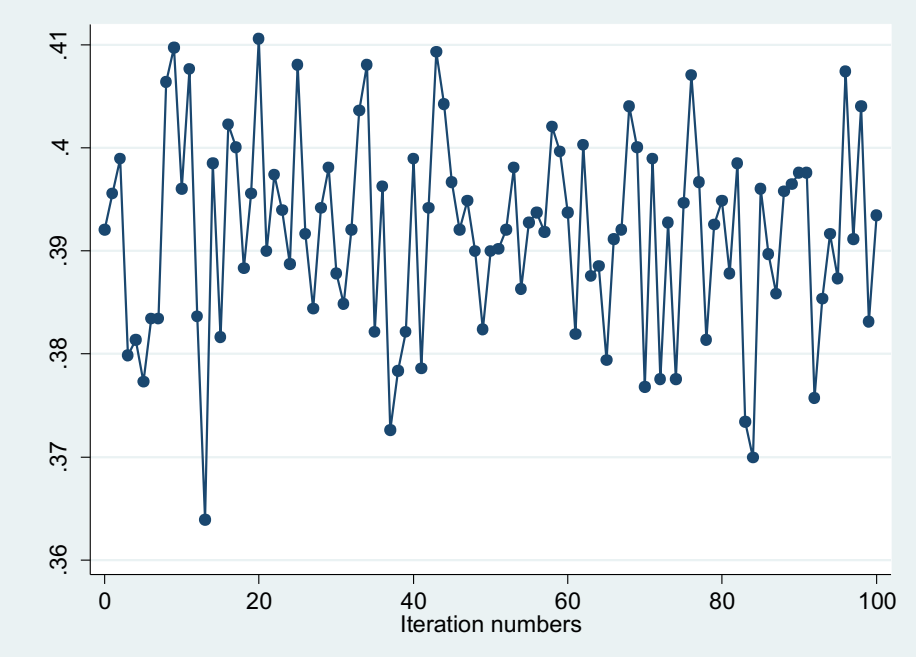
Variable	Observations per m			
	Complete	Incomplete	Imputed	Total
parmh	4554	1005	1005	5559
fincomebin	1878	3681	3681	5559
pany01_10	5546	13	13	5559
pany01_13	4497	1062	1062	5559
any01_15	3252	2307	2307	5559
schoolabs10bin	5476	83	83	5559
schoolabs13bin	4424	1135	1135	5559
earlyparenth~d	3926	1633	1633	5559
loweduatt	3490	2069	2069	5559
baseho	2233	3326	3326	5559
parmon13	3547	2012	2012	5559
cdisc13	3546	2013	2013	5559
parsol13	3551	2008	2008	5559
parcont13	3546	2013	2013	5559

```
(complete + incomplete = total; imputed is the minimum across m
 of the number of filled-in observations.)
```

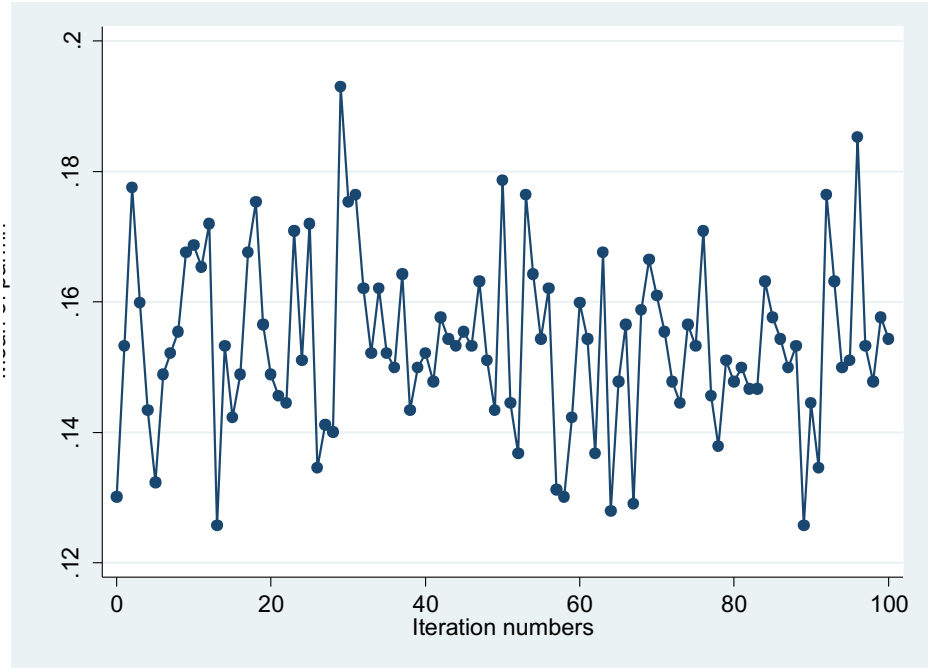
ii. Cross-Sectional Analyses at Age 13

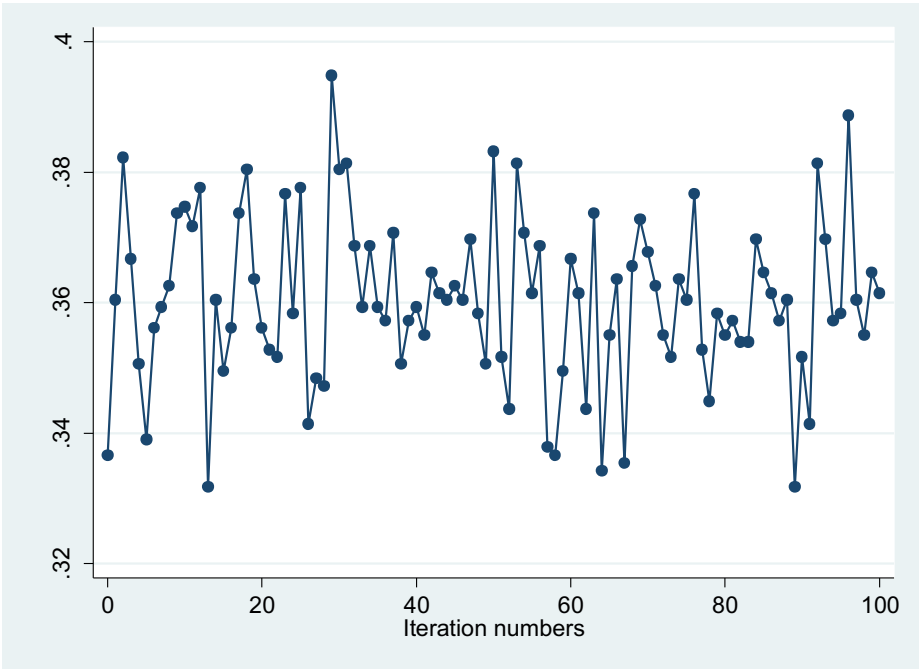
Low Household Income





History of Parental Mental Illness





Monte Carlo Error Terms

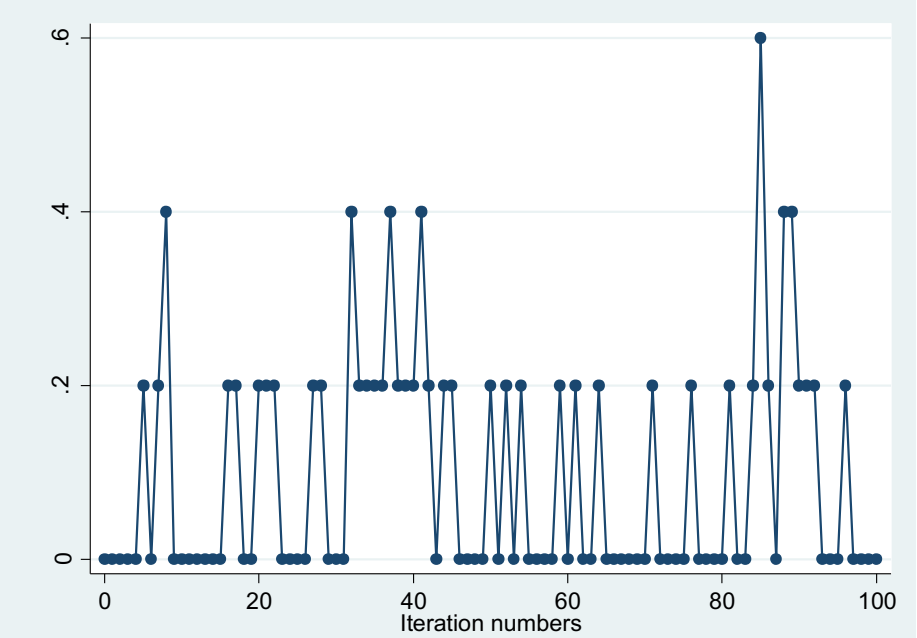
```
. mi estimate, mcerror: logistic pany01_13 asthma13 sex fincomebin parmh

Multiple-imputation estimates                     Imputations     =         67
Logistic regression                               Number of obs   =       5041
                                                  Average RVI     =     0.4642
                                                  Largest FMI     =     0.6765
DF adjustment:   Large sample                     DF:     min     =     146.13
                                                          avg     =   1.97e+07
                                                          max     =   7.36e+07
Model F test:       Equal FMI                     F(   4, 1924.7) =       2.68
Within VCE type:          OIM                     Prob > F        =     0.0304
```

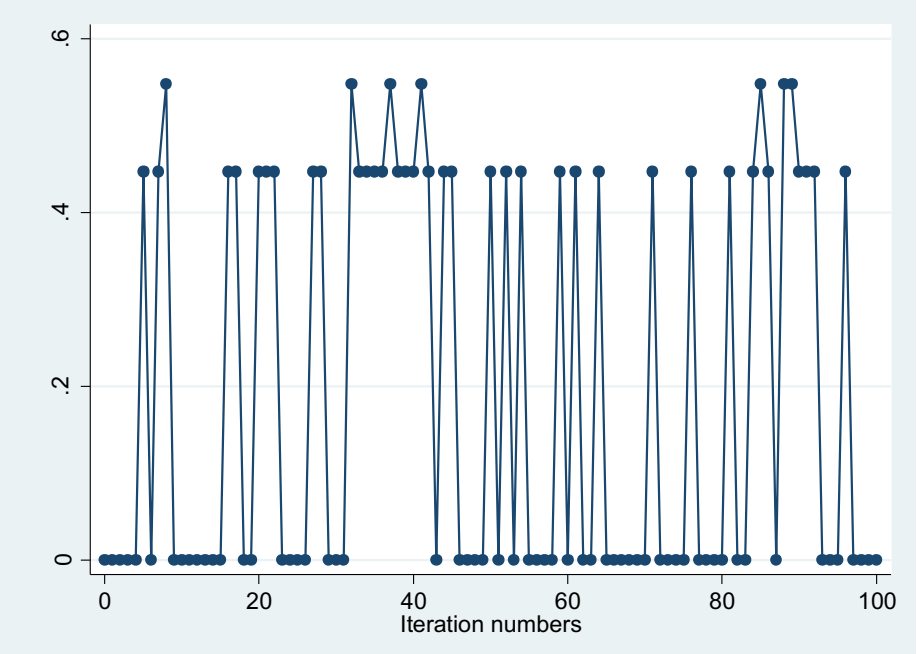
pany01_13	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
asthma13	.2532122	.1407326	1.80	0.072	-.0226186	.529043
	.0006872	.0000305	0.01	0.001	.0007102	.0006688
sex	-.512191	.1422777	-3.60	0.000	-.7910501	-.2333319
	.000531	.000028	0.00	0.000	.0005106	.0005561
fincomebin	-.0132091	.3051809	-0.04	0.966	-.6163477	.5899295
	.0303393	.0170918	0.10	0.080	.042762	.0486914
parmh	.0989427	.2082829	0.48	0.635	-.3096027	.5074882
	.0114678	.0033409	0.06	0.042	.0153021	.0107991
_cons	-2.953094	.1230677	-24.00	0.000	-3.194469	-2.711719
	.0065721	.0022958	0.43	0.000	.009632	.0059208

Note: values displayed beneath estimates are Monte Carlo error estimates.

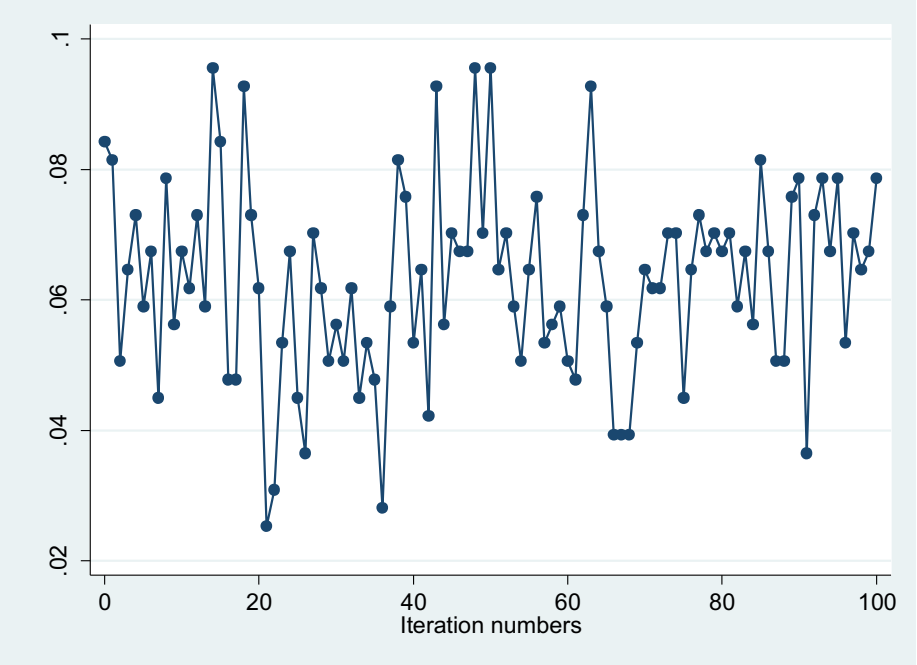
iii. Longitudinal Analyses

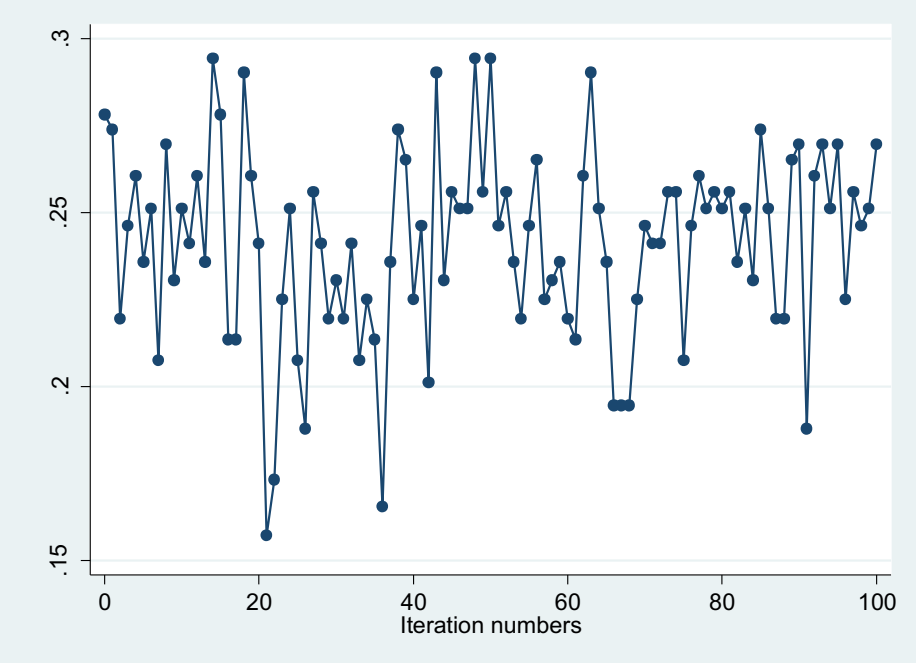
DAWBA 10 Years



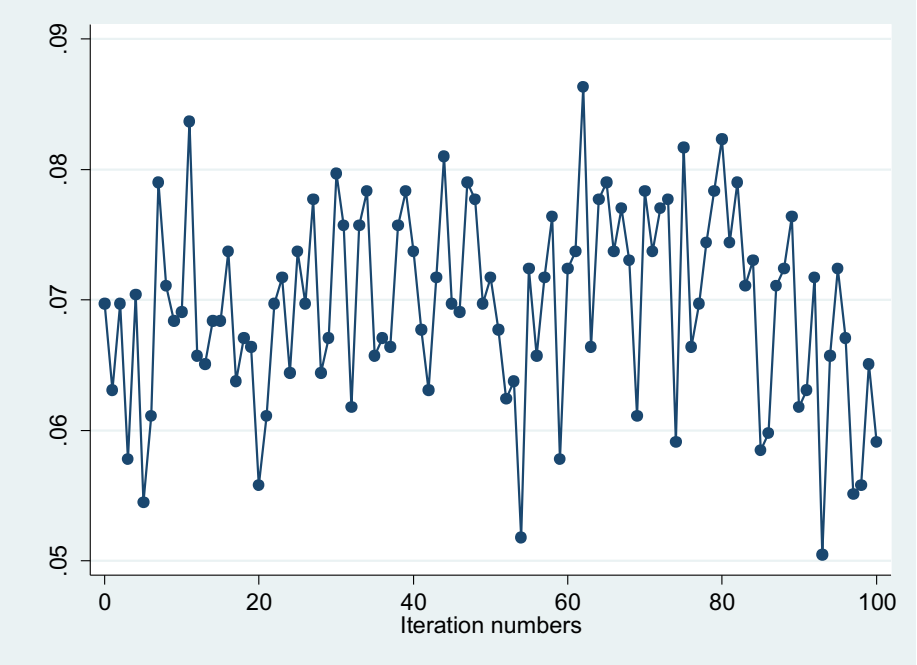


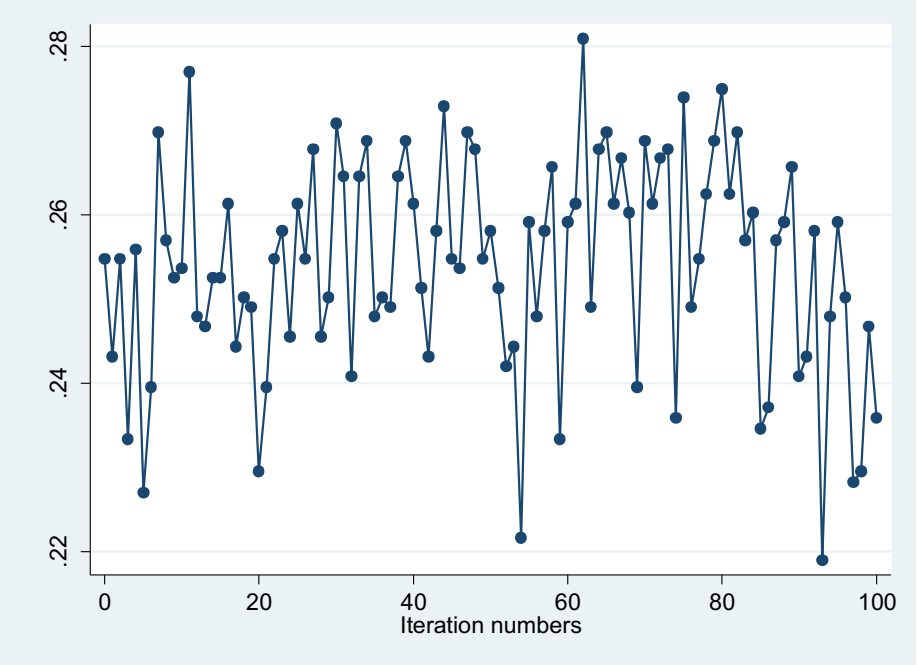
DAWBA 13 Years



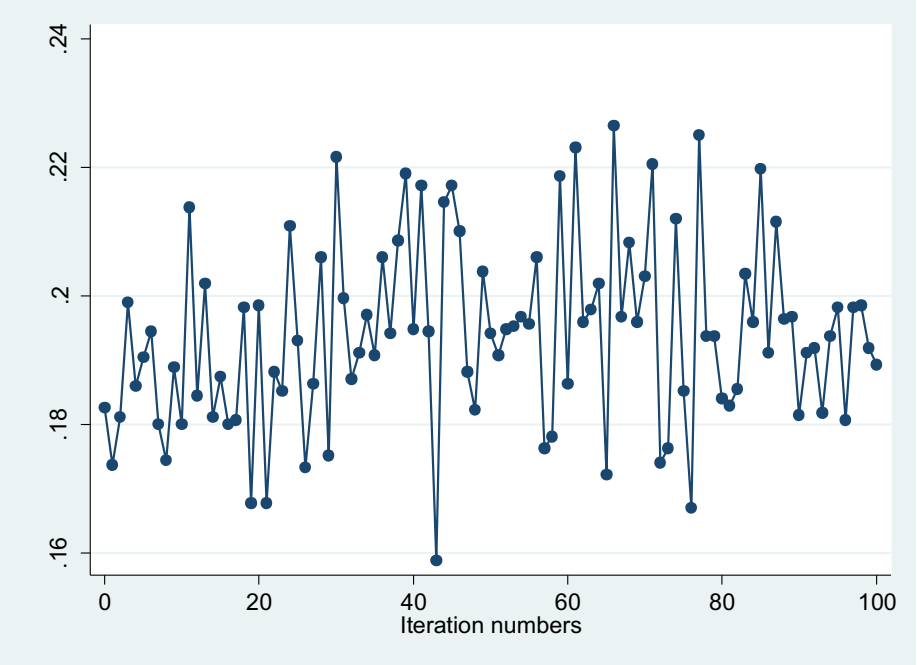


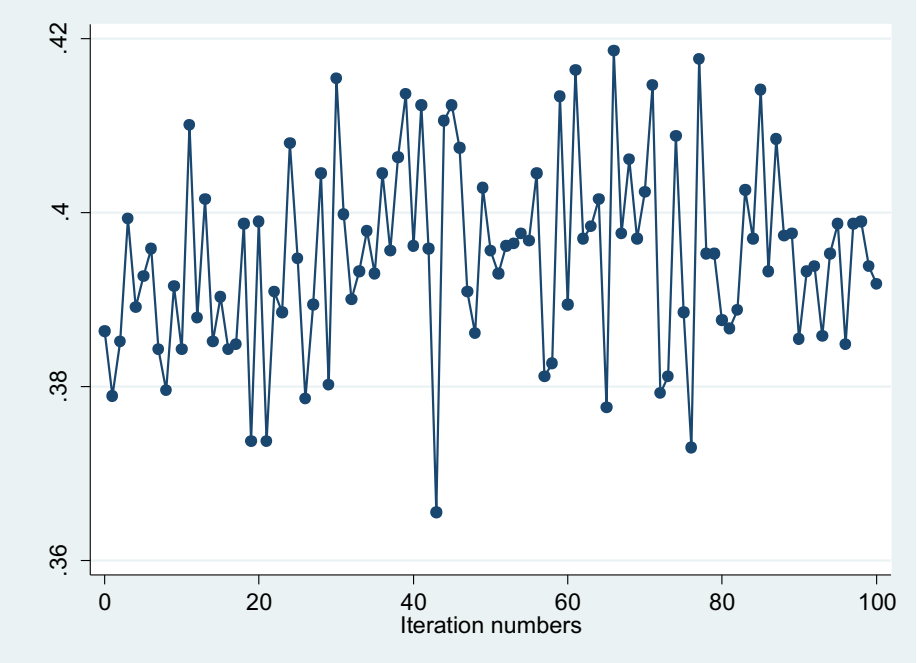
DAWBA 15 Years



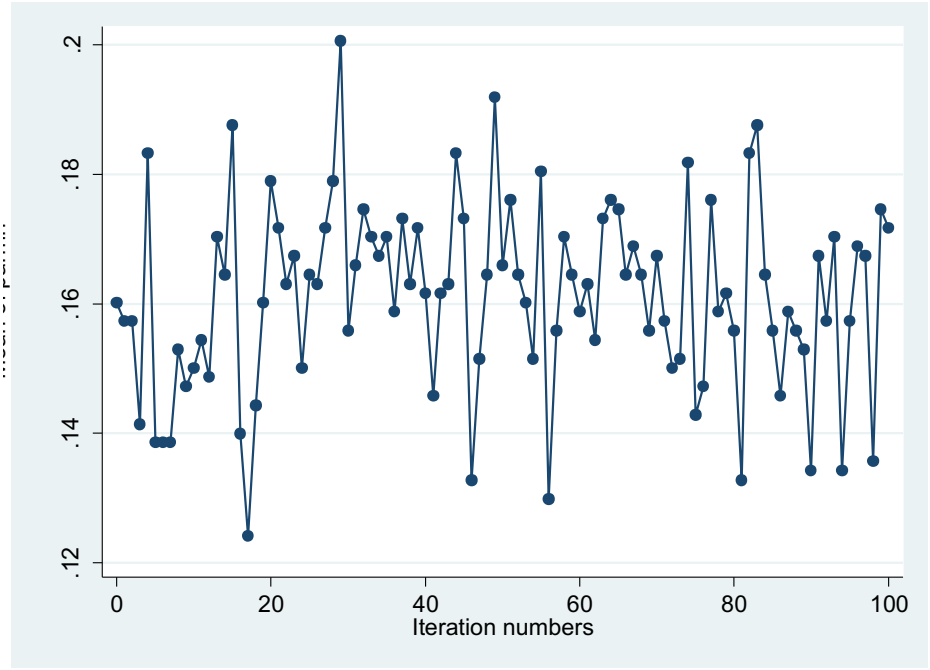


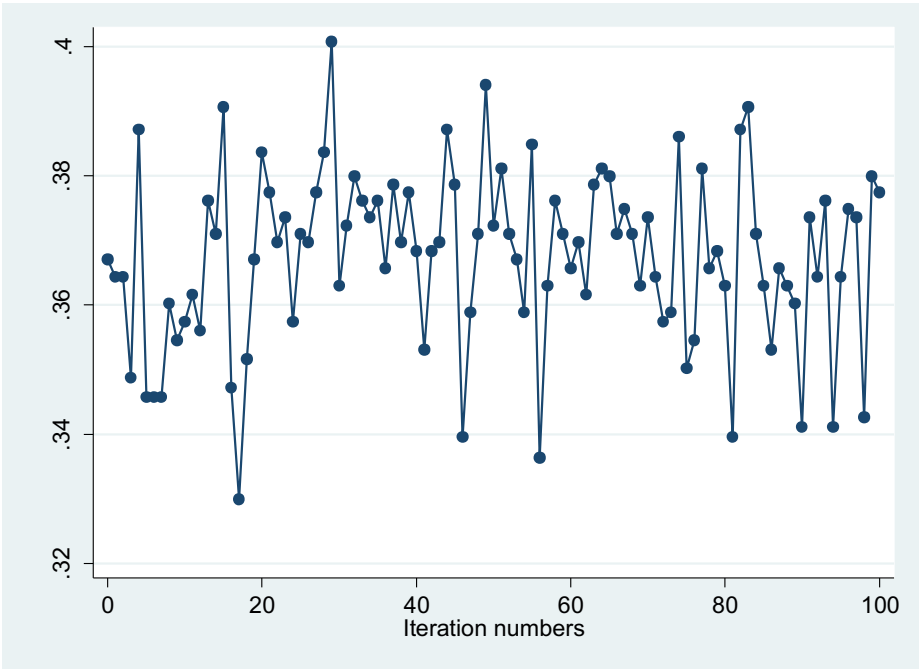
Low Household Income





History of Parental Mental Illness





Monte Carlo Error Terms

```
Multiple-imputation estimates                   Imputations     =         67
Logistic regression                             Number of obs   =       4011
                                                Average RVI     =     0.3273
                                                Largest FMI     =     0.5810
DF adjustment:   Large sample                   DF:     min     =     198.37
                                                        avg     =  974609.81
                                                        max     = 3021953.66
Model F test:       Equal FMI                   F(   4, 3081.6) =       4.61
Within VCE type:          OIM                   Prob > F        =     0.0010
```

pany01_10	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
longasthma	.4422992	.1439051	3.07	0.002	.1602502	.7243481
	.0013494	.0000704	0.01	0.000	.0013232	.0013889
sex	-.4178542	.149232	-2.80	0.005	-.7103436	-.1253647
	.0012371	.0000826	0.01	0.000	.0012759	.0012189
fincomebin	.3679542	.255245	1.44	0.151	-.1353876	.871296
	.0235082	.0143224	0.12	0.033	.0360453	.0382015
parmh	.27414	.2042041	1.34	0.180	-.1263888	.6746688
	.0110958	.0036598	0.07	0.022	.0160261	.0097279
_cons	-3.075274	.1395036	-22.04	0.000	-3.348798	-2.80175
	.006382	.0019037	0.29	0.000	.0082981	.0063988

Note: values displayed beneath estimates are Monte Carlo error estimates.

```
. mi estimate, mcerror: logistic pany01_13 longasthma sex fincomebin parmh

Multiple-imputation estimates                     Imputations     =         67
Logistic regression                               Number of obs   =       4011
                                                  Average RVI     =     0.6183
                                                  Largest FMI     =     0.6942
DF adjustment:   Large sample                     DF:     min     =     138.69
                                                          avg     =    2651.66
                                                          max     =    6191.68
Model F test:       Equal FMI                     F(   4, 1431.9) =       4.14
Within VCE type:          OIM                     Prob > F        =     0.0024
```

pany01_13	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
longasthma	.5812301	.1693487	3.43	0.001	.2492478	.9132125
	.0065987	.0016247	0.06	0.000	.0085631	.005857
sex	-.5784554	.1808535	-3.20	0.001	-.9330162	-.2238946
	.0076138	.0017342	0.05	0.000	.0081232	.0085687
fincomebin	.1913766	.3464373	0.55	0.582	-.4936051	.8763582
	.0348935	.02104	0.12	0.078	.060722	.048133
parmh	.2477354	.2478245	1.00	0.318	-.2389256	.7343965
	.0170934	.0062498	0.08	0.038	.0235067	.0185054
_cons	-3.28507	.1606012	-20.45	0.000	-3.60006	-2.97008
	.0085786	.0024591	0.31	0.000	.0102504	.0094717

Note: values displayed beneath estimates are Monte Carlo error estimates.

```
. mi estimate, mcerror: logistic any01_15 longasthma sex fincomebin parmh

Multiple-imputation estimates                     Imputations     =         67
Logistic regression                               Number of obs   =       4011
                                                  Average RVI     =     1.1150
                                                  Largest FMI     =     0.7256
DF adjustment:   Large sample                     DF:     min     =     126.85
                                                          avg     =     335.19
                                                          max     =     539.22
Model F test:       Equal FMI                     F(   4,  849.8) =       3.72
Within VCE type:          OIM                     Prob > F        =     0.0052
```

any01_15	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
longasthma	.6132657	.1704571	3.60	0.000	.2782362	.9482953
	.0129271	.0051228	0.12	0.000	.0154074	.0175192
sex	.2328484	.1636033	1.42	0.155	-.0885296	.5542264
	.011735	.0044598	0.08	0.024	.0149852	.0144775
fincomebin	.1490835	.3072256	0.49	0.628	-.4588675	.7570346
	.0316425	.0201042	0.12	0.084	.0593735	.0416372
parmh	.4366318	.2363239	1.85	0.066	-.0289737	.9022374
	.020909	.0106069	0.12	0.017	.0296289	.0300411
_cons	-3.244421	.1729027	-18.76	0.000	-3.584495	-2.904346
	.0138622	.0059495	0.66	0.000	.0179367	.0186173

Note: values displayed beneath estimates are Monte Carlo error estimates.