Persistent back pain in emerging adults: an analysis of the 1970 British Birth Cohort Study

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Declaration

Throughout the course of this thesis I received advice from my supervisory team (Professor George Peat, Dr Elaine Nicholls, Dr Rosie Lacey, Dr Ross Wilkie and Dr Martin Thomas). The preliminary outline of this research project was proposed by Professor George Peat. Initial discussion with my supervisors suggested the potential use of the 1970 British Birth Cohort as a resource for exploring persistent back pain in emerging adulthood. The rest of this thesis including decisions regarding study design, conduction and subsequent analysis were that of my own; in addition to all findings, interpretations and conclusions.

Dr Nadia Corp gave advice regarding search terms utilised within the scoping review undertaken on risk factors within emerging adulthood for low back pain.

All BCS70 recruiting, tracing and data collection was done by the responsible research institute at each sweep and was not conducted personally by myself in any manner. References for each individual sweep for acknowledgement of contributors can be found within the methods chapter. Professor George Peat gained free access to the BCS70 data through the UK Data Service via registration. Statistician Dr Elaine Nicholls and myself worked together to set up and clean the BCS70 data within SPSS. Dr Nicholls gave statistical advice throughout and gave specific assistance when multiple imputation was undertaken.

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Abstract

Low back pain (LBP) is a common, often long-term problem which occurs at all stages of life from childhood to old age. This thesis focuses on persistent LBP in 'emerging adulthood' (18-29 years), a developmental stage characterised by delayed subscription into adulthood in which formative behavioural transitions and unique cumulative exposure occur which could influence long-term health outcomes. LBP research within this period has relatively limited evidence on the frequency and specific causes. Emerging adults and adolescents experience sleep disturbance commonly, through increased social and educational demands. The aim of this thesis was to estimate prevalence of persistent LBP in emerging adulthood, its association with comorbidity, and the possible effect of sleep disturbance.

Methods:

I conducted three analyses using data from the 1970 British Birth Cohort Study (BCS70): (i) cross-sectional prevalence study of persistent LBP at age 29 years (n=11,226); (ii) cross-sectional analytic study of the associations of persistent LBP at 29 years with a range of physical and mental health co-morbidities ; (iii) nested case-control analysis investigating the association between sleep disturbance during childhood and emerging adulthood (ages 10, 16, 21, 26, 29 years) and persistent LBP at age 29 years.

Results:

The estimated lifetime, 12-month, and annual consultation prevalences for persistent LBP at age 29 years were 14.9% (95% CI 14.2, 15.5), 11.1% (10.5, 11.7) and 6.4% (6.0, 6.9) respectively. 81.1% reported their persistent LBP began in emerging adulthood. Compared to 29-year-olds without persistent LBP, those with persistent LBP were more likely to report a wide range of other health conditions (e.g. prevalence odds ratio (OR) for asthma = 1.35 (1.07, 1.70); for eating disorder = 2.62 (1.80, 3.82)), although they were generally not more

likely to seek help for these co-morbidities. Persistent LBP commencing in emerging adulthood was associated with sleep disturbance at age 26 and 29 years ((adjusted OR 1.32 (1.05, 1.65) and 1.46 (1.23, 1.73) respectively) but not at age 10, 16 and 21 years. Reporting sleep disturbance at multiple age points showed a dose-response relationship.

Conclusion:

Persistent LBP by the end of 'emerging adulthood' is already common and associated with multiple physical and mental health co-morbidities Sleep disturbance in childhood does not appear to be a risk factor however the role of sleep disturbance in emerging adulthood itself, perhaps as a cause but also as an effect of persistent LBP, warrants further investigation.

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Abbreviations and acronyms

BCS70	1970 British Birth Cohort Study
CAPI	Computer assisted personalised interview
CLS	Centre for Longitudinal Studies
CM	Cohort member
CWP	Chronic widespread pain
DALY	Disability adjusted life years
GB	Great Britain
GBD	Global burden of disease
HSE	Health and Safety Executive
IASP	International Association of the Study of Pain
ICD	International Classification of Diseases
LBP	Low back pain
MSK	Musculoskeletal
NCDS	National Child Development Study 1958
NSHD	National Survey of Health & Development study 1946
NVQ	National Vocational Qualification
ONS	Office of National Statistics
RMI	Rutter Malaise Index
SDI	Sociodemographic Index
SOC	Standard Occupational Classification
UK	United Kingdom
USA	United States of America
YLD	Years lost to disability
YLL	Years of life lost

1 Background

This background chapter begins by briefly considering some aspects of the definition of low back pain (LBP) within epidemiological research, before then summarizing estimates of the occurrence and impact within the general population. The focus of this thesis is on LBP in emerging adulthood and so this developmental stage of life is then critically introduced along with a synthesis of estimates of LBP specifically in this part of the life course.

1.1 Low back pain definitions

1.1.1 Anatomical Location

An explicit anatomical definition of LBP adopted by researchers is pain residing 'between the lower costal margins and the gluteal folds' as initially defined by Anderson (1977). However, there are have been many other definitions used within the LBP field of research. In one systematic review involving 165 studies, only a small percentage (26.3%) of the prevalence estimates used the LBP anatomical definition proposed by Anderson (1977). Other more simplistic anatomical definitions used by other studies included in the systemic review were more common, such as 'low back' or 'back' (Hoy *et al.*, 2012).

1.1.2 Specific and Non-Specific

Back pain can be sub-classified as specific or non-specific. Specific back pain infers that there is an underlying pathoanatomical process. In a study undertaken in primary care by Deyo and Weinstein (2001), causes of back pain presentations consisted of 0.01% infection, 0.7% tumour or metastasis, 3% spondylolisthesis and 4% with a compression fracture. Other examples of specific LBP include radicular syndrome, ankylosing spondylosis and osteoporosis. Non-specific back pain on the other hand is a diagnosis of exclusion and is more common, and is suggested to be responsible for around 90% of LBP cases (Koes, Van Tulder and Thomas, 2006).

The impact of changing LBP definitions (e.g. specific or non-specific causes) can be seen in population estimates within different iterations of the Global Burden of Disease (GBD) study. Estimates in the 2004 GBD study were considerably lower than the 2010 GBD estimates for LBP related disability adjusted life years (DALY). DALY is defined as the combination of years lost to disability (YLD) and years of life lost (YLL)(WHO, 2014). For example, LBP in 2004 was globally ranked the 105th largest cause of DALYs, whereas in 2010 it rose to sixth (Hoy *et al.*, 2014). The 2004 GBD study excluded mild non-specific LBP (which constitutes the majority of LBP), and instead two out of the three definitions used for LBP centred on intervertebral disc disorders. These disorders require imaging (e.g. x-ray), which large population studies often do not have access to. Other factors in addition to the cause of LBP could have also influenced the rank difference seen between the two GBD studies. In the 2004 GBD study, LBP duration was required to be a minimum of four days, in comparison to the 2010 GBD study which required a minimum of one day. These differences listed in the 2004 GBD study, not elaborated on at the time, could explain the significant change in LBP DALY figures between 2004 and 2010 GBD (Hoy *et al.*, 2010, 2014; Buchbinder *et al.*, 2013).

1.1.3 Duration

The LBP duration is classically subdivided into acute, subacute and chronic as first proposed by Nachemson and Bigos in 1984 (cited in de Vet et al. 2002). Acute LBP within the literature is generally accepted as an episode of LBP lasting less than six weeks. A subacute episode is an episode lasting between six and 12 weeks. Chronic pain, unrelated to cancer, has been described by the International Association of the Study of Pain (IASP) to last between three to six months (Merskey & Bogduk 1994). This is based upon the principle laid out by Bonica (1953), stating that pain continuing beyond the expected healing time should be considered as chronic in nature.

Von Korff & Dunn (2008) argued that using duration alone to define chronic pain could be too simplistic and does not fully encompass other factors such as disability, psychological and behavioural factors. They state the term chronic pain does not differentiate between the different severities of pain persisting past three months (mild vs severe). Von Korff & Dunn (2008) used a Risk Score; this score was calculated by factoring together activity limitation, depression score, pain intensity, life interference, the number of pain sites and days. The study found that in comparison to the standard definition of chronic pain (number of pain days), that the Risk Score had superior prognostic value in predicting factors such as unemployment related to pain or pain medication use. They proposed that the use of the Risk Score could shift the emphasis away from the restrictive label of 'chronic pain' based on use of the number of pain days alone, which does not fully account for the variable long term nature of chronic pain. They proposed instead a re-focus on a more comprehensive measure of prognosis which encourages a more holistic approach to treatment by considering multiple contributing factors.

The movement away from defining LBP by duration alone, was further supported by the National Institute for Health and Care Excellence (NICE) and IASP. In the most recent recommended NICE guidelines for LBP and sciatica, they state 'we have moved away from the traditional duration-based classification of low back pain (acute, subacute and chronic) and have considered low back pain to be a continuum where risk of poor outcome at any time point is almost certainly more important that the duration of symptoms' (NICE, 2016 p. 23). A taskforce from the IASP proposed chronic LBP should be defined as 'pain in 1 or more anatomic regions that persists or recurs for longer than 3 months and is associated with significant emotional distress or significant functional disability' (Treede *et al.*, 2015). The 11th revision of the International Classification of Diseases (ICD) will publish this as the universal definition in 2018.

1.1.4 Recurrence

A systematic review by de Vet et al. (2002) found that 31 out of 81 papers reviewed contained a categorical LBP recurrence definition. Upon examination of the 31 papers, they concluded that the recurrence (or episode) definition reasoned by each individual paper was not based on scientific principle, but rather on methodological practicality or 'arbitrary' definitions. The definition proposed by de Vet et al. for LBP recurrence is 'pain in the lower back lasting for more than 24 hours, preceded and followed by a period of at least a month without low back pain', which gives a clear duration of recurrence and the required LBP free period of time to denote recovery.

This view was shared by Stanton et al. (2009). They demonstrated in their systematic review on recurrence definitions, that just under 10% of the studies included used the same definition of recurrence and only 38% of studies involved reported a recurrence definition. What seems to be problematic is disentangling whether an individual is having a recurrence or a flare-up of a current episode. Within Stanton et al.'s (2009) systematic review, there was a large difference in how studies defined recurrence (i.e. length of time LBP needs to be present) and this varied from hours to weeks. A minority of studies (13%) gave a set definition of a recovery period absent from LBP. Therefore it is likely, as Stanton et al. suggested, that some of these studies are not estimating recurrence but also participants with concurrent chronic pain (eight of the studies in the systematic review used persistent pain and recurrence interchangeably). Both of these systematic reviews highlight the discrepancy within the field of recurrence and Stanton et al. proceeded to propose the definition of recurrence formerly given by de Vet et al. (2002) as a way to achieve uniformity.

1.1.5 Summary: consensus towards a universal LBP definition

Multiple criteria can be used to define LBP in epidemiological studies. LBP can be characterised as described above, by anatomical location, presumed cause, temporal aspects such as duration and recurrence, and by risk of future pain and disability. Nevertheless, other definitions regarding severity and functional impairment also require consideration. The variety of definitions used for LBP, can in part be explained by researchers utilising secondary data (data the researcher has not personally constructed or collected) and this often leads to the adoption of pragmatic LBP classifications.

The use of heterogeneous definitions of LBP can limit the future pooling of data and comparison of estimates between studies. However, the situation may be improving. One systematic review focusing on LBP in children found that newer papers (2002-2013) were more likely than older papers (1980-2001) to adopt and cite well used LBP definitions and criteria (Calvo-Muñoz, Gómez-Conesa and Sánchez-Meca, 2013).

Another step towards improvement was the gathering of consensus for a universal classification of LBP as a result of a modified Delphi study. Twelve countries represented by 28 back pain experts, gave both minimal and optimal definitions. The definition they ultimately proposed considered anatomical location, exclusion, frequency and duration. The Delphi study's minimal definition defines LBP as 'within the last 4 weeks between the inferior margin of the 12th rib and inferior gluteal folds (indicated on an anatomical diagram) that is bad enough to limit usual activities or change the daily routine for more than 1 day' (Dionne *et al.*, 2008). The GBD study adopted a comparable definition from 2010 onwards, excluding activity limitation (Hoy *et al.*, 2014); activity limitation was subsequently included in 2015 (Vos, 2016).

1.2 Disability and economic cost

The GBD project provides extensive global estimates and trends through annual epidemiological studies. The 2016 GBD report showed that LBP was the seventh largest burden of disease in 2016, out of 333 diseases and injuries as defined using DALYs (Abajobir *et al.*, 2017a, 2017b). Within all the 195 territories and countries incorporated into the study, LBP consistently retained its top ten position amongst diseases causing the largest amount of YLD. GBD researchers compare development between countries using the Sociodemographic Index (SDI) (a measure of fertility, education and income of countries); with the United Kingdom (UK) and United States of America (USA) as examples of high SDI countries. LBP is the second largest leading burden of disease in countries with a high SDI in 2016, only second to ischaemic heart disease. In addition, LBP was within the top five diseases across all SDI ranks (high, middle and low). When focusing on the UK in particular, LBP again holds its position as the second largest health burden and its first position in causing the greatest amount of YLD.

LBP has an equally profound impact on the economy although precise estimates are often difficult due to case definitions used. The UK Office of National Statistics (ONS) estimated in 2016 that 30.8 million working days were lost due to musculoskeletal related problems (defined as upper limb problems, back and neck pain); this was second only to minor illnesses for the number of work days lost (ONS, 2016). In comparison, the 2014 ONS report defined back, neck and muscle problems as musculoskeletal (MSK). In this previous report back, neck and muscle problems ranked first as the leading cause of working days lost (30.6 million days) (ONS, 2014). Regardless of the definition used by ONS, it is clear that MSK problems, particularly back and neck problems, impact considerably on working days lost.

The Health and Safety Executive (HSE) estimated the number of days lost from injuries sustained at work. The HSE disclosed that over 3.4 million days were lost due to back

disorders caused at work, with 15.9 days on average per case in 2016. Individually, lumbar pain was the most common MSK illness reported (Health and Safety Executive 2016). HSE's estimate of 3.4 million is significantly lower than ONS's estimate of 30.8 million in same calendar year. This difference between the two estimates is because the HSE reports on back pain individually and the ONS in comparison accounts for multiple MSK related problems e.g. neck, back and muscle pain. Additionally, the difference in part can be explained by HSE's focus on back problems *caused by the workplace*; whereas the ONS report encompasses all causes of back pain (e.g. idiopathic, work, sport-related or chronic disease).

A well-cited study estimated that in the year 2000 LBP in total cost the UK economy £12.3 billion, with £9.1 billion estimated to be lost due to morbidity related loss of productivity (Maniadakis and Gray, 2000). There have since been few studies undertaken to provide more up-to-date UK estimates. Dagenais et al. (2008) undertook a systematic review looking at the international variation of the economic burden of LBP, giving cost estimates in dollars. The only UK study included out of twenty-seven studies was that done by Maniadakis & Gray (2000). This review attempted to consider both indirect and direct costs. Due to the large heterogeneity in research methodology the study found it difficult to give a reliable estimate, ultimately reporting an estimate they consider likely to be incorrect and underrepresentive of the true figure ($19.6 to $118.8 billion). Despite this, they state that even according to the smallest estimate, LBP causes an immense impact on all sectors of society that warrants substantial attention (Dagenais, Caro and Haldeman, 2008). A more recent study in the USA, estimated $87.6 billion of health care spending was spent in 2013 on low back and neck pain (Dieleman *et al.*, 2016).

1.3 Occurrence of LBP over the life course

1.3.1 The natural history of back pain episodes

Back pain episodes have the greatest amount of improvement within the first month of onset, as shown by a systematic review (Pengel *et al.*, 2003). The researchers found that the rate of improvement slows more prominently towards the end of three months. In the small amount of remaining individuals who had chronic pain (LBP lasting greater than three months), the level of disability and pain was consistent at one-year follow-up.

Chronic sufferers tend to form the minority of adults suffering with LBP (Dunn et al. 2013). These individuals have been noted in the literature to be susceptible to have another episode, due to the episodic course of LBP (Korff, 1994; Lemeunier, Leboeuf-Yde and Gagey, 2012; Kongsted *et al.*, 2016). Point prevalence estimates capture this by showing different individuals reporting LBP pain at different times. A longitudinal cohort study by Kjaer et al. (2011) in children, demonstrated one-month back pain prevalence of 33% at age nine, 28% at age 13 and 48% at age 15 years. Of these children, only 7% of those who participated at all three sweeps in this study (n= 261) consistently reported back pain at all three follow-up ages (9, 13 and 15 years). Researchers focusing on adult LBP have also highlighted this point, noting that if it is not the same individuals reporting pain at different observed time points, these prevalence figures must include both estimates for first (incident) LBP episodes and recurrent episodes of LBP (Dunn et al. 2013).

Although point prevalence estimates are helpful to assist measuring the size of the problem at a certain time, they are not beneficial for determining the severity, duration and stage of the LBP (Axén and Leboeuf-Yde, 2013). Over the last ten years, research has shifted to predicting the course of LBP trajectories, moving away from the traditional acute and chronic definitions. A review of research on the longitudinal trajectories of LBP by Kongsted et al. (2016), recommends comprehensive 'Principal Trajectory Patterns' for LBP based on

consensus among included papers. Subcategories include intensity, variability (persistent, fluctuating, episodic and single) and change (rapidly improving, gradually improving and progressing pain). These subcategories illustrate the variation in the natural history of LBP amongst patients. Within the review, severity trajectories indicated that patients with high severity reported greater disability and depression. In comparison, individuals reporting mild LBP had less physical and psychological disturbance. The review found in primary care populations the most common cluster was 'infrequent' or mild LBP, with severe consistent pain found in approximately 20% of sufferers (one in five). The natural course of LBP based upon these different trajectories, are suggested to be reasonably consistent over time in adults (Dunn, Campbell and Jordan, 2013; Kongsted *et al.*, 2016). Dunn, Campbell and Jordan (2013) in particular demonstrated that membership with a specific trajectory to be comparable seven years later.

1.3.2 Estimates of the recurrence of low back pain

The recurrence of LBP, having a second or subsequent episode of LBP, is often difficult to estimate. A recent systematic review, which focused on the risk of recurrence in patients who recovered from a LBP episode in the last year, demonstrates this point. The researchers had great difficulty performing a meta-analysis because of the heterogeneity, low quality and limited number of the studies meeting the inclusion criteria (da Silva *et al.*, 2017). The small number of studies available in the review was partially due to the difficulty of differentiating survival and inception cohorts. Survival cohorts consist of participants who have had a resolved episode of LBP. Problematically, this previous episode could have occurred anything from a few months to a few years before. In comparison, inception cohorts require study participant recruitment within a defined short time period after an episode of LBP. Failure to distinguish between these two cohorts leads to bias within estimates of recurrence, as these two types of cohorts have different risks of developing recurrent LBP (da Silva *et al.*, 2017). A systematic review focusing on inception

cohorts experiencing an episode of LBP within the previous three weeks, reported a one year recurrence of 56 - 88% (Pengel *et al.*, 2003).

1.3.3 Incidence

Given the concept of LBP as typically a recurrent, episodic condition, incidence can refer to the rate of first or new episodes. First event incidence is defined as an individual's first lifetime episode of LBP. Episode incidence is the initiation of a new episode of LBP in an individual with a preceding history of LBP. Estimates of first event incidence are therefore expected to be lower than those for episode incidence that includes recurrent episodes. These definitions of incidence both assume that the onset of an episode of LBP can be clearly identified. Where the onset is insidious over time, the distinction between incidence and prevalence may become blurred. Prevalent cases identified at a given point in time are more likely to be chronic in nature (Silman and Macfarlane, 2002; Dunn, Hestbaek and Cassidy, 2013).

Adult estimates for incidence rates include a recent American study which estimated the clinically significant incidence rate of LBP as 1.39 per 1,000 person-years, based on LBP defined as cases presenting to 100 accident and emergency departments between January 2004 and December 2008 (Waterman, Belmont and Schoenfeld, 2012). It is unclear what type of incidence (first event or episode) this estimate provides. Additionally, although this estimate might account for more clinically severe cases, some research has shown that factors such as gender and disability outweighed pain severity as a determinant for seeking care related to LBP (Ferreira *et al.*, 2010). Therefore, Waterman et al.'s (2012) clinically significant estimate of LBP might under-represent individuals who consult primary care, or individuals with LBP who forego any medical input despite having significant pain. Estimates from a longitudinal Canadian study undertaken by Kopec et al. (2004) was comparatively much larger and indicated an LBP incidence rate of 44.1 per 1,000 person-years. This

difference could be explained by Kopec et al.'s (2004) study using the definition of LBP as that diagnosed by a health practitioner (e.g. hospital or primary care), with the authors stating that due to their definition of LBP they also may not have captured all back pain episodes, such as milder cases who did not consult.

Incidence estimates for adults using proportions include a systematic review undertaken by Hoy et al. (2010). The study estimated that annual first episode incidence ranged between 6.3 to 15.4% and the annual episode incidence ranged between 1.5 to 36%. They note that the episode incidence estimate does not consider multiple episodes within the designated time period and therefore could be underestimating the true episode incidence.

Within children (< 18 years), incidence estimates include a recent systematic review which estimated a mean annual incidence of 15% (using two studies); however, there was no specification on whether this accounted for first event incidence or episode incidence (Kamper, Yamato and Williams, 2017). These figures are likely to be inaccurate due to the low quality of the two papers included. In adolescents (defined as eight to 18 years) the one year incidence of LBP has been estimated to range from 11.8-33% in a systematic review on idiopathic spinal pain (Jeffries, Milanese and Grimmer-Somers, 2007), which is similar to that previously quoted for adults.

Understanding when incidence is highest for LBP in the life course is complicated due mainly to methodological differences between studies across the life course. Leboeuf-Yde & Kyvik (1998) used a Danish population of 29,424 participants aged between 12-41 years, and found that between the ages of 12-14 years the cumulative lifetime incidence of LBP had the steepest gradient increase. This large study used an anatomical picture outlining LBP (below 12^{th} rib and above inferior gluteal fold) with different duration options. Research by Waxman et al. (2000) showed that participants that were between 25-34 years of age significantly reported more new onset LBP than any other age group. Although, it is

worth considering that the minimum age of study participants within the aforementioned study was 25 years and therefore could not account for incidence for younger ages. Kopec et al. (2004) in contrast found back pain to have the highest incidence between the ages of 45-64 (incident rate 51.9 per 1,000 person years) in an adult Canadian study. They defined back pain using a questionnaire where study participants self-reported diagnosis by a healthcare professional (no duration was reported). It is not clear what type of incidence Kopec et al. (2004) and Leboeuf-Yde & Kyvik (1998) were defining.

Given the complexity of capturing first event or episode incidence of LBP and the inconsistency of LBP definitions it is unsurprising that estimates from published studies are quite heterogeneous and a single acceptable estimate is elusive. Hoy et al. (2010) suggested that a further problem is the expense of longitudinal studies in comparison to cross-sectional studies, which could explain why incidence estimates are much less common than prevalence estimates.

1.3.4 Prevalence

A study by Hoy et al. (2014) examining the 2010 GBD estimates, found that the global age-standardised (one day) point prevalence of LBP was 9.4%. They also found that the prevalence among women was slightly lower than in men (8.7% and 10.1% respectively).

A systematic review conducted by Hoy et al. (2012) also presented further global estimates; however, greater detail to classification showed how methodology influenced these estimates. The researchers did this by noting whether the studies reviewed (n=165) considered activity limitation, the episode length required for inclusion, and the defined anatomical location. The use of the definition of 'low back' and 'posterior aspect of the body from the lower margin of the twelfth ribs to the lower gluteal folds' had a significantly greater mean prevalence than when 'back' was used for anatomical location. There was little difference between the lifetime and one year prevalence estimates (38.9%, 38.0%),

although these figures were significantly higher than that of the one month period prevalence of LBP (30.8%) (Hoy et al. 2012). The lowest estimate found by Hoy et al. (2012) was the point prevalence (18.3), which is almost double that reported by Hoy et al. (2014) above. This is most likely due to the methodological variation between the two studies. Hoy et al.'s (2014) study inclusion criteria explicitly defined LBP as pain between the lower gluteal fold and lower rib lasting greater than 24 hours. In comparison Hoy et al.'s (2012) estimate was a composite of all point estimates within studies included, using a variety of different definition criteria e.g. duration, anatomical location and activity limitation. This methodological choice by Hoy et al.(2012) was undertaken to meet their objective of investigating the effect 'case definition, prevalence period, and other variables have on prevalence'.

Hoy et al. (2012) also gave estimates for gender. Males had a significantly lower point and one-month prevalence than females. However, for the one-year and lifetime prevalence there was no significant difference in respect to gender. When considering age, the trend reported within the study showed increased prevalence into adolescence with a subsequent drop between 20-29 years of age; however this difference was not significant. Then the maximum prevalence occurred between 40-69 years of age before ultimately decreasing.

The age-related pattern of increasing prevalence throughout adulthood but then apparently lower prevalence in old age shown by Hoy *et al.* (2012) is also supported by Dionne, Dunn and Croft (2006). In this study, the prevalence of mixed and benign back pain followed the same trend, with back pain in the elderly characteristically decreasing. Researchers have put forward similar proposals as to why there is reduced reporting in the elderly, with determinants such as competing co-morbidities, depression, cognitive impairment affecting recall, altered pain perception and use of proxy reporting playing a

key role (Bressler *et al.*, 1999; Dionne, Dunn and Croft, 2006). Another factor for decreased reporting in the elderly could be retirement, which would remove ongoing exposure of occupational factors related to back pain. Dionne, Dunn and Croft's (2006) study also demonstrated the opposite to be true for disabling or severe LBP, which was associated with a linear rise in prevalence with age.

Published prevalence estimates at the other end of the age spectrum, childhood and adolescence, have a very broad range. In a systematic review with 56 studies, the LBP lifetime prevalence (up to age 21) was estimated to be between 7%-72% (Jeffries, Milanese and Grimmer-Somers, 2007). This range narrowed when the prevalence measure was adjusted to point, one month and one-year prevalence (1%-38.5%, 9.8%-36%, 3%-56%, respectively). The researchers queried the role recall played in affecting their results and found estimates had greater variation when participants had to recall previous LBP over a greater period of time. A more recent meta-analysis by Calvo-Muñoz et al. (2013) focused on the 9-18 years age group (mean age, 13.6 years) and found a significant increase in prevalence with age. Estimates reported for point, one month, one year and lifetime prevalence were 12.0%, 18.3%, 24.5% and 39.9% respectively.

Recent work within the Lancet Child and Adolescent Health journal, suggest that the children of today experience a prolonged adolescence and that adolescence should be extended from age 18 (or 19 as suggested by World Health Organization) to the age of 24 years (Goodburn, Ross and WHO, 1995; Sawyer *et al.*, 2018). A developmental phase, emerging adulthood, has been proposed which supports this notion and LBP estimates within this age period is scarce in comparison to both adulthood and childhood estimates.

1.4 Occurrence of LBP in emerging adulthood

1.4.1 Emerging adulthood

The psychologist Jeffrey Arnett first coined the term emerging adulthood in 2000, characterising a period of early adult development from the ages of 18 to 25/29 years. Arnett proposed that this particular developmental life stage had become apparent with changes in the previous decades and that this period of life could be viewed as distinctive from childhood, adolescence and adulthood (Arnett, 2000). For clarity childhood is commonly stated to be between the ages of zero to 19, with adolescence (ages 10 to 19) forming a subsection of childhood which accounts for distinct changes resulting from puberty (Goodburn, Ross and WHO, 1995). The age of majority in the UK is 18, upon which an individual is deemed an adult in both the eyes of the government and from a legal perspective. However, beyond this there is debate as to what other factors contribute to adult status within society. Studies by Arnett found that the majority of 18-25 year old Americans felt that they were neither an adolescent nor an adult. When asked what caused self-identification as an adult, there were three main themes: independent decisions, personal responsibility and financial independence (Arnett, 1994, 1997). Arnett proposed that large contextual change within society over the last few decades has created space for this distinct developmental age of emerging adulthood. This occurs due to multiple factors: older average age of marriage, later parenthood, greatest occupational variability, highest level of risk taking, increased rates of young people within further education and greater gender equality (Arnett, 2000). Arnett contends that 18 to 29 year olds in particular, have 'relative independence from social roles and from normative expectations. Having left the dependency of childhood and adolescence, and having not yet entered the enduring responsibilities that are normative in adulthood' (Arnett, 2000 p. 469). Five themes were noted to arise in this developmental age (feeling 'in between', self-focus, possibility, instability and identity exploration) which delay subscription into adulthood (Arnett, 2000).

He noted, however, that this concept could only exist in cultures in which its young societal members have this capacity for independence (usually industrialised countries). Even within industrialised countries, there are those who do not experience emerging adulthood. This could be through personal disposition or lacking the means to foster these opportunities e.g. lower social classes (Arnett, 2000).

1.4.2 Opposition to the concept of emerging adulthood

While the concept of emerging adulthood has stimulated a growing body of research focused on this period of life over the last decade (Swanson, 2016), it has not gained universal acceptance. Prominent criticism of Arnett's concept of emerging adulthood includes the lack of transparency of the methodology used to underpin the work justifying emerging adulthood and the limited applicability to populations in non-industrialised countries or working class individuals (Arnett 2004, p. 17; Côté 2014). Although Arnett personally accepts that lower classes do experience emerging adulthood, this is however (in his view) over a shortened period of time (Arnett et al. 2011, p. 49). Emerging adulthood could also be limited by its dependence on societal context and Arnett acknowledges that emerging adulthood potentially could be replaced by new theories in future. This questions how long this proposed developmental stage will remain relevant as society evolves over time (Arnett *et al.*, 2011).

To be accepted as a developmental life stage, something distinct must happen in the defined age period. There are concerns that emerging adulthood does not meet this requirement (Hendry and Kloep, 2010). Other theorists argue that emerging adulthood is actually a 'choice' by individuals between 18-29 years, and this postponement (labelled as emerging adulthood) is instead caused by other factors such as the current economic state and personal circumstances (Schoon and Schulenberg, 2013). One researcher in particular comments that labelling this moratorium of adulthood as a 'choice' or as 'normal' in young

people can have serious implications economically and socially if incorporated into policy (Côté, 2014).

The use of emerging adulthood as a developmental life phase, however flawed, still provides a potentially useful and novel perspective within a life course approach on LBP prevalence and determinants. Although more commonly defined as 18 to 25 years of age within research, the use of the broader age range of 18 to 29 years is equally supported within Arnett's (2004) work. This extended range is specified to be more appropriate in countries with a higher SDI due to greater prolongment of factors such as marriage in comparison to countries with a lower SDI (Arnett, 2004 p. 7). Furthermore this definition provides a slightly extended window to examine the maximal exposure of determinants within this transitional phase and is the definition this thesis will subsequently adopt.

1.4.3 Incidence

The incidence of LBP in emerging adulthood is prone to all the aforementioned difficulties associated with estimating LBP incidence in the general population. Only one incidence figure was found fitting the emerging adulthood age range (18 to 29 years). A longitudinal study (n=10,007) showed an incidence rate of 34.4 per 1,000 person years for back pain in 18 to 24 year olds (Kopec, Sayre and Esdaile, 2004). This estimate for emerging adults is comparably lower than the back pain incidence previously mentioned within the same study for adults aged 45-64 years (51.9 per 1,000 person years) (Kopec, Sayre and Esdaile, 2004).

1.4.4 Prevalence

Searching for LBP prevalence figures referring explicitly to the age range defined by Arnett's emerging adulthood was limited; this is understandable because the term is rooted in psychological theory that has not fully translated into MSK research. Much like incidence, there are estimates for prevalence for childhood, adolescence and adulthood. However, it

is rare in literature to find many systematic reviews or papers that report estimates specifically within the 18 and 29 years range. In a study by Coenen et al. (2017), 1249 participants gathered from the Western Australian Pregnancy Cohort (Raine) Study completed questionnaires at ages 17, 20 and 22 years old. The questionnaires focused on the severity of LBP and its impact (e.g. seeking help from any health professional, use of medication, leave related to work or school and activity interference), with the participants subsequently split into four different prevalence and impact trajectories ('low', 'increasing', 'decreasing' and 'high'). The researchers found that most participants were in the low pain and severity trajectory (53%), the majority of whom were men (n= 363/661). Women were in the majority for the other clusters, particularly the 'high' pain grouping (75%). They found that across all five impact domains, the increase in prevalence was significant from 17 to 22 years of age, from 32% at 17 years to 45% at 22 years old in those reporting LBP in the last four weeks. The use of trajectory clusters helped identify that 30% of the participants were within the 'high' or 'increasing' groups at age 22 years. This indicates that even within young adulthood LBP poses as a significant health issue that requires preventative measures.

Another study by Leboeuf-Yde & Kyvik (1998) attempted to identify when during the life course LBP first becomes problematic, using a population sample of 29,424 participants. The study found a one year period prevalence of just over 50% by age 21 years for males and 22 years for females, with estimates remaining consistent thereafter. The study however did not evaluate the questionnaire it used for LBP in adolescents nor did it state a minimum duration or consider activity limitation and severity, which could influence estimates. Despite this, the research undertaken by Leboeuf-Yde & Kyvik (1998) contributes to a growing body of evidence suggesting that LBP starts earlier in life; with the prevalence of LBP among children and adolescence thought to be increasing, with figures akin to that of adult estimates (Jeffries et al. 2007; Dunn et al. 2013; Calvo-Muñoz et al. 2013). This idea

of LBP occurring earlier in the life course is supported by Dunn et al. (2013), who proposed that the 'vulnerability' for LBP commences at a younger age than previously thought, which can potentially frame LBP outcomes in future. Dunn et al. (2013) suggest that taking a more life course approach to the epidemiology of LBP is an important research agenda; this would allow a greater understanding of how different determinants affect different developmental life stages. Consensus among other researchers also allude to giving greater attention to investigating younger age groups (Kjaer *et al.*, 2011; Calvo-Muñoz, Gómez-Conesa and Sánchez-Meca, 2013).

1.4.5 Prevalence of chronic pain

Chronic pain estimates exist in children and adults. However within the 18 to 29 year age range these figures are lacking. Although studies included participants within the emerging adult age range they did not stratify specifically for this age range. Therefore, child and adult chronic LBP estimates studies will be shown. Despite two systematic reviews looking into chronic LBP estimates, due to poor methodological heterogeneity among LBP studies, it was difficult to extract accurate estimates during this period (McBeth and Jones, 2007; Meucci, Fassa and Xavier Faria, 2015). A systematic review on chronic LBP prevalence estimates demonstrated a lifetime period prevalence of 51-84%, 12-month period prevalence of 36-67% and a 1 month period prevalence of 31-42% in adults aged 18 years and older (McBeth and Jones, 2007). Due to the fact that prevalence studies are more likely to capture long standing cases than episodes transient or periodic in nature, these latter estimates are higher than acute LBP estimates for adults (Hoy et al. 2012). In comparison, a systematic review in children (aged <18 years) focusing on the prevalence of chronic LBP, gave a one-month and a one-week period prevalence estimate of 18-24% and 9-25% respectively (King *et al.*, 2011).

Problematically, as with all reporting, is vulnerability to recall bias; particularly estimates over a long period of time e.g. 12-month and lifetime estimates. This applies to both adults and children (Jeffries, Milanese and Grimmer-Somers, 2007; McBeth and Jones, 2007).

1.5 Summary: persistent back pain in emerging adulthood

LBP is a common and growing problem. LBP causes a substantial burden both to the economy with millions of working days lost and to the individual as the greatest cause for years lost to disability (among all diseases). The recognition of the recurrent nature of LBP and the use of group-based trajectory modelling have contributed to a move away from the orthodox understanding of LBP as simply acute or chronic in nature and towards a nuanced view of the course of LBP. This more nuanced definition is now reflected in national clinical guidelines that generally signal a move towards risk/prognosis-based stratification of LBP for management.

Although age-related patterns of the prevalence of back pain are sensitive to the definition used, e.g. anatomical site and prevalence period measure, the severity threshold applied, and the method of data collection (e.g. in children whether by validated self-report or parent-completed questionnaires), the overlap in prevalence estimates among adults and among children would suggest that the onset of LBP typically commences before adulthood. Investigating emerging adulthood allows further understanding of LBP prevalence in a developmental age between childhood and established adulthood, in which estimates for LBP (particularly chronic LBP) is relatively sparse. As a transitional life phase where young individuals are processing their identity and forming behavioural patterns (e.g. risk engagement), emerging adulthood is arguably distinctive from that of other developmental stages. Established through contextual change in society over the last few decades, it may feature unique (levels of) exposures and identity exploration between the age of 18 and 29 years. The use of emerging adulthood within this research is not to lessen

the importance of developmental periods such as childhood and adulthood, but rather to investigate the occurrence and determinants of LBP through a novel lens. Investigating LBP early in the life course allows greater exploration not only of LBP prevalence but also of the role of determinants in childhood and the risk of subsequently developing LBP. The hope is that such investigation gives insight into a period where psychosocial and behavioural patterns are still being formed and that might therefore provide an important period to intervene and shape future LBP outcomes in adulthood.

2 Determinants of LBP in emerging adulthood

In order to explore low back pain (LBP) within childhood and emerging adulthood this thesis utilised data from the longitudinal 1970 British Birth Cohort Study (BCS70). Further information regarding the BCS70 and rationale for its use can be found in within the methodology chapter (p. 47). Given the anticipated heterogeneity of the literature and the rich breadth of the BCS70 in respect of LBP, a simple scoping search of the literature was performed for two main purposes: to inform potential exposures of interest for subsequent empirical analysis of BCS70 data in this thesis; and to identify determinants that may be important potential confounders in any such analysis.

2.1 Scoping search

2.1.1 Methods

Databases searched included EMBASE, Medline and PsycINFO, from January 1946 to December 2017. PsycINFO in particular was selected due to the psychological origin of Arnett's concept of emerging adulthood. After attending workshops on 'undertaking a systematic review' within the Research Institute for Primary Care & Health Sciences, at Keele University, discussion with colleagues informed a search strategy with key terms which can be found in the Appendix 1. The search terms for risk factors replicated those used by Forbes et al. (2016). Due to the large number of studies returned on the initial search, an iterative process was used to refine the search strategy.

Titles and abstracts were screened for relevance by a researcher (MN). The full-text articles for those considered relevant were obtained and judged against the eligibility criteria by the same researcher. The inclusion criteria consisted of either a cross-sectional, cohort or case-control study design with a minimum of 100 study participants. The latter, while being somewhat arbitrary, would exclude studies likely to have insufficient statistical power. The

sampling frame was emerging adults between the ages of 18-29 years. This could consist of studies that included participants of a wide age range which included emerging adults by presenting age-stratified results.

The outcome of interest was first LBP event or the onset of an episode of LBP or the presence of LBP, reported in association with a given determinant. If the outcome was failed surgery, spondylolisthesis, or other specific pathology (e.g. ankylosing spondylitis), this would lead to exclusion. Finally, studies were excluded if they were not written in English. If the inclusion criteria were met, information on the determinants that had been investigated and reported was extracted from relevant full-text articles.

2.1.2 Findings

A total of 1762 full-text papers were identified as relevant and 57 studies were included in the final review. Studies mainly included participants recruited from settings such as universities and specific occupations (particularly nursing and the military). Few studies were focused exclusively on age ranges consistent with emerging adulthood LBP studies. Instead they tended to cover a wide age range (e.g. adult population), but presented results stratified by age. The determinants of LBP that were the focus of these studies were broadly grouped into psychological, social, biological and physical factors for the purposes of summarizing, but are categorized more finely in Table 2.1.

Psychological determinants

A wide variety of psychological determinants appeared to have been investigated, including aspects of personality (e.g. anxiety traits, emotional disturbance, neuroticism) (Klaber Moffett *et al.*, 1993; Feyer *et al.*, 2000; Kennedy *et al.*, 2008), antisocial behaviour, exposure to domestic violence (Bonomi *et al.*, 2009; Paradis *et al.*, 2016) and mental health disorders such as depression and obsessive compulsive disorder (Christensen *et al.*, 2015).

Several studies had investigated cognitive factors, such as perceived stress, locus of control, and coping skills (Klaber Moffett *et al.*, 1993; Khatun, Ahlgren and Hammarström, 2004; Larsen and Leboeuf-Yde, 2006; Karahan *et al.*, 2009; Mitchell *et al.*, 2009; George *et al.*, 2012; Ganesan *et al.*, 2017).

Social determinants

Occupation in itself was thoroughly covered, with research predominantly in professions with high prerequisites for manual handling. There was a particular focus on the type of occupation undertaken and related working conditions (Nyland and Grimmer, 2003; Van Nieuwenhuyse *et al.*, 2004; Videman *et al.*, 2005; Mitchell, O'Sullivan, Burnett, Straker and Rudd, 2008; Karahan *et al.*, 2009; Ernat *et al.*, 2012; George *et al.*, 2012; Hafeez *et al.*, 2013; Vincent-Onabajo *et al.*, 2016; Lallukka *et al.*, 2017). Poor support, both occupationally or socially (e.g. marital status) was studied (Khatun, Ahlgren and Hammarström, 2004; Van Nieuwenhuyse *et al.*, 2004; Ganesan *et al.*, 2017). The association of LBP with sport was undertaken with particular attention to the type of sport, and the prevalence and intensity of activity (Cakmak *et al.*, 2004; Khatun, Ahlgren and Hammarström, 2004; Leggat, Smith and Clark, 2008; Mattila, Saarni, *et al.*, 2008; Mitchell *et al.*, 2009, 2010; Hayes, Smith and Cockrell, 2009; Hangai *et al.*, 2010; Lorusso, Vimercati and L'Abbate, 2010; Roy, Lopez and Piva, 2013; Triki *et al.*, 2015; Maselli *et al.*, 2015; Fett, Trompeter and Platen, 2017; Ganesan *et al.*, 2017).

Biological and physical determinants

There was a wide range of biological determinants including non-modifiable factors such as biological markers and genetics (Shiri *et al.*, 2008; Hartvigsen *et al.*, 2009) to modifiable factors such as dietary factors (e.g. caffeine intake, alcohol consumption) (Khatun, Ahlgren and Hammarström, 2004; Aggarwal *et al.*, 2013). Smoking or tobacco use had been investigated frequently (Khatun, Ahlgren and Hammarström, 2004; Mattila, Saarni, *et al.*,

2008; Mattila, Sahi, *et al.*, 2008; Karahan *et al.*, 2009; Alkherayf *et al.*, 2010; Mitchell *et al.*, 2010; Hafeez *et al.*, 2013; Triki *et al.*, 2015). Another important risk factor was reporting previous episodes of LBP, with the suggestion that even in emerging adulthood previous episodes of LBP in adolescence or childhood could be associated with an increased risk of future back pain episodes (Videman *et al.*, 2005; Mattila, Sahi, *et al.*, 2008; Roy and Lopez, 2013; Fett, Trompeter and Platen, 2017; Ganesan *et al.*, 2017).

Posture both whilst stationary and non-stationary were broadly investigated (Nyland and Grimmer, 2003; Videman *et al.*, 2005; Mitchell, O'Sullivan, Burnett, Straker and Smith, 2008; Paalanne *et al.*, 2008; Mitchell *et al.*, 2009, 2010; Aggarwal *et al.*, 2013; Mohan *et al.*, 2015; Ganesan *et al.*, 2017). Poor quality furniture or the type of furniture used whilst studying was researched (Van Nieuwenhuyse *et al.*, 2004; Aggarwal *et al.*, 2013; Lourenço *et al.*, 2015; Mohan *et al.*, 2015; AlShayhan and Saadeddin, 2017), as well as factors such as vibration or lifting heavy weights, which were incurred occupationally or domestically (Van Nieuwenhuyse *et al.*, 2004; Shiri *et al.*, 2008; Karahan *et al.*, 2009; Heuscher *et al.*, 2010; Aggarwal *et al.*, 2013; Roy and Lopez, 2013; Roy, Lopez and Piva, 2013; Mohan *et al.*, 2015; AlShayhan and Saadeddin, 2017; Ganesan *et al.*, 2017).

Table 2.1 Overview of risk factors studied in association with low back pain through the period of emerging adulthood, stratified by study design

Risk factor	Studies	CS (n)	CC (n)	CO (n)	Total (n)
Gender	Khatun, Ahlgren and Hammarström, 2004; Shiri *et al.*, 2008; Ndetan *et al.*, 2009; George *et al.*, 2012; Triki *et al.*, 2015; Rodríguez-Romero *et al.*, 2016; Ganesan *et al.*, 2017	4		3	7
Anthropometric					
Body Mass Index	Khatun, Ahlgren and Hammarström, 2004; Shiri *et al.*, 2008; Ernat *et al.*, 2012; Aggarwal *et al.*, 2013; Furtado *et al.*, 2014; Frilander *et al.*, 2015; Triki *et al.*, 2015	5		2	7
Birth weight	Hestbaek *et al.*, 2003			1	1
Ergonomics					
Weight lifting	Van Nieuwenhuyse *et al.*, 2004; Karahan *et al.*, 2009; Heuscher *et al.*, 2010; Aggarwal *et al.*, 2013; Roy and Lopez, 2013; Roy, Lopez and Piva, 2013; Mohan *et al.*, 2015; AlShayhan and Saadeddin, 2017; Ganesan *et al.*, 2017	7		2	9
Furniture	Mohan *et al.*, 2015; AlShayhan and Saadeddin, 2017	2			2
MSK mobility, strength and posture	Nyland and Grimmer, 2003; Van Nieuwenhuyse *et al.*, 2004; Videman *et al.*, 2005; Mitchell, O'Sullivan, Burnett, Straker and Smith, 2008; Paalanne *et al.*, 2008; Mitchell *et al.*, 2009, 2010; Aggarwal *et al.*, 2013; Lourenço *et al.*, 2015; Mohan *et al.*, 2015; Ganesan *et al.*, 2017; Ye *et al.*, 2017	10		2	12
Previous Low back pain	Feyer *et al.*, 2000; Videman *et al.*, 2005; Mattila, Sahi, *et al.*, 2008; Roy and Lopez, 2013; Ganesan *et al.*, 2017	2		3	5
Sedentary behaviour					
Use of TV or computers	Van Nieuwenhuyse *et al.*, 2004; Leggat, Smith and Clark, 2008; Aggarwal *et al.*, 2013; Hafeez *et al.*, 2013; Mohan *et al.*, 2015; Ye *et al.*, 2017	6			6
Study hours	Ganesan *et al.*, 2017	1			1
Socioeconomic status	Khatun, Ahlgren and Hammarström, 2004; Hestbaek *et al.*, 2008; Mattila, Sahi, *et al.*, 2008; Noll *et al.*, 2016	3		1	4
Family history of low back pain	Hartvigsen *et al.*, 2009; Aggarwal *et al.*, 2013; Ganesan *et al.*, 2017	2		1	3
Smoking	Khatun, Ahlgren and Hammarström, 2004; Mattila, Saarni, *et al.*, 2008; Mattila, Sahi, *et al.*, 2008; Karahan *et al.*, 2009; Alkherayf	5	1	2	8

Risk factor	Studies	CS (n)	CC (n)	CO (n)	Total (n)
	et al., 2010; Mitchell *et al.*, 2010; Hafeez *et al.*, 2013; Triki *et al.*, 2015				
Psychological	Klaber Moffett *et al.*, 1993; Feyer *et al.*, 2000; Khatun, Ahlgren and Hammarström, 2004; Larsen and Leboeuf-Yde, 2006; Mattila, Sahi, *et al.*, 2008; Kennedy *et al.*, 2008; Alkherayf and Agbi, 2009; Bonomi *et al.*, 2009; Leijon and Mulder, 2009; Mitchell *et al.*, 2009, 2010; Karahan *et al.*, 2009; Christensen *et al.*, 2015; Noll *et al.*, 2016; Paradis *et al.*, 2016; Ganesan *et al.*, 2017	8	1	7	16
Occupational	Nyland and Grimmer, 2003; Khatun, Ahlgren and Hammarström, 2004; Van Nieuwenhuyse *et al.*, 2004; Videman *et al.*, 2005; Mitchell, O'Sullivan, Burnett, Straker and Rudd, 2008; Karahan *et al.*, 2009; Ernat *et al.*, 2012; George *et al.*, 2012; Hafeez *et al.*, 2013; Vincent-Onabajo *et al.*, 2016; Lallukka *et al.*, 2017	7		4	11
Physical activity					
General	Cakmak *et al.*, 2004; Khatun, Ahlgren and Hammarström, 2004; Leggat, Smith and Clark, 2008; Mitchell *et al.*, 2009, 2010; Hayes, Smith and Cockrell, 2009; Hangai *et al.*, 2010; Lorusso, Vimercati and L'Abbate, 2010; Ernat *et al.*, 2012; Lunde *et al.*, 2015; Noll *et al.*, 2016; Rodríguez-Romero *et al.*, 2016; Fett, Trompeter and Platen, 2017; Ganesan *et al.*, 2017	10		4	14
Specific sports	Mattila, Saarni, *et al.*, 2008; Maselli *et al.*, 2015; Triki *et al.*, 2015	1		2	3
Sleep	Bonvanie *et al.*, 2016; Noll *et al.*, 2016	1		1	2
Fatigue	Triki *et al.*, 2015			1	1
Other					
Alcohol	Khatun, Ahlgren and Hammarström, 2004	1			1
Diet	Aggarwal *et al.*, 2013; Ganesan *et al.*, 2017	2			2
Ethnicity	Knox, Orchowski and Owens, 2012	1			1
Diabetes	Shiri *et al.*, 2008	1			1
Biological markers	Eivazi and Abadi, 2012	1			1
Falls	Cakmak *et al.*, 2004; Mohan *et al.*, 2015	2			2
School performance	Khatun, Ahlgren and Hammarström, 2004; Mattila, Saarni, *et al.*, 2008	1		1	2

CS Cross-sectional study; CC Case-control study; CO Cohort Study

2.1.3 Summary

This relatively simple scoping search identified a wide range of potential determinants of LBP in emerging adulthood that have been investigated previously. The magnitude, direction and validity of any associations found were not considered in this review, although published systematic reviews of determinants of LBP in childhood, adolescence, and adulthood have tended to find relatively limited consistent evidence of associations for many of those factors included (Hoy *et al.*, 2010; Ramond *et al.*, 2011; Balagué *et al.*, 2012; Huguet *et al.*, 2016; Kamper, Yamato and Williams, 2017).

Nevertheless, in the context of this thesis the identification of potential determinants serves two purposes: to highlight those factors which require consideration as potential confounders for later analyses within this thesis, and to suggest relatively under explored determinants that might usefully be investigated within the BCS70 data.

2.1.4 Selection of exposure for further investigation

The scoping review identified several potential exposures that had been minimally explored (e.g. <3 studies) in emerging adults. These exposures included: family history of back pain, birthweight, diet, alcohol, ethnicity, biological markers, falls, fatigue, sleep, furniture and school performance. This thesis sought to look at an exposure using a lifecourse epidemiology approach and which might be relevant at multiple ages through childhood into emerging adulthood. The sweeps available within the BCS70 for childhood and emerging adulthood were at ages 10, 16, 21, 26 and 29. Therefore the exposure of interest would need to be measured at all required time points within the BCS70 and this excluded birthweight, diet, alcohol, family history of back pain, school performance, furniture and falls as potential exposures. Exposures such as biological markers were not undertaken within the BCS70. Another question for choosing the exposure was if the risk factor was

practically preventable, which led to the exclusion of ethnicity and school performance. Lastly, there was consideration whether the causal pathway of the exposure was clear. One example of this was fatigue, which could be argued to be an intermediate step between poor sleep and back pain. Therefore after taking all these considerations into account, sleep was considered. The exposure of sleep was in comparison to other potential exposures was relatively consistently defined, available at all BCS70 sweeps of interest, and could be targeted in terms of prevention.

There is a growing body of evidence demonstrating the biological plausibility of linking sleep problems to pain (Finan, Goodin and Smith, 2013). Studies in the general adult population are beginning to gain consensus in showing that poor sleep can predict LBP and other MSK related-outcomes (expanded upon below) (Mork *et al.*, 2014; Mundal *et al.*, 2014; Generaal *et al.*, 2017; Uhlig *et al.*, 2018). Exploring the natural history of sleeping problems and pain earlier, in a less investigated period in the lifespan such as childhood and emerging adulthood could give a greater understanding of this relationship.

2.2 Sleep and its potential relevance to LBP in emerging adulthood

2.2.1 Brief introduction to Sleep

Sleep has been defined as 'a recurrent, easily reversible condition characterised by relative quiescence and by greatly increased threshold for response to external stimulation' (Ernest Hartmann, 1973). Whilst recognised as fundamental to survival, there remains no definitive answer to why humans spend an estimated third of the life course sleeping (Everson, Bergmann and Rechtschaffen, 1989; Montagna *et al.*, 2003).

Somatic explanations of the function of sleep emphasise the role of sleep in coordinating metabolism and tissue function, principally the regulation of the immune and endocrine systems (e.g. cytokines and growth hormones) (Frank 2006; Adam and Oswald 1977). Neural metabolic theories draw attention to the role of sleep in aiding brain tissue

detoxification and restoration (Siegel, 2005; Frank, 2006). A further large body of research has centered around the neural-cognitive hypothesis of sleep, involving the facilitation of brain plasticity (e.g. neural development and memory consolidation) (Frank, 2006). The sheer breadth of theories and explanations affirm that understanding the role of sleep is a highly complex and multifaceted subject.

2.2.2 Sleep physiology and disorders

Circadian and homeostatic control of sleep timing

The control of when sleep occurs is through both the circadian system and the homeostatic system. The circadian system is the body's internal body clock which oscillates over a 24-hour period to control many physiological processes; sleep, temperature, endocrine and autonomic functions. For sleep in particular, the circadian rhythm regulates the sleep wake cycle and requires external stimuli, chiefly light, to coordinate the circadian system (Horne, 1988). This can be defined as 'Process C'. The homeostatic system, responsible for stabilisation of the body's internal environment, is thought to drive the need to sleep within the human body. This is speculated to occur through 'Process S', denoted as the exponential build-up of sleep initiating chemicals in the brain through the day, which stimulate the body to sleep beyond a certain 'threshold'. Reduction of these chemicals occur proportionally with time spent asleep; as the level passes below a set 'threshold', this prompts wakefulness. The interplay between these two processes ('Process S' and the circadian 'Process C' from Borbély's (1982) two-process model) is thought to modulate sleep.

The stages of sleep

Sleep has different stages which can be divided into non-rapid eye movement sleep (NREM) and rapid eye movement sleep (REM) (Aserinsky and Kleitman, 1953). NREM sleep consists

of sleep stages one to four. Stages three and four are combined, to form slow wave sleep (SWS) (Colten and Altevogt, 2006). In NREM sleep there is a reduction in the body's vital signs and skeletal muscle activity, in comparison to REM sleep, where there is greater variation in physiological measures (Lavigne et al. 2007).

The invention of electroencephalography (EEG) by Hans Berger (1929), allowed the discovery of brain wave activity and the identification of sleep stages. The combination of EEG, electroculogram (EOG) recording eye movement and electromyogram (EMG) assessing muscle tone, forms the gold standard of representing sleep measurement polysomnography (Moorcroft, 2013). Each sleep stage displays distinctive characteristics on polysomnography. These stages are cyclical during the period of sleep and the structural composition of these stages in healthy sleep is called sleep architecture (Colten and Altevogt, 2006). The composition of time spent cycling through different stages increases with age (Lavigne et al. 2007). In comparison the total amount of sleep recommended, decreases with age as seen below in table 2.2.

Table 2.2 The National Sleep Foundation's recommended sleep hours stratified by age

Age	Recommended total sleeping time (hours)
Neonate (0-3 months)	14 - 17
Infant (4-11 months)	12 - 15
Toddler 1-2 (years)	11 - 14
Pre-school (3-5 years)	10 - 13
School aged children (6-13 years)	9 - 11
Teenagers (14-17 years)	8 - 10
Young Adults (18-25 years)†	7 - 9
Adults	7 - 9
** As recommended by the National Sleep Foundation* (Hirshkowitz *et al.*, 2015) *† Age range used for young adults is that classically defined for emerging adulthood*	

Sleep disorders

There are many different sleeping disorders. In adults sleep deprivation, insomnia and obstructive sleep apnoea (OSA) are among the most prevalent, with adolescents demonstrating a similar pattern (Walia and Mehra, 2016; Ophoff *et al.*, 2018). This contrasts

within younger children (age 6-12) who more commonly experience disorders relating to nocturnal enuresis, sleep terrors, sleep walking and OSA (Ophoff *et al.*, 2018). This section will go on to mainly summarise insomnia and (arousal) parasomnias; the latter defined as 'abnormal behavioural or physiological events occurring at different sleep stages' (Ohayon and Guilleminault, 2005).

Insomnia

The symptoms of insomnia classically include sleep difficulties with initiation, maintenance, early morning waking and the experience of unrefreshed sleep (Thorpy, 2012). Prevalence estimates of insomnia in the general population are dependent on the definition used and can vary based on the frequency, duration, functional impairment or if a diagnostic criteria is specified (Ohayon, 2002). Even when diagnostic criteria are defined, prevalence can vary depending on the type of diagnostic criteria used. For example, higher prevalence rates are reported using the Diagnostic and Statistical Manual of Mental Disorders (DSM) criteria and lower prevalence reported when using more rigorous International Classification of Disease (ICD) criteria (Roth *et al.*, 2011). Therefore, due to the heterogeneity of definitions the point prevalence of insomnia varies considerably: 28.8-48.0% (symptoms alone), 8.5-13.0% (symptoms with daytime dysfunction), and 4.4-6.0% (diagnostic criteria) (Ohayon, 2002). Insomnia can have secondary causes, some of which include mental health and substance misuse. One study demonstrated 40% of insomnia suffers had a mental health co-morbidity (Ford and Kamerow, 1989). Once accounting for these psychiatric and other physical primary causes, the point prevalence estimate for primary insomnia alone in a large scale European study was 3% in adults using the DSM 4th edition diagnostic criteria (Ohayon and Reynolds, 2009). Diagnosis of primary insomnia is achieved through taking a sleep history, after ruling out any suspected secondary causes.

Arousal parasomnias

Arousal parasomnias are related to NREM sleep. During the initial few hours of sleep as children transition out of slow wave sleep, disorders such as sleep walking and night terrors occur (Guilleminault *et al.*, 2003). Sleep walking involves inappropriate, unconscious coordinated motor movement during sleep (usually <15 minutes), these motor movements can be complex and there is potential for accidental injury (Howell, 2012). The common age for sleep walking is between eight to 12 years of age and a systematic review estimated a point prevalence of 5.0% (95% CI 3.8–6.5) in children (Stallman and Kohler, 2016).

Night terrors consist of an episode of arousal (whilst still unconscious) with fear-like expressions, screaming and the inability to be comforted; with the potential of injury, e.g. running into things to 'escape' nightmare (Mason and Pack, 2007; Stores, 2009). During night terrors, there is a strong autonomic response (including raised heart rate and sweating) and after the episode the majority of children are unable to recall the event (Avidan and Kaplish, 2010). The point prevalence of night terrors at age five is estimated to be 13.4% and tends to tail off with increasing age, with the age 13 point prevalence estimated to be 5.3% (Petit *et al.*, 2015).

2.2.3 Sleep measurement

Sleep can be measured subjectively or objectively, e.g. by using polysomnography. With the former in particular, there is great discussion on the validity for different questionnaires for specific sleep disorders and use in certain demographics (Spruyt and Gozal, 2011; Erwin and Bashore, 2017). A brief overview of each measurement, with advantages and disadvantages, can be seen in table 2.3.

Table 2.3 Sleep measurement overview: advantages and disadvantages

Measurement	Description	Advantages	Disadvantages
Polysomnography	Combination of: • Electroencephalography • Electroculogram • Electromyogram Undertaken in lab whilst patient sleeps. Allows identification of sleep disorders e.g. OSA	• Provides comprehensive measurements of sleep architecture • Objective measurement e.g. use of multiple sleep latency test for daytime sleepiness	• Expensive. Use of sleep lab, equipment and trained technicians • Not helpful with individuals with long periods of wakefulness • Undertaken over a period of one to two days • Artificial and uncomfortable sleep environment • Difficult with children
Actinography	Wrist unit (akin to watch) which monitors movement, gives information on total sleep time	• Non-invasive • More cost effective than *Polysomnography* • Allows hourly surveillance for long periods of follow-up	• Does not show sleep architecture or sleep behaviours, only shows activity • Movement artefact • Non-compliance
Videosomnography	Video recording of sleep, gives particular insight into infant sleep and parasomnias	• Convenient (e.g. based at home) • Can see sleep behaviours e.g. sleeping walking	• Does not show sleep architecture • Dependent on quality of set-up • Time inefficient
Self-reported questionnaires or sleep diaries	Examples include Pittsburgh sleep quality index (PSQI) or standard sleeping log	• Cost effective • Large scope of sleep questions • Allows measurement of subjective measures e.g. restorative sleep	• Reliant on parent's insight into child's sleeping pattern or individual's insight into own sleeping patterns.

Measurement	Description	Advantages	Disadvantages
			• Subject to recall bias

OSA; obstructive sleep apnoea.
Modified from (Sadeh, 2015).

2.2.4 Sleep in adolescents

Distinct biological changes related to puberty and sleep wake regulation within teenagers have been associated with increased daytime-sleepiness and a delayed circadian phase (e.g. preference for later bedtimes and waking times) (Carskadon *et al.*, 1980; Crowley, Acebo and Carskadon, 2007). This alongside external factors such as extra-curricular activities and usage of electronics before bedtime, is thought to explain the change in sleep patterns in adolescence (Carskadon, 1990; Van Den Bulck, 2004; Crowley, Acebo and Carskadon, 2007). An international meta-analysis by Gradisar et al.(2011) on sleeping patterns, demonstrated that adolescents aged 15 and older, often have insufficient total sleeping time (<8 hours) on school nights. This association did not extend to weekend nights. This is partly explained by other studies that show evidence that teenagers tend to sleep 1-2 hours more over the weekend, unrestricted from school pressures to wake early, in an attempt to 'catch up' from weekday sleep deficit (Crowley, Acebo and Carskadon, 2007; Knutson and Lauderdale, 2009). Support from Carskadon and Acebo (2002) demonstrate that this trend is unlikely to be due to a changed requirement of total sleep time in adolescents, as when given the chance, teenagers in three longitudinal studies met the total sleep requirement sufficiently (Carskadon *et al.*, 1980). The combination of biological predisposition, coupled with external factors and early school starts is proposed to create a 'vulnerability' in teenagers for sleep problems (Carskadon, 1990; Lund *et al.*, 2010). This sleep deficit in adolescents is regarded as a serious public health problem by the American Academy of Paediatrics; associated with higher rates of car accidents, substance abuse and poor academic performance (Johnson and Breslau, 2001; Danner and Phillips, 2008; Dewald *et al.*, 2010; Au *et al.*, 2014).

2.2.5 Sleep in emerging adults

Emerging adulthood appears to be associated with a distinct change in sleep patterns related to timing (Roenneberg *et al.*, 2004; Lund *et al.*, 2010). Roenneberg et al. (2004) showed that the increased delay in the circadian phase seen throughout adolescence peaks at age 20 years. Thereafter, the circadian preference becomes increasingly earlier (e.g. inclination to go to bed earlier and rise earlier). Interestingly, Roenneberg et al. (2004) suggests this change from maximal circadian delay (or late sleeping times) in the early twenties marks the true transition from adolescence into adulthood. These physiological changes in emerging adults combined with the increased time demand through occupational or university membership and higher social commitments alter sleep related risk (Petrov, Lichstein and Baldwin, 2014). In general and taking into consideration the distinct change in sleep timing, some researchers argue that the young adult demographic should not be synonymous with the wider adult population in regard to sleep (Becker, Langberg and Byars, 2015; Fatima *et al.*, 2017).

The sleep deficit shown in adolescence appears to continue into emerging adulthood, with 20-60% of young adults reporting sleeping problems and those reporting sleeping problems shown to be at an increased risk of reporting poor health (Steptoe, Peacey and Wardle, 2006; Lund *et al.*, 2010; Becker *et al.*, 2018). Sleeping problems in adolescence are associated with reporting sleeping problems in emerging adulthood and established adulthood (Dregan and Armstrong, 2010; Fatima *et al.*, 2017). These studies linking sleep problems to poor health or future sleep problems considered factors such as body mass index, smoking, anxiety, depression and stress; with varying levels of association shown depending on the type of sleep problem defined (e.g. daytime functioning) (Steptoe, Peacey and Wardle, 2006; Dregan and Armstrong, 2010; Lund *et al.*, 2010; Fatima *et al.*, 2017; Becker *et al.*, 2018).

2.2.6 Plausible mechanisms for the association between sleep and pain

The field exploring the pathological mechanisms underlying sleep and pain is still very much in its 'infancy' (Okifuji and Hare, 2011). Chronic pain is associated with arousal during sleep, shortened total sleep time and difficulty with sleep maintenance (Moldofsky *et al.*, 1975; Wittig *et al.*, 1982). Some of the most commonly implicated mechanisms which explain the association include opioid regulation, neuroendocrine axis activation, neurotransmitter interplay, immunoregulation and emotion (Bjurstrom and Irwin, 2015).

Natural opioids produced by the body play a role within the central descending pain pathways. Sleep deprivation is associated with alteration in the synthesis of endogenous opioids and the expression of opioid receptors (Nascimento *et al.*, 2007; Finan, Goodin and Smith, 2013). Interestingly, multiple sites with these opioid receptors are implicated in the function and regulation of both sleep and pain (Desjardins, Brawer and Beaudet, 1990; Sastre *et al.*, 1996; Foo and Mason, 2003). In animal studies, sleep deprivation has been shown to reduce the efficacy of opioid based analgesia (Nascimento *et al.*, 2007). The activation of the hypothalamic-pituitary-adrenal (HPA) axis, responsible in normal physiology for the release of cortisol in relation to stress, can be prolonged in chronic pain and has sleep attenuating effects (Roehrs and Roth, 2005). HPA axis activation in combination with the sympathetic nervous system is suggested to explain the increased arousal experienced within sleep in primary insomnia (Roehrs and Roth, 2005). Several neural transmitters including serotonin, acetylcholine, dopamine and adenosine have been suggested to have a role in both pain (therapeutic or signaling) and sleep regulation; the imbalance or dysregulation of these neural chemicals comprise a large area of interest (Sitaram and Gillin, 1979; Ribeiro, Sebastião and De Mendonça, 2002; Roehrs and Roth, 2005; Monti and Monti, 2007; Monti and Jantos, 2008; Kwon *et al.*, 2014). Immunologically, the release of inflammatory cytokines in acute injury is mimicked in the body after sleep deprivation (Mullington *et al.*, 2010). Lastly the complex interplay between emotion, sleep

and pain may also further understanding, with poor mood being shown to be associated with increased reporting of pain (Turk and Okifuji, 2002). Although it is not clear exactly how mood interacts (e.g. anxiety and depression) with the sleep-pain association, there is research supporting its role as a mediator (Jansson-Fröjmark and Lindblom, 2008; O'Brien *et al.*, 2010; Mirõ *et al.*, 2011).

For LBP in particular, poor sleep has been suggested to reduce muscle relaxation, potentially inducing muscle fatigue related to poorer postural instability as demonstrated in healthy young adults (Smith and Haythornthwaite, 2004; Akulwar, Mulgaonkar and Somaiya, 2017). Understanding the biological plausibility of the association between sleep and pain is extremely complex. This section provides a brief but by no means exhaustive summary with further expansion on the pathophysiology beyond the remit of this thesis.

2.2.7 Sleep and pain: a bi-directional relationship

Both sleep and pain commonly co-exist: two-thirds of individuals with chronic pain report sleeping problems, and over half of those with sleeping problems (insomnia) report chronic pain (Taylor *et al.*, 2007; Lavigne *et al.*, 2011). Increased sleep time (>9 hours) as well as sleep deprivation (< 6hrs) has been shown to have a curvilinear association with pain (Edwards *et al.*, 2008). A substantial amount of research has been undertaken to understand the bidirectional relationship between sleep and pain. Despite this, the existence of a causal role for sleep disturbance on the development of pain is contested (Finan, Goodin and Smith, 2013). Differences in exposure measurement (e.g. objective or subjective), the participant age group and the particular type of pain investigated (e.g. rheumatoid arthritis) result in highly heterogeneous evidence (Tang *et al.*, 2012).

However, sleep problems, such as insomnia and sleep deprivation, may be associated with greater pain reporting on the following day (Raymond *et al.*, 2001; Edwards *et al.*, 2008; Lewandowski *et al.*, 2010). Sleep deprivation has further been shown to lower the pain

threshold to noxious stimuli in healthy participants, however, not all research regarding the associations between sleep and hyperalgesia in humans has been consistent (Moldofsky and Scarisbrick, 1976; Kundermann *et al.*, 2004; Lautenbacher, Kundermann and Krieg, 2006; Okifuji and Hare, 2011).

Longitudinal studies have demonstrated that issues with sleep can predict the onset of pain. Sleeping problems at baseline have been shown to be predictive of new onset headaches (tension, migraine or non-specified) in longitudinal British and Norwegian studies with follow-up at one and eleven years respectively (Boardman *et al.*, 2006; Ødegård *et al.*, 2011; Sivertsen *et al.*, 2014). Sivertsen *et al*. (2014) also found a significantly increased risk between sleeping problems reported in pain free participants at baseline and incident MSK problems (arthrosis, rheumatoid arthritis and osteoporosis).

2.2.8 Sleep and musculoskeletal pain

Further work has been undertaken to understand the relationship between sleep and musculoskeletal (MSK) pain specifically. In studies exploring the predictive ability of pain and sleep, sleep was found to be the stronger predictor of subsequent pain in comparison to the ability of pain to predict subsequent sleep problems. This finding was consistent across chronic pain, fibromyalgia, temporomandibular disorders and juvenile polyarticular arthritis (Bigatti *et al.*, 2008; Edwards *et al.*, 2008; Lewandowski *et al.*, 2010; Quartana *et al.*, 2010; Bromberg, Gil and Schanberg, 2012; Tang *et al.*, 2012).

Sleep, chronic widespread pain and adulthood

The primary outcome of many longitudinal studies exploring the association between sleep and MSK pain in adults, focuses on chronic widespread pain (CWP). CWP is broadly described as the longstanding involvement of multiple pain sites throughout the body, which can include additional features such as fatigue (Mansfield *et al.*, 2017). In one study with a 17 year follow-up of female participants aged 20-50 years, disturbed sleep at

baseline was associated with incident CWP with an adjusted odds ratio (OR) of 2.1 with a 95% confidence interval (CI) of 1.2-3.4 (Nitter, Pripp and Forseth, 2012). In a shorter longitudinal study with a 6 year follow-up, Generaal *et al.* (2017) showed in participants free from pain at baseline, that reported insufficient hours of sleep (≤6 hours) or insomnia had an increased the risk of CWP onset (hazard ratios of 1.52; 1.22, 1.90 and 1.60; 1.30, 1.96, respectively). The researchers were particularly interested in the role of depression as mediator in the sleep pain relationship and found after accounting for symptoms of depression, the results were still significant but weakened. Thereby supporting its role in mediating the association to a certain extent. Aili *et al.* (2015) carried out a prospective study of five years (n=1599), which investigated if there was an association between sleep disturbance and developing multi-site pain (≥3 sites) in pain free participants at baseline. They found that poor sleep, defined as high score on the modified Karolinska Sleep questionnaire, was associated with an odds ratio of 4.55 (95% CI 1.28, 16.12). The authors note though, that care should be applied with interpretation due to the imprecision of the confidence interval. Despite this, even the lowest estimate still indicates an increased risk with poor sleep and the onset of multi-site pain. Using the Norwegian HUNT survey, Uhlig *et al.* (2018) demonstrated an increased risk in CWP free participants with self-reported insomnia at baseline and subsequent CWP complaints, with a risk ratio of 1.58 (95% CI 1.26, 1.98). Using the same HUNT survey, Mundal *et al.* (2014) demonstrated that sleep problems were a strong predictor of persistent CWP after an 11 year follow-up (adjusted OR 1.30 95% CI 1.12, 1.51).

Sleep, LBP and adulthood

In the aforementioned study by Uhlig *et al.* (2018) into CWP, the authors also presented the associations between sleep problems and for specific pain sites, including LBP (defined by annotating pain sites on a morphological diagram which had been present for greater than

three months). They found that pain free participants who reported insomnia at baseline were at an increased risk of reporting LBP at the 11 year follow-up (RR 1.36 95% CI 1.11, 1.68). Using the earlier wave of the Norwegian HUNT survey (HUNT 1) as baseline, Mork *et al.* (2014) sought to explore the association between sleeping problems and chronic MSK pain, with specific analysis exploring the mediating role of BMI and physical activity. Follow-up again was over an 11 year period. Sleep problems were defined as 'never', 'sometimes' and 'often/always' in the last 4 weeks and LBP was defined as indicated in the HUNT study above. Their work demonstrated a significant dose-response relationship with reporting sleeping problems 'sometimes' and 'often/always' at baseline (males ('often/always' RR 1.51 95% CI 1.20, 1.91) and females ('often/always' RR 1.66 95% CI 1.41, 1.95)) and incident chronic LBP at follow-up.

The association between chronic LBP and sleep, has been explored in a systematic review. Kelly *et al.*(2011) found 17 studies (with varying study designs) meeting their criteria, after screening five databases. Studies graded of moderate quality, supported the association between chronic LBP and multiple types of sleeping problems including increased sleep disturbance, reduced sleep duration and quality. Although there was generally consensus for the association between chronic LBP and other sleep related problems (sleep efficiency, day dysfunction and unrefreshed sleep), these were from papers appraised as low in quality.

Sleep, LBP and childhood

A recent systematic review by Andreucci et al. (2017) looked explicitly at the relationship between sleep problems and the onset of MSK related pain in prospective studies focusing principally on childhood and adolescence (ages 6-19 years). They found 13 relevant studies, the majority of which were deemed high quality. The researchers found overall that childhood sleep problems (related to daytime tiredness, sleep duration, and quality) did not

increase the risk of subsequent MSK pain (back, neck, shoulder and widespread pain). Of the three prospective studies that covered LBP, there was varying support for the relationship between sleep duration or daytime tiredness (only in girls) and LBP onset.

Only two of these three LBP-focused studies within the systematic review specifically investigated the association between sleep quality and subsequent LBP. Auvinen *et al.* (2010), undertook a longitudinal cohort study which examined if poor sleep (related to quality or quantity) at age 15/16 years increased the risk of neck, shoulder and LBP at two year follow-up. They sought to investigate adolescents reporting at two time points, using a subsample (n=1,773) from the 1986 Finnish Birth Cohort. They used validated subjective measures, both for their exposure and outcome of interest. The sleep quality and quantity measure was based on sleep duration, frequency of nightmares, general sleeping issues and daytime tiredness. For MSK pain, participants were asked if within the last six months they had any pain experienced in the body, with written and visual cues for the different MSK pain sites (including LBP). The participants, due to the nature of birth cohorts, were asked a wide breadth of questions and therefore were likely to be blinded to the study's outcome of interest. Parental socioeconomic class, mood, smoking, sedentary, physical activity and baseline pain status were considered potential confounders by the authors and therefore included as covariates in logistic regression modelling. Results illustrated that only adolescent girls, with insufficient (OR 2.41 95% CI 1.34, 4.34) or intermediate (OR 1.66 95% CI 1.09, 2.53) sleep quality or quantity reported at age 15/16 years demonstrated positive associations with LBP at follow-up, showing a dose-response relationship. Females only had a significant association with day tiredness (OR 2.42 95% CI 1.24, 4.71). The confidence intervals overall are relatively wide and therefore lack precision. However, the general direction of association even using the most conservative estimates, indicate in general adolescent girls with sleep issues or tiredness are at increased risk of subsequent LBP.

The authors highlighted the potential for attrition bias given follow-up response was 68% and those followed up tended to be healthier (e.g. non-smokers) than those lost to follow-up at age 18 years. The paper did not report LBP duration and severity. The authors note that not elaborating on the exclusion criteria, i.e. menstrual related back pain, could account for why they found a higher LBP prevalence in females and could potentially introduce some information bias. Auvinen *et al. (*2010) also comment that not including anxiety or distress, may have resulted in some residual confounding. The measure used in multivariate modelling for depression constitutes one question ('I feel unhappy, sad or depressed') with response denoted by frequency (often, sometimes and never). This crude ordinal measure potentially may not sufficiently adjust for the severity of depressive symptoms, therefore there may be some residual confounding.

Szpalski *et al. (*2002) also undertook a two-year longitudinal study in children between the ages of 9 and 12 years. They focused on identifying risk factors for subsequent LBP in young children. Various risk factors were investigated which ranged from engagement in leisure activities, backpack usage and history of parental back pain. Participants (n=287) consisted of primary school children from the state school system in one Belgian city. To be included, children needed to be examined by the allocated school doctor at both time points. Half way during the study there was alteration of state school medical examination location to outside the city, causing a loss of 105 possible participants at follow-up. Sleep was measured using a general validated subjective questionnaire with questions focused on quality of sleep, falling asleep, maintenance and tiredness. In addition children also had a physical medical examination (e.g. spinal palpation). No clinical investigations were routinely carried out. Using logistic regression the authors adjusted for the following confounders; body mass index, sporting activity, parental history of LBP and depression. The results showed that only not walking to school was associated with new onset of LBP at follow-up. They did not demonstrate any of the sleep variables within the multi-variate

model, and did not report figures for estimates pertaining to sleep. There could be potential confounding through not adjusting in particular for socioeconomic class which has been associated with LBP in children and adults (Huguet *et al.*, 2016). Accounting for this, perhaps using the parent's socioeconomic class could have helped better inform the reader regarding the loss of 26.8% (105/392) of participants through change in medical examination location midway through the study. This may introduce selection bias because of the inability to account for the characteristics of the missing data. For example, children in lower socioeconomic groups may have been unable to attend these outer city appointments through both parents working full time or lack of transportation.

Sleep, LBP and emerging adulthood

Research has explored the relationship between sleep and LBP, a large proportion of which is undertaken in adult populations. Although some participants within late emerging adulthood are represented usually, their proportions are small. The majority of studies with a broad age range, as expected, adjust for age group and rarely utilize age group stratification.

There is only one single study, undertaken by Bonvanie *et al. (*2016), to the best of knowledge, which explores the association as well as the directionality between sleep problems and chronic pain (including MSK pain) in emerging adulthood. The authors used the Dutch Tracking Adolescents' Individuals lives survey, to recruit 1668 participants which reported at the fourth (age 19) and fifth (age 22) survey waves. Sleep problems were defined using a five item questionnaire (Nottingham Health Profile), which was validated and compared to the Pittsburg Sleep Questionnaire Index, a well-established subjective sleep measure. The outcome of chronic pain (any of neck, shoulder, back, limbs) was measured using a questionnaire validated for use in young adults and those responding 'yes' were asked explicitly about duration, frequency, daily interference and severity; with

further consideration of pain medication usage. The authors used statistical methods such as mediation modelling and cross lagged models to achieve their aims, taking into consideration age, sex and socioeconomic class within the analyses, in addition to the four key mediators of interest.

They found that reporting sleep problems at age 19 years significantly increased the likelihood of reporting new onset or persistence of chronic pain (any type of pain lasting more than 3 months with a severity score greater than five out of ten) at age 22; this increased association was also seen for MSK pain severity. However chronic pain, MSK severity and headache severity reported at age 19 years did not predict sleep problems at age 22. Only fatigue was shown to mediate the relationship between LBP and sleep. Bonvanie *et al. (*2016) comment that the sleep measure they used did not allow them to account for the frequency or severity of sleep problems due to limited response options (e.g. yes or no). They also remarked on the difficulty of accounting for fatigue (as defined in questionnaire to be unrelated to a known health or 'obvious' cause), which the authors argue could attenuate the results if the participant attributes their fatigue to their co-existent sleeping problem which they deem as an 'obvious' cause, thereby potentially contributing to some information bias. Lastly the researchers conclude that only having a few variables for fatigue or physical activity might compromise measurement quality and could result in some residual confounding. Overall this high standard paper, gives clear biological plausibility of the relationship between sleep and pain and suggests future research should explore further mechanisms which may mediate this association.

2.3 Conclusion

Sleep problems within adolescents and emerging adulthood are common due to both innate internal biological changes and external pressures. Biological plausibility for the association between sleep disturbance and pain are gaining momentum. Results so far in

childhood studies related to sleep disturbance and LBP have shown mixed results. Novel work investigating this trend in emerging adults appears promising, with results akin to that of adult studies demonstrating more consistent support for the association between sleep and pain. Although a few studies have covered the course of pain, there is scarce understanding of the transition of sleeping disturbance through childhood in relation to the development LBP in early adulthood. This is important given changes within sleep physiology in adolescents and emerging adulthood, in addition to the growing consensus that LBP originates earlier within the life-span. Further work is needed to build upon the limited prevalence estimates of chronic back pain within emerging adults, with the scope to account for extended years of potential exposure using the extended age definition of this developmental phase (18-29 years).

2.4 Thesis aims and objectives

The overall aim of this thesis was to provide prevalence estimates for persistent LBP in emerging adulthood, its association with comorbidity, and to explore the association with sleep disturbance reported through adolescence and emerging adulthood.

Using data from the BCS70, the specific objectives were:

1. To estimate the prevalence of persistent back pain in emerging adulthood, the proportion of this that begins in emerging adulthood and the proportion that have sought medical care.
2. To provide a comparative description of health among emerging adults with persistent back pain and those without persistent back pain.
3. To investigate the relationship between sleep disturbance in adolescence and emerging adulthood and the risk of new onset persistent back pain in emerging adulthood.

3 Methodology

This chapter aims to meet the aforementioned objectives through use of two cross-sectional studies and a nested case-control study. The type of studies used will also be briefly overviewed, giving strengths and limitations of their utilisation. There will be discussion on the use of the 1970 British Birth Cohort Study (BCS70), how the data collection was conducted and how subsequent statistical analyses were carried out.

3.1 Birth cohorts

3.1.1 Overview

Birth cohorts comprise individuals who were born in the same specified period of time and birth cohort studies often aim to follow participants up from cradle to grave. They are rich sources of data collected prospectively throughout the life course, with longitudinal insights on exposure to multiple factors and health related outcomes. In addition to their intrinsic value, different birth cohorts can also be compared to better inform researchers about disease patterns (e.g. increasing incidence rates), with insight into period effects (e.g. introduction of a vaccination) or generational effects (e.g. environmental and societal exposures which are unique to membership within that cohort) (Szklo and Nieto, 2014).

3.1.2 Previous British birth cohorts

There have been nineteen birth cohort studies within Britain to date, see table 3.1.

Table 3.1 British birth cohorts

Cohort	Year commenced	Sampling region	Size of participants at initial recruitment
1921 Lothian Birth Cohort	1921	Scotland	550
1936 Lothian birth Cohort	1936	Scotland	1091
National Survey of Health and Development (NSHD)	1946	England, Wales and Scotland	5,362
Newcastle Thousand Families Study	1947	Newcastle, Northern England	1,142
National Child Development Study (NCDS)	1958	England, Wales and Scotland	17,416
1970 British Birth Cohort Study (BCS70)	1970	England, Wales and Scotland	17,195
Merthyr Allergy Study	1982	South Wales	453
The Leicester Respiratory Cohorts	(1) 1985-1990 (2) 1993-1997	East Midlands, England	(1)1,650 (2) 8,700
Isle of Wight Birth Cohort Study	1989-1990	Isle of Wight	1,456
Avon Longitudinal Study of Parents and Children (ALSPAC)	1990-1992	Bristol, South West of England	14,062*
North Cumbria Community Genetics Projects (NCCGP)	1995-2003	Cumbria, North West England	~8000
Manchester Asthma and Allergy Study (MAAS)	1995-1997	Manchester, North West of England	1,184
Study of Eczema and Asthma To Observe the effects of Nutrition (SEATON)	1997-1999	Edinburgh, Scotland	1,924
Southampton Women's Survey (SWS)	1998-2002	Southampton, South of England	3,158*
Millennium Cohort Study (MCS)	2000	England, Wales, Scotland and Northern Ireland	18,818
The Gateshead Millennium Study (GMS)	2000	Gateshead, North East of England	1,029
Growing Up in Scotland	(1) 2004/2005 (2) 2010/2011	Scotland	(1) 5,217 (2) 6,127
Born in Bradford (BiB)	2007-2010	Bradford, North of England	13,776*

Cohort	Year commenced	Sampling region	Size of participants at initial recruitment
Growing Up in Wales: The Environments for Healthy Living study	2009-2015	Swansea, Wales	526*

**specifically for children included in the study.*

Use of these cohorts has led to vast amounts of published research focusing on interests ranging from educational performance to social deprivation. Many health outcomes have also been investigated. However back pain has been explored to a lesser extent. Within the National Survey of Health and Development (NSHD) Study and National Child Development Study (NCDS) birth cohorts specifically, only three studies to date are shown to focus on back pain (Lake, Power and Cole, 2000; Power *et al.*, 2001; Muthuri, Kuh and Cooper, 2018). This was checked using the Centre for Longitudinal Studies (CLS) and Medical Research Council bibliographies, the organisations responsible for the NCDS and NSHD.

3.1.3 Decision to use the 1970 British Birth Cohort Study data

To date, using the CLS bibliography, there was no previous study which had previously investigated back pain within the BCS70. This would allow exploration of an under-utilised source of data representative of Great Britain (GB), substantial in participant size and breadth of included variables. There is no cost of accessing and analysing the data, therefore 'bona fide' researchers have the opportunity to apply for access to the data from the eight sweeps already undertaken (Elliott and Shepherd, 2006). Therefore, this thesis used five sweeps within the BCS70 to investigate the variables of interest e.g. sleep and low back pain (LBP) through adolescence and emerging adulthood. Sweeps used for adolescence included the age 10 and 16 cohort waves (Butler, Bynner and University of London. Institute of Education. Centre for Longitudinal Studies, 2016, 2017). Sweeps used for emerging adulthood included the age 21, 26 and 29 waves (Bynner, 2016; Bynner and University of London. Institute of Education. Centre for Longitudinal Studies, 2016;

University of London. Institute of Education. Centre for Longitudinal Studies, 2016). The BCS70 is the most recent British cohort which has investigated the age range of interest. Most evidence supporting the concept of emerging adulthood as a life stage was undertaken in the last decade before the millennium, which coincides with the years the BCS70 participants also became emerging adults.

3.2 1970 British Birth Cohort Study data

3.2.1 Sweeps

The study population consisted of targeting 17,212 individuals born between the fifth and eleventh of April 1970 within England, Wales, Scotland and Northern Ireland. Participants from Northern Ireland were excluded after the age 10 survey. Participants have been followed up at definite time points called 'sweeps'. The eight sweeps where undertaken in the following ages: birth (1970), age five (1975), age 10 (1980), age 16 (1986), age 26 (1996), age 29 (1999/2000), age 34 (2004/2005) and age 42 (2012). The birth sweep is defined as sweep zero. There are also sub-sample data collections at further age points, for example the age 21 sweep. Stewardship of the BCS70 over these eight sweeps has changed. The maintenance of the cohort study has occurred through the dedication and collaboration of multiple research centres, with the cohort currently under the supervision of the CLS (CLOSER, 2018). Through the generosity of numerous funders for each individual sweep, the cohort has remained viable. Any additional information on the cohort can be found in the published BCS70 cohort profile (Elliott and Shepherd, 2006).

3.2.2 Target and observed study participants

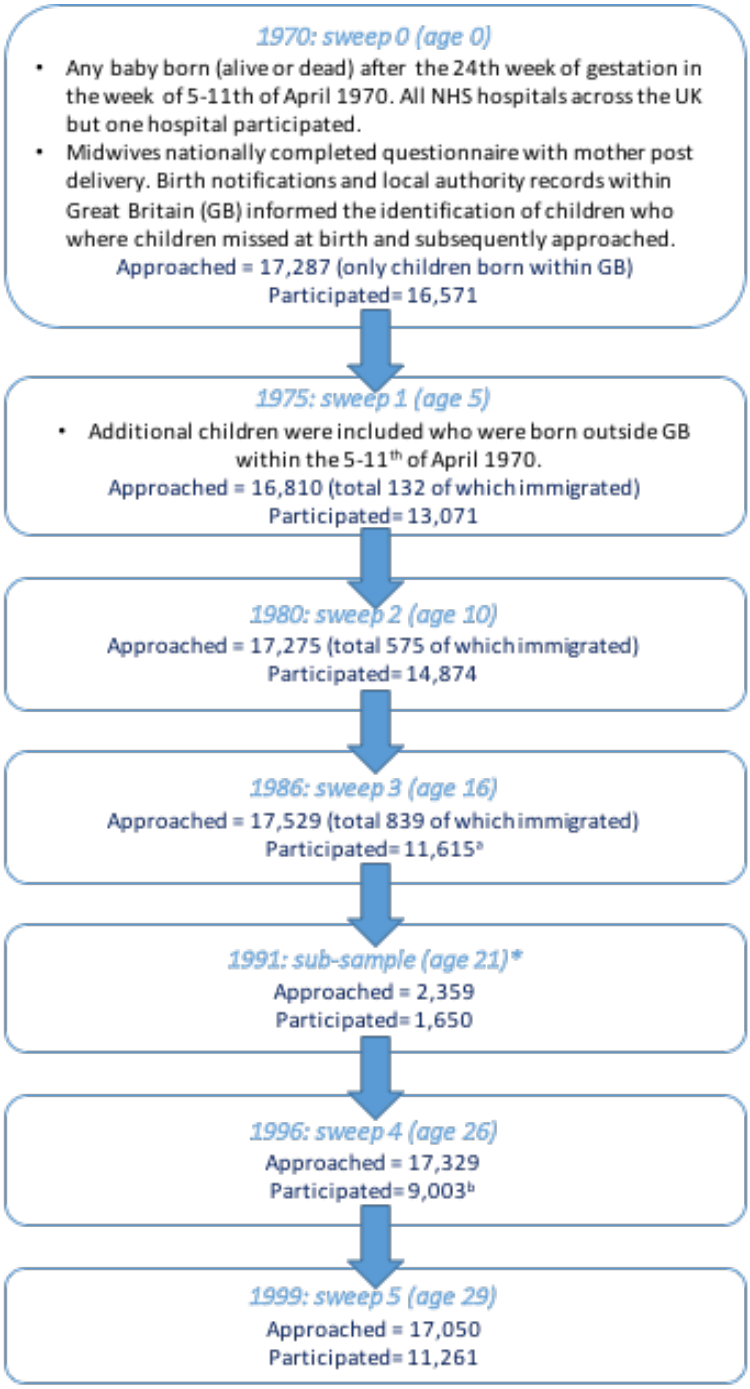
The focus of the thesis will be on the sweeps undertaken from age 10 to age 29, covering the very start of adolescence through to the end of emerging adulthood. Therefore, only these sweeps of interest will be elaborated on further. The data from the BCS70 is reported

using two samples: longitudinal and cross-sectional. Cross-sectional target samples were formed from cohort members (CM) who were born in the specified week in April 1970, who had not temporarily/permanently emigrated or passed away. This therefore included immigrants who were born outside of GB, with additional recruitment of these individuals to help increase the size of the cohort (continued until the age 16 survey). The longitudinal target sample only included participants who were born in GB on the specified week in April 1970, who did not permanently emigrate or had not passed away. The observed sample for both the longitudinal and cross-sectional samples was defined as participants who were able to be contacted, interviewed and complete at least one section of the questionnaire.

There is great complexity when using the BCS70 data. The number of study participants targeted to be approached and the actual numbers of participants who were included have been the subject of many technical reports (Plewis, Calderwood and Hawkes, 2004; Elliott and Shepherd, 2006; Heywood and Johnson, 2016). These reports are revised and added to every few years when a new report is released to incorporate successive BCS70 waves.

The data used within this thesis is derived from the cross-sectional data sample and from here on will only be referred to. The overview of the approached target samples and the final samples that participated at different sweeps within the BCS70 can be seen below in figure 3.1.

Figure 3.1 BCS70 cross-sectional sample approached and achieved



BCS70; British Birth Cohort Study.
*sub-sample.
[a]Lower than expected recruitment due to national teaching strike.
[b]Lower than expected recruitment due to decreased funding leading to limited tracing of participants.
Additional recruitment from immigration was stopped after sweep 3.
Approached: All those born on the 5-11th of April 1970, regardless of country of birth who were currently living in Britain at that sweep.
Participated: All those who participated within the BCS70 at that sweep by filling out at least one section of the survey.
The discrepancy between *approached* and *participated* are through loss of study participants by emigration, death, non-response and inability to be traced.
Taken from 1970 British Birth Cohort Study User Guide to the Response and Death Datasets (Heywood and Johnson, 2016).

3.2.3 Data collection

The data collection was undertaken using different approaches and was dependent on the sweep of interest. At age 10 and 16 CMs were traced using school registers available from councils and general practice registries. Questionnaires were given to parents, teachers and the CM. The CM also attended medical examinations at both the age 10 and 16 sweeps. Tracing of the age 21 CMs involved recruiting a sub-sample which was done through sending opportunistic birth cards to those with a current address still available; face-to-face or telephone interviews were undertaken with trained research staff.

At age 26, CMs were traced using birthday cards. However, collaboration with Family Health Service Authorities and the Driver and Vehicle Licensing Agency was also utilised to identify a greater amount of updated CM household addresses. Data collection was done using a postal questionnaire. Lastly, the age 29 sweep used all the aforementioned methods of tracing in addition to those listed in table 3.2. Data were collected by trained research staff using face to face interviews deploying the use of computer assisted personalised interviewing (CAPI), software incorporated to help improve the quality of the data collected. A separate self-reported questionnaire was also given during the interview.

Table 3.2 Tracing methods undertaken in the age 29 survey of the BCS70

Tracing methods
• Posting birthday card • Previous address or contact details • Postcode databases • Media advertisements • Electoral register databases • Health Authorities address records • Driver and Vehicle Licensing Agency address records • Ministry of Defence records • National Health Service Central Register (deaths emigrations and NHS enrolment)

BCS70; 1970 British Birth Cohort Study.
Taken from NCDS/BCS70 1999-2000 Follow-ups Guide to the Combined Dataset (Shepherd, 2001).

3.2.4 Ethics

Ethical approval for data collection was sought by the responsible research institution was given at each successive BCS70 sweep. For the initial first few sweeps ethical permission by the local research ethics committee (LRECS) until the age 29 follow-up in 2000. At this time ethical permission was given by the NHS Research Ethics Committees (RECs) for all the subsequent sweeps. Informed consent was always sought at each individual sweep using informational leaflets and letters, which initially was gained through parents and transitioned to consent given from the CM themselves. Data collected was anonymised and indexed using a unique identification number. Access to the data, was gained through registration to the UK Data Service.

3.3 Three studies using 1970 British Birth Cohort Study data

In this thesis, three studies were undertaken using BCS70 data. These were (1) a prevalence study to estimate the prevalence of persistent back pain at age 29 years; (2) a cross-sectional analytic study to compare description of health among emerging adults with persistent back pain and those without persistent back pain; and (3) a nested case-control study to investigate the relationship between sleep disturbance in adolescence and emerging adulthood and the risk of new onset persistent back pain in emerging adulthood. Analysis for all studies was conducted using SPSS version 24 unless otherwise stated.

3.3.1 Overview of study designs used

Cross-sectional studies are observational and can either have (1) descriptive (for prevalence estimation) or (2) analytic (for evaluating an association of interest) purposes. Cross-sectional studies are undertaken in a defined period of time, in which both the exposure and outcome of interest are present. In table 3.3 below, strengths and limitations for cross-sectional studies can be seen.

*Table 3.3 Strengths and limitations of cross-sectional studies**

Strengths
• Inexpensive. • Can have multiple outcomes and exposures. • Use of disease status at defined point limits recall bias. • Time efficient (e.g. one time point data collection needed).
Limitations
• Unable to infer the direction of causality between exposure and outcome. • Does not account for brief episodes or episodes in which death occurs shortly after the development of disease. More likely to include chronic disease sufferers.

**modified from* (Silman and Macfarlane, 2002).

The cross-sectional studies undertaken in this thesis used data from CMs at age 29 years (sweep 5), i.e. upper age limit used to demarcate emerging adulthood.

The nested case-control study design consists of looking at an outcome of interest and retrospectively examining study participant exposure to specific determinants, in a defined cohort. Strengths and limitations of case-control studies are summarised below in table 3.4.

*Table 3.4 Strengths and limitations of case-control studies**

Strengths
• Superior for exploring rarer disease outcomes. • In comparison to other studies is less time exhaustive and less expensive. • Allows multiple exposures of interest to be explored. • Useful for diseases with greater latency periods.
Limitations
• Cannot investigate multiple outcomes. • Reverse causality can still be an issue in some circumstances (e.g. unclear when disease ultimately started). • Is vulnerable particularly to selection bias through unrepresentative population recruitment into the study of interest and to recall bias. Recall bias can occur when study participants with the outcome of interest, are potentially more motivated when recollecting previous life events. • Inefficient for rare exposures. • Can be difficult to form incidence estimates.

**modified from* (Hennekens and Buring, 1987).

The benefits of using a nested case-control study include the attenuation of some biases case-control studies experience. For example, the use of a cohort in which the data has prospectively collected before the outcome has occurred reduces the chance of potential recall bias.

3.3.2 Study 1: Cross-sectional prevalence study of persistent back pain

Objectives: To estimate the prevalence of persistent back pain in emerging adults and the proportion of this that begins in emerging adulthood. To inform the latter, by examining the consistency of recall of study participants who reported when their persistent back pain first commenced.

Prevalence estimates include (1) lifetime period prevalence of persistent back pain at age 29 years; (2) 12-month period prevalence of persistent back pain at age 29 years; (3) 12-month consulting prevalence for persistent back pain at age 29 years.

Study design: Cross-sectional prevalence study.

Participants: BCS70 CMs at age 29 years (sweep 5).

Variables: Variables used in this study can be seen in table 3.5. CAPI lead to a specific flow of questions asked to participants within the BCS70 dependent on the answers they reported to the primary stem question (figure 3.2). All responses were binary yes or no questions, except for the age persistent back pain first started variable (continuous measure).

Table 3.5 Variables included in the cross-sectional prevalence study

Age at Survey	Variable	Question	Response options
29	backme1: MC	Have you ever had or been told you had "persistent back pain, lumbago or sciatica" or "chronic fatigue syndrome better known as ME"?*	1. Persistent back pain, lumbago or sciatica 2. Chronic fatigue syndrome 3. Neither 4. Don't know
	cl1age13	How old were you when you first had persistent back pain?	Age between birth and 30 years
	cl112m13	Have you had persistent back pain in the last 12 months?	1. Yes 2. No 3. Don't know
	cl1doc13	Have you seen a doctor in the past 12 months about your persistent back pain?	1. Yes 2. No
	BD6CNTRY: 2000	Country of Interview†	1. England 2. Wales 3. Scotland 4. Northern Ireland
	dmsex	Cohort member sex	1. Male 2. Female
26	b960637	Do you often have backache?	1. Yes 2. No
16	pd1.1	Do you have backache?	1. Most of the time 2. Some of the time 3. Rarely or never

**Multi-code: therefore could respond both.*

† Same response frequencies as standard region of residence variable (without sub-division of English counties) therefore used as a proxy measure of residence.

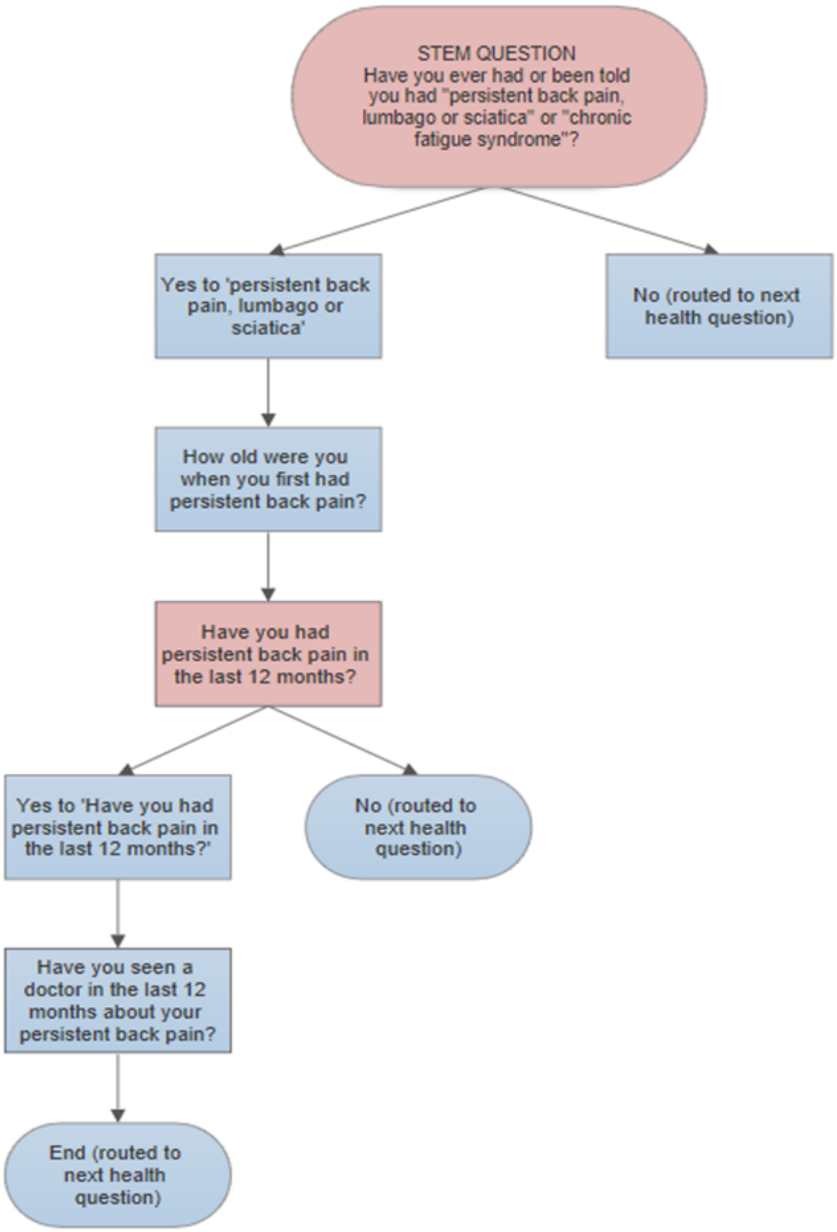


Figure 3.2 Question flow of persistent back pain variables at age 29 years

Due the question flow in the CAPI system (figure 3.2), only those who answered 'yes' to the main stem question 'Have you ever had or been told you had "persistent back pain, lumbago or sciatica" or "chronic fatigue syndrome better known as ME"?' were asked additional persistent back pain questions. A data imputation decision was made with the assumption that participants who answered 'no' to stem 'back pain ever' variable would also have answered no to 'persistent back pain in the last 12 months' variable and no to the 'seen doctor within the last 12 months' variable. This allowed calculation of the 12-month

prevalence and annual consulting prevalence of persistent back pain using the original denominator reporting for the 'back pain ever' variable (backme1: MC).

Cohort members who reported 'don't know' and 'not answered' (these options were only available for the variables relating to lifetime prevalence and 12-month prevalence (backme1: MC and cl112m13)) were excluded.

Statistical analysis: For Study 1, prevalence estimates for the three outcomes of interest were calculated, both overall and stratified by sex or country of residence, using frequency tables and cross-tabulations. Associated 95% confidence intervals (CI) were calculated, both for the prevalence estimates and also the difference in prevalence between each level of the stratifying factors. This was done using MedCalc for Windows, version 15.0 (MedCalc Software, Ostend, Belgium).

3.3.2.1 Recall accuracy of onset of persistent back pain in emerging adulthood

In order to assess the consistency of recall of study participants reporting their persistent back pain commenced during emerging adulthood, the variable 'how old were you when you first had persistent back pain?' asked at the age 29 survey and the back pain variables from cross-sectional data at age 26 and 16 were used. To be included cohort members had to provide responses to variables cl1age13 and either the b960637 or pd1.1 variable(s). Testing recall also informed how the age 16 and 26 back pain variables should be defined to best fit the definition of persistent back pain, to help address the inconsistency in variable wording. See table 3.5 for reference.

The age 26 back pain variable remained unchanged. The age 16 back pain variable had three possible responses: 'most of the time', 'some of the time' and 'rarely or never'. Two definitions were tested within the recall sub-analysis (table 3.6).

Table 3.6 Two definitions tested for the definition of persistent back pain at the age 16 variable 'do you have backache?' for the recall analysis conducted within the cross-sectional prevalence study

Persistent back pain definition (1)	Persistent back pain definition (2)
Yes: Reporting backache ✓ 'most of the time' ✓ 'some of the time' No: reporting backache ✓ 'rarely or never'	Yes: Reporting backache ✓ 'most of the time' No: reporting backache ✓ 'some of the time' ✓ 'rarely or never'

Table 3.7 An example two by two table showing the recall of participants who reported back pain at age 16 and reported the age they first experienced persistent back pain reported at age 29

		Response at age 16 to 'Do you have backache?' (Reference Standard)	
		True (Present)	False (Absent)
Self-reported age at which persistent back pain started recalled at age 29	<=16 (+)	True positive a	False positive b
	17-30 (-)	False negative c	True negative d

In order to assess recall a modified two by two table was formed based on a classical sensitivity and specificity two by two plot. As shown in table 3.7 for demonstrative purposes and the explanation of which can be found within Appendix 2.

Using these two by two plots correct and incorrect recall was calculated (table 3.7 and equation 3.1).

Equation 3.1 Calculation of correct and incorrect recall accuracy used within recall analysis for consistency

$$\frac{true\ postives + true\ negatives}{true\ postives + true\ negatives + false\ positives + false\ negatives} =$$

$$\frac{a + d}{a + b + c + d} = correct\ recall\ proportion$$

$$\frac{false\ postives + false\ negatives}{true\ postives + true\ negatives + false\ positives + false\ negatives} =$$

$$\frac{b + c}{a + b + c + d} = incorrect\ recall\ proportion$$

3.3.3 Study 2: Cross-sectional analytical study investigating co-morbidity and consultation

Objectives: To provide a comparative description of health among emerging adults with persistent back pain and those without back pain.

To compare amongst cases and controls (1) prevalence of self-reported illnesses and mental health symptoms; (2) amount of self-reported co-morbidity; (3) propensity to consult for individual illnesses or mental health symptoms; (4) amount of self-reported co-morbidity consulted for.

Study design: Cross-sectional association study.

Participants: BCS70 cohort members at age 29 years (sweep 5).

Outcomes of interest: Persistent back pain in emerging adulthood was the outcome of interest and was defined as cohort members who participated in the 29-year follow-up and who: reported 'yes' to ever experiencing persistent back pain, reported first onset of persistent back pain during emerging adulthood (age 18 to 29 years) and had suffered persistent back pain within the last 12 months.

Participants classed as having persistent back pain in emerging adulthood were compared to all other cohort members who participated in the 29-year follow-up but reported 'no' to ever having persistent back pain (backme1: MC). If participants reported their back pain to commence outside emerging adulthood or did not report persistent back pain within the last 12 months or did not report the age of onset they were excluded from the study.

Variables: The health section within the survey included questions on 28 health illnesses and eight mental health conditions separately, see table 3.8. For the 28 illnesses, the flow of questions was identical to that as explained in figure 3.2 and consisted of an initial stem question 'Have you ever had or been told you had [insert disease]?' If the cohort member reported 'yes', subsequent questions asked included: 'How old were you when you first had [insert disease]?', 'Have you had [insert disease] in the last 12 months?' and 'Have you seen a doctor in the past 12 months about your [insert disease]?'.

For specifically migraines, participants were prompted by being asked if they had a 'migraine or severe headaches associated with vomiting or dizziness'. Allergic rhinitis was included in addition to hay fever, which the survey described as a 'persistent runny nose when you haven't got a cold'.

Table 3.8 28 physical health illnesses and eight mental health conditions included in cross-sectional association study on co-morbidity and consulting

Physical health Illnesses	Mental health conditions*
Peptic ulcers	OCD-type symptoms
Eating disorder	*(feeling compelled to repeat certain actions or thoughts)*
Chronic fatigue syndrome	Mania-type symptoms
Renal/bladder problems	*(feeling overexcited or over confident)*
Bronchitis	Schizophrenia-type symptoms
Migraine	*(hearing or seeing things, which other people haven't)*
Hypertension	Phobia-type symptoms
General gynaecological problems†	*(feeling anxious or scared about objects or situations)*
Mouth ulcers	Anxiety symptoms
Crohn's disease	*(feeling generally anxious or jittery)*
Irritable Bowel Syndrome	Depressive symptoms
Contact dermatitis	*(feeling low, depressed or sad)*
Menstrual problems†	Alcohol dependency
Allergic rhinitis	*(had problems with alcohol)*
Cold sores	Drug dependency
Fungus infections	*(had problems with drugs)*
Psoriasis	
Ulcerative Colitis	
Asthma	
Other skin conditions	
Eczema	
Hay fever	
Acne	
Diabetes	
Hernia	
Gallstones	
Fits	
Cancer	

**with symptom group used in survey (cohort members were never asked for specific mental health condition by name).*
†limited to female cohort members only.

For mental health conditions specifically, participants were given a card with a list of symptom groups (representing individual mental health conditions) to report if they had sought help for in the last eight years. The participant needed to report 'yes' to be asked subsequently 'Do you still have this problem?' and 'Have you seen a specialist or been to a hospital for this problem in the last 12 months?' Responses to the former were 'yes, most of the time', 'yes, some of the time' and 'no'. Reporting yes to most or some of the time was coded as yes to having the mental health illness at age 29. These symptoms for clarity are reported as the disease they pertain to.

Due to the different phrasing of questions for mental health, estimates were not comparable between the two health sections (for descriptive simplicity the two sections are labelled 'physical health' and 'mental health') and therefore have been presented separately.

To calculate prevalence the same data imputation decision used in section 3.3.1 for 12-month prevalence and annual consulting prevalence for persistent back pain, was applied to all 28 physical illnesses. A similar process was also undertaken for the mental health symptoms, if the CM did not report saying 'yes' to the mental health group of symptoms in question, they were coded as responding 'no'. It is worth noting that the 28 physical illnesses have 12-month prevalence estimates and the mental health symptoms have point prevalence estimates due to the inconsistency of variables.

The calculated total number of different types of consultations attended did not include consultations for persistent back pain or gender-specific consultations.

Covariates: Covariates measured at age 29 included; sex, socioeconomic class, body mass index, physical activity and smoking. Highest education achievement (academic or vocational) was used as a measure for socioeconomic class using the National Vocational Qualification (NVQ). This decision was made as NVQ had the least amount of missing data compared with other possible measures for socioeconomic class at age 29 sweep, e.g. standardised occupational class. The variable used for NVQ was a composite variable of many individual variables related to highest educational achievement, which ranged from academic grades such as O-levels to apprenticeships. The CLS formulated a system in which they classified a wide range of qualifications, either vocational or academic, into an overall NVQ class (see Appendix 3 for further details). CMs with no academic or vocational qualifications were included and coded in the derived variable under 'none'.

Physical activity was measured by the average activity level score, a proxy variable adapted from previous research based on the amount of exercise reported factored up to one month, multiplied by the level of activity intensity (Juneau *et al.*, 2014). Current smokers were defined as having a daily or occasional habit, consistent with the definition used by the ONS cited in previous BCS70 studies (Daly *et al.*, 2016).

Statistical analysis: For Study 2, descriptive statistics (mean and standard deviation, median and inter-quartile range, or numbers and percentage, as appropriate) were used to describe the key characteristics of cases and controls. Logistic regression was used to estimate odds ratios (OR) and 95% CIs for the associations tested. Logistic regression was used for this analysis as the outcome was binary (case or control) and it allowed multiple covariates to be included within the models utilised (table 3.9).

Table 3.9 Models utilised in in analytical cross-sectional study on co-morbidity and consultation

Crude	Model 1	Model 2
• No adjustment performed	• Socioeconomic class (highest achieved NVQ) • Sex (if stratification for sex not applied)	• Socioeconomic class (highest achieved NVQ) • Sex (if stratification for sex not applied) • Average activity score • Smoking • BMI

BMI body mass index (kg/m^2); NVQ National Vocational Qualification (academic or vocational).

3.3.4 Study 3: Nested case-control study investigating sleep disturbance and persistent back pain commencing during emerging adulthood

Objectives: To investigate the relationship between sleep disturbance in adolescence and emerging adulthood and the risk of new onset persistent back pain in emerging adulthood.

To explore the association between developing persistent back pain in emerging adulthood and (1) sleep disturbance at a specific age in adolescence and emerging adulthood; (2) reporting sleep disturbance at multiple age points; (3) the transition between reporting sleep disturbance from adolescence to emerging adulthood; (4) parasomnias reported at age 10.

Study design: Nested case-control study.

Participants: BCS70 cohort members at age 29 (sweep 5), age 26 (sweep 4), age 21 (sub-sample), age 16 (sweep 3) and age 10 years (sweep 2).

Variables:

Case definition: Cases were defined identical to the outcome definition listed in 3.3.3: study participants at the age 29 survey who reported ever having had persistent back pain, having it within the last 12 months, and the onset of persistent back pain reported to commence within emerging adulthood, 18-29 years (variables = backme1: MC, cl112m13, cl1age13).

Control definition: Controls were defined as participants who reported 'no' to ever having persistent back pain at the age 29 (backme1: MC). This automatically inferred that these participants also reported 'no' to variables cl112m13 and cl1age13 (see figure 3.2), as these were stem questions which were only available if the participant reported persistent back pain in the initial question (backme1: MC).

Cohort members were excluded from the study if they reported persistent back pain outside emerging adulthood or did not report the age their persistent back pain started or did not report having an episode within the last 12 months. The decision was made to make

all non-cases (that were not excluded) the controls. The rationale for this arose from pragmatically looking at the age 29 survey response and how common the exposure of persistent back pain was. The logic applied was that more selection bias or complication of the data would occur if some controls were removed in an attempt to increase control to case ratio.

Exposures of interest: Sleep disturbance variables can be seen in table 3.10, below. There were two analyses carried out using the nested case-control study. The primary analysis focused on reporting *any* sleep disturbance; therefore for ages 16, 21, 26 and 29 reporting 'yes' to either problems with falling and staying asleep or early waking was coded as reporting 'yes' to sleep disturbance. At the age 16 variables specifically, only reporting 'most of the time' was coded as 'yes'. For the age 10 variables specifically, which were reported by a parent, the response to the stem question m36 (has child sleeping difficulty?) was used as a proxy measure for sleep disturbance.

Table 3.10 Sleep disturbance variables included in the nested-case-control study

Survey (age)	Variable	Question	Response options
29	mal06	Usually have difficulty falling or staying asleep?	1. Yes 2. No
	mal07	Usually wake unnecessarily early in morning?	1. Yes 2. No
26	b960642	Usually have great difficulty in falling/staying asleep?	1. Yes 2. No
	b960643	Usually wake unnecessarily early in the morning?	1. Yes 2. No
21	vbe6	Do you usually have great difficulty in falling or staying asleep?	1. Yes 2. No
	vbe7	Do you usually wake unnecessarily early in the morning?	1. Yes 2. No
16	c5o6	Do you have great difficulty sleeping?	1. Most of the time 2. Some of the time 3. Rarely or never
	c5o7	Wake unnecessarily early in mornings?	1. Most of the time 2. Some of the time 3. Rarely or never
10†	m36	Has child sleeping difficulty?*	1. Yes 2. No 3. Not stated
	m37	Getting off to sleep	1. Yes 2. Not stated
	m38	Waking during the night	1. Yes 2. Not stated
	m39	Waking early in the morning	1. Yes 2. Not stated
	m40	Nightmares or night terrors	1. Yes 2. Not stated
	m41	Sleepwalking	1. Yes 2. Not stated

† Reported by parent.
**Umbrella stem question. If reported 'yes' in questionnaire, below was 'if yes which of the following does he/she have?' with yes tick boxes for variables for m37 to m41.*

For the secondary analysis, specific sleep disturbances were investigated. The variables at all age sweeps were separated to represent two types of sleeping disturbances: (1) problems falling or staying asleep (2) early waking. For the age 10 sweep this meant specifically combining variables m37 and m38 for sleep problems related to falling or staying asleep. Parasomnias (variables m40 and m41) were also included in the secondary analysis. A data imputation decision was made for all age 10 sweep variables, that if a study

participant reported ‘no’ at the stem question (m36), ‘no’ would have also been reported for all subsequent variables (m37 to m41).

Covariates: Confounders were informed through use of the scoping review undertaken in chapter 2 (section 2.1.2 p. 23). Covariates considered for inclusion within logistic regression models used in the nested case-control study can be seen within table 3.11. The exception of which is pregnancy, which although included within the table, will be accounted for by doing a restricted analysis exploring sleep disturbance in females who have never been pregnant and developing persistent back pain which started during emerging adulthood.

Table 3.11 Covariates considered as potential confounders within nested case-control study

Confounder	Sweep	Coded definition	Methods	Comments
Sex	10, 16, 21, 26 and 29	Male or Female.	Use of age 29 sweep sex variable and if missing use each prior sweep in reverse chronological order until sex identified (e.g. age 29 → 26 → 21 → 16→ 10).	Maximises use of data.
Household Socioeconomic class	10 and 16	Father's SOC at age 10 sweep (if father's SOC is absent use mother's SOC). Thereafter if absent use of father's SOC from age 16 sweep, if absent use mother's SOC).	Use of 1980 SOC from the Office of Population Censuses and Surveys.	Use of SOC as measure of socioeconomic status was more consistent to compare at ages 10 or 16 to ages 26 or 29. This was in comparison to other possible measures of socioeconomic status; (1) net pay of parents at age 10 or 16 and CM net pay at age 26 or 29 (2) literacy/athematic scores at age 10 or 16 and highest academic or vocational achievement age 26 or 29. Previous research adopted a similar stance (Power *et al.*, 2001).
CM socioeconomic class	26 and 29	Use of CM age 29 SOC (if missing use of age 26 SOC).	Use of 1990 SOC from the Office of Population Censuses and Surveys.	Age 29 SOC variable had less missing data than the age 26 SOC variable, therefore formed the primary variable (rationale identical for household SOC primary choice variable).

Confounder	Sweep	Coded definition	Methods	Comments
Maternal persistent back pain	10 and 16	*Yes:* Mother reports backache 'most of the time' at either age 10 or age 16. *No:* Mother reports any other option than 'most of the time' at both age 10 and age 16 for backache. *Missing:* missing at both or one of the age 10 and age 16 maternal LBP variables.	*Age 10:* Likert scale. A score of 0 coded as 'rarely or never' and a score of 100 coded as 'most of time'. *Age 16:* 'do you have backache?' Response options were 'rarely or never', 'some of the time' or 'most of the time'.	Using maternal reporting of 'persistent' back pain, allows consideration of a genetic component for LBP causation e.g. lumbar disc degeneration as suggested by other research (Battié *et al.*, 2007; Livshits *et al.*, 2011).
Chronic illness or disability in the household	10 and 16	*Yes:* any household member reported to have chronic illness or disability at age 10 or 16. Score out of 2 given for the number of sweeps chronic illness in the household was reported (ordinal measure). *No:* no-one in household member reported to have chronic illness or disability at BOTH age 10 or 16. *Missing:* reports missing at both or one of the age 10 and age 16 surveys.	Variable defined as '[in the last 5 years] has anyone in the house had any severe or prolonged illness (medical, surgical or psychiatric) or any handicap or disability? Please include illness in mother, father other adults and children in house' at both age 10 and 16 sweeps. The amount of time points chronic illness was reported in the household formed an ordinal measure e.g. 2 time-points, 1 time-point or 0 time-points.	Previous research papers highlighted the importance of chronic pain within the household in both children and adults alike (Shraim *et al.*, 2014; Campbell *et al.*, 2018). Only able to measure this at age 10 and 16 sweeps, due to the difficultly of tracking when CM left childhood household or availability of similar chronic illness in the household variables at the 21, 26 and 29 sweeps.

Confounder	Sweep	Coded definition	Methods	Comments
Previous LBP	16	*Yes:* backache reported as 'most of the time' or 'some of the time' (any previous back pain). *No:* backache reported as 'rarely or never'.	Use of age 16 backache CM variable (Response options were 'rarely or never', 'some of the time' or 'most of the time').	Age 16 sweep only age with LBP recorded before the period of emerging adulthood which was utilised within the case definition. Age 10 sweep did not have a LBP variable.
Physical activity	16 and 29	*Age 29: score (0-122).* *Age 16: score (0-130) leading to binary outcome.* *High sports participation:* ≥mean = yes. *Low sports participation:* <mean= no.	Age 29: modified methodology used by Viner and Cole (2006) to account for physical activity level using 'how often CM takes part in any exercise activity' and 'how often CM gets out of breath/sweaty during exercise?' Two modifications include (1) factoring score up to 1 month instead of 2 months; (2) score of 0 recoded to represent frequency of CMs reporting 'no' to 'do regular exercise?' variable. Age 16: addition of 'F20' variables (all sports activities in school and all sports out of school) to form overall average activity score and then formatted into a binary outcome as per Juneau *et al.*, (2014).	Unable to consider age 10 due to lack of appropriate variables. Physical activity was not measured at the age 21 and 26 sweeps.

Confounder	Sweep	Coded definition	Methods	Comments
Depression	16 and 29	*Age 16 and 29:* *Yes:* severest response to any of the following variables; (1) 'do you feel miserable or depressed?'; (2) 'feeling unhappy or depressed?'; (3) 'feeling worthless as a person?'. *No:* any other response to three variables cited above.	For both age 16 and 29 for the variables 'feeling unhappy or depressed?' and 'feeling worthless as a person?' the responses were 'no more than usual', 'rather more than usual' and 'much more than usual'. For the variable 'do you feel miserable of depressed?' at the age 16 survey possible responses were 'rarely or never', 'some of the time' or 'most of the time'. At the age 26 survey only a binary response of yes or no was available for this variable.	The BCS70 has the RMI score for psychological morbidity measured at ages 16, 21, 26 and 29, however the back pain variables used to define the outcome of interest and the sleep disturbance were the variables used to derive the RMI score. The GHQ12 for mental health disorders was also available but only at age 29. Therefore, three variables were combined to form the depression covariate (only one of the variables was contained within the RMI), all variables of which were recorded at both the age 16 and 29 sweeps.
Body mass Index (kg/m^2)	16 and 29	BMI at both age 16 and 29 was measured in kg/m^2 using continuous measure.	At both age 10 and 16 sweeps, BMI was calculated using metric measurements for height and weight. Any imperial measurements were converted to metric to facilitate this.	BMI has been commonly investigated regarding both LBP and sleep apnoea. The latter of which known to cause sleep disturbance.

Confounder	Sweep	Coded definition	Methods	Comments
Smoking	16 and 29	*Age 29:* using rationale given in section 3.3.3 (p. 62) covariate section. Smoker: occasionally or every day. Non-smoker: never smoked. Ex-smoker: used to smoke but do not now. *Age 16:* Smoker: occasionally or current smoker. Non-smoker: never or previously smoked.	Age 29 smoking variable 'which of the following describes your smoking habit?' had the following responses 'never smoked', 'used to smoke', 'occasionally smokes' and 'smokes everyday'. Age 16 smoking variable 'What kind of smoker are you?' had the following responses 'never smoked a cigarette', 'smoked >= 3 months ago', 'smoke < 1 cigarette a week' and 'smoker defined as >=1 cigarette a week'. The latter two responses were coded as smoker status.	Age 29 definition for smoking status was done as per ONS recommendations and with a previous BCS70 study (Daly *et al.*, 2016). Age 16 definition was adapted to be similar as possible to the smoking definition at age 29. Unable to differentiate if CM was ex-smoker from 'smoked >= 3 months ago' therefore added within non-smoker category.
Pregnancy (restricted females only)*	29	*Been Pregnant:* Yes to 'ever been or got someone else pregnant' and female. *Never Been Pregnant:* No to 'ever been or got someone else pregnant' and female.	At age 29 all CMs were asked 'if ever been or got someone else pregnant'. BCS70 defined pregnancy as 'live births, still births, abortions and miscarriage'.	Pregnancy was considered as a confounder due to its inherent possibility to cause LBP through biological causes e.g. increased lumbar lordosis. Also subsequent sleep disturbance related to caring for infant(s) or young children.

BCS70 1970 British Birth Cohort Study; BMI body mass index (kg/m^2); CM cohort member; GHQ12 General Health Questionnaire; LBP low back pain; ONS Office of National Statistics; RMI Rutter Malaise Index; SOC Standard Occupational Classification.

**Not entered as a co-variate in logistic regression. Use of restricted analysis of females stating 'no' to 'ever pregnant' variable undertaken.*

Statistical analysis: Descriptive statistics and cross-tabulation were utilised. ORs with 95% CIs were formed using logistic regression, with adjustment of covariates incorporated within seven main models. The sleep disturbance variables at age 10, 16, 21, 26 and 29 years, were chronologically entered, forming models 1 to 5. For example model 2 included adjustment for sleep disturbance at age 10 and age 16 years. The principle for adjusting for sleep disturbance at other ages was to see if any particular age alone was important for developing persistent back pain in emerging adulthood. Model 6 further adjusted for confounders within childhood (age 10 and 16 years) and model 7 further adjusted for confounders within emerging adulthood (age 21, 26 and 29). The specific covariates included in models 5-7 can be seen below in table 3.12.

Table 3.12 Models 5-7 utilised in the nested case-control study

Model 5	Model 6	Model 7
Sleep disturbance reported at all time-points including: • Age 10 • Age 16 • Age 21 • Age 26 • Age 29	Covariates in model 5 and all confounders measured at age 10 or 16: • Childhood household SOC • Maternal history of persistent back pain • Chronic illness in the household • Previous back pain reported by CM • Physical activity • BMI • Smoking • Depression	Covariates in model 6 and all confounders measured at age 26 or 29: • SOC of CM • Physical activity • BMI • Smoking • Depression

BMI Body Mass Index (kg/m^2); CM cohort member; SOC Standard Occupational Classification.

Use of multiple imputation:

Imputation is defined as the utilisation of available data from study participant variables to predict variable outcomes for missing study participant data (Bland, 2000). Multiple sweeps were used in the analysis for Study 3, reducing sample size, and hence increasing the potential for selection bias.

To address this, multiple imputation was employed in Study 3 to impute the missing data prior to analysis, as it cannot be assumed that data are missing completely at random (MCAR) (Bland, 2000). An imputation model was constructed using the variables listed in table 3.13 (i.e. to include all variables in the analysis for Study 3) and was used to predict the missing data. In the imputation model, continuous and ordinal variables were modelled using linear regression and binary variables with logistic regression (an approach supported by Wu, Jia and Enders (2015)). The estimation algorithm used was selected using the automatic setting option in SPSS (either the Markov Chain Monte Carlo (MCMC) algorithm or chained equations), as this approach selects the estimation algorithm that is most suitable for the data being imputed. The imputation model was run multiple times to generate a set of imputed datasets, with the number of datasets chosen to equal the maximum percentage of missing data (White, Royston and Wood, 2011). The analysis models of interest (as described above) were then applied to each imputed dataset. Results were pooled across datasets using Rubin's rules to generate an overall odds ratio estimate of interest. The table demonstrating missing data frequency for cases and controls can be seen in chapter 6 table 6.3 p. 107.

Table 3.13 Variables included in imputation model, stratified by level of measurement assigned

Nominal	Ordinal	Continuous
• Case-control status • Gender • Sleep disturbance age 29 • Sleep disturbance age 26 • Sleep disturbance age 21 • Sleep disturbance age 16 • Sleep disturbance age 10 • Maternal history of persistent back pain • CM previous history of low back pain • Physical activity age 16 • Ever pregnant • Smoking age 16 • Depression age 29 • Depression age 16	• Chronic Illness in the household • Smoking age 29	• BMI age 29 • BMI age 26 • BMI age 16 • BMI age 10 • Physical activity age 29 • NVQ age 29 • Malaise Rutter Inventory Score age 29 • Malaise Rutter Inventory Score age 16 • Adult SOC • Household (childhood) SOC

BMI Body Mass Index (kg/m^2); CM cohort member; NVQ National Vocational Qualification; SOC Standard Occupational Classification.

Variables computed to test cumulative sleep disturbance or the transition from adolescence to emerging adulthood were not included in the imputation model but formed subsequently using the imputed estimates. In results chapter 6, use of the imputed data is expanded upon in comparison to complete case data results (complete case data constitutes the original data from BCS70 before imputation).

4 Results I: Descriptive estimates of persistent back pain in emerging adulthood

The following results chapter presents findings from the prevalence study described in chapter 3, Section 3.3.2 (p. 57) using the 1970 British Birth Cohort Study (BCS70) age 16, 26 and 29 data. Estimates are presented with 95% confidence intervals (CI).

4.1 Lifetime prevalence

At wave 5 in 1999, when cohort members (CM) were aged 29 years, 11,226 of 11,261 participants (51.5% female) responded to the stem question on lifetime experience of persistent low back pain. Overall 1,665 reported ever having or being told they had persistent back pain, lumbago or sciatica (lifetime prevalence rate (excluding 'don't know' and 'not answered') 14.9%; 95% CI 14.2, 15.5; table 4.1). The lifetime prevalence was significantly higher among females than males (table 4.2) and among participants in England (table 4.3).

Table 4.1 Responses to persistent back pain ever variable at age 29 years, stratified by sex

'Have you ever been told you had...'	Male		Female		Overall	
	N	*%*	N	*%*	N	*%*
Persistent back pain, lumbago or sciatica	729	*13.4*	936	*16.2*	1,665	*14.8*
Chronic fatigue syndrome	23	*0.4*	51	*0.9*	74	*0.7*
Neither of these	4,691	*86.1*	4,781	*82.8*	9,472	*84.4*
Don't know	0	-	3	*0.1*	3	*<0.1*
Not answered	7	*0.1*	5	*0.1*	12	*0.1*
Total	5,450	*100.0*	5,776	*100.0*	11,226	*100.0*

Table 4.2 Lifetime prevalence of persistent back pain at age 29 years, stratified by sex

		Lifetime prevalence*			Difference	
	N	n	%	95% CI	%	95% CI
Overall	11,211	1,665	14.9	14.2,15.5		
Male	5,443	729	13.4	12.5,14.3	Ref	
Female	5,768	936	16.2	15.3,17.2	2.8	1.5, 4.1

CI Confidence interval.
**excludes 15 respondents reporting 'don't know' and 'not answered'.*

Table 4.3 Lifetime prevalence of persistent back pain at 29 years, stratified by country

		Lifetime prevalence*			Difference	
	N	n	%	95% CI	%	95% CI
Scotland	1,040	125	12.0	10.1, 14.2	Ref	
England	9,561	1457	15.3	14.5, 16.0	3.3	1.1, 5.3
Wales	625	83	13.3	10.8, 16.2	1.3	-1.9, 4.7

CI Confidence interval
**Excludes 15 respondents reporting 'don't know' or 'not answered'.*

4.2 12-month period prevalence

Of the 1,665 respondents at age 29 years reporting ever having persistent back pain, 1,240 (74.5%) reported having persistent back pain within the past 12 months. The resultant 12-month period prevalence estimate for persistent back pain at age 29 years was 11.1% (95% CI 10.5, 11.7) and was significantly higher among females than males (table 4.4).

Table 4.4 12-month period prevalence of persistent back pain at age 29 years, stratified by sex

	12-month period prevalence†*				Difference	
	N	n	%	95% CI	%	95% CI
Overall	11,210	1,240	11.1	10.5, 11.7		
Male	5,443	556	10.2	9.4, 11.1	Ref	
Female	5,767	684	11.9	11.0, 12.7	1.7	0.5, 2.9

CAPI Computer Assisted Personal Interviewing; CI Confidence interval.
†Data imputation. Original denominator reporting to 'persistent back pain ever' variable used (n= 11226) as stem questions were only asked in CAPI system if 'yes' was reported. Assumes those who reported 'no' to 'persistent back pain ever' variable were also 'no' to 'persistent back pain in the last 12 months'.
**Excludes 16 respondents reporting 'don't know' or 'not answered'.*

4.3 Proportion consulting a doctor within the last 12 months

Participants were only asked if they consulted a doctor if they reported 'yes' to both 'back pain ever' and having 'persistent back pain within the last twelve months', through the Computer assisted personalised interviewing (CAPI) stem system. Overall, of 1,240 respondents reporting persistent back pain and indicating that this was present in the previous 12 months, 717 (57.8%) reported having seen a doctor for this in the past 12 months. This proportion was higher among females than males (62.1% vs 52.5%). The resultant 12-month consultation prevalence estimates are given in table 4.5, and show the significantly higher consulting rate for persistent back pain at age 29 years among females compared to males.

Table 4.5 Annual consultation prevalence for persistent back pain at age 29 years, stratified by sex

	Annual consultation prevalence†*				Difference	
	N	n	%	95% CI	%	95% CI
Overall	11,210	717	6.4	6.0, 6.9		
Male	5,443	292	5.4	4.8, 6.0	Ref	
Female	5,767	425	7.4	6.7, 8.1	2.0	1.1, 2.9

CI Confidence Interval; CAPI Computer Assisted Personal Interviewing.
†Data imputation. Original denominator reporting to 'persistent back pain ever' variable used (n= 11226) as stem questions were only asked in CAPI system if 'yes' was reported. Assumption those who reported 'no' to 'persistent back pain ever' variable = 'no' to 'Seen a doctor regarding persistent back pain in last 12 months' variable.
**Excludes 16 respondents reporting 'don't know' or 'not answered'.*

4.4 Proportion of persistent back pain that began in emerging adulthood

In response to the CAPI stem question 'ever had persistent back pain', participants who reported 'yes' (1665/11226), were asked the question 'age persistent back pain first started'. Only one participant did not give a response to the latter variable (1664/11226). Figure 4.1, demonstrates a negatively skewed histogram illustrating the response to the 'age first started' variable. A proportion of 81.1% (1349/1664) reported persistent back pain commencing during emerging adulthood.

Looking at figure 4.2, below, the reported first onset of persistent back was not influenced by sex. From the ages of 15-30 years, the cumulative percentage had a linear trend.

Figure 4.1 Frequency of the self-reported age at which persistent back pain first started

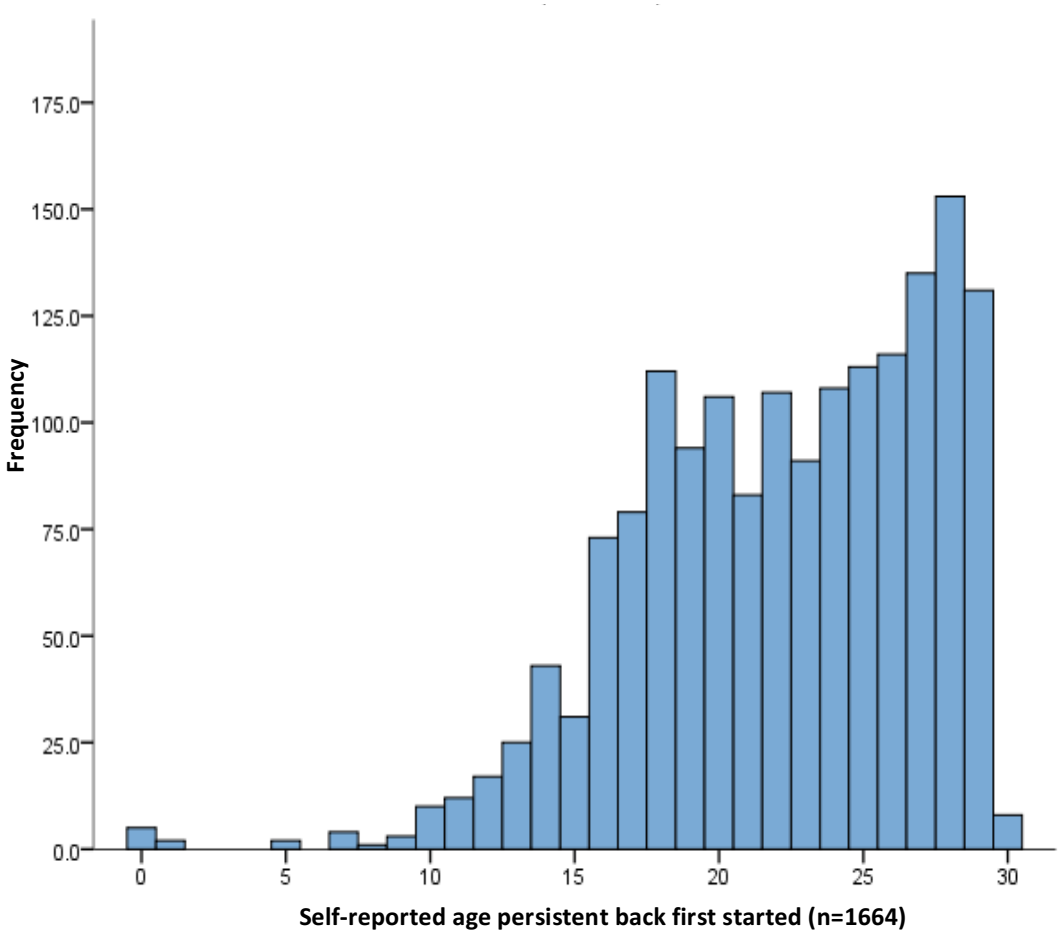
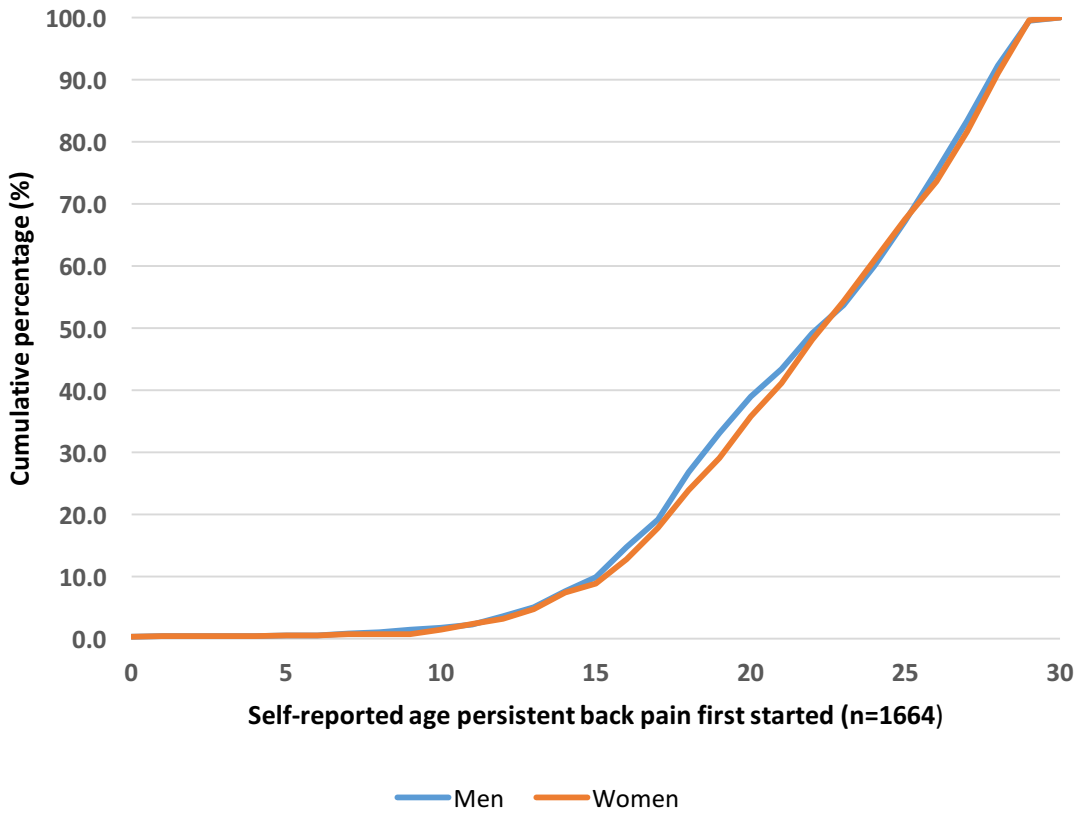


Figure 4.2 Cumulative percentage of the self-reported age at which persistent back pain first started stratified for sex



4.5 Accuracy of self-reported age of onset of persistent back pain

To check the recall agreement of the age 29 variable 'age persistent back pain first started', cross-sectional data at age points 16 and 26 were used to check for the consistency of persistent back pain reporting.

4.5.1 Age 16 recall analysis

The response rate for the age 16 back pain question can be seen below in table 4.6.

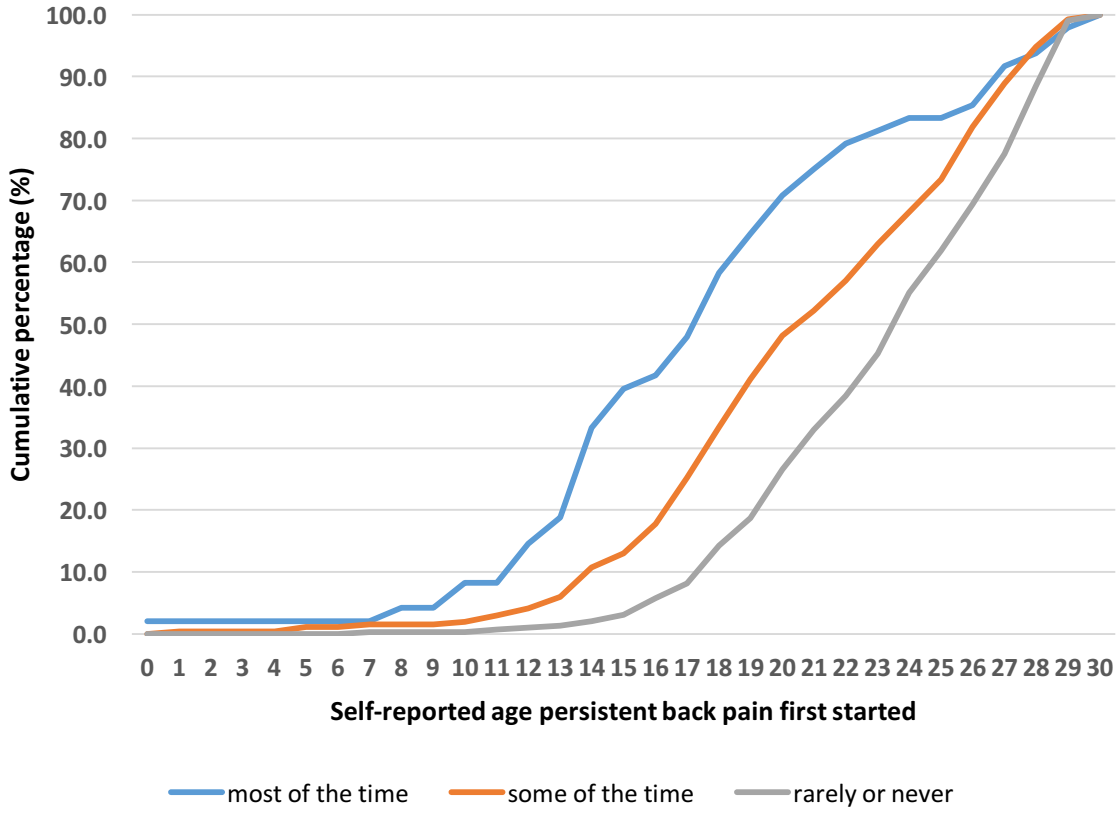
Table 4.6 Participant response to the back pain variable reported at age 16 and age persistent back pain first started as reported at age 29

'Do you have backache?'	Age persistent back pain first started: <=16 or 17-29 years		Total
	<=16	17-30	
Most of the time: N (%)	20 (41.7)	28 (58.3)	48 (100.0)
Some of the time: N (%)	48 (17.8)	222 (82.2)	270 (100.0)
Rarely or never: N (%)	17 (5.8)	277 (94.2)	294 (100.0)
Total: N (%)	85 (13.9)	527 (86.1)	612 (100.0)

Descriptive analysis was performed separately on each response for the age 16 back pain variable and compiled into a cumulative percentage graph to compare the spread of data (figure 4.3).

Using figure 4.3, the graph demonstrates that the responses 'rarely or never' and 'some of the time' for the age 16 back pain variable were more heavily weighted towards an older onset of persistent back pain. 5.8% of respondents who cited 'rarely or never' and 17.8% of respondents who cited having back pain 'some of the time', reported persistent back pain occurring before or at age 16. In comparison, a greater proportion of respondents who cited having back pain at age 16 'most of the time' (41.7%), stated their persistent back pain commenced before or at age 16.

Figure 4.3 Cumulative percentage of the self-reported age at which persistent back pain first started stratified by response to age 16 back pain variable; 'rarely or never', 'some of the time' and 'most of the time'



In table 4.7, using the age 16 back pain variable defined as 'yes' coded as experiencing back pain 'most' and 'some of the time', the correct recall response was 56.4% and the incorrect recall response was 43.6%.

Table 4.7 A two by two table showing the recall of participants who reported at the age 16 back pain variable and reported at age 29 the age they first experienced persistent back pain

		Response at age 16 to 'Do you have backache?' with yes coded as 'some and most of the time' and no coded 'rarely or never' (Reference Standard)		
		Back pain present	Back pain absent	Total
Self-reported age at which persistent back pain started recalled at age 29	<=16 (+)	68	17	85
	17-30 (-)	250	277	527
	Total	318	294	612

In comparison to the age 16 variable used above in table 4.7 which identified 250 'false negatives', there was substantially less 'false negatives' (n=28) when the variable was *recoded* as 'yes' defined as experiencing back pain 'most of the time' only (table 4.8). Using this *recoded* age 16 variable, the correct recall response was 84.8% and the corresponding incorrect recall response was 15.2%.

Table 4.8 A two by two table showing the recall of participants who reported at the age 16 back pain variable (recoded) and reported at age 29 the age they first experienced persistent back pain

		Response at age 16 to 'Do you have backache?' with yes coded as 'most of the time' and no coded 'rarely or never and some of the time' (Reference Standard)		
		Back pain present	Back pain absent	Total
Self-reported age at which persistent back pain started recalled at age 29	<=16 (+)	20	65	85
	17-30 (-)	28	499	527
	Total	48	564	612

4.5.2 Age 26 recall analysis

The same process was undertaken for age 26 recall; table 4.9 demonstrates the response rate for the age 26 back pain variable.

Table 4.9 Participant response for back pain variable at age 26 and age persistent back pain first started reported at age 29

'Often have backache?'	Age persistent back pain first started: <=26 or 27-30		Total
	<=26	27-30	
Yes: N (%)	576 (84.6)	105 (15.4)	681 (100.0)
No: N (%)	240 (57.7)	176 (42.3)	416 (100.0)
Total: N (%)	816 (74.4)	281 (25.6)	1097 (100.0)

In reference to table 4.10, the correct recall response from participants was 68.6% and the incorrect recall response was 31.4% at age 26.

Table 4.10 A two by two table showing the recall of participants who reported at the age 26 back pain variable and reported at age 29 the age they first experienced persistent back pain

		Response at age 26 to 'Do you have backache often?' (Reference Standard)		
		Back pain present	Back pain absent	Total
Self-reported age at which persistent back pain started recalled at age 29	<=26 (+)	576	240	816
	27-30 (-)	105	176	281
	Total	681	416	1097

4.5.3 Recall analysis stratified for sex

At both age points the recall percentages between males and females were relatively similar, to a lesser extent for respondents aged 16 (table 4.11). The accuracy of recall was superior at age 16 in comparison to age 26.

Table 4.11 A table demonstrating the agreement of recall for participants reporting at age 16 and/or 26, who also reported at age 29 the age they first experienced persistent back pain; stratified for sex

Age 16*		
	Correct recall (%)	Incorrect recall (%)
Overall	84.8	15.2
Male	81.8	18.2
Female	86.2	13.8
Age 26		
	Correct recall (%)	Incorrect recall (%)
Overall	68.6	31.4
Male	68.9	31.1
Female	68.3	31.7

**Age 16 recall using recoded variable; 'yes' defined as reporting back pain 'most of time', 'no' defined as reporting back pain 'some of the time' and 'rarely or never'.*

5 Results II: Co-morbidity and consultation

The following results chapter presents findings from the cross-sectional association study of 1970 British Birth Cohort Study (BCS70) age 29 data, the methods for which are given in chapter five, Section 3.3.3 (p. 62). Associations are presented as odds ratios (OR) with 95% confidence intervals (CI).

5.1 Descriptive characteristics

For the cross-sectional prevalence study, 11261 participants were available from the age 29 survey from the BCS70. There were 35 missing cases. Out of the remaining 11,226 participants 678 were excluded, as they did not meet the inclusion criteria for case or control status, leaving a total of 10,548 study participants.

Characteristics of the 1,002 cases with persistent back pain and 9,546 controls are shown in table 5.1. Compared to controls, cases had a higher proportion of females, lower educational attainment and occupational class, and were more likely to be obese and to smoke.

Table 5.1 Descriptive characteristics of cases and controls: BCS70 29 year follow-up (1999-2000)

Age 29 variables		Cases with persistent back pain (n=1002)		Controls (n=9546)	
		N	%	N	%
Female		560	*55.9*	4,832	*50.6*
Region					
	England	863	*86.1*	8,090	*84.7*
	Wales	55	*5.5*	542	*5.7*
	Scotland	84	*8.4*	914	*9.6*
Highest level of achievement*					
	None	153	*15.3*	1,234	*12.9*
	NVQ Level 1	107	*10.7*	815	*8.5*
	NVQ Level 2	303	*30.2*	2,977	*31.2*
	NVQ Level 3	151	*15.1*	1,341	*14.1*
	NVQ Level 4	260	*25.9*	2,719	*28.5*
	NVQ Level 5	28	*2.8*	458	*4.8*
Adult SOC					
	I Professional	34	*4.1*	532	*6.4*
	II Managerial-technical	249	*30.4*	2,891	*34.7*
	III Skilled non-manual	203	*24.8*	2,114	*25.4*
	III Skilled manual	191	*23.3*	1,694	*20.4*
	IV Partly skilled	117	*14.3*	917	*11.0*
	V Unskilled	26	*3.2*	172	*2.1*
Body Mass Index (kg/m^2)					
	< 25	542	*55.4*	5,444	*58.3*
	25-29.9	291	*29.7*	2,820	*30.2*
	>29.9	146	*14.9*	1,078	*11.5*
Smoking					
	Never smoked	368	*36.8*	4,323	*45.3*
	Ex-smoker	198	*19.8*	1,812	*19.0*
	Occasional or regular smoker	435	*43.5*	3,406	*35.7*
Average activity score (0-112)					
	Median (IQR)	16.0 *(0.0, 40.0)*		20.0 *(4.0,40.0)*	

IQR Inter-quartile range; NVQ National Vocational Qualification; Standard Occupational Classification 1990.
**academic or vocational.*

Due to the presence of effect modification when stratifying for sex, results for total number of co-morbidities and different types of consultations sought are presented separately for males and females.

5.2 Co-morbid physical health: 12-month prevalence

In the last 12 months, study participants (cases and controls) reported commonly suffering from hay fever (18.3%), migraines (11.5%), eczema (9.3%), asthma (7.3%) and Irritable bowel syndrome (IBS) (5.2%). Among female participants, gynaecological-related illness (general and menstrual) was also relatively prevalent. After adjustment, 15 of the 28 self-reported physical illnesses were significantly more likely to be reported by those with persistent back pain that commenced during emerging adulthood (table 5.2).

For a number of illnesses, the derived odds ratios indicated strong positive associations with persistent back pain commencing during emerging adulthood compared with controls (peptic ulcer, eating disorders, chronic fatigue syndrome, renal/bladder problems and bronchitis), although the small numbers informing these analyses often resulted in wide CIs and low precision.

Individuals with self-reported migraine in the last year had a 1.97 times higher odds of reporting persistent back pain commencing during emerging adulthood than those who did not report migraine, with a relatively narrower CI (95% CI 1.65, 2.35) due to the higher prevalence of migraine (n=1,217). A similar trend but to a lesser extent was seen in those with hypertension and IBS.

Table 5.2 Prevalence of self-reported illness in last 12 months and their association with persistent back pain at age 29 years

	Prevalence amongst cases %	Prevalence amongst controls %	Crude OR (95%CI)	Adj. OR (95%CI)*	Adj. OR (95%CI)‡
Peptic ulcers	2.6	0.6	4.08 (2.57, 6.47)	4.03 (2.53, 6.42)	3.85 (2.41, 6.14)
Eating disorder	3.9	1.3	2.98 (2.07, 4.29)	2.78 (1.93, 4.01)	2.62 (1.80, 3.82)
Renal/bladder problems	4.6	2.0	2.41 (1.73, 3.35)	2.31 (1.66, 3.22)	2.30 (1.64, 3.22)
Chronic fatigue syndrome	0.9	0.4	2.33 (1.12, 4.84)	2.33 (1.12, 4.84)	2.41 (1.15, 5.04)
Bronchitis	2.4	1.1	2.25 (1.44, 3.53)	2.20 (1.40, 3.45)	2.11 (1.33, 3.35)
Migraine	19.9	10.7	2.08 (1.76, 2.46)	1.99 (1.68, 2.37)	1.97 (1.65, 2.35)
Hypertension	5.6	2.8	2.05 (1.53, 2.75)	2.00 (1.07, 1.40)	1.83 (1.34, 2.49)
General gynaecological problems†	10.0	5.6	2.01 (1.50, 2.70)	2.00 (1.49, 2.69)	1.78 (1.30, 2.42)
Irritable Bowel Syndrome	8.5	4.7	1.88 (1.48, 2.40)	1.79 (1.40, 2.29)	1.77 (1.38, 2.28)
Mouth ulcers	1.5	0.9	1.87 (1.07, 3.26)	1.86 (1.06, 3.25)	1.79 (1.01, 3.19)
Contact dermatitis	2.7	1.5	1.78 (1.18, 2.70)	1.70 (1.12, 2.57)	1.72 (1.13, 2.62)
Crohn's disease	0.5	0.3	1.77 (0.68, 4.60)	1.79 (0.69, 4.66)	2.08 (0.80, 5.47)
Menstrual problems†	16.6	11.2	1.71 (1.36, 2.15)	1.57 (1.23, 2.00)	1.49 (1.16, 1.91)
Allergic rhinitis	4.5	2.8	1.66 (1.20, 2.29)	1.68 (1.22, 2.33)	1.63 (1.17, 2.28)
Cold sores	3.1	2.0	1.60 (1.09, 2.35)	1.60 (1.09, 2.35)	1.39 (0.92, 2.08)
Fungus infections	1.8	1.1	1.60 (0.97, 2.64)	1.55 (0.92, 2.62)	1.55 (0.92, 2.62)
Psoriasis	3.8	2.6	1.48 (1.04, 2.09)	1.44 (1.02, 2.05)	1.33 (0.93, 1.90)
Asthma	9.6	7.1	1.39 (1.11, 1.74)	1.37 (1.10, 1.72)	1.35 (1.07, 1.70)
Other skin conditions	2.6	1.9	1.38 (0.91, 2.09)	1.37 (0.90, 2.08)	1.36 (0.89, 2.08)
Ulcerative Colitis	0.3	0.2	1.36 (0.41, 4.57)	1.38 (0.41, 4.64)	1.23 (0.36, 4.20)
Eczema	10.9	9.0	1.24 (1.00, 1.53)	1.20 (0.97, 1.49)	1.17 (0.94, 1.45)
Hay fever	20.8	18.0	1.19 (1.01, 1.40)	1.22 (1.04, 1.43)	1.24 (1.05, 1.46)
Acne	2.0	1.7	1.16 (0.73, 1.85)	1.16 (0.73, 1.86)	1.17 (0.72, 1.90)

		Prevalence amongst cases %	Prevalence amongst controls %	Crude OR (95%CI)	Adj. OR (95%CI)*	Adj. OR (95%CI)‡
Hernia		0.7	0.6	1.08 (0.49, 2.36)	1.08 (0.49, 2.38)	1.08 (0.49, 2.38)
Diabetes		0.8	0.8	1.04 (0.50, 2.17)	1.04 (0.50, 2.17)	1.04 (0.50, 2.18)
Gallstones		0.2	0.2	0.95 (0.22, 4.08)	0.88 (0.21, 3.79)	0.47 (0.06, 3.56)
Fits		0.8	0.5	-	-	-
Cancer		0.2	0.3	-	-	-
Total count of co-morbidities reported						
Males						
None	3,018	49.3	59.4	1	1	1
One	1,431	29.4	27.6	1.28 (1.02, 1.61)	1.29 (1.03, 1.62)	1.29 (1.02, 1.62)
Two	471	12.2	8.8	1.66 (1.21, 2.28)	1.70 (1.24, 2.33)	1.71 (1.25, 2.36)
Three or more	236	9.0	4.6	2.62 (1.82, 3.78)	2.62 (1.82, 3.80)	2.44 (1.67, 3.55)
Females						
None	2,421	29.1	46.7	1	1	1
One	1,658	33.2	30.5	1.75 (1.40, 2.18)	1.78 (1.42, 2.20)	1.76 (1.41, 2.21)
Two	784	20.4	13.9	2.36 (1.83, 3.04)	2.37 (1.83, 3.05)	2.27 (1.74, 2.95)
Three or more	529	17.3	8.9	3.11 (2.37, 4.08)	3.13 (2.38, 4.11)	3.07 (2.32, 4.06)

FOOTNOTES FROM TABLE 5.2 CONTINUED

CI Confidence interval; OR Odds ratio.

† Females only (not included in count of co-morbidities to allow comparison).

** Adjusted for sex and socioeconomic status.*

‡ Adjusted for sex, socioeconomic status, body mass index, average activity score, smoking.

N indicates total individuals in both cases and controls who self-reported illness.

Ordered by magnitude of crude OR for self-reported illness.

(-) insufficient power to run analysis.

Looking at the total count of co-morbidities reported (table 5.2), overall male participants reported a smaller proportion of co-morbidities in comparison to females. Female cases had a considerably larger proportion reporting three or more co-morbidities than their respective controls. Both males and females reporting any additional co-morbidity were at a significantly higher risk of reporting persistent back pain starting during emerging adulthood, demonstrating a dose response relationship.

5.3 Co-morbid mental health symptoms: point prevalence

Mental health symptoms related to depression (9.6%) and anxiety (3.9%) were the most prevalent in all study participants. Cases with persistent back pain were associated with increased reporting of symptoms pertaining to OCD, schizophrenia, phobia, anxiety and depression (table 5.3).

Table 5.3 Prevalence of self-reported mental health symptoms at age 29 and their association with persistent back pain at age 29 years

		Prevalence amongst cases %	Prevalence amongst controls %	Crude OR (95%CI)	Adj. OR (95%CI)*	Adj. OR (95%CI)‡
OCD-type symptoms[a]		2.0	0.6	3.33 (2.00, 5.56)	3.22 (1.92, 5.38)	3.07 (1.83, 5.14)
Mania-type symptoms[b]		0.6	0.2	2.49 (1.01, 6.14)	2.49 (1.01, 6.13)	2.31 (0.93, 5.70)
Schizophrenia-type symptoms[c]		1.1	0.5	2.34 (1.21, 4.55)	2.22 (1.14, 4.31)	2.16 (1.11, 4.21)
Anxiety symptoms[e]		7.4	3.6	2.16 (1.66, 2.80)	2.05 (1.58, 2.67)	1.94 (1.49, 2.54)
Phobia-type symptoms[d]		5.1	2.5	2.13 (1.56,2.90)	2.03 (1.49, 2.77)	1.95 (1.43, 2.67)
Depressive symptoms[f]		16.9	8.8	2.11 (1.76,2.52)	2.06 (1.72, 2.47)	1.92 (1.59, 2.32)
Alcohol dependency[g]		1.0	0.5	1.95 (0.99,3.87)	2.00 (1.01, 3.98)	1.67 (0.81, 3.45)
Drug dependency[h]		0.8	0.4	1.87 (0.87,3.99)	1.85 (0.86, 3.97)	1.70 (0.79, 3.67)
Total count of mental health symptoms reported						
Males						
None	4,755	85.5	92.9	1	1	1
One	225	8.1	4.0	2.21 (1.52, 3.20)	2.18 (1.50, 3.16)	2.10 (1.44, 3.06)
Two	88	2.3	1.7	1.49 (0.77, 2.89)	1.45 (0.74, 2.83)	1.23 (0.61, 2.48)
Three or more	88	4.1	1.5	2.98 (1.76, 5.05)	2.83 (1.66, 4.82)	2.57 (1.50, 4.40)
Females						
None	4,541	73.9	85.4	1	1	1
One	599	18.2	10.3	2.05 (1.62, 2.59)	2.03 (1.60, 2.57)	1.95 (1.53, 2.49)
Two	146	4.1	2.5	1.86 (1.18, 2.94)	1.84 (1.16, 2.91)	1.82 (1.14, 2.90)
Three or more	106	3.8	1.8	2.46 (1.51, 4.01)	2.38 (1.46, 3.88)	2.32 (1.42, 3.81)

CI Confidence interval; OCD Obsessive-compulsive disorder; OR Odds ratio.

** Adjusted for sex and socioeconomic status.*

‡ Adjusted for sex, socioeconomic status, body mass index, average activity score, smoking.

N indicates total individuals in both cases and controls who self-reported mental health symptoms.

Ordered by magnitude of crude OR for self-reported mental health symptoms.

[a] 'feeling compelled to repeat certain actions or thoughts'; [b] 'feeling overexcited or over confident'; [c] 'hearing or seeing things, which other people haven't'; [d] 'feeling anxious or scared about objects or situations'; [e] 'feeling generally anxious or jittery'; [f] 'feeling low, depressed or sad'; [g] 'had problems with alcohol'; [h] 'had problems with drugs'.

However only anxiety and depression related symptoms had precise estimates due to the higher prevalence of cases. Females had a markedly higher proportion of cases reporting one or more co-morbid mental health symptoms than controls. Males overall had less self-reported co-morbid mental health symptoms in comparison to females.

For both sexes, there was a significant association for reporting one and three or more types of mental health symptoms in those with persistent back pain; however, the association for reporting two types of mental health symptoms was only seen in females and not males (table 5.3).

5.4 Propensity to consult for co-morbid illness and mental health symptoms

Among cases and controls who reported each co-morbid physical illness and mental health symptoms, the proportion who had consulted subsequently in the previous 12 months was generally high and appeared broadly similar between cases and controls although estimates were imprecise due to small numbers in many instances (table 5.4 and 5.5).

Out of the physical illnesses, only consulting for migraines (OR 1.64 95% CI 1.19, 2.27) and IBS (OR 1.84 95% CI 1.10, 3.08) in the last 12 months was shown to have an increased odds of developing persistent back pain which commenced during emerging adulthood (table 5.4). There was no association between the propensity to consult for any mental health symptom (within secondary care) and developing the outcome of interest (table 5.5).

Table 5.4 Proportion consulting in the last 12 months for each self-reported illness (%) and its association with persistent back pain at age 29 years

	Proportion of cases that consulted§ %	Proportion of controls that consulted§ %	Crude OR (95%CI)	Adj. OR (95%CI)*	Adj. OR (95%CI)‡
Peptic ulcers	84.6	87.1	0.82 (0.22, 2.99)	0.62 (0.15, 2.56)	1.56 (0.11,2.78)
Eating disorder	46.2	53.9	0.73 (0.36, 1.50)	0.77 (0.37, 1.63)	0.66 (0.29, 1.48)
Renal/bladder problems	78.3	82.9	0.74 (0.34, 1.65)	0.74 (0.32, 1.74)	0.80 (0.33, 1.91)
Chronic fatigue syndrome	66.7	86.5	0.31 (0.06, 1.67)	0.19 (0.02, 1.51)	-
Bronchitis	83.3	86.4	0.82 (0.25, 2.70)	0.65 (0.18, 2.33)	0.64 (0.18, 2.35)
Migraine	52.3	39.3	1.69 (1.25, 2.30)	1.62 (1.19, 2.22)	1.64 (1.19, 2.27)
Hypertension	92.9	84.0	2.48 (0.85, 7.23)	2.31 (0.78, 6.85)	2.17 (0.72, 6.52)
General gynaecological problems†	89.3	92.3	0.69 (0.27, 1.81)	0.71 (0.27, 1.87)	0.76 (0.28, 2.01)
Irritable Bowel Syndrome	65.9	53.3	1.69 (1.04, 2.74)	1.71 (1.04, 2.81)	1.84 (1.10, 3.08)
Mouth ulcers	26.7	11.7	2.75 (0.72, 10.48)	2.01 (0.47, 8.71)	1.07 (0.19, 6.08)
Contact dermatitis	37.0	49.3	0.61 (0.26, 1.41)	0.60 (0.25, 1.42)	0.54 (0.22, 1.35)
Crohn's disease	100.0	92.6	-	-	-
Menstrual problems†	67.7	72.0	0.82 (0.51, 1.31)	0.81 (0.50, 1.31)	0.76 (0.47, 1.26)
Allergic rhinitis	42.2	39.5	1.12 (0.59, 2.12)	1.10 (0.57, 2.11)	1.20 (0.59, 2.41)
Cold sores	16.1	15.0	1.09 (0.39, 3.08)	1.12 (0.39, 3.23)	0.99 (0.30, 3.29)
Fungus infections	50.0	55.6	0.80 (0.30, 2.17)	0.76 (0.27, 2.11)	0.78 (0.25, 2.44)
Psoriasis	57.9	48.4	1.47 (0.74, 2.93)	1.34 (0.66, 2.74)	1.27 (0.59, 2.73)
Asthma	69.8	68.1	1.08 (0.68, 1.72)	1.03 (0.64, 1.66)	0.91 (0.56, 1.48)
Other skin conditions	57.7	54.1	1.16 (0.50, 2.65)	1.16 (0.48, 2.79)	1.02 (0.41, 2.55)
Ulcerative Colitis	66.7	95.2	0.10 (0.04, 2.29)	-	-
Eczema	43.1	45.3	0.91 (0.61, 1.37)	0.95 (0.63, 1.43)	0.96 (0.63, 1.46)
Hay fever	37.0	30.1	1.37 (1.02, 1.85)	1.29 (0.95, 1.75)	1.26 (0.93, 1.73)
Acne	60.0	58.2	1.08 (0.42, 2.78)	1.20 (0.41, 3.55)	1.26 (0.41, 3.86)

		Proportion of cases that consulted§ %	Proportion of controls that consulted§ %	Crude OR (95%CI)	Adj. OR (95%CI)*	Adj. OR (95%CI)‡
Hernia		57.1	71.0	0.55 (0.11, 2.69)	0.46 (0.08, 2.62)	0.49 (0.07, 3.32)
Diabetes		87.5	95.9	0.30 (0.03, 3.28)	0.35 (0.03, 4.14)	0.21 (0.01, 3.54)
Gallstones		50.0	90.0	0.11 (0.01, 2.55)	0.17 (0.01, 5.45)	-
Fits		75.5	88.9	0.38 (0.06, 2.39)	0.24 (0.03, 2.17)	0.11 (0.01, 2.49)
Cancer		100.0	100.0	-	-	-
Total count of different types of consultations sought						
Males						
None	4,098	70.1	80.4	1	1	1
One	739	21.0	16.1	1.54 (1.20, 1.96)	1.53 (1.20, 1.96)	1.54 (1.20, 1.97)
Two	170	6.3	3.0	2.41 (1.58, 3.67)	2.34 (1.54, 3.57)	2.21 (1.43, 3.40)
Three or more	56	2.5	1.0	2.99 (1.53, 5.83)	3.02 (1.54, 5.92)	3.02 (1.53, 5.96)
Females						
None	3,522	52.3	66.8	1	1	1
One	1,274	28.6	23.1	1.58 (1.29, 1.94)	1.57 (1.28, 1.93)	1.57 (1.28, 1.94)
Two	413	10.9	7.3	1.91 (1.42, 2.57)	1.90 (1.41, 2.56)	1.80 (1.32, 2.45)
Three or more	183	8.2	2.8	3.70 (2.60, 5.28)	3.65 (2.56, 5.21)	3.41 (2.36, 4.95)

CI Confidence interval; OR Odds ratio.

† Females only.

** Adjusted for sex and socioeconomic status.*

‡ Adjusted for sex, socioeconomic status, body mass index, average activity score, smoking.

§ Proportion of participants that went on to consult for [insert illness] in the last 12-months, after reporting [insert illness] in the last 12-months.

N indicates total individuals in both cases and controls who self-reported illness.

Ordered by magnitude of crude OR for self-reported illness.

(-) insufficient power to run analysis.

5.5 Consultations for multiple co-morbidities

Overall, there was evidence of a graded relationship between persistent back pain and the number of co-morbid physical illnesses consulted for in the past 12 months (table 5.4). This was present regardless of sex and remained after adjustment for covariates.

This pattern was less marked for mental health symptoms, although this may be due to the very low prevalence of some of these symptoms. In general, for both males and females, cases with persistent back pain had a higher proportion that reported seeking secondary consultation for mental health symptoms than controls in the previous 12 months (table 5.5). Crude odds ratios for females consulting for one to two mental health related symptoms or males consulting for greater than three mental health related symptoms demonstrated an association with persistent back pain commencing during emerging adulthood; however, after full adjustment this association did not hold. The effect of adjusting for socioeconomic class (using highest National Vocational Qualification) in men particularly, showed strong evidence of positive confounding.

Table 5.5 Proportion consulting in the last 12 months for each self-reported mental health symptoms (%) and its association with persistent back pain at age 29 years

		Proportion of cases that consulted§ %	Proportion of controls that consulted§ %	Crude OR (95%CI)	Adj. OR (95%CI)*	Adj. OR (95%CI)‡
OCD-type symptoms[a]		50.0	51.7	0.93 (0.34, 2.58)	0.86 (0.29, 2.55)	1.29 (0.38, 4.40)
Mania-type symptoms[b]		50.0	56.5	0.77 (0.13, 4.65)	0.48 (0.06, 3.92)	0.32 (0.01, 8.25)
Schizophrenia -type symptoms[c]		72.7	53.3	2.33 (0.55, 9.95)	2.66 (0.53, 13.42)	-
Anxiety symptoms[e]		35.1	41.8	0.76 (0.45, 1.28)	0.72 (0.43, 1.23)	0.77 (0.45, 1.32)
Phobia-type symptoms[d]		45.1	41.3	1.17 (0.64, 2.15)	1.16 (0.62, 2.18)	1.16 (0.62, 2.20)
Depressive symptoms[f]		33.1	33.4	0.99 (0.70, 1.41)	0.97 (0.68, 1.39)	0.93 (0.64, 1.33)
Alcohol dependency[g]		40.0	36.7	1.15 (0.29, 4.62)	1.11 (0.26, 4.79)	1.10 (0.19, 6.32)
Drug dependency[h]		50.0	58.5	0.71 (0.16, 3.24)	1.01 (0.17, 5.93)	0.58 (0.07, 4.71)
Total count of different types of specialist mental health consultation sought						
Males						
None	4,999	94.6	97.2	1	1	1
One	76	2.3	1.4	1.66 (0.85, 3.25)	0.36 (0.18, 0.71)	0.39 (0.20, 1.43)
Two	29	0.7	0.6	1.27 (0.38, 4.20)	0.58 (0.23, 1.48)	0.53 (0.20, 1.38)
Three or more	52	2.5	0.9	2.94 (1.50, 5.76)	0.43 (0.11, 1.69)	0.44 (0.11, 1.75)
Females						
None	5,125	92.1	95.4	1	1	1
One	171	4.8	3.0	1.68 (1.10, 2.55)	0.63 (0.28, 1.42)	0.69 (0.30, 1.55)
Two	51	1.8	0.8	2.18 (1.09, 4.38)	1.05 (0.42, 2.59)	0.99 (0.39, 2.49)
Three or more	45	1.3	0.8	1.65 (0.73, 3.70)	1.34 (0.46, 3.87)	1.52 (0.52, 4.44)

CI Confidence interval; OCD Obsessive-compulsive disorder; OR Odds ratio.

** Adjusted for sex and socioeconomic status.*

‡ Adjusted for sex, socioeconomic status, body mass index, average activity score, smoking.

§ Proportion of participants that went on to consult for [insert disease symptoms] in the last 12-months, after reporting [insert disease symptoms] in the last 12-months.

N indicates total individuals in both cases and controls who self-reported mental health symptoms. Ordered by magnitude of crude OR for self-reported mental health symptoms.

[a] 'feeling compelled to repeat certain actions or thoughts'; [b] 'feeling overexcited or over confident'; [c] 'hearing or seeing things, which other people haven't'; [d] 'feeling anxious or scared about objects or situations'; [e] 'feeling generally anxious or jittery'; [f] 'feeling low, depressed or sad'; [g] 'had problems with alcohol'; [h] 'had problems with drugs'.

(-) insufficient power to run analysis.

6 Results III: Sleep disturbance and persistent back pain in emerging adulthood

The following results section presents findings from the nested case-control study using 1970 British Birth Cohort Study (BCS70) data (age 10, 16, 21, 26 and 29 years), the methods for which are described in chapter three, Section 3.3.4 (p. 67). Associations are presented as odds ratios (OR) with 95% confidence intervals (CI).

6.1 Descriptive characteristics of cases and controls

1,002 cases with persistent back pain at age 29 years that began in emerging adulthood were identified, along with 9,546 controls without persistent back pain (table 6.1). 678 cohort members (CM) reporting lifetime persistent back pain at age 29 years that either began before age 18 years or had apparently resolved at age 29 years were excluded.

Based on complete case data, compared with controls, cases were more likely to be female, smoke, have lower educational attainment, and lower occupational class as adults (table 6.1). There was a higher proportion of cases who grew up with someone in the household with chronic illness and who reported depressive symptoms (age 16 and 29) in comparison to controls. Cases at age 29 also had higher average Rutter Malaise Index (RMI) score for psychological morbidity. Lastly, cases tended to report a lower level of physical activity (age 29) and belong to a lower adult socioeconomic class than controls.

Table 6.1 Descriptive characteristics of cases and controls: BCS70 age 10, 16, 21, 26 and 29 year follow-up (1970-2000)

	Cases with persistent back pain (n=1,002)		Controls (n=9,546)	
	N	%	N	%
Female	560	*55.9*	4,832	*50.6*
Region				
England	863	*86.1*	8,090	*84.7*
Wales	55	*5.5*	542	*5.7*
Scotland	84	*8.4*	914	*9.6*
Adult SOC†				
I Professional	34	*4.1*	532	*6.4*
II Managerial-technical	249	*30.4*	2,891	*34.7*
III Skilled non-manual	203	*24.8*	2,114	*25.4*
III Skilled manual	191	*23.3*	1,694	*20.4*
IV Partly skilled	117	*14.3*	917	*11.0*
V Unskilled	26	*3.2*	172	*2.1*
Household (childhood) SOC‡				
I Professional	46	*5.2*	547	*6.4*
II Managerial-technical	213	*24.0*	2,120	*25.0*
III Skilled non-manual	85	*9.6*	930	*11.0*
III Skilled manual	381	*42.9*	3,446	*40.6*
Household (childhood) SOC continued‡				
IV Partly skilled	134	*15.1*	1,109	*13.1*
V Unskilled	30	*3.4*	336	*4.0*
Maternal history of persistent back pain§	57	*10.4*	518	*9.7*
Chronic Illness in the household				
None	329	*47.5*	3,711	*54.7*
1 time point	278	*40.2*	2,310	*34.1*
2 time points	85	*12.3*	759	*11.2*
Previous history of LBP††	162	*47.6*	*1,419*	*37.7*
Average activity score				
At age 29 (0-112)‡‡				
Median (IQR)	16.0 *(0.0, 40.0)*		20.0 *(4.0, 40.0)*	
At age 16 (0-130)§§				
Low physical activity	164	*48.0*	*1,795*	*50.1*
High physical activity	178	*52.0*	*1,788*	*49.9*
Ever pregnant *	384	*68.6*	3,039	*62.9*
Body Mass Index (kg/m^2)				
At age 29				
Mean (SD)	25.4 *(5.1)*		24.9 *(4.5)*	
At age 26				
Mean (SD)	23.9 *(4.0)*		23.6 *(3.7)*	
At age 16				
Mean (SD)	21.6 *(3.2)*		21.3 *(3.3)*	
At age 10				
Mean (SD)	17.0 *(2.1)*		16.9 *(2.1)*	
Smoking				
At age 29				
Never smoked	368	*36.8*	4,323	*45.3*
Ex-smoker	198	*19.8*	1,812	*19.0*
Occasional or regular smoker	435	*43.5*	3,406	*35.7*
At age 16				
Never or previously smoked	264	*70.0*	3,104	*73.4*
Occasional or regular smoker	113	*30.0*	1,124	*26.6*

		Cases with persistent back pain (n=1,002)		Controls (n=9,546)	
		N	%	N	%
Highest level of academic or vocational achievement					
	None	153	*15.3*	1,234	*12.9*
	NVQ Level 1	107	*10.7*	815	*8.5*
	NVQ Level 2	303	*30.2*	2,977	*31.2*
	NVQ Level 3	151	*15.1*	1,341	*14.1*
	NVQ Level 4	260	*25.9*	2,719	*28.5*
	NVQ Level 5	28	*2.8*	458	*4.8*
Malaise Rutter Inventory Score					
At age 29 (0-24)					
	Median (IQR)	4.5 *(2.0, 8.0)*		2.0 *(1.0, 5.0)*	
At age 16 (0-22)					
	Median (IQR)	9.0 *(6.0, 12.0)*		8.0 *(5.0, 12.0)*	
Depressive symptoms¶¶					
At age 29		45	*13.4*	336	*9.2*
At age 16		262	*26.4*	1,756	*18.6*

CM Cohort member; IQR Inter-quartile range; LBP Low back pain; NVQ National Vocational Qualification; SD standard deviation; SOC Standard Occupational Classification.
**Females only.*
†Cohort member SOC at age 29 (if missing, cohort member SOC at age 26).
‡Father's SOC at age 10 survey (if missing, mother's SOC at age 10 then father's SOC at age 16 then mother's SOC at age 16).
§Maternal history of persistent back pain: Mother reported backache 'most of the time' at age 10 or 16 survey.
¶Parents reported anyone living within cohort member's household who had 'severe or prolonged illness (medical, surgical or psychiatric) or any handicap or disability' at age 10 and/or age 16.
††CM report backache 'most of the time' or 'some of the time' at age 16 survey.
‡‡If CM reported no to 'do regular exercise?' average activity score = 0. Score formed using variables 'How often CM takes part in any exercise activity' and 'How often CM gets out of breath/sweaty during exercise?' used modified version of score adopted from (Juneau *et al.*, 2014) *p. 71.*
§§Combination of variables 'all sports in school' and 'all sports outside of school', with total score formed. Low activity level = < mean, high activity = ≥ mean. Adopted from (Viner and Cole, 2006).
¶¶Depression age 16 and 29: Reporting yes to the severest response to any of the following variables 'do you feel miserable or depressed?' or 'feeling unhappy or depressed?' or 'feeling worthless as a person?'.

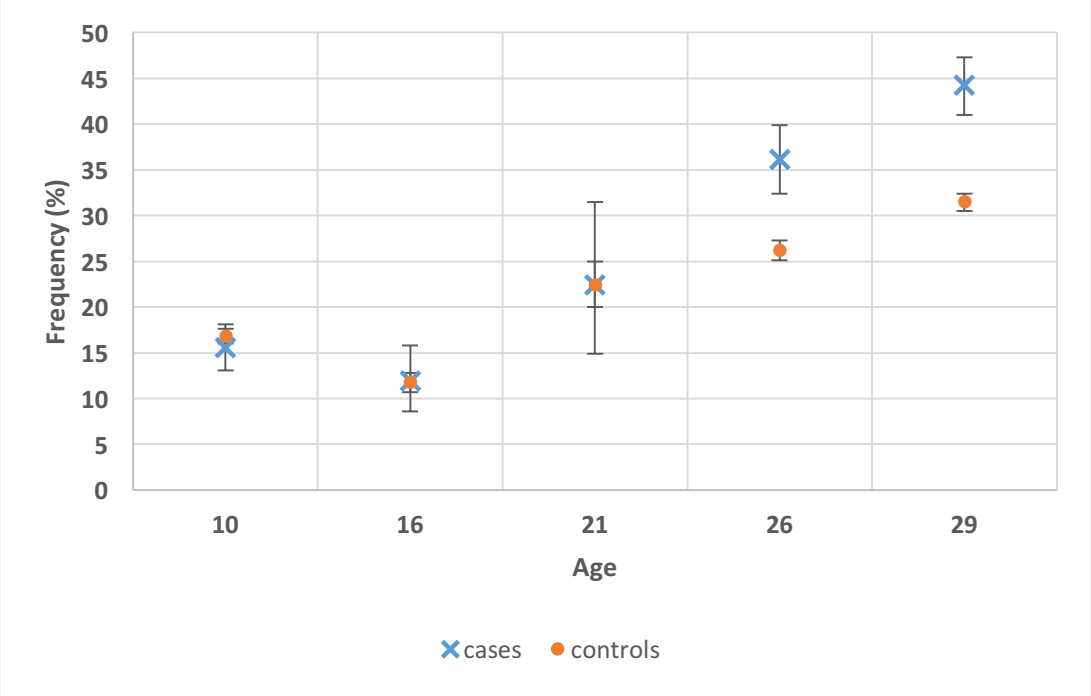
Self-reported sleep disturbance increased through adolescence and emerging adulthood (table 6.2 and figure 6.1) with a difference between cases and controls for sleep disturbance evident at age 26 and 29.

Table 6.2 Frequency of sleep disturbance in cases and controls: BCS70 age 10, 16, 21, 26 and 29 year follow-up (1970-2000)

Frequency of sleep disturbance reported		Cases with persistent back pain (n=1,002)		Controls (n=9,546)	
		N	%	N	%
At age 29					
	Any	438	*44.2*	2,977	*31.5*
	Falling or staying asleep	297	*29.9*	1,773	*18.7*
	Early waking	330	*33.3*	2,298	*24.3*
Age 26					
	Any	234	*36.1*	1,694	*26.2*
	Falling or staying asleep	159	*24.5*	1,061	*16.4*
	Early waking	162	*24.9*	1,202	*18.6*
Age 21*					
	Any†	24	*22.4*	252	*22.4*
	Falling or staying asleep	13	*12.1*	152	*13.5*
	Early waking	15	*14.0*	171	*15.2*
Age 16					
	Any	40	*11.9*	436	*11.8*
	Falling or staying asleep	15	*4.4*	219	*5.9*
	Early waking	33	*9.7*	282	*7.6*
Age 10					
	Any	134	*15.5*	1,388	*16.8*
	Falling or staying asleep	112	*12.9*	1,023	*12.4*
	Early waking	18	*2.1*	242	*2.9*
	Sleeping walking	15	*1.7*	166	*2.0*
	Night terrors	14	*1.6*	239	*2.9*

**Sub sample used at age 21.*

*Figure 6.1 Frequency of self-reported sleep disturbance for cases with persistent back pain commencing during emerging adulthood and controls with no persistent back pain ever (ages 10-29 years)**



**Sub sample used at age 21*

6.2 Missing data and imputation

Excluding the 21 year follow-up in which only a subsample of cohort members were surveyed, only 2,852 of 10,548 (27.3%) cohort members included in the case-control analysis provided complete data for exposure at all four time points (age 10, 16, 26 and 29 years) with most missing exposure data occurring at age 16 (table 6.3). Similarly, the 16 year sweep had the most missing data for other covariates.

Table 6.3 Frequency of missing data within cases and controls

	Amount of missing data			
	Cases with persistent back pain (n=1,002)		Controls (n=9,546)	
	N	%	N	%
Gender	0	*0.0*	0	*0.0*
Sleep disturbance age 29	10	*1.0*	85	*0.9*
Sleep disturbance age 26	353	*35.2*	3,081	*32.3*
Sleep disturbance age 21*	895	*89.3*	8,421	*88.2*
Sleep disturbance age 16	665	*66.4*	5,839	*61.2*
Sleep disturbance age 10	137	*13.7*	1,296	*13.6*
NVQ age 29	0	*0.0*	2	*0.0*
Adult SOC	182	*18.2*	1,226	*12.8*
Household (childhood) SOC	113	*11.3*	1,058	*11.1*
Maternal history of persistent back pain	455	*45.4*	4,228	*44.3*
Chronic Illness in the household	310	*30.9*	2,766	*29.0*
CM previous history of low back pain	662	*66.1*	5,787	*60.6*
Physical activity age 29	2	*0.2*	8	*0.1*
Physical activity age 16	660	*65.9*	5,963	*62.5*
Ever pregnant †	0	*0.0*	0	*0.0*
BMI age 29	32	*3.2*	254	*2.7*
BMI age 26	465	*46.4*	4,239	*44.4*
BMI age 16	629	*62.8*	5,630	*59.0*
BMI age 10	209	*20.9*	2,103	*22.0*
Smoking age 29	0	*0.0*	0	*0.0*
Smoking age 16	248	*24.8*	2,113	*22.1*
Malaise Rutter Inventory Score age 29	0	*0.0*	0	*0.0*
Malaise Rutter Inventory Score age 16	248	*24.8*	2,113	*22.1*
Depression age 29	10	*1.0*	88	*0.9*
Depression age 16	667	*66.6*	5,911	*61.9*

CM Cohort member; BMI Body Mass Index (kg/m^2); LBP Low back pain; NVQ National Vocational Qualification; SOC Standard Occupational Classification.
** Sub sample recruited at age 21.*

Data were seldom missing completely at random and restricting analysis to only those cases and controls providing complete exposure data at each time-point may introduce bias and a loss of precision. An illustration of this, using sleep disturbance at age 29 as an example, is provided in Appendix 4. Missing data on potential confounders introduces additional potential for bias. To reduce the impact of this bias on models utilising logistic regression analyses, the decision was made to use multiple imputation to account for the missing data. The methods for imputation are described in chapter three (section 3.3.4 (p. 67)).

A comparison of the estimated crude associations between exposure at each age and the outcome of persistent back pain at age 29 years using imputed data versus complete case analysis is shown in table 6.4.

Similar patterns of overall association and precision of estimates are seen but with attenuation of estimates, particularly at age 21, the time-point with most missing data.

Table 6.4 Univariate logistic regression demonstrating the association between the age sleep disturbance was reported and developing persistent back pain commencing during emerging adulthood; comparing the use of imputed and complete case data

Age	Male		Female		Overall	
	OR	95% CI	OR	95% CI	OR	95% CI
Imputed data						
10	0.88	(0.66,1.19)	0.93	(0.72,1.20)	0.91	(0.75,1.11)
16	0.90	(0.54,1.50)	0.99	(0.68,1.44)	0.97	(0.69,1.35)
21	1.13	(0.67,1.89)	1.14	(0.71,1.82)	1.12	(0.72,1.76)
26	1.69	(1.33,2.14)	1.52	(1.23,1.87)	1.58	(1.35,1.86)
29	1.78	(1.46,2.17)	1.70	(1.42,2.03)	1.72	(1.51,1.97)
Complete case analysis						
10	0.88	(0.65,1.18)	0.92	(0.71,1.19)	0.91	(0.75,1.10)
16	0.74	(0.37,1.49)	1.11	(0.74,1.65)	1.01	(0.72,1.43)
21	0.94	(0.45,1.97)	1.06	(0.57,1.98)	1.00	(0.62,1.61)
26	1.67	(1.28,2.19)	1.56	(1.25,1.94)	1.59	(1.34,1.88)
29	1.77	(1.45,2.16)	1.70	(1.42,2.03)	1.72	(1.51,1.97)

CI Confidence interval; OR Odds ratio.

The main analysis in the subsequent sub-sections (6.3, 6.4 and 6.5) uses imputed BCS70 data. Secondary analyses into specific sleep problems, sub-section 6.6, uses the complete case data (original BCS70 data).

6.3 'Sensitive period hypothesis'

The following analysis explores whether sleep disturbance at one age is more strongly associated with the outcome than sleep disturbance at other ages.

When adjusting for reporting previous sleeping problems in the life course (table 6.5), there does not seem to be substantial alteration in the overall significance of the association

between the age sleep disturbances had been reported and persistent back pain in comparison to table 6.4.

Table 6.5 Association between the age sleep disturbance was reported and developing persistent back pain which first commenced during emerging adulthood adjusted for potential confounders (models 1-5)

Age	Model 1	Model 2	Model 3	Model 4	Model 5
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
10	0.91 (0.75, 1.11)	0.91 (0.75, 1.11)	0.91 (0.74, 1.11)	0.90 (0.74, 1.10)	0.89 (0.73, 1.09)
16	-	0.97 (0.70, 1.36)	0.95 (0.67, 1.35)	0.87 (0.61, 1.25)	0.83 (0.58, 1.18)
21	-	-	1.13 (0.72, 1.78)	0.97 (0.59, 1.61)	0.90 (0.53, 1.50)
26	-	-	-	1.62 (1.29, 2.04)	1.39 (1.11, 1.74)
29	-	-	-	-	1.60 (1.36, 1.89)

CI Confidence interval; OR Odds ratio.
Using imputed data.
Model 1-5 in chronological age order of sleep disturbance. Model 1: Age 10 only entered. Model 2: Age 10 and 16. Model 3: Age 10, 16 and 26. Model 4: Age 10, 16, 21 and 26. Model 5: Age 10, 16, 21, 26 and 29.

Sleep disturbance reported at age 26 and 29 was significantly associated with developing persistent back pain which commenced during emerging adulthood after full adjustment (table 6.6); this was not seen for sleep disturbance reported at age 10, 16 and 21. The model estimates for covariates adjusted within the model can be seen in Appendix 6.

Table 6.6 The association between the age sleep disturbance was reported and developing persistent back pain which first commenced during emerging adulthood adjusted for potential confounders (models 5-7)

Age	Model 5	Model 6	Model 7
	OR (95% CI)	OR (95% CI)	OR (95% CI)
10	0.89 (0.73, 1.09)	0.90 (0.73, 1.10)	0.91 (0.74, 1.12)
16	0.83 (0.58, 1.18)	0.76 (0.53, 1.09)	0.76 (0.53, 1.09)
21	0.90 (0.53, 1.50)	0.86 (0.51, 1.45)	0.80 (0.47, 1.38)
26	1.39 (1.11, 1.74)	1.35 (1.07, 1.69)	1.32 (1.05, 1.65)
29	1.60 (1.36, 1.89)	1.55 (1.31, 1.84)	1.46 (1.23, 1.73)

BMI Body Mass Index (kg/m^2); CM Cohort member; CI Confidence interval; OR Odds ratio.
Using imputed data.
Model 5: adjusted for sleep disturbance reported at age 10, 16, 21, 26 and 29 years.
Model 6: adjusted for childhood household Standard Occupational Classification, maternal history of persistent back pain, chronic illness in the household, CM previous back pain, activity level, BMI, smoking, depression and covariates in model 5. (All confounders from either age 10 or 16).
Model 7: adjusted for with adult Standard Occupational Classification, average activity score, BMI, depression, smoking and covariates in model 6. (All confounders from either age 26 or 29).

In addition, a stratified analysis was conducted (using the complete case data) to explore whether the observed associations at age 26 and 29 years differed by adult social class. This showed no strong, consistent evidence of differences in the direction and strength of associations for the fully adjusted model (Appendix 8).

When the analysis was restricted to females who had never been pregnant, although there was no significant association with sleep disturbance found at any age after full adjustment (table 6.7), the overall magnitude of the odds ratios found were only slightly smaller than the (overall gender) odds ratios found in table 6.6. Sleep disturbance reported at age 26 had an odds ratio of 1.55 (with full adjustment). Despite the lower CI including the null, the upper confidence interval for the true strength of association at age 26 could still be potentially marked (95% CI 1.00, 2.40). The estimates overall due to the smaller sample size of non-pregnant females (variable asked at age 29), accounts for the decreased precision of estimates.

*Table 6.7 The association between the age sleeping disturbance was reported and developing persistent back in emerging adulthood adjusted for potential confounders (models 5-7); restricted to females who have never been pregnant**

Age	Model 5	Model 6	Model 7
	OR (95% CI)	OR (95% CI)	OR (95% CI)
10	0.83 (0.52, 1.33)	0.81 (0.50, 1.29)	0.82 (0.51, 1.32)
16	0.82 (0.43, 1.56)	0.78 (0.40, 1.51)	0.78 (0.40, 1.52)
21	0.94 (0.47, 1.91)	0.93 (0.45, 1.92)	0.87 (0.41, 1.82)
26	1.57 (1.02, 2.42)	1.55 (1.00, 2.41)	1.55 (1.00, 2.40)†
29	1.34 (0.93, 1.94)	1.31 (0.90, 1.91)	1.37 (0.93, 2.01)

BMI Body Mass Index (kg/m^2); CI Confidence interval; OR Odds ratio.
Using imputed data.
† Non-significant (p=<0.05).
Model 5: adjusted for sleep disturbance reported at age 10, 16, 21, 26 and 29 years.
Model 6: adjusted for childhood household Standard Occupational Classification, maternal history of persistent back pain, chronic illness in the household, CM previous back pain, activity level, BMI, smoking, depression and covariates in model 5. (All confounders from either age 10 or 16).
Model 7: adjusted for with adult Standard Occupational Classification, average activity score, BMI, depression, smoking and covariates in model 6. (All confounders from either age 26 or 29).
**Pregnancy definition includes; live births, still births, abortions and miscarriage.*

6.4 'Cumulative exposure hypothesis'

Further investigation was undertaken to see if there was an association between multiple episodes of sleep disturbance across the early life-course and developing persistent back pain as an emerging adult. Looking at table 6.8, reporting sleep disturbance at more than one age point prior to, and including age 29 does seem to be significantly associated with developing the outcome of interest; demonstrating a dose-response relationship. Descriptive patterns (Appendix 5) demonstrate that the majority of respondents who reported sleep disturbance at two or more age points, reported sleeping disturbance at age 26 and age 29.

Table 6.8 Association between onset of persistent back pain in emerging adulthood and number of time-points sleep disturbance was reported between age 10 and 29 years

	Male		Female		Overall	
Number of time points sleep disturbance reported	OR	95% CI	OR	95% CI	OR	95% CI
1	1.24	(0.90,1.70)	1.24	(0.96,1.61)	1.24	(1.02,1.52)
2	1.46	(1.02,2.10)	1.50	(1.11,2.04)	1.49	(1.17,1.88)
3	1.86	(1.25,2.78)	1.72	(1.18,2.52)	1.78	(1.32,2.40)
4+	1.65	(0.87,3.13)	1.61	(0.93,2.79)	1.63	(1.04,2.54)

CI Confidence interval; OR Odds ratio.
Using imputed data.
**all time points (including age 21).*

6.5 'Sensitive transition hypothesis'

The potential transition from adolescence where no sleep disturbance is reported, into emerging adulthood where sleep disturbance is reported was investigated in respect of altering the odds for developing persistent back pain which commenced during emerging adulthood. The highest odds for developing persistent back pain within emerging adulthood was seen when sleep disturbance is reported at age 26 alone (OR 1.57 (95% CI 1.31, 1.88)), see table 6.9. However, this is not too dissimilar to reporting sleep disturbance at both age 16 and 26 (OR 1.48 (95% CI 1.03, 2.14)).

Table 6.9 Association between onset of persistent back pain in emerging adulthood and change in sleep disturbance between age 16 and 26 years

Age sleeping problem reported	OR (95% CI)
Neither 16 or 26 (reference)	1
16 only	0.77 (0.46, 1.30)
26 only	1.57 (1.31, 1.88)
Both 16 and 26	1.48 (1.03, 2.14)

CI Confidence interval; OR Odds ratio.
Using imputed data.
Age 16 time-point represents adolescence and age 26 time-point represents emerging adulthood.

6.6 Specific sleep problems

The relationship between reporting specific sleep disturbances and the onset of persistent back pain commencing during emerging adulthood was undertaken as exploratory secondary analysis using the complete data set.

6.6.1 Specific sleep problems: early waking and falling or staying asleep

The overall pattern of significant association was similar regardless of the specific type of sleep problem reported (tables 6.10 and 6.11). The risk of developing persistent back pain is slightly higher in those reporting problems with falling or staying asleep at age 29 (OR 1.85 (95% CI 1.60, 2.14)) and at age 26 (OR 1.65 (95% CI 1.36, 2.00)) than in those reporting problems with early waking. However, the confidence intervals were relatively imprecise.

Table 6.10 Univariate logistic regression demonstrating the association between the age problems with early waking was reported and developing persistent back pain commencing during emerging adulthood

Age point problems with early waking reported	Male		Female		Overall	
	OR	95% CI	OR	95% CI	OR	95% CI
10	0.62	(0.29,1.34)	0.77	(0.41,1.44)	0.70	(0.43,1.14)
16	0.92	(0.44,2.12)	1.41	(0.91,2.18)	1.31	(0.90,1.92)
21*	1.01	(0.44,2.36)	0.84	(0.39,1.83)	1.10	(0.62,1.94)
26	1.58	(1.18,2.13)	1.39	(1.09,1.78)	1.45	(1.21,1.76)
29	1.52	(1.23,1.88)	1.59	(1.32,1.93)	1.55	(1.35,1.79)

CI Confidence interval; OR Odds ratio.
**Age 21 sub-sample.*
Using the complete case data.

Table 6.11 Univariate logistic regression demonstrating the association between the age problems with falling or staying asleep was reported and developing persistent back pain commencing during emerging adulthood

Age point problems with falling or staying asleep reported	Male		Female		Overall	
	OR	95% CI	OR	95% CI	OR	95% CI
10	1.05	(0.76,1.45)	1.04	(0.79,1.36)	1.05	(0.85,1.30)
16	0.32	(0.08,1.33)	0.91	(0.51,1.64)	0.74	(0.44,1.27)
21*	1.68	(0.58,4.84)	0.88	(0.42,1.85)	1.13	(0.62,2.07)
26	1.42	(1.03,1.95)	1.79	(1.41,2.28)	1.65	(1.36,2.00)
29	1.96	(1.58,2.43)	1.77	(1.45,2.15)	1.85	(1.60,2.14)

CI Confidence interval; OR Odds ratio.
**Age 21 sub-sample.*
Using the complete case data.

6.6.2 Specific sleep problems: sleep walking and night terrors

There does not seem to be a significant association between reporting sleep walking at age 10 and reporting persistent back pain commencing during emerging adulthood, see table 6.12. Although, individuals who reported night terrors at age 10 demonstrated a protective association with the outcome of interest (OR 0.55 (95% CI 0.32, 0.95)).

Table 6.12 Univariate logistic regression demonstrating the association between reporting specific sleep problems at age 10 and developing persistent back pain commencing during emerging adulthood*

Age	Male		Female		Overall	
	OR	95% CI	OR	95% CI	OR	95% CI
Sleep walking	0.68	(0.28,1.70)	0.98	(0.51,1.89)	0.86	(0.50,1.47)
Night terrors	0.48	(0.21,1.10)	0.64	(0.31,1.32)	0.55	(0.32,0.95)

CI Confidence interval; OR Odds ratio.
Using the complete data set.
** Parental report at age 10 survey.*

7 Discussion

In this final chapter, findings from each of preceding studies are summarised, critically interpreted within context of current and previous findings, and their implications considered.

7.1 Summary of findings

The main findings from the analyses of 1970 British Birth Cohort Study (BCS70) data can be seen below in tables 7.1, 7.2 and 7.3.

Table 7.1 Overview of results from analyses of BCS70 data: study 1

Objective 1: To estimate the prevalence of persistent back pain in emerging adulthood, the proportion of this that begins in emerging adulthood and the proportion that have sought medical care
• The lifetime prevalence of persistent back pain at age 29 years (i.e. by the end of emerging adulthood) was 14.9% (95% CI 14.2, 15.5). The 12-month period prevalence of persistent back pain at age 29 years was 11.1% (95% CI 10.5, 11.7). • Among those reporting persistent back pain at age 29 years, 81.1% reported that this began during emerging adulthood (18 years or older). • 57.8% of those who reported persistent back pain at age 29 years had consulted a doctor regarding their pain in the past 12 months. This translates into an annual consultation prevalence for persistent back pain of 6.4% (95% CI 6.0, 6.9) in adults aged 29 years.

CI Confidence interval; OR Odds ratio.

Table 7.2 Overview of results from analyses of BCS70 data: study 2

Objective 2: To provide a comparative description of health among emerging adults with persistent back pain and those without back pain
• At age 29 years, those reporting persistent back pain were more likely to report a wide range of other health conditions compared to respondents with no persistent back pain. These included common conditions such as migraine, irritable bowel syndrome (IBS) and menstrual problems, as well as less common disorders such as chronic fatigue syndrome, bronchitis and contact dermatitis. The magnitude of the increased odds ranged from 20% (hay fever, asthma) up to three-fold (peptic ulcer, eating disorder). A higher prevalence of several mental health symptoms was also observed among those with persistent back pain. These included symptoms commonly linked to obsessive-compulsive disorder, mania, anxiety and depression. • Women reported a higher proportion of co-morbidities and consultation attendance than men for both physical illness and mental health related symptoms. • Reporting any additional number of physical co-morbidities demonstrated a significant dose response relationship with developing persistent back pain regardless of gender. Results for men and women were mixed for reporting any number of co-morbid mental health symptoms and developing persistent back pain. • Those with persistent back pain had a higher risk of consulting for specific physical illnesses such as migraine and IBS than those without persistent back pain ((OR 1.64 95% CI 1.19, 2.27) and (OR 1.84 95% CI 1.10, 3.08) respectively). Individuals with persistent back pain were also more likely to consult for any additional number of co-morbid physical illnesses. However, after adjustment for potential confounders, no such association was seen between persistent back pain and (secondary care) specific mental health symptom consultation (e.g. depression) or the number of mental health related consultations.

CI Confidence interval; OR Odds ratio.

Table 7.3 Overview of results from analyses of BCS70 data: study 3

Objective 3: To investigate the relationship between sleep disturbance in childhood, adolescence and emerging adulthood and the risk of new onset persistent back pain in emerging adulthood.
• Sleep disturbance at age 26 and 29 years was significantly associated with persistent back pain that began in emerging adulthood ((OR 1.32 (95% CI 1.05, 1.65) and OR 1.46 (95% CI 1.23, 1.73) respectively). However, no such association was found in those reporting sleep disturbance at age 10, 16 and 21 years. In exploratory analyses, the overall same pattern was seen for specific sleep problems ('early waking' or 'falling and staying asleep'). • In the restricted analysis of females who had never been pregnant, the same pattern of results was seen for sleep disturbance in both males and females. Although not statistically significant, this is most likely due to less precise confidence intervals resulting from the smaller sample size. This suggests the association between sleep disturbance and persistent back pain in emerging adulthood in females is not explained by childbirth. • Reporting sleep disturbance at multiple age points showed a significant dose-response relationship with developing persistent back pain up to 3 time points. Thereafter the association between reporting sleeping disturbance at four or more time points showed a smaller magnitude of association. This could be due to the inclusion of childhood time points (e.g. 10 and 16), which were shown above to have no association, indicating a difference in associations for sleep problems in emerging adulthood and for sleep problems in childhood. • There was limited support for this thesis' 'sensitive transition hypothesis'. As reporting sleep disturbance alone in emerging adulthood (OR 1.57 (95% CI 1.31, 1.88)) was similar to reporting sleep disturbance in both adolescence and emerging adulthood (OR 1.48 (95% CI 1.03, 2.14)).

CI Confidence interval; OR Odds ratio.

7.2 Comparison to the literature

7.2.1 Prevalence estimates

Due to the heterogeneity of low back pain (LBP) definitions, it is important to clearly outline the definition used within this thesis in order to appropriately compare prevalence estimates with studies using other definitions. The definition of persistent back pain within the BCS70 prevalence study was self-reported being told or having 'persistent back pain, lumbago or sciatica' within a defined period of time (ever or last 12 months). The lifetime prevalence of persistent LBP was 14.9% (95% CI 14.2, 15.5) and the 12-month period prevalence was 11.1% (95% CI 10.5, 11.7) in emerging adults (age up to 29 years). Based on previous comparisons, this type of definition and its requirement for the pain to have been 'persistent', would be expected to result in relatively lower estimates than studies using anatomical location and less stringent criteria for the duration or frequency of symptoms (Hoy *et al.*, 2012). Despite the use of the word 'persistent' alone to denote duration and 'back or lumbago' alone to indicate anatomical location within the BCS70, the results were similar to prevalence estimates given in a longitudinal study by Hestbaek, Leboeuf-Yde and Kyvik (2006) which had more explicit criteria for their case definition. These researchers also investigated persistent back pain, but they explicitly defined duration as LBP present for longer than 30 days and defined anatomical location as pain residing between below the 12th rib and above the lower gluteal fold (with anatomical illustration for participant reference). This study showed at follow-up, where participants were between 28 to 30 years of age, a 12-month period prevalence of 11% for persistent LBP (Hestbaek, Leboeuf-Yde and Kyvik, 2006). Both this thesis' and Hestbaek, Leboeuf-Yde and Kyvik's (2006) estimates were expectedly smaller than the 12-month period prevalence of 42.4% for LBP found by Ganesan et al.(2017). This may be because Ganesan et al.'s (2017) study (with 90.6% of participants between the ages of 20-29 years) did not report their definition for LBP.

Further comparison of emerging adult estimates with published child and adult chronic low back pain estimates is challenging. For adults, a systematic review estimated a lifetime period prevalence of 51-84% and 12-month period prevalence of 36-67% for chronic LBP (McBeth and Jones, 2007). The latter estimate was expectedly higher than the 12-month period prevalence found within this thesis for emerging adults, due to the fact that studies within the review were age-standardised and estimates will account for increased prevalence of LBP shown within established adulthood (Dionne, Dunn and Croft, 2006; Hoy *et al.*, 2012). Prevalence estimates for children are limited and generally use shorter periods of time. A systematic review by King et al.(2011) suggested for children (age 8 to 18 years) a one-month prevalence for chronic LBP of 18-24%, using estimates from two studies. These estimates are higher than those within this thesis which used a longer period of prevalence (12 months) and older participants (emerging adults). One explanation for this could be methodological variation. King et al. (2011) acknowledged within their review the inconsistency of pain definitions and overall lack of quality of included papers. Further inspection of these two studies forming the child chronic LBP one-month prevalence estimate within the review, found a lack of comparability to the BCS70 analysis due to the chronic LBP definitions they used (Watson *et al.*, 2002; Petersen, Brulin and Bergström, 2003). The study by Watson *et al.* (2002) defined chronic LBP as pain in the classical LBP area illustrated in an anatomical diagram and experiencing this pain for more than 24 hours in the last month. Petersen, Brulin and Bergström (2003) grouped together participants who reported having backache 'about everyday' and participants who reported backache 'about every month' within the last six months to define their 'recurrent monthly' chronic prevalence estimate (18%). Despite these clear methodological differences, the recall analysis completed within the BCS70 at age 16 (see section 4.5.1 p 85) does support these two studies, indicating that LBP is prevalent at a younger age regardless of specified duration. Reconciling these studies with this thesis' finding that 81.1% of participants

reported their persistent back pain to start after childhood and during emerging adulthood is difficult. Perhaps one explanation could be the representativeness of the BCS70 participants of the general population at age 29 years. The age 29 BCS70 sweep is under-representative of males from a lower socioeconomic group particularly (Mostafa, Wiggins and Centre for Longitudinal Studies., 2014). One other suggestion could be that although there is a fair proportion of recurrent episodes of LBP when individuals enter adulthood, it may first be perceived to be a *persistent problem* in emerging adulthood. This perception could be because many childhood episodes are either forgotten or discounted, as indicated within other child LBP studies (Hestbaek *et al.*, 2006; Jeffries, Milanese and Grimmer-Somers, 2007).

Unfortunately, due to differences in the phrasing of LBP questions within each sweep of the BCS70, comparison of child and adult back pain estimates was not possible and therefore this analysis was unable to demonstrate how LBP prevalence changed from childhood into adulthood.

The annual consultation prevalence found within the BCS70 analysis was 6.4% (95% CI 6.0, 6.9). This was comparable to that found within other UK estimates; a study by Jordan *et al.* (2014) gave an annual back pain consultation prevalence of between 3-5%. The BCS70 consultation estimate is most likely higher than that found by Jordan *et al.* (2014) because of this thesis' chronic definition, and the tendency of these chronic cases to consult more. Alternatively Jordan *et al.* (2014) comment that their consultation estimate could be lower than expected as some of the back pain consultations could have been missed as they were coded differently under a different consultation category e.g. coded as generalised pain.

7.2.2 Co-morbidity and consultation

Results from this thesis are similar to the associations between LBP and co-morbidity found within adult populations. Schneider et al.(2007) also showed significant associations between LBP and co-morbid hay fever, asthma, migraine and hypertension. They also found an association with peptic ulcers (OR 1.49 (95% CI 1.24, 1.79)), in agreement with the strong but less precise association found within this thesis (OR 3.85 (95% CI 2.41, 6.14)). The association between peptic ulcers and persistent low back pain may be explained by the chronic use of non-steroidal anti-inflammatory drugs (NSAIDS) for pain relief. The evidence for NSAID use and the increased risk of developing peptic ulcers is well established (McQuaid and Laine, 2006; Massó González *et al.*, 2010).

Schneider et al's (2007) work demonstrated the strongest association with LBP and co-morbid other musculoskeletal (MSK) problems, which the BCS70 analysis was unfortunately not able to consider (no additional specific MSK variables other than LBP at age 29 sweep). In concordance with this thesis, an adult cross-sectional study looking at subjective health complaints (n= 457) found that those on sick leave due to LBP had significantly more headaches (OR 1.6 95% CI 1.2, 2.1), anxiety (OR 2.2 95% CI 1.3, 3.6) and depression (OR 1.7 95% CI 1.2, 2.4) (Hagen *et al.*, 2006). Hagen et al. (2006) indicated that their findings suggest that LBP sufferers could have a 'syndrome' with a specific picture or constellation of health complaints consisting of depression, anxiety, sleeping difficulty, headaches, spinal and leg pain. They indicated that this was different to the non-specific pain picture seen within IBS sufferers. However, the results found within this thesis conflict with Hagen et al.'s (2006) interpretations, and instead seem to support a non-specific constellation of health complaints. This was shown in the wide variety of significantly higher self-reported physical illnesses (e.g. asthma) and mental health symptoms (e.g. obsessive-compulsive disorder) in emerging adults with persistent back pain. One systematic review further

supporting this non-specific picture demonstrated LBP to be significantly associated with reporting respiratory, cardiovascular, gastrointestinal and other pain symptoms (headaches) (Hestbaek et al. 2003). It is worth considering that the differences seen in subjective health complaint presentations may vary between emerging adult or general adult populations and chronic or acute LBP populations.

Another key consideration is the validity (degree to which a hypothesis is or 'concept is accurately measured') of subjective health complaints within emerging adults (Heale and Twycross, 2015). A study conducted by Fosse and Haas (2009) indicated that subjective health complaints within adolescents and emerging adults was a valid measure of general health (physical and mental). One manner in which to test this validity could be to compare this thesis' emerging adult prevalence estimates of health complaints (physical illness and mental health symptoms) within with objectively measured disease estimates i.e. medically confirmed. Hypertension could be an example of this, which is diagnostically defined as blood pressure exceeding 140/90mmHg and is reported within age 16-24 years to range between 1-5% (Public Health England 2018). The prevalence found for hypertension at age 29 years among participants in the analyses in this thesis was 3%, which is in keeping with the estimate reported by Public Health England.

Reporting any physical co-morbidities demonstrated a significant dose response relationship with developing persistent back pain regardless of gender (this was also seen for females who reported any number of mental health symptoms). As to why subjective health complaints are more likely in those with persistent LBP, some researchers suggest that this could be due to the shared risk factors such as engagement with unhealthy behaviours or anxiety (Schneider et al. 2007; Hestbaek et al. 2003).

7.2.3 Sleep disturbance and persistent back pain in emerging adults

The prevalence of sleep disturbance within emerging adults in the BCS70 was 22.4-32.4% (overall for ages 21, 26 and 29) and this was similar to that previously reported in emerging adults (20-60%) (Becker et al. 2018; Steptoe et al. 2006; Lund et al. 2010). The results of the BCS70 sleep analysis were not consistent with the results found within Bonvanie *et al.'s* (2016) study however, which demonstrated that sleep problems were associated with chronic pain (including MSK pain severity) in younger emerging adults (ages 19 to 22). In comparison this thesis found no association in younger emerging adults (age 21). It is worthwhile considering that the BCS70 age 21 sweep was a sub-sample and did have the largest amount of missing data to impute (88.3%). Therefore, this association should be interpreted with caution. Results from the BCS70 sleep analysis demonstrate a novel association within older emerging adults (age 26 and 29 years). This thesis found no association between sleep disturbance in adolescence (age 10 and 16 years) and developing persistent back pain within emerging adulthood, the results of which are consistent with the systematic review conducted by Andreucci et al. (2017). This review indicated that within children MSK related pain was not associated with sleep problems. Within the review, two studies showed mixed stances regarding the association between sleep quality and LBP (Szpalski *et al.*, 2002; Auvinen *et al.*, 2010). This BCS70 sleep study supported the null association found by Szpalski et al. (2002). However due to the fact the BCS70 sleep analysis results were not stratified, this thesis therefore could not comment on the possibility of a gender preference for the association between sleep quality and subsequent LBP as shown in females by Auvinen et al.(2010).

Caution should be taken with interpretation and further investigation is required for the association seen with night terrors. Even though the analysis of BCS70 found a protective association for having night terrors at age 10 years and reporting persistent LBP that

commenced during emerging adulthood, it is worth considering both plausibility and confounding factors. In terms of plausibility, there seems to be limited biological and psychological rationale to explain how night terrors at a young age (which are immediately forgotten by the sufferer after each episode) could affect persistent pain in later life. No adjustment was undertaken for the exploratory secondary analysis into specific sleeping problems and therefore residual confounding could also explain the association seen.

7.3 Strengths and Limitations

7.3.1 Strengths

Strengths of the studies undertaken in this thesis include the use of a large cohort study with a substantial breadth of variables available for use. The BCS70 data was collected longitudinally from study participants at multiple age points. Despite data collection requiring considerable resources, both financial and administrative (e.g. tracing), use of these data was completely free of cost for the present analyses. Many sleep disturbance studies investigating the emerging adult age group utilise convenience university student samples and these students may have unique sleeping schedules which may not be generalisable to emerging adults who do not attend university. Therefore, a strength of this study is the use of a large nationally representative population for recruitment. Although there was missing data within this large cohort, this was taken into account and multiple imputation was used in an attempt to address this.

Exposure data used in the nested case-control analysis in this thesis were prospectively ascertained, thereby limiting the potential for recall bias. Recall bias arises when participants have an incorrect recollection of their past exposure status. This is a form of information bias, which is when poor data collection and study definitions cause substantial amounts of individuals within a study to be misclassified (Szklo and Nieto, 2014). The amount of inaccurate recall may be the same among cases and control (non-differential

misclassification) or may be different for cases than for controls (differential misclassification) (Szklo and Nieto, 2014). A related issue is the potential for misclassification of the age at onset of persistent back pain due to reliance upon recall: at age 29 years, study participants had to recall the age they first experienced persistent back pain. To investigate this, analyses were undertaken checking agreement between recalled age at onset and prospectively gathered data on the presence of back pain at ages 16 and 26 years. Agreement was relatively good (68.6-84.8%) and it is likely these agreement estimates are conservative (Appendix 2). Lastly, misclassification of outcome status through interviewer bias (in which the interviewer augments the way questions are delivered thereby potentially changing the study participant's response) was low within the BCS70. This was due to the fact that researchers of the BCS70 had no knowledge of the thesis' hypotheses and therefore could not influence the outcome of participant interviews (Szklo and Nieto, 2014).

7.3.2 Limitations

General limitations

The concept of 'emerging adulthood' itself emerged from Arnett's work in the 1990s (Arnett, 2000) and which was coincident with the maturing of the members of the BCS70 cohort. In some respects, they may have been the first observed cohort to experience emerging adulthood. However, each birth cohort is likely to experience emerging adulthood differently, creating cohort effects. This might limit the generalisability of findings from one cohort to another. More recent generations (e.g. born 1995-2018) could potentially even experience emerging adulthood for a longer length of time. Within the same generation it might be argued that cohort members experience emerging adulthood differently (perhaps not at all). Stratified analysis by adult social class did not suggest strong evidence to support this although further exploration of this idea might may be warranted.

The conduction of scoping search within chapter two (p. 22) was useful for informing possible determinants to investigate however, as it was undertaken independently, there is no additional external research to confirm its findings.

The validity of the studies undertaken within this thesis comprises as key area of consideration for potential limitations. Despite its strengths, this large longitudinal study is likely to have some inaccurate recall among participants. With all three studies, persistent back pain was defined as it was initially asked at the age 29 sweep 'have you ever had or been told you had persistent back pain, lumbago or sciatica?' This definition might have lacked validity as it did not use an anatomical image of the commonly accepted location of LBP 'below the 12th rib and above the lower gluteal fold', nor did it define other important factors: length of chronicity, severity and functional impairment. This could lead to ambiguity to what exactly constitutes as 'persistent' back pain as the experience of pain is subjective from individual to individual and a more objective measure could have helped address this. However, it is worth considering that the BCS70 was conducted during a time (1980 to 2000) when there was much less consensus on LBP research definitions and the responsible research institute therefore could not take these more recently established criteria into consideration. Additionally, the BCS70 definition did not specify or exclude specific causes of persistent back pain (e.g. ankylosing spondylitis or spondylolisthesis), therefore this thesis was unable to account for these individuals within our cases or perform a sensitivity analysis. However, participants with a specific cause of back pain are likely to form a minority of those reporting persistent back pain within the cohort (Deyo and Weinstein, 2001; Koes, Van Tulder and Thomas, 2006). An additional exclusion factor not considered in the BCS70 was menstrual related back pain, which could perhaps account for the increased LBP prevalence seen within females within the prevalence study undertaken in this analysis.

Neither variables for LBP or sleep disturbance used validated questionnaires. However, another study used exactly the same variables to define sleep disturbance in an earlier British Birth Cohort Study (1958). They commented on similarity of these variables to other validated measures (Diagnostic and Statistical Manual of Mental Disorders 4th edition criteria and Jenkins Sleep Scale) and that it was adequate when used to explore general sleep quality rather than specific sleep disorders (Martin *et al.*, 2009; Dregan and Armstrong, 2010; Jenkins, 2018).

Another main limitation of this thesis' analyses is consistency. The BCS70 with its impressive breadth of data was prone to inconsistency, which is not unforeseen as the study data had four centres taking stewardship of its conduct through the first five sweeps. Both persistent back pain and sleep disturbance variables were worded inconsistently across waves. Case or exposure status might have been misclassified due to the ambiguity or lack of validity of some of the questions used to define variables in the analysis. This was particularly noticeable in the way the back pain questions were asked and made comparing 'persistent back pain' at age 29 to earlier sweeps (age 16 and 26) in the recall analysis particularly challenging (see table 3.5 p. 58). This also prevented a direct comparison of the prevalence of persistent pain across different ages within BCS70 cohort members. Another example of inconsistency was the use of parental reporting for sleep disturbance at the age 10 sweep. Evidence for the validity of this suggests that parental reporting could either lead to either an overestimation or underestimation of sleeping problems due to the differing perspective or awareness of the parent in comparison to that of the child (Owens *et al.*, 2000; Dayyat *et al.*, 2011). Usage of parental sleep reports is common but there is recommendation to ideally use an objective measure (e.g. polysomnography) in conjunction to a subjective measure (Dayyat *et al.*, 2011; Spruyt and Gozal, 2011). At age 16, the sleep disturbance variable 'do you have great difficulty sleeping?' lacked consistency in comparison to all other sweeps, in which there was explicit inclusion of

'falling or staying asleep' or 'early waking' within the variable definition. The age 16 sweep was also the only sweep which did not have binary outcomes ('yes' or 'no') for variables and instead utilised ordinal levels of measurement ('most of the time', 'some of the time' and 'rarely or never'). This meant that pragmatic definitions were adopted for variables at this age point. Although these factors mentioned could lead to misclassification of exposure or outcome, it is unlikely that this was differential with respect to case/control status and the influence from this selection bias for the binary outcomes utilised in analyses would most likely lead to underestimation within the derived odds (Szklo and Nieto, 2014).

In both the cross-sectional studies and the nested case-control study, a limitation was the ability to infer causality. For the cross-sectional studies, this is inherent due to the study design, as the exposure and outcome of interest were collected at the same time period. For the nested case-control study investigating sleep disturbance, this was due to the way cases were defined (persistent back pain commencing in emerging adulthood between the ages of 18 to 29). Therefore, the results using the age points with the period of emerging adulthood (21, 26 and 29) could be due to persistent back pain causing sleep disturbance, rather than sleep disturbance causing persistent back pain. This bi-directional relationship between sleep and pain has been shown in other studies undertaken in other chronic pain pathologies such as fibromyalgia and rheumatoid arthritis; with some research indicating that pain predicts sleeping problems (Nicassio and Wallston, 1992; Affleck *et al.*, 1996; Smith *et al.*, 2008).

In the majority of instances, deliberate efforts were made to reduce the role of chance in this thesis by using a sufficiently large cohort to perform logistic regression analyses. There however were a minority of instances in which a substantial sized cohort was not possible; such as for the analysis into descriptive health, when stratification led to small numbers or analysis was performed on rare diseases e.g. Crohn's disease. In these circumstances, the

data sometimes lacked power for some analyses, which may have led to an increased risk of a type two error, in which a true association is missed and a null hypothesis is incorrectly retained (Bowers, 2013).

As with any study that runs multiple comparisons, there is a possibility that despite preventative measures some of these results could be due to chance because the large number of analyses performed (as within this thesis). Using a significance level of 0.05 consequently means that for every 100 associations tested, five will be due chance (Althouse, 2016). Although measures can be performed to account for this (e.g. Bonferroni corrections), this was not undertaken. The concept of requiring Bonferroni corrections for all instances of multiple comparisons has been forcibly challenged by Rothman (1990), particularly within circumstances where analyses are exploratory; as is the case within this thesis which looked to gain an initial sense in a wide range of co-morbidities. Therefore, although there is acknowledgement of the potential of chance in some of these findings, the intention for their use was not as standalone results but as a potential prompt for future research considerations (Althouse, 2016).

Alternative research methods which could have given further understanding of causality, such as the autoregressive cross-lagged approach shown in the study by Bonvanie *et al.* (2016) which also explored chronic pain and sleep in emerging adults, could provide further insights into causal associations but were beyond the scope of this thesis.

Specific limitations of studies:

Cross-sectional analytical study

Illnesses or mental health symptoms reported were not confirmed by a medical professional and therefore could potentially lack validity. The wording of the survey questions meant the study was limited in gaining information about repeat consultations

for individual illnesses or consultations regarding co-morbid MSK disorders, the latter of which has been shown to be of importance in other research (Schneider *et al.*, 2007). Similarly, the wording of the consulting and prevalence questions were complex; physical illness was directed towards 12-month prevalence whilst consulting in primary care vs mental health related illness was directed towards point prevalence at age 29 and consulting in secondary care. This made comparison of these two analyses inappropriate. Furthermore, participants who had not actively sought help (e.g. consultation) for their mental health were unable to respond to a mental health questionnaire. This was ultimately due to the phrasing of the stem question on the symptom card (only allowed to report 'yes' if they had sought help for symptoms in last 8 years). Anxiety and depression were not adjusted for in the analysis as inclusion of these potential confounders could strongly affect the associations found for mental health related analysis due to issues with multicollinearity (where two variables are highly related and account for similar variance within statistical models) (Alin, 2010). Adjustment for depression and anxiety was also not applied to analysis for physical illness either to maintain uniformity throughout the cross-sectional analytical analysis.

Nested case-control study

There was a substantial amount of missing data at particular age points within the case-control study. Although this is common within any large longitudinal study, considerations must be made as to how representative the study sample is to the wider reference population to account for selection bias. Selection bias can occur when there are substantial missing cases/cases lost to follow-up, as these individuals could have certain characteristics which put these individuals at an altered risk of developing back pain (the outcome) (Szklo and Nieto, 2014). This is particularly troublesome when the reason these cases are missing is due to having developed the outcome e.g. disabling back pain, which

leaves them unable to participate within the survey. At sweeps age 29 and 10 this was much less likely due to a smaller level of missing data, however at age 16 and 26 there was a higher risk of selection bias (age 21 was a sub-sample and therefore the smaller sample size was expected). This can be seen in table 6.3 (p. 107) for reference. Missing data, particularly at the age 16 sweep, was stated in part to be due to a national teaching strike and this was problematic as some of the surveys were administered at school (Elliott and Shepherd, 2006). For each participant at age 16 there were 18 separate surveys to complete (including parental, teacher and health visitor surveys) and this volume of questionnaire-burden may have been unacceptable in terms of methodological resources to ensure completion for all parties involved. For the age 16 and 26 sweep, the technical reports by the BCS70 indicate as mentioned above that response was under-representative particularly of males from a lower socioeconomic group (Mostafa, Wiggins and Centre for Longitudinal Studies., 2014). Attempts were undertaken at each sweep to understand non-response; this can be found alongside response rates in the technical reports for each individual sweep on the Centre for Longitudinal Studies website (Centre for Longitudinal Studies, 2018).

Multiple confounders were considered. However, there is acknowledgement that some variables used to account for these potential confounders were imperfect and pragmatic methods were undertaken often, specifically when adjusting for depression (see rationale table 3.11 p. 71). The variables utilised were not comprehensive or validated and potentially leave residual confounding for depression. Another potential confounder which was not included was anxiety. Within the BCS70 there was a score available for psychological distress, the Rutter Malaise Inventory (RMI), combining both anxiety and depression which would have been ideal. Another advantage of the RMI score was that it was recorded at all sweeps of interest. However, the RMI score was formed by all the variables used to define the exposure (sleep) and the outcome (persistent back pain). In

addition, the RMI included the anxiety and depression variables of interest for confounding. There were concerns that utilising multiple variables from the same psychological distress score would lead to issues with collinearity within logistic regression. Within the BCS70 at age 16 and 29 years, all five potential anxiety variables originated within the RMI questionnaire. For depression, variables were available both within the RMI score and in another section completely separate from the RMI score. Therefore, the choice was made to minimise the use of variables originating from within the RMI by selecting depression; with only one of the three variables used to form the depression covariate within the RMI.

There were other confounders that could have been considered. Two of these included fatigue and stress but issues such as measurement validity and rationalising their casual mechanism led to their exclusion. Other general confounders that could have been considered was medication use, particularly medication used to aid with sleep (e.g. sedating antihistamines or benzodiazepines). These medications could have altered the strength of association seen between sleep and pain. However, this was not possible using the BCS70 data as medication usage was not ascertained. Other factors that might arguably have been considered as confounders include alcohol intake and drug use. Alcohol and drugs variables were available within the BCS70. Both substances are likely to influence normal physiological sleep (Ebrahim *et al.*, 2013; Thompson *et al.*, 2017) although their role as independent causes of low back pain seems less clear and therefore may not be regarded as strong confounders.

7.3.3 Clinical implications

This thesis gives little evidence indicating that any reduction in sleep disturbance in adolescence (age 10 and 16 years) could impact on subsequent rates of back pain; much in line with other work (Andreucci, Campbell and Dunn, 2017). However, improving sleep in emerging adulthood may be beneficial. This association observed in emerging adulthood

may be due to factors such as reverse causality and residual confounding. However it is also possible that sleeping problems have a relatively short induction period as seen within this thesis and other research which limited follow-up to within two to three years (Bonvanie *et al.*, 2016). The results found regarding the sleep analysis in the BCS70 require further research and replication before being considered within the context of policy. If the results of the thesis were assumed to be true and consistently reproduced, improving sleep in emerging adults could improve prevention of the occurrence or impact of persistent LBP on individuals. Although improvement as shown within the findings might not be dramatic and is most likely modest, in terms of how prevalent back pain is, this would argue in favour of change within the direction of policy. In addition to the thesis' modest finding, there are three additional factors that also support this notion. Firstly, better targeting of sleep may help improve current and prospective pain severity in different pain groups in addition to LBP (e.g. chronic widespread pain) (Edwards *et al.*, 2008; Lewandowski *et al.*, 2010; Aili *et al.*, 2015; Bonvanie *et al.*, 2016; Generaal *et al.*, 2017). Secondly, in the wider context, sleep problems need to be addressed due to how prevalent they are in the reference population without persistent back pain (22.4-31.5%), as shown within the BCS70 emerging adult controls. Research in general indicates that problems pertaining to sleep are becoming a growing problem internationally (Steptoe, Peacey and Wardle, 2006). Thirdly this policy direction should be supported given that there is growing research purporting that better sleep hygiene is beneficial for multiple other outcomes than LBP alone. Recent research within the Lancet demonstrated that in a large UK (n= 91,105) study, utilising both objective (accelerometer) and subjective (questionnaire) measures, disruption to the body clock (through increased night activity via sleep disturbance) was associated with a higher risk of not only poorer mental health outcomes but also mental health disease (bipolar disorder and major depressive disorder) (Lyall *et al.*, 2018). This was supported by this thesis' finding that emerging adults with persistent back pain were more likely to report a variety of

mental health symptoms. Other researchers have further indicated that individuals suffering from insufficient sleep are more vulnerable to future cardiovascular disease including heart attacks and hypertension (Laugsand *et al.*, 2011; Fernandez-Mendoza *et al.*, 2012).

The most appropriate method to effectively attempt to address sleep hygiene as a problem within emerging adulthood would be within policy and public health as indicated above. One important question is if sleep is currently considered as a risk factor for chronic pain or wider health problems in the public domain. Currently, the Global Burden of Disease (GBD) project does not utilise sleep disturbance or deprivation as risk factor for 'policy attention' within their systematic analysis of the 2015 GBD Study (Forouzanfar *et al.*, 2016). In comparison, a recent joint initiative by Public Health England and Business In The Community has formed a Sleep and Recovery Toolkit, an online informative tool which educates and encourages individual users and businesses alike to engage in healthier sleeping behaviours (Business In The Community, 2018). This initiative was prompted by evidence from the Rand Corporation, who conducted an international study on loss of productivity and cost of sleep deprivation. The researchers reported that sleep deprivation through decreased productivity (via absenteeism and mortality) costs the UK over 30 billion pounds annually (RAND Corporation, 2017). Within secondary care, the importance of sleep management (e.g. use of a sleep diary to aid tracking pain severity) is highlighted by prominent health bodies within their guidelines (British Pain Society, 2013; Royal College of Anaesthetists, 2015). On an individual level, interested people are also able to receive advice regarding sleep freely through the NHS Choices website, specifically in relation to helping reduce chronic pain (NHS Choices 2018).

However, a limitation of these current initiatives is that specialised sleep diaries are only prompted for use for individuals within secondary care services who are referred to pain

management clinics or palliative care. In addition, use of free health resources (NHS Choices) will only occur if the importance of sleep is recognised by emerging adults. There is little directed focus on sleep hygiene within emerging adults. This is important, as these individuals are shown (within this thesis) to have a relative degree of persistent back pain already and form a high risk group for sleep problems. Therefore, use of public health campaigns through television or public transport advertisements could provide greater access to the majority of emerging adults; a population known for its recruitment difficulty. This would help to challenge the normalisation of erratic sleeping patterns and encourage better sleeping behaviours in these emerging adults who are formalising behavioural patterns as they transition into independent adults.

Addressing these problems in a clinical context (one patient at a time) may be less efficient than population-wide public health action. This thesis found that emerging adults with persistent LBP are more likely to report and seek multiple consultations for co-morbid conditions (physical and mental) than those without persistent back pain. This finding instead, would be more fittingly addressed within primary care. General practitioners should be aware of repeat consulters for multiple co-morbidities at this relatively young age (age 29) as a high risk group to have persistent back pain. Possible recommendations could include making sleep diaries (with next day pain tracking) available for use for these individuals within primary care. This could emphasise the importance of sleep and potentially prevent or reduce LBP severity, in additional to other health benefits. Tailoring such advice or interpretation in emerging adulthood might require specific considerations of the determinants of sleep problems in this phase of life e.g. the influence of drugs and alcohol. Further research to improve understanding of these determinants is needed.

Additional recommendations for further work can be seen in table 7.2 below.

Table 7.4 Suggestions for future research

• Explore the effect of age on LBP prevalence rates using the same cohort e.g. BCS70 with the same definition at subsequent age points. • Further work is needed to understand the role of sleep within LBP. Future research investigating the association between sleep disturbance and LBP should aim to utilise objective sleep measures e.g. polysomnography, as only one paper in systematic review exploring association between poor sleep and chronic LBP used this (Kelly *et al.*, 2011). Other objective measures such as heart rate devices, accelerometers and phone health apps to collect data could also be considered due to their growing viability and popularity with technological advancement. Another consideration could be further studies exploring the same association between LBP and sleep in emerging adults undertaken in cohorts other than BCS70, to investigate the role of cohort effects. • Conduction of longitudinal studies with a shorter induction period within emerging adulthood. • Qualitative research to gain understanding why emerging adults with persistent back pain are more likely to subjectively report co-morbidities but not necessarily consult for them. • This thesis has shown the feasibility of exploring back pain using the BCS70 data and the relatively large sample size available. Future studies could relatively efficiently explore a wide range of other risk factors available within this birth cohort across the life course.

BCS70; 1970 British Birth Cohort Study.

7.4 Conclusions

Based on novel analyses from the rich BCS70 data, this thesis has demonstrated that persistent back pain in emerging adults is not only common (affecting one in seven in their lifetime) but the majority of cases commence during emerging adulthood. These individuals are already displaying patterns of multimorbidity with other physical illnesses and mental health related symptoms at this relatively early age. Sleep disturbance in childhood and adolescence does not appear to be a strong risk factor, although persistent LBP in emerging adulthood (age 26 and 29 years) is associated with a higher rate of current sleep disturbance. This is either due to relatively short induction period, an unmeasured confounder or reverse causation. Regardless, targeting sleep in the form of better sleep hygiene has been demonstrated to improve pain severity. Improving sleep hygiene in emerging adulthood may or may not impact on the rates of persistent LBP, but public campaigns to improve sleep hygiene are nevertheless recommended given the scale of the problem and wider potential benefits beyond pain management alone.

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9 Appendix

Appendix 1

Table A.1 Search strategy for scoping review with key terms for exposure, population and outcome of interest

Risk factors†	Emerging Adulthood	Low back pain
Risk factor* Risk factor [exploded MESH] Epidemiologic studies [exploded MeSH] Odds ratio"[exploded MeSH] Multivariate analysis[exploded MeSH] Logistic Models[exploded MeSH] Prevalence[exploded MeSH] Incidence[exploded MeSH] odds ratio [Title or abstract] risk ratio [Title or abstract] relative risk [Title or abstract] risk [Title or abstract] predict*[Title or abstract] correlat*[Title or abstract] etiol*[Title or abstract] aetiol*[Title or abstract] prevalence[Title or abstract] incidence[Title or abstract] rate*[Title or abstract])	Adolescen* Students* Students [MESH] Emerging adult* Early adult* Late adolescen* Transition to Adult* Young adult* Young adult* [MESH] Youth* Young Professional* Young men* Young women*	Lumbar adj3 pain* Coccydynia* Coccyx adj3 pain* Spondylosis* Lumbago* Low back pain* Sciatic* (low or lower) adj3 back pain* (low back or lower back) adj3 pain* (low or lower) adj3 spinal pain* (low spinal or lower spinal) adj3 pain* (low or lower) adj3 back ache* (low or lower) adj3 backache* (low back or lower back) adj3 ache* (low or lower) adj3 back disorder* Low back pain MESH Sciatic MESH Coccyx MESH Spondylosis MESH

†Search terms for risk factors replicated those used by Forbes et al. (2016).
Words highlighted in red were ultimately removed from the search strategy to refine search.

Appendix 2

A.2 Expanded explanation of table 3.7 for further reference

Using table 3.7 (chapter three) for demonstrative purposes in the following explanation, the age 16 time point will be used to explain how recall consistency was checked.

A true positive would be if participants report back pain at age 16 and also correctly recall their persistent back pain starting at or before age 16. A true negative would be reporting no back pain at age 16 and reporting persistent back pain commencing after the age of 16. In table 3.7 the true positives and true negatives are signposted in green.

Taking into account the nature of back pain, although labelled classically as a false positive above, a participant that reports persistent back pain earlier on e.g. age 13 but does not report any back pain at age 16 could still have consistent recall. This is because although the participant did not suffer with back pain at the time the BCS70 sweeps were conducted, it is possible that they still could have suffered unrecorded episodes in between. However, it is still possible that these 'false positives' could also be participants that incorrectly remembered when their persistent back pain first started e.g. actually started later. In table 3.7 the false positives therefore are highlighted as amber, due classification ambiguity of these cases into correct or incorrect recall.

The false negatives are participants who cite back pain at 16 but report the age they first started to have persistent back pain was after age 16 (indicated in table 3.7 as red).

Appendix 3

Table A.3 The classification of academic, applied and vocational qualifications into the BCS70 derived National Vocational Qualification variable (None to class 5).

BCS70 National Vocational Qualification classification	Academic	Applied	Vocational
None	None	None	None
1	GCSE grade D-G CSEs grades 2-5 Scottish standard grades 4-5 Other Scottish school qualification	Foundation GNVQ Other GNVQ	NVQ level 1 Other NVQ Units towards NVQ RSA Cert/Other Pitmans level 1 Other vocational qualifications HGV
2	GCSE grade A*-C O levels grade A-C O levels grade D-E CSE grade 1 Scottish standard grades 1-3 Scottish lower or ordinary grades	Intermediate GNVQ BTEC First Certificate BTEC First Diploma	NVQ level 2 Apprenticeships City & Guilds Part 2/Craft/Intermediate City & Guilds Part 1/Other RSA First Diploma Pitmans level 2
3	A level AS levels Scottish Highers Scottish Cert of 6th Year Studies	Advanced GNVQ BTEC National Diploma ONC/OND	NVQ level 3 City & Guilds Part 3/Final/Advanced Craft RSA Advanced Diploma Pitmans level 3
4	Degree HE Diploma	BTEC Higher Certificate/Diploma HNC/HND	NVQ level 4 Professional degree level qualifications Nursing/paramedic Other teacher training qualification City & Guilds Part 4/Career Ext/Full Tech RSA Higher Diploma
5	Higher Degree		NVQ level 5 PGCE

Appendix 4

A.4 Illustration of selection bias due to missing data

Less than 1% of cases and controls had missing sleep disturbance data at age 29 years. The crude cross-sectional association between sleep disturbance and persistent back pain is shown below.

Table A.4.1 Frequency of sleep disturbance reported in cases and controls using complete case data at age 29 sweep

		Case-control status		
		Case	Control	Total
Self-reported sleep disturbance recalled at age 29	Yes	438	2,977	3415
	No	554	6,484	7038
	Total	992	9461	10453

OR= ad/bc = 438 x 6484 / 2977 x 554 = 2839992/1649258 = 1.72 (95% CI 1.51, 1.97)

OR; Odds ratio.

If analysis were restricted to those with complete exposure data at all 4 ages (10, 16, 26, 29) the estimated crude odds ratio would be biased (towards the null) and have a wider confidence interval as shown below.

Table A.4.2 Frequency of sleep disturbance reported at the age 29 sweep in cases and controls who reported at all four sweeps (age 10, 16, 26 and 29) using complete case data*

		Case-control status		
		Case	Control	Total
Self-reported sleep disturbance recalled at age 29	Yes	79	701	780
	No	161	1,911	2072
	Total	240	2612	2852

OR = ad/bc = 79 x 1911 / 701 x 161 = 150969/112861 = 1.34 (95% CI 1.01, 1.77)

**Age 21 sub-sample therefore excluded.*

OR; Odds ratio.

Appendix 5

Table A.5 The descriptive reporting patterns for all study participants (cases and controls) who reported to sleep disturbance variables at all age points (10, 16, 26 and 29) using complete case data

Number of sweeps CM reported 'YES' within	Frequency of CMs reporting	Age 10	Age 16	Age 26	Age 29
0	1,345	NO	NO	NO	NO
1	280	YES	NO	NO	NO
	109	NO	YES	NO	NO
	224	NO	NO	YES	NO
	291	NO	NO	NO	YES
2	26	YES	YES	NO	NO
	28	NO	YES	YES	NO
	231	NO	NO	YES	YES
	42	YES	NO	YES	NO
	65	YES	NO	NO	YES
	35	NO	YES	NO	YES
3	18	YES	YES	YES	NO
	12	YES	YES	NO	YES
	60	NO	YES	YES	YES
	62	YES	NO	YES	YES
4	24	YES	YES	YES	YES
TOTAL	2,852				

CM; Cohort member
Using the complete data set.

Appendix 6

Table A.6 The association between the age sleeping problems were reported and developing persistent back pain which first commenced during emerging adulthood; with demonstration of the association of covariates within models

	Model 5	Model 6	Model 7
Exposure	OR (95% CI)	OR (95% CI)	OR (95% CI)
10	0.89 (0.73, 1.09)	0.90 (0.73, 1.10)	0.91 (0.74, 1.12)
16	0.83 (0.58, 1.18)	0.76 (0.53, 1.09)	0.76 (0.53, 1.09)
21	0.90 (0.53, 1.50)	0.86 (0.51, 1.45)	0.80 (0.47, 1.38)
26	1.39 (1.11, 1.74)	1.35 (1.07, 1.69)	1.32 (1.05, 1.65)
29	1.60 (1.36, 1.89)	1.55 (1.31, 1.84)	1.46 (1.23, 1.73)
Childhood covariates			
Household SOC	-	1.02 (0.96, 1.08)	0.98 (0.93, 1.05)
Maternal LBP history	-	1.03 (0.76, 1.39)	1.00 (0.75, 1.35) †
Chronic Illness in household (1)*	-	1.33 (1.12, 1.57)	1.32 (1.12, 1.56)
Chronic Illness in household (2)*	-	1.26 (0.97, 1.63)	1.21 (0.93, 1.58)
Previous LBP	-	1.41 (1.12, 1.76)	1.39 (1.11, 1.75)
Physical activity	-	1.13 (0.91, 1.40)	1.12 (0.90, 1.40)
BMI	-	1.03 (1.00, 1.05)	1.02 (0.98, 1.05)
Smoking	-	1.13 (0.90, 1.41)	0.94 (0.71, 1.25)
Depression	-	1.32 (0.93, 1.86)	1.27 (0.89, 1.81)
Adult covariates			
Adult SOC	-	-	1.12 (1.05, 1.20)
Physical activity	-	-	1.00 (1.00, 1.00) †
BMI	-	-	1.02 (1.00, 1.04) †
Smoking (1) ‡	-	-	1.27 (1.03, 1.57)
Smoking (2) ‡	-	-	1.36 (1.10, 1.69)
Depression	-	-	1.25 (1.06, 1.47)

BMI Body Mass Index (kg/m^2); CM Cohort member; CI Confidence interval; OR Odds ratio; SOC Standard Occupational Classification.
Using the imputed data.
†Non-significant (p=<0.05).
Model 5: adjusted for sleep disturbance reported at age 10, 16, 21, 26 and 29 years.
Model 6: adjusted for childhood household SOC, maternal history of persistent back pain, chronic illness in the household, CM previous back pain, activity level, BMI, smoking, depression and covariates in model 5. (All confounders from either age 10 or 16).
Model 7: adjusted for with adult SOC, average activity score, BMI, depression, smoking and covariates in model 6. (All confounders from either age 26 or 29).
**Number signifies number of time points chronic illness in the household is reported.*
‡(1) ex-smokers in reference to non-smokers. (2) Smokers in reference to non-smokers.

Appendix 7

Supplementary complete case data analysis from the chapter six sleep analysis.

Table A.7.1 Sleep disturbance exposure and case-control status; stratified by the time point reported at (age 10,16,21,26 and 29 surveys) using complete data

	Cases N (%)	Controls N (%)	Total N (%)
Age 29			
Exposed	438 (44.2)	2977 (31.5)	3415 (32.7)
Non-exposed	554 (55.8)	6484 (68.5)	7038 (67.3)
Total	992 (100.0)	9461 (100.0)	10453 (100.0)
Age 26			
Exposed	234 (36.1)	1694 (26.2)	1928 (27.1)
Non-exposed	415 (63.9)	4771 (73.8)	5186 (72.9)
Total	649 (100.0)	6465 (100.0)	7114 (100.0)
Age 21*			
Exposed	24 (22.4)	252 (22.4)	291 (22.4)
Non-exposed	83 (77.6)	873 (77.6)	956 (77.6)
Total	107 (100.0)	1125 (100.0)	1232 (100.0)
Age 16			
Exposed	40 (11.9)	436 (11.8)	476 (11.8)
Non-exposed	297 (88.1)	3271 (88.2)	3568 (88.2)
Total	337 (100.0)	3707 (100.0)	4044 (100.0)
Age 10			
Exposed	134 (15.5)	1388 (16.8)	1522 (16.7)
Non-exposed	731 (84.5)	6862 (83.2)	7593 (83.3)
Total	865 (100.0)	8250 (100.0)	9115 (100.0)

**Sub-sample at age 21 survey.*
Using complete case data.
Exposure = reporting any of the following sleep disturbances: difficulty with either waking early, getting or staying asleep.

Table A.7.2 Exposure to early waking and case-control status; stratified by the time point reported at (age 10,16,21,26 and 29 surveys) using complete data.

	Cases N (%)	Controls N (%)	Total N (%)
Age 29			
Exposed	330 (33.3)	2298 (24.3)	2628 (25.1)
Non-exposed	662 (66.7)	7163 (75.7)	7825 (74.9)
Total	992 (100.0)	9461 (100.0)	10453 (100.0)
Age 26			
Exposed	162 (24.9)	1202 (18.6)	1364 (19.2)
Non-exposed	488 (75.1)	5266 (81.4)	5754 (80.8)
Total	650 (100.0)	6468 (100.0)	7118 (100.0)
Age 21*			
Exposed	15 (14.0)	171 (15.2)	186 (15.1)
Non-exposed	92 (86.0)	954 (84.8)	1046 (84.9)
Total	107 (100.0)	1125 (100.0)	1232 (100.0)
Age 16			
Exposed	33 (9.7)	282 (7.6)	315 (7.7)
Non-exposed	308 (90.3)	3452 (92.4)	3760 (92.3)
Total	341 (100.0)	3734 (100.0)	4075 (100.0)
Age 10			
Exposed	18 (2.1)	242 (2.9)	260 (2.9)
Non-exposed	847 (97.1)	8008 (87.1)	8855 (97.1)
Total	865 (100.0)	8250 (100.0)	9115 (100.0)

**Sub-sample at age 21 survey.*
Using the complete case data set.
Exposure = reporting sleeping problems related to early waking.

Table A.7.3 Exposure to problems with getting or staying asleep and case-control status; stratified by the time point reported at (age 10,16,21,26 and 29 surveys) using complete data

	Cases N (%)	Controls N (%)	Total N (%)
Age 29			
Exposed	297 (29.9)	1773 (18.7)	2070 (19.8)
Non-exposed	695 (70.1)	7689 (81.3)	8384 (80.2)
Total	992 (100.0)	9462 (100.0)	10454 (100.0)
Age 26			
Exposed	159 (24.5)	1061 (16.4)	1220 (17.1)
Non-exposed	491 (75.5)	5406 (83.6)	5897 (82.9)
Total	650 (100.0)	6467 (100.0)	7117(100.0)
Age 21			
Exposed	13 (12.1)	152 (13.5)	165 (13.4)
Non-exposed	94 (87.9)	973 (86.5)	1067 (86.6)
Total	107 (100.0)	1125 (100.0)	1232 (100.0)
Age 16			
Exposed	15 (4.4)	219 (5.9)	234 (5.7)
Non-exposed	324 (95.6)	3515 (94.1)	3839 (94.3)
Total	339 (100.0)	3734 (100.0)	4073 (100.0)
Age 10			
Exposed	112 (12.9)	1023 (12.4)	1135 (12.5)
Non-exposed	753 (87.1)	7227 (87.6)	7980 (87.5)
Total	865 (100.0)	8250 (100.0)	9115 (100.0)

**Sub-sample at age 21 survey.*
Using the complete case data set.
Exposure = reporting sleeping problems related to getting or staying asleep.

Table A.7.4 Exposure to specific sleep problems and case-control status; stratified by type of sleep problem reported at (age 10,16,21,26 and 29 surveys) using complete data.

	Cases N (%)	Controls N (%)	Total N (%)
Sleep walking			
Exposed	15 (1.7)	166 (2.0)	181 (2.0)
Non-exposed	850 (98.3)	8084 (98.0)	8934 (98.0)
Total	865 (100.0)	8250 (100.0)	9115 (100.0)
Night terrors			
Exposed	14 (1.6)	239 (2.9)	253 (2.8)
Non-exposed	851 (98.4)	8011 (97.1)	8862 (97.2)
Total	865 (100.0)	8250 (100.0)	9115 (100.0)

Using the complete case data set.
Reported at age 10 survey by parent.

Table A.7.5 Association between onset of persistent back pain in emerging adulthood and number of time-points sleep disturbance reported between age 10 and 29 years using complete data

Original	Male		Female		Overall	
Number of time points sleeping problems reported	OR	95% CI	OR	95% CI	OR	95% CI
1	1.15	(0.63,2.08)	1.11	(0.77,1.60)	1.13	(0.82,1.54)
2	2.20	(1.16,4.14)	1.30	(0.83,2.03)	1.54	(1.07,2.22)
3+	1.11	(0.38,3.28)	1.56	(0.85,2.88)	1.42	(0.84,2.41)

CI Confidence interval; OR Odds ratio.
Using complete case data.
**only has 10, 16, 26 and 29 sleep disturbance variables.*

Table A.7.6 The association between onset of persistent back pain in emerging adulthood and change in sleep disturbance at age 16 and 26 using the complete data

Age sleeping problem reported	OR (95% CI)
Neither 16 or 26 (reference)	1
16 only	0.60 (0.31, 1.62)
26 only	1.49 (1.11, 2.01)
Both 16 and 26	1.72 (1.02, 2.88)

CI Confidence interval; OR Odds ratio.
Using complete case data.
Age 16 time-point represents adolescence and age 26 time-point represents emerging adulthood.

Appendix 8

Table A.8 The association between the age sleep disturbance was reported and developing persistent back pain which first commenced during emerging adulthood adjusted for potential confounders (using model 7), stratified by adult socioeconomic class.

		Adult socioeconomic position†		
	Overall	High	Mid	Low
	aOR (95%CI)	aOR (95%CI)	aOR (95%CI)	aOR (95%CI)
Age:				
26 years	1.32 (1.05, 1.65)	1.51 (1.06, 2.15)	1.16 (0.85, 1.59)	1.35 (0.83, 2.21)
29 years	1.46 (1.23, 1.73)	1.27 (0.93, 1.72)	1.36 (1.04, 1.77)	1.57 (1.03, 2.39)

Using imputed data.

† Based on occupation at age 29 years classified using Standard Occupational Classification. High = professional/managerial; Mid = skilled occupation (manual/non-manual); Low = partly skilled/unskilled.

aOR (95%CI) adjusted odds ratio with 95% confidence interval, adjusted for sleep disturbance reported at age 10, 16, 21, 26 and 29 years, childhood household Standard Occupational Classification, maternal history of persistent back pain, chronic illness in the household, previous back pain, activity level, BMI, smoking, depression, average activity score, BMI, depression, smoking.