Epidemiology of Childhood Anxiety: Longitudinal perspectives.

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Submitted in accordance with the requirements for the degree of
Doctor of Clinical Psychology (D. Clin. Psychol.)
The University of Leeds
Academic Unit of Psychiatry and Behavioural Sciences
School of Medicine

2011

The candidate confirms that the work submitted is his/her own and that appropriate credit has been given where reference has been made to the work of others

Acknowledgements

I would like to thank my supervisors, Professor Stephen Morley and Dr. David Owens for their support and encouragement and also to thank Dr. Sam Cartwright-Hatton, Professor Susan Bogels, and Professor Silvia Schneider for their contributions to the beginnings of this project back in 2006. All of your expertise and knowledge have been invaluable. Professor Pat Cohen gave up her personal time to contribute data to the project and for that I am extremely grateful. Thanks to Laura Miller from the ALSPAC data team, who has always been happy to answer my many and wide ranging questions.

Abstract

Introduction: Anxiety is cited as one of the most common mental disorders of youth, with serious implications for academic and social outcomes and future psychopathology. Research has increased greatly in the last 25 years but there are still large gaps in our understanding of the descriptive epidemiology of anxiety and the majority of research focuses on the aetiology of adult disorder. The aim of this thesis was to use the best available evidence from studies using a prospective design and diagnostic outcome measures, to understand the onset and trajectory of anxiety through the lifespan and to determine whether childhood anxiety predicts adult anxiety disorders

Method: Principal Investigators from all prospective longitudinal studies of child mental health were approached in order to gain access to diagnostic data relating to anxiety disorders in youth. Two studies released appropriate data which are analysed here to determine prevalence, first onset, and course of anxiety, with adult outcome assessed in the one cohort that released appropriate adult data. These data are then synthesised with the published data in order to provide a coherent summary of the current picture of the descriptive epidemiology of anxiety disorders, in particular social anxiety and generalised anxiety or overanxious disorder.

Results: New data from a UK birth cohort show the different anxiety disorders to have specific patterns of prevalence and onset, suggesting early onset for separation anxiety and specific phobia. Analysis of data from New York suggests moderate homotypic continuity of social anxiety and overanxious disorder in childhood and adolescence. When examined together the available data show the importance of methodological considerations when determining the prevalence of anxiety in childhood and suggest that although substantial proportions of children will suffer from anxiety most will be disorders of short duration with favourable outcomes. There are, however, consistently across studies 20-30% with chronic anxiety who are likely to have poor outcomes. It is clear that a substantial proportion of adult sufferers have early onset but the figures are inconsistent across different studies.

Discussion: The results are discussed in light of the wider literature, and implications for methodology and clinical applications are presented. The limitations of the current approach and directions for future research are briefly outlined.

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Chapter One: Introduction.

Overview.

This thesis uses data from around the world to attempt to understand the onset, course, and outcome of one of the most prevalent forms of psychopathology – anxiety disorders. When determining the most effective timing and methods of prevention and intervention, and allocating precious resources, we need to consider the question; do anxious children grow up to become anxious adults?

This chapter will give a clear rationale for a project that will analyse novel prospective data and attempt to synthesise these new data with existing findings from longitudinal epidemiological studies in the United States, Europe and New Zealand. The aim of the project is to better understand the distribution of anxiety disorders in time and space through the lifespan. It is hoped that by accurately describing the epidemiology of anxiety disorders in young people we can reliably inform research in the aetiology and interventions for anxiety disorders, and develop a better understanding of the risks associated with anxiety in childhood and adolescence. A literature review will collate and critique evidence from baseline and cross-sectional studies of the onset, course, and outcome of anxiety disorders, in order to give an overview of how anxiety disorders in childhood and adolescence have largely been described and understood. The review will highlight the areas that remain controversial or unclear. This chapter will also outline the problems with using cross-sectional designs, the use of clinical samples, and provide a clear rationale for using prospective longitudinal studies with standardised diagnostic data, to understand the epidemiology of anxiety. This is followed by a detailed summary of the existing analysis from the prospective data sources and the areas of consensus and confusion will be highlighted to direct further analysis and synthesis of data.

Literature Review.

Progress so far: Research into child and adolescent anxiety disorders.

A recent systematic review of published research into childhood and adolescent anxiety disorders in the last 25 years demonstrated that peer reviewed research has significantly increased over recent decades. In comparison to research into adult disorders, however, child and adolescent papers make up approximately 10% of

published research (Muris and Broeren, 2009). Furthermore, when examining the focus of these papers, Post Traumatic Stress Disorder and Obsessive Compulsive Disorder receive the majority of research attention despite comparatively low prevalence rates in this population. In their review Muris and Broeren, alongside other recent authors in the field, point to a lack of understanding of descriptive epidemiology (namely the onset, course and outcome) of specific disorders; an important area that the current project hopes to address.

A sound empirical knowledge of the onset, course, and outcome of anxiety disorders in childhood and adolescence in the general population is proposed in this thesis to be an important endeavour. It provides the starting point for conducting relevant research into the aetiology of childhood anxiety and for the successful implementation of treatment and prevention programmes. The societal burden of disease in young people referred for treatment has been shown to be significant, suggesting a renewed focus on intervention is important and necessary (Bodden, Dirkson, & Bögels, 2008). Non-clinical community samples will be the focus of the current study, as drawing conclusions regarding the epidemiology of anxiety from clinical data presents a number of difficulties. Firstly, many cases of clinically significant disorder never seek professional help - in one large community study it was shown that only 14.3% of diagnosed cases of anxiety disorders had ever had contact with a mental health professional, (Costello, Egger, & Angold, 2005). Secondly, it has been shown that clinically referred samples may not be representative of the majority of those suffering from anxiety disorders; for example, they experience significantly increased comorbidity (Carron & Rutter, 1991). A focus on community samples allows a better understanding of the incidence of disease in the population, and allows more accurate understanding of the need and focus for public health interventions.

Describing the development of childhood anxiety in time and space: the difficulties in using cross-sectional designs.

A clear understanding of the onset, course, and outcomes of child and adolescent anxiety is vital in understanding how best to direct and use resources. It allows us to better understand the aetiology, determine malign and benign course and outcomes, and effectively target prevention and treatment of anxiety disorders for young people. It is argued that anxiety in early life is prevalent, causes distress and interferes with developmental processes, and is associated with greater psychopathology in later life. There is, therefore, a possible need to redress the balance between the amount of research conducted in adult and child samples illustrated by Muris and Broeren (2009)

in order to better understand these processes in younger populations. It is proposed that a clear overview of the descriptive epidemiology is crucial to highlighting the populations at risk, providing a rationale to ensure that the available resources are deployed as efficiently and effectively as possible.

It is argued that studies of a cross sectional design are less useful when attempting to fully understand the trajectory of anxiety disorders through the lifespan, due to a number of considerable difficulties that arise in understanding and combining data from such sources. The current project will attempt to synthesise published data from longitudinal, prospective studies regarding prevalence, age at onset, course and outcome of the different childhood anxiety disorders, and to add to this evidence through the analysis and synthesis of data collected from prospective longitudinal studies but so far not analysed. Throughout the report it will be argued that prospective longitudinal data, preferably from birth cohorts, are the best epidemiological data we have available; these data will therefore be the main focus of this thesis.

Anxiety is widely cited as one of the most prevalent forms of mental disorder with the earliest onset (see for example Kessler et al. 2005; Merikangas, Nakamura, & Kessler,2009; Pine and Klein, 2008). However, detailed data regarding the onset, course and outcome are absent and prevalence estimates are frequently based on self report measures administered at one time point (cross-sectional data). It has been suggested that cross-sectional studies may underestimate the prevalence of psychiatric disorders in the population. Jaffa, Harrington, Cohen, & Moffitt (2005), point out that prospective studies consistently show the cumulative prevalence of receiving a diagnosis of any psychiatric disorder before the age of 16 to be just under 40%: 36.7% (Costello, Mustillo, Erkanli, Keeler, & Angold, 2003) 38.3% (Kim-Cohen et al., 2003) and 39% (Cohen et al., 1993). These rates are significantly higher than those reported by cross-sectional research. Jaffa and colleagues therefore conclude that single wave studies, are highly likely to significantly underestimate the prevalence of psychiatric disorders in childhood and adolescence. It is, therefore, suggested that cross-sectional research will also significantly underestimate anxiety disorders in this population.

There is a growing body of research using standardised diagnostic measures, which aim to improve the reliability of data on mental disorders. The prevalence rates that

are reported by such studies, however, can still vary greatly as they are sensitive to a number of factors, in particular the criteria that were employed for diagnosis, the range of ages included in the study, and the source of symptom information. Even within individual studies, outcomes can vary substantially dependent upon the methods that were used to produce the final prevalence rates. For example, Breton et al. (1999) found prevalence rates of any anxiety disorder ranging from 3.9% to 14.6% within the same sample of 6-14 year olds, when using different informants and methods of combining informant information. Also the use of impairment as a criterion for diagnosis can have a major effect on the prevalence rate reported within one sample; Romano, Tremblay, Vitaro, Zocolillo, & Pagani (2001) found that rates decreased from 21.9% to 8.9% within one large sample of 14-17 year olds, when impairment was required for diagnosis. These issues all can be seen when standardised measures of anxiety are used in prospective studies; however, the multiple follow ups means that we can still see meaningful patterns within the data. It makes comparisons between studies difficult (this will be discussed further later in the thesis) but in cross-sectional studies these differences make comparisons extremely difficult and often meaningless.

The major problem is that cross sectional studies often examine a rather limited age range, e.g. Kashani et al. (1987) examined only 14-16 year olds, and Lavigne et al. (1996) looked at 2-5 year olds. This makes it impossible to examine changes in the prevalence of disorder through the course of childhood and adolescence, or to discern when the disorder becomes most prevalent and has its peak onset. Unfortunately, it is not possible to compare across cross-sectional studies that have examined different age ranges, in order to get an overview of a wider age range, because of methodological differences in the studies and the way they apply the diagnostic interview (as discussed above). To illustrate these difficulties, consider the following cross-sectional studies: Puura et al. (1998) used diagnostic interviews to ascertain prevalence in a large sample of 8-9 year olds in Finland; Breton et al. (1999) provides prevalence rates for French Canadian 9-11 year olds; Lynch, Mills, Daly, & Fitzpatrick (2006) provide prevalence rates for Irish 12-15 year olds; and Kashani et al. (1987) also used diagnostic interviews to assess prevalence in 14-16 year olds in the USA. These studies provide prevalence estimates for large samples, and together provide data from middle childhood through adolescence. However, the use of different sampling techniques and diagnostic tools and possible cultural differences makes it impossible to use these disparate cross-sectional studies to plot the change in

prevalence of anxiety disorders from 9-16 years and to expect to form a valid or reliable picture of how anxiety develops from childhood into adolescence.

In summary, a cross-sectional design can be useful in planning service provision for a specific age group in a specific location; however, it is less useful when attempting to gain a wider understanding of the development of anxiety, and for plotting the onset and course of psychiatric disorders through childhood and adolescence.

Anxiety in childhood: A normal part of growing up?

Anxiety disorders are among the most prevalent disorders in adulthood with (according to one major European study) approximately 6% of the population suffering clinical impairment from such a disorder over a twelve month period and 14% reporting that they have experienced it in their lifetime, (Alonso et al., 2004). Retrospective reports from clinically anxious adults suggest that the majority of these disorders began at an early age, (Christie-Burke, Burke, Regier, & Rae, 1990; Kessler et al., 2005; Manfro et al., 2003). In childhood samples, a systematic review of cross-sectional data suggests that anxiety is more prevalent than depressive or conduct/oppositional disorders in preadolescent children, (Cartwright-Hatton, McNicol, & Doubleday, 2006). It is widely written and accepted that anxiety disorders are the most common psychopathology in both childhood and adolescence (see for example Merikangas et al. 2009 or Pine & Klein, 2008). When looking at early childhood even the most conservative methodology suggests that over 3% of children in a large UK sample of under 10's (N=7997) suffer from anxiety with impairment to their functioning in a 12 month period, (Ford, Goodman, & Meltzer, 2003). Two large prospective studies of psychopathology in late childhood and adolescence estimated the cumulative risk of developing an anxiety disorders before the age of 16 to be approaching 10% (Costello et al. 2003; Lewinsohn, Rohde, Seeley, & Fischer, 1993). Furthermore, prevalence rates of most anxiety disorders (excluding separation anxiety disorder and overanxious disorder) have been shown to steadily increase throughout adolescence, (Beesdo-Baum, Knappe, & Pine, 2009; Bittner et al., 2007; Offord et al., 1992).

Childhood and Adolescent Anxiety: A growing problem?

A review, that included two meta analyses, carried out in the United States examined the reported prevalence of anxiety symptoms from the 1950's to the 1990's and suggested that anxiety in both college students and children has increased significantly over this period (Twenge, 2000). In her extensive paper Twenge carried

out a meta-analysis of 99 studies that used a well validated self report tool, the Children's Manifest Anxiety Scale (CMAS) with school children aged between nine and seventeen. The cohort data and demographic information were used to determine the association between self reported levels of anxiety and the year of birth. Significant associations were found even when controlling for geographical location, socio economic factors, race, and urban vs. rural setting. The increase in anxiety across this period was large; 0.99 SD higher in 1981 than in 1954. Twenge reports that school children in the 1980's were on average more anxious than psychiatric patients in the 1950's. It is notable that the year of birth explained over 20% of the variance; more than that explained by family or environmental factors. When attempting to explain this increase she examined economic differences in the cohorts; however, this did not explain the differences over time.

A review of time trends internationally reports an unclear picture of the changing trends in emotional disorders, with parents and children reporting stable or declining levels of emotional disorders between 1970's and 1990's in Scandinavia; alternatively, young people in Greece and Scotland report significant increases between the early 1980's and late 1990's (Maughan, Lervolino, & Collishaw, 2005). A study carried out in the UK that examined trends in mental disorders between 1974, 1986, and 1999 in adolescents found a more recent increase in emotional disorders between 1986 and 1999; no change was found between 1974 and 1986 (Collishaw, Maughan, Goodman, & Pickles, 2004). Using standardised measures with imputed adjustments to ensure accurate compatibility, 15-16 year olds in 1999 were demonstrated to be 1.5 times as likely to report clinical levels of emotional disorders than in 1986 (OR = 1.5; 95% CI .93-2.42). Collishaw, Maughan, Natarajan, & Pickles (2010) went on to examine more recent changes in emotional disorders over the twenty year period between 1986 and 2006. Similarly they found increases in both parent and child reported emotional problems for girls and in parent reported emotional problems for boys. These findings suggest that emotional disorders including anxiety are a growing problem, particularly in the UK.

If these cohort changes hold true and continue to increase they are an important consideration not just for clinical psychology and psychiatry but for politicians and policy makers. Changes in the prevalence of distress that has been demonstrated by comparing birth cohorts leads us to ask questions about the causes of causes; i.e. what are the social conditions that drive the psychological or intrapersonal "causes"

that clinical psychologists might be interested in? It might be postulated that economic hardship is a driver of anxious psychopathology but this was not found to be the case by Twenge (2000). Maughan et al. (2005) demonstrate the international differences in time trends, not all nations are experiencing this increase in population levels anxiety, and Wilkinson and Pickett (2009) use international data to suggest that social inequality, rather than economic hardship is responsible for the increase in psychological distress. By examining anxiety in nations (and different American states) where there are different levels of inequality, correlational data is used to demonstrate an association between increasing levels of anxiety and a larger gap between rich and poor. They postulate that this inequality may underlie some of the aetiological factors investigated in relation to increased anxiety (e.g. parenting efficacy). All of the data described above are based upon self reported symptoms of anxiety, when we look to the diagnostic tools used in many of the prospective studies we can see that these studies are relatively recent in their data collection. For example, the Gallagher (2008) review covered seven cohorts born between 1965 and 1985. The vast majority of these prospective studies, however, are cohorts that were born in the 1970's giving a limited range to examine time trends. Furthermore, there are currently no diagnostic data available for different birth cohorts from the same country. Information about time trends using diagnostic data rather than self report is currently lacking and would add a great deal to the argument regarding the changing prevalence of psychopathology in young people over time. It is hoped that the detailed analysis of descriptive epidemiology will make this task easier for future researchers comparing anxiety diagnoses across different cohorts.

What are the implications of anxiety disorders for young people?

As well as being highly and increasingly prevalent, anxiety disorders in childhood and adolescence are thought to be harmful in a number of domains. For instance, childhood anxiety has been found to be associated with poor social and academic outcomes (Chansky & Kendall 1997; King & Ollendick 1989; Last, Hansen, & Franco, 1997; Strauss, Frame, & Forehand, 1987) and evidence from longitudinal research also suggests that pre-pubertal anxiety is a significant risk factor for later suicidal behaviour, substance misuse, and conduct problems, (Weissman et al. 1999,) major depression (Wittchen, Nelson, & Lachner, 1998), and for severe anxiety in later life, (e.g. Gregory et al. 2007). The weight of evidence is compelling. It is possible, however, that a third variable could be the "causal" association between childhood anxiety and such outcomes; poor attachment, a negative family environment, or economic and social deprivation could feasibly cause children to both suffer with

clinical levels of anxiety in childhood and to develop significant problems later in life, and the mediating or moderating influence of anxiety disorder is yet to be fully investigated. A study that has examined the greatest range of outcomes for young people is the Christchurch Health and Development Study in New Zealand (Woodward & Fergusson, 2001). Young people who met diagnostic criteria for anxiety disorders between 14 and 16 years old were shown to have a greater risk not just for later anxiety disorders but also for drug dependence, nicotine and alcohol dependence, suicidal behaviour, underachievement in education and early parenthood. An impressive number of covariates were examined that included individual factors (the presence of any other DSM-III disorders at baseline), family factors (parental alcoholism and discipline style), and social factors (maternal educational qualifications and social class). When including these covariates adolescent anxiety disorders was still associated with more anxiety disorders, depressive disorders, illicit drug use, and lower educational attainment in later life. This suggests that the presence of anxiety disorders in this age group adds further developmental risk to individual, family, and social risk factors.

What can be done about it? Treatment and prevention programmes for anxiety in young people.

We are aware that a proportion of young people are suffering from anxiety disorders that impair their functioning and that these disorders are associated with poor outcomes for the young person; so what do we have to offer? Psychological interventions for anxiety in adolescence have received increasing research attention in the last 25 years and effective Cognitive Behavioural Therapies (CBT) have been developed for this population. A review of Randomised Controlled Trials (RCT) is beyond the scope of this thesis; however, a meta-analysis carried out in 2004 suggests that CBT for anxiety in adolescents to be an efficacious treatment; however, the review highlighted the lack of data for interventions in younger children (Cartwright-Hatton, Roberts, Chitsaban, Fothergill, & Harrington, 2004). A later review and meta-analysis of 20 studies that examined CBT in samples ranging from 3-16 years, with most studies beginning in middle childhood (six to eight years old) found an extremely impressive pre-post Effect Sizes (d= 0.94). When compared to a control group an effect size of d= 0.61 suggests CBT to be a relatively efficacious treatment for children and adolescents (Ishikawa, Okajima, Matsuoka, & Sakano, 2007). It has been proposed that the use of adult models to understand childhood anxiety and to develop treatments appear to be effective in older children and adolescents but it seems possible that younger children are less likely to be able to

make use of such therapy due to their stage of cognitive development (Piacentini & Bergman, 2001). In their review Ishikara and colleagues included CBT aimed at parents, as this is one way to administer to younger children who may not have the cognitive capacity to engage with CBT and they found that there is little difference between effect sizes for interventions aimed at children, parents, or the family as a whole. A recent RCT made use of an adapted behavioural parent training programme for parents of young anxious children (aged three to ten) with impressive results (Cartwright-Hatton et al. 2011). Following ten weekly two hour parenting groups over 60% of the treated group were free of their primary anxiety disorders diagnosis, compared to only 15% of those in the treatment as usual group. These gains were maintained at 12 month follow up and parental report measures continued to improve over this period. The Macquarie University Preschool Intervention Project in Australia also uses a parenting intervention for very young children who are displaying behavioural inhibition, a temperament characterised by withdrawal and hesitancy in novel situations, which has been shown consistently to be a risk factor for the development of anxiety disorders. Intervention at this early point has been shown to be effective at reducing the number of diagnosable anxiety disorders in childhood (Rapee, 2002; Rapee, Kennedy, Ingram, Edwards, & Sweeney, 2005). These important developments mean that we now have evidence based psychological interventions for children and young people at all stages of development.

In terms of preventing anxiety disorders, a great deal of work in Australia has been ongoing in the last twelve years to evidence a programme that can be delivered in schools to help children develop confidence, resilience, and social skills with the aim of preventing the development of anxious and depressive psychopathology. The FRIENDS for life programme has a growing and impressive evidence base that now shows it to be effective in reducing anxiety and depression up to six years after exposure. The programme can be adapted to be effectively delivered to both children and adolescents and can be delivered by psychologists, or is also effective when delivered by teachers and school nurses (Dadds, Spence, Holland, Barrett, & Laurens, 1997; Farrell & Barrett, 2007; Hau, 2001; Lock & Barrett, 2003; Lowry-Webster, Barrett, and Dadds, 2001).

The technology is, therefore, available to intervene effectively in young people's distress and to reduce or prevent the number of people suffering from anxiety. A better understanding of the descriptive epidemiology allows us to effectively target

these interventions and prevention programmes and adult follow up data allows us to ask questions about the necessity and cost effectiveness of, large scale strategies such as the FRIENDS programme and its ability to produce better outcomes for anxious children and adults.

Summary.

Anxiety disorders are a prevalent disorder in adulthood and cross-sectional data suggests that they are also highly prevalent in early life and that adolescent anxiety disorders are associated with poor outcomes in later life (in addition to confounding developmental risks). Cross-sectional data, however, have some important limitations, which may lead to underestimates of prevalence and has limited utility in describing the onset, course, and outcomes of anxiety. There are concerns that anxiety is a growing problem in the UK and it represents a substantial burden of disease. We have effective treatments and prevention programmes for tackling anxiety in childhood and adolescence so it is argued that the identification of children who are suffering childhood anxiety disorders and the effective targeting of intervention, is best served through an accurate understanding of the epidemiology of anxiety disorders. I will now briefly discuss the relevant findings from clinical, self report, and cross-sectional studies of anxiety disorders before reviewing the prospective findings.

When are anxiety disorders most prevalent: The clinical picture.

Clinical data from referred children show separation anxiety and simple phobias to be the most prevalent disorders of childhood and adolescence. Last, Perrin, Hersen and Kazdin (1992) examined 188 consecutive referrals for children with anxiety disorders over three years and found in nearly 30% the primary diagnosis was for separation anxiety, 20% were simple phobia, 15% social anxiety, 10% panic and less than 10% were diagnosed with obsessive compulsive disorder or post traumatic stress disorder. In this sample of 5-18 year olds the youngest reported onset was for separation anxiety (7.5 years) and the latest for panic disorder (14.1 years). There were few reported differences across gender and high rates of comorbidity both with other anxiety disorders and heterogenous psychopathology including behavioural problems.

Community studies of anxiety disorders.

The first review of epidemiological data from community (i.e. non-clinical) samples was undertaken sixteen years ago (Angold & Costello, 1995). The most remarkable

finding was that of unanimity across different designs and populations; demonstrating far more robust estimates than found in clinical samples. This review suggested that anxiety was a prevalent disorder in childhood and adolescence. The most recent unpublished review and meta-analysis of the prevalence of anxiety through early childhood to late adolescence shows the growing attention to the epidemiology of anxiety in such samples, and presents interesting findings (Costello, Egger, Copeland, Erkanli, & Angold, in prep). This review includes over 50 epidemiological studies using community samples of between two and 18 year olds and uses statistical methods to combine large quantities of prevalence data from studies using varying designs (see Table 1). The findings demonstrate that anxiety disorders are highly prevalent throughout childhood and adolescence, and show that these estimates are stable and reliable in adolescence despite the differing populations and methods employed. It is notable that the percentage of young people reporting that they suffer from anxiety disorders is not markedly different to some of the large studies reporting prevalence of anxiety in adulthood (Alonso et al 2004). These data alone suggest that we look again at the vastly increased resources focused on adult anxiety; however, in order to provide robust evidence for this redirection we need to understand not just prevalence but also be able to determine between the many cases of anxiety that spontaneously remit and have a benign course and outcome, and those that interfere with development and confer risk for later life.

Table 1. Calculated Prevalence for individual anxiety disorders in childhood and adolescence (Costello et al. in prep)

	Age 6-12 Years				Age 13-18 Years			
Anxiety disorders	Mean (%)	SE (%)	2.5%	97.5%	Mean (%)	SE (%)	2.5%	97.5%
Any	12.3	5.4	7.1	28.2	11.0	0.5	10.3	12.2
GAD	1.7	1.2	0.9	5.0	1.9	0.5	1.3	3.3
Separation Anxiety	3.9	1.5	2.6	8.5	2.3	0.9	1.4	4.8
Social Anxiety	2.2	2.2	1.0	8.8	5.0	1.3	3.5	8.4
Specific Phobia	6.7	3.6	4.0	18.0	6.7	1.6	4.7	10.9
Panic Disorder	1.5	3.2	0.2	8.9	1.1	0.3	0.7	1.8

Changing prevalence and patterns of onset.

The DSM-IV contains ten anxiety disorders (America Psychiatric Association, 1994). It has been suggested that these different diagnostic categories may not be applicable to younger populations, especially very young children (see for example Merikangas et al., 2009). However, Beesdo-Baum et al. (2009) reviewed the literature in relation to the development of DSM V and found that temporal patterns (e.g. age at onset) support diagnostic categories for specific phobia, separation anxiety, social anxiety, generalised anxiety disorder, panic disorder, and agoraphobia. When Costello et al (in prep) examined individual anxiety disorders, prevalence in children (six to 12 year olds) and adolescents (13-18 year olds) appeared mostly consistent across the two age groups. An increase in social anxiety and a decrease in separation anxiety from childhood into adolescence is, however, evident (see Table 1) suggesting that separation anxiety has early onset with less cases in later life and social anxiety has a later onset. Furthermore, there are some disorders (namely specific phobia) that show consistently higher prevalence than many other anxiety disorders (e.g. generalised anxiety disorder). Differences in prevalence and patterns of onset such as these are used to argue for the validity and utility of these different diagnostic categories in childhood. In preschool children, however, all disorders have been shown to be equally prevalent (Egger & Angold, 2006; Briggs-Gowan Carter, Skuban, & Horowitz, 2001) which offers support for the lack of applicability of specific diagnostic categories to very young children and general difficulties in the assessment of this population (Merikangas et al. 2009). The reporting of high levels of comorbidity in younger children is also used to support the argument that individual diagnostic categories are less useful in these younger populations; for example a recent RCT reported high levels of comorbidity between diagnoses of anxiety disorders in children under ten, (Cartwright-Hatton et al. 2011).

Understanding the course and outcome of anxiety.

Despite the difficulties with cross-sectional data outlined previously Costello and colleagues (in prep) have provided an extremely useful and concise meta-analysis that provides clear evidence that anxiety disorders in childhood and adolescence are highly prevalent and suggests that many disorders have their first onset in this early stage of development. However, using prevalence data alone to argue for the redirection of resources to understanding anxiety in younger populations is insufficient. There is currently a lack of clarity and contradictory findings regarding whether anxiety disorders in children are merely transitory or have a chronic course and problematic outcome. It is possible that the adolescent and childhood samples

do not overlap and represent distinct populations; one with a childhood and one with an adolescent onset. It has previously been believed that anxiety disorders remit quickly, with a number of studies in clinical populations supporting this hypothesis (Aschenbrand, Kendall, Webb, Safford, & Flannery-Schroeder, 2003; Last, Perrin, Hersen, & Kazdin, 1996). In studies of very young children, however, parent reports of their children's emotional problems have been used to demonstrate that symptoms are persistent over the course of a year (Briggs-Gowan, Carter, Bosson-Heenan, & Horowitz, 2006) and a recent examination of a number of different risk factors in preschool children found that anxious symptoms (along with child temperament) in preschoolers were the best predictor of anxiety symptoms at 6 and 8 years old (Mian, Wainwright, Briggs-Gowan, & Carter, 2011) suggesting in fact that very early symptoms are important predictors of later psychopathology. In longer term follow up (at 10 to 11 years old) parent reported internalising and externalising symptoms at preschool uniquely predict their diagnostic counterpart (disorder) using the DSM-IV; Children with parent reported internalising symptoms in kindergarten have a three - fold odds of meeting diagnostic criteria for an anxiety or depressive disorder in pre adolescence, (Mesman & Koot, 2001). So there are some difficulties in understanding the importance and predictive validity of early disorders and symptoms. Clinical studies show that the majority of childhood anxiety disorders remit, but early symptoms have been shown to be persistent over the course of a year and to be associated with later disorder. The recent testing of ecological models of anxiety by Mian et al. (2006) suggest that child factors (symptoms) are far better predictors of later anxiety than external factors, so the hypothesis that the association between early symptoms and later psychopathology is the product of a third social or family factor (e.g. social disadvantage or insecure attachment) seems less likely. There is disagreement in the literature as to whether early anxiety is a persistent disorder with a malign course or a common disorder with a remitting course.

An additional problem with using prevalence data to argue for the redirection of resources is that many of the cross sectional studies citing high prevalence estimates have been questioned due to the impairment criterion they use; it is argued, for example, that many specific phobias do not interfere with daily living and without this impairment to functioning the prevalence estimates are inflated and it is questionable if there is any need for intervention; as specific phobias are one of the most common in young people the removal of many of these phobias significantly decreases the overall prevalence of anxiety. When strict impairment criteria are applied many

disorders prevalence is much reduced but there remains a substantial proportion of the population with anxiety diagnoses. For example Carter et al. (2010) used a diagnostic interview to examine anxiety in kindergarten children and when they applied the impairment criteria they nearly halved the reported prevalence of anxiety disorders; however 9% were diagnosed with specific phobia and 2.2% with separation anxiety, still suggesting a high proportion of anxiety in this young population. It is relevant to the current thesis that anxiety disorders have been shown to be most affected by changing impairment criterion in comparison to other forms of psychopathology. In one large study using impairment criteria for each symptom and then applying a global measure of functioning reduced prevalence by up to 90% when compared to impairment applied only at the syndrome level, (Shaffer et al. 1996). It is, therefore, necessary to produce consistent estimates using methods which have clear criteria for reaching diagnosis and associated level of impairment. The use of standardised diagnostic interviews and DSM-IV or ICD-10 criteria can be helpful in alleviating these difficulties and have been demonstrated to reveal a substantial proportion of children with functionally impairing anxiety disorders (e.g. Carter et al.2010). The current project will, therefore, only use data from studies that have used standardised diagnostic measures with clear impairment criteria.

What do standardised diagnostic data tell us about the persistence and course of childhood and adolescent anxiety disorders?

Anxiety disorders in adulthood have been shown to be persistent over long term follow up. For example, a study of young adults in Zurich showed panic disorder to be a highly stable disorder over the seven-year follow-up (Vollrath & Angst, 1989). In clinical samples stability of panic disorder was supported over a twelve and eight year follow up respectively, and similar continuity was found for generalised anxiety disorder and social anxiety, (Bruce et al. 2005; Yonkers, Bruce, Dyck, & Keller, 2003). As discussed above, parent reports of very young children's anxious symptoms have been shown to be persistent over a 12 month period, (Briggs-Gowan et al. 2001) and to be predictive of preadolescent disorder (Mesman & Koot 2001). In childhood samples, however, there are inherent difficulties in distinguishing between developmentally normal childhood fears and anxieties, and pathological anxiety, and the use of self report tools which provide continuous data make these findings difficult to interpret. It appears that the presence of developmentally normal "fears" (Ollendick, Matson, & Helsel, 1985) providing the continuum from normal to abnormal anxiety, and the high prevalence of anxiety in young populations, may have led to the

contention that anxiety disorders are merely extremes of normal development and, therefore, transitory if the sufferer is a child or young person.

As already mentioned in the previous section, the contention that anxiety is not persistent and is usually transitory has been supported by a number of short term follow up studies of clinical samples that have shown the vast majority of children to be free of their primary anxiety diagnosis within a short period of time, leading to the conclusion that the course of childhood anxiety disorders is remitting and less malignant than the course of adult disorders (Aschenbrand, et al. 2003; Cantwell & Baker, 1989; Foley, Pickles, Maes, Silberg, & Eaves, 2004; Last et al. 1997; Last et al. 1996). The issue with these studies is that they use a single diagnostic follow up over a relatively short period (18 months to five years) to ascertain whether the participant is "well" or remains ill, they also often focus upon only one disorder; for example Cantwell & Baker, (1989) examined OCD and Foley et al. (2004) looked at separation anxiety. Alternatively the other studies do not distinguish between outcomes of the different anxiety disorders and examine "any anxiety disorders".

A recent naturalistic study carried out by Carballo and colleagues (2010) in paediatric psychiatric clinics in Spain, followed nearly 2000 children over fourteen years. They report the persistence of most anxiety disorders (particularly social anxiety and specific phobias) to be very high. Over 80% received the same diagnosis at 75 % of consultations (minimum number of consultations was three). In adolescents the persistence was lower (between 60% and 70%). This is still very high in comparison to the other clinical studies cited and may reflect the large sample size offering greater accuracy, or alternatively may be a result of the naturalistic design and human reasoning, with clinicians being increasingly likely to reassign a diagnosis once they have previously recorded it, and those who remit not attending clinic, which could lead to an artificial inflation of the persistence of the disorders. Prospective studies using community samples and a standardised diagnostic interview which is administered by an interviewer who is "blind" to previous diagnoses offer a valid and reliable method without these confounds to explore these discrepant findings in samples other than those presenting for treatment.

The current study is interested in whether the contention of a benign course is true for most young people and all anxiety disorders, or if anxiety is in fact persistent in some cases. It is suggested that the presence of some anxiety disorders in childhood and

adolescence may be more problematic and may cause significant impairment and risk for psychopathology in later life. The fact that studies often treat the anxiety disorders as a homogenous group may have contributed to the propagation of the theory that anxiety disorders in childhood are transitory, as there is emerging evidence that some disorders are at increased risk of later psychopathology (e.g. separation anxiety, Bruckl et al. 2007). It is also proposed that short term studies of clinically referred children have previously underestimated the predictive power of early anxiety, due to the "waxing and waning" course of many anxiety disorders in early adolescence. In Chapter Two data from the Early Developmental Stages of Psychopathology (EDSP) study from Dresden, Germany will be presented, which demonstrate using a prospective design that although homotypic continuity (same specific diagnosis at baseline and follow up) may be low for anxiety disorders in adolescence, there is a great deal of psychopathology associated with a baseline anxiety diagnosis. This finding held true for both a short term (19 months; Wittchen et al. 2000) and long term (10 year) follow up, (Beesdo-Baum et al. 2009). It is clear that in order to understand the persistence of anxiety disorders, particularly those that do not seek treatment but cause significant impairment, longitudinal studies that regularly use standardised diagnostic interviews to examine anxiety disorders throughout the lifespan, provide the best empirical data.

Summary.

As it is increasingly evident that anxiety is prevalent in early life, there is a need to understand the course of anxiety disorders and whether this anxious population of children become anxious adolescents and adults. There are mixed findings from the clinical literature with some short term longitudinal studies with relatively small samples showing the majority of cases to have remitted, and a longer term naturalistic study showing a high degree of persistence of anxiety diagnoses. A number of limitations of both these designs have been outlined; including the lack of data available to examine the course of individual disorders. Some prospective data shows that separation anxiety may be a good predictor of later psychopathology and it is proposed that the use of large scale epidemiological studies with diagnostic data over a long period of development provide the best way to examine persistence of anxiety and determine outcomes for these disorders. It seems important that we fully understand these patterns, as it may be possible to identify the disorders and/or individuals at risk of persistent disorders so that we can better target resources to

those who are least likely to experience spontaneous remission and suffer long term risk for psychopathology.

Age at onset.

Age at onset is one of the least studied areas of descriptive epidemiology. Kessler et al. (2007) suggest this is due to reluctance amongst researchers to rely on retrospective reports to calculate survival distributions and a lack of resources for prospective studies of mental disorders to collect diagnostic data at regular enough intervals, and with large enough samples, to map distributions across the lifespan. Age of onset is important for two main reasons; first it can be used to calculate lifetime risk for disorders and secondly it is vital in targeting research on the prevention of mental disorders. Kessler et al (2007) also point to the evidence of a relationship between early onset and increased severity of mental disorders (notably generalised anxiety disorder; Kessler, Keller, & Wittchen, 2001).

Costello's review of 50 epidemiological studies provides strong evidence that anxiety is prevalent in childhood and adolescence and we can therefore assume that a large number of young people have their first onset at this time. However, specific age of onset for anxiety disorders has largely been assessed using retrospective reports from clinical samples, i.e. by simply asking sufferers when they first remember experiencing key features or symptoms. Such data, collected from adults, support the contention that many anxiety disorders were first experienced in early childhood. In the National Comorbidity Survey of adults in the USA Kessler et al. (2005) found the median reported age of onset for anxiety disorders to be as low as 11 years; despite the wide range of ages included in the survey (15-54 years). In their review of retrospective studies of age at onset, Ost & Treffers (2001) report that the mean age of onset for animal phobias ranges from 4.4 to12.8 years and for other specific phobias it ranges from 8.1 to 20.6 years. In the same review, social anxiety was reported to begin in adolescence, with a mean onset of between 15.7 and 20 years. However, the retrospective nature of these reports, with some adults recalling symptoms from 50 or 60 years earlier, calls into question the reliability of such data. From a recent review of the test-retest reliability of reports of lifetime childhood disorders, it could be summarised that retrospective information did not exceed moderate reliability, (Muller & Schneider, by personal correspondence). Mannuzza Klein, Klein, Bessler, & Shrout (2002) also found the predictive power of diagnosing child psychiatric disorders retrospectively in adulthood to be very low (only 27% of

children diagnosed with ADHD were later identified in adulthood) suggesting that this method could underestimate childhood onset, and will often lack specificity.

A number of cross-sectional studies have aimed to address the problems inherent in using adult samples to address the question of age at onset by using diagnostic interviews with children and adolescents, reducing the time between onset and recall. Such studies are relatively scarce and are subject to some of the same methodological difficulties as retrospective studies with adults. Three such studies findings are summarised in Table 2. Keller et al. (1992) interviewed 275 parents and their children to investigate the onset of separation anxiety and overanxious disorder. Giaconia et al. (1994) examined the onset of specific phobias and social anxiety in 386 adolescents. Wittchen, Stein, & Kessler (1999) investigated the onset of social anxiety in boys and girls separately in the baseline investigation of a sample of 3021

Table 2. Cross sectional mean age of onset data from community samples of children and adolescents

	Specific Phobia	Separation Anxiety	Social Anxiety	OAD	Panic Disorder	Agoraphobia
Giaconia et al. 1994	6.7years	----	10.8 years	----	----	----
Keller et al. 1992	----	8 years	----	10 years	----	----
Wittchen, et al. 1998; 1999;2000	----	----	11.5 girls 12.5 boys	----	14.5years	12.6 years

14-24 year olds in the Dresden study. From this same baseline sample Wittchen et al. (1998) also examined the onset of panic and agoraphobia. These studies suggest that the onset of social anxiety may be much earlier than those reported by adults retrospectively, (e.g. Ost & Treffers, 2001). It is also of note that panic disorder is generally thought to be a disorder with a peak onset in early adulthood; however, the findings of Wittchen, Lieb, Schuster, & Oldehinkl (2000) suggest it may well have significant onset in adolescence. There is, therefore, cross-sectional evidence using large samples of children and adolescents indicating retrospective data from adults may underestimate the early onset of disorders, and suggesting that many anxiety disorders have their onset in childhood and adolescence. However, it should be noted that the mean age at onset will always be heavily influenced by the age of the

sample in which the onset is assessed, making cross sectional cohort data problematic for establishing key periods or peak onset.

Costello et al (in prep) attempted to include age at onset in their review; however, only the authors' study (Great Smoky Mountains Study; Costello et al. 2003) had assessed and reported age at onset for anxiety disorders in the diagnostic interview. This study reported the median age of onset for any anxiety disorder as eight years old, significantly below reported in adult studies (e.g. 11 years; Kessler et al. 2005). When examining the median and interquartile ranges for each disorder, the findings demonstrate that the majority of disorders have their onset before the age of 10, with only panic and agoraphobia having their onset in adolescence (at 12 and 18 years respectively). It is notable that in a population of 16 year olds, only panic, OCD, and generalised anxiety disorder had any reported cases of onset after the age of 11: Panic onset range 12-15 years; obsessive compulsive disorder 8-13 years; generalised anxiety disorder 0-13 years, (Costello et al. 2004). Also, using data from this same population, the window of onset appears to be large for disorders such as generalised anxiety disorder (12 years) but extremely short for other anxiety disorders e.g. separation anxiety disorders (four years). These indications of early onset provide support to the adult data and suggest an underestimation of early onset (Kessler et al. 2005). Although the Great Smoky Mountains is a longitudinal study, the calculation of age at onset relies on parent and child reporting of their first recollection of key features of the diagnosis; in essence it is still a cross-sectional and retrospective account of age at onset. Many claims regarding epidemiology, particularly age at onset, are made from such data. For example, Merikangas et al. (2009) talk about the temporal patterns of onset taken from prospective studies. However, on closer inspection, although the studies discussed are prospective in design, the data they refer to are retrospective.

Cross sectional studies of children and young people, whilst an improvement on adult retrospective designs, remain limited in a number of respects: Firstly, despite the use of standardised diagnostic interviews, when assessing age at onset these studies generally ask the parent and child to recall the age at which they first remember key symptoms. Wittchen, Lachner, Wunderlich, & Pfister, (1998) demonstrated that the Munich version of the Composite International Diagnostic Interview ((M-CIDI), although reliable in later adolescence, is not able to reliably determine age at onset in prepubescent participants, and although attempts have been made to alter diagnostic

tools in order to make them better at reliably assessing age at onset in children and adolescents, (Shaffer et al., 1996; Wittchen et al. 1999), these measures remain retrospective in nature, with the inherent error that this brings. Also, Wittchen et al (1998) have demonstrated that 23-32% do not clearly remember when the disorder had its onset, calling into question the validity of retrospective measures in many cases. They also found that assessing onset of *full diagnostic criteria* rather than key features of the disorder has a large and significant effect; they demonstrated that onset of the full disorder was, on average reported two to three years later. This is an important distinction, and one that is often ignored. Onset questions relating to key features of the disorder are advocated in most standardised diagnostic manuals for anxiety disorders, depressive conditions require full diagnostic criteria to be met to attribute onset of the disorder; however, this is not consistent across all mental disorders. This project will examine age at onset using prospective data and current diagnostic criteria in order to address these issues.

What can we learn from long term follow up?

Using child or adolescent samples only informs us regarding the age at onset for those suffering anxiety in childhood or adolescence. It cannot provide data regarding the onset for those suffering in later life and tell us if these populations overlap. Do young people suffering from anxiety disorders go on to suffer from these same disorders in adulthood? Longitudinal data that follows participants into adulthood is required to answer these questions. By using standardised diagnostic interviews to plot prevalence rates through childhood and adolescence into adulthood, and calculating first incidence rates at a number of follow ups through the lifespan it is hoped that the existing data from childhood and adolescence will be able to demonstrate more clearly the peak ages at onset for each anxiety disorder. The longitudinal data from birth cohorts that are now into adulthood are able to provide these data without the biases of using a cross sectional sample, which will always be influenced by the age of the cohort and impeded by difficulties in recalling symptoms, syndromes, and/or diagnostic criteria accurately.

Summary.

There exists a large amount of data appertaining to the prevalence of anxiety and some data that have attempted to examine the onset and course of anxiety disorders in younger populations. Prevalence data suggest anxiety disorders are a big and growing problem in childhood. It is important, however, that we distinguish between

disorders that cause the child impairment to functioning (and so require intervention) and those that do not. In order to do this, standardised diagnostic interviews with clearly defined impairment criteria, are required. Self report data from parents suggests that early symptoms of anxiety are persistent and predictive of later anxiety disorders. Clinical samples suggest that when we follow up anxious children they are often well after a period of up to five years; however, the use of only one follow up and the focus on individual disorders (e.g. obsessive compulsive disorder and separation anxiety) may mask the malign effects of some anxiety disorders and cannot examine the possible waxing and waning of disorders through different developmental stages or key risk periods. Clinical populations with a single follow up do not allow us to fully explore the course and outcome of early anxiety or understand the risk that these early anxiety disorders' confer for later anxiety disorders or other forms of psychopathology. The current cross sectional data demonstrate that anxiety is a prevalent disorder in childhood and adolescent populations, suggesting substantial onset of disorder in this population. We know that parents and children report earlier onset than have been reported by adults in retrospective studies. However, the "age at onset" findings are always heavily influenced by the age of the sample being questioned and we know that asking about symptoms rather than asking about the onset of an anxiety disorders can significantly affect the onset by as much to two to three years. It is, therefore, argued that it is necessary to look to the longitudinal, prospective data that uses standardised diagnostic interviews at multiple follow ups in childhood and adolescence (and preferably into adulthood) in order to provide accurate and reliable estimates and better understand the development of anxiety disorders through the lifespan. It must be noted that although diagnostic interviews provide the de facto "gold standard" for this kind of research, a recent review and meta-analysis found agreement between standardised diagnostic interviews and clinician assigned diagnoses to be low to moderate in most disorders, including internalising disorders (0.28). Mean kappa levels were reported as higher in child samples than in adult sample (0.39 vs. 0.31); however, the child sample was substantially smaller and complicated by the combination of informants – the same issue faced in many of the current studies (Rettew, Lynch, Achenbach, Demenci, Ivanova, 2009). They conclude that rather than one method of assessment being inferior it must be acknowledged that findings from standardised diagnostic interviews may not be generalisable to clinical experience and practice. Wittchen et al (1999) suggests that without the clinical "outcome" in a diagnostic interview the respondent

may lack motivation to respond honestly and thoughtfully. The findings, therefore, may underestimate disorder and may not map onto clinical cases found in services.

Prospective Longitudinal Data.

Gallagher (2008) carried out a systematic search of the literature and collated all available publications from seven longitudinal studies meeting the strict inclusion criteria (see Appendix One); these studies are presented in Table 3. All relevant data to answer questions regarding prevalence, age at onset and outcome of anxiety disorders were reviewed and reported. The conclusions from the review will now be briefly summarised:

Although a large quantity of prevalence data were reported across the seven studies reviewed, the selection of data to report and the manner in which they are reported varies substantially between and within studies. To illustrate this point, when examining prevalence there are often no reported figures for any anxiety disorders and it is not possible to calculate this from the data reported due to high rates of comorbidity and the limited number of disorders included. In other cases, only rates for "any" anxiety disorder are reported, meaning that judgements about the individual disorders cannot be made. In none of the studies are publication of rates for both the individual disorders and rates for any anxiety disorder available at every follow up; therefore, it was not possible to reliably plot the prevalence rates through childhood and adolescence for all the studies, or to combine the data across studies. It was also not possible to ascertain the peak age at onset for anxiety disorders. The review confirmed that anxiety disorders are a prevalent problem amongst children and adolescents and that the prevalence rates reported in large scale longitudinal research are robust despite a range of temporal and geographical differences and differing approaches to data collection and analysis. The evidence reviewed also suggests that the majority of adult anxiety disorders have their onset in childhood.

Robust Prevalence Data.

When examining prevalence in the longitudinal studies reviewed, anxiety disorders in later childhood and adolescence have been reported to be present in 9.7% of 11 year olds in the Dunedin study, New Zealand (Anderson et al., 1987) 9.2% of 12-13 year olds in the Taiwan Panel Study (Gau et al., 2005) and 9.2% of 12-17 year olds in the

Table 3. Studies from Gallagher (2008) review.

Study/Authors	Design	Published data relating to anxiety disorders
Bremen Adolescent Study (BJS.) Bremen, Germany. *Essau (2005);Essau, Conradt & Petermann (1999);Essau, Conradt & Petermann (2000) Essau, Conradt & Petermann (2002)*	Diagnostic interviews in adolescence (12-17 years) and 15 months later.	Reported for AAD and specific anxiety disorders at baseline and T1.
Christchurch Health & Development Study, (CHDS). Christchurch, New Zealand *Fergusson, Horwood & Lynskey (1993) Fergusson & Horwood (2001);Horwood & Fergusson (1998)*	Birth cohort study. Diagnostic interviews at 15 and 18 years old with both parent and child.	Reported for AAD at T1 and T2
Dunedin Study. Dunedin, New Zealand. *Anderson, Williams, McGee, & Silva (1987);Feehan, McGee, Raja & Williams (1994);Gregory et al (2007) Kim-Cohen et al (2003; McGee et al (1990);Newman et al (1996)*	Birth cohort study. Diagnostic interviews with children/adolescents at 11, 13, 15, 18, 21, 26, & 32	Reported for AAD and (in some cases specific anxiety disorders) at baseline and six follow ups.
Great Smoky Mountains Study (GSMS) North Carolina, USA *Costello et al (1996); Costello et al (1988) Costello, Mustillo, Erkanli. Keeler & Angold (2003)*	Overlapping cohorts using diagnostic assessment. Baseline age 9-13.	Reported for each age group and individual disorders at 9-13.
Children in the Community Study (CIC). New York State, USA *Cohen, Cohen & Brook (1993); Cohen et al (1993); Pine, Cohen, Gurley, Brook& Yuju (1998);*	Overlapping cohorts' design of children from 10-20 using diagnostic assessments at 2.5 and 8 year follow up.	Reported for Any anxiety disorder, OAD, separation and social anxiety disorders.
Oregon Adolescent Depression Project. Oregon, USA *Lewinsohn et al. (1993)*	Single 12 month follow up 14-18 at baseline.	Point prevalence and lifetime prevalence at baseline and T1
Taiwan Epidemiological Study of Mental Disorders. Taiwan. *Gau, Chong, Chen & Cheng (2005)*	Cohort of 12-13 years followed up using diagnostic interviews yearly for three years.	Reported for AAD and specific anxiety disorders at T1, T2 & T3.

Bremen Study, Germany (Essau, Conradt, & Petermann, 2002). These rates are remarkably similar across different studies carried out at different times and in different countries. Rates of separation anxiety also appear relatively robust with rates of 3.5% found in the Dunedin study at age 11 (Anderson et al., 1987) and in the Great Smoky Mountains Study in the US at age 9-13 (Costello et al., 1996) and rates of 3% found in the New York sample, also US, at age 14-16 (Cohen et al., 1993). The prevalence of social anxiety appears more varied, which may indicate that it is less stable over the age ranges studied than some of the other disorders. Alternatively, changes in diagnostic criteria of social anxiety disorders in childhood from DSM-III to DSM-IV, most importantly removing overanxious disorder and implementing generalised anxiety disorder, and changing criteria from a phobia to an anxiety disorder, may well have influenced the stability of longitudinal assessments of social anxiety.

Childhood Onset and Adult Outcomes.

Three main lines of evidence were reviewed to understand onset and course of anxiety. These were: follow-back analyses; cumulative prevalence rates; and first incidence data. Follow-back analyses examine adults or adolescents in the later assessments who meet diagnostic criteria for an anxiety disorder, to determine at what age they first received a diagnosis. Using follow-back analyses, the Dunedin study demonstrated that 80.5% of 21 year olds diagnosed with an anxiety disorders had a diagnosis before the age of 18 suggesting persistence in this age group, (Newman et al., 1996). At 26, of those receiving an anxiety diagnosis, 61.5% had previously received a diagnosis between the ages of 11 and 15 (Kim-Cohen et al.2003). This figure is higher still when looking at adults with more severe anxiety, defined as those accessing treatment suggesting an early onset for many of the severe adult anxiety disorders. The New York study has similar findings when examining individual disorders. In their sample of 17-26 year olds, 81% of those with specific phobias had received their diagnosis at baseline or first follow up in early adolescence; in those with social anxiety and generalised anxiety disorder the number of diagnoses first made in early adolescence was even higher at over 95%, (Pine Cohen, Gurley, Brook, & Ma, 1998).

Cumulative prevalence data tell us the percentage of the sample who received at least one diagnosis of anxiety before a particular age. Cumulative prevalence of anxiety disorders reported by both the Great Smoky Mountains Study and the Oregon Adolescent Depression Project suggest that the number of children and adolescents

who will have received a diagnosis by the time they are 16 years old is relatively high. The Great Smoky Mountains report a cumulative prevalence by 16 years of 9.9% (Costello et al., 2003) and 9.2% in the Oregon study (Lewinsohn et al., 1993). These findings are remarkably similar despite differing methods and follow-up periods. Moreover, as previously discussed these prevalence are approaching the lifetime incidence reported in the adult literature; e.g. Alonso et al. (2004) lifetime prevalence rate of any anxiety disorder of 14%. The fact that over 9% of 16 year olds have reached diagnosis could suggest that a large proportion of lifetime anxiety disorders are first diagnosed before the age of 16. However, this contention must be treated with caution as the adult and adolescent study methods are not identical and it is of course possible, although unlikely, that the anxious adult population has no overlap with the population of anxious children. Moreover, the retrospective nature of the collection of cumulative prevalence data from an adult sample requires people to remember diagnoses from, in some cases, 50 to 60 years ago, which introduces a measure of error (and most probably underestimation) to such adult studies.

Problems with relying on “lifetime” incidence (asking whether the individual has ever experienced symptoms in their lifetime) can be illustrated by comparing them to 12-month prevalence (have you experienced symptoms in the last twelve months); they are often remarkably similar. Costello et al. (2004) note the similarity in lifetime and twelve month prevalence found in adults (18-54) and adolescents (15-17) in the National Comorbidity Survey (NCS). They conclude that this either refers to an epidemic of anxiety in the 12 months prior to the survey, extreme stability of anxiety through the lifespan, or indicates high rates of forgetting for earlier incidences of anxiety. Wittchen, Lieb, Pfister, & Schuster (2000) notes a similar trend in the Early Development Stages of Psychopathology study in Dresden, and propose that high rates of forgetting are the most likely explanation given all other sources of evidence for stability. Comparisons between adult and child cumulative incidence rates are, therefore, made tentatively and require longitudinal data to determine any truth in this contention.

First incidence data calculate the percentage of participants that are diagnosed with a disorder that have not received that diagnosis at any previous follow ups; i.e. those receiving that diagnosis for the first time within the study period. For example, the number of a birth cohort who were diagnosis free at baseline (age 10), and at two year follow up (age 12) but receive a diagnosis at five year follow up (age 15) will

allow us to calculate the percentage of the sample with their first onset at 13 to 15 years of age in the cohort. First incidence data from the studies reviewed give the onset of a disorder between two specific ages and can be useful in furthering our understanding of peak age of onset. The Bremen study shows that 6.9% of 12-18 year olds received a diagnosis of an anxiety disorder for the first time during the study period of 15 months. This would suggest that adolescence is a significant period for the development of anxiety disorders. Unfortunately these data were not presented for each anxiety disorder.

The Oregon Study, using very similar methodology, reports first incidence over the study period of 12 months for young people between the ages of 14-18 as much lower at just 0.6%, suggesting that peak onset is likely to be either before the age of 14 or alternatively in adulthood. The discrepancy between these two studies is somewhat surprising considering the use of similar methods to collect data on incidence over the follow up period. The Oregon finding seems low in comparison to other studies and could reflect cultural differences between Germany and the USA or alternatively reflect differences between the individual disorders each study subsumed under any anxiety disorder. The data reviewed by Gallagher (2008) would suggest that peak onset for most disorders are more likely to be before the age of 14 rather than in adulthood. The fact these studies begin collecting data in adolescence presents a problem as these may well not be the true first diagnosis. Also, as illustrated here, the use of the any anxiety disorder criterion rather than examining the individual disorders is problematic when examining incidence in limited age ranges and may well be heavily influenced by a small number of specific anxiety disorders. Examining incidence of individual disorders is important to our understanding of the temporal onset of anxiety disorders in this period and will be a focus of the current project. Using repeated follow ups to determine the changes in new cases of each disorder over time will be most helpful in understanding the patterns of new onset.

Conclusions regarding the outcome of childhood anxiety were limited due to the available data; however the review did suggest that the majority of anxious adults were first diagnosed in early life. These conclusions were drawn largely from the findings of two major longitudinal studies in the United States (the New York study) and New Zealand (Dunedin Study). The New York study presents a seven year follow up of young adults suggesting that childhood anxiety presents, on average a two to three fold increased risk for adult anxiety disorders. Interestingly, as reported above,

they also found that most adult psychopathology was preceded by a childhood diagnosis of anxiety disorders; however, as the prevalence rates in the New York study are particularly high (unfortunately no cumulative prevalence data are reported), this may not mean that early disorder is a particularly useful predictor of adult disorder. When examining the likelihood of adult disorders having had their onset in adolescence this varies but remains consistently high (overanxious disorder OR = 4.99; social anxiety OR = 5.64; specific phobia = 10.61) Pine et al. (1998). This increasingly strong relationship with adult disorders dependent upon severity of early disorders is also shown in reverse (i.e. severe adult disorder is more likely to begin in childhood) in the Dunedin data (Gregory et al. 2007). Authors reporting longer term follow up from the Dunedin birth cohort in New Zealand also found that the majority of adults diagnosed with anxiety disorders had their first onset in late childhood or adolescence; this was particularly evident in severe adult cases, defined as those seeking treatment for their disorder (Gregory et al. 2007; Kim-Cohen et al. 2003). This was a consistent finding in the two longitudinal studies that examine the continuity of disorder from adolescence into young adulthood and is supported by data following young adults into later life which show high stability and a low incidence of new cases (Vollrath & Angst, 1989; Yonkers et al. 1996). It is clear that more investigation of the longitudinal data into later life is required in order to gain a better understanding of the predictive power of early anxiety disorders in adult psychopathology and this requires multiple follow ups of cohorts beginning early in development and continuing into adulthood.

Conclusions thus far.

Prevalence data show childhood to be a significant period of onset for anxiety disorders and the most recent review, which statistically combines the findings of 50 cross-sectional studies showed childhood and adolescent anxiety disorders to be equally prevalent but estimates in adolescence to be more reliable. Separation anxiety was found to decrease from childhood to adolescence and social anxiety increases in adolescence suggesting peak onset for separation anxiety to be earlier and social anxiety to be in adolescence, furthermore, providing support for distinct anxiety diagnoses in childhood samples. Cross-sectional prevalence data, even when they are determined by standardised diagnostic interviews, are not able to accurately plot the onset and course of anxiety though the different developmental stages. Longitudinal prospective data are best placed to answer these questions and the

available data suggests that cross-sectional data may underestimate prevalence. Clinical and self report data have shown inconsistent findings in whether or not anxiety in childhood and adolescence is transitory or a stable disorder that leaves the sufferer at increased risk of later anxiety or other psychopathology. The persistence of anxiety disorders and their stability over time is important to understanding the course of anxiety through the lifespan, and to understanding which disorders carry the greatest risk for anxiety in later life. Again, longitudinal data with multiple follow ups from childhood into adulthood is best placed to answer these questions and allow the identification of the disorders and age groups at greatest risk of persistent disorders and those who may suffer only for a short time.

Early data from retrospective and cross-sectional studies of adults suggest that the mean age at onset for anxiety disorders to be around 10 or 11 years; with onset of specific phobia and separation anxiety disorders to be in early childhood, social anxiety in adolescence, and panic, agoraphobia, and generalised anxiety disorder to have their onset in adulthood. However, evidence from younger samples of children and adolescents suggest that these may be missing the early onset of some disorders, and is supported by the findings of the Costello review. Retrospective reports using improved methods of data collection (e.g. Wittchen et al., 2000) support the early onset of separation anxiety, social anxiety, and specific phobias but show significant adolescent onset for disorders previously thought to have their onset in adulthood (agoraphobia, generalised anxiety and panic disorder). Problems with biases in “onset” according to the age of the population can only be addressed using prospective samples with data available into adulthood. However, prospective age at onset data (incidence rates) are currently only available for samples of older adolescents (Essau et al 2002; Lewinsohn et al. 1993; Wittchen et al. 2000). These findings suggest that although adolescence has *significant* onset, it appears likely that peak onset is earlier or later in adulthood. Incidences of specific anxiety disorders have not yet been calculated using longitudinal data.

The Gallagher (2008) review of the prospective, diagnostic data relating to anxiety disorders concludes that although there is a multitude of data collected around the world, there is a distinct lack of data available to plot rates, and compare onset and course of anxiety disorders from the seven longitudinal studies identified. The patterns of data, however, do suggest a high prevalence of anxiety disorders amongst children and adolescents and provides evidence that longitudinal data produce more

robust prevalence than cross sectional data, but not necessarily higher estimates. Cumulative incidence at 16 years of age is high and approaching cumulative incidence found in adult samples. Caution is needed in drawing such comparisons due to the different methods employed; however, this points to significant early onset of disorders that requires further investigation. Evidence from longitudinal studies that follow participants into adulthood suggests that although most childhood disorders appear to remit, many adult disorders had their first onset in childhood or adolescence. This is an important contention for supporting the argument for the redirection of resources to research into the development of childhood anxiety rather than the current focus on adult disorders. These contentions have been given increasing credence in recent reviews; however, further understanding of the patterns of specific disorders at specific ages will add significantly to our understanding of the epidemiology of anxiety disorders and we must be able to identify the children and adolescents whose anxiety puts them at risk for future anxiety disorders and those for whom the disorder is transitory, in order to make best use of the available resources.

Aims.

In this project I plan to analyse data from existing sources of prospective longitudinal data to meet three main aims:

1) To update the systematic search and review of the prospective, longitudinal studies examining anxiety disorders of childhood and adolescence that have been published to date.
2) To gain access to longitudinal data that began collecting standardised diagnostic information in childhood or adolescence that has not yet been used to plot prevalence and first incidence of anxiety disorders at specific ages or developmental stages.
3) To use the new data to calculate the stability of anxiety diagnoses through the lifespan and determine the outcomes for anxious children in later life.
4) To synthesise all published prospective, diagnostic data that relates to the onset, stability, and outcome of childhood and adolescent anxiety disorders with the new analyses to provide a comprehensive review of the current epidemiological data appertaining to anxiety

Chapter Two: A systematic search to update Gallagher (2008) in 2010

Background.

A systematic review of the literature was carried out in 2006 (Gallagher, 2008; see Appendix One for search/inclusion/exclusion criteria.) This review revealed 15 epidemiological studies that had collected diagnostic data regarding anxiety disorders from children or adolescents at a minimum of two points in time, (see Appendix Two). It was hoped that a full review of these published studies that have employed the most robust methodology would allow the mapping of the onset, course, and outcome of anxiety disorders across the lifespan. It was proposed that further comparison and synthesis of data from around the world would make the review a robust source of developmental epidemiology for clinicians and researchers. However, the conclusions of this review were limited by the lack of analysis and publication of epidemiological data relating to anxiety disorders. In many cases data about age at onset have been omitted from reporting because the focus of the study was directed towards other matters, such as local service planning (e.g. the Great Smoky Mountains Study; Costello et al. 1996) or a focus on externalising problems and/or social rather than clinical outcomes (e.g. the Christchurch study; Fergusson & Horwood, 2001). When data examining anxiety disorders are presented, often the focus is on the social and diagnostic correlates, (e.g. GSMS) or age and gender differences in anxiety disorders (Children in the Community Study, New York; Cohen et al., 1993). Another issue lies in anxiety disorders being combined with depression and analysed and reported as internalising problems or emotional disorders (Ontario Child Health Study, Offord et al. 1992; British Child and Adolescent Mental Health Survey, Ford et al. 2003).

Literature Search.

In order to attempt to answer the research questions outlined in the Introduction (Chapter One), the literature search performed in 2006 was carried out again in October 2010 in order to establish if any further longitudinal data regarding anxiety disorders had been published in the preceding four years.

Studies relevant to this review were identified using a number of search strategies. First, electronic databases were searched using the search terms [(CHILD* or ADOLESCEN*) and (ANXIETY* or PSYCHIATRIC* or DISORDER) and (EPIDEMIOLOG* or PREVALENCE or INCIDENCE or ONSET or LONGITUDINAL). PsycInfo (2000 -2010) and Medline (2000-2010) were both searched using these terms. The Principal Investigators (PI) and lead researchers/authors associated with all 15 studies revealed by the 2006 search (see Appendix Two) were contacted where possible and websites were searched for any further publications or articles that may be in press. Finally, the reference lists of all relevant papers were scrutinised for further relevant studies.

The search terms located 1185 relevant articles from the year 2000 to the present day (October 2010). The titles and abstracts were searched by the author to establish relevance to the research questions, the use of a standardised diagnostic interview to determine anxiety status, and a prospective, longitudinal design (data collected at a minimum of two points in time,) were required. Seven relevant articles were identified through the electronic and website search. A critical review of the papers identified, the Wittchen et al. (2000) chapter that was omitted from the original 2008 review, and with the unpublished review kindly provided by E. J. Costello, Principal Investigator of the Great Smoky Mountains Study, will now be presented. The review aims to build upon the literature reviewed in Chapter One to provide an up to date understanding of the descriptive epidemiology of anxiety disorders and provide further rationale for the novel analysis of existing prospective data.

The Early Developmental Staged of Psychopathology study (EDSP): Dresden, Germany.

The Dresden study was not included in the Gallagher (2008) review because anxiety diagnoses were believed to be published for baseline disorders only. However, the Gallagher (2008) search had failed to pick up data published in a book chapter (Wittchen et al. 2000) that was brought to light with the publication of Beesdo-Baum et al. (2009). This chapter draws from data at baseline and first follow up (15-20 months). Prevalence and incidence of anxiety disorders in those who were aged 14 to 17 years at baseline are discussed. Cumulative or “lifetime” prevalence for anxiety is extremely high (27.2%); however, overall prevalence rates for any anxiety disorder

fell between baseline and first follow up (14.5% to 10.4%). Incidence data and lifetime prevalence for the anxiety disorders in this period are presented in Table 4.

Table 4. Incidence and lifetime prevalence reported by Dresden study at 20 month follow up (Wittchen et al. 1999)

Disorder	Incidence	Lifetime Prevalence
Any Anxiety Disorder	8%	21.3%
Panic Attack	2.7%	3.2%
Panic Disorder	0.6%	0.7%
Agoraphobia	0.7%	3%
Phobia NOS	2.1%	6%
Social Phobia	2.1%	5.8%
Specific Phobia	3.9%	13.7%
GAD	0.1%	0.3%

The incidence rates reported here are for a similar age range to those reported in the Oregon Adolescent Depression Project by Lewinsohn et al (1993); however the Dresden incidence is much higher than the 0.6% reported for anxiety disorders in the Oregon study. This may be due to the use of different methods of collecting and combining the data. However, this discrepancy is puzzling as both studies looked at similar age ranges, used diagnostic interviews, followed the adolescents up over a similar period, and both sought any new anxiety diagnoses since the baseline assessment.

There is evidence of reduced reliability of diagnoses reported from over a three month period to determine diagnostic criteria (Angold, Erkanli, Costello & Rutter, 1996) and this reduced reliability is likely to substantially affect the estimates of incidence when asking about symptoms over a period of greater than a year. Lifetime prevalence as calculated from a one off interview is even more problematic as there are significant issues with reliability and rates of forgetting of earlier symptoms and distress (Costello et al 2004). In apparent recognition of these issues, Wittchen et al. (2000) also reports the point prevalence of the Dresden data (the symptoms must be current and present at the time of interview); these data are reproduced in Table 5. Only panic attacks and panic disorder are reported at both follow ups at using these criteria; both appear to increase in this period.

The findings from the first follow up demonstrate that although late adolescence (between 14 and 19) is a significant period of onset it appears from the comparison with lifetime prevalence rates, (which should be treated with caution but are assumed to be conservative,) that peak onset for the majority (two thirds) of anxiety disorders are earlier in childhood and adolescence.

Table 5. Point prevalence at baseline and 20 month follow up (Wittchen et al. 1999)

Disorder	**Point Prevalence Baseline**	**Point Prevalence 20 months**
Any Anxiety Disorder	14.5%	----
Panic Attack	1.9%	3.5%
Panic Disorder	0.3%	0.8%
Agoraphobia	1.9%	---
Phobia NOS	2.9%	---
Social Phobia	2.9%	
Specific Phobia	9%	---
GAD	0.2%	---

When examining the stability of disorders in late adolescence Wittchen and colleagues (2000) report that 19.7% of those meeting criteria for an anxiety disorder at baseline meet full criteria at 20 months. Fortunately 38.2% were completely well, displaying no symptoms at all; however, 47.9% remained symptomatic or met criteria for a "subthreshold" diagnosis. It is unclear why the reported values reach a value over 100% as these appear to be mutually exclusive categories. Panic disorder and specific phobias were the most stable with 44% and 30% respectively still meeting diagnostic criteria. Agoraphobia and phobia not otherwise specified were the most likely to have remitted; 75.4% and 93% respectively. These two disorders colour the picture of stability significantly. When examining all anxiety disorders together 87.3% have remitted; however this is largely due to agoraphobia and phobia not otherwise specified. It seems that some of the less stable anxiety disorders in the short term (e.g. generalised anxiety and panic) actually appear to have the least favourable outcomes in the longer term. For example, only 22% of those with generalised anxiety are symptom free at ten year follow up; although the same disorder may have low stability it places the individual at risk for later psychopathology and subthreshold symptoms are often present. The heterotypic continuity data are provided in support of the contention that rather than being transitory and having a favourable outcome

some anxiety disorders wax and wane in their level of symptoms, but confer high risk for later psychopathology.

Separation anxiety, as a disorder that remits in adulthood, has been proposed as a risk factor for other disorders, namely, panic disorder. Bruckl et al. (2007) showed that separation anxiety in childhood placed the individual at a much increased risk not specifically for panic disorder but for a range of psychopathology. Furthermore, Beesdo-Baum and colleagues (2009) present data from four waves of assessment in the Dresden study reporting data from ten year follow up of the sample of 14 to 24 year olds. Analysis of these data provide further evidence to support the contention that anxiety has an unstable course in adolescence with many disorders having only moderate stability across the follow up periods. However, it also clearly demonstrates that although anxiety may remit in the short term heterotypic continuity is high; anxiety in adolescence is a significant risk factor for anxious and depressive psychopathology in adulthood. Ten year follow up of the 14 to 24 year olds at 23 to 34 years demonstrates that a sizeable proportion (35-41%) of adolescents meet criteria for the same anxiety disorder (strict homotypic continuity) and what is more only 10 to 14% were without psychopathology, with 70% suffering from an emotional disorder (depression or anxiety). Of those who were diagnosed with social anxiety at baseline only 13% were free of psychopathology at 10 years; 35% met criteria for social anxiety (strict homotypic continuity) and 64% were diagnosed with an anxiety or depressive disorder (heterotypic continuity). When examining generalized anxiety disorder and post traumatic stress disorder no one diagnosed at baseline was free from psychopathology at ten years. It is of note that in both generalized anxiety and post traumatic stress disorder sample sizes were small as these are rare disorders in this age group (generalized anxiety disorders; 0.2% N = 3); however, this is still a clinically important finding.

Beesdo-Baum and colleagues (2009) use the prospective data from all follow ups in the Dresden data (plus presumably the lifetime prevalence although this is not stated) to cumulate recently assessed new cases across the lifespan into adulthood (from 0 to 34 years) for both males and females for all anxiety disorders. These graphs illustrate the onset of separation anxiety and specific phobia to be in early childhood, with the onset of panic, agoraphobia and social anxiety having a less clear peak, with somewhat later onset and significant new cases continuing to appear into adulthood. Comparison of this data with the use of retrospective data demonstrates that rather

than steadily increasing through childhood and adolescence into adulthood there are key stages of development where onset is more likely and this differs across anxiety disorders. Most anxiety disorders have their onset prior to 14 where there is a flattening of new cases and social anxiety appears to be a disorder that continues to have incident cases whereas generalised anxiety has slower onset and a flatter curve suggesting less new cases in older adolescents. Gender differences were few; however, males were shown to have an earlier onset for specific phobias and a later onset for generalized anxiety disorder. This is potentially of interest when thinking about the direction of resources and prevention programmes.

Summary.

The Dresden study provides a great deal of insight into the course and outcome of anxiety disorders that begin in adolescence. There are some data relating to new onset of cases in adolescence and they show that there are significant "new" cases of anxiety appearing in adolescence. It is likely, however, that some cases of anxiety disorder had an earlier onset but as data collection begins late in development earlier cases are missed. Lifetime prevalence has issues with reliability or recall, so caution is required when interpreting these survival graphs. Interesting data relating to the persistence of anxiety disorders emerges from the long term follow up of young people. The findings show that, as has been demonstrated previously in clinical samples, anxiety disorders are transient and remit in around 80% of cases over the course of two years. However, by using symptoms and subthreshold measures of psychopathology and comparing across different disorders to examine outcome there appears to be very few anxious young people who can be considered "well" at ten year follow up. The data also highlight the importance of looking at individual anxiety disorders, as the seemingly benign course of anxiety from the first look at the analysis is largely due to agoraphobia and phobia not otherwise specified. Furthermore, short term transience can be associated with poor long term outcomes in some disorders (e.g. generalized anxiety disorder) suggesting that long term follow up is crucial in understanding the stability and risk conferred from early anxiety disorders. The Dresden group propose that early anxiety does not have a linear course but anxiety disorders remit and change their symptom profile through the course of development but in many disorders leave the young person at a much increased risk of later psychopathology.

The Great Smoky Mountains Study of Youth (GSMS): USA.

The GSMS data were included in the 2008 review to describe prevalence (in particular cumulative prevalence) rates across childhood and adolescence. The GSMS also examined associations between childhood disorders (separation anxiety, overanxious or generalized anxiety disorder, and social anxiety) with diagnoses in adolescence. Since the 2006 search Costello et al (in prep) have used the data from the GSMS and conducted a review and meta-analysis of the prevalence of anxiety through early childhood to late adolescence. This review includes over 50 epidemiological studies using community samples of 2 to 18 year olds and uses statistical methods to combine large quantities of prevalence data from studies using various designs. Their review demonstrates the growing attention to the epidemiology of anxiety in such samples, and presents interesting findings (Costello et al. in prep).

Similar to the conclusions from longitudinal data drawn from Gallagher (2008) Costello et al (in prep) conclude that anxiety disorders are highly prevalent in childhood and adolescence. Costello and colleagues compare the prevalence of anxiety disorders across childhood and adolescence, and proportions appear remarkably similar. The rate of anxiety disorders between two and eight years (9.4%) was only slightly below the mean for the whole sample (2 to 18 years; 10.1%) suggesting that anxiety is as prevalent in young children as in adolescents. There is, however, increased variability across this younger age range; for example, existing evidence suggests that prevalence in four to six year olds is significantly higher than two to three year olds (Briggs-Gowan et al. 2001). Prevalence of anxiety disorders in 6 to 12 year olds was calculated to be 12.3%; however, when examining the confidence intervals there is a large amount of variability, (95% CI; 7.1-28.2%). In adolescents (13 to 18 years) rates of 11% were calculated, with significantly narrower confidence intervals (95% CI;10.6-11.4%) reflecting the increasing precision of estimates and consistent findings across adolescent studies. It is as yet unclear whether this is an artefact of the way data is combined from parents and children in younger samples, or reflects a true variability in the prevalence of anxiety disorders across the various samples. It is clear from the Gallagher (2008) review and similar reviews carried out by other authors (Costello et al. 2004; Beesdo-Baum et al 2009) that one of the factors affecting prevalence is the assessment period; for example, much lower rates are reported when asking whether the child has a symptom present currently (point prevalence estimate) in the last three months (three month prevalence estimate), at any point in the last 12 months (12 month prevalence estimate) or whether they have experienced the symptoms at any

point in time (lifetime prevalence estimates). Costello et al (in prep) helpfully overcome this problem through their use of complex meta-analytic methods; however this is an interesting finding in itself that requires further attention and has implications for the descriptive epidemiology of anxiety disorders.

A notable finding of Costello and colleagues (in prep) review, similar to that of Gallagher (2008), is that anxiety disorders are, in some cases, shown to be more prevalent in child and adolescent samples than in samples of adults (Alonso et al. 2004; Kessler et al. 2005). This supports the high cumulative prevalence rates shown in the Great Smoky Mountains Study (Costello et al. 2004) and the Oregon Adolescent Depression Project, (Lewinsohn et al. 1993). It cannot be determined whether this demonstrates continuity of disorders, as it may not be the same population suffering in both childhood and adolescence. However, this evidence suggests that the large focus of resources and research upon adult anxiety may require further consideration. This review suggests not only that anxiety disorders are prevalent but that they cause significant impairment to young people's functioning in many cases. The data from this unpublished review have been referred to in some detail in Chapter One and so this will not be repeated here (see Table 1).

They do, however, report data from the GSMS regarding age at onset when the sample are aged 21 years. The median age at onset is eight years with new cases of all disorders appearing at the age of 21. However, as demonstrated in Table 6 the mean ages of onset for anxiety disorders demonstrate a surprisingly early onset, and the interquartile range suggests that "peak" onset may be a suitable description for some disorders (e.g. separation anxiety) but not others (e.g. generalised anxiety disorder) where onset is over a longer period of time, (see Table 6.)

Table 6. Mean age at onset at age 21 in the Great Smoky Mountains Study.

Anxiety Disorder	**Mean**	**Interquartile Range**	
		Lower	**Upper**
Any	7 years	6	11
Separation Anxiety	6 years	4	8
Specific Phobia	6 years	3	11
Social Anxiety	9 years	5	12
Generalised Anxiety	9 years	0	13

These data from an early adult sample show 50% of anxiety disorders to have their first onset between 6 and 12 years. This is compelling evidence for the redirection of resources to younger people. It is unfortunate that it is not clear how these data were calculated and whether the authors have used the prospective data to calculate onset or used self reported onset. It seems unlikely that retrospective data would be used in this sample; however, these data will be used cautiously in this thesis due to uncertainty around the exact methods used.

The Mannheim Study, Germany.

The Mannheim study was excluded from the original review as the longitudinal diagnostic data were reported only for "emotional" or "neurotic" disorders in the earlier publications (Esser, Schmidt, & Woerner, 1990). However, a recent publication from the study presents 18 year follow up data using ICD-10 criteria to diagnose anxiety disorders (Fichter, Kohlboeck, Quadflieg, Wyschkon, & Esser, 2009). Children were aged three to 15 years at baseline and nine to 22 at first follow up. The baseline data used for this paper is from the first follow up of the study (nine to 22 years) and it is unclear if they are using the "current" (i.e. point prevalence) or "past" (symptoms present in the last five years). Unfortunately the sample is relatively small (N=269; original sample N=396) and the majority of participants were over 15 years old at what will be referred to as "baseline" for this study. Despite the small sample size Fichter and colleagues have presented the data separately for 9-11, 12-14 and 15-22 year olds. The findings support a reduction in psychopathology from childhood into adolescence and adulthood and this is true for both anxiety disorders and phobias, and is supported by the Dresden data presented above. At baseline, prevalence is measured using symptom criteria plus having a severity rating of two or more (two relates to moderate impairment; range 0-4): 23% of 9-11 year olds; 13% of 12-14 year old girls and 10% of boys; 16.5% of 15-22 year old females and 10% of males were described as suffering from an anxiety or phobic disorder.

When looking at these individuals as adults 18 years later 12 month prevalence is much lower. The same psychiatric interview showed 4.2 - 8.7% of females and 3.4 - 4.2% of males meeting criteria for anxiety or phobia. This may be due to the comparison between disorders in the "last five years" in childhood and "last twelve months" in adulthood. However this is unclear, so it is possible that it is a comparison between point prevalence in childhood and 12 month prevalence in adulthood, which

would make the decreases even more striking. Only two women (0.8%) of the adult sample (N=269) met criteria for “severe” anxiety or phobia (rating of 4) at both time points (continuous severe anxiety/phobic symptoms.) In this cohort 3.1% of the sample received a diagnosis of “severe” anxiety or phobia in adulthood and had reported no symptoms at baseline (i.e. this could be considered the incidence or first onset of severe anxiety in adulthood). The use of this data to talk about adult onset must be tentative in a population who has had only one baseline follow up and are now aged 27-40 years old; however, the decreasing prevalence supports the contention that most adult cases are “new cases” in this sample. Unfortunately the data are not presented as a percentage of the anxious adult sample but for the sample as a whole making comparisons with other studies more difficult.

The Mannheim sample is small and the number of cases in adulthood is relatively few, so it is difficult to examine patterns of remission and onset in a meaningful way. None of the 9-11 year olds diagnosed with anxiety or phobia meet criteria 18 years later suggesting full remission in this small sample (N= 3). These findings do not appear to lend support to the contention that adult disorders most often have an early onset. Possible factors to explain this discrepancy with the findings of the Dresden, Dunedin and New York studies could be that the Mannheim study has a relatively small sample, does not use the same psychiatric interview/criteria at both follow ups, and there may be international differences between America, New Zealand, and Germany. However, compatible findings between the New York and Dunedin studies and those from Dresden, Germany suggest that the cultural explanation is unlikely. It seems more likely that the use of only one baseline assessment and such a long period of follow up, coupled with the use of different methods of determining diagnostic status, and the relatively small sample explain these discrepant findings. Despite these seemingly contradictory findings relating to the proportion of stable disorders and early onset of adult disorders, Odds Ratios show that anxiety and phobias did confer risk for adult psychopathology (OR=1.7) and this increased when looking specifically at phobias in childhood or adolescence and ICD 10 anxiety disorders at 18 year follow up (OR=2.3). These OR’s are more conservative but comparable to those reported in the New York study by Pine and colleagues (1998) over a much shorter follow up.

These findings could be considered problematic in one respect in that they appear to show only a limited relationship between early onset anxiety or phobia and later anxiety or psychopathology. However, the data still demonstrate a relationship

between early onset and adult disorders, specifically between early phobias and adult anxiety disorders. The use of only two periods of assessment with a small sample, over such a long follow up period when the Dresden data is beginning to provide clear evidence that anxiety waxes and wanes over childhood and adolescence (Wittchen et al. 2000) offers a possible and meaningful explanation of the discrepancy between Mannheim and studies such as Dunedin and New York which have larger samples and more importantly multiple follow ups across childhood and adolescence.

Teen Health 2000 (TH2K).

The TH2K paper was published in 2009. A cohort of 4,175 11-17 year-olds in Texas, USA were interviewed using the Diagnostic Interview Schedule for Children (DISC) to establish rates of DSM-IV mental disorders. Of those, 3134 were interviewed one year later (Roberts, Roberts, & Chan, 2009). Prevalence of any anxiety disorder was 6.3% (CI 95%; 5.4-7.2%) in this sample. The proportion of the sample experiencing their first incidence of an anxiety disorder in the previous 12 months is reported as 2.9% (CI 95%; 2.3-3.6%). Incidence is then broken down by age. Twelve month incidence of anxiety disorders for those who were 11-12 years old at first interview were found to be similar but less than that for the overall sample at 2.6% (CI 95%; 1.4-3.8%). In 13-15 year olds there was an increased incidence reported of 3.6% (CI 95%; 2.7-4.6%). Going into later adolescence, in 16 to 17 year olds incidence was somewhat lower at 2.2% (CI 95%; 1.1-3.3%). This suggests that *early* adolescence (13 to 15 years old) may be an important period of onset, supporting the contention of Wittchen and colleagues (2000) that early adolescence is the last stage of significant onset for the majority of anxiety disorders. However, the combining of individual disorders into "any anxiety disorder" makes further extrapolation of meaning from these data difficult.

National Survey of Health and Development (NSHD): Medical Research Council

This UK birth cohort (N= 3279), born between 3rd March and 9th March 1946, were not included in the original review because the adolescent measures of anxious symptoms were teacher report questionnaires rather than diagnostic interviews. Therefore, this study does not meet criteria for inclusion in the original review. However, the results of the long term follow up of this cohort are of interest to the current research questions. The baseline assessments took place at 13 and 15 years

old. Colman, Wadsworth, Croudace, & Jones, (2007) report that 70% of individuals meeting diagnosis for an internalising disorder at *both* 13 and 15 (persistent disorders) met criteria in adulthood (36, 43 or 53 years) compared to only 25% of those who did not meet criteria in adolescence. There was no significant difference between rates of adult psychopathology in those who met criteria at *either* 13 or 15 years and those not meeting criteria for an internalising disorder in adolescence. This suggests that the persistence of internalising disorders in adolescence is significant in its prediction of adult disorder. A second paper looks at the course of internalising disorders from adolescence to late adulthood (53 years) and distinguished six categories relating to the onset, course, and outcome of internalising disorders. The results are presented in Table 7.

Table 7. Continuity and onset of internalising symptoms in NHSD (Colman et al. 2007)

Onset and Continuity	**N**	**%**
No disorder	2071	44.8%
Continuous disorder (moderate)	1553	33.6%
Continuous disorder (severe)	78	1.7%
Onset in adulthood (moderate)	524	11.3%
Onset in adulthood (severe)	132	2.9%
Onset in adolescence remitted.	269	5.8%

These data must be treated with caution as the “diagnosis” of mental disorder is not the same across the five follow ups. However, the degree of continuity is striking across such a long follow up period. When examining the 1900 individuals who are believed to have an internalising disorder in adolescence we can see that adolescent disorders do not appear to have a favourable outcome in over three quarters of cases (85.8%). Only 14% of those with adolescent disorder did not meet diagnostic criteria in adulthood. Unfortunately the data is not broken down for anxious and depressive disorders; this makes the use of this data extremely limited in answering the current research questions; however, it does point to the long term continuity of anxiety and depression as being moderate (35.3% over forty years) and points to the importance of accurate understanding of the stability of disorders in understanding outcome.

British Child and Adolescent Mental Health Survey: Office of National Statistics.

The first wave of the British Child and Adolescent Mental Health Survey (BCAMHS) was conducted in 1999 using the Development and Wellbeing Assessment (DAWBA) diagnostic interview with 12,529 children aged 5 to 15 years; the cross sectional data was cited in the introduction of the Gallagher (2008) review (Office of National Statistics, 1999). A 2004 "follow up" used a new sample rendering it a second cross sectional study (N = 7977) (Office of National Statistics, 2004). However, in 2007 the second cohort were followed up three years on creating a prospective sample (N = 7329). As with the National Survey of Health and Development reported above, depression was, unfortunately, included with anxiety disorders to form the group "emotional disorders". It is unclear why this decision was taken but the extremely small numbers of children reaching diagnostic criteria for depressive disorders may be of significance; prevalence of anxiety in the baseline survey were 2.2% for 5 to 10 year olds and 4.4% for 11 to 16 year olds giving an overall prevalence for the sample of 3.3%. Depressive disorders, however, were present in only 0.9% of children and adolescents with rates as low as 0.2% in 5 to 10 year olds, (N = 7797; Office of National Statistics 2004). Despite this limitation the findings are included here as the data was stratified by age and offers a UK sample from young children to adolescents. This is of particular interest as the current project will analyse data from a UK birth cohort in the 1990's. Furthermore, the remarkably low incidence of depressive disorders in the "Emotional Disorders" sample lends itself to interpretation of the data in relation to the course and outcome of anxiety disorders.

Table 8. Persistence of emotional disorders by age: BCAMHS (Office of National Statistics 2007)

Age at Baseline	**Persistence** % of those with emotional disorders in 2004
5-7 years	26%
8-10 years	12%
11-13 years	40%
14-16 years	21%

Emotional disorders were persistent in 30% of children reaching diagnostic criteria over the three year follow up (33% girls; 27% boys). In Table 8 the persistence of emotional disorders is presented for each age group (ages given at baseline). It appears that disorders in 11-13 year olds are particularly stable for well over a third of cases still meet diagnostic criteria three years later.

When looking at onset of new disorders the incidence or number of new internalising diagnoses for the whole sample of children and adolescents was 3% (4% girls, 3% boys). It appears that the three year incidence rate increased with age (see Table 9). The use of a measure that asks parents and/or young people to recall symptoms over such a long period (three years) will introduce a significant amount of error; it could be that these rates are most likely more reflective of a shorter period of time and may lead to an underestimation of new cases.

Table 9. Incidence of emotional disorders between 2004 and 2007

Age at baseline	Incidence Rates
5-7 years	2%
8-10 years	3%
11-13 years	4%
14-16 years	5%

Although these data are not suitable for answering the research questions in terms of the specific onset, course and outcome of anxiety disorders in this large UK sample will provide a useful comparison for the UK data analysed in Chapter Four the Results which uses the same diagnostic tool (DAWBA).

Summary.

In the four years since the last systematic search a relatively small amount of new data has been analysed and published that relates to the onset, course and outcome of anxiety disorders in childhood and adolescence. Some studies that did not meet criteria for the original review have been included here in order to try and help build the picture of the epidemiology of internalising disorders in general and to understand where anxiety fits with this picture.

Prevalence.

Costello and colleagues (in prep) have provided a thorough and illuminating review and meta-analysis of prevalence across childhood and adolescence that demonstrates the substantial proportion of children and adolescents in the community who have significant issues with diagnosable and functionally impairing anxiety disorders. These disorders are demonstrated to be as prevalent in childhood as in adolescence and proportions are approaching those found in large scale epidemiological studies of adults. Despite similarities in prevalence of the anxiety disorders in childhood and adolescence, separation anxiety stands out as a diagnosis of childhood and social anxiety as a disorder of adolescence, as would be expected from the clinical and cross-sectional data. The associated error in the childhood estimates is, however, much greater than those reported for studies in adolescence, highlighting the difficulties in measuring anxiety in younger populations.

Age at onset data.

New data from the TH2K study provide additional data for understanding age at onset. The 12 month incidence rates for different age ranges in this cohort give specific data that when combined with onset data from other studies supports the contention that early adolescence may be a significant stage in development where the onset of anxiety disorders is prevalent. These data are unfortunately not provided for individual anxiety disorders and, like other studies reviewed, the first data collection was not until late childhood making it impossible to know if the incidence is true first onset or whether some anxiety disorders may have been present at earlier ages but were not recorded. These data, however, can add to our understanding of incidence in adolescence. Incidence of individual disorders reported in the Dresden study demonstrate substantial proportions of the sample displaying onset of separation anxiety and specific phobias in later adolescence; however, these must be examined in the context of the differing lifetime prevalence of different disorders (i.e. some disorders are simply rarer) and, as in the TH2K "first" onset will most likely be underestimated due to the first data collection taking place at such a late stage in development when we know that anxiety is prevalent in much younger children. The major limitation of the onset data from these two studies is that patterns of onset through development cannot be determined, as incidence is only calculated once and samples are not broken down by age. The data from the Great Smoky Mountains Study from when the cohort reach adulthood suggests early onset (middle childhood) for most anxiety disorders, with separation anxiety having a short window of peak onset and generalised anxiety having a much wider window covering all of childhood

and adolescence. It is unclear how these data are calculated but they do suggest a much earlier peak onset for many disorders than has previously been reported with very few disorders after the age of 14, as supported by the incidence curves from the Dresden data.

Continuity and stability.

The Dresden data lend support to the contention that early anxiety disorders do not have a linear course and wax and wane through childhood and adolescence but are associated with psychopathology in later life, with different patterns emerging for the various anxiety disorders. The Dresden data examine the course and outcome of individual disorders and two important patterns emerge from the data: First that the seeming "remission" of early anxiety disorders may well be due to the "any anxiety disorder" category often employed in longitudinal studies. The high rates of remission reported may, at least in part, be accounted for by a lack of stability in agoraphobia and phobia not otherwise; Secondly, that both generalised anxiety and social anxiety, which in short term studies appear to be transient, also have the least favourable outcomes in the longer term. These are interesting findings and illustrate the need to examine anxiety disorders as separate entities rather than always subsumed under "any anxiety disorder" in order to better understand the patterns of disorders through the lifespan which can be explored in longitudinal studies. Importantly the Dresden data show that although homotypic continuity of anxiety disorders may be moderate, when we look at symptomatic and subthreshold cases of anxiety, and look to other forms of psychopathology, (particularly depressive disorders) these young people report their disorders to be extremely stable over the long term follow up and have a much increased risk of psychopathology, if not mental disorder.

Adult outcomes.

Two studies included in the above review have recently followed up cohorts that were first examined in childhood and adolescence and are now well into adulthood. These are the Mannheim study (Fichter et al. 2009) and the Medical Research Council National Survey of Health and Development (Colman, et al. 2007). Although these studies have flaws in their methodology in terms of inclusion in a meta-analysis they provide an opportunity to make comparisons with the compelling data from the Dunedin and New York studies that adult onset of many anxiety disorders are rare and that the majority of cases have their onset in childhood or adolescence. The Mannheim study has generated diagnostic status in a way that is not easy to compare with other similar studies; it does, however, use ICD-10 as the adult outcome

measure. The small sample and use of only two data collection points 18 years apart may explain why the data suggest a larger proportion of adult onset than has been found in the Dunedin or New York studies, which have the benefit of multiple waves of diagnostic assessment. The Mannheim study would suggest only a small number of women remain anxious who had been diagnosed with anxiety disorders in childhood. Although the proportion of the sample diagnosed with anxiety decreases substantially in adulthood, most of these cases were first diagnosed in adulthood. Fichter and colleagues, however, do report that when using the ICD-10 criteria as an outcome variable, there is a moderate predictive relationship between childhood anxiety and adult psychopathology more generally (OR = 1.7) and particularly between phobias and later anxiety disorders (OR = 2.3). This finding of a specific relationship between early onset anxiety and anxiety in later life supports the findings from the New York study (Pine et al. 1998).

The second study with long term follow up (Colman et al. 2007) unfortunately does not report anxiety disorders separately from depression. They report onset and continuity of internalising disorders. The results of their 40 year follow up, however, support the findings of the Dunedin and New York studies and suggest a large percentage of those with adult disorders were first diagnosed in adolescence with only a small proportion of the sample having onset of "severe" disorders in adulthood (2.9%); remarkably similar to the reports from the New York and Dunedin follow back analyses. Despite the inclusion of depression this adds credibility to the contention that adult psychopathology, particularly significant or severe cases frequently have an early onset. The findings also show that only stable disorders are associated with psychopathology in adulthood, an interesting finding that has not been examined before.

UK data on onset and stability of internalising disorders.

Data from the British Child and Adolescent Mental Health Survey (BCAMHS) were included in this chapter despite the fact that data was combined for depression and anxiety to make an "emotional disorders" category (Office for National Statistics, 2007); it is predicted that this may be due to the small numbers of children meeting criteria for a depressive disorder, particularly for 5 to 10 year olds. Inclusion is due to the focus of the current project on a large UK birth cohort for which the BCAMHS data may provide an interesting and important comparison. The data are broken down in a way which allows persistence and incidence to be examined in a young sample. Although the British Child and Adolescent Mental Health Survey appears to

demonstrate prevalence rates significantly lower than that of the other studies reviewed (e.g. emotional disorder rates that are more similar to rates of individual anxiety disorders in other large studies) the data show a steady increase in the number of incident cases (first onset) of emotional disorders throughout childhood into adolescence. They also report that emotional disorders appear to be stable in around a third of anxious children, with some variability dependent upon the age at first diagnosis; children first diagnosed at 11 to 13 years appear to be the most stable over a three year period when compared to groups of older adolescents of younger children.

Conclusions.

The findings presented here from the updated literature review offer some support to the major contentions of Gallagher (2008). It is widely accepted that anxiety disorders are prevalent in childhood and adolescence; however, the Costello et al. (in prep) meta-analysis suggests that anxiety disorders may be equally prevalent in childhood and adolescence (dependent upon diagnosis) but that earlier disorders incur higher degrees of measurement error. Anxiety disorders appear to have an early onset (in childhood or early adolescence) with some having a clear peak age at onset and others having a larger window of opportunity for new cases to arise. There remain, however, significant issues with data available to assess age at onset prospectively. The data collection begins too late in the child's development, is taken only between two time points, or does not distinguish between anxiety and depressive disorders.

The course of anxiety appears to be non-linear in many cases and may wax and wane over time, it is increasingly probable that they are, in some cases, significant risk factors for adult psychopathology - specifically adult anxiety disorders. The course and outcome for the specific disorders follow individual patterns, therefore, it is probable that the favourable outcomes often described in short term follow up studies looking at all anxiety disorders together, may reflect the course of a small number of prevalent disorders (e.g. phobia not otherwise specified) and so conceals the malignant course of other anxiety disorders.

An increased interest in the long term outcomes of adolescent anxiety and depression is evident from the evidence reviewed and there is some support for the contention that adult anxiety disorders are associated with, and frequently preceded by, earlier anxiety disorders. However, research examining the specific onset and course of the individual anxiety disorders is still absent. Information regarding younger children is

also lacking, particularly studies that follow these young children into adulthood to determine the outcome of very early anxiety disorders as opposed to those from adolescence. Onset of any anxiety disorder is beginning to be the focus of research attention and so can be described for a number of samples; however, the data required to answer important questions about the targeting of resources require more precise identification of the onset of individual disorders, when they are most likely, and the parameters of these "peak" stages of onset. These data are not yet available.

It remains unclear whether anxiety in childhood and adolescence is stable or transitory in the majority of cases. If anxiety is highly prevalent and most cases of childhood and adolescent disorder remit, is early anxiety a good enough predictor of adult anxiety disorders for preventative strategies to be effective (and cost effective) in reducing the prevalence of adult anxiety disorders? Alternatively can it be argued that the treatment of anxiety disorders in children should be our major focus regardless, in order to reduce distress and long term impairment? The work from the Dresden study also suggests that subthreshold disorders may require further attention when examining the distress and impairment associated with early onset disorders. The large numbers of children who receive anxiety diagnoses in large epidemiological studies, however, may point to anxiety in childhood as a poor predictor of later psychopathology and the contention that only persistent internalising disorders are reasonable predictors of adult disorders (Colman et al 2007) suggests that more powerful ways of predicting poor outcomes require further investigations. These are important questions, as needless intervention in benign cases could have unintended consequences, which could interfere in normal development and stigmatise children needlessly.

The current study will attempt to analyse new data in light of these findings and assimilate them into the current picture of the epidemiology of anxiety with the hope of highlighting areas where conclusions appear more robust, and to attempt to answer the question of whether the anxious child is likely to become an anxious adult.

Chapter Three: Method.

Recruitment.

Rather than recruiting individual participants, this study required me to recruit prospective longitudinal studies of child and adolescent mental health. The aim was to gain permission from Principal Investigators to access diagnostic data that has already been collected but not yet analysed or published relating to the descriptive epidemiology of anxiety disorders. The original review (Gallagher, 2008) demonstrated that the data to understand the descriptive epidemiology have been collected in many different countries (see Table 3 and Appendix 2). Most of this data, however, has not yet been used to answer questions regarding the epidemiology of anxiety in this level of detail.

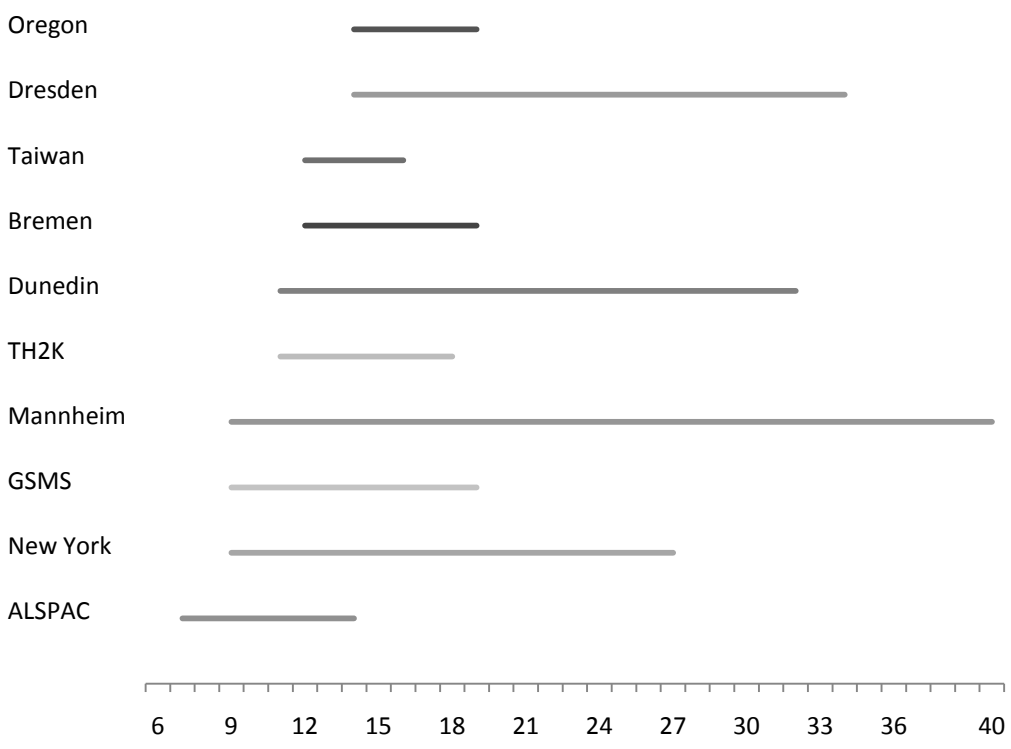

Figure 1. Age ranges in prospective longitudinal studies

The aim was to acquire the diagnostic status for anxiety disorders, determined by a standardised diagnostic interview that has been assigned to each child at baseline and any subsequent follow ups. For some studies this may only be one follow up

(e.g. Bremen, Christchurch, and Oregon studies), for others it is as many as eight (Dunedin). Similarly some studies assess over short periods (two years or less) whilst others cover up to 40 years (see Figure 1).

By acquiring such data, it would be possible to establish the age (or developmental stage) at which a young person is most likely to receive their first diagnosis of each anxiety disorder, (determining peak age at onset in a sample) and make comparisons across the different samples. We are also able to examine the continuity of anxiety disorders; whether they are stable and continue to present a problem over time, or remit as the young person moves into adolescence and adulthood. Where data have been collected into adulthood we are also able to explore outcomes for anxious children and adolescents; do they continue to suffer from anxiety or has it ceased to be a problem in adulthood?

Design.

The original plan was to gain access to enough raw diagnostic data from large samples to allow the manipulation of data into a state where they could easily be compared and combined. The data would be broken down into appropriate age cohorts to make data sets compatible and then it would be possible to calculate the proportion of new cases of each anxiety disorder at each developmental stage, the proportion of those with stable anxiety disorders at different points in their development, and the risks (as calculated by Odds Ratios) of later disorder for those who suffer anxiety early in life, and the proportion of adult disorders that had their onset earlier in life. This would have provided us with a full review and then a meta-analysis of large scale epidemiological data.

The proposed analysis.

The original plan for the analysis, which was presented to the PI's, based on access to the data presented in Figure 1 was the same for all data sets. They differed only in the number of analyses proposed, dependent upon the age ranges and number of follow ups in each data set. For some studies follow back analysis and examining adult outcomes are not feasible due to the age ranges included. A brief outline of these proposed analyses will now be presented:

The first step would be to code diagnoses of each anxiety disorder as absent or present and then break down cohorts according to their age. Ideally this will use

similar methods for combining informant data, and the same impairment and prevalence criteria but these differences can be worked with. The age groups would be dependent upon the age range included and the sample size; ideally there would be no more than a three year range in the ages of each group. This allows comparisons between the proportions of children with each anxiety disorder at each age/stage, for each follow up; in the past, even cohorts that cover large age ranges have often been analysed as a whole. These data can then be used to determine the proportion of children receiving their first diagnosis of each anxiety disorder at each follow up. By calculating the proportion of new cases for each follow up and each age we can determine patterns over the life course in order to identify when the highest number of emerging cases appear - the peak age at onset. When samples begin collecting data later in life caution must be used in interpreting these as "first" onset. The next step is to use samples that have collected data in late adolescence and adulthood to look at the diagnostic outcomes for those with and without anxiety in early life and determine the risk associated with early anxiety when the individual reaches adulthood. In order to determine these outcomes we would use a number of methods. First, calculating the proportion of child or adolescent anxiety cases that meet diagnostic criteria at later follow ups (proportion of anxious children with chronically stable disorders), the likelihood (as determined by Odds Ratios) that those with child or adolescent anxiety receive a diagnosis in later life; and the proportion of adults with anxiety disorders that met diagnostic criteria in early life (follow back analysis). Wherever possible, data sets would then be combined in order to carry out the same analysis on a large amalgamated sample.

The planned data analyses are, therefore, relatively simple and largely rely on descriptive statistics and contingency tables to calculate proportions and Odds or Risk ratios. Despite this simplicity, if data could be compared and combined across a wide range of studies internationally then the picture regarding the onset, stability, and outcome would be much clearer, and international comparisons could be useful in thinking about the differences and similarities cross-culturally and methodologically and ensures that the samples of anxious youths are sufficient to carry out the whole range of analysis with suitable power. Figure 1 demonstrates that although there is a wealth of diagnostic data collected, there are no prospective studies that collect diagnostic data on preschool children and only very few that begin in middle childhood. This means that calculating first onset for some disorders would be very difficult. Furthermore, very few longitudinal studies have begun collecting data in

childhood and continued into adulthood (The Dunedin and New York studies are exceptions to this problem). The majority of studies begin late in childhood or in adolescence. The period between ages 12 and 18 is the age range covered by the greatest number of prospective longitudinal studies; the majority of meaningful comparisons and synthesis would, therefore, be in this period of adolescence. Although some disorders may be associated with adolescent onset, many first onsets of anxiety disorders may be missed. The limitations of a number of these studies for answering the questions outlined above and for meta analysis is, therefore, apparent. To undertake these analyses requires cooperation from some of the longitudinal studies that have collected data over a long period of time - 10 years or more. A number of studies identified New York, Dunedin and Dresden in particular, offer these data and their inclusion would be necessary in order for the research aims to be feasible.

Approaching Principal Investigators to share appropriate data.

In order to gain access to data that could be used to meet the aims of the project, I contacted the Principal Investigators (PI) from the studies contained in the 2008 review (see Table 3), and also the PI from the Dresden study. A letter and an e-mail to each individual researcher was written outlining my plans to carry out a large scale review and meta-analysis of prospective longitudinal data relating to the epidemiology of anxiety disorders. I requested access to diagnostic data that could be used to generate and estimates of the prevalence, onset, stability, course and outcome of anxiety disorders in childhood and adolescence, and into adulthood where possible in order to amalgamate large data sets and have a large anxious population. The letters and e-mails aimed to establish the research groups' ability and inclination to share longitudinal data regarding diagnostic status of anxiety disorders in their respective studies.

The only study that I did not attempt to contact was Dr. Gau from the Taiwan Epidemiological Study of Mental Disorders as it was evident that they did not collect appropriate data for the majority of the planned analysis of this project. The Principal Investigators were identified using web resources and personal contacts and both e-mail and postal addresses were sought. Individual letters were then written and sent by both post and e-mail. Some PI's were also contacted by telephone or in person by a Dutch contact, Prof. Susan Bögels, an internationally prominent researcher in childhood anxiety who examined my PhD thesis, which included the Gallagher (2008) review.

Of the seven studies with appropriate data for inclusion, two responded immediately to say that they were unfortunately unable to share data at this time due to constraints on visiting researchers and data sharing projects during data collection periods. These studies were the Great Smoky Mountains Study (GSMS) in the United States and the Dunedin study in New Zealand. However, Prof Costello the PI from the GSMS kindly sent an in prep article (see Chapter One and Two, Costello et al in prep) that she thought would be useful to understanding age at onset and stability. The Dunedin study pointed us towards the data that they have already published as this contains a large quantity of suitable data appropriate for comparison and inclusion in the planned synthesis. The PI of the Bremen Study Prof. Cecilia Essau was contacted by Prof Susan Bogels and was reported initially to be very willing to share data but there were a number of difficulties negotiating authorship with this research group so this offer was subsequently withdrawn. The Oregon Adolescent Depression Project (OADP) in the Unites States and the Christchurch project in New Zealand did not respond to any correspondence. As the age ranges in these two studies are limited to later in adolescence this was not followed up further. The Early Developmental Stages of Psychopathology (EDSP) study in Dresden initially responded to say that they would be able to share data and negotiations began. The Children in the Community study in New York also agreed to release diagnostic data.

Application for Data.

The Avon Longitudinal Study of Parents and Children (ALSPAC; also known as "Children of the 90's") is a large birth cohort study carried out in Bristol in the UK. Children were born between 1991 and 1992. A formal query was e-mailed to the ALSPAC data managers at Bristol University to determine whether they had collected diagnostic outcomes for mental disorders. This revealed that the Development and Wellbeing Assessment (DAWBA) has been collected at ages 7, 10, 13/14, and 17/18 years. I was then asked to apply to the ALSPAC team of Principal Investigators through a data request application process. This process checks the feasibility and ethics of the request and ensures that no one else would be, or is currently, using these data for a similar purpose. A fee of £700 for the administration and data support was also required; I applied to the Max Hamilton fund to ensure this funding was available and was successful in both applications.

Negotiation.

Early Developmental Stages of Psychopathology – Dresden, Germany.

The original request for the data to be used to calculate prevalence, onset, course and outcome at all ages (using the sample of 14-17 year olds at baseline), in order for them to be included in a meta-analysis with data from Dunedin and New York was met with a positive response. The researchers suggested that data could be shared either through the research statistician completing analysis on my behalf, or that I would go to Dresden and register as a visiting researcher to carry out the analysis with his support. The second option was favoured as this allowed me to learn about the processes and systems used in this particular study. However, after arranging a visit and booking flights insufficient data were secured from other studies, which precluded the meta-analytic methods that were outlined in the original data request. The researchers in Dresden were concerned that I could not publish the EDSP data alone as this mapping of the onset, course, and outcome of anxiety disorders is something that the research group wished to publish in the future. Unfortunately this venture was curtailed at short notice.

Children in the Community study (CiC) - New York.

Personal contact through one of the lead researchers (Daniel Pine) who peer reviewed the original Gallagher (2008) review ensured ongoing contact with the PI of the New York study Professor Patricia Cohen despite her retirement. The original request was for all data regarding diagnostic status for anxiety disorders at all follow ups for those that were “children” (i.e. under 16 years of age) at baseline. This request was met with a positive response; however, Prof. Cohen was clear that there are a large number of different issues with these data that meant sharing all the data requested was neither possible nor desirable as some diagnoses were not considered to be reliable or valid. Prof. Cohen was able to provide data for the sample who were less than 14 at baseline and look at continuity and new onset of anxiety and depression over the two follow ups providing data from late childhood/early adolescence (<14), later adolescence (<17) and adulthood (+18) for both social anxiety disorder and overanxious disorder/generalised anxiety disorder.

Methodology of included studies:

Avon Longitudinal Study of Parents and Children (ALSPAC).

Participants.

ALSPAC recruited 14,541 pregnant women resident in Avon, UK with expected dates of delivery 1st April 1991 to 31st December 1992. 14,541 is the number of pregnancies for which the mother enrolled in the ALSPAC study and had either returned at least one questionnaire or attended a "Children in Focus" clinic by 19/07/99.

Out of the initial 14,541 pregnancies, all but 69 had known birth outcome. Of these 14,472 pregnancies, 195 were twin, three were triplet and one was a quadruplet pregnancy meaning that there are 14,676 foetuses in the initial ALSPAC sample. Note that of these 14,676 foetuses, 14,062 were live births and 13,988 were alive at 1 year. When the oldest children were approximately seven years of age, an attempt was made to bolster the initial sample with eligible cases that failed to join the study originally. As a result, when considering variables collected from the age of seven onwards (and potentially abstracted from obstetric notes) there are data available for more than the 14,541 pregnancies mentioned above. The number of new pregnancies not in the initial sample that are currently represented on the built files is 542. Of these 542 additional pregnancies 6 were twin, meaning that the number of additional children that need to be considered is 548. The total sample size for analyses using child based questionnaire data collected after age seven is therefore 15,224. Note that of the total sample of 15,224 foetuses 14,610 were live births and 14,535 were alive at 1 year.

Standardised diagnostic measures.

The diagnosis of mental disorders was assigned according to the administration and scoring of the Development and Wellbeing Assessment (DAWBA) administered to families at ages 7, 10, 13/14, and 17/18. This is a valid and reliable measure of diagnostic status of mental disorders using ICD-10 and DSM-IV (Goodman, Ford, Richards, Gatward, Meltzer, 2000). Respondents were the target child's biological mother in over 97 % of cases, with fathers, step fathers, mother figures, and the child themselves completing in a small proportion of families. Diagnostic status for the children at 17/18 years old was not yet calculated and so was not made available for

this thesis. In the first instance the diagnostic status was calculated using the original method of clinicians' rating symptoms, syndromes, and disorders. Goodman et al (2010) then developed a computer algorithm in order to identify probabilities of caseness. This algorithm was then applied to the DAWBA at all follow ups producing five levels of probability: <0.01; 0.05; 0.15; 0.50; >0.70. A mental disorder is assigned at a value of 0.50 or >0.70.

Ethical approval for the use of DAWBA data.

ALSPAC has its own Law and Ethics Committee that reviews all proposals for new data collection and approves policies for data handling and analysis. Proposals for new data collection are also approved by the Local Research Ethics Committees (LRECs). Ethical approval for this study was, therefore, obtained from the ALSPAC Law and Ethics Committee.

The Children in the Community (CiC) Study, New York.

During the early and middle 70's, Drs. Leonard Kogan and Shirley Jenkins co-directed a national study in the United States designed to develop an indicator of the physical health and the social, emotional, and cognitive functioning of children in geographic areas based on local census and county-level indicators. The resulting index included Divorce rate, Infant mortality, percentage in Poverty, Out-of-wedlock births, and rate of Venereal disease and was labeled Disorganized Poverty or DIPOV (employing the initials of the indicators). The DIPOV indices for the 62 counties of New York state in 1970, 1971, and 1972 were examined and two counties were selected for study: omitting the New York City area as too unique to be representative of the USA, Albany County was identified on the DIPOV scale as one of the counties with the highest DIPOV index and adjacent Saratoga county as one of the lowest. Census tracts or block groups were selected with a range of DIPOV scores roughly representing the US as a whole in rural, small town, suburban, city, and central city sites. In each area a target child was randomly selected for inclusion in each household with one or more children between the ages of 1 and 10. Mothers or mother-substitutes were interviewed with regard to the family and environment as a whole and in depth with regard to the randomly sampled child. About 85% of qualified households completed interviews. This constitutes the "baseline" of the New York study.

The Children in the Community study has collected data on about 800 families since 1975. Over 225 articles and two books have explored wide-spread issues regarding mental health and mental disorders. Grant support has come from three institutes of the National Institutes of Health (NIMH, NICHD, NIDA), the National Institute of Justice, and the William T. Grant Foundation.

This entire sample includes subjects who were born from late 1964 to early 1975. Major waves of data collection have been carried out at mean ages 5, 14, 16, 22, 33 and 38. The data that were released for inclusion in the current study were selected by Professor Cohen in order to address the research questions regarding onset, stability, course and outcome of child and adolescent anxiety disorders. Only diagnostic data for social anxiety and overanxious disorder (later generalised anxiety disorder) were released and the data were provided for three follow ups where the mean age of the original sample were 14, 16, and 22 years. The sample used for the new analysis included only those who were under 14 at baseline so the sample is significantly reduced (N= 436) and the groups are defined as childhood/early adolescence (< 14 years), later adolescence (< 17 years), and adulthood (over 18 years).

Analysis and synthesis of data.

With the data that were made available the analysis plan was significantly reduced as not all of the planned analysis aims could be met using the small number of studies available for inclusion. Amalgamation of the data sets to conduct a meta-analysis was not possible.

ALSPAC

The ALSPAC data offer a unique opportunity to examine age at onset in a young sample of children in the UK and to plot the prevalence and age at onset in an extremely large birth cohort and examine continuity of anxiety disorders in this age range.

A large amount of data were released, including demographics, questionnaire measures (who completed the questionnaire; when, etc) and scores for each individual item on the DAWBA for all anxious and depressive disorders. The first task was to analyse the missing data; to determine the demographic differences between families who had chosen to complete the DAWBA at baseline and those who had not.

This was done using the SPSS file to create contingency tables and calculate Odds Ratios and Effect Sizes. The missing cases were coded separately for each follow up to allow analysis of drop out through the course of the study.

Prevalence of anxiety at age 7, 10 and 13 were then calculated using SPSS descriptive statistics. New cases of onset were determined using contingency tables to determine the proportion of the sample at each follow up who had received a diagnosis who had not met criteria at an earlier follow up (new onset). These proportions were recorded for each anxiety disorder at each stage of follow up. Figure 2 demonstrates how these contingency tables were calculated and presented.

		Time 2	
		Yes	No
Time 1	Yes	Stable Disorder	Remitted Disorder
	No	New onset	Never anxious.

Figure 2. Demonstration contingency table.

The proportion of those who had met criteria for an anxiety disorder and continued to do so at the next follow up (stability) was also calculated for anxiety disorders as a whole but not for each anxiety disorder as confidence intervals showed an unacceptable degree of imprecision due to the extremely small numbers. The proportion of stable disorders over the course of the study so far were also calculated as any person who was diagnosed with anxiety at two or more follow ups.

No follow back analysis or Odds Ratios were calculated as age 13 to 14 is still considered to be early in development and so not represent a good measure of "outcome" or address the research questions proposed.

New York.

The data received from the New York sample was in a form that meant very little analysis was required or indeed possible. Professor Cohen had used my analysis plan to allow her to undertake all the data cleaning. She had, therefore, extracted the data that were both appropriate and necessary to determine proportions of onset, stability and outcome in children who were under 14 at baseline. Unfortunately these data were only provided for social anxiety, overanxious disorder at baseline and generalised anxiety in the follow ups, and depressive disorders. The other anxiety disorders had inconsistencies in coding and diagnostic categories that Professor

Cohen felt would render them unreliable in this analysis. Data was presented in contingency tables.

Prevalence of each disorder was calculated as the proportion of the sample meeting criteria for each disorder in early adolescence, later adolescence and adulthood. No prevalence for “any anxiety disorder” could be calculated but for social anxiety and generalised anxiety. Then we calculated the proportion of cases that were considered “new”; i.e. the young person had not met criteria at any of the previous waves of data collection for both social anxiety and overanxious/generalised anxiety disorder; those who had met criteria for overanxious disorder at baseline were not considered to have a new case of generalised anxiety disorder if they were diagnosed at follow up. The proportion of cases of social anxiety and overanxious disorder that continued to meet criteria was also calculated (stable disorders) at first and second follow up. It was not possible to produce estimates for all of those who had met criteria at two or more follow ups from the contingency tables. However, follow back analyses were used, calculating the proportion of adults who had received a diagnosis at either of the earlier waves of data collection.

Synthesis.

As there was not sufficient data available to perform the planned meta-analysis, the synthesis relied upon the comparisons of proportions, and the use of graphical displays to examine patterns in the data that suggest robust findings, contradictions, and methodological problems in drawing conclusions regarding the epidemiology of anxiety disorders.

Chapter Four: Results.

Analysis of New Data.

The analysis of the ALSPAC data from the UK will be discussed first as it is a larger data set, which has allowed the current study to conduct more novel analysis. This will be followed by the presentation of the data released from the Children in the Community study carried out in New York. These data refer to overanxious/ generalised anxiety disorder and social anxiety only.

ALSPAC

The data had been coded by the ALSPAC team into diagnostic categories using the algorithms outlined in Goodman et al. (2010). PASW 15 (SPSS) was used to analyse the diagnostic data and Confidence Interval Analysis (Altman, 2005) was used to calculate confidence intervals. The demographics, raw item data, and probability ratings generated by the computer algorithms were sent to the author in an SPSS file. The initial data set that was received contained diagnostic status at age seven determined using clinician ratings; the second database included diagnostics computed solely by the algorithms and also included diagnostic status at age 10 and age 13/14. The latter was therefore used for the analyses. Table 10, however, contains comparisons of the two prevalence estimates, determined either by clinician ratings or the computer algorithm at age seven to understand the effects of employing such a method to calculate diagnostic status.

Table 10 shows that the prevalence of any anxiety disorder appears higher when the clinician rating is applied rather than the DAWBA algorithm. Children are nearly twice as likely to be diagnosed with any anxiety disorder when they are assessed by a clinician rather than when applying the DAWBA algorithm (OR = 1.8). With individual disorders the differences appear smaller and suggest that this differential might be due to the inclusion of “anxiety not otherwise specified” in the original analysis of the DAWBA data (NB this diagnosis is not computed using the algorithm.) For some individual disorders, however, such as generalised anxiety disorder, a larger effect is demonstrated (OR = 2.4) with clinician ratings meaning a diagnosis is two to three times as likely as when using the algorithm. The method of rating had no effect on the

diagnosis of separation anxiety suggesting that some anxiety diagnoses are less likely using the DAWBA algorithm while others are more robust to the application of different criteria. It seems fair to conclude that this computerised method, despite offering advantages in terms of time and cost efficiency, may lead to conservative estimates of anxiety in young children. Unfortunately the data were not available to determine whether this discrepancy remains true as the sample become older.

Table 10. Prevalence of anxiety disorders determined by clinician rating or computer algorithm.

	DAWBA clinician % (95% CI)	**DAWBA algorithm % (95% CI)**
Any Anxiety Disorder	3.11% (2.8 - 3.5%)	1.7% (1.5 - 2.0%)
Generalised Anxiety Disorder	0.5% (0.4 - 0.7%)	0.2% (0.1 - 0.3%)
Obsessive Compulsive Disorder	0.1% (0.1 - 0.2%)	0.01% (0- 0.1%)
Separation Anxiety	0.8% (0.7-1.1%)	0.8% (0.7 - 1.1%)
Social anxiety	0.3% (0.2 - 0.4%)	0.1% (0.1 - 0.2%)
Specific Phobia	1.0% (0.9 - 1.3%)	0.9% (0.7 - 1.1%)
Anxiety Not Otherwise Specified (NOS)	0.8% (0.6 - 1.0%)	---

Missing Data.

The ALSPAC birth cohort is extremely large (N = 15 211) and of those children 55% (N = 8252) completed the Development and Wellbeing Assessment (DAWBA), a standardised diagnostic assessment of mental disorders (Goodman et al. 2000) at aged seven. At aged ten 51.4% (N=7820) completed the DAWBA, and at aged 13-14 years 46.7% (N = 7102) completed the DAWBA. In such a large cohort, determining whether there are important demographic differences between those who completed the baseline DAWBA at age seven and those who did not, is a difficult task - even small differences reach statistical significance. I examined five variables: Mother's age at birth; mothers educational qualifications; ethnicity; social class; parents' marital status. Effect Size (ES) was calculated for the continuous variable of mother's age at

birth. We calculated mean age at birth of those responding (M = 28.97) and of those not responding (M = 26.64) and used the pooled standard deviation (SD = 4.868) to calculate Effect Size (Cohen's d = 0.48) which suggested a small effect, (Cohen,

Table 11. Demographic differences in the DAWBA completers and non-completers

Demographic Data		**Baseline DAWBA completed** (N = 8252)	**Baseline DAWBA not completed** (N = 6958)	**Chi Square.**
Mothers Highest Educational Qualification	A levels or degree.	N=3324 40%	N= 1086 15.6%	χ^2 = 397.2; df = 2; N =12483; p<0.001
	O levels, CSE's or vocational qualifications	N= 4661 56.5%	N= 3412 49%	
		Missing = 3.5%	Missing = 35.4%	
Child Ethnicity	White	N= 7555 92%	N= 3976 57.1%	χ^2 = 64.2; df = 1; N = 12142; p<0.001
	None White	N = 301 3.6%	N= 310 4.5%	
		Missing = 4.4%	Missing = 38.4%	
Social Class	I, II, III (non manual)	N = 5726 69.4%	N=2376 34.1%	χ^2 = 161.1; df = 1; N = 10111; P<0.001
	III (manual), IV, V	N= 1117 13.5%	N=892 12.8%	
		Missing = 7.1%	Missing = 53.4%	
Marital Status	Widowed, Divorced, Separated	N= 396 4.8%	N=3593 51.6%	χ^2 = 352.0; df = 2; N=13236; p<0.001
	Married	N= 6256 75.8%	N=415 6%	
	Never Married	N= 1134 13.7%	N= 1442 20.7%	
		Missing = 5.7%	Missing = 21.7%	

1992). Mother's age appears to have a "small" effect on families' choice to take part in the diagnostic interview with those who were older more likely to take part Table 11 reports Chi Square tests of association, which demonstrate significant relationships between the four demographic variables examined and completion of the DAWBA at baseline. These data suggest that those who completed the DAWBA are mothers who are better educated, have higher social status, are more likely to be married, and are less likely to have non-white children. The demographic data for the children who did not complete the DAWBA was also, as might be expected, more likely to be missing (see Table 11) ;for example only 47% of families who had not completed the DAWBA had data for social class recorded in comparison to 83% of respondents who completed the DAWBA. It is, therefore difficult to draw firm conclusions regarding the comparisons of the two samples; however, the trend in the missing data clearly suggests that disadvantaged families are less likely to be represented in the sample that was assessed for mental disorders.

Prevalence

The prevalence of any anxiety disorder in the birth cohort at ages 7, 10 and 13/14 years was calculated, looking at possible sex differences.

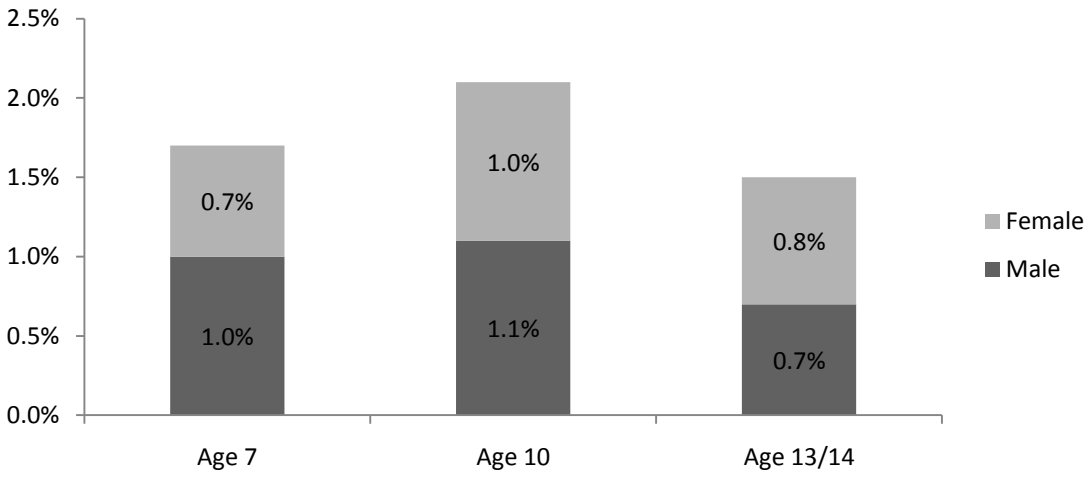

Figure 3. Point Prevalence of any anxiety disorder in the ALSPAC study.

Figure 3 shows the percentage of children meeting criteria for any anxiety disorder at ages 7, 10 and 13 years. In the baseline sample (aged seven; N = 8252) 142 children met diagnostic criteria for any anxiety disorder; 1.7% (95% CI; 1.5 - 2.0%). At age 10 (N = 7820) three years later 166 children met diagnostic criteria for any anxiety disorder; 2.1% (95% CI; 1.8 - 2.5%). This dropped at age 13/14 (N = 7102), 109

young people met diagnostic criteria for any anxiety disorder; 1.5% (95% CI; 1.3 - 1.8%)

When examining gender differences more males than females received a diagnosis of any anxiety disorder at age seven; 2% (N = 86) of males versus 1.4% (N = 56) of females (OR = 1.5; 95% CI; 1.1-2.0%); χ^2 (1, N = 8252) = 4.86 p = 0.03. Gender differences in prevalence are no longer significant at ages 10 and 13 years; p = 0.88 and p = 0.23 respectively. As we are interested in the patterns of onset and course of anxiety in the sample, and the prevalence of diagnosable disorder are low the data will be analysed as a whole sample in order to increase precision of estimates. However this increased prevalence of anxiety disorders in young boys will be discussed in relation to previous research in the Discussion (Chapter Five).

Table 12. Point and cumulative prevalence (with 95% confidence intervals) for anxiety disorders in the ALSPAC cohort

	GAD	**OCD**	**Separation Anxiety**	**Social anxiety**	**Specific Phobia**
7 Years (N = 8252)	0.2% (0.1-0.3%)	0.01% (0-0.1%)	0.8% (0.7-1.1%)	0.1% (0.1-0.2%)	0.9% (0.7-1.1%)
10 Years (N= 7820)	0.4% (0.3-0.6%)	0.1% (0.0-0.1%)	1.1% (0.9-1.3%)	0.3% (0.2 -0.5%)	0.9% (0.7-1.1%)
13 Years (N= 7102)	0.4% (0.3-0.6%)	0.1% (0.0-0.1%)	0.6% (0.4-0.7%)	0.5% (0.3-0.6%)	0.5% (0.4-0.7%)
Cumulative Prevalence	0.8% (0.6-1%)	0.4% (0.1-0.4%)	2% (1.7-2.4%)	0.7% (0.5-0.9%)	2% (1.7-2.4%)

The prevalence data in Figure 3 and Table 12 demonstrate that the proportion of children currently meeting DAWBA diagnostic criteria for any anxiety disorder is highest at 10 years old in this sample, largely due to the number of children meeting criteria for specific phobia and separation anxiety at this age. The prevalence of social anxiety steadily increases through childhood to 0.5% in early adolescence. Generalised anxiety disorder and obsessive compulsive disorder are relatively rare with generalised anxiety slowly increasing. Specific phobia remains constant between 7 and 10 years but nearly halves between 10 and 13 suggesting remission and reduced incidence of specific phobias in early adolescence. This finding is supported by the first onset data shown in Figure 4. Although the proportions of anxiety disorder are relatively low the confidence intervals demonstrate precise estimates in this sample.

Onset.

Onset data were calculated using contingency tables to determine the number of children receiving their first diagnosis of an anxiety disorders at age 7, 10 and 13/14 years. Onset or first incidence refers to the number of children who currently meet diagnostic criteria who have not previously received a diagnosis. The proportions of new cases at each age are displayed in Figure 4.

Despite the small numbers of children meeting diagnostic criteria prospective data clearly show specific patterns in the onset of anxiety disorders emerging as childhood moves into adolescence (see Figure 4 and Table 13). New onset of any anxiety disorder decreases steadily through late childhood into early adolescence largely due to the decline in incidence of separation anxiety and specific phobia. This finding supports the contention that the peak onset for both separation anxiety and specific phobia is in middle childhood. Social anxiety and obsessive compulsive disorder on the other hand shows increasing numbers of new cases into later childhood and adolescence; this pattern is similar for GAD with incidence increasing between seven and 10.

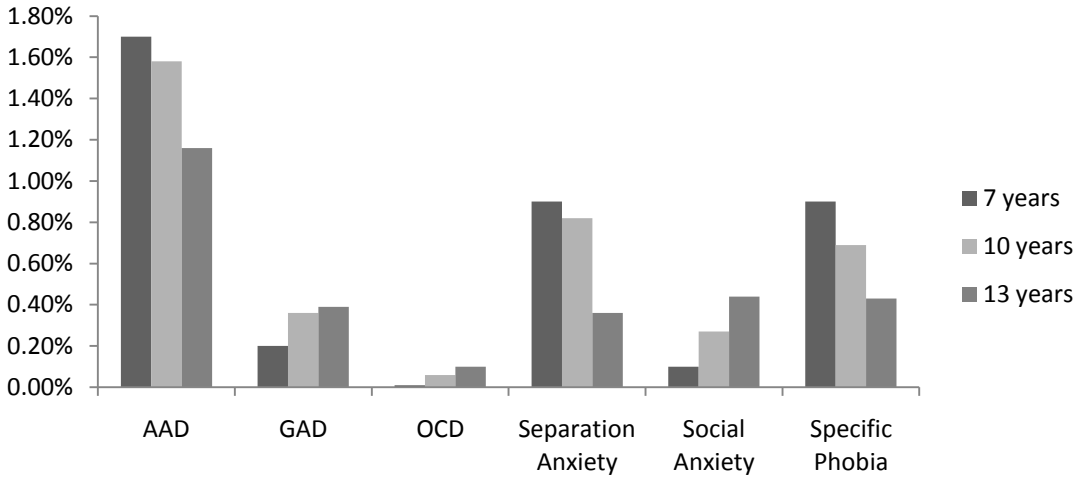

Figure 4. First onset of anxiety disorders at ages 7, 10 and 13-14 years in the ALSPAC cohort.

Chi Square test of Linear by Linear association was used to determine whether these trends were statistically significant. The decrease in any anxiety disorder was shown to be significant χ^2 (1, N= 6315) = 8.26 p = 0.004. The decrease in onset of separation anxiety was also found to be significant χ^2 (1, N=6315) = 19.28 p =0.001 as was the case for specific phobia χ^2 (1, N = 6315) = 11.96 p = 0.001. The

increasing incidence of social anxiety in this period is also significant χ^2 (1, N = 6315) = 7.4 p = 0.007 as was the increase in generalised anxiety disorder χ^2 (1, N = 6315) = 4.4 p = 0.036. The slight increase in obsessive compulsive disorder did not reach statistical significance (p = 0.17).

Table 13. New onset of anxiety: percentage of the sample with a new incidence of anxiety disorders (95% Confidence Intervals)

	Any Anxiety Disorder	Generalised Anxiety Disorder	Obsessive Compulsive Disorder.	Separation Anxiety	Social Phobia	Specific Phobia
7 Years (N= 8252)	1.7% (1.1-2.0%)	0.2% (0.1-0.3%)	0.01% (0- 0.1%)	0.8% (0.7-1.1%)	0.1% (0.1-0.2%)	0.9% (0.7-0.1%)
10 Years (N= 6679)	1.6% (1.3-1.9%)	0.4% (0.2-0.5%)	0.1% (0. - 0.1%)	0.8% (0.6-1.1%)	0.3% (0.2-0.4%)	0.7% (0.5-0.9%)
13 Years (N= 6315)	1.2% (0.9-1.4%)	0.4% (0.3-0.6%)	0.1% (0-0.2%)	0.4% (0.2-0.5%)	0.4% (0.3-0.6%)	0.4% (0.3-0.6%)

Table 13 reports the proportion of new cases of each disorder. Confidence intervals demonstrate these estimates to be precise. In order to be able to compare the ALSPAC data with those reported by other cohort studies we also calculated the cumulative incidence of anxiety disorders. The results can be found in Table 12 and are displayed in Figure 5.

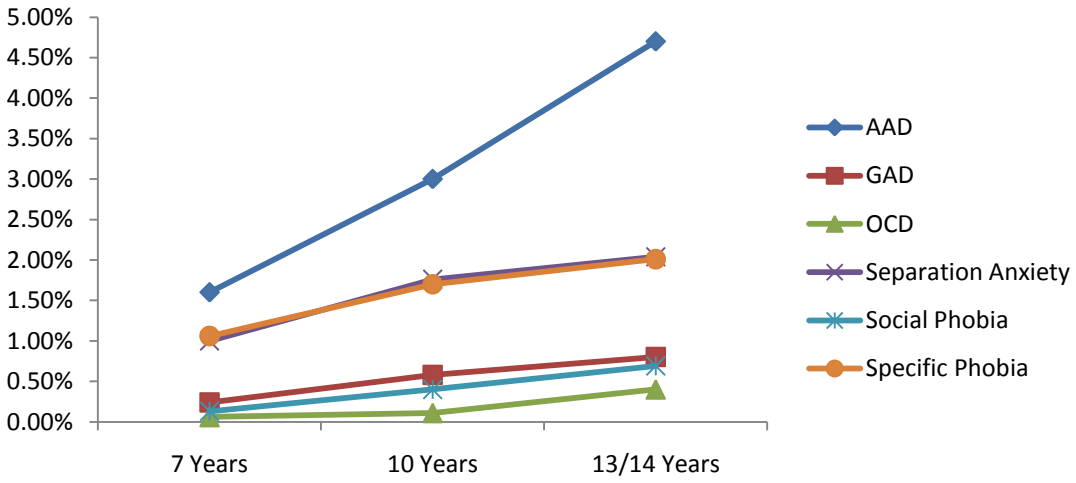

Figure 5. Cumulative incidence of anxiety disorders in the ALSPAC study

Cumulative incidence represents the total number of young people who have met the diagnostic criteria for an anxiety disorder over the course of the study. We can see

that nearly one in 20 thirteen year olds have met criteria for an anxiety disorder at one of the three points of data collection (4.7%; 95% CI 4.2-5.2%). As would be expected from the onset data we can see that separation and specific phobia flatten off and social anxiety steadily increases. Obsessive compulsive disorder and generalised anxiety disorder are rare and show small increases.

Course: Stability and Remission of Anxiety Disorders.

When examining the course and outcome of anxiety disorders it was evident that a significant number of children who had been diagnosed with anxiety disorders were missing from follow up. It was difficult to make sense of this drop out as the sample configures slightly differently at each follow up and the number of those completing at all three follow ups is relatively low (N = 5614) Figure 6 demonstrates the rates of attrition in children diagnosed with an anxiety disorder in comparison to those who did not receive a diagnosis. The figure sets out the drop outs as a percentage across the three study stages and shows that across the follow ups children previously diagnosed with an anxiety disorder appear to be somewhat more likely to drop out over the course of the study. A Chi Square test was used to explore this difference; drop out between age seven and age 13 to 14 years was significantly more likely in those previously diagnosed with an anxiety disorder than those who had not received a diagnosis; χ^2 (1, N= 6070) = 8.2 p = 0.004.

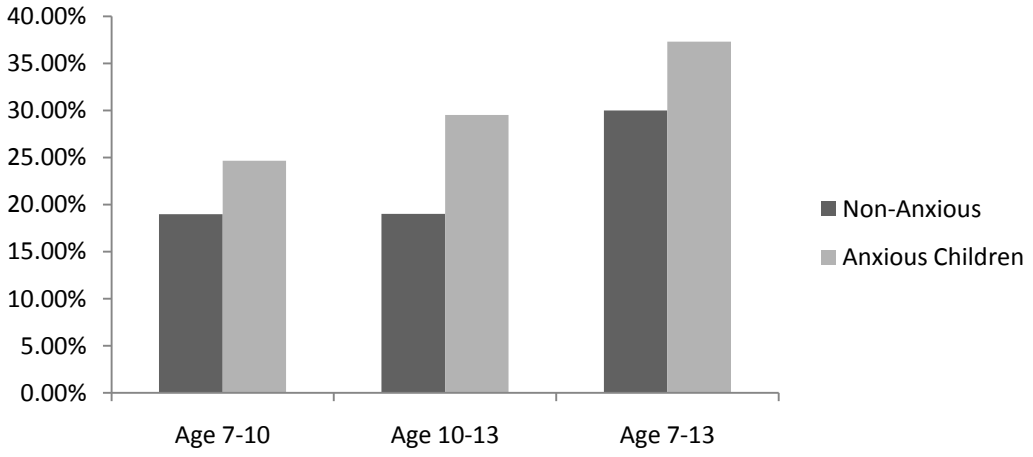

Figure 6. Comparing attrition of children previously diagnosed with anxiety disorders and attrition for those without.

A stratified analysis using Mantel-Haenszel correction was used to examine the effects of confounding demographics on the drop out of anxious children. Maternal social class and maternal educational qualification were initially chosen as potential

confounds as they have previously been shown to predict completion of the DAWBA at baseline and these data were collected for the majority of completers at baseline. Stratified analysis has been described as “the primary tool (or, more accurately, should be the primary tool) for evaluating and controlling confounding…” (pg 73, Rothman, 1971).

Table 14. Completion of the DAWBA according to diagnostic status of anxiety at aged seven adjusted for maternal highest qualification

	Completed DAWBA	**Dropped Out**	**Total**	**Proportion completing (%)**	**Odds Ratio**
Total	**6070**	**2182**	**8252**	**73.6%**	
Non-Anxious	5981	2218	8199	73.0%	OR = 1.6 (1.1-2.6)
Anxious	89	53	142	62.7%	
Highest Ed Q					
Non-Anxious	2505	616	3121	80.3%	OR = 1.2 (0.7-2.2)
Anxious	47	14	51	72.5%	
Lowest Ed Q					
Non-Anxious	2931	1394	4325	67.8%	OR = 1.8 (1.1-2.8)
Anxious	40	34	74	54.1%	
					Mantel-Haenszel adjusted OR = 1.6 (1.1-2.2)

When comparing non-completion of the DAWBA amongst anxious and non-anxious seven-year-olds we calculated that anxious children are more likely to fail to complete the DAWBA at age 13 (OR= 1.7; 95% CI 1.5-2.2). When comparing families reporting themselves to be in the three lowest bands of social class to those in the three highest, the likelihood of non-completion of the DAWBA is slightly lower; (OR= 1.4; 95% CI 1.2-1.7). However, mothers with O level or vocational qualifications were shown to be at three times the odds of not completing the DAWBA at age 13 (OR = 3.0, 95% CI 2.6-3.4) when compared to mothers with A levels or Degree level qualifications. A stratified analysis compares the drop out of anxious and non-anxious children stratified by a third, possibly confounding variable. In this analysis we used

maternal highest educational qualification as this factor has been shown to be associated with drop out. Table 14 demonstrates that, when the data are stratified according to mother's highest educational qualification, the relationship between anxiety status and drop out appears stronger for those whose mothers have the lowest educational qualifications (OR=1.8) rather than higher educational qualification (OR=1.2). The pooled Odds Ratios with Mantel-Haenszel adjustment, however, showed that the effect of anxiety on DAWBA completion remains (OR = 1.6; 95% CI 1.1-2.2). Those children with anxiety at aged seven are less likely to complete the DAWBA at age 13 regardless of this confounding social factor.

The finding that more children previously diagnosed with anxiety do not complete the subsequent DAWBA might lead to the estimates of stability being conservative; however, these estimates were calculated for any anxiety disorder and are presented below.

Of those children who took part in further diagnostic interviews, 21.1% (N = 30; CI 95%; 15.2-28.6%) of the 142 children diagnosed with anxiety at age seven were also found to be currently anxious at age 10, and 8.5% (N = 12; CI 95%: 4.9 - 14.2%) of anxious seven year olds continue to meet criteria at age 13. Stability appears to be further reduced between 10 and 13 years, with over 85% achieving remission (N = 22; 13.3%; CI 95%: 8.9-19.3%). When we look across the whole period only 3.5% (N = 5; CI 95% 1.5 - 8%) of anxious children received a diagnosis of a current anxiety disorder at age 7, 10, and 13; this is only 0.1% of the sample who completed the DAWBA at all three follow ups (N= 5614).

Outcome.

As the data we have access to only allow us to calculate disorders until the age of 14 the outcome for this cohort cannot be explored further than the data presented above for the continuity and new onset of disorders in early adolescence. It is clear that the majority of children diagnosed with a current anxiety disorder do not currently meet diagnostic criteria at three year follow up. A significant minority, however, (approximately 20% of ten year olds and 10% of 13 year olds) continue to meet diagnostic criteria following an earlier diagnosis.

The New York "Children in the Community" study.

The New York study began in the 1970's and the whole cohort was aged 9-18 years at baseline. The following data were released for the sample of children who were 9-14 at baseline in order to carry out analysis on first incidence, continuity, and outcome.

Prevalence

Twelve month prevalence data across the age groups and follow ups for the New York sample are published and were included in the original review (Gallagher, 2008) so will not be presented here. Prevalence in the younger sample that were released for the current project are presented in Figure 7 and were calculated for each age group by combining the number suffering from each disorder at each follow up, in the method used by the New York researchers in the original analysis.

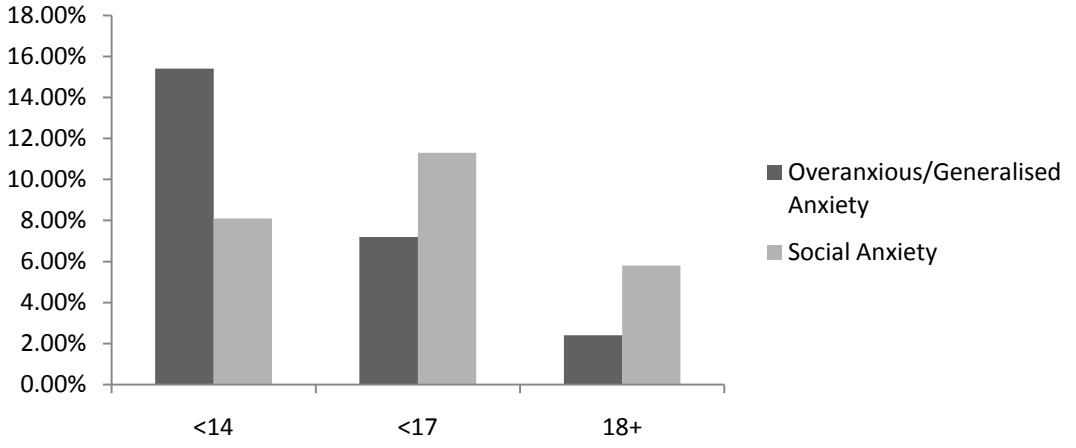

Figure 7. Prevalence of overanxious disorder and separation anxiety in early adolescence, later adolescence and adulthood in the New York study

Any anxiety disorder was not calculated for this sample due to the limited data. Data were released, however, for overanxious disorder/generalised anxiety disorder and social anxiety. The DSM-III which included overanxious disorder was used at baseline (< 14 years) and first follow up (<17 years) and then replaced with generalised anxiety disorder in adulthood with the advent of DSM-IV. The data demonstrate a reduction in the proportion of adolescents meeting criteria for overanxious disorder in later adolescence and an even greater reduction in the proportion of adults meeting criteria for generalised anxiety disorder. It is unclear if this is due to a decrease in such symptoms (namely worry) as the sample reach adulthood, or if the decrease is due to the new diagnostic criteria assessing a different

constellation of symptoms. The prevalence of social anxiety increases from early to later adolescence and then decreases (to below the prevalence in early adolescence) as the sample reach adulthood.

Onset.

The proportion of the sample with new onset of both overanxious disorder and social anxiety were calculated at all three follow ups. Overanxious disorder shows a marked decrease in new onset between early and late adolescence suggesting a remission of the disorder and decreasing rates of new onset, adult onset of generalised anxiety appears consistent with onset of overanxious disorder in late adolescence. Figure 8 shows that despite the increasing prevalence of social anxiety in adolescence (see Figure 7) new cases are decreasing, suggesting that onset of social anxiety is not common in adulthood in this sample. Chi square tests of Linear by Linear Association showed these trends to be significant for both overanxious disorder χ^2 (1, N=400) = 53.8 $p < 0.001$ and social anxiety χ^2 (1, N = 300) = 5.2 $p = 0.02$

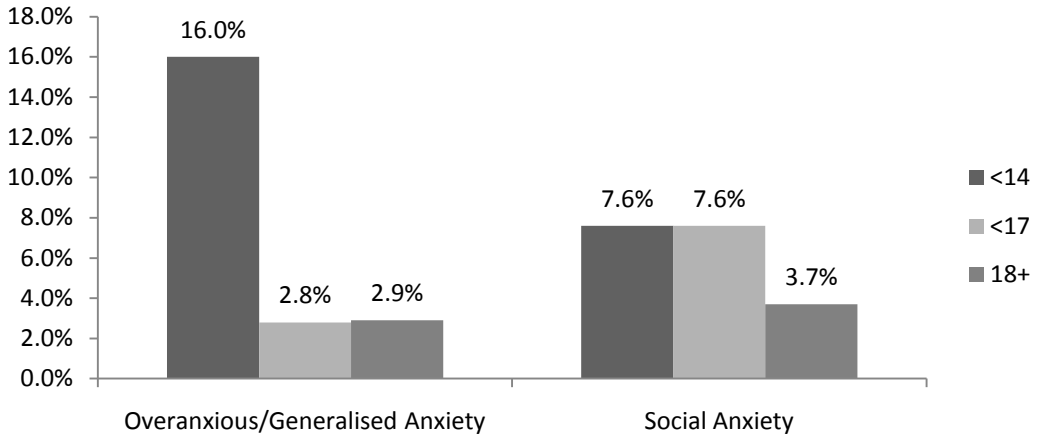

Figure 8. New onset of overanxious disorder and social anxiety in adolescence and adulthood in the New York study.

In line with the data presented above, which suggests that overanxious disorder has decreasing prevalence and onset as the young person gets older, the cumulative incidence is fairly flat (see Figure 9). Social anxiety disorder demonstrates a more steady increase in cumulative incidence through adolescence and adulthood; however, there is a slight flattening as fewer new cases are diagnosed in later life and cases from later adolescence remit.

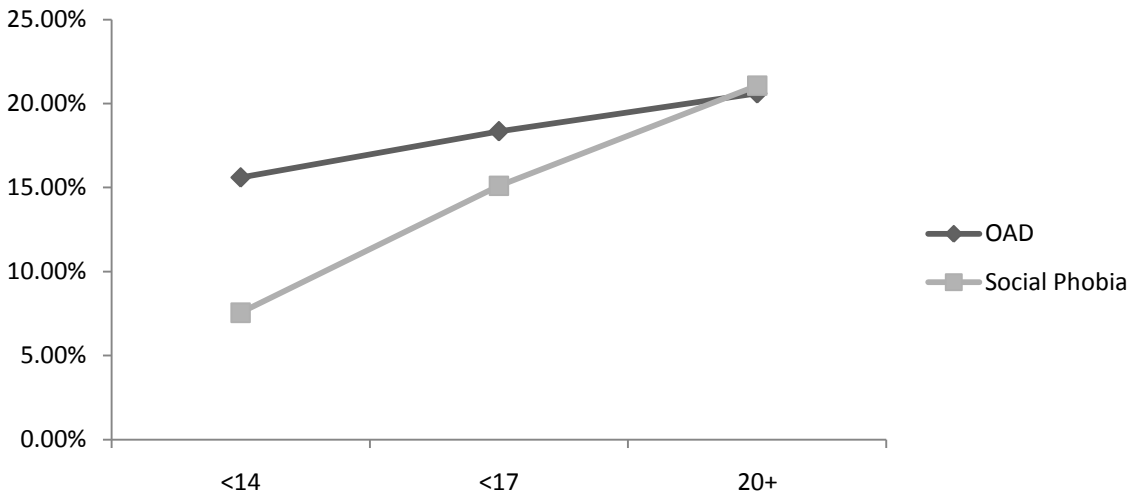

Figure 9. Cumulative incidence of overanxious/generalised anxiety disorder and social anxiety in the New York study.

Course: Stability and remission of social anxiety and overanxious disorder.

Only disorder specific homotypic continuity can be examined using the data made available for the current project. The diagnostic data show social anxiety to be moderately stable from early to late adolescence, becoming increasingly stable into adulthood; 45% (95% CI: 21.3 – 72.4%) of those with social anxiety in early adolescence still meet criteria for social anxiety in late adolescence and this stability decreases in adulthood with 19.2% (95% CI: 8.5 – 37.9%) of those first diagnosed in early adolescence receiving an adult diagnosis. Stability from late adolescence to adulthood is slightly lower at 17% (95% CI 8.9 – 30.1%), but confidence intervals show this estimate to be more precise.

The stability of overanxious disorder shows a different picture. Although 33% (95% CI: 16.3 – 56.3%) of those diagnosed with overanxious disorder meet criteria for the same disorder as older adolescents, this falls to 11% (95% CI: 3.1 - 32.8%) who meet criteria for generalised anxiety disorder in adulthood. Of those diagnosed with overanxious disorder in later adolescence only 6.5% (95% CI: 1.8-20.7%) continue to meet criteria in adulthood. The large confidence intervals' suggest these estimates are only moderately precise.

Outcome.

Pine and colleagues (1998) examined stability and outcome of anxiety disorders in the New York sample, looking at the risk conferred in adulthood from childhood and adolescent disorders; this is discussed in the synthesis section which follows in this

chapter. There is, therefore, relatively little novel analysis that might add to these findings. However, in order to synthesise effectively and make direct comparisons with the Dunedin study it was thought to be useful to carry out "follow back analysis" with the data released for the current project. Of the adults (aged 18+) meeting criteria for generalised anxiety disorder, 40% (95% CI 19.8-64.3%) had received a prior diagnosis of overanxious disorder in early adolescence (<14 years) and 14.3% (95% CI 4.0-39.9%) of adults had received a diagnosis of overanxious disorder in late adolescence (<17). Follow back analysis of social anxiety shows that 27.8% (95% CI 12.5-50.9%) of adults receiving a diagnosis of social anxiety had previously received a diagnosis in early adolescence, and 34.8% (95% CI 18.8-55.1%) had received a diagnosis of social anxiety in late adolescence. Estimates of the number of adults with their "first" diagnoses in late adolescence will be confounded by those who also suffered in early adolescence, as continuity was moderate for these disorders and there was a lack of raw data to calculate overlap so these estimates may be somewhat inflated whenf added together.

Appendix Three visually represents the overlap between the populations of anxious under fourteens, under seventeen's and adults to allow a clearer understanding of the analysis and missing data for both overanxious and social anxiety disorder.

Synthesis of Data: Understanding the contribution to the wider picture.

It remains extremely difficult to synthesise data due to methodological differences between the prospective longitudinal studies that have collected standardised diagnostic data on anxiety disorders. The original requests for raw data were to enable the synthesis of onset, course and outcome data for different age groups in a meaningful way. The data that were requested in order for these analyses were, unfortunately, not obtained. The novel data analysed above and the relevant published data cover a range of ages with modest overlap and begin relatively late in development, Figure 10 demonstrates the relatively small degree of overlap and the late starting age for most longitudinal studies. The novel data and the currently published data allow comparisons only for limited age ranges and for a small number of studies. Only New York and Dunedin follow from childhood to adulthood, the ALSPAC and Great Smoky Mountains Study begin in childhood but do not yet provide data into adulthood, and the majority of studies begin in adolescence and allow only a

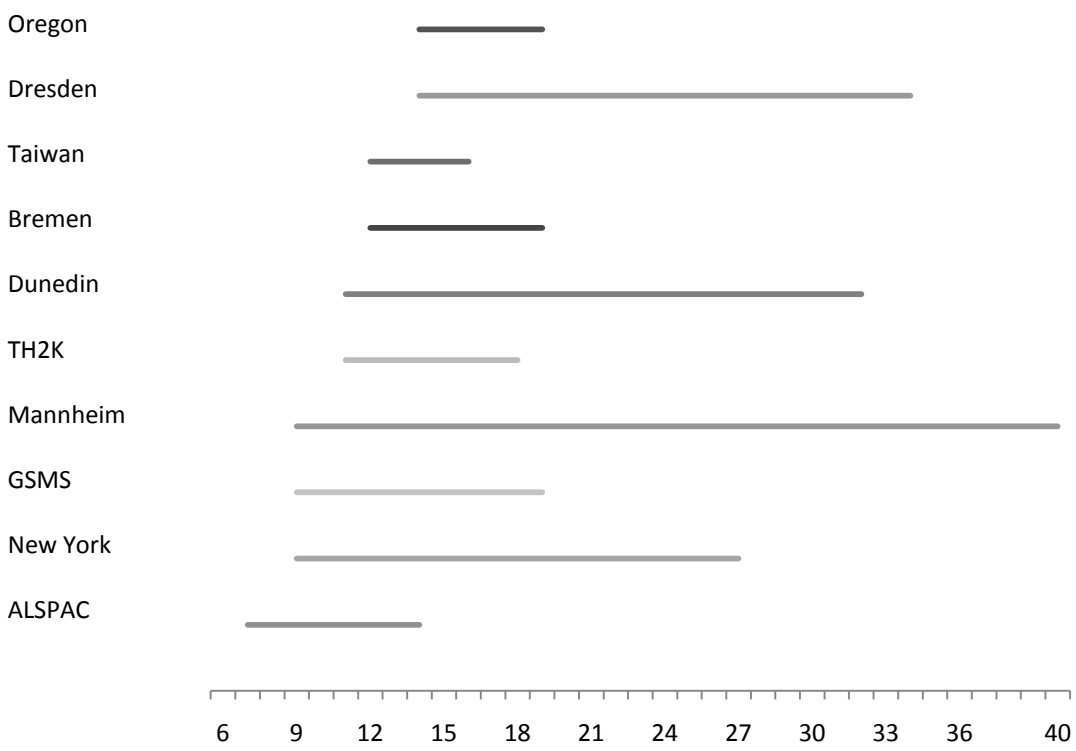

Figure 10. Age ranges of longitudinal prospective studies (reproduced from Chapter Three)

short period of follow up. However, it has been possible to compare patterns in the data using graphical displays.

Prevalence.

Figure 11 plots the reported prevalence of any anxiety disorder in a number of studies where data were available for comparison. Due to a range of methodological differences and temporal or cultural differences comparisons must be made with some caution.

The Bremen data were not included as they report only lifetime prevalence and New York could not be included as no prevalence can be calculated for any anxiety disorder. Figure 11 shows clear discrepancy in both the magnitude of the prevalence and the changing patterns over time. In the Dunedin data anxiety disorders increase in prevalence throughout childhood and into adolescence where other studies

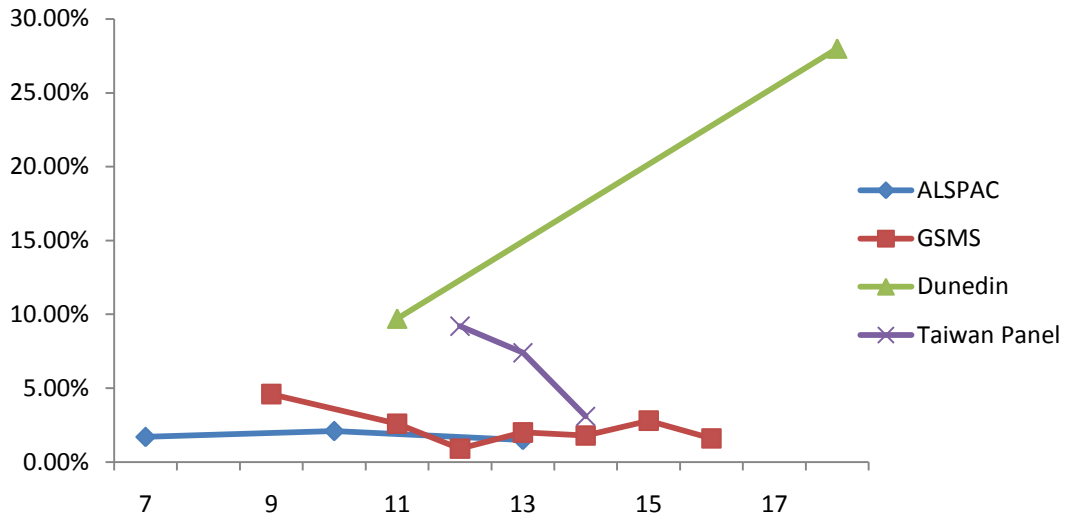

Figure 11. Prevalence of anxiety disorders in longitudinal prospective studies.

demonstrate a fluctuating pattern, as can be seen in the ALSPAC and Great Smoky Mountains data. Alternatively, there is also a fall in prevalence demonstrated by the Taiwan panel study. It was proposed that the large differences between the findings of the studies demonstrated in Figure 11 may be attributable to the core period of assessment that is used in the diagnostic interview and so comparisons across the same age groups using different prevalence criteria are presented in Figure 12. The comparisons demonstrate that studies which require symptoms to have been present in the last twelve months have much higher rates than those that require symptoms to be present only in the last six months which are in turn greater than in the last three months or currently present (point prevalence).

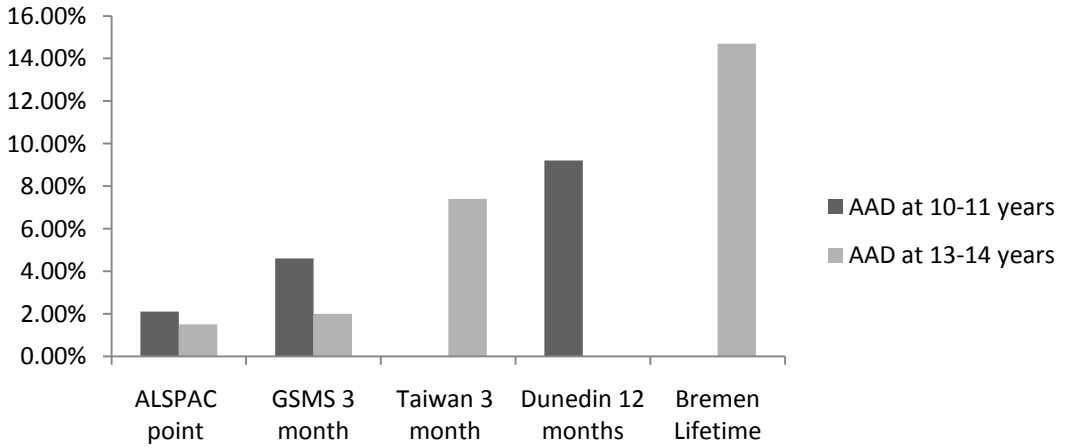

Figure 12. Prevalence of any anxiety disorder at 10-11 and 13-14 years using different prevalence criteria.

More similar rates are seen when we compare the ALSPAC data with studies that require symptoms to be present in the last three months. Figure 13 compares the Great Smoky Mountains Study in the USA with the ALSPAC data.

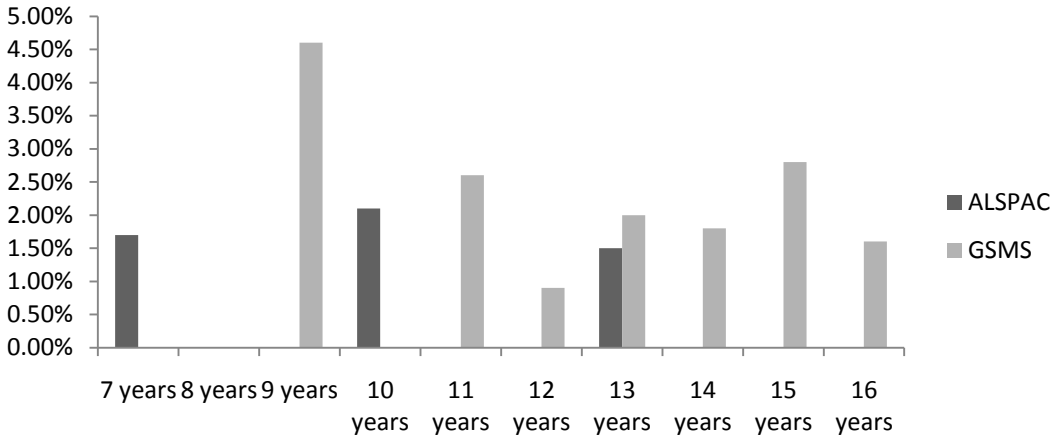

Figure 13. Great Smoky Mountains Study (three months) and ALSPAC (point) prevalence data.

Cumulative (lifetime) prevalence of anxiety disorders in late adolescence has previously been calculated by both the Oregon Adolescent Depression Project (8.8%; 14-18 years) and Great Smoky Mountains Study (9.9%; 16 years). These data were calculated from 12 month and three month prevalence data respectively and exactly how these data are calculated is unclear. It must, therefore, be assumed from the study design that they are taken from lifetime prevalence estimates at interview. They are higher than that calculated above using the ALSPAC cohort at aged 13 to 14 years (4.7%) This would, however, be expected in a younger sample and is also likely to be affected by the use of the point prevalence criterion.

Onset

No other studies have reported new incidence in children across more than one follow up. The ALSPAC data demonstrates decreasing onset of anxiety disorders in 7 to 13 year olds, with increasing proportions of new cases of generalised and social anxiety but progressively fewer new cases of separation anxiety and specific phobias. The New York data show the peak onset of overanxious disorder to be before the age of 14 and suggest significant onset of social anxiety before the age of 18, with relatively few cases of adult onset in either disorder. Figure 14 compares the proportion of new cases of anxiety identified for each study, plotted against the period of follow up (represented by the age of sample) The seemingly conservative rates of onset over 12 months reported by Lewinsohn et al (1993) in the Oregon study (0.6% in 14-18

year olds) affects the patterns considerably. If it were taken in isolation (without looking at the Dresden or Bremen data) the Oregon data would suggest that new onset progressively reduces in later adolescence. This finding is supported by the TH2K data which report an overall incidence for 11-16 year olds of 3% (Roberts et al. 2009). They then break this down by age; incidence increases from 2.6% to 3.6% between 11 and 14 year and then drops to 2.2% in 15 to16 year olds, suggesting peak incidence at around 14 years and that incidence begins to decrease in later adolescence. However, there is a much higher proportion of onset reported in the Bremen and Dresden studies. The Bremen study calculated an incidence rate of 6.9% over a 15 month period in a sample of 12-18 year olds. The Dresden incidence data show similarly high figures of 8% over a 15 month period in 14-19 year olds. Incidence of social anxiety (2.1%) and specific phobias (5.7%) were particularly high; generalised anxiety shows incidence of only 0.1% in this population of adolescents.

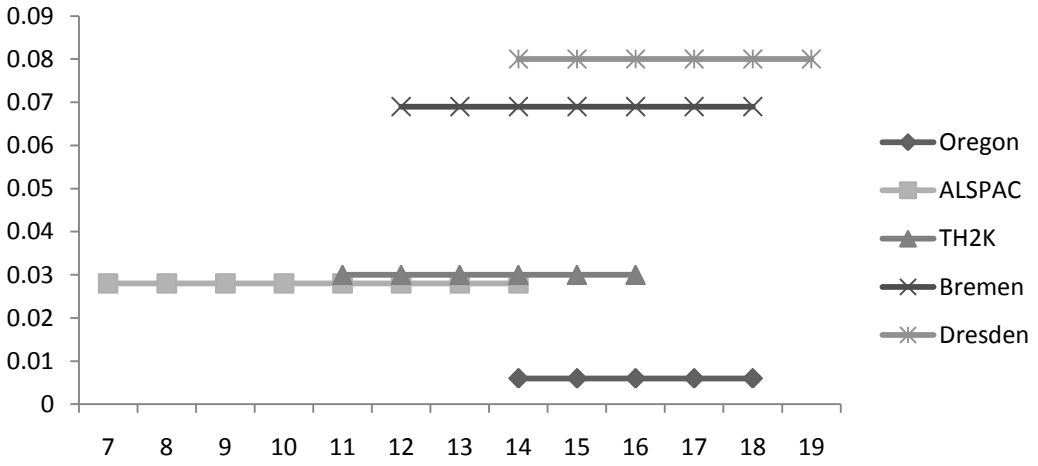

Figure 14. Proportion of young people with new incidence of anxiety disorders according to age range and length of follow up.

Relatively high onset rates have been proposed by some authors to demonstrate the lack of stability in anxiety disorders in this age group. If we use the Dresden data as an illustration, Wittchen et al (2000) report that over 15 months the overall prevalence of anxiety disorders drops and there are significant number of “new” cases (see Figure 15). It has been postulated that anxiety disorders in younger samples may be less stable and we can see that the cumulative prevalence is only 0.6% less than adding point prevalence at all three follow ups together, so we examined the new ALSPAC data in this way. Figures 16 and 17 demonstrate similar patterns to those in

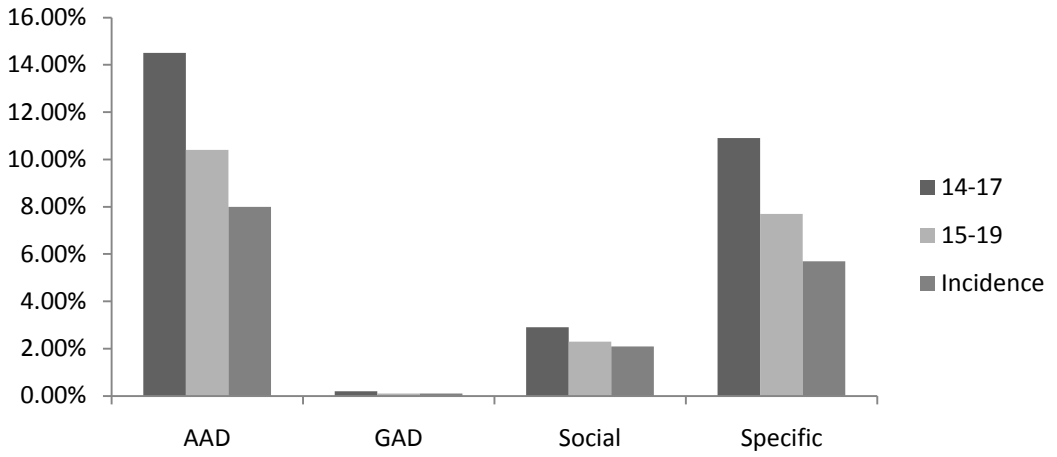

Figure 15. Prevalence and incidence in the Dresden study at baseline (14-17 years) and first follow up (15-19 years). (Wittchen et al. 2000)

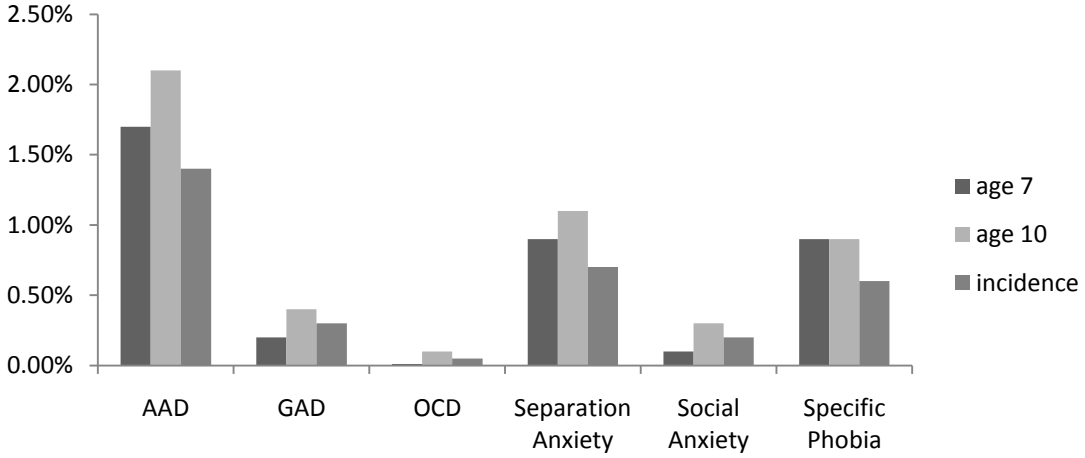

Figure 16. Prevalence and incidence of anxiety disorders in the ALSPAC at age 7 and 10

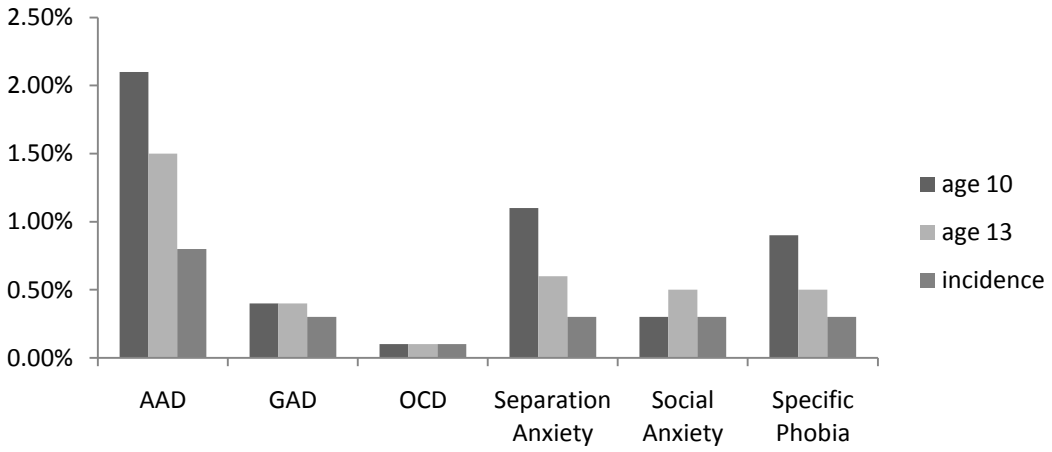

Figure 17. Prevalence and incidence of anxiety disorders in the ALSPAC at ages 10 and 13.

the adolescent Dresden data in the ALSPAC study in childhood and early adolescence.

Figure 16 shows the prevalence and onset of anxiety at seven and ten years and Figure 17 shows the prevalence and onset between ten and thirteen years. Both Figure 16 and Figure 17 show that new disorders make up a sizeable proportion of the disorders present, but there is evidence of increased stability as the child gets older with around half of the identified anxiety disorders being new cases and around a half stable, rather than two thirds or more being new disorders. The data from all three figures taken together suggest that the onset of any anxiety disorder decreases through childhood and continues to decrease through adolescence with a possible spike in mid adolescence. Separation anxiety has progressively fewer cases of new onset as the child gets older; social anxiety and generalised anxiety on the other hand have progressively more cases of new onset through childhood and into adolescence.

Cumulative Incidence and patterns of onset.

The Dresden study use cumulative incidence curves calculated using the Kaplan-Meier survival method to demonstrate the patterns for new onset of cases in childhood, from the data that they have collected later in life. Figure 18 uses data from Wittchen et al (2000) and Beesdo-Baum et al. (2009) and compares it with the cumulative incidence from the ALSPAC data. The incidence of the Dresden data is of a greater magnitude (as they use 12 month prevalence and also a different method of calculating diagnostic criteria) and shows a clear pattern of flattening of new incidence at age 14 ; unfortunately the lack of data does not allow us to examine this truly prospectively in the ALSPAC data; predicted outcomes, however, using a log linear trend line show a less clear picture of flattening. Cumulative incidence curves have not been produced for other studies with this data. We only have data for lifetime incidence calculated for later adolescence which may not be taken from prospective data and is reported at over 9% (Oregon and Bremen studies).

When we look at the individual disorders that we have data for we can see that social anxiety has a cumulative prevalence that continues to increase into later adolescence. Although there is significant onset in childhood and early adolescence new cases are continuing to emerge later in life, supported by the adulthood incidence data in the New York data (see Figures 19 and 20). Although the low prevalence of social anxiety in the ALSPAC study makes visual comparisons difficult Figure 19 demonstrates the pattern of increasing onset of social anxiety through childhood into

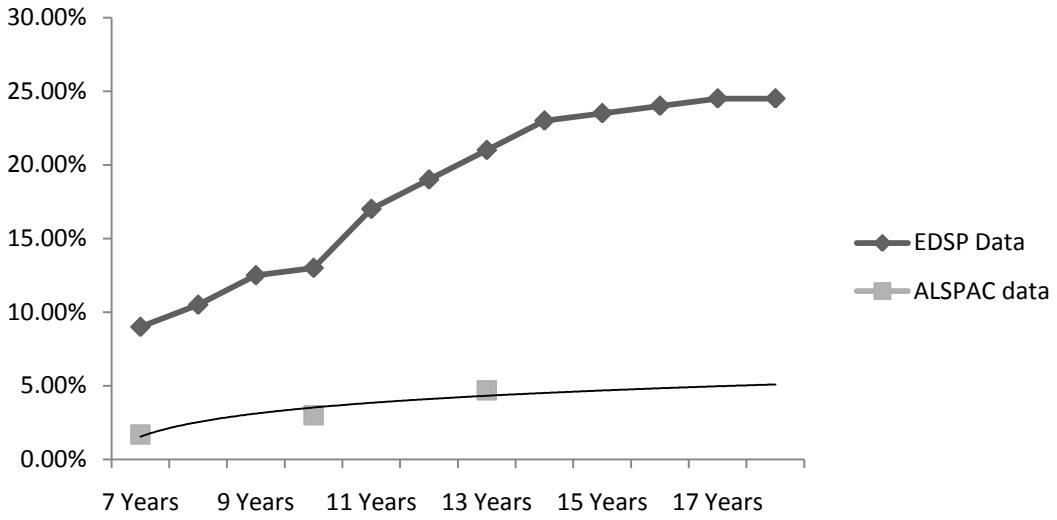

Figure 18. Cumulative incidence/onset curves for anxiety disorders in the ALSPAC and Dresden studies.

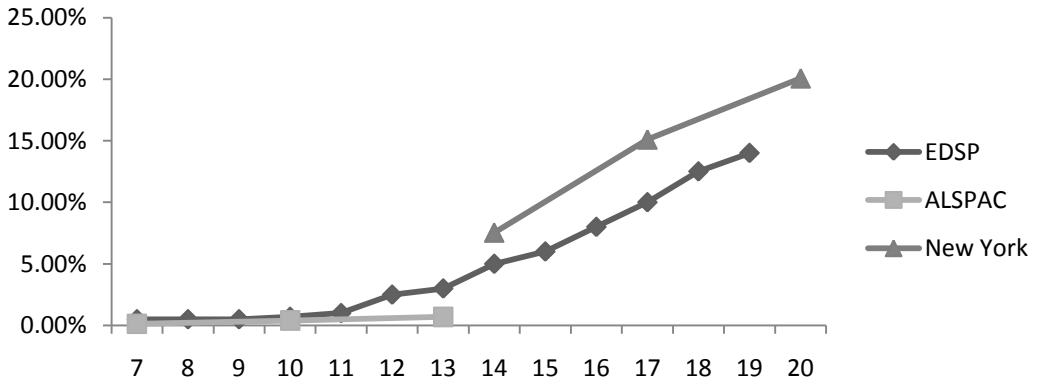

Figure 19. Cumulative Incidence/onset curves for social anxiety in the ALSPAC, Dresden, and New York studies.

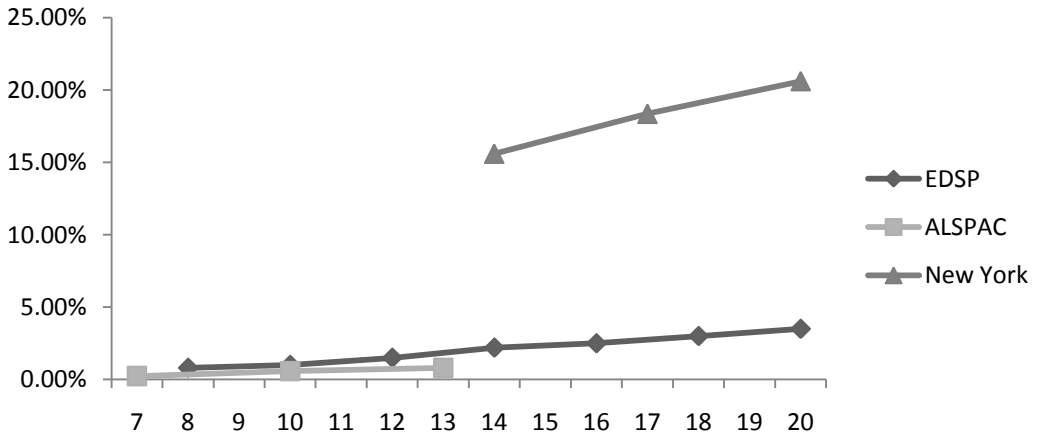

Figure 20. Cumulative Incidence (Onset curves) for overanxious/generalised anxiety disorder in the ALSPAC, Dresden and New York studies.

early adolescence. Whereas Figure 20 shows that overanxious/generalised anxiety disorder has a lower cumulative incidence and a much more conservative increase with a flatter curve through later adolescence demonstrating a slowing of the number of new cases in this period.

Stability of anxiety disorders in childhood and adolescence.

The course and outcome of anxiety disorders over time is an area that has received far more attention in the existing literature. The ALSPAC data, however, demonstrates the stability of anxiety disorders in a childhood sample, the course and outcome of anxiety in this younger age group is currently missing from the existing literature. We can compare the stability of anxiety in this younger sample with the stability of internalising disorders in the BCAMHS sample.

The ALSPAC data demonstrate that approximately one in five children diagnosed with an anxiety disorder at age seven still meet criteria three years later at age 10 (21.1%) and only 13% who were aged 10 at baseline meet criteria at age 13. BCAMHS used the DAWBA on a cohort of children who were aged five to seven years old at baseline and 26% continued to meet criteria for an emotional disorder three years later. Mirroring the drop in the stability of anxiety in the ALSPAC data, only 12% of those who were 8-10 at baseline continued to meet criteria for an emotional disorder three years later; the stability rose sharply to 40% for children who were 11-13 years old at baseline; however there are no comparison group yet analysed for the ALSPAC cohort. The BCAMHS data (like the TH2K study) are essentially splitting a sample by age rather than examining change over time as the ALSPAC data allows. These data should be treated with appropriate caution but provide an interesting comparison, showing similar patterns of changing stability in childhood.

Comparing stability of anxiety disorders in different samples.

The stability of anxiety calculated from the ALSPAC data in early childhood contribute to a consistent picture of stability reported in prospective longitudinal studies, (see Table 15.) These findings support the contention that around 20% of anxiety disorders are continuous across short periods of time, but that at least 30% of anxious children will suffer from anxiety again, over longer term follow up. These findings appear to hold true regardless of the age group examined or the length of time between the diagnostic interviews.

Table 15. Stability of anxiety diagnoses

Study	Follow up period	Stable Disorders	Method
ALSPAC	36 months	21.1%	A
Bremen	15 months	22.6%	A
Dresden	15-20 months	19.7%	A
ALSPAC	6 years	36.6%	B
Dresden	10 years	30%	B
GSMS	8 years	28.6%	B

A = Stability between two points in time B = Anxiety present at two or more follow ups

Stability of individual anxiety disorders – overanxious disorder.

Due to the small numbers of children reaching diagnostic criteria, continuity of individual anxiety disorders were shown to have unacceptably large confidence intervals so are not reported for the ALSPAC sample. The baseline and first follow up stability of overanxious disorder in the New York study was reported in Cohen et al. (1993) and were calculated for a sample of 250 9-18 year olds, with 22.8% of those with overanxious disorder continuing to meet criteria after 2.5 years (rising to 50% in those with "severe" overanxious disorder at both follow ups) This finding for overanxious disorder presents more evidence to support the data in Table 15 that around 20% of disorders are stable in childhood and adolescence. Odds Ratios were used to demonstrate the increase in risk of further overanxious disorder from a baseline diagnosis across the severity levels (mild overanxious disorder OR= 3.27, moderate overanxious disorder OR = 8.63, severe overanxious disorder OR = 17.25).

The analysis of overanxious disorder in the younger data set looked at the stability of overanxious disorder in those who were under 14 at baseline and then in adolescence and early adulthood. Moderate stability was shown from early to late adolescence (33% continue to meet diagnostic criteria from baseline, aged under 14 years and first follow up, aged under 17 years), suggesting that continuity is higher in a younger sample with the same follow up period; stability drops to only 11% of those diagnosed with overanxious disorder before the age of 14 meeting criteria for generalised anxiety in adulthood. This could, however, be due to the changing diagnostic criteria in adulthood from overanxious to generalised anxiety disorder, and the overanxious symptoms may still be present but at a sub-threshold level for a generalised anxiety diagnosis. This pattern of stability for overanxious disorder in adolescence is similar

to the findings reported in the Great Smoky Mountains Study (9-16 year olds) where stability of overanxious disorder in adolescence was shown to be moderate; 28.6% of the sample received an overanxious disorder diagnosis at two or more follow ups (Bittner et al. 2007).

Stability of individual anxiety disorders – social anxiety disorder.

Using the analysis of the younger sample of the New York study presented above, adolescent social anxiety appears to be moderately stable over a three year period, with nearly half the cases assigned in early adolescence (45%) continuing to meet diagnostic criteria in later adolescence. When we look at stability from early adolescence into adulthood (19%) and late adolescence to adulthood (17%) these findings look far more similar to those reported for the sample as a whole, where stability of social anxiety over a six and a half year follow up was reported at 20%, (Pine et al. 1998). The new analysis found 19% of those receiving a diagnosis of social anxiety in childhood or early adolescence were diagnosed with social anxiety in adulthood. This decreases from 45% of those diagnosed with social anxiety in early adolescence continuing to meet criteria later in adolescence. In the GSMS study (9-16 years study period) social anxiety was shown to be stable in 14.3% of cases. This is comparable to the 20% reported for the whole New York sample but is somewhat lower than that reported in the novel analysis of the New York data (45%) which covers a more similar age range. The Dresden ten year follow up data, however, report stable social anxiety disorder in 35% of their sample of 14-24 year olds over ten years Beesdo-Baum et al. (2009) and only 15.8% over the 15 month follow up, suggesting short term transience but remaining at increased risk for later social anxiety. The New York data reported here suggest that early onset social anxiety is moderately stable in adolescence, but this stability reduces in adulthood. Despite this, over half of the adult sample had met diagnostic criteria for social anxiety in childhood or adolescence.

Stability of individual anxiety disorders – simple phobia.

Simple phobia was also examined in the Dresden study, and has been shown to be highly predictive of adult mental disorders with only 10% of those who had received a simple phobia diagnosis being without psychopathology in adulthood; 41% continued to meet criteria for simple phobia and 73% having an anxious or depressive disorder (Beesdo-Baum et al. 2009). Homotypic stability over the 15 month follow up was lower at 30.1% (Wittchen et al. 2000) Unfortunately this cannot be corroborated by

the New York data as simple phobia had a number of issues with the data and so could not be shared for this purpose.

Outcome: Follow back analysis of adult data.

Follow back analyses were carried out for the whole data set by Pine and colleagues (1998). In this analysis the proportion of adults with anxiety disorders that had received a prior diagnosis of anxiety disorder was over 90% across the anxiety disorders and Newman and colleagues (1996) similarly report that 80.5% of 21 year olds in the Dunedin study had received a previous diagnosis in childhood or adolescence, and of those suffering with anxiety disorders at age twenty six 54.5% had received their first diagnosis before the age of fifteen (Kim-Cohen et al 2003). When looking at longer term adult follow up Gregory et al. (2007) employed follow back analysis on the Dunedin cohort at age 32 found that 30% of adults with anxiety disorders had met criteria for an anxiety disorder at ages 11 to 15.

Looking at the follow back analysis of generalised anxiety in the younger sample from the New York study suggests that a more modest but substantial proportion of adults diagnosed with generalised anxiety disorder were previously diagnosed with overanxious disorder in childhood (40%) and a smaller proportion diagnosed later in adolescence (14.3%). The Dunedin study reports that 66% of adults with generalised anxiety disorder had their first diagnosis in childhood or adolescence (Kim-Cohen et al. 2003.

Of adults with social anxiety disorder around a third received their first diagnosis in childhood or early adolescence (27.8%) and slightly more received their first diagnosis in later adolescence (34.8%). Kim-Cohen et al (2003) report from the Dunedin data that 50% of 26 year olds received their first diagnosis of social anxiety between 11 and 15.

Chapter Five: Discussion.

Overview.

This chapter will outline the findings of the novel analysis undertaken in this thesis and how these findings integrate with the published longitudinal prospective data reviewed in the Introduction (Chapter One) and Updated Review (Chapter Two). These findings will then be discussed in the context of the wider field and assertions made regarding the descriptive epidemiology of anxiety disorders using retrospective and cross-sectional research. The implications of the project for developing research methods to improve the understanding of the descriptive epidemiology of anxiety disorders will then be discussed. The clinical implications for intervention and prevention will be briefly discussed followed by limitations and ideas for future research.

Summary of findings.

Avon Longitudinal Study of Parents and Children (ALSPAC).

The ALSPAC analysis adds significantly to our understanding of the onset and course of anxiety in younger children. Anxiety disorders are present in approximately two to three of every hundred children at any one time in middle childhood to early adolescence, and prevalence is highest at age ten. New onset of anxiety disorders decreases over this period of development and most disorders remit; they are not present at three-year follow up. However a small but significant proportion of anxious children (around 20%) continue to meet diagnostic criteria at three-year follow up and over a third of anxious children meet diagnostic criteria at two or more follow ups, suggesting that disorders may wax and wane over time.

Significantly more boys than girls met criteria for an anxiety disorder at age seven but this gender difference was not found at age 10 or at 13/14. Boys were at around 50% more risk of anxiety disorders than their female counterparts. Increased prevalence of anxiety in boys in middle childhood has been reported previously using diagnostic interviews (Mesman & Koot, 2001). In some publications anxiety is reported separately for boys and girls and almost always girls are reported to be at increased risk of anxiety diagnoses; Costello et al (in prep), however, in their meta-analysis were

not able to examine gender differences as not enough studies reported boys and girls separately. Lewinsohn, Lewinsohn, Gotlib, Seeley, & Allen, (1998) examined possible confounds of gender differences, and found that anxiety remained more prevalent in females but the differences are small and rarely significant. However this was in an adolescent sample. The fact that adolescent and adult anxiety disorder is more prevalent in females may have an impact on perceptions of gender differences in younger populations, and this data supports the contention that this may be erroneous. There is data emerging that suggests in younger children males may be at increased risk. Examining gender differences in these populations, therefore, appears an area for further examination.

Stability of anxiety disorders in this sample seems low with nearly 80% of anxious seven-year-olds free from their diagnosis by age ten. However, when we use the Great Smoky Mountains method of examining "continuous" disorder (anyone who has met criteria at two or more follow ups) nearly 40% of anxious children have a "stable" disorder. This suggests that anxiety disorders wax and wane to some extent over this period of development with chronic disorders not taking a linear course in some cases. Using the computer algorithm was shown in the current study to produce conservative estimates in comparison to clinician diagnoses, and using "point" prevalence (symptoms must be currently present) also reduces the proportion of children who are assigned a diagnosis of anxiety disorder. It is therefore unsurprising that the prevalence of anxiety reported for the ALSPAC cohort is low in comparison to other studies in samples of a similar age. An important finding is that, of those who receive a diagnosis of anxiety disorder, the proportion who have a stable diagnosis both in shorter term follow up (around 20%) and over multiple follow ups (between 30 and 40 %) are consistent with the proportions found in studies using less conservative methods - even those that have examined stability of anxiety in older children and adolescents.

Missing Data.

Examination of missing data in this sample, both for those who chose not to complete the DAWBA at baseline and for those who did not complete at all follow ups, demonstrates a pattern of attrition that must be considered when interpreting the findings. In support of the findings of Wolke and colleagues (2010), in the ALSPAC sample in relation to risk factors for behavioural problems, non-completion of the DAWBA appears to be associated with economic and social disadvantage - a

population that would be expected to have a high prevalence of mental disorders when we look at the data for adults, (Jenkins et al. 1997; Murali & Oyebode, 2000; Pollitt, 2004). Furthermore, families that completed the DAWBA at baseline whose child met criteria for an anxiety disorder were less likely to complete the DAWBA at later follow ups than those who did not. Non-completion occurred more often in families who reported social disadvantage but, when this was taken into account, anxiety status was still associated with increased drop out. These findings suggest that prevalence might be conservative estimates in this sample, particularly for the stability estimates, as we do not know the outcome for a substantial proportion of anxious children who were lost to follow up.

Children in the Community – The New York Study.

The data released to me from the New York study also provide new and interesting findings in relation to onset and stability of social and generalised anxiety in later childhood and adolescence.

Social Anxiety

The findings show that the prevalence of social anxiety peaks in later adolescence and decreases to below the prevalence reported in childhood or early adolescence once the sample reach adulthood. This is somewhat surprising as social anxiety is often referred to as a disorder of later adolescence rather than childhood. As would be expected from this pattern the onset of new cases also decreases once the individual reaches adulthood - suggesting peak onset in adolescence; the proportions of new cases are similar for the samples in early and later adolescence, so identifying exactly when a first diagnosis is most likely may not be possible. This may well reflect an extended period of "peak" onset in later childhood and early adolescence. Unfortunately, the breakdown of the data according to smaller age groups as originally planned was not possible, precluding the examination of these patterns in more detail.

The stability of social anxiety in adolescence over a three year follow up was shown to be moderate with 45% of those receiving a diagnosis before the age of 14 continuing to meet criteria three years later. Over a six year follow up, around a fifth of those diagnosed in early adolescence met criteria again in adulthood (19.2%) and slightly less (17%) who were diagnosed later in adolescence continued to meet criteria in adulthood, suggesting that social anxiety has greater stability in early adolescence and then remits. Follow back analyses suggest that of the sample with adult social

anxiety around a third of cases began in early adolescence and around a third in later adolescence. The majority of adult cases appear, therefore, to have received their first diagnosis in childhood or adolescence. This finding must be treated with caution as there was considerable overlap (45%) between the early and late adolescent cases so this estimate may be inflated.

Overanxious Disorder.

Overanxious disorder has its peak prevalence in childhood or early adolescence (<14 years) with the onset of new cases being highest at this time and remaining low for late adolescence and adulthood. The stability of overanxious disorder is greatest over the three year follow up between early and later adolescence with only one in ten early disorders resulting in adult generalised anxiety disorder. Around a third of children and early adolescents (<14) continued to meet diagnostic criteria for overanxious disorder three years later in later adolescence (<17). Continuity between late adolescence and adulthood was lower than that between early adolescence and adulthood (6.5%) suggesting that disorders with later onset are less stable or perhaps reflecting the difference between the populations diagnosed with overanxious disorders and generalised anxiety disorder. Using follow back analyses around 40% of adults with generalised anxiety disorder had received a prior diagnosis of overanxious disorder in early adolescence and less than 15% had met criteria for overanxious disorder in later adolescence, again suggesting that a substantial proportion of adult disorders have early onset, but that conversely most adolescent disorders have a benign outcome, particularly in adolescence. Since the advent of DSM IV (APA 2000) overanxious disorder is not currently in commonly use but Bittner et al (2007) argue that it is useful as a predictor of later psychopathology and its use should be reconsidered; however as we only examined its relationship with generalised anxiety disorder in this sample, these data only suggest that early onset of overanxious disorder is somewhat stable and has a weak relationship with later generalised anxiety disorder. Its predictive value may be associated with anxiety (or depressive) disorders other than generalised anxiety disorder which could, unfortunately, not be examined using the current data.

Prevalence of anxiety disorders in the New York sample is high and it is possible that the use of DSM-III and the overanxious disorder diagnosis contributes to these high estimates, as the prevalence of GAD appears consistently lower than overanxious disorder. The New York study also asked about symptoms at any time in the last year

(twelve month prevalence data), which has also been shown to increase the estimates.

The proportion of adult disorders first diagnosed in adolescence in the younger sample of the New York cohort is substantial (although not as high as those reported by Pine et al. (1998) in the full cohort). The high prevalence recorded by the New York study over a large number of follow ups, however, leaves a large pool of young people reaching criteria for anxiety disorders; it is, therefore, important that follow back data are examined in the light of the stability and outcome of childhood disorders, to determine a true picture of the outcomes of early anxiety and the true costs of early onset. (Appendix Three presents these combined data visually). Two thirds of all adolescents diagnosed with overanxious disorder are diagnosis-free at three-year follow up. This is a substantial proportion who still suffers the same diagnosis; however, nearly 90% of those children or young adolescents are free from a worry related diagnosis in adulthood. Of those diagnosed with social anxiety in childhood and adolescence, social anxiety is estimated to be stable over three years in just under half of cases, and around 20% of cases from childhood are still present in adulthood. Although it appears that most adult disorders have their onset earlier in life, due to the smaller proportions of adults receiving these diagnoses it appears crucial to the targeting of resources that those young people with stable and chronic anxiety disorders are identified if effective intervention and relapse prevention are to be offered.

It was unfortunately not possible to determine differences in the attrition from the New York sample as the necessary demographic data were not released for analysis here. The New York sample is representative of New York State, from where it was taken. Previous publications, however, have alluded to the drop out of those with increased social disadvantage following baseline data collection and supplementation with a group of children meeting certain demographic criteria was undertaken to address this attrition (Cohen et al. 1993a). No further detailed analysis of this drop out is to be found in the published literature.

Synthesis

Directly synthesising data, (combining the data sets) from different studies was not possible for a number of reasons that are discussed in the “Implications for methodology” section later in this chapter. However, every effort was made to make

meaningful comparisons and determine common patterns and discrepancies between the new data and the existing prospective longitudinal studies.

Prevalence criteria.

When attempting the synthesis and comparisons of data from different studies it became clear that there is a robust effect of the amount of time preceding the interview that symptoms are required to have been present in order to contribute to a diagnosis. This has been discussed briefly in reference to the discrepant magnitudes of prevalence reported here for the ALSPAC and New York data. Some studies (e.g. Bremen study) have used a "lifetime" criterion when first asking young people or their parents about mental disorders "Have you ever experienced…" However it has been shown using the same samples that asking "Have you in the last twelve months experienced…" demonstrates twelve month and lifetime prevalence of mental disorders to be almost identical. When attempting to make sense of this finding Costello et al (2004) suggest that there was either an epidemic of anxiety in the 12 months preceding the interview or there are high rates of forgetting for disorders before this period. When people are asked about the presence of symptoms or disorders in the last six months, prevalence reduces. Prevalence reduces further using a three month criterion and even further when the disorder is required to be currently present.

Costello and colleagues (2004) conclude in their review that prevalence of anxiety is robustly reported at 2-4% using three month or point prevalence and between 10 and 20% using six or twelve month prevalence criterion. The lack of difference between lifetime and 12 month prevalence is discussed by the authors with reference to high rates of forgetting for disorders occurring longer than twelve months ago; there is little discussion, however, of what this difference means in terms of low estimates using point prevalence. If the lifetime prevalence reduction is due to "forgetting" is the increase in prevalence using twelve month criteria rather than shorter periods also due to misremembering? It has already been shown that asking about symptoms from over three months ago has limited reliability (Angold et al. 1996). It is possible, therefore, that some of the "diagnoses" may not have met diagnostic criteria had the parent or child been questioned about their symptoms closer to the time that they were experiencing them. Twelve month prevalence might, therefore, include a number of subthreshold cases and reflect an over estimation of true "caseness". Alternatively, this discrepancy (which appears to have a "dose-response" relationship;

see Figure 12, Chapter Four) may add weight to the argument that anxiety disorders in childhood and adolescence are usually transient disorders. If a disorder is stable and symptoms occur continuously over a year or more, then we would expect limited differences between point and twelve month prevalence.

As the effect of different prevalence criteria have been investigated within the same sample (e.g. the EDSP in Dresden, Wittchen et al. 2000) and robust prevalence has been reported for different anxiety disorders in samples that use the same prevalence criterion (Gallagher, 2008), we can conclude that these discrepant findings are not due to true differences in the prevalence of anxiety in the samples compared. Diagnostic interviews have a minimum duration as well as impairment criteria; for example generalised anxiety disorder symptoms must have been present for at least three months, specific phobias symptoms must have been present for at least six months. Consequently, it is important to be clear that this assertion is not suggesting that these transient disorders are not significant, distressing, and associated with functional impairment for children. However it does suggest that the twelve month prevalence data be treated with some caution, and adds weight to the contention that anxiety disorders are present in a large number of children, most of who will experience spontaneous remission relatively quickly and may not be at risk for future disorders.

One of the main difficulties with this robust finding is that the use of differing prevalence criteria precluded the combination of data sets, as this difference is activated during the interview and unless multiple interviews are used then this data cannot be deconstructed. Agreement on the prevalence criterion that allows sufficient reliability but also sufficient sample size is important in helping prospective studies to produce comparable data. This would allow the amalgamation of data sets as originally proposed in this thesis; in these sets stringent prevalence criteria can be applied and the combination of large samples ensures that the anxious sample is large enough to carry out appropriate analysis.

Onset data.

The use of different prevalence criteria (twelve month versus three month versus point prevalence) contribute to difficulties in comparing prevalence, course, and outcome of anxiety disorders in different studies. Patterns in onset can also be affected by these inconsistencies as studies may provide onset data based upon a new disorder in the

last twelve months (Dresden and New York) or since the last diagnostic interview (Oregon and Bremen studies) or alternatively stipulate that the disorder must be present at the time of interview (ALSPAC). The biggest problems, however, are that, until the current study, only onset between two time periods has been reported, large age ranges have been explored as a single group, and there has been very little exploration of the changing patterns of onset for the different anxiety disorders. It does not appear to be the case that the incidence is as clearly affected by the different criteria as prevalence has been shown to be. Extremely low onset was reported in the Oregon study of 14 to 18 year olds and these researchers include all symptoms in the preceding 15 months - a similar time frame to Dresden and Bremen which also examined onset in adolescence over a period of 12-24 months but found 13 times the number of new cases. The TH2K study in Holland on the other hand found more moderate onset in this period (under half of the Bremen and Dresden incidence) with a peak in mid adolescence. There are no clear answers for this discrepancy; however the diagnoses included in "any anxiety disorder" may have been instrumental in these differences. Unfortunately this is not clear from the published data. The Great Smoky Mountains study report age at onset for the sample at age 21 years and report very early onset for a number of anxiety disorders, with a median age at onset for any anxiety disorder of only seven years. Specific phobia and separation anxiety have a median age at onset of six years, but also the median onset for social anxiety and generalised anxiety is only nine years old. It is unfortunately unclear from what data these findings were calculated from as the study began collecting data when the children were nine years old; it does however, offer support for the picture of onset we see in the ALSPAC data in an adult sample. The late starting age of most of the samples is a serious issue for determining age at onset from the prospective data.

The existing onset data are unimpressive in describing onset in adolescence. The new ALSPAC data confirm the cross-sectional findings regarding the onset of separation anxiety and specific phobia in early childhood and support the contention that these disorders have a short window of peak onset (particularly separation anxiety) whereas other disorders (such as generalised anxiety disorder) appear to have a much longer window, supporting the findings of Costello and colleagues (in prep) regarding the periods that might be considered "peak" onset. The New York data suggest that adolescence may well be the key period of onset for social anxiety and that this is consistent from late childhood into adolescence, perhaps suggesting social anxiety also has a wide window of onset. It is important to note that many of

the studies reviewed begin data collection late in the child's development meaning that many apparently new cases may not represent the first time that the disorder has been present - missing "peak" onset for early disorders such as separation anxiety and specific phobias. The patterns illuminated by the ALSPAC sample over three follow ups in childhood and early adolescence support the contention of peak onset of many anxiety disorders in childhood that was reported in the Great Smoky Mountains data.

Cumulative incidence (onset curves) from survival analysis have been used in the Dresden publications; using this method to compare data from the ALSPAC, New York, and Dresden studies shows clear patterns of onset in social and generalised anxiety despite differences in the magnitude of prevalence in the different studies. When excluding the New York data and looking at all anxiety disorders we can see that, after 14 years of age, onset appears to flatten significantly suggesting that childhood and early adolescence are the key developmental stages for the onset of anxiety. When examining the New York data alongside the Dresden and ALSPAC findings social anxiety shows incidence continuing to increase into late adolescence whereas generalised anxiety flattens off. These synthesised data support the contention that anxiety disorders have their peak onset in early life. The data regarding course, stability and outcome, however, suggests that as these numbers fall the majority of these disorders will remit.

Course and stability.

Exploring the course and stability of anxiety disorders as a group of disorders offers a clear and consistent picture across different samples and age ranges. When we use the Dresden data in adolescence and the ALSPAC data in childhood we can see that the vast majority of identified anxiety disorders are incident disorders in both younger and older samples. When looking specifically at the anxious children in three samples (Dresden, Bremen, and now ALSPAC) we can see that they have all reported stability of close to 20% over the course of one to three year follow up. Similarly robust findings can be seen when stability is measured by reporting those who meet diagnostic criteria at two or more follow ups. It is reported that 30-40% of childhood and adolescent disorders can be classified as stable according to the Great Smoky Mountains Study (Bittner et al. 2007), the ALSPAC data, and in an adolescent-to-adult sample in the Dresden study, (Beesdo-Baum et al. 2009).

Stability appears greater for this sample of the New York cohort in childhood and adolescence (over the three year follow up) than from adolescence into adulthood. This is to be expected in the light of the falling prevalence of overanxious and social anxiety disorders in adulthood, as the majority of early anxiety disorders remit and fewer new cases have their onset. Overanxious disorder in particular appears to have limited stability when adulthood generalised anxiety is the outcome. Looking at the heterotypic continuity reported in the Dresden study for generalised anxiety disorder (Beesdo-Baum et al 2009) and Great Smoky Mountains study for overanxious disorder (Bittner et al. 2007) it is possible that these "worry" disorders may well have greater heterotypic predictive power (being predictive of other forms of psychopathology and other anxiety disorders). This could, unfortunately, not be investigated in the current study.

Wittchen et al. (2000) first suggested the theory that anxiety disorders wax and wane over the course of childhood and adolescence, appearing transitory but conferring increased risk for adult mental disorders - other anxiety disorders and also depressive disorders. This was later given additional credence from the ten year follow up data from the Dresden study where Beesdo-Baum et al (2009) reported that 35% of cases of social anxiety diagnosed at 14 to 17 years are present at ten year follow up. When we look at the relationship with other mental disorders they report an additional 29% meeting criteria for any anxiety or depressive disorder and a further 19% meeting criteria for another form of psychopathology. Therefore, only 13% of adolescents diagnosed with social anxiety are diagnosis free at ten year follow up. Generalised anxiety in adolescence is associated with 100% stability over the ten year follow up, but the proportion of stable cases of generalised anxiety and other mental disorders are not reported, most likely due to the small sample size (N=3). We can see this pattern to some extent in the ALSPAC data where a third of the stable disorders remitted and then reappeared in adolescence. When we include heterotypic continuity in this way, or look at anxiety disorders as a whole group, the more moderate stability and favourable outcomes shown from the New York data looking solely at homotypic stability look less encouraging.

Summary of stability synthesis.

There is a great deal of consistency in the findings relating to the stability of anxiety disorders in the synthesised data. The ALSPAC data demonstrates this level of stability to be present in a much younger sample than has been examined before. It

appears that around one in five cases of anxiety in childhood and adolescence are stable in the short term and that a larger proportion (over a third) remit and then reappear, demonstrated in the greater degree of stability calculated over multiple follow ups, often covering longer periods of time. Stability of both social anxiety and overanxious disorder were shown, in the New York data analysed in this thesis, to be greater in adolescence with both disorders remitting in the majority of cases in adulthood; they may well however, be associated with other anxiety disorders or other psychopathology. The Dresden data provides interesting findings regarding the association between these early anxiety disorders and later psychopathology. Homotypic continuity in the study is moderate and comparable to those proportions reported above; however, when we look at who is "well" in adulthood ten years later there are very few of the sample who do not meet criteria for a mental disorder of some kind. The data analysed here could not examine these patterns but suggest that even when we use the most stringent diagnostic homotypic continuity criteria a substantial proportion of anxiety disorders have poor long term outcomes.

Outcome.

As very few studies follow children or adolescents into adulthood, the data for studying outcome are also somewhat limited. Anxiety disorders, however, have been shown in the existing literature and in this thesis to be a prevalent mental disorder in childhood and adolescence, which in most cases appear to remit by adulthood but are stable in a sizable minority of cases across adolescence (overanxious and social anxiety in particular). Adult follow up of adolescent disorder suggests that early anxiety is harmful in a number of domains that include the risk of future psychopathology (Woodward and Fergusson, 2001). The conclusions of the Gallagher (2008) review included the contention that most adult anxiety disorders had their first onset in childhood or adolescence, based largely upon the findings from the original New York sample and the Dunedin data. The new finding from a large UK cohort, reported in Chapter Two - that only adolescents who met criteria for an internalising disorder at both follow ups (stable disorder) were at increased risk of internalising disorders in adulthood (forty years later) provides an interesting context to examine findings regarding outcome and risk associated with the early onset of anxiety disorders, (Colman et al. 2007).

The consistent finding that anxiety disorders are prevalent in childhood but most often remit in the short term, and are even less stable into adulthood should not be ignored

as robust predictors of adult disorder are required for effective intervention. The data presented here suggest that early disorder itself may not be a good enough predictor of adult anxiety disorders. The lack of a clear relationship in the New York data is troubling in light of the Mian and colleagues (2011) model which suggests that early symptoms are the best predictors from early development of later anxiety disorder status. This is perhaps because early childhood is a period where anxiety symptoms are less common and, therefore have a stronger predictive relationship. It is also clear that the self report measure is a general measure of anxiety symptoms and the homotypic continuity examined here is less useful in predicting outcomes. Pine and colleagues (1998) used the whole sample of the New York study to conduct a follow back analysis. Despite finding that 98% of adults with social anxiety were diagnosed at an earlier wave of data collection they urge the reader to exercise caution in their interpretation. This is due to the extremely high prevalence of anxiety in the New York sample and the moderate to low stability of many anxiety disorders, which led to a large proportion of the sample receiving a diagnosis of an anxiety disorder at some point in the study. Unfortunately cumulative prevalence is not reported to tell us exactly what proportion received a diagnosis over the whole time frame; however it is presumably high from the high prevalence and moderate stability reported. This supports the contention that early anxiety may not be a good predictor of adult anxiety disorder, as they can make up nearly a third of the sample in some cases and the majority of these disorders remit. This is also supported by the significant but modest Odds Ratios with those with early onset anxiety at two to three times the odds of suffering from an anxiety disorder in adulthood as those without an early disorder. Better predictive value is ascertained from rating anxiety disorders on severity; where severe disorders confer up to 11 times the risk (Pine et al. 1998).

The younger sample examined here from the New York study showed that overanxious/generalised anxiety and social anxiety demonstrated the pattern described by Pine et al (1998) in the sample as a whole. Although a significant proportion of adult disorders begin earlier in life, most childhood and adolescent disorders have remitted. The proportion of adult disorders with early onset was, however, more moderate than the earlier reported findings for the whole sample. Unfortunately we were not able to examine these patterns in other anxiety disorders. The homotypic stability of anxiety disorders reported in the ten year follow up of the Dresden sample are somewhat higher, suggesting that anxiety in adolescence might be more closely related to anxiety later in life than childhood disorders. This was not,

however, supported in the New York data where late adolescent disorder appears less stable This may relate to the findings of Costello and colleagues (in prep) who found estimates of anxiety in adolescence much more precise and reliable with much smaller confidence intervals than estimate in childhood samples. Issues of the "stability" of disorders may reflect issues with the measurement in anxiety in younger populations as much as the "true" course of anxiety. However, some of the preliminary data from the New York analysis reported here actually suggests that adult social anxiety and overanxious disorder is more commonly diagnosed in childhood than later in adolescence. This presents a somewhat confusing picture, but may suggest that disorders with an earlier onset can have less favourable outcomes, as reported by Kessler et al. (2007).

Results in the wider context.

More recently the literature relating to childhood and adolescent anxiety often begins with statements regarding the high prevalence, early onset, persistent course, and poor outcomes of anxiety disorders. This thesis, although in part aiming to provide more clear evidence to support some of these claims, and direct the reader to the importance of a better understanding of anxiety in younger populations, it simultaneously hopes to highlight some of the complexities of the descriptive epidemiology of anxiety. This is in part due to the complexity of measuring anxiety disorders in these populations and the different picture of anxiety that is gained from examining its trajectory at different points in the lifespan. By determining the patterns of anxiety in time and space more accurately it is hoped that resources can be used more effectively to identify risk factors for persistent anxiety with a poor outcome.

So what do the collected findings from the well designed, prospective longitudinal studies presented in this thesis tell us about the descriptive epidemiology of anxiety disorders that we did not already know from cross-sectional and/or self report data and what findings do they merely confirm?

In terms of prevalence the extremely high prevalence cited (usually one in ten children) although a fairly robust finding when asking about symptoms in the previous 12 months, it is clear that a much smaller number of children suffer from anxiety at any given time when we look to more accurate point prevalence data and that the transience of disorders also finds some support within these data. This finding is replicated in adult data where point prevalence was reported at less than half of the twelve month prevalence (Alonso et al. 2004). Many children may forget about

previous diagnoses when asked about lifetime, and it is likely that when we try to measure symptoms from longer than three months prior to the interview, a degree of overestimation may be possible, as respondents struggle to remember whether symptoms met criteria. The reduction in reliability when using longer windows to assess prevalence has been documented previously (Angold et al 1996). The consistent discrepancies either point to overestimation or that anxiety diagnoses are transient over a 12 month period.

The findings regarding the patterns of prevalence and new onset support the contentions made from retrospective and cross sectional studies regarding the age at onset for anxiety disorders being particularly early for separation anxiety and specific phobia and show that even for the disorders that are more rare and associated with later onset there are significant cases appearing in very young samples. Age at onset data is still very limited in prospective data for many of the reasons outlined earlier in this discussion. However, the significant trends found in patterns of onset using the ALSPAC data provides robust age at onset data in a sample that has previously been explored only retrospectively or in clinical samples and support the very early onset of anxiety disorders reported in the Great Smoky Mountains study (Costello et al. in prep). In their review of cross sectional data Ost & Treffers, (2001) suggest mean age at onset for social anxiety to be between 15.7 and 20 years; this is contested by the prospective findings from the New York study which suggest the onset in this sample, which follows the young people into early adulthood was much earlier. Separation anxiety patterns of onset in the ALSPAC data similarly suggest an earlier onset than has previously been suggested in cross sectional studies (Keller et al 1992) and this is supported by the adult data from the Great Smoky Mountains (Costello et al. in prep). Although previous cross sectional findings which use enhanced methods for determining age at onset to examine specific phobias and social anxiety report remarkably similar “mean age” to support the findings from the ALSPAC data (Giaconia et al. 1994; Wittchen et al 1998; 1999).

The use of standardised diagnostic interviews to determine disorder rather than measures of symptoms is far more precise and ensures that these disorders are of sufficient duration and associated with impairment. Self report data from parents has suggested that internalising symptoms are “persistent” or at least predictive from preschool to preadolescence in between 38 and 50% of cases, suggesting a high degree of stability in these symptoms (Briggs-Gowan et al. 2006). We cannot

comment on preschool data as diagnostic interviews with this sample have not been carried out, however, the persistence of diagnosable anxiety disorder between seven and ten appears to be low in comparison (one in five) and this figure has also been repeated in adolescence (Wittchen et al. 2000; Essau et al. 2002). Persistence of diagnosable anxiety in young samples, therefore, appears relatively low compared to when using parent reports of symptoms. It must be noted that this study is only able to examine homotypic continuity, so those who are diagnosis free may be suffering from another mental disorder. In a clinical sample the persistence of anxiety diagnoses over a period of three to four years has previously been found to be around a fifth of cases (18%; Last et al. 1996) which is remarkably similar to the stability or persistence reported from the ALSPAC data, Dresden study (Wittchen et al. 2000) and Bremen study (Essau et al. 2002). The transience of anxiety disorders appears to be confirmed by prospective data in large community samples; however, where these data really add to the picture of the descriptive epidemiology of anxiety disorders is in the long term follow up into late adolescence and in some cases adulthood as described above.

Retrospective findings that adults with anxiety report the onset of their symptoms in early life (Kessler et al. 2005) are supported to a degree by the prospective longitudinal findings. However, the picture is far more complex. Prevalence of anxiety in adulthood in a large US sample was found to be 18% using a 12 month criterion (Kessler et al. 2005) and 14% in a large European study (Alonso et al. 2004). These represent high proportions of the adult population. Point prevalence data for a large adult sample in Europe is reported at 6% (Alonso et al. 2004), which is substantially higher than the point prevalence of anxiety in childhood or adolescence reported in the ALSPAC sample. Magnitude of prevalence aside, we know that there continue to be new cases of most anxiety disorders (with the exception of separation anxiety) throughout the life span and the current New York data suggests that over half the cases of generalised anxiety disorder and nearing two thirds of the adult cases of social anxiety had their first onset in childhood or adolescence. This does, however, leave a larger proportion to be categorized as “adult onset” than reported in the early adulthood Dunedin data or the whole sample New York analyses. It is possible that a large number of cases had early onset but due to their transience were not picked up in the period of data collection, were forgotten, or that first onset was prior to the first diagnostic interview and then latent or subthreshold until adulthood. These estimates may, therefore, be conservative.

Colman and colleagues' (2007) study of internalising disorders at 40 year follow up suggest very few cases of adult onset of severe disorder (less than 3%) and even for moderate disorders (less than 12%). However, the Dunedin study with its multiple follow ups that are closer together, so decreases the chances of cases being "missed", report that childhood onset decreases as the sample get older (80% at 21 years of age, 65% at 26 years of age, 40% at 32 years of age). This pattern suggests that there is significant onset of anxiety disorders in later adulthood. It could be that there are two types of anxiety sufferers; those who have early onset and wax and wane through childhood and adolescence with a substantial proportion with a stable anxiety disorder, but for whom the majority are diagnosis free in adulthood, and those without anxiety in early life and pure adult onset. This group may have anxiety with a different aetiology and be more closely related to environmental/social factors or events rather than temperament and early experiences. The evidence that early psychopathology has particularly poor outcomes could be seen to support this (Kessler et al. 2007). The lack of studies with multiple follow ups in adulthood, however, precludes further examination of this hypothesis.

Implications for methodology.

The ALSPAC data regarding patterns of prevalence and onset fully support Beesdo-Baum et al. (2009) contention regarding the applicability of distinct anxiety diagnoses to a sample of children as young as seven. The temporal trends are clear and significant and would be unlikely to emerge if all anxiety disorders were measuring similar constructs or symptoms.

There are a number of reasons why this thesis was not able to answer the research questions about the epidemiology of anxiety disorders that it set out to answer in the manner that was intended. Firstly, the difficulties in gaining access to longitudinal prospective data that is very expensive to collect and can be used to answer a plethora of research questions relating to psychopathology, prevented the planned breakdown of "raw" diagnostic data which would have allowed more synthesis of data. Secondly, despite a vast amount of diagnostic data having been collected around the world, the complexities of measuring anxiety in child and adolescent populations and the many differences in the design of the studies means that comparison of the available and published data is challenging. Some of these challenges have already

been discussed in some detail earlier in the discussion. The main challenges to making sense of the plethora of data are the changing prevalence criterion, changes to diagnostic categories, the attrition of those who are more socially disadvantaged and anxiety disordered, and the small sample of anxious children that are left even when we use extremely large birth cohorts. There is also a distinct lack of data on young children and studies that continue to follow children past adolescence.

The use of 12 month prevalence criterion appears to be common in prospective studies (e.g. Christchurch, Dresden, Dunedin, and New York) however, with the finding of Angold et al (1996) that using greater than three month prevalence decreases reliability has led to the Great Smoky Mountains to report three month prevalence, and the Oregon study use point prevalence. Even with the raw data it would not be possible to combine across these studies as the difference lies in the way that the participants are asked the questions. Although 12 month prevalence may be less reliable, the increased estimates it provides allow analysis of a larger sample of anxious children, (e.g. exploring patterns of continuity within individual anxiety disorders and examining gender differences which were not possible with the ALSPAC data due to small numbers). The "subthreshold" disorders may well be important but it is important that they are correctly identified and dealt with as such. The change in prevalence criterion appears to have little impact on the calculations of stability or course of anxiety disorders, suggesting that the choice to use this criterion may affect only the prevalence estimates, which appear to be robustly affected by the application of such criteria.

Another factor affecting the precision of estimates of prevalence, onset, stability and outcome may well be the representativeness of the samples - even in large birth cohorts such as the ALSPAC study. The analysis of missing data in prospective studies is somewhat lacking and inconsistent in its findings. The New York data report drop out of the most disadvantaged of their cohort and so took steps to recruit to fill this gap (Cohen et al. 1993). Representative birth cohorts with wide ranging demographic data offer a unique opportunity to examine the difference between families who choose to take part in diagnostic interviews. Dunedin in New Zealand report no demographic differences apart from more single mothers in the small proportion of the birth cohort who did not take part (14%; Anderson et al. 1987); however, the ALSPAC cohort in the UK shows a much larger proportion of families choosing not to complete the diagnostic measure (54%) and, as has been reported

previously (Wolke et al 2010), non-completion is associated with social disadvantage in a number of domains. Some studies have found attrition to be unrelated to diagnostic status (e.g. Great Smoky Mountains Study; Bittner et al 2007) but the ALSPAC data demonstrated that anxiety status was associated with drop out even when social disadvantage was taken into account. The Dresden study have shown specific phobia to predict drop out (Bruckl et al. 2007), suggesting that anxiety may well be a predictor of drop out and further impact upon the epidemiological picture, particularly of the stability and outcome of anxiety disorders.

Figure 1 (also 9) demonstrates the lack of overlap in studies of childhood and adolescence; there are many studies which collect these data but comparisons of different samples at different points in development are not as straightforward as might be hoped due to the reasons outlined above and that data are mostly available for a short window in later childhood and adolescence with relatively few in middle childhood, none in early years to examine the earliest cases of onset, and even fewer with data into adulthood in order to examine long term outcomes and distal risk from childhood anxiety. Studies that collect data from birth into adulthood often appear to see late childhood or early adolescence as the key period to examine mental disorders; however, data for these earlier time points may be warranted due to the extremely early onset of separation anxiety and specific phobias, and to answer the question regarding whether the early onset of many adult disorders is missed in the early years. There are now standardised diagnostic tools to establish diagnostic status in children aged two to five years (The Preschool Age Psychiatric Assessment; Angold, Egger, & Carter, 2007)

Clinical Implications.

The clinical implications of the data presented and synthesised here are limited. However, they are often cited in support of the direction of clinical resources and so this section will discuss the possible implications of the current picture of anxiety and raise questions regarding the feasibility of a population based approach or a “high risk” approach (Rose, 1992) to the prevention of anxiety disorders and the identification of those requiring intervention.

So is early anxiety a useful predictor of adult anxiety? If it is can we intervene successfully? In the whole sample analysis of the New York data (Pine et al 1998)

and the Dunedin study (Gregory et al. 2007) although early onset was present in the vast majority of adult cases both these studies report extremely high prevalence and moderate stability of anxiety disorders. Unfortunately neither study reports cumulative prevalence; however, we can assume from the available evidence from prevalence and stability data that it was high. So although a substantial proportion of adult disorders have their first onset early in life, most cases of anxiety disorder that are identified early will remit. The adult population is smaller and so the percentages can become confusing. When we look at actual sample size in these studies they are small, which is why the amalgamation of data sets is vital to gaining a better understanding of the patterns in specific anxiety disorders and their relationship to other disorders. If we combine across multiple follow ups then we see the same patterns; there is a sizable proportion of chronic sufferers, and the large pool of anxious youths contribute to the adult sample more than would be expected by chance, but not necessarily at a rate that makes early anxiety a good predictor of later anxiety status. Therefore, due to their transience, screening for mental disorders may not be a useful method of determining the risk of later disorder and any required intervention.

The multiple follow up studies suggest that anxiety disorders are "stable" (i.e. present at two or more follow ups) in around a third of cases (or more) in later childhood and adolescence, the fact that these studies use diagnostic interviews means that we know that these are of suitable duration, severity and impact upon the individuals functioning to suggest that intervention would be required and helpful in many cases. It would also be likely that intervention could have long term impacts on the prevalence of anxiety in adulthood as we know that in many studies despite actual number being relatively small, over half (and in some studies as many as 98% of cases) have been reported to have their onset early in life. It is also important to look to studies that have looked at prediction of other mental disorders and heterotypic continuity which suggest that early anxiety is a predictor of other mental disorders and other forms of anxiety which it may be possible to prevent with timely and effective intervention in childhood or adolescence (Beesdo-Baum et al 2009; Woodward & Fergusson, 2001)

The acceptance of claims regarding the extremely high prevalence of anxiety, its early onset, and malign outcomes ignores the subtle and complex trajectory that anxiety takes, and may well be as erroneous as earlier claims that anxiety is transient in early

life and can be ignored. Employing the most stringent diagnostic criteria, increasing awareness of the effects of the prevalence criterion employed, and recognising the effects of drop out on large longitudinal studies can help this more nuanced view of anxiety disorders be explored and examined. Most cases of early anxiety appear to remit but there are a consistent proportion of those who are suffering chronic anxiety through their early development, and some whose anxiety appears to follow them into adulthood. It seems important that this smaller population are correctly identified and intervention offered to have an impact on the burden of disease. This would suggest a more specific "high risk" strategy than simply identifying those at risk of anxiety disorders. We are not yet at a stage where we are able to accurately identify those who will go on to develop anxiety disorders, so we are not yet able to accurately identify high risk "subgroups" within anxious populations. Current examples of taking a "high risk" approach include identifying children who exhibit behavioural inhibition (Rapee, 2002). However, as with anxiety disorders themselves, a high proportion of these toddlers will not go on to develop anxiety. Is this strategy precise enough to justify the expense of intervention and the stigmatisation of the young child as "at risk" of mental disorder?

If, in answer to the difficulties in identifying those at risk early on we argue for the screening of young children for anxiety disorders we may well reveal an enormous sample of young people – do we have the resources to intervene in all cases and more importantly should we? It seems clear that if we were to screen groups of children then we would not be able to use such time intensive and stringent methods as diagnostic interviews and would, therefore, find substantial proportions of children and young people meeting criteria for anxiety disorders. The use of population wide prevention programmes (such as FRIENDS) in order to cut out screening and reach all young children without stigmatising could, therefore, be argued to be the best approach and has been rolled out in Australia and is beginning to be used in other parts of the world. The rationale for such programmes often includes citation of the 12 month prevalence studies that show 10 to 20% of young people suffering from an anxiety disorder. It could be argued that there are a number of difficulties in the accuracy and reliability of these figures for supporting this approach (Angold et al. 1996). The results from the Dresden study, however, suggest that adolescent anxiety disorders may have multiple pathways leading to poor outcomes, and the Dunedin data strongly links treatment seeking anxiety disorders in adulthood to early onset, providing support for this use of resources. There is no available evidence that the

prevention programmes reduce anxiety in adulthood, only in childhood and adolescence (due to the relatively recent set up and evaluation of the projects) – is it possible that as most childhood anxiety disorders are remitted by adulthood that we could be removing an "inoculation" effect of experiencing anxiety early in life? Or is it more likely that by taking a population approach and preventing distress and impairment from anxiety in childhood the prevention programmes will lead to adult outcomes?

This is of course not a question that can currently be answered. It is clear, however, that even when using the most stringent criteria (as seen in the ALSPAC data presented in this thesis) a substantial proportion of children meet diagnostic criteria in the course of their early development, and of those who do not, evidence is emerging that a sizable proportion suffer impairment from the subthreshold symptoms of anxiety (e.g. Wille, Bettge, Wittchen, Ravens-Sieberer & the BELLA study group 2008). Is it not, therefore, ethical to attempt to identify and offer the effective interventions that have been developed for such children? In order to do this we would need to direct resources to better screening and education for parents, health and education professionals regarding identifying young people's anxiety.

Limitations.

One of the major limitations of the analysis of stability and outcome is that despite the large sample size from the ALSPAC data and the moderate sample size for the New York data when we begin to look at determining estimates from the anxious sample they are relatively small. This may provide an argument for using more relaxed prevalence criterion, or including a measure of subthreshold disorders in order to be able to study the course and outcomes of children suffering from anxious symptoms and associated impairment. Combining data sets would allow us to get larger samples without compromising the precision of our estimates but this is not currently viable, as the current project testifies. The large confidence intervals in the New York data are due to the relatively small number of children falling into each disorder, and caution must be taken when interpreting results from such small samples. Appendix Three which illustrates the numbers involved in the New York analysis of course and outcome attempts to highlights this problem, and if we look to the Dresden data regarding generalised anxiety disorder we can see that although 100% continued to meet criteria for a mental disorder, as this is a relatively rare disorder in both

childhood and adulthood the actually sample size is three, despite the moderate cohort size (N= 1035).

It would be expected when we look to the vast number of prospective studies that have taken place around the world that the data to answer the most simple questions would be readily available and that it would be relatively easy to combine samples that use standardised measures in order to create adequate sampling; this thesis is testament to the fact that it is not at all easy due to the many methodological differences and logistical difficulties described above.

Due to the data for only two anxiety disorders being released from the New York study and the small numbers of anxious children in the ALSPAC sample this thesis has not been able to add to the understanding of the temporal patterns of prevalence, onset of different disorders and the risk conferred from many early anxiety disorders (e.g. separation anxiety and specific phobia), for other mental disorders later in life. There is strong evidence from the Dresden study that separation anxiety in early life is a strong predictor of other anxiety disorders later in childhood and adolescence with a steadily increasing risk of anxiety in comparison to children without the disorder (Bruckl et al. 2007) and evidence that heterotypic continuity of many anxiety disorders is high, with people reporting experiencing symptoms for the majority of the ten year follow up (Beesdo-Baum et al. 2009). Investigation of the relationship between early anxiety and later depressive disorders that has also been demonstrated in the Dresden sample was also not possible for the same reasons. This is an important area of anxiety disorders research that appears to be growing and the current data from the Dresden study suggests that the relationships between anxiety and psychopathology is specific (as reported in the New York data, Pine (1998)) but also confers risks for other mental disorders later in life (Beesdo-Baum et al. 2009) and this has big implications for prevention and intervention. It is unfortunate that further examination of these relationships was not possible in the current thesis, as only examining homotypic continuity seriously limits the applications of the longitudinal analyses conducted.

Another similar limitation, which may also be considered strength, is the use of strict diagnostic thresholds rather than examining data at different levels of severity. There is discussion and preliminary evidence that there are also a group of children who do not meet diagnostic criteria, but are suffering serious impairment from their anxious

symptomotology, they are ignored by the current study (Angold & Costello, 1995; Costello et al. in prep; Wille et al. 2008). However, the use of a method which uses a high threshold for caseness can also be very useful when arguing for the redirection of resources to the children and adolescents most in need. The very high prevalence estimates sometimes cited in relation to anxiety may be difficult for policy makers to make sense of and appear to pathologise a large proportion of children.

The analysis completed on the new data could have used more complex modelling of the data to test the relationships between early and late anxiety, but instead uses descriptive statistics and Odds Ratios. This simple approach was taken because the complex nature of the confounding factors would have required extensive demographic data on the sample in order to make meaningful models. At this stage in understanding descriptive epidemiology of anxiety the use of complex models was judged to be less important than deconstructing the data to see what story they tell us about the distribution of anxiety disorders in time and space. The current methods were judged to be most appropriate from looking at the methods of other prominent researchers in the field (see for example, Dunedin study Gregory et al. 2007, GSMS Costello et al 2004) and appropriate literature on research methods (Kelsey, Whittenmore, Evans, & Thompson, 1996).

Future Directions.

Access to the adult data from the ALSPAC sample (at age 18) will soon be available and examining the outcomes for this sample will provide an interesting comparison to the existing studies for outcomes in adulthood. The planned metaanalysis of data proposed in this thesis appears an even more worthy endeavour when examining the current picture. Amalgamation of some of the large data sets reviewed would allow the planned comparisons of onset, stability, and outcome with large enough samples of anxious children and adolescents to look at heterotypic continuity across anxiety disorders even when using the most stringent criteria. Many of the studies described in this thesis are ongoing and more data is due to be released that will provide more pieces for the puzzle and almost certainly raise new questions.

Tracking the prevalence of anxiety is undoubtedly important for planning services and interventions, it is also important, however, in providing a standardised measure to determine the mental health of young people in society. If the increases reported in

the UK continue to increase then this may be indicative of the need for change in not only mental health services but in wider social policy. Standardised criteria allow these changes in cohorts to be accurately tracked and large birth cohorts offer a unique opportunity to understand the changes in anxiety diagnoses through the generations.

Work to prevent increasing childhood anxiety and effectively intervene for young sufferers is increasing around the world. In order to effectively deploy diminishing resources it will be crucial to have accurate models of risk for anxiety disorders, and specifically for chronic anxiety, to target resources efficiently. Recent models suggest that child factors (anxious symptoms and anxious temperament) are the best predictors of childhood disorders compared with social and environmental factors (Mian et al 2011). The continued investment in research to better understand these early manifestations of anxiety, therefore, appears a valuable approach in attempting to better understand the risk and how to prevent poor outcomes for young children. Looking at impairment associated with symptoms that do not reach diagnostic thresholds will also be an important area for future research.

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Appendix One - Search, Inclusion and Exclusion criteria of Gallagher (2008)

Search Criteria.

Studies relevant to this review were identified using a number of search strategies. First, electronic databases were searched using the search terms [(CHILD* or ADOLESCEN*) and (ANXIETY* or PSYCHIATRIC* or DISORDER) and (EPIDEMIOLOG* or PREVALENCE or INCIDENCE or ONSET or LONGITUDINAL). PsycInfo (1906 -2006) and Medline (1950-2006) were both searched using these terms. In consultation with experts in the area, a list of relevant papers, authors working in the field, and ongoing studies was also compiled in order to try to access unpublished data. Finally, the reference lists of all relevant papers were scrutinised for further relevant studies, and a manual search was conducted of The Archives of General Psychiatry for issues not available for electronic searching (1959-1993).

Inclusion Criteria.

Studies were included if they had a psychiatric, epidemiological focus, conducted the first diagnostic assessment before the age of 18, and followed up the participants at least once with a further diagnostic assessment. It was a requirement that the diagnosis be made through the use of a standardised diagnostic interview, (either with the parent or child or both) and that it assess current diagnoses. Studies either employing large community samples or a two stage screening process were included. Two stage studies test a large sample using a screening tool and then carry out further diagnostic assessment in a high risk sample and a control sample, selected from the screening, in order to weight the prevalence of diagnoses to the general population

Exclusion Criteria.

Studies were excluded if they used self-report measures to reach diagnosis because of the limited diagnostic validity. Studies where data were retrospectively reported were also excluded because of potential memory biases, which might lead to lack of reliability in determining accurate age at onset of symptoms and syndromes. Studies that reported diagnoses of “emotional disorders,” “neuroses” or “affective disorders” without reporting “any anxiety disorder” or specific anxiety disorders were also excluded. If anxiety disorders were only reported at one stage of the longitudinal design, these studies were also excluded.

Appendix Two: Prospective longitudinal studies identified for Gallagher (2008) review.

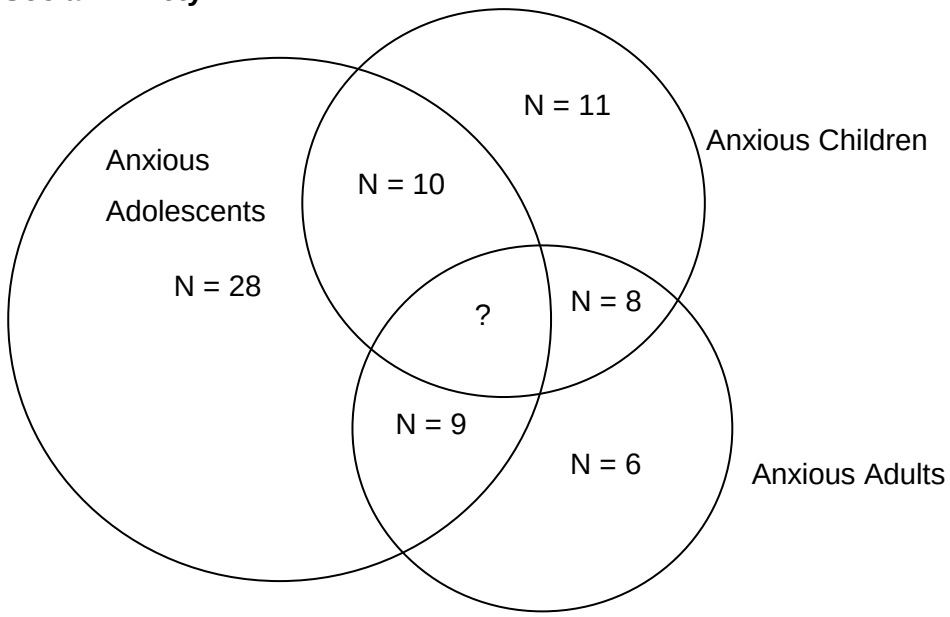
Study/Authors	Design	Data	Included/ Excluded
Bremen Adolescent Study (BJS.) Germany. *Essau (2005)* *Essau, Conradt & Petermann (1999)* *Essau, Conradt & Petermann (2000)* *Essau, Conradt & Petermann (2002)*	Diagnostic interviews in adolescence and 15 months later.	Reported for "any anxiety disorder" and specific anxiety disorders at T1 and T2.	**INCLUDED**
Christchurch Health & Development Study, (CHDS). New Zealand *Fergusson, Horwood & Lynskey (1993)* *Fergusson & Horwood (2001)* *Horwood & Fergusson (1998)*	Birth cohort study. Diagnostic interviews at 15 and 18 years old with both parent and child.	Reported for "any anxiety disorder" at T1 and T2	**INCLUDED**
Dunedin Study. New Zealand. *Anderson, Williams, McGee, & Silva (1987)* *Feehan, McGee, Raja & Williams (1994)* *Gregory et al (2007)* *Kim-Cohen et al (2003)* *McGee et al (1990)* *Newman et al (1996)*	Birth cohort study. Diagnostic interviews with children/adolescents at 11, 13, 15, 18, 21, 26, & 32	Reported for "any anxiety disorder" and (in some cases specific anxiety disorders) at baseline and six follow ups.	**INCLUDED**
Early Developmental Stages of Psychopathology (EDSP). Dresden, Germany. *Wittchen, Nelson & Lachner (1998)* *Wittchen, Stein & Kessler (1999)*	Standardised Munich CIDI used to reach diagnosis, followed up at 15 and 30 months.	Only data analysed & reported regarding anxiety disorders is for baseline.	**EXCLUDED**
From Boy to Man. Finland *Puura et al (1998)* *Sourander et al (2004)* *Sourander et al (2005).*	Uses self-report measures/medical records to determine diagnosis at follow up.	----------	**EXCLUDED**

Great Smoky Mountains Study (GSMS) USA *Costello et al (1996)* *Costello et al (1998)* *Costello, Mustillo, Erkanli. Keeler & Angold (2003)*	Overlapping cohorts using CAPA diagnostic assessment.	Reported for each age group and individual disorders at 9-13.	**INCLUDED**
Isle of Wight Study GBR *Graham & Rutter (1973)* *Rutter & Graham (1966)* *Rutter, Tizard, Yule, Graham & Whitmore (1976),* *Rutter, Tizard & Whitmore (1970)*	Diagnostic assessments (specially developed for this study) at 10-11 and 14-15.	Reports data for "emotional disorders" or "neurotic disorders" no data for anxiety disorders. (Anxiety disorders reported at baseline only)	**EXCLUDED**
Mannheim Study Germany *Esser Scmidt & Woerner (1990)*	Children interviewed using Isle of Wight interview at 8, 18 and 25.	Reports data for "emotional disorders" or "neurotic disorders" not anxiety disorders.	**EXCLUDED**
New York Longitudinal Study. USA *Cohen, Cohen & Brook (1993)* *Cohen et al (1993)* *Pine, Cohen, Gurley, Brook & Yuju (1998)* *Velez, Johnson & Cohen (1989)*	Overlapping cohorts design of children from 10-20 using diagnostic assessments at 2.5 and 8 year follow up.	Reported for "any anxiety disorder" and specific anxiety disorders.	**INCLUDED**
Ontario Child Health Study. Canada *Bowen, Offord & Boyle (1992)* *Boyle et al (1987)* *Offord et al (1987)* *Offord et al (1992)*	Single follow up on children from 4-11 (8-16 at T2)	Reported for "emotional disorders" at T1 and T2.	**EXCLUDED**
Oregon Adolescent Depression Project. *Lewinsohn, Hops, Roberts, Seeley & Andrews (1993)*	Single follow up on children from 14-18 after a year.	Point prevalence and lifetime prevalence at T1 and T2. ----------	**INCLUDED**

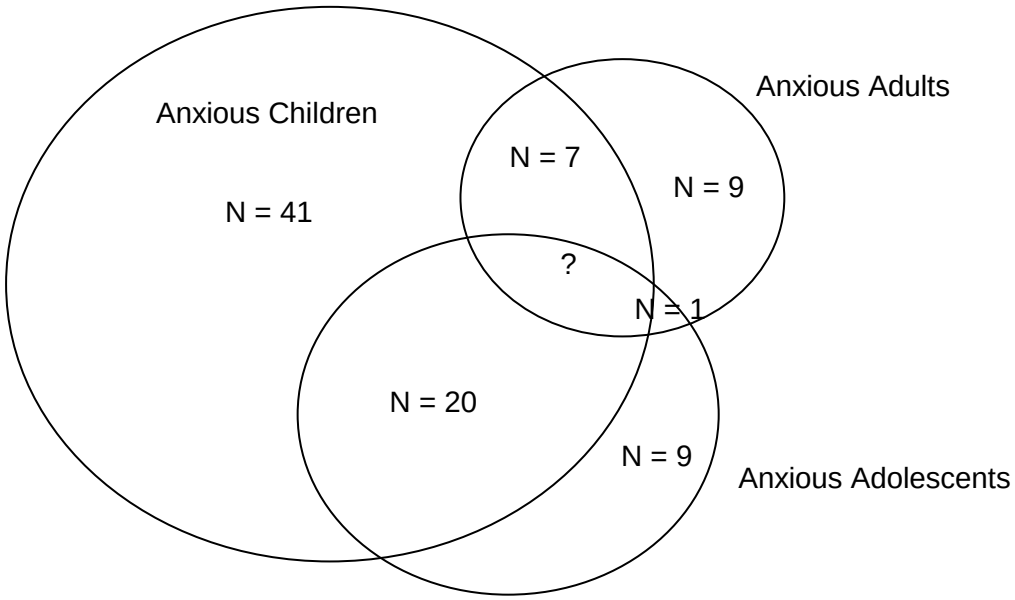
Psychopathology from Adolescence into Adulthood. Holland. Ferdinand & Verhulst (1995)	Self report data collected at two yearly intervals for eight years.		**EXCLUDED**
Taiwan Epidemiological Study of Mental Disorders. Taiwan. *Gau, Chong, Chen & Cheng (2005)*	Cohort of 12-13 years followed up using diagnostic interviews yearly for three years.	Reported for any anxiety disorders and specific anxiety disorders at T1, T2 & T3.	**INCLUDED**
TRAILS (Development of Psychopathology In Early Adolescence). Holland. *Oldehinkl & Ormel (EMBARGO*)	Uses self-report rather than diagnostic interview.	----------	**EXCLUDED**
Zurich Adolescent Psychology & Psychopathology Study (ZAPPS) Zurich Epidemiological Studies of Child And Adolescent Psychiatric disorders (ZESCAP) Switzerland. *Merikangas, Zhang, Aveneoli, Acharaya, Neuenschwander, & Angst, (2003)* *Steinhausen, (2006)* *Steinhausen & Winkler Metzke (2003)* *Steinhausen, Winkler Metzke, Meier, & Kannenberg, (1998)*	A longitudinal study using diagnostic interviews with parents of 7-16 year olds and adolescents at first follow up.	Only data analysed and reported is for baseline.	**EXCLUDED**

Appendix Three. Visual representations of the stability and follow back analysis in the New York data.

Social Anxiety



Overanxious Disorder



NB Circles areas are to scale in order to represent the number of people in each population, positioning however is merely estimated, as are the number in each group from the overlapping cohorts.