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Research report

Recent trends in the incidence of anxiety and prescription of anxiolytics and hypnotics in children and young people: An e-cohort study

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ABSTRACT

Background: Little is known regarding the recognition of anxiety in children and young people (CYP) in primary care. This study examined trends in the presentation, recognition and recording of anxiety and of anxiolytic and hypnotic prescriptions for CYP in primary care.
Method: A population-based retrospective electronic cohort of individuals aged 6–18 years between 2003 and 2011 within the Secure Anonymised Information Linkage (SAIL) Databank primary care database was created. Incidence rates were calculated using person years at risk (PYAR) as a denominator accounting for deprivation, age and gender.
Results: We identified a cohort of 311,343 registered individuals providing a total of 1,546,489 person years of follow up. The incidence of anxiety symptoms more than tripled over the study period (Incidence Rate Ratio (IRR)=3.55, 95% CI 2.65–4.77) whilst that of diagnosis has remained stable. Anxiolytic/hypnotic prescriptions for the cohort as a whole did not change significantly over time; however there was a significant increase in anxiolytic prescriptions for the 15–18 year age group (IRR 1.62, 95% CI 1.30–2.02).
Limitations: There was a lack of reliable information regarding other interventions available or received at a primary, secondary or tertiary level such as psychological treatments.
Conclusions: There appears to be a preference over time for the recording of general symptoms over diagnosis for anxiety in CYP. The increase in anxiolytic prescriptions for 15–18 year olds is discrepant with current prescribing guidelines. Specific guidance is required for the assessment and management of CYP presenting with anxiety to primary care, particularly older adolescents.

1. Introduction

Mental health issues are of growing concern and a source of controversy in children and young people (CYP) in the United Kingdom (U.K). They are associated with significant morbidity and have been found to contribute to adverse life outcomes (such as educational underachievement) and serious disruptions to CYP's lives and those of their families (Patel et al., 2007). It is estimated from Office of National Statistics population survey data that, at any one time, four per cent of CYP, have a clinically diagnosable or relevant emotional disorder (anxiety or depression; Office of National Statistics, 2004). Anxiety disorders are thought to be among the earliest psychiatric conditions to manifest with an estimated median age of onset of 11 years (Kessler et al., 2005). Earlier age of onset appears to be associated with greater severity and poorer long term outcomes (Ramsawh et al., 2011). Concerns are amplified by the persistence of childhood or adolescent mental health issues into adulthood (Costello et al., 2006) where up to a fifth of the adult population may be affected by a common mental disorder at any one time (McManus et al., 2009; Leray et al., 2011).

There are fears that we are medicalising unhappiness with consequent over diagnosis and excessive treatment (Dowrick and Frances, 2013). This is particularly relevant in CYP where there is a

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normal developmental range of anxiety-related phenomena (e.g. stranger anxiety, fear of the dark, existential questioning) as they develop cognitively and emotionally and engage with the world. Significant increases in the rates of psychotropic prescriptions in CYP have been found in America (Olfson et al., 2002), Europe (Steinhausen and Bisgaard, 2014) and the UK (Middleton et al., 2001; Rani et al., 2008) over the past three decades. Such findings contribute to concern over the medicalisation of normal human experience, particularly following the release of the Diagnostic and Statistical Manual of Mental Disorders 5 (DSM-5; American Psychiatric Association, 2013). This revision has been heavily criticised for pathologising normal human behaviour such as eccentricity, loneliness and sadness (Watts, 2012), and for its potential to cause excessive and inappropriate use of medication in children (Gaughwin, 2014).

Access to services in primary care represents a key factor in the management of CYP mental health issues. Research utilising routinely collected data in primary care in the UK has identified a fall in recorded diagnoses and rise in recorded symptoms of depression alongside an increase in new antidepressant prescriptions in both adults (Rait et al., 2009) and CYP (Wijaars et al., 2012). Adult data suggests that this recording behaviour is being applied to anxiety disorders (Walters et al., 2012); however there are currently no such data available on CYP and little is known regarding the use of anxiolytics and hypnotics in this population in this setting. There are no specific National Institute of Clinical Excellence (NICE) guidelines available for the management of anxiety in CYP. There are NICE guidelines for anxiety (which relate principally to adults; NICE, 2011), depression for CYP (which includes mixed anxiety and depression; NICE, 2005) and for the assessment and treatment of social anxiety disorder (NICE, 2013). These all highlight some considerations for the management of anxiety in CYP. Psychological therapies should be the first line of treatment. Pharmacotherapy should not be routinely offered to treat social anxiety disorder in young people and antidepressants should only offered for moderate to severe depression, in conjunction with psychological treatments. The relative effectiveness of psychological and pharmacological treatments for anxiety disorders in children and young people has been assessed in trials (RUPP, 2001; POTS, 2004; Beidel et al., 2007; Walkup et al., 2009). These findings suggest that CBT, sertraline and their combination are all possible options for the treatment of these disorders in childhood. However, uncertainties remain whether: there is an age below which medication is unsuitable; what the duration of treatment should be; and the impact of stopping a course of medication. These concerns, together with parental preference for psychological over pharmacological interventions for their children, are clearly reflected in these guidelines. There are no hypnotics or anxiolytics licensed in the United Kingdom for the treatment of anxiety in CYP. Hypnotics in CYP are only indicated for occasional use for night terrors and somnambulism (sleepwalking) and anxiolytics only to relieve acute anxiety (and related insomnia) caused by fear (e.g. before surgery) (British National Formulary Sections 4.1.1 and 4.1.2; British Medical Association and Royal Pharmaceutical Society of Great Britain, 2014).

This is the first study examining trends in the incidence of recorded: anxiety diagnoses, anxiety symptoms, mixed anxiety and depression, panic attacks/panic disorder and the use of hypnotics and anxiolytics in CYP in primary care using routinely collected data.

2. Aims

The aim of this study is to examine trends in the incidence of anxiety diagnoses and symptoms, recording of mixed anxiety and depression, panic attacks/panic disorder, hypnotic and anxiolytic prescriptions in CYP in primary care.

3. Method

3.1. Design

A retrospective electronic cohort study was conducted utilising the Secure Anonymised Information Linkage System (SAIL databank; www.saildatabank.com) developed in the Health Information Research Unit (HIRU) at the College of Medicine, Swansea University.

3.2. Ethical approval

Approval was granted from the HIRU Information Governance Review Panel (IGRP), an independent body consisting of a range of government, regulatory and professional agencies, which overseas study approvals in line with permissions already granted to the analysis of data in the SAIL databank (Lyons et al., 2009; Ford et al., 2009). We plan to follow the key points of the MRC/Wellcome Trust data sharing policy

3.3. Data source

The Secure Anonymised Data Linkage (SAIL) databank is an expanding data repository (over 2 billion records) of anonymised person based linkable data to support research. SAIL was established by the HIRU at Swansea University in 2004 and forms part of the Health e-Research Collaboration UK (HeRC UK), led by the Medical Research Council (MRC) and based in the Centre for the Improvement of Population Health through e-Records Research (CIPHER). CIPHER is a UK Clinical Research Collaboration (UKCRC) Public Health Research Centre of Excellence set within the Farr Institute at the College of Medicine at Swansea University. Policies, structures and controls are in place to protect patient confidentiality, along with a high performance computing infrastructure and a reliable matching, anonymisation and encryption process, which is achieved in conjunction the NHS Wales Informatics Service. Data are imported into SAIL via a split file approach, whereby demographic and clinical data are separated at source later to be rejoined fully encrypted with an allocation of a unique identifier. This split file method ensures anonymisation and confidentiality, whilst maintaining the facility of data linkage at the level of the individual to any of the datasets housed in SAIL (Lyons et al., 2009; Ford et al., 2009). This allows data from sources including general practice records, hospital admissions and demographic information to be linked at patient level whilst maintaining anonymity.

In this study data were utilised from: NHS Administrative Register (NHS AR) a register of all individuals registered with a Welsh General Practitioner or who have ever had contact with the NHS; General Practice Database (GPD) attendance and clinical information for all general practice interactions including symptoms, investigations, diagnoses and prescribed medication. Individual practices sign up, currently there are 195 practices (out of 474 in Wales) covering a population of over 1.9 million which contains regularly updated data; Welsh Index of Multiple Deprivation assigns all Lower Super Output Areas in Wales a deprivation score. This score is derived from eight separate domains of deprivation including income, employment and education.

The SAIL databank was interrogated using structured query language (SQL).

3.4. Study population and setting

Individuals aged from 6 to 18 years between 1st of January 2003 and 31st December 2011 were identified. Data collection began either six months from GP registration or at the study onset whichever was the later to exclude the risk of retrospective recording. Data collection ended at the end of registration with a SAIL supplying GP, date of death, 19th birthday or the study end whichever was the sooner. Individuals supplying a minimum of six months of data based on these criteria (and therefore registered with a SAIL supplying GP for a minimum of one year) were included in the cohort. Each individual could supply more than one period of data provided the above criterion were met. For each year, data were collected between the start and end dates identified when constructing the original cohort or, between the 1st of January and the 31st of December if an individual's period of data collection spanned beyond these dates.

3.5. Measures

Demographic information (age, gender, lower super output area based deprivation quintile using the Welsh Index of Multiple Deprivation) were collected. Age and residential information for each individual was collected based upon the onset of data collection for each year. Age was described according to categories of 6–10, 11–14 and 15–18 years in accordance with other studies of this type (Wijaars et al., 2012) except where numbers were small when 6–14 and 15–18 age ranges were used.

Other measures were taken from GP computer records using primary care Read codes. The Read codes and algorithms being used to identify a new episode of symptoms/diagnoses of anxiety have been developed and utilised in previous research (Supplementary Table 1) (Walters et al., 2012; John et al., 2015). These included GP recording of i) diagnoses of anxiety e.g. chronic anxiety, generalised anxiety disorder, anxiety state, ii) anxiety symptoms e.g. anxiousness, iii) mixed anxiety and depression, iv) panic attacks and panic disorders. We included emotional disorders with an onset usually in childhood but excluded codes for phobias, obsessive compulsive disorders, post-traumatic stress disorder, behavioural disorders, hyperkinetic disorders, conduct disorders and disorders of social functioning in keeping with other studies(Rait et al., 2009; Wijaars et al., 2012; Walters et al., 2012). We excluded adjustment disorders as conceptually they are an intermediate health condition between normal responses to stress and more severe emotional disorders such as anxiety and depression (Casey and Doherty, 2012). Annual prevalence of each subtype was measured. An annual prevalent case was defined as an individual with any record of a given subtype in a target year (Frisher et al., 2004). Cohorts for each year were interrogated to identify individuals with new (incident) diagnosis/symptoms of anxiety, mixed anxiety and depression and panic disorder/panic attacks defined as no record of a given subtype in the previous 12 months. Participants may have more than one episode recorded for each subtype as long a period of at least 12 months exists between entries in keeping with previous studies of this type (Rait et al., 2009; Wijaars et al., 2012; Walters et al., 2012). Data were also collected on incident anxiolytic and hypnotic prescriptions by BNF (British Medical Association and Royal Pharmaceutical Society of Great Britain, 2014) categories (Sections 4.1.1 and 4.1.2) excluding barbiturates (Section 4.1.3) and antihistamines (Section 3.4.1) (Supplementary Table 2).

Routine data does not explicitly link medication prescription with diagnosis. Individuals with an anxiolytic prescription were further analysed in an attempt to identify the indication for which the medication was prescribed. Routinely collected electronic GP data records were reviewed for 6 months either side of the initial prescription date for depression and anxiety diagnosis and symptoms before searching for other possible indications (Gardarsdottir et al., 2007). These were: pain, enuresis, attention deficit hyperactivity disorder, conduct disorders, autism, headaches, migraine prophylaxis sleep problems, other codes of interest (including tearfulness and psychosis), irritable bowel syndrome, stress, phobias and obsessive disorders, dissociative disorders and eating disorders. If an individual prescribed relevant anxiolytic/hypnotic medication had anxiety or depression diagnoses/symptoms recorded then it was assumed that this medication was prescribed for this indication and no other indications were examined.

3.6. Statistical analysis

Annual incidence rates were calculated using person years at risk (PYAR) as a denominator. For example a person who supplied six months of data to the study would contribute 0.5 years to the denominator. Poisson regression was undertaken to investigate the adjusted associations between incidence of recorded anxiety symptoms/diagnoses, mixed anxiety depression, panic attack/panic disorder, hypnotic and anxiolytic prescription on the one hand and, year of diagnosis, gender, age group and deprivation on the other. Annual prevalence rates were also calculated utilising PYAR as a denominator. This is a more appropriate unit rather than number of registered cases because each individual's duration of follow-up is not fixed (Frisher et al., 2004).The significance of variables in the Poisson regression modelling was assessed using Wald tests. Robust standard errors for the estimated incidence rate ratios (IRRs) were utilised to account for clustering within practices. Analysis was conducted using SPSS version 20 for Windows.

4. Results

4.1. Sample characteristics

There were 311,343 registered GP patients aged 6–18 years between 1st January 2003 and 31st December 2011 in the SAIL databank providing a total of 1,546,489 person years of follow up. The mean follow-up time was 5.0 years. Annual prevalence of all anxiety subtypes and anxiolytic and hypnotic prescriptions during the study period are shown in Supplementary Tables 1 and 2 respectively. There has been a significant increase in prevalence in all subtype diagnoses and symptoms except mixed anxiety and depression. The prevalence of anxiety diagnosis increased from 1.97 cases per 1000 person years at risk (95% confidence interval CI 1.77–2.20) in 2003 to 2.53 (95% CI 2.28–2.79) in 2011 of 6–18 year olds. The prevalence of anxiolytic prescriptions was 1.90 cases per 1000 person years at risk (95% CI 1.70–2.12) in 2003 and 2.66 (95% CI 2.41–2.93) in 2011. During the study period there were 3297 new anxiety diagnoses (3151 individuals), and 1435 incident recordings of anxiety symptoms (1384 individuals) and 1093 new cases of mixed anxiety and depression (1076 individuals) (Table 1). A total of 2492 individuals received 2638 incident anxiolytic prescriptions and 1680 individuals received 1730 incident hypnotic prescriptions (Table 2). Only 227 individuals received incident prescriptions for both anxiolytics and hypnotics. For all subtypes the majority of records represent incident as opposed to prevalent cases (Fig. 1).

Adjusted incident rate ratios for year, gender, age group and deprivation for anxiety diagnosis, anxiety symptoms, panic attack/panic disorder and mixed anxiety and depression are shown in Table 1 and for hypnotic and anxiolytic prescriptions in Table 2. All incident anxiety subtypes increased with age and were nearly twice as likely in females (panic attack/panic disorder IRR 2.64, 95% CI 2.38–2.93; anxiety diagnosis IRR 1.88, 95% CI 1.75–2.02; anxiety symptoms IRR 1.84, 95% CI 1.66–2.04) and mixed anxiety

Table 1
Incidence rate ratios (IRR) for anxiety diagnosis, anxiety symptoms, panic attack/panic disorder and mixed anxiety and depression.

Variable		Anxiety diagnosis		Anxiety symptoms		Panic attack/Panic disorder		Mixed anxiety depression	
		Events	IRR(95%CI)[a]	Events	IRR(95%CI)[a]	Events	IRR(95%CI)[a]	Events	IRR(95%CI)[a]
Gender	**Male**	1186	Reference (P^b < 0.0001)	523	Reference (P^b < 0.0001)	457	Reference (P^b < 0.0001)	289	Reference (P^b < 0.0001)
	Female	2111	1.88(1.75–2.02)	912	1.84(1.66–2.04)	1142	2.64(2.38–2.93)	804	2.92(2.59–3.28)
Age group	**6–10**	754	0.45(0.4–0.52)	308	0.44(0.36–0.53)	413	0.29(0.24–0.35)	84	0.09(0.04–0.19)
	11–14	389	(P^b < 0.0001)	153	Reference (P^b < 0.0001)	138	Reference (P^b < 0.0001)	8	Reference (P^b < 0.0001)
	15–18	2154	3.18(2.95–3.43)	974	3.47(3.05–3.96)	1048	2.82(2.54–3.12)	1001	13.74(10.95–17.24)
Deprivation[c]	**1**	596	(P^b < 0.0001)	219	Reference (P^b < 0.0001)	265	Reference (P^b < 0.0001)	152	Reference (P^b < 0.0001)
	2	539	1.04(0.92–1.18)	274	1.44(1.21–1.71)	265	1.15(0.98–1.36)	130	0.99(0.83–1.18)
	3	735	1.15(1.04–1.27)	340	1.46(1.22–1.74)	361	1.27(1.1–1.47)	221	1.34(1.13–1.59)
	4	614	1.09(0.98–1.22)	281	1.37(1.14–1.65)	326	1.31(1.12–1.52)	259	1.8(1.51–2.14)
	5	812	1.33(1.2–1.47)	319	1.42(1.2–1.67)	382	1.4(1.21–1.63)	326	2.09(1.79–2.44)
Year	**2003**	306	Reference (P^b =0.120)	65	Reference (P^b < 0.0001)	123	Reference (P^b < 0.0001)	146	Reference (P^b < 0.0001)
	2004	366	1.05(0.91–1.22)	130	1.74(1.27–2.37)	179	1.28(1.07–1.53)	163	0.93(0.73–1.19)
	2005	361	1.02(0.89–1.16)	134	1.78(1.33–2.38)	188	1.32(1.12–1.56)	141	0.8(0.67–0.95)
	2006	371	1.05(0.91–1.21)	154	2.04(1.5–2.77)	177	1.24(1.04–1.49)	112	0.63(0.5–0.8)
	2007	411	1.17(1.02–1.33)	169	2.25(1.67–3.02)	210	1.48(1.27–1.73)	107	0.6(0.49–0.73)
	2008	358	1.02(0.88–1.18)	166	2.21(1.64–2.99)	179	1.27(1.07–1.51)	107	0.6(0.51–0.71)
	2009	386	1.11(0.99–1.25)	183	2.46(1.82–3.33)	204	1.47(1.23–1.74)	107	0.61(0.51–0.73)
	2010	376	1.13(0.99–1.28)	205	2.88(2.17–3.82)	172	1.28(1.02–1.62)	107	0.64(0.49–0.84)
	2011	362	1.2(1.02–1.41)	229	3.55(2.65–4.77)	167	1.38(1.11–1.72)	103	0.68(0.54–0.86)

[a] Adjusted for calendar year, gender, age and deprivation.
[b] based on Wald test.
[c] Deprivation: 1=least deprived; 5=most deprived.

Table 2
Incidence rate ratios (IRR) for hypnotic and anxiolytic prescriptions.

Variable		Hypnotics		Anxiolytics	
		events	IRR(95%CI)[a]	events	IRR(95%CI)[a]
Gender	**Male**	674	Reference (p^b =0.323)	1073	Reference (P^b < 0.0001)
	Female	1056	1.65(1.5–1.82)	1565	1.54(1.42–1.68)
Age group	**6–10**	154	0.46(0.33–0.65)	538	0.35(0.3–0.41)
	11–14	81	Reference (P^b < 0.0001)	213	Reference (P^b < 0.0001)
	15–18	1495	10.82(8.94–13.11)	1887	3.89(3.52–4.3)
Deprivation[c]	**1**	278	Reference (P^b < 0.0001)	440	Reference (P^b < 0.0001)
	2	296	1.23(1.04–1.45)	463	1.21(1.06–1.39)
	3	335	1.12(0.95–1.32)	609	1.29(1.15–1.45)
	4	365	1.39(1.18–1.63)	548	1.32(1.16–1.5)
	5	453	1.59(1.36–1.85)	576	1.28(1.11–1.46)
Year	**2003**	172	Reference (P^b < 0.0001)	214	Reference (P^b=0.014)
	2004	213	1.05(0.85–1.30)	286	1.17(0.95–1.43)
	2005	188	0.9(0.73–1.10)	278	1.11(0.91–1.36)
	2006	185	0.89(0.71–1.10)	305	1.22(1–1.48)
	2007	187	0.9(0.73–1.11)	315	1.27(1.03–1.55)
	2008	197	0.95(0.78–1.15)	311	1.25(1.02–1.53)
	2009	207	1.01(0.82–1.24)	331	1.35(1.12–1.63)
	2010	212	1.07(0.88–1.32)	297	1.26(1.05–1.52)
	2011	169	0.95(0.74–1.21)	301	1.41(1.17–1.71)

depression three times as likely (IRR 2.92, 95% CI 2.59–3.28) than in males (Table 2). For all anxiety subtypes the gender difference increased with age. The female: male ratio in the 6–14 years age group compared to the 15–18 year age group is 1.47:1 to 2.16:1 for anxiety diagnosis, 1.37:1 to 2.14:1 for anxiety symptoms, 1.80:1 to 3.09:1 for mixed anxiety and depression, and 2.33:1 to 2.83:1 for panic attack/panic disorder. Anxiolytic prescription rates were significantly higher for females (IRR 1.54, 95% CI 1.42–1.68) as were hypnotic prescription rates (IRR 1.54, 95% CI 1.42–1.68).

The most deprived areas were at higher risk of all subtypes compared with the least deprived areas (panic attack/panic disorders IRR 1.40 95% 1.21–1.63; anxiety diagnosis IRR 1.33, 95% CI 1.20–1.47; anxiety symptoms IRR 1.42, 95% CI 1.20–1.67; mixed anxiety depression IRR 2.09, 95% CI 1.79–2.44). Children from the most deprived quintile were more likely to be diagnosed with anxiety compared to those in the least deprived quintile between the ages of 15–18 years (IRR 1.37, 95% CI 1.21–1.56) but not between the ages of 6 and 14 years (IRR 1.23, 95% CI 0.96–1.59). This analysis was not performed for symptoms or prescriptions due to small numbers.

4.2. Trends over time-anxiety

Trends over time of anxiety diagnoses, anxiety symptoms, panic attack/panic disorder and anxiolytic mixed anxiety and depression are shown in Fig. 2. A small non-significant increase in the incidence of anxiety diagnoses is apparent from 1.82 cases per 1000 PYAR in 2003 to 2.37 cases in 2011 (IRR=1.20, 95% CI 1.02–1.41). The incidence of anxiety symptoms more than tripled from 0.39 cases per 1000 PYAR in 2003 to 1.50 cases per 1000 PYAR in 2011 (IRR=3.55, 95% CI 2.65–4.77). In contrast incidence of mixed anxiety and depression fell from 0.87 to 0.67 cases per 1000 person years over the study period (IRR=0.68, 95% CI 0.54–0.86). Incidence of panic attack/panic disorder increased from 0.73

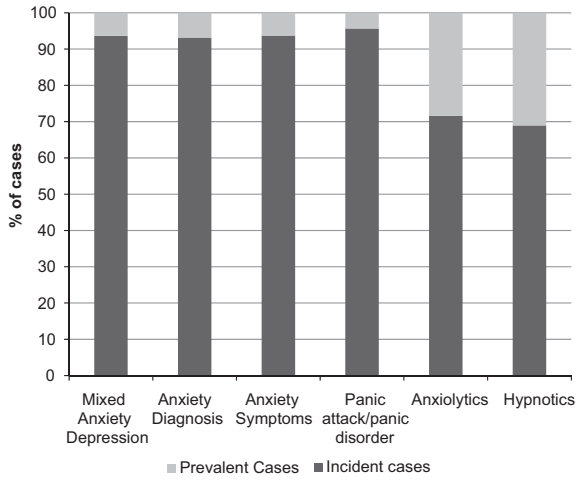

Fig. 1. Annual incident and prevalent cases of all subtypes and anxiolytic and hypnotic prescriptions recorded from 2003–2011.

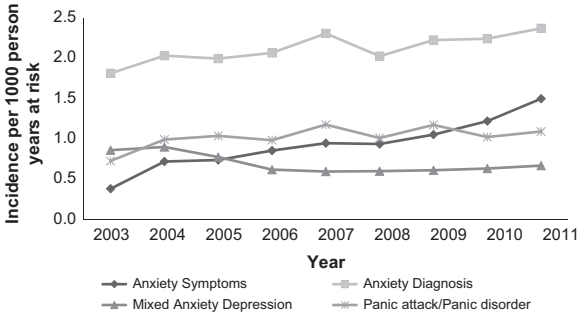

Fig. 2. Incidence of anxiety diagnosis, symptoms, panic attack/panic disorder and mixed anxiety and depression over time.

to 1.09 cases per 1000 person years from 2003 to 2011 (IRR=1.38, 95% CI 1.11–1.72).

An initial increasing trend in incident anxiolytic prescriptions is evident up until 2007 however very little change is seen after this point resulting in a non-significant increase over the study period from 1.27 to 1.97 cases per 1000 person years (IRR=1.41, 95% CI 1.17–1.71). While anxiolytic prescriptions for the cohort as a whole did not change significantly over time, there was a significant increase in prescriptions for 15–18 year age group (Fig. 3) from 3.00 to 4.91 cases per 1000 person years (IRR=1.62, 95% CI 1.30–2.02). The majority of new anxiolytic prescriptions were for diazepam which made up around three quarters of new prescriptions over all. This was followed by hydroxyzine hydrochloride. Incidence of new diazepam prescriptions increased from 0.93 cases per 1000 PYAR in 2003 to 1.40 cases per 1000 PYAR in 2011. Incidence of new prescriptions of hydroxyzine hydrochloride increased from 0.25 to 0.43 cases per 1000 PYAR during the study period. Where incident cases had 1 year or more GP follow-up data (n=2386) 942 received two or more prescriptions (39%; 95% CI 38–41) and 340 received five or more prescriptions (14%; 95% CI 13–16). Of those receiving multiple prescriptions 559 were given their second prescription within six months of the initial prescription date (59%; 95% CI 56–62).

Incident hypnotic prescriptions remain relatively stable over time with an overall non-significant decrease from 1.02 to 0.84 cases per 1000 PYAR (IRR=0.95, 95%CI 0.74–1.21). Of the 1730 incident prescriptions only 235 were made for those aged 6–14. The low rates of prescriptions each year mean that analysis of trends over time for this younger age group was not meaningful. In contrast to anxiolytic prescriptions there was a small non-significant decrease

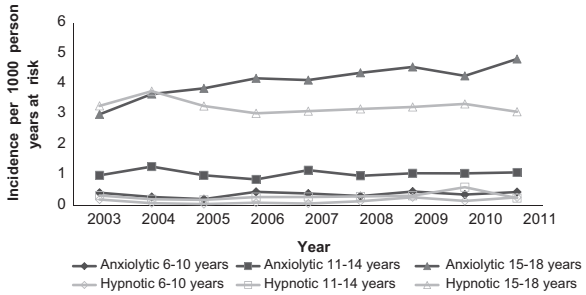

Fig. 3. Incidence of anxiolytic and hypnotic prescriptions by age group over time.

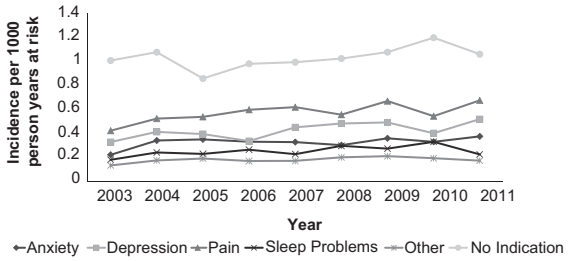

Fig. 4. 3 Combined incident anxiolytic and hypnotic prescriptions by indication over time.

from 3.28 to 3.08 cases per 1000 PYAR over time for those aged 15–18 (IRR=0.95, 95% CI 0.72–1.24). The most frequently prescribed hypnotic medication was zopiclone making up just over half of new prescriptions. This was followed by temazepam. Of those where at least one year of follow-up data was available following prescription (n=1541) 621 received two or more prescriptions (40%; 95% CI 38–43) and 215 received five or more prescriptions (14%; 95% CI 12–16). Of those who received at least one additional prescription 378 were given their second prescription within six months (61%; 95% CI 57–65).

Indications associated with incident anxiolytic and hypnotic medications are shown in Fig. 4. The most commonly associated indication was pain. Incidence of prescriptions associated with pain increased from 0.42 to 0.67 cases per 1000 PYAR from 2003 to 2011. Incidence of prescriptions associated with anxiety also increased from 0.21 in 2003 to 0.37 in 2011 cases per 1000 PYAR. The only other indication which reached sufficient numbers to be analysed separately was sleep problems with an incidence of 0.18 cases per 1000 PYAR in 2003 and 0.22 in 2011. Incident prescriptions associated with other indications remained at a low level throughout the study period with 0.13 cases per 1000 PYAR in 2003 and 0.17 cases per 1000 person years at risk in 2011. Incidence of prescriptions for which no indication could be found fluctuated throughout the study period beginning at 1.01 cases per 1000 person years in 2003 decreasing to 0.86 in 2005 before climbing back up to 1.06 cases in 2011.

5. Discussion

5.1. Main findings

Since 2003 the incidence of anxiety symptoms in CYP recorded in primary care has more than tripled, with a comparatively stable trend in anxiety diagnoses over time. New prescriptions for anxiolytics have remained at a stable rate for those aged 6–14; however, new prescriptions have significantly increased over time for those aged 15–18 years. This trend is not reflected with hypnotic prescriptions which show a comparatively stable trend

over time. Where data is available it appears that around 40% of new prescription of hypnotics and anxiolytics are associated with multiple prescriptions in the subsequent year.

5.2. Strengths and limitations

The main strength of this study is its population based sample size. There is no clear reason to believe the results would differ for the entire population of Wales or the entire population of UK children.

The results of the current study reflect trends in presentation to primary care, recognition and treatment by GPs and the way in which depression and anxiety in children and young people is recorded in primary care. However this is likely to be an underestimate of incidence in the community as routine data does not capture individuals who do not present to their GP or, with whom depression or anxiety is discussed, but not recorded. This is common feature of all routinely collected database studies and results are not intended as an estimate of time trends of the population as a whole. An additional limitation of utilising routine data is that the indication for which a medication is prescribed is not specifically recorded and can only be inferred based on other diagnoses around the time of prescription. While work examining the indications for which a prescription is made in this study is a good indication of trends over time, the number of individuals for which no indication is recorded is likely to be inflated. This is due to the nature of the current cohort and the possibility that not all individuals were registered with SAIL supplying GP at the time when a diagnosis was recorded. Further work is needed to fully elucidate the diagnoses which may be linked to this increase in prescribing.

A further limitation is the lack of information regarding whether and what interventions have been received at secondary and tertiary mental healthcare levels for children and adolescents who are prescribed hypnotics and anxiolytics. In the United Kingdom, general practitioners are frequently requested to provide prescriptions for patients who are actively followed up by specialist mental healthcare, where tailored and carefully supervised use of anxiolytics/hypnotics may be appropriate. Our findings may be influenced by a cohort effect as the CYP investigated age through the study period. The large proportion of individuals compared to events (e.g. 3297 new anxiety diagnoses compared to 3151 individuals) and prescriptions (e.g. 2492 individuals received 2638 incident anxiolytic prescriptions) suggests that this was not a major effect. We did not explore prescriptions for antidepressants which may be indicated for these disorders since this has been done previously (Wijaars et al., 2012).

The read codes, not specific to children, utilised in this study have been previously validated against adult survey data (John et al., 2015). The use of survey data in order to validate read codes has a distinct advantage over many other data base studies (Rait et al., 2009; Wijaars et al., 2012; Walters et al., 2012). However it may not be appropriate to use adult survey data to validate codes utilised for CYP. Further research is needed to examine whether GPs employ the same coding for both adults and young people.

5.3. What this study adds

There has been considerable debate in the literature regarding an increasing tendency in primary care to diagnose depression and anxiety in patients presenting with sadness or distress and to offer them antidepressant or anxiolytic medication (Dowrick and Frances, 2013), in relation to pathologising normal human experience (Watts, 2012). This is of particular concern in CYP (Gaughwin, 2014) where such presentations, particularly if they are not persistent may reflect 'normal' processes. Psychotropic prescriptions for CYP are continuing to rise across western cultures (Olfson et al., 2002; Steinhausen and Bisgaard, 2014; Middleton et al., 2001; Rani et al., 2008). This is the first study to examine the way in which anxiety problems are recognised and recorded and to assess prescribing of hypnotics and anxiolytics in primary care for CYP. The persistence of mental health issues into adulthood (Costello et al., 2006) and associated adverse life outcomes (Patel et al., 2007) make recognition and proper treatment of anxiety and other mental health issues in this group important in terms of future life outcomes for the individual and future demands on services. Further research is needed to fully understand the dramatic increase in symptoms of anxiety.

These results may reflect a genuine increase in anxiety in the young population, increased awareness on the part of GPs or increased help-seeking behaviour on the part of children and young people. The increase in anxiolytic prescriptions in 15–18 year olds over the study period is not in keeping with NICE guidelines for both generalised anxiety disorder in adults (NICE, 2011) and social anxiety disorder in children and young people (NICE, 2013). NICE recommends that SSRIs are the first line pharmacotherapy for treating adults with generalised anxiety disorder (NICE, 2011). It may be that the increase in anxiolytic prescriptions is partially attributable to the controversy surrounding SSRI use in adolescents (Committee of Safety of Medicines, 2003) resulting in GPs perceiving anxiolytic medication as a safer or more acceptable alternative. However it is not possible to draw this conclusion based on the data available and more research is required to fully understand the reasons for this increase.

A recent review of the assessment and management of anxiety disorders in CYP highlights that much is still unknown regarding the safety of anxiolytic medication, particularly with regards to benzodiazepines and longer term treatment, in this age group and further emphasises psychological interventions as a first line treatment (Creswell et al., 2014). In particular trials of benzodiazepines in children and young people with anxiety have yielded mixed results with improvements in anxiety, depression, psychomotor excitation, and hyperactivity, but combined with increased sedation, activation, headache, and nausea (Simeon and Ferguson, 1987). Other trials have found no statistically significant differences to placebo and concerns remain over disinhibition in children and long term tolerance (Simeon et al., 1992). Thus whatever the underlying cause, the increase in anxiolytic prescriptions demonstrated in this study is of concern. There is a need for further research into the safety of these medications, and for specific guidance for treating anxiety disorders in CYP.

A recent study from The Health Improvement Network (THIN) databank has found that recording of incident anxiety diagnoses in primary care has declined over recent years with a concurrent increase in incident cases of anxiety symptoms in adults (Walters et al., 2012). Labelling of mixed anxiety and depression was also found to nearly halve over the study period. Such results are reflected with diagnoses and symptoms of depression. Overall results suggest that GPs are increasingly using non-specific symptom terms for recording common mental disorders for both adults, and CYP. This decrease in recording of diagnoses may be partially attributable to increasingly cautious diagnostic behaviour by GPs. However, an additional factor that may be of influence is the updated Quality and Outcomes Framework (QOF; British Medical Association, NHS Employers, 2006). Financial incentives are given for general practices that follow guidelines for stepped care for patients with suspected depression. Studies suggest the QOF provides a disincentive to record a diagnosis of depression and GPs report the use of alternative labels such as 'low mood' (Mitchell et al., 2011). The current study

demonstrates similar diagnostic behaviour for anxiety where QOF incentives do not exist, so additional factors such as perceived stigma may also be contributing to this finding.

5.4. Implications

The increase in symptoms of anxiety and anxiolytic prescriptions highlight the need for further research and guidance regarding the recognition and management of anxiety in young people presenting to primary care. Anxiolytics are not licenced for use in anxiety, depression or pain in this age group. The increase in new prescriptions of anxiolytics in 15–18 year olds is at odds with NICE recommendations, where they exist, which state that pharmacotherapy should not be routinely offered in the treatment of social anxiety disorder in young people (NICE, 2013). Furthermore treatment of anxiety in adults with benzodiazepines, which comprise the majority of anxiolytic medications, is specifically discouraged (NICE, 2011). The increase in symptoms of anxiety highlight the need for specific guidelines on how CYP suffering with anxiety should be assessed and treated, particularly older adolescents where pharmacotherapy is increasing. This increase may reflect the paucity of resources at the primary care level for family-based and psychological therapies for CYP who suffer from emotional disorders, and difficulties in accessing specialist care. The establishment of the Primary Mental Health worker resource available to general practices through the Mental Health Measure (Welsh Government, 2010) legislation in Wales may have a positive impact in providing more resources for non-pharmacological interventions, as may the provision of schools based counselling (Welsh Government, 2013) in Wales since 2008, thereby reducing the need for anxiolytic prescription for this group of patients. It would be important to repeat this study in the future to ascertain the impact of greater resources for mental healthcare at the primary healthcare level.

Further research is needed to fully understand the indications for which, hypnotic and anxiolytic medication are being prescribed particularly given the large proportion of hypnotic and anxiolytic prescriptions for which no indication can be found. It appears that prescriptions associated with pain have increased since 2003. Prescriptions for which no indication could be found have also increased over the study period further highlighting the need for more research in this area. It may be that GPs record the indication as free text or assume they will know the indication from the prescription or it may be GPs are increasingly choosing not to record depression or anxiety in this group or that medications are being prescribed for indications beyond those examined here.

Awareness that GP's are increasingly using non-specific symptom codes rather than formal diagnoses for both anxiety and depression is important for future research based on routinely collected data. While results here provide a measure of GP recording behaviour, future research may focus on the impact of a diagnosis compared with recording of symptoms on patient outcomes. This would provide further information on the impact of adherence to QOF guidance. The degree of linkage possible utilising the SAIL databank means that outcomes including educational data and hospital admissions could be examined. Future studies may aim to explore whether the way in which a mental health issue is recorded has an impact on care or outcomes for the patient.

6. Conclusion

Since 2003 the incidence of anxiety symptoms in CYP recorded in primary care has more than tripled, with a comparatively stable trend in the incidence of anxiety diagnoses. Anxiolytic prescriptions for 6–14 year olds have not changed significantly over time but have increased significantly for 15–18 year olds which is out of keeping with current prescribing guidelines. These results may reflect a genuine increase in anxiety in CYP, increased awareness on the part of General Practitioners or increased help-seeking behaviour. This study highlights the need for specific guidelines on how CYP with anxiety should be assessed and managed in primary care, particularly in older adolescents and for further guidance on the use of anxiolytics and hypnotics.

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Conflicts of interest

The authors have no conflicts of interest to report.

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Appendix A. Supporting information

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