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ORIGINAL ARTICLE

Prescribing for young people with attention deficit hyperactivity disorder in UK primary care: analysis of data from the Clinical Practice Research Datalink

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Abstract

Guidance on management of attention deficit hyperactivity disorder (ADHD) in the UK was issued by the National Institute for Clinical Excellence in 2008. No UK study has examined all psychotropic prescribing in young people with ADHD since the introduction of the guidance; this is especially relevant due to the high prevalence of psychiatric comorbidity in this population. The aim of this study was to describe primary care prescribing of ADHD and other psychotropic medications for young people with ADHD. The analysis of records of patients with an ADHD diagnosis in the UK Clinical Practice Research Datalink from 2005 to 2013 was performed. Estimation of the prevalence of prescribing of ADHD and other psychotropic medications over 8-year follow-up for cases aged 10–20 years in 2005 was carried out. Of 9390 ADHD cases, 61.6% [95% confidence interval (CI) 60.6–62.5%] had a prescription at some point for ADHD medication. Prescribing of other psychotropic medications was higher in girls than in boys (36.4% vs. 22.7%; $p < 0.001$). ADHD prescribing prevalence declined steeply between the ages of 16 and 18 from 37.8% (95% CI 36.6–38.9) to 23.7% (95% CI 22.7–24.6%). There was a parallel increase in prescribing of other psychotropics from 3.8% (95% CI 3.4–4.3%) to 6.6% (95% CI 6.0–7.3%). There is scope to optimise the management of ADHD and psychiatric comorbidities in young people, and there is a need for sustainable models of ADHD care for young adults, supported by appropriate training and specialist services.

Keywords Primary health care · Prescribing · ADHD · Comorbidities

Introduction

Children, young people and adults with attention deficit hyperactivity disorder (ADHD) are at greater risk of experiencing a broad spectrum of poorer outcomes, including higher rates of mortality, injuries and accidents, as well as educational and occupational underachievement (Lichtenstein et al. 2012; Shaw et al. 2012; Dalsgaard et al. 2015; Chang et al. 2014). There are also increased rates of comorbidity with other psychiatric disorders including anxiety, depression and substance misuse, the peak age of emergence for many of these being in late adolescence and early adulthood (Biederman et al. 1991; Copeland et al. 2011; Jensen and Steinhausen 2015; Fayyad et al. 2016). Such coexisting disorders may affect functioning and adherence to medication and furthermore may go undiagnosed and hence untreated (Kooij et al. 2010; Bolea-Alamanac et al. 2014). However, despite the significance of comorbidities in ADHD, prescribing of other psychotropic medications in young people with the condition has been little studied, with most studies focussing on the prescription of ADHD medication only and/or on younger children (Birnbaum et al. 2013; Sikirica et al. 2013).

Moving from adolescence to adulthood, ADHD symptoms can become less overt (for example, manifesting as inner restlessness and disorganisation) and even be mistaken for the signs of other common psychiatric comorbidities (Asherson et al. 2007). Sibley et al.'s (2015) systematic review of persistence suggested that 40–50% of adolescents with ADHD still met criteria for a diagnosis in adulthood where recommended methods such as age-appropriate symptom thresholds were used. However, despite evidence for

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symptom persistence, internationally, studies of prescribing patterns such as those by Johansen et al. (2015) in the USA and Zetterqvist et al. (2013) in Sweden indicate that there are high rates of treatment discontinuation in late adolescence. Previous UK studies of primary care prescribing have also reported a steep fall in prescribing prevalence of ADHD medication coinciding with the period during which transition from child to adult services takes place (Wong et al. 2009; McCarthy et al. 2012a, b), but these studies used data collected before new guidance was issued by the National Institute for Clinical Excellence (NICE) in 2008. This guidance recommends that young people with ADHD should be reassessed at school-leaving age to determine whether they need to continue treatment into adulthood, and also states that drug treatment is the first-line treatment for adults with moderate or severe levels of impairment resulting from their ADHD. Our recent paper (Newlove-Delgado et al. 2017) used the UK Clinical Practice Research Datalink to examine time to cessation of ADHD medication from age 16, including the most recently available data from 2005 to the end of 2013. However, despite the developments in guidance in treating those reaching adulthood the median time to cessation that we reported was 1.5 years, suggesting a continuing disparity between expected levels of symptom persistence and continuation of medication.

However, no UK study has to date examined all psychotropic prescribing in primary care (both ADHD and non-ADHD medications) in children and young adults with ADHD over this more recent time period, which represents an important gap. In the UK, general practitioners (GPs, primary care doctors) are the 'gatekeepers' to specialist services such as child and adolescent psychiatry clinics or paediatric neurodevelopmental clinics. Whilst GPs do not usually undertake diagnosis of ADHD and comorbidities in children and young people, they are often responsible for prescribing regular medication under shared-care arrangements. When young people reach the age boundary for child services at 16–18, there is considerable variation nationally in the services available to them if ongoing treatment is needed (Hall et al. 2015), with some areas of the UK having no available Adult ADHD service to support GPs in prescribing and other aspects of ADHD management. Consequently, knowledge of the more recent patterns both of prescribing of ADHD medication and other psychotropic medications in primary care will allow greater understanding of current practice in managing ADHD and comorbidities in young people. This will contribute to recommendations for commissioning of services, practice and training to improve assessment and wider availability of appropriate management for ADHD and comorbid conditions.

The primary objective of this study was, therefore, to examine the prevalence of primary care prescribing of drugs used to manage ADHD and of other psychotropic medications from 1 January 2005 to 31 December 2013 for people with ADHD aged 10–20 in 2005.

Methods

Study design

This analysis of prescribing uses data from the UK Clinical Practice Research Datalink (CPRD), a large clinical database run by the Medicines and Healthcare products Regulatory Agency (MHRA) which includes prescribing and consultation data from primary care practices across the country (Herrett et al. 2015). We used the CPRD to report the prescribing prevalence of ADHD and other psychotropic medications and the prevalence of recorded psychiatric comorbidities in people with a recorded ADHD diagnosis as defined below. We included cases with ADHD aged from 10 to 20 at any point between 1 January 2005 and 31 December 2005 and analysed the data available on these cases from 1 January 2005 until 31 December 2013. This allowed the study of patterns of primary care prescribing during the period of transition from child to adult services, which usually takes place between the ages of 16 and 18 years.

Inclusion criteria

To be included, firstly, cases needed to be aged 10–20 at some point between 1 January 2005 and 31 December 2005. Secondly, they needed to have a record of an ADHD diagnosis coded in their files at some point between birth and the end of the study period on 31 December 2013. ADHD diagnoses were defined as any of the 22 CPRD medical codes and primary care terms (based on ICD-10 F90 categories) (World Health Organisation 1992) that relate to an ADHD diagnosis (Newlove-Delgado et al. 2017).

Identification of prescriptions and comorbid psychiatric diagnoses

To identify prescriptions of ADHD medication, the files of included cases were searched for prescription records coded with any of the CPRD product codes referring to British National Formulary (BNF) categories of ADHD medication—e.g. stimulants, dated within the study period (Joint National Formulary 2015). Other psychotropic medication prescriptions were identified by searching for records of medications included in BNF Sections 4.1, 4.2 and 4.3 (anxiolytics, antidepressants, mood stabilisers and drugs used in psychoses and related disorders). Antipsychotics and mood stabilisers were grouped together as one category. Comorbid psychiatric diagnoses were identified by searching

for codes relating to ICD-10 classifications for the main categories of disorder.

Analysis

Stata SE13 (Statacorp 2015) was used for all data analysis. Prescribing prevalence of ADHD medication was reported, firstly, as the percentage of all cases with a recorded prescription at any point within the study period, and, secondly, by age. For the analysis of prescribing by age, if the case's registration with a CPRD practice ended before the end of a year then that was counted as an incomplete year and the case was not included. As CPRD does not provide the full date of birth, the age was designated as the age of the case at the end of the calendar year for this analysis.

We also reported the prevalence of prescribing for non-ADHD psychotropic medication and the prevalence of psychiatric comorbidities. We reported prescribing by category of comorbidity. We reported the prevalence of concurrent prescriptions of ADHD and other psychotropic prescriptions occurring in the same calendar year. Finally, to examine secular changes, we reported prevalence of prescribing of ADHD medication by year.

All protocols using patient-level data from the CPRD are reviewed for scientific quality and approved by the Independent Scientific Advisory Committee (ISAC) on behalf of the National Research Ethics Service Committee. This study protocol (13_213) was granted ISAC approval in January 2013.

Results

Sample characteristics

There were 9390 patients with ADHD who met the inclusion criteria. Of these, 7876 (83.9%) were male. The median length of time for which follow-up data were available was 8.7 years (interquartile range 3.2–9.2 years).

Psychiatric comorbidities

Over a quarter of cases (26.0%, 2440/9390) in the sample had another psychiatric diagnosis recorded at some point during follow-up. The most common categories of comorbid psychiatric disorder were autism spectrum disorders (ASD) (9.9%) and anxiety or depressive disorders (9.3%) (Table 1). Psychiatric comorbidity was more prevalent in females than in males (29.4% vs. 25.3%, $p = 0.001$).

Prescribing at any point during follow-up

Of all patients, 61.6% (95% CI 60.6–62.5%) had at least one prescription for an ADHD medication during the study period. This percentage was similar between males and females (61.8% vs. 60.4%).

A quarter of all cases (24.9%; 95% CI 24.0–25.8%) had at least one prescription for another psychotropic medication at some point during the study period, with the most commonly prescribed category being antidepressants (Table 2). Females had a higher prevalence of being prescribed a non-ADHD psychotropic medication (36.4% vs 22.7%, $p < 0.001$), in particular of being prescribed antidepressants and anxiolytics.

Of those with a recorded comorbidity, 49.2% (95% CI 47.1–51.1%) had a prescription for a non-ADHD

Table 1 Percentage of ADHD cases that had comorbid psychiatric disorders

Disorder category	Percentage of cases with the disorder recorded at any point during follow-up		
	All cases ($N = 9390$) (95% confidence interval)	By gender	
		Males ($N = 7876$) (%)	Females ($N = 1154$) (%)
Any comorbid psychiatric disorder	26.0% (25.1–26.9%)	25.3	29.4
Autism spectrum disorder (ASD)	9.9% (9.3–10.5%)	10.3	7.7
Anxiety- or depression-related disorder	9.3% (8.7–9.9%)	8.1	15.9
Conduct/oppositional defiant disorder	5.2% (4.8–5.7%)	5.5	3.8
Substance/alcohol misuse-related disorder	2.1% (1.8–2.4%)	2.0	2.6
Any tic disorder	2.1% (1.8–2.4%)	2.3	1.0
Any personality disorder	1.9% (1.6–2.2%)	1.5	4.0
Bipolar affective disorder or psychosis	0.46% (0.32–0.59%)	0.50	0.26

Table 2 Percentage of ADHD cases that were prescribed non-ADHD psychotropic medication by gender and age

Medication category (British National Formulary 2015)	Percentage with at least one prescription at any point during follow-up		
	All cases ($N=9390$) (95% confidence interval)	By gender	
		Males ($N=7876$) (%)	Females ($N=1154$) (%)
Any non-ADHD psychotropic medication	24.9% (24.0–25.8%)	22.7	36.4
Antidepressants	16.0% (15.3–16.8%)	13.6	28.7
Anxiolytics	5.8% (5.3–6.2%)	5.1	9.2
Antipsychotics and mood stabilisers	10.7% (10.1–11.3%)	10.5	11.4

psychotropic medication at any point versus 16.8% (95% CI 16.0–17.7%) of those without recorded comorbidity. In those with a comorbid disorder, prescribing of non-ADHD psychotropic medication was higher amongst females than in males (64.4% vs. 45.7%; $p<0.001$).

There were clear differences between diagnostic groups on examining non-ADHD psychotropic prescribing (Table 3). Antipsychotic and mood stabiliser prescribing was highest amongst those with a recorded tic disorder (42.4% had a prescription at some point). Unsurprisingly, participants with a recorded diagnosis of anxiety or depression were more likely than other groups to be prescribed antidepressants.

Concurrent prescribing of ADHD and psychotropic medications

Just under 1 in 10 cases (8.8%, 95% CI 8.3–9.4%) had a prescription for both an ADHD medication and a non-ADHD psychotropic medication within the same calendar year. This percentage was higher amongst females (11.1% vs. 8.4% in males).

Prescribing by age

Prescribing by age is summarised in Fig. 1. Over the transition period from child to adult services there was evidence of rapidly falling prevalence. Amongst 16-year-olds, prevalence of prescribing of ADHD medication was 37.8% (95% CI 36.6–38.9%) falling to 23.7% (95% CI 22.7–24.6%) in 18-year-olds. In contrast, for other psychotropic prescriptions, from the age of 16 onwards there was a clear rise so that at the age of 18, 6.6% (95% CI 6.0–7.3%) had a prescription.

As Fig. 2 demonstrates, patterns of ADHD medication prescribing by age followed a similar pattern in each year of the study period, with the sharpest drop in prescribing consistently seen between the ages of 16 and 18 years.

Discussion

Summary

Our results clearly demonstrate a marked decline in the prevalence of ADHD prescribing over the period in which transition from child to adult services takes place in the UK and a parallel rise in the prevalence of other psychotropic prescribing. A quarter of all cases had a prescription at some point

Table 3 Percentage of ADHD cases that were prescribed psychotropic medication by type of recorded psychiatric comorbidity

Type of recorded psychiatric comorbidity	Percentage prescribed a drug from British National Formulary category of medication at any point during the study period (95% confidence interval)		
	ADHD medication	Antidepressants	Antipsychotics or mood stabilisers
No recorded comorbidity ($N=7055$)	61.0% (60.0–62.2%)	10.3% (9.6—11.0%)	6.4% (5.9–7.0%)
Any recorded comorbidity ($N=2335$)	63.1% (61.1–65.0%)	33.4% (31.5–35.3%)	23.6% (21.9–25.4%)
Autism spectrum disorder ($N=927$)	67.7% (64.7–70.7%)	19.3% (16.9–22.0%)	25.1% (22.4–28.0%)
Conduct/oppositional defiant disorders ($N=490$)	63.7% (59.3–67.8%)	17.6% (14.4–21.2%)	18.2% (15.0–21.8%)
Depression- or anxiety-related disorders ($N=876$)	58.8% (55.5–62.0%)	60.8% (57.6–64.0%)	22.2% (16.9–28.6%)
Tic disorders ($N=198$)	63.6% (56.7–70.1%)	22.2% (16.9–28.6%)	42.4% (35.7–49.5%)

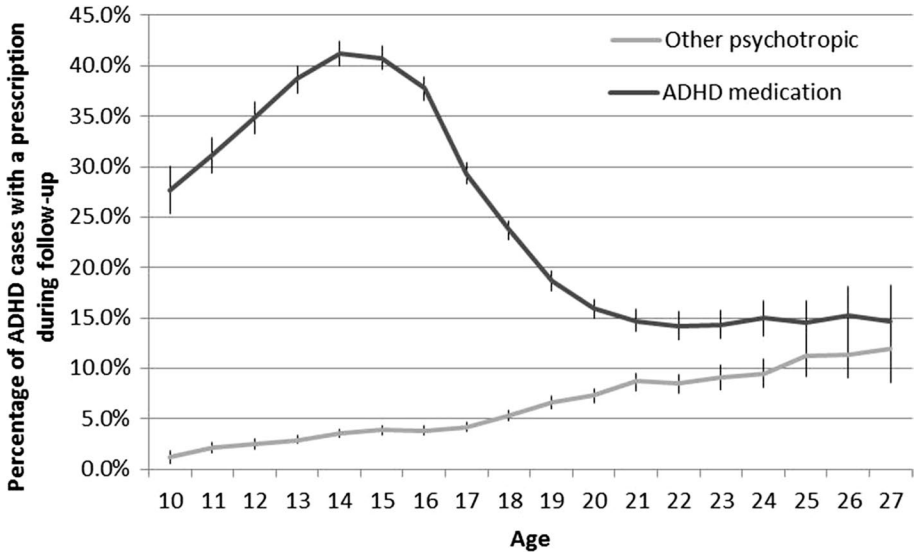

Fig. 1 Percentage of ADHD cases that were prescribed ADHD medication and other psychotropic medications by age. Bars indicate 95% confidence interval

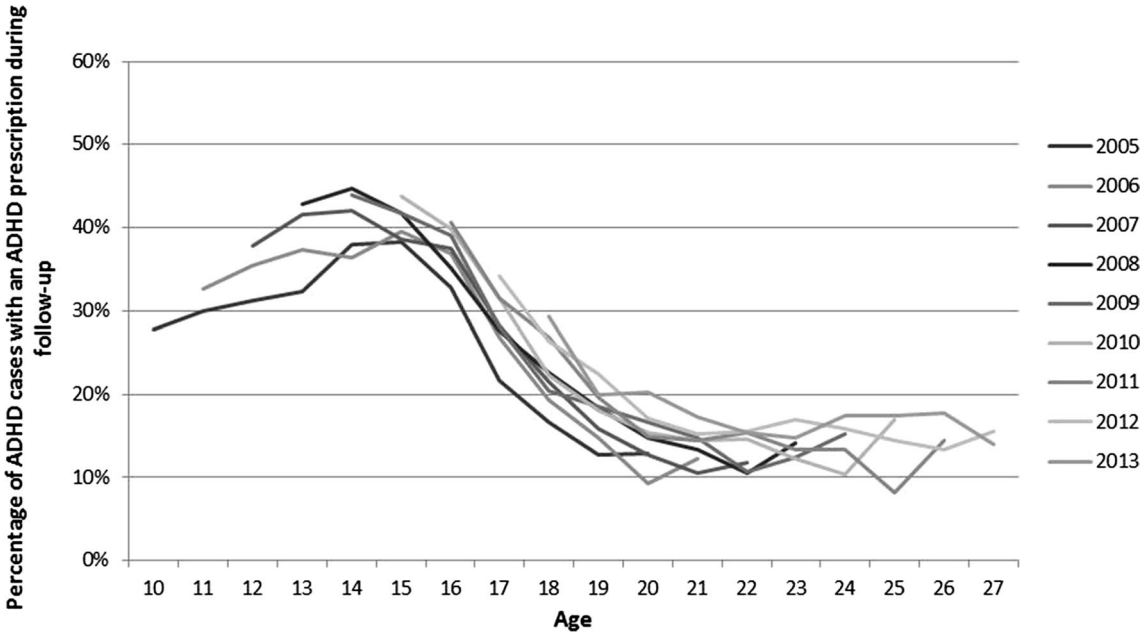

Fig. 2 Percentage of ADHD cases that were prescribed ADHD medication by age and study year

for non-ADHD psychotropic medication. We found that girls with ADHD were more likely to have a recorded diagnosis of comorbid depression or anxiety alongside ADHD and to be prescribed non-ADHD psychotropic medication.

Strengths and limitations

The chief strength of this analysis was the use of high-quality and recent data from a national database capturing current practice in primary care prescribing until the end of 2013, covering a period following the introduction of the UK NICE ADHD guidance.

In the UK, primary care databases are likely to provide the fullest picture of prescribing due to widespread shared-care protocols for ADHD (Ford et al. 2008). However, they fail to capture the smaller proportion of prescribing taking place in specialist services which might include shorter-term trials. Prescribing for those who de-registered from their practice would also no longer be captured in CPRD if they did not re-register with a CPRD-affiliated practice. These cases might represent a slightly different population,

for example, those moving away for education. Although estimates of validity of diagnoses in the CPRD are generally high, particularly for non-acute conditions, relying on clinician-coded diagnoses of ADHD to select cases might introduce bias (Herrett et al. 2010).

Perhaps the most significant limitation of this study when considering the implications regarding under-treatment or the appropriateness of treatment is that the data set did not contain information on several important factors that may influence prescribing. Data were not available on the severity of ADHD and of comorbid conditions, or on the specific indication for medication.

Comparison with existing literature

The decline in prescribing of ADHD medication in late adolescence that we describe coincides with the period of transition from child to adult services. The decline appears steeper and in excess of what would be expected from follow-up studies of persistence of symptoms (Faraone et al. 2006; Sibley et al. 2015). When examining secular trends, this pattern was still evident in the most recent years (2012 and 2013) included in this study. In contrast, Johansen et al.'s (2015) US study of ADHD prescribing found a much more gradual drop in the use of medication between the ages of 12 and 23 years, which supports the suggestion that prescribing will be heavily influenced by external factors such as service availability and attitudes of prescribers and patients (Hall et al. 2015; Matheson et al. 2013).

The proportion of adults with ADHD who are prescribed drugs for ADHD appears to have risen over time, albeit from a very low base. In 2008, NICE estimated that 1.2% of UK adults with ADHD were currently receiving ADHD medication, compared to our finding that 14–15% of adults over 20 had a prescription. This rise has been reported in previous studies covering earlier and overlapping time periods in the UK, as well as worldwide by Johansen et al. (2015), Zetterqvist et al. (2013), McCarthy et al. (2012a, b) and Raman et al. (2018). Therefore, this study, which uses prescribing records from between 2005 and 2013, may underestimate current 2018 rates of prescribing due to rapid changes in practice and service development. However, very recent reports highlight concern that some UK Adult ADHD services may be in the process of being decommissioned, and others have expanding waits, both factors which could act to influence prescribing prevalence and practice (Iacobucci 2018).

The rise in the prevalence of non-ADHD psychotropic prescribing in late adolescence is not unexpected, given that this is the peak age for emergence of new mental health diagnoses, whilst ADHD symptoms decline with age (Copeland et al. 2011). It is, however, plausible that these prescribing trends might represent prescribing of antidepressant or other psychotropic medications at the expense of treating ADHD, as symptoms of ADHD in adults may be less well recognised or mistaken for those of other psychiatric disorders (Kooij et al. 2010; Asherson et al. 2007).

Comorbidity is considered to be the rule rather than the exception in children and adults with ADHD (Jensen and Steinhausen 2015; Fayyad et al. 2016), and yet in this study only a quarter of all cases had a recorded comorbid psychiatric diagnosis during the study period. Of particular note was the very low prevalence of recorded substance or alcohol use disorders. Estimates from comorbidity studies are usually based on screening clinical samples using diagnostic instruments that will actively detect difficulties, and in our study diagnoses were recorded in routine practice. It is not possible to determine whether comorbid disorders were detected but not recorded. It is feasible, however, to suggest that the low prevalence we report could reflect under-diagnosis of certain common comorbid conditions.

Almost a fifth of cases with a comorbidity had a concomitant prescription of ADHD and other psychotropic medications, which is similar to the findings of Sikirica et al.'s (2013) European study. The overall prevalence of antipsychotic and mood stabiliser prescribing in our sample was 10%, which is in line with the results of a US study by Birnbaum et al. (2013) estimating that approximately 11% of young people with ADHD were also prescribed antipsychotics. A quarter of those with recorded comorbid ASD had antipsychotic or mood stabiliser prescriptions. Similarly, worldwide psychopharmacology studies suggest that antipsychotics are the most commonly prescribed class of drug in adults and children with ASD (Hsia et al. 2014; Jobski et al. 2016; Piñeiro-Dieguez et al. 2016), with a recent US study reporting that 20% of insured children with ASD were prescribed antipsychotics and 9% mood stabilisers (Madden et al. 2017).

Finally, our findings imply that females are more likely to be pharmacologically treated in primary care for psychiatric comorbidities with ADHD than males. The literature does suggest that there are gender differences in the identification and management of ADHD. Girls may face higher barriers to referral and to receiving a diagnosis (Maniadaki et al. 2006; Groenewald et al. 2009; Ohan and Visser 2009). Given that the females in our sample *had* been clinically recognised and referred, they may have represented a more severely affected group than males.

Implications for research and practice

Whilst this was a UK-based study, there are aspects which are generalizable internationally. For example, the challenges of transition and the fall in prescribing in ADHD medication over this period are described across international health systems (Johansen et al. 2015; Broad et al.

2017). Primary care physicians in many developed countries including the USA also have an important role in the management of ADHD in this group, meaning that the messages from this research will be relevant to international primary care practice and research (Bolea-Alamanac et al. 2014; Patel et al. 2017). The findings on the decline in ADHD prescribing, the gender differences in other psychotropic prescribing and the recorded prevalence of comorbid disorders all suggest that there is scope to optimise the management of ADHD over the transition period and improve the identification and treatment of psychiatric comorbidities amongst adolescents and adults.

Recent studies by Hall et al. (2015) have reported on inadequate provision of specialist services for this group in the UK. Furthermore, UK GPs perceive a range of barriers in managing adolescent mental health problems, including time and lack of training (O'Brien et al. 2016), and also report problems in gaining access to such specialist services for their patients (Roberts et al. 2013). Current UK guidance recommends that ADHD medication requires occasional review by a specialist, and where such services are not available this will limit the GP's ability to prescribe (NICE 2018). Ongoing efforts are therefore required to support and encourage holistic treatment where it may be helpful to the young adult with ADHD. Sustainable models are needed to provide age-appropriate services to advise and liaise with primary care and support shared-care protocols (Coghill 2015; Young et al. 2016). There is a strong case for further training for GPs and specialists not only on ADHD but on psychiatric comorbidities in the context of ADHD in both genders.

In terms of future research, in order to invest in improving ADHD management, the various models of delivering services need to be evaluated in terms of outcomes, cost-effectiveness and acceptability. A better understanding of the perspectives of service users themselves might also increase engagement with pharmacological and non-pharmacological interventions. Similarly, relatively little is known about what might influence the specific ADHD prescribing practices of clinicians in primary care. Further research into their perspectives and diagnostic and treatment practices is likely to help identify and address barriers to improved management.

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Compliance with ethical standards

Conflict of interest The authors declare no competing interests.

Ethical approval All protocols using patient-level data from the CPRD are reviewed for scientific quality and approved by the Independent Scientific Advisory Committee (ISAC) on behalf of the National Research Ethics Service Committee. This study protocol (13_213) was granted ISAC approval in January 2013.

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