Article

Adverse Drug Reaction Reporting and Prescribing Trends of Drugs for Attention Deficit Hyperactivity Disorder in Primary Care England, 2010–2019

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Abstract

Objective: We investigated the prescription trends and adverse drug reactions (ADRs) of ADHD drugs in primary care, England between 2010 and 2019. **Methods:** The Prescription Cost Analysis database presenting the primary care prescriptions data and the Interactive Drug Analysis Profiles presenting all suspected ADRs reported for each drug were screened. The data were analyzed using linear regression analysis to examine the annual average change per year. **Results:** The prescription items dispensed for ADHD showed an average 11.07% (95% CI 10.54–11.60, $p = .001$) increase per year and there was a mean 11.54% (95% CI 11.03–12.06, $p = .001$) increase per year in the costs. The overall reporting of serious and fatal ADR was reduced by 1.79% per year for ADHD drugs. Guanfacine showed a 40% mean increase per year. **Conclusion:** The increasing use of ADHD drugs within primary care in England could be a result of multiple factors such as growing ADHD prevalence. (*J. of Att. Dis. 2022; 26(3) 467-475*)

Keywords

adverse drug reactions, attention deficit hyperactivity disorder, cost, England, prescriptions

Introduction

ADHD is defined as a neurodevelopmental disorder that appears in early childhood, characterized by a continuous behavioral pattern of severe inattention, motor hyperactivity, and impulsivity, with symptoms often continuing into adulthood (American Psychiatric Association, 2013; Thapar, 2016). ADHD has been recognized as a significant public health issue due to its early onset, high prevalence, adverse outcomes, the persistence of symptoms beyond childhood (in at least two-thirds of patients), and association with secondary co-morbid mental disorders (Fayyad et al., 2017; Thapar, 2016; Turgay et al., 2012). The worldwide prevalence of ADHD in children and adolescents (aged <18 years) has been estimated to be around 2.2%, ranging from 0.1% to 8.1% (Fayyad et al., 2017). A higher prevalence in males compared to females has been a strongly consistent epidemiological finding; a male to female ratio varied, ranging from 3:1 to 16:1 depending on different countries (Nøvik et al., 2006).

The two main classes of pharmacological agents available for the treatment of ADHD include stimulants and non-stimulant medications. Stimulants include methylphenidate, dexamphetamine, and lisdexamfetamine, and non-stimulants such as atomoxetine and guanfacine are currently licensed in the United Kingdom (UK) for the treatment of ADHD in children, adolescents, and adults (Supplemental Table S1). The prescribing trends of ADHD medications in the UK have been previously reported but without serious or fatal ADR data (Beau-Lejdstrom, 2016; Renoux et al., 2016). Furthermore, published studies have mainly utilized the patient-level database, while investigation on the population-level ADHD drug utilization trends has been limited, where only one study available with the findings too old (10 years ago) to be relevant (Ilyas & Moncrieff, 2012). The investigation of the current prescribing trends is important as it provides valuable insights into the use of stimulants and non-stimulant medications for the treatment of ADHD, which may help in optimization of their prescribing, since misuse, overuse, and underuse of these medications can lead to wastage and health hazards, particularly for medicines (e.g., stimulants) that are associated with a high risk of adverse reactions.

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Given the increased prescribing trends of ADHD medications, the costs of ADHD medications have become another research focus. From 1993 to 2003, there was a three-fold increase in the use of ADHD medications globally, but a nine-fold rise in global spending (the U.S. $2.4 billion in 2003) (Scheffler et al., 2007). In England, the total annual cost for the stimulants and other drugs prescribed for ADHD was 29 million (National Institute for Health and Care Excellence (NICE), 2018). In addition, the cost of ADHD medications in England rose by 88.9% on average per year between 1998 and 2010 (Ilyas & Moncrieff, 2012). In an Irish cohort study conducted between 2002 and 2011, the net ingredient cost of ADHD medications showed an approximate 20-fold rise from €68,945 to €1,410,433 (Boland et al., 2015). The investigation of the trends in costs associated with the use of ADHD medications is important as the increasing number of prescriptions is one of the main contributing factors to increased cost (Kreling et al., 2001). Furthermore, there is a considerable debate in the literature over the association between inflation and the increased cost of medication. While the current belief is that medication prices would have increased at the rate of inflation (Hernandez et al., 2020; Pharmaceutical Research and Manufacturers of America, 2020) some researchers found that the increase in the cost of medications significantly exceeded inflation (Hernandez et al., 2020). Therefore, the primary aim of this study was to investigate and compare the trends of use in different classes of ADHD drugs to establish whether there has been an overall increase or decrease in the use of ADHD drugs between 2010 and 2019. The secondary aims of this study were to assess ADHD drug-related serious and fatal events and to determine the inflation-adjusted costs of ADHD drugs dispensed in primary care in England between 2010 and 2019.

Methods

Data Source: Prescription Costs Analysis (PCA)

Prescription Cost Analysis (PCA) database, which was downloaded from the NHS Business Services Authority website, consists of all the details of prescriptions written by general practitioners and non-medical prescribers (pharmacists, nurses, etc) (The NHS Business Services Authority (NHSBSA), 2019). The database also includes prescriptions written by hospital doctors and dentists provided they are dispensed in the community, and any prescriptions written in Wales, Scotland, Northern Ireland, and the Isle of Man but dispensed in England. However, any prescriptions written in England but dispensed outside England or the items dispensed in hospitals or private prescriptions are not covered by the database. The database is internally audited to 99% accuracy (NHS Digital, 2019).

The ADHD drugs which are dispensed are listed according to the British National Formulary (BNF) therapeutic classification in the PCA database. From the PCA database, we extracted data related to ADHD drugs dispensed by Pharmacy and Appliance contractors in England and dispensed by doctors and supplied under personal administration in England. A single medicine prescribed on a prescription form by a doctor (nurse/pharmacist etc) is referred to as a prescription item. The extracted data is arranged and separated by month, including every single prescription item—separating each drug into each formulation, and strength. The drug quantity is dependent on the product's formulation and is measured in units. Specifically, we recorded the number of total units dispensed (e.g., tablets, capsules, milliliters)—specific for each strength and brand. In addition, we also recorded the net ingredient cost—the price of the medicines as outlined by the drug tariff, or manufacturer or wholesaler (where appropriate), which is described as the drug's basic price before the discounts are applied and the cost for dispensing is added (NHS Digital, 2019).

Serious and Fatal Events

The Medicines and Healthcare Products Regulatory Agency (MHRA) ensures the safety, quality, and efficacy of the medicines and medical devices promoting public health and safety of patients. The Yellow Card Scheme run by the MHRA is a system used to report any suspected adverse drug reactions or incidents involving medicines and medical devices by the patients and healthcare professionals in the UK (Yellow Card, 2020). The Yellow Card Scheme can be used to identify unknown issues and investigate for any defective or fake medicines so that action can be taken if necessary.

The total number of fatal and serious ADR events were recorded for all the ADHD drugs from the year 2010 to 2019 fatal and serious ADR events are reported based on the following criteria: (1) patient died due to reaction, (2) life-threatening, (3) resulted in hospitalization or prolonged inpatient hospitalization, (4) congenital abnormality, (5) involved persistent or significant disability or incapacity, or (6) if the reaction was deemed medically significant (Yellow Card, 2020).

Data Analysis and Presentation

The extracted data were analyzed using Microsoft Excel and SPSS version 24. The monthly data obtained from the PCA was extracted and tabulated according to each ADHD drug and the total quantities and items dispensed for each drug per month were calculated—summarizing all formulations and strengths. The quantities for each month were then summed to find the total quantities or items dispensed per year in units of thousands. The total number of prescription items and costs for each ADHD drug was worked out for

Table 1. Prescription Items Dispensed and Costs of ADHD Drugs 2010 and 2019.

	Thousands of prescription items		Inflation-adjusted costs, £000s	Costs, £000s
Drug class, *n* (%)	2010	2019	2010	2019
Methylphenidate	662	1,235	32,224	41,271
Dexamphetamine	46	48	1,625	4,855
Lisdexamfetamine	0.01	191	2.6	13,185
Atomoxetine	87	142	9,683	9,190
Guanfacine	—	37	—	2,947
Total ADHD drugs, *n*	797	1,652	43,533	71,448
ADHD drugs as proportion of BNF total, %	0.086	0.147	0.480	0.787

2010 and 2019 to examine the trends in both prescriptions and costs of different categories of drugs over 10-year (2010–2019). Analysis and presentations of costs were presented in terms of an inflation-adjusted cost in years prior to 2019, using The Bank of England inflation calculator (Bank of England, 2020).

The proportion of total prescription numbers and costs accounted for by all ADHD drugs combined in both 2010 and 2019 were obtained. The contribution made by different ADHD drugs to prescriptions and costs in both years was also obtained. We also presented the total prescriptions normalized to per 1,000 Clinical Commissioning Group (CCG) population for the year 2019, serious/fatal adverse drug reactions (ADRs) for various ADHD drugs normalized to the number of ADHD items prescribed during the last 10 years, and Costs of ADHD drugs normalized to the number of ADHD items prescribed during the last 10 years. The number of ADHD medication prescriptions as a proportion of total BNF-listed medication was calculated by dividing the total number of ADHD medication by the total number of BNF-listed medication and multiplying with 100. A similar approach was used to calculate the total cost of ADHD medication and cost of ADHD medication as a proportion to the cost of total BNF-listed medication. Linear regression analysis was performed with the year as the independent variable and prescription items (quantity & items dispensed) and costs as the dependent variables, using data from each year (starting from 2010), with p-value $<.05$ indicated statistical significance. We calculated and presented the average annual percentage increase by dividing the regression coefficient by the baseline prescriptions or costs from 2010 (Ilyas & Moncrieff, 2012).

Results

Trends in ADHD Drugs Prescriptions

Overall, there was an increase in the quantity of all ADHD drugs dispensed (Supplemental Figure S1), with an exception of dexamphetamine. The most dispensed medicine was methylphenidate with a big difference compared to the other medications. Methylphenidate showed a significant increase in the prescription items dispensed from 2010 to 2019.

Another stimulant drug, dexamphetamine maintained a mixed trend in the prescription items dispensed over the years, whereas other drugs showed an increasing trend. Atomoxetine was the second most dispensed drug from 2010 to 2017, following behind methylphenidate. In 2010, lisdexamfetamine was the lowest dispensed ADHD drug, but it showed a sharp increase from 2012 to 2019 and surpassed atomoxetine to be the second most prescribed item in 2018 after methylphenidate. The utilization for guanfacine started in 2016, where it showed a steady rise in the items dispensed.

Comparison of the prescription items dispensed between 2010 and 2019 showed that the total number of ADHD drugs dispensed in 2019 nearly increased by 90% as compared to 2010 (Table 1). However, the total number of drugs listed in the BNF also increased from 2010 to 2019. Hence, the total percentage of ADHD drug items dispensed as a proportion of the total number of drugs listed in the BNF, increased by 56% from 0.086% to 0.147%. Dexamphetamine showed a similar trend in the number of prescription items from 2010 to 2019. Lisdexamfetamine showed the highest increment from 2010 to 2019. The costs showed a rise from 0.480% (inflation-adjusted) in 2010 to 0.787% in 2019 for ADHD drugs as a proportion of BNF in total.

Figure 1 presents the costs of ADHD prescription items over the last 10 years, normalized to the respective number of prescription items. All five drugs showed an increase in costs over the years. However, when the cost of ADHD drug was normalized to the respective number of prescription items, we observed decreased in cost per prescription item was for three drugs (methylphenidate, lisdexamfetamine, and atomoxetine), and increased for two drugs (dexamfetamine and guanfacine). The per-item cost of dexamphetamine was increased from £28 in 2010 to £101 in 2019 whereas the per-item cost of lisdexamfetamine item was decreased from £328 in 2010 to £69 in 2019 (Figure 1).

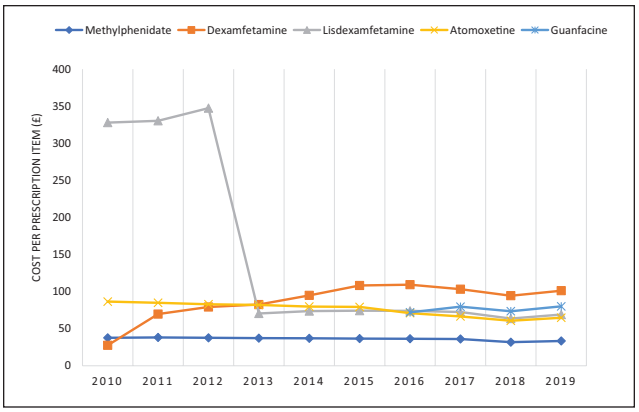

Figure 1. Costs of ADHD drugs normalized to the number of ADHD items prescribed during the last 10 years.

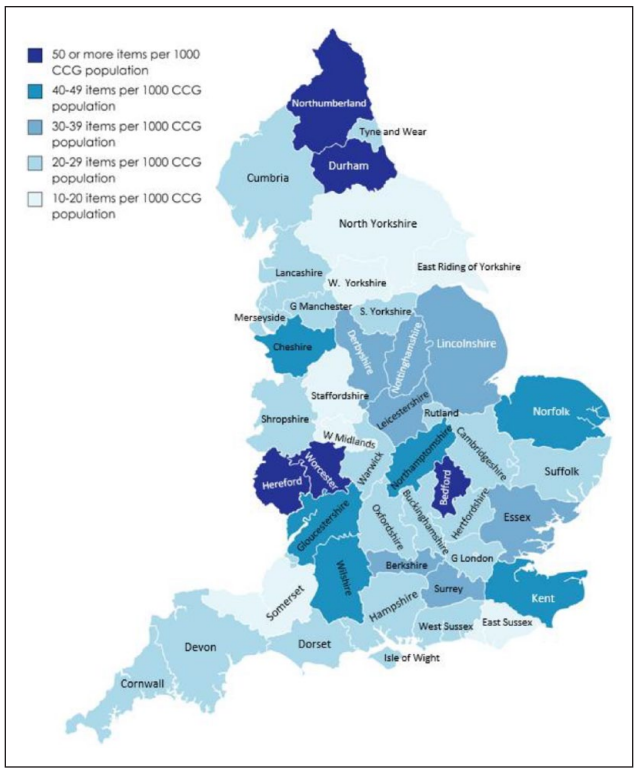

Figure 2. Total prescription items for ADHD drugs, normalized to per 1,000 CCG population for the year 2019.

The geographical differences were evident in Figure 2 highlighting the regions with the highest and lowest rates of ADHD prescriptions shown by different shades of blue (darkest for highest usage). The lowest ADHD prescribing regions were North Yorkshire (12.12 per 1,000 CCG population) and East Riding of Yorkshire (12.35 per 1,000 CCG population). The highest prescribing regions were Durham (62.38 per 1,000 CCG population), Herefordshire, and Worcestershire (55.78 per 1,000 CCG population).

From 2010, the regression analysis shows an 11.07% increase in the total ADHD prescriptions per year (Table 2). Dexamphetamine showed a decrease in the prescriptions dispensed per year though it was not significant statistically. On average, an 11.54% increase per year was seen for the costs of total ADHD drugs from 2010 to 2019. A statistically significant increase ($p < .05$) was shown for most of the drugs except atomoxetine.

Serious and Fatal Outcomes

Supplemental Figure S2 displays the trend of the total number of ADRs with ADHD drug usage over the last 10 years. Methylphenidate had the highest number of reporting for serious or fatal ADR events in the UK from 2010 to 2019. The number of serious and fatal ADR events with methylphenidate showed a peak of 85 reports in 2011 and then a constant decrease with two peaks in 2015 and 2017. The lowest reporting for serious and fatal ADR events with the use of methylphenidate was in 2018 which coincided with the highest quantity dispensed. Dexamphetamine had the lowest number of serious or fatal ADR events reported from 2010 to 2019 compared to all other ADHD medications. From 2010 to 2015, the second-highest reporting of serious and fatal ADR events was observed for atomoxetine, however, it showed a decline after 2015.

Figure 3 display the trend of the total number of ADRs with ADHD drug usage over the last 10 years, normalized to the respective number of prescription items. Figure 3 showed a decrease in the numbers of ADRs per million prescription items for five ADHD drugs. In 2019, the number of ADRs per million items was lowest for methylphenidate (39 ADRs per million items) and highest for guanfacine (462 ADRs per million items).

Table 3 shows an average of 1.79% decrease in the reporting of serious and fatal ADR events for total ADHD drugs per year as a percentage of baseline. Guanfacine showed a 40% increase while dexamphetamine had an 11.5% increase in the reporting for serious and fatal ADR events. Methylphenidate, lisdexamfetamine, and atomoxetine had fewer serious and fatal ADR events reporting in 2019 as compared to 2010.

Discussion

The present study aimed to explore the trends in prescriptions, adverse events, and costs of drugs for ADHD between 2010 and 2019 in England. Overall, there was an increase in the prescription and cost trends for most of the ADHD medications. The increasing trend in ADHD prescriptions was consistent with the data reported in the United States, Canada, Australia, Japan, Hong Kong, Western and Northern Europe for children, adolescents, and adults (Raman et al., 2018).

Table 2. Regression Analysis of Yearly Trends in Prescriptions (Items Dispensed) and Cost.

Items	Prescription trends		Prescriptions, mean change per year as % of baseline[a] (95% CI)	Cost trends		Costs, mean change per year as % of baseline[a] (95% CI)
	Regression coefficient (95% CI)	*p*		Regression coefficient (95% CI)	*p*	
Methylphenidate	61.98 (58.37, 65.60)	.001	9.37 (8.82, 9.92)	194876.76 (169160.95, 220592.56)	.001	7.81 (6.78, 8.84)
Dexamphetamine	−0.48 (−1.01, 0.11)	.100	−1.05 (−2.22, 0.24)	31805.60 (15410.55, 48200.65)	.003	25.29 (12.26, 38.33)
Lisdexamfetamine	17.67 (12.03, 23.31)	.001	294500 (200500, 388500)	126605.06 (87718.73, 165491.39)	.001	64342.63 (44580.0, 84105.26)
Atomoxetine	6.07 (5.03, 7.01)	.001	7.01 (5.81, 8.10)	14888.70 (−2999.59, 32776.98)	.090	1.99 (−0.40, 4.37)
Guanfacine	10.10 (5.26, 14.95)	.024	217.11 (113.07, 321.37)	84645.84 (50455.91, 118835.76)	.020	252.621 (150.58, 353.66)
Total ADHD drugs	87.85 (83.62, 92.09)	.001	11.07 (10.54, 11.60)	388953.54 (371652.99, 406254.10)	.001	11.54 (11.03, 12.06)

[a]% change was calculated by dividing the regression coefficient by baseline prescriptions or costs from 2015 as given in Table 1.

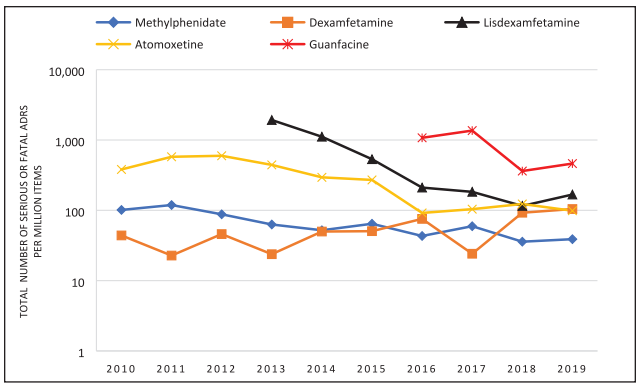

Figure 3. Serious/fatal adverse drug reactions (ADRs) for various ADHD drugs normalized to the number of ADHD items prescribed during the last 10 years.

The increasing trend for the prescribing of ADHD medications is a result of many factors including increased prevalence and improved diagnosis of ADHD in recent years in the UK, which creates a possibility for higher rates of pharmacological treatment (Renoux et al., 2016). Besides, the GPs had been involved more actively in the management of ADHD and frequently prescribed ADHD drugs which were often done by specialists in the past (Renoux et al., 2016). However, this increasing trend also raised concerns regarding overdiagnosis and inappropriate ADHD medication prescribing (Raman et al., 2018).

As reported previously, between 1998 and 2010, the use of ADHD drugs increased by 25.6% (22.7–28.5) (Ilyas & Moncrieff, 2012). However, in this study, the percentage increase per year between 2010 and 2019 was only 11.07% (10.54–11.60), suggesting a drop of almost 15% per year. In another study conducted using the UK CPRD database (patient-level), the overall prescription rates increased by around 700% between 1998 and 2010 (Renoux et al., 2016), but our study using population-level database showed a rise of around 90% from 2010 to 2019. The bigger increase initially (before 2010) could be related to the broken stigma around ADHD, resulting in an increased diagnosis of this condition. The increased awareness in public may also lead to initial higher rates of prescriptions.

However, over the years, the observed drop in the increasing trend of prescribing in our study could be due to adequate recognition of ADHD patients and their treatment for children in the UK as most people have been detected earlier (Beau-Lejdstrom et al., 2016). Besides, the drop in the increasing trend could also be due to the trial of other non-pharmacological interventions before prescribing ADHD drugs. The 2018 updated guidelines by The National Institute for Health and Care Excellence (NICE) in the UK specifies that pharmacological therapy should not be the first-line treatment for school-aged children and young adults with ADHD (Beau-Lejdstrom et al., 2016). Furthermore, the drop in the increasing trend could also be due to the reporting of severe adverse events, although there have not been any warnings for ADHD drugs licensed in the UK (Beau-Lejdstrom et al., 2016).

Our results of individual ADHD drugs complied with the findings in previous studies (Beau-Lejdstrom et al., 2016; Ilyas & Moncrieff, 2012; Renoux et al., 2016). Methylphenidate accounted for the most prescriptions throughout the years from 2010 to 2019 with an average 9.37% increase every year. It is first-line treatment according to the NICE guidelines because its efficacy is proven in a higher number of clinical studies (Cortese et al., 2018), suggesting a good balance of efficacy against side effects in ADHD. This drug also has a wider range of formulations (short and extended-release) available in the UK (Bolea-Alamañac et al., 2014). However, the high use of methylphenidate may also be a result of over-prescribing as this drug can be misused to improve cognitive function (Care Quality Commission, 2016).

Atomoxetine (non-stimulant) was another first-line medication used to treat ADHD symptoms in the past, alongside methylphenidate. However, with the change in NICE guidelines which recommends the use of lisdexamfetamine as first-line (alongside methylphenidate), lisdexamfetamine had become the most frequently prescribed ADHD drug after methylphenidate. Lisdexamfetamine was given unlicensed under the brand name Vyvanse before the entry of

Table 3. ADRs of ADHD Drugs Reported from January 2010 to December 2019 in the UK.

Items	Reporting of serious and fatal ADR events		Serious and fatal ADR events, mean change per year as % of baseline[a] (95% CI)
	Regression coefficient (95% CI)	*p*	
Methylphenidate	−3.37 (−6.79 to 0.059)	.053	−5.03 (−10.13 to 0.09)
Dexamphetamine	0.23 (−0.85 to 0.55)	.127	11.5 (−42.5 to 27.5)
Lisdexamfetamine	−0.57 (−5.35 to 4.21)	.757	−4.75 (−44.58 to 35.08)
Atomoxetine	−5.32 (−9.39 to −1.25)	.018	−16.12 (−28.45 to −3.79)
Guanfacine	2.00 (−100.70 to 104.70)	.846	40 (−2014 to 2094)
Total ADHD drugs, *n*	−2.78 (−9.65 to 4.09)	.370	−1.79 (−6.23 to 2.64)

[a]% change was calculated by dividing the regression coefficient by baseline serious and fatal ADR events from 2015.

Elvanse in the UK. After the launch of lisdexamfetamine dimesylate (Elvanse) in the UK, and its inclusion in the BNF, in 2013, we observed a big jump in items dispensed and quantity for this drug as shown in our study. The approval was based on the results from phase 3 trials including children and adolescents with ADHD (Coghill et al., 2013). Lisdexamfetamine displayed a better efficacy as compared to atomoxetine based on a prospective comparison, and methylphenidate (osmotic release oral system) according to post hoc comparison (Frampton, 2018). It has a similar adverse effect profile compared to other stimulating agents and is also well tolerated.

The steady decrease in dexamphetamine is justified by the rare use of this drug because it is not used as first-line in primary care as per the indications in NICE and BNFC. This is also due to the licensing of another stimulant (lisdexamfetamine) which is preferred because dexamphetamine is more susceptible to abuse compared to lisdexamfetamine. Moreover, the longer effect of lisdexamfetamine helps lower the stigma associated with someone taking multiple doses in a day, particularly at school or the workplace (NICE, 2018b). There has also been an 11.5% increase in the reporting for serious and fatal events reported for dexamphetamine as shown in our study (Bolea-Alamañac et al., 2014).

Atomoxetine showed a constant increase in the number of items prescribed and was the second most prescribed item for ADHD from 2010 to 2017; however, a decrease was seen for the proportion of prescriptions to total ADHD drug use. Atomoxetine lacks stimulant effects as it does not have a direct effect on dopamine availability. Therefore, it has less potential for abuse as compared to other ADHD drugs (Bolea-Alamañac et al., 2014). It is also commonly prescribed because it can be given to patients in whom stimulants are contraindicated, or who are not tolerant or responsive to methylphenidate. It is also used for patients who are at risk of stimulant misuse or abuse (NICE, 2019). According to the data from the meta-analysis of clinical trials, there is little difference in the clinical efficacy of atomoxetine and stimulants (Care Quality Commission, 2016). The decrease of atomoxetine as a proportion of total ADHD drugs is most likely due to the licensing of another non-stimulant, guanfacine in 2016. A 217.11% rise per year was seen for the prescriptions of guanfacine after it was licensed in the UK in 2016.

Adequate treatment of ADHD patients is very cost-effective as found in a systematic review involving children, adolescents, and adults (Doshi et al., 2012). The cost of a drug is an important factor as NICE generally consider costs when approving drugs. The changing trends in prescriptions are directly related to the costs of pharmacological treatment. ADHD drugs cost less than 1% of total BNF drugs, in terms of both inflation cost and actual cost in 2019. From 2010 to 2019, we found an average of 11.54% increase per year in the prescription costs in the study conducted. However, previous studies showed a mean increase of 88.9% per year over the 13 years (1998–2010) (Ilyas & Moncrieff, 2012). This was due to a higher jump in the rate of prescriptions dispensed during the previous years as compared to recent years as demonstrated in our study. The increasing trend in costs was consistent with the previous studies in other settings (Boland et al., 2015; Ilyas & Moncrieff, 2012; Scheffler et al., 2007).

Our analysis showed that the cost of dexamphetamine was increased from £28 per item in 2010 to £101 per item in 2019 whereas the cost of lisdexamfetamine item was decreased from £328 per item in 2010 to £69 per item in 2019. Dexamphetamine had a decrease in the number of prescriptions prescribed every year, but the cost of this drug increased by an average of 25.29% every year. This could be due to the huge increase in price for dexamphetamine items, for example, the price of 5 mg (28) dexamphetamine tablets increased from £3.00 in 2010 to an average of £24 in 2018 (OpenPrescribing, 2020). Lisdexamfetamine was the second most prescribed item after methylphenidate. In fact, the average increment of the cost of lisdexamfetamine per year was the largest among all the ADHD drugs. Regardless of the high price for lisdexamfetamine, a cost-utility analysis for adults in the UK, found that lisdexamfetamine was

more cost-effective as compared to extended-release methylphenidate and atomoxetine (Zimovetz et al., 2018). Methylphenidate had a very significant difference in the number of items dispensed as compared to other drugs, which justified the highest net ingredient cost reported with methylphenidate from 2010 to 2019. In a study conducted by Ilyas and Moncrieff (2012), methylphenidate accounted for the majority of the cost (57%) in ADHD drugs in 2010 which aligned with our results showing methylphenidate as the highest contributor in cost for 2019 (58%). The approval of newer longer-acting stimulants and non-stimulants dramatically increases the cost of ADHD medications (British National Formulary (BNF), 2019). Although some patients may need pharmacological treatments for a time-limited period, most others may need them indefinitely. Therefore, these increases can contribute to financial hardship which may lead patients to be non-compliant toward ADHD medications or completely avoid filling prescriptions.

Most of the ADHD medications used are effective and well-tolerated, however, some patients experience adverse events associated with the treatment provided. There was a decrease in the reporting for serious and fatal ADR events for most of the ADHD medications. Dexamphetamine and guanfacine showed a slight increase for serious and fatal ADR events from 2010, but they had low reporting compared to other drugs in general. Methylphenidate had the highest number of reporting for serious and fatal ADR events.

Methylphenidate was the most common ADHD drug dispensed, and hence more frequent reporting of adverse drug events. Nevertheless, we observed that the number of serious and fatal events showed an average 5.03% decrease every year. In 2010, 67 serious adverse events were reported as compared to 48 serious adverse events in 2019; there were no fatalities reported in 2010 and 2018. The highest reporting of fatal ADR events (three fatalities) was seen in 2011, 2012, and 2015.

On the other hand, guanfacine showed an average of 40% increase in the reporting of serious and fatal ADR events per year with the highest reporting in 2017, although it was the least prescribed drug in that year. This could be because guanfacine was launched in the UK in 2016 and is a relatively new drug to be prescribed in the UK, where patients were asked to report any adversities. Another possible reason might be that the prescribers may have adopted a more cautious approach and were more vigilant in identifying and reporting ADRs because of their lack of familiarity with the new medication; however, the reporting decreased in the next year as the prescribers gained more confidence in using the medication.

Our study is limited by the fact that the population-level dataset is not based on a sample from individual patients, therefore individual characteristics such as gender, ethnicity, and age cannot be investigated. Therefore, an increase in the number of prescriptions can also indicate a rise in population size or longer usage of the medication which cannot be determined from this study. Furthermore, this study investigated prescribing rates that may not reflect the actual use or consumption of medication by the patients. In addition, a prescription cost analysis was based on the PCA database providing details of all community prescriptions in England where the drugs issued in hospitals are not covered. Furthermore, the investigation of serious and fatal ADR events through the UK Yellow Card Scheme had limitations as not all patients report their adverse effects because it is not mandatory. There was also no information about indication, patient's information, hospital data, etc.

Conclusion

In summary, the overall rate of prescribing for ADHD medication increased significantly between 2010 and 2019 in England. Among the five licensed drugs in the UK, methylphenidate (Stimulant) was the most frequently prescribed item throughout the years, and hence the costliest and most reporting for serious and fatal events. There was an 11.54% increase in the trends for costs for all ADHD drugs. This could be due to the increased population, increased diagnosis of ADHD, increased number of patients receiving pharmacological treatment, and the use of drugs for a longer period. The total and the inflation-adjusted costs in 2019 accounted for less than 1% of the total BNF drugs. The reporting for serious and fatal ADR events for ADHD medications showed an overall decrease, though with an increment for guanfacine as this was introduced in 2016 and is a relatively new drug.

Author Contributions

All authors were investigators in the study and participated in the study design, interpretation of the study results, and in the drafting, critical revision, and approval of the final version of the manuscript. SSH conducted the statistical analysis.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Ethics Approval

This study used anonymized information from the NHSBSA database; therefore, institutional ethics approval was not required.

Consent to Participate

This study used anonymized information from the NHSBSA database; therefore, informed consent was not required.

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Availability of Data and Material

The data that support the findings of this study are available from the NHS study, please contact NHSBSA (https://www.nhsbsa.nhs.uk).

Supplemental Material

Supplemental material for this article is available online.

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