Impact of deprivation, dementia prevalence and regional demography on prescribing of anti-dementia drugs in England 2009-2019: a time trend analysis

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Abstract

Aim This study aimed to examine trends in prescribing of anti-dementia drugs in primary care in England between 2009-2019 and to investigate the impact of deprivation, regional demography and disease prevalence on prescribing practices. Methods Analysis of publicly available government data from various sources pertaining to primary care prescribing and demographics was conducted. All primary care prescription data pertaining to anti-dementia drugs and antipsychotic drugs in England between 2009-2019 were extracted and adjusted for inflation and populations changes. Data across English Clinical Commissioning regions and groups were compared to explore the association between prescribing trend, deprivation, regional demography and dementia prevalence. Anti-psychotic drugs prescribing trends were used as reference comparators. Results The number of prescription items for anti-dementia drugs in England increased by approximately three-folds from 24 items/1,000 populations in 2009 to 70.9 items/1,000 populations in 2019; prescribing of antipsychotics increased by 37.6%. In 2019, the least deprived areas had approximately twice the rate of prescribing of anti-dementia drugs compared to the most deprived areas [median (IQR) values of 46.7 (36.6-64.8) vs 91.23 (76.2-95.1) items/1,000 populations respectively]. A weak positive correlation (Pearson's correlation-coefficient 0.371, p=0.413) was observed between dementia prevalence and prescribing rates. Conclusions The three-fold rise in the number of prescription items for anti-dementia drugs in the study period reflects the policy emphasis on early diagnosis and treatment of dementia. Higher rates of prescribing in the least deprived areas may be reflective of higher life expectancy, better diagnoses and access to treatments. Such differences need to be investigated further.

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Introduction

Globally, there are over 47 million people are living with dementia, with this figure set to reach 135.46 million by 2050 [1]. As of 2019, a total of 472,890 people in England have a coded diagnosis of dementia [2].

The National Institute of Clinical Excellence (NICE) guideline on Dementia in England recommends acetyl-cholinesterase (AChE) inhibitors: donepezil, galantamine and rivastigmine as recommended monotherapies for the management of mild to moderate Alzheimer's disease (AD) [3]. The NICE guideline recommend that the N-methyl-D-aspartate (NMDA) receptor antagonist, memantine, should be used to treat moderate AD in patients who are intolerant or have a contraindication to AChE inhibitors. Memantine is also recommended to be used in patients with an established diagnosis of AD when AChE inhibitors are already being used. The NICE guidelines also recommend AChE inhibitors for the treatment of non-Alzheimer's

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dementia; however, they do not have a UK marketing authorisation for this purpose and therefore must be prescribed off-label [3].

In addition to AChE inhibitors and memantine, antipsychotics are recommended for the management of non-cognitive symptoms of dementia. These symptoms of dementia include agitation, aggression, distress and psychosis. Currently in the UK, risperidone and haloperidol are the only antipsychotics with a UK marketing authorisation for the treatment of non-cognitive symptoms associated with dementia [3].

In the last decade, there has been an increased emphasis on the diagnoses and management of dementia in primary care, prior to any psychiatric referrals. The National Dementia Strategy (NDS) published in 2009 in England emphasised the need to improve public and professional awareness and understanding of dementia as well as early diagnosis and treatment [4]. The Quality and Outcomes Framework (QoF) is a voluntary annual reward and incentive programme for all general practices in England. This incorporates better diagnosis and management of dementia, including a follow-up care plan in primary care, as one of the key quality indicators [5].

Evaluation of prescribing practices in dementia have predominantly focused on minimising the potentially inappropriate use of antipsychotics for treatment of non-cognitive symptoms [6-9]. However, a time trend analysis of prescribing of drugs used in the management of dementia, in the context of recent policy emphases on better diagnosis and management of dementia in primary care, have not been investigated to a similar extent. In addition, the link between deprivation, prevalence and prescribing for dementia remains poorly understood. Geographical and deprivation level variations in prescribing practices can inform stratification of targeted interventions to identify linked co-morbidities and reduce health inequalities. The aim of this study was to analyse the trends in prescribing of anti-dementia drugs in primary care in England from 2009 to 2019 and to investigate the impact of deprivation and regional demography on prescribing practices.

Methods

Ethical consideration

This study represents secondary analysis of the information retrieved from publicly available anonymised datasets and does not warrant formal ethical approval.

Study Design and Population

A longitudinal study of national primary care prescribing datasets were undertaken using NHS Digital sources, namely- OpenPrescribing.net and Prescription Cost Analysis (PCA) [10,11]. OpenPrescribing.net is a national online prescribing data resource hosted by the Evidence-Based Medicine DataLab at the University of Oxford. The resource provides general practice level prescribing data which is published each month from NHS Digital for all prescriptions written by general practitioners and other non-medical prescribers who are attached to the practices. This includes the number of items prescribed and the actual cost of the medication [12]. PCA statistics are provided by NHS Digital and present prescription data regarding the number of items and the net ingredient cost (NIC) of all prescriptions dispensed by the NHS in the community in England [13].

Data Extraction and Analysis

Prescription data from January 2009 to December 2019 for anti-dementia drugs, relating to British National Formulary (BNF) Section 4.11 [14], were included. Data on donepezil, galantamine, rivastigmine and memantine were extracted. Prescription patterns relating to 10 of the most and the 10 of the least deprived Clinical Commissioning Groups (CCGs) as per the Office of National Statistics (ONS) Index of Multiple Deprivation (IMD) in 2015 [15] (Supplemental material 1) were also extracted and analysed to explore the link between prescribing patterns and deprivation. The CCGs are clinically-led autonomous NHS bodies involved in planning and commissioning healthcare services for their locality. The 10 most deprived and the 10 least deprived CCGs included in the analysis covered a population of 2.8 million and 2.3 million respectively. All data were adjusted for population estimates for each year at national, regional and CCG level [16].

Costs of prescription items were adjusted for inflation using the ONS Consumer Price Index (CPI) for pharmaceutical products [17]. Dementia prevalence for 2017-18 data was obtained from Quality and Outcomes Framework Datasets [18] All data were extracted, independently checked for accuracies and analysed using Microsoft Excel and SPSS V21. The Independent-Sample Median test was used to analyse the differences in the median value for prescription items and costs across NHS England Commissioning Regions for each year. The Independent-Samples Mann-Whitney U Test was used to examine the variation in prescription items and costs across categories of the most and least deprived areas in England. P values of <0.05 were considered significant. Data trends on antipsychotic drugs, including haloperidol and risperidone, were also similarly extracted and analysed to be used as a comparator drug class.

Results

Prescribing of anti-dementia drugs between 2009 and 2019

The number of prescription items dispensed in England for the pharmacological treatment of dementia (anti-dementia drugs, BNF Section 4.11) increased by approximately three folds from 24 prescription items per 1,000 populations in 2009 to 70.9 prescription items per 1,000 populations in 2019, reflecting an increase of 195.4% (table 1, figure 1).

Donepezil was the most commonly prescribed anti-dementia drug both in 2009 and 2019, accounting for 64.0% and 52.0% of all anti-dementia prescribing respectively. Of all anti-dementia drugs, highest increase was noted for prescribing of memantine which increased from 4.5% in 2009 to 34.7% in 2019. Prescriptions for galantamine decreased over the same period by 40% (table 1).

The results presented an overall decrease in the cost incurred from prescribing drugs for dementia, increasing by 17.5% from 2009 to 2011 but then drastically decreasing by 82.0% from 2011 to 2019. This resulted in an overall decrease in costs of 81.7% from 2009 to 2019 (table 1, figure 2).

The costs of prescribing rivastigmine peaked in 2012 at £342.69 per 1,000 populations, followed by a substantial reduction in costs by 88.8% in the following year between 2012 and 2013. Overall, the costs of memantine increased by 61.8% 2009 to 2019, peaking in 2013 at £434.54 per 1,000 populations. A significant reduction in the costs of donepezil by 40.0% was observed between 2011 and 2012. Donepezil's cost per item decreased by the largest proportion from 2019 to 2009 which decreased by 98.8% over the 10-year period (table 1, figure 2).

Prescribing of antipsychotics drugs: 2009 – 2019

The prescribing of all antipsychotic drugs showed a steady increase of 37.6% over the 10-year period (table 1, figure 3). Antipsychotic prescribing was consistently higher than prescribing of anti-dementia drugs, however, the rate of increase in prescribing for anti-dementia was higher in the study period. In particular, prescriptions of haloperidol and risperidone also increased from 2009 to 2019 by 13.2% (table 1, figure 3). Costs of prescribing of all antipsychotic drugs decreased by 71.4% from 2009 to 2019 (table 1, electronic supplemental material 2). Both antipsychotics and anti-dementia drugs presented an initial increase in costs from 2009 to 2011, followed by a decrease from 2011 to 2016. Haloperidol and risperidone showed a decrease in costs from £421.10 to £301.79 (-28.33%) per 1000 populations from 2009 to 2019 (electronic supplemental material 2).

Association between deprivation and prescribing

Prescribing in the least deprived areas was substantially higher than that in the most deprived areas from 2015 to 2019 (table 2). The median (IQR) prescription items for the least deprived CCGs for all five observations was 75.68 (72.32-86.67) compared with 44.62 (43.03-44.85) items per 1,000 populations in the most deprived areas (p = 0.008). Similarly, the median (IQR) costs of prescribing per 1,000 populations in the most deprived areas across all five observations was £255.18 (233.48-320.74) compared with £625.87 (563.25-654.78) in the least deprived areas (p=0.008) (table 2). There was a larger observed variation in both items and cost data within the most deprived areas compared to the least deprived areas (table 2).

Variations across NHS England Commissioning Regions

Prescription items for dementia increased from 2015 to 2019 in every NHS England commissioning region (electronic supplemental material 3). Prescribing was consistently highest in the North East and Yorkshire region and lowest in the Midlands for the duration of the measured time period. In 2009, the North East and Yorkshire region, a total of 85.6 prescription items per 1,000 populations were prescribed compared with 41.2 per 1,000 populations in the Midlands. Similarly, in 2019, the North East and Yorkshire region prescribed 101.4 items per 1,000 population, 96% higher than the 51.8 items prescribed in the Midlands (table n) (p=0.015). A significant difference in the median costs of prescribing was also observed (p=0.001). A weak positive correlation between prevalence of dementia and prescription of anti-dementia drugs was observed (Pearson's correlation coefficient 0.371, p= 0.413).

Discussion

This overall aim of this study was to examine prescribing trends and associated costs of anti-dementia drugs in primary care in England and to investigate the impact of deprivation, regional demography and disease prevalence on prescribing practices and patient access to these drugs. This study demonstrates a three-fold rise in prescribing of anti-dementia drugs in England in the last 10 years. The increase is reflective of the policy emphases on the early and better diagnosis and management of dementia in primary care in England. Alzheimer's disease and other dementias currently rank as the leading and second most common cause of death amongst females and males in England respectively [19]. In 2011 and 2014, there were updates to the coding framework in primary care used to code the cause of death. These changes also required dementia to be identified as the underlying cause of death rather than 'other health conditions'. An updated national strategy has been launched in 2020 in England which aims to continue to emphasise early diagnoses, treatment and support for investigation and provision of newer therapies [20]. The prescription data analysed in this study triangulates well with the increasing prevalence and mortality data.

The number of prescription items for the NMDA receptor antagonist, memantine, presented the largest percentage increase over the 10-year period. This notable increase emerged in 2011 and may be causally linked with an update to the NICE guidelines in the same year. Prior to 2011, memantine was only recommended for use in clinical trials for patients with moderate to severe AD [21]. However, following the update to the NICE guidelines, memantine was recommended for patients with moderate to severe AD who had a contraindication to AChE inhibitors [22]. This increase in prescribing of memantine in 2011 is concurrent with the trends observed in another study [23].

From 2009 to 2019, the cost per item of all anti-dementia drugs (BNF Section 4.11) decreased by over 50%. Donepezil and memantine saw the largest reduction in this value, decreasing by 98.8% and 92.9% respectively. The observed reduction in costs coincides with galantamine's patent in January 2012, donepezil's in February 2012 and rivastigmine's in July 2012. Memantine, the NMDA receptor antagonist, lost exclusivity in April of 2014.

Analysis at Clinical Commissioning Group level found an inverse relationship between deprivation and prescribing patterns. This is concurrent with previous findings reporting that in English practices, patients with dementia are 27% more likely to receive a dementia prescription in the least deprived areas compared with those in the most deprived areas [24]. Furthermore, these differences could be related to factors affecting life expectancy based on deprivation considering the late onset feature of dementia.

The variations in prescribing rates were higher in the most deprived regions compared to the least deprived regions. Regional variations in prescribing rates were also observed with no clear cut 'North-South' divide observed in the datasets. The data is suggestive of the presence of pockets of 'deprivation' and 'affluence' in all regions [25, 26]. These differences need to be investigated further.

This study also shows that prescription of all antipsychotic medication increased during the 10-year study period. The National Dementia Strategy (NDS) published in 2009 aimed to reduce antipsychotic use among

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people with dementia, however, the trends in prescribing of antipsychotics from 2009 to 2019 has not reflected a change in prescribing practices [4, 27]. Previous studies which has looked into prescribing of antipsychotics following the launch of the NDS, also suggested no notable change in prescribing rates 4 years following the implementation of this strategy [6].

Strengths and Limitations

National prescribing datasets covering all patients registered with a general practice in England were included in this study. We did not investigate record of the indications, reasons or length of treatment for the drugs prescribed. Furthermore, the 10 most and 10 least deprived CCGs are only representative of the two extremes, they do not represent the entire population of England. It is important to note that the data regarding the prescriptions and costs of antipsychotics were not exclusively related to prescribing for dementia. Antipsychotics can be used for the treatment of multiple other disorders, such as psychosis, schizophrenia, bipolar disorder and major depression, as well as other off-label uses [28,29].

Implications for Practice and Research

Quality, appropriateness and off-label prescribing of drugs for dementia treatment need to be investigated in light of the rising trends in the data. With a greater emphasis on diagnosis and treatment in primary care, evaluations of prescriber behaviours, expertise and skills are important to ensure that prescribing is evidence based. The deprivation level differences in rates of prescribing need to be investigated further. In addition, wide variations in the rate of prescribing within the most deprived areas warrant further investigation. The continued rising trend observed for prescribing of antipsychotic drugs requires further research to identify the contribution of dementia to the observed trend.

Conclusions

In the last 10 years, there has been a nearly 3-fold rise in the number of prescription items for anti-dementia drugs. The rising trend in primary care prescribing demonstrates greater participation of the sector in the diagnosis and treatment of dementia in addition to specialist psychiatry care. Least deprived regions have approximately twice as high prescribing rate compared to most deprived regions. Higher rates of prescribing in the least deprived areas may be reflective of higher life expectancy, better diagnoses and access to treatment compared to the most deprived areas. Such differences need to be investigated further.

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Conflict of interest statement

All authors declare no conflicts of interest.

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Data availability statement (if applicable to the manuscript type)

All data pertaining to this study are reported in this manuscript.

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Table 1 Prescription items and costs of all anti-dementia drugs (BNF Section 4.11) and antipsychotic drugs in England in 2009 and 2019.

Anti-dementia Drugs
Donepezil*
Rivastigmine*
Galantamine*
Memantine*
Total anti-dementia drugs
Anti-psychotic drugs
Haloperidol & Risperidone, n (%)**
All antipsychotic drugs
Total: anti-dementia drugs + antipsychotic drugs
Percentage refers to proportion of all anti-dementia prescription items; **Percentage refers to proportion of all antipsychotic

Table 2 Prescriptions items and costs of anti-dementia drugs (BNF Section 4.11) in the 10 most and 10 least deprived CCGs in England per 1,000 populations from 2015 to 2019.

Year, n*
2015
2016
2017
2018
2019
Percentage (%) median change from 2015 to 2019
Median all years
n= sum of prescription and costs for 10 CCGs for each year per 1,000 populations; BNF: British National Formulary; CCG

Figure legends

Figure 1 Prescription items of all anti-dementia drugs (BNF Section 4.11) per 1,000 populations in England from 2009 to 2019.

BNF: British National Formulary

Figure 2 Costs of prescribing for all anti-dementia drugs (BNF Section 4.11) per 1,000 populations in England from 2009 to 2019, adjusted for inflation

BNF: British National Formulary

Figure 3 Prescription items for anti-dementia drugs (BNF Section 4.11) and all antipsychotic drugs per 1,000 population in England from 2009 to 2019.

BNF: British National Formulary

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