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Trends in diagnosis and treatment for people with dementia in the UK from 2005 to 2015: a longitudinal retrospective cohort study

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Summary

Background The objectives of this study were to describe changes in the proportion of people diagnosed with dementia and the pharmacological treatments prescribed to them over a 10 year period from 2005 to 2015 at a time of UK policy strategies and prioritisation of dementia. We aimed to explore the potential impact of policy on dementia care.

Methods In this longitudinal retrospective cohort study, we included all patients registered at a Clinical Practice Research Datalink (CPRD) practice between July 1, 2005, and June 30, 2015, with a diagnosis of dementia defined using Read codes. The main outcomes were the number and proportion of acceptable patients, who met the CPRD threshold for data quality, in a GP practice defined by the CPRD as contributing up-to-standard data with a diagnosis of dementia and the number and proportion of these with a prescription for an antidementia or antipsychotic medication. We examined the prevalence of dementia diagnosis and prescribing by calendar quarter, and stratified by age, sex, and UK country (England, Scotland, Wales, or Northern Ireland). We investigated the use of antidementia drugs, alone and in combination, antipsychotics, antidepressants, anxiolytics, and hypnotics. The trend in the proportion of patients with a diagnosis of dementia, before and after the introduction of the UK National Dementia Strategy, was estimated using an interrupted time-series analysis.

Findings 8966224 patients were identified in the CPRD whose most recent registration period overlapped the study period. Of these, 128249 (1.4%) had a diagnosis of dementia before the end of the study period. The proportion of people diagnosed with dementia in the UK doubled from 0.42% (19635 of 4640290 participants) in 2005 to 0.82% (25925 of 3159754 participants) in 2015 (χ^2 test for trend, $p < 0.0001$), and the proportion of those who received antidementia medication increased from 15.0% (2942 of 19635) to 36.3% (9406 of 25925). The interrupted time-series analysis showed a significant acceleration in the rate of diagnosis of dementia after the introduction of the UK National Dementia Strategy ($p < 0.0001$). There was a large reduction in antipsychotic drug prescription in dementia from 22.1% (4347 of 19635) in 2005 to 11.4% (2943 of 25925) by 2015.

Interpretation Over the 10 years studied, there is evidence of a sustained positive change in diagnosis rates of dementia and in the quality of drug treatment provided to those diagnosed. The prescription of antidementia drugs more than doubled and the prescription of potentially hazardous antipsychotics halved after the introduction of national dementia strategies. These data support the formulation and delivery of national policy to improve the quality of care for people with dementia.

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Introduction

In 2014, 850000 people in the UK were estimated to have dementia, supported by approximately 540000 family carers.¹ These numbers are set to rise markedly both in the developed and in the developing world as the population ages in the coming decades.^{2,3} Dementia causes irreversible and continuing decline in global intellectual, social, and physical functioning; behavioural and psychological disturbances are also common. The illness is a major challenge to health and social services. The current cost to the UK economy is estimated at £26 billion per year,^{1,4} and the effect on families is profound, with around 40% of family carers developing depression or anxiety,^{5,6} which might lead to the person with dementia entering a care

home. Dementia has become a national priority within the UK. The Prime Minister's 2012 and 2015 Challenges on Dementia identified aspects of particular importance: prevention, research, awareness, tackling stigma, and diagnosis with high quality post-diagnostic support.

A priority identified in 2009 in the National Dementia Strategy for England⁷ and confirmed in subsequent policy is the need to increase the rate of diagnosis of dementia. The National Dementia Strategy estimated that only a third of people with dementia ever received a diagnosis of dementia. An estimate for England based on routine data in 2011–12 suggested that 42% of the estimated number of people with dementia had been diagnosed.⁸ However, determining the national diagnosis

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For more on the Prime Minister's 2012 Challenges on Dementia see https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/215101/dh_133176.pdf

For more on the Prime Minister's 2015 Challenges on Dementia see https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/414344/pm-dementia2020.pdf

Research in context

Evidence before this study

No formal literature search was done. Articles were identified through searches of the authors' own files. The National Dementia Policy in England over the past decade has been to increase the proportion of people with dementia receiving a diagnosis as a gateway to good management. This includes receiving appropriate medication. Systematic reviews of antipsychotics have shown these are often ineffective and cause substantial harm, whereas reviews of acetylcholinesterase inhibitors including from the Cochrane Collaboration have shown clinically significant benefit. To our knowledge, only one previous peer-reviewed study has examined the benefit of this policy and it did not examine more recent changes or prescriptions of antipsychotics, antidepressants, anxiolytics, or hypnotics.

Added value of this study

With use of the Clinical Practice Research Datalink, a representative database from UK primary care, there is evidence of a sustained increase in diagnosis rates of dementia and in the quality of drug treatment provided in those diagnosed between 2005 and 2015. The policies of increasing the use of antidementia drugs (more than doubled) and avoiding potentially hazardous antipsychotics (halved) have proved successful.

Implications of all the available evidence

This study, together with previous data, provides evidence that national policy can change medical practice, despite a systematic review of earlier trials of interventions to increase diagnosis rate, which found them to be unsuccessful. Furthermore, it shows that improvements can be made in the quality of care for the increasing number of vulnerable individuals with dementia.

rate is complicated as there are difficulties in estimating both the number of people with a diagnosis of dementia and the actual number in the population with dementia.⁹ In such calculations, the numerator depends on general practitioners reporting accurately in the annual Quality and Outcomes Framework the number of people registered with dementia in their care.¹⁰ The number registered has risen rapidly by 10% a year in England, from 232 000 in 2008–09 to 344 000 in 2013–14. The denominator is derived from a consensus view based on several surveys done between 1989 and 2011, but since March, 2015, the estimate has been based on the CFAS II study.¹¹ Given these uncertainties, one report estimated that the diagnosis rate for England in 2012–13 could have been as low as 36% or as high as 54% and for 2013–14, their best estimate was 50% (344 000 of 686 000).¹²

Concomitant with improving diagnosis in dementia is the challenge of providing high quality support, care, and treatment. On the basis of available evidence, and as part of a comprehensive package of care, national guidelines recommend three acetylcholinesterase inhibitors—donepezil, galantamine, and rivastigmine—for the management of mild to moderate Alzheimer's disease and memantine for people with severe Alzheimer's disease (or those with moderate Alzheimer's disease who are intolerant of acetylcholinesterase inhibitors).¹³ The same guidelines, similarly to many international initiatives, discourage the routine use of medication for non-cognitive symptoms or challenging behaviour. In particular, antipsychotic medication should only be used in dementia when absolutely necessary and should be time limited and regularly reviewed. This is because antipsychotic medication is of limited efficacy,¹⁴ associated with an increased mortality and morbidity,^{15,16} and often can be successfully withdrawn.¹⁷ Indeed, only one antipsychotic, risperidone, is licensed for the treatment of dementia-related behavioural disturbances, and it is specifically for up to

6 weeks treatment of persistent aggression in Alzheimer's dementia unresponsive to non-pharmacological approaches and where there is a risk of harm to the patient or others.

Information on secular trends in dementia diagnosis and its treatment is important to understand the effect of policies, clinical guidance, and the provision of treatments in dementia. Given the limitations of universal routine data collection in primary care in the UK, it can be helpful to make use of the established databases available, such as the Clinical Practice Research Datalink (CPRD).¹⁸ This initiative collects data for patient characteristics, diagnoses, investigations, prescriptions, and referrals to secondary care from over 670 participating practices (covering approximately 6·9% of the population of the UK).

We aimed to use CPRD data to describe changes in the proportion of patients diagnosed with dementia and associated drug treatments over time (specifically the use of antidementia drugs, alone and in combination; antipsychotic medications, excluding prochlorperazine which is prescribed for dizziness; antidepressants; anxiolytics; and hypnotics).

Methods

Study design and patients

In this longitudinal retrospective cohort study, we included all patients whose most recent active registration at a CPRD practice overlapped with the study period July 1, 2005, to June 30, 2015. We further identified all patients with a diagnosis of dementia before the end of the study period based on the definition used in the Quality and Outcomes Framework and defined using Read codes, the standard clinical terminology system used in general practice in the UK.¹⁰ Diagnoses were identified from the patient electronic record with no additional verification with the general practitioner.

Patients were eligible for inclusion in the analysis for a specific calendar quarter if they were registered for

For more on the Clinical Practice Research Datalink see <http://www.cprd.co.uk/intro.asp>

the whole of that quarter in a practice assessed to be up-to-standard in terms of data quality by the CPRD research team. The CPRD has broad National Research Ethics Service Committee ethics approval for purely observational research such as this study. No individual patient consent was required.

Outcomes

The main outcomes of interest were a diagnosis of dementia and prescriptions for an antidementia drug, an antipsychotic (excluding prochlorperazine), an anxiolytic, a hypnotic, or an antidepressant. Combination therapy for antidementia drugs was defined as having a prescription for an acetylcholinesterase inhibitor and memantine on the same day. Where dates of diagnoses or prescriptions were missing, these event records were excluded. All code lists are available from the study authors on request.

Statistical analysis

The number and proportion of patients with a diagnosis of dementia was examined by calendar quarter, and stratified by age, sex, and UK country (England, Scotland, Wales, and Northern Ireland). The trend in the proportion of patients with a diagnosis of dementia was estimated using interrupted time-series analysis¹⁹ using a binomial generalised linear model with first order lagged residuals and seasonality accounted for by adjusting for calendar quarter. The intervention was defined as the launch of the National Dementia Strategy in 2009.

We analysed three measures of antidementia drug prescription by calendar quarter: in the total study population, in people with a diagnosis of dementia, and in those specifically with a diagnosis of Alzheimer's disease. The number and proportion of patients with a prescription for an antidementia drug was examined by calendar quarter, and stratified by the drug substance as well as age, sex, and UK country. The use of combination antidementia therapy was also considered in patients with a diagnosis of dementia.

In patients with a diagnosis of dementia, the number and proportion of patients with a prescription for an antipsychotic (overall and atypical vs typical antipsychotics), an anxiolytic, a hypnotic, or an antidepressant was also examined by calendar quarter. All analyses were done with Stata, version 11.2.

Role of the funding source

There was no funding source for this study.

Results

8966224 patients were identified in the CPRD whose most recent registration period overlapped the study period. Of these, 128249 (1.4%) had a diagnosis of dementia before the end of the study period, two-thirds (84254 [66%]) of whom were female.

Across the UK, the proportion of people with a dementia diagnosis increased significantly from 0.42%

(19635 of 4640290) to 0.82% (25925 of 3159754; χ^2 test for trend, $p < 0.0001$) during the study period with similar proportional increases seen in both men and women. An increase was seen in all areas of the UK. In England, the proportion of people with a diagnosis of dementia increased from 0.41% (14936 of 3651585) in July–September, 2005, to 0.74% (21462 of 2916792) in January–March, 2014 (figure 1). The proportion was consistently higher in Scotland and Northern Ireland than in England and Wales. However, data for the second quarter of 2015 show that the proportion in England (18145 [0.82%] of 2225185) is now closer to that seen in Scotland (3991 [0.88%] of 455034) and Northern Ireland (1336 [0.90%] of 148043). A recent increase in diagnoses in Wales has also been observed. Diagnosis recording rates increased as expected with age (figure 1). An increase in the diagnosis rate over time was consistently seen regardless of age although the proportional increase in the rate of diagnosis was higher in older patients, with

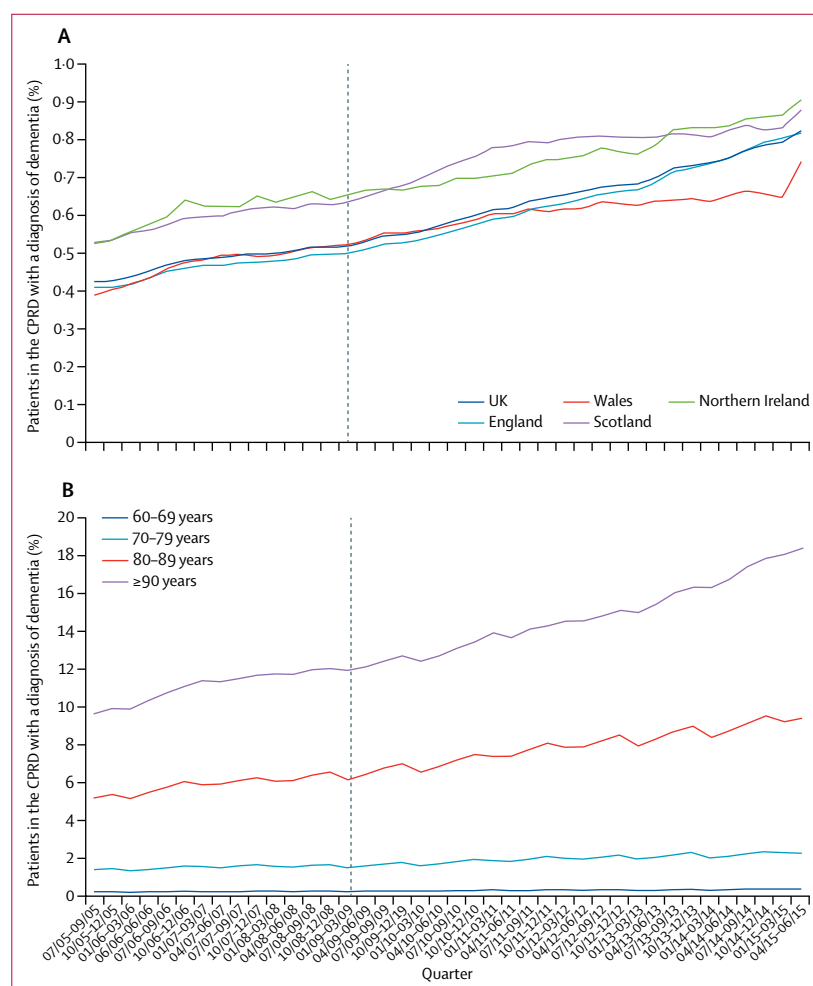


Figure 1: Proportion of CPRD population diagnosed with dementia in the UK by region (A) and age (B) between July, 2005, and June, 2015

Dates are month/year. Dotted line indicates launch of National Dementia Strategy (February, 2009). CPRD=Clinical Practice Research Datalink.

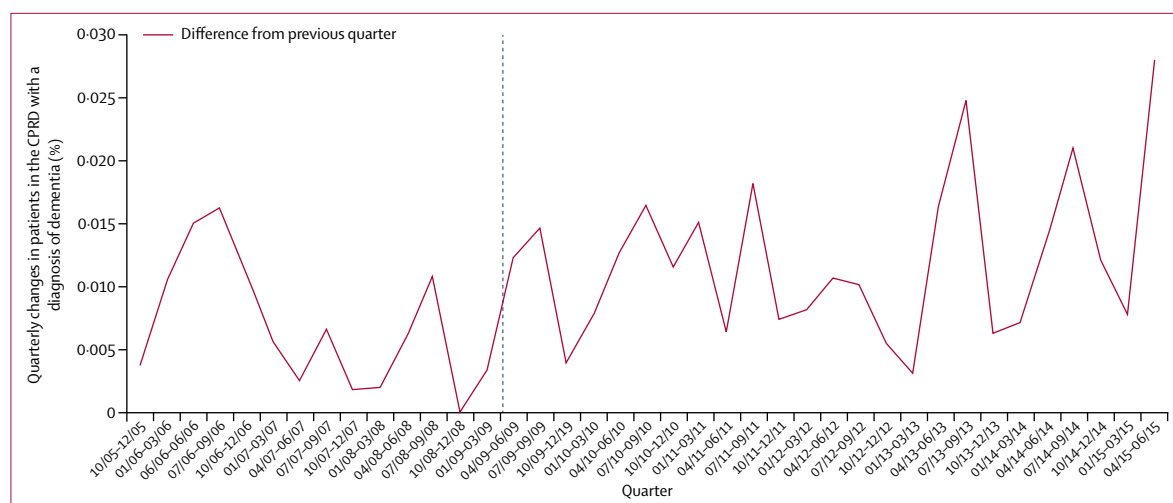


Figure 2: Quarterly changes in the proportion of patients in the CPRD with a diagnosis of dementia
Dotted line indicates launch of National Dementia Strategy (February, 2009). Dates are month/year. CPRD=Clinical Practice Research Datalink.

the prevalence of diagnosis in those aged 90 years or older almost doubling.

With the use of estimates from the interrupted time series, we can see that before the introduction of the National Dementia Strategy, the proportion of patients with a diagnosis of dementia was increasing (quarter on quarter odds ratio [OR] 1.014, 95% CI 1.012–1.015, $p < 0.0001$). After introduction of the programme, there was no evidence of a stepped change in the rate of diagnosis of dementia (OR 0.996, 95% CI 0.988–1.004, $p = 0.37$), but a significant acceleration in the trend in the proportion of patients with a diagnoses was observed (Wald test, $p < 0.0001$). The quarter on quarter change in the overall diagnosis rate is shown in figure 2, which also suggests an acceleration in recorded diagnoses in recent years compared with previous years.

43 718 (0.49%) people in the total population were prescribed an antidementia drug during the study with the rate of current prescribing increasing approximately four-fold over the 10 year study period (from 3752 [0.08%] of 4 640 290 in 2005 to 10 069 [0.32%] of 3 159 754 in 2015), largely accounted for by an increase in the use of donepezil (2524 [0.05%] in 2005 to 5948 [0.19%] in 2015) and memantine (220 [0.01%] in 2005 to 2572 [0.08%] in 2015; data not shown). Prescribing was more common in women and in people over the age of 80 years. The rate of prescribing has increased across the UK and is consistently highest in Northern Ireland.

There were 37 246 patients with a diagnosis of dementia and a prescription for an antidementia drug (figure 3). This means that approximately 6500 people (15% of the total) were prescribed an antidementia drug without a diagnosis of dementia clearly recorded in their primary care record. Over the 10 year study period, the rate of prescribing of antidementia drugs in patients with a diagnosis of dementia has risen from 2942 (15.0%) of 19 635 in 2005 to 9406 (36.3%) of 25 925 in 2015. The

most commonly prescribed antidementia drug across the whole period was donepezil. A large increase in the prevalence of use of memantine has been seen since the start of 2012. The difference between the number of identified patients with dementia with a prescription for an antidementia drug and the number of patients with a prescription regardless of diagnosis implies that a small proportion of patients are receiving a prescription for an antidementia drug without a documented and logistically extractable dementia diagnosis.

Patients with a diagnosis of Alzheimer's disease (46 047 [36%] of 128 249) were more likely to be prescribed an antidementia drug than those with other diagnoses (figure 4). By 2015, about 55% (6075 of 10 980) of those with Alzheimer's disease were prescribed an antidementia drug. Prescribing levels of donepezil and memantine increased from 17.5% (1225 of 6994) in 2005 to 35.7% (3925 of 10 980) in 2015 and from 1.8% (126 of 6994) in 2005 to 13.2% (1453 of 10 980) in 2015, respectively, but remained low for galantamine and rivastigmine.

Since 2010, concomitant use of a acetylcholinesterase inhibitor and memantine for the treatment of dementia has increased from 96 (0.4%) of 26 066 of those with dementia at the start of 2010 to 435 (1.7%) of 25 925 by quarter 2 of 2015.

The prescription of antipsychotic drugs in patients with dementia has significantly decreased from 4347 (22.1%) of 19 635 in 2005 to 2943 (11.4%) of 25 925 by 2015 (figure 5). There was a greater reduction in prescribing of the older (typical) medications (from 1837 [9.4%] to 488 [1.9%]) than the atypical ones, which increased from 2667 (13.6%) of 19 635 in mid-2005 to 3931 (16.8%) of 23 424 in late 2007 before decreasing again to 2502 (9.7%) of 25 925.

There have also been changes in the prescribing rates of hypnotics and antidepressants in patients with

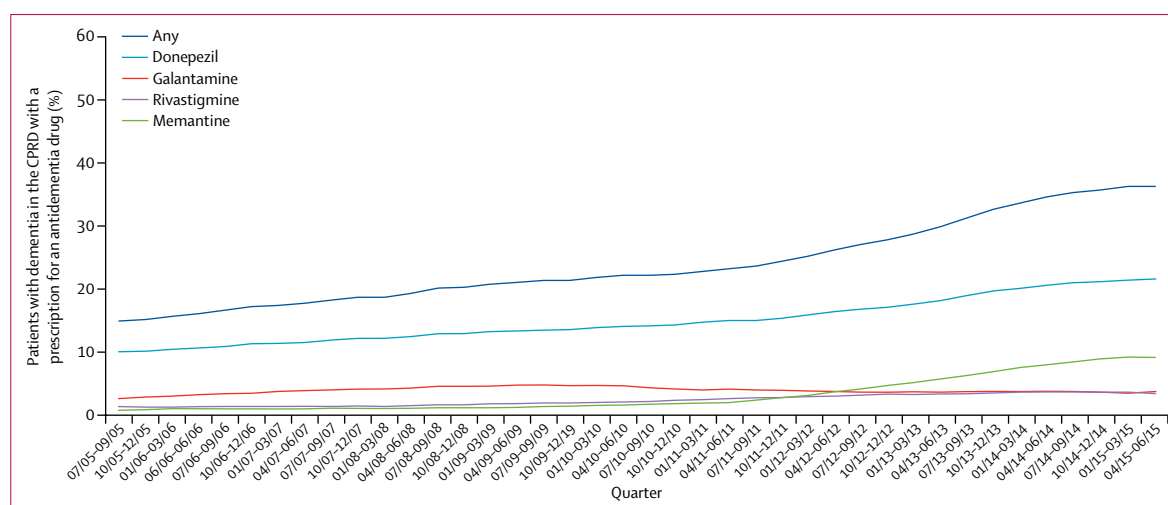


Figure 3: Proportion of patients with a diagnosis for dementia prescribed an anticholinergic drug

Dates are month/year. CPRD=Clinical Practice Research Datalink.

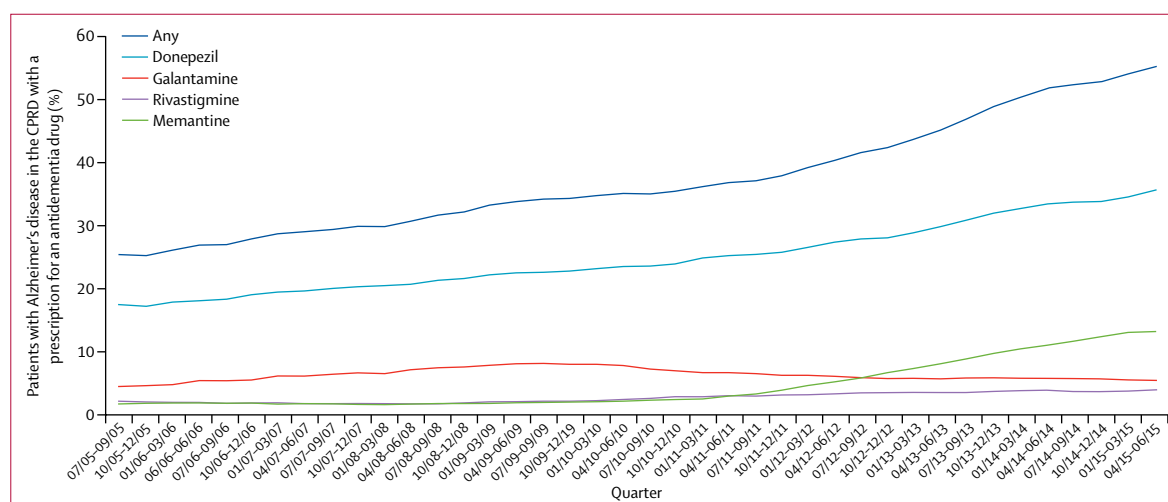


Figure 4: Proportion of patients with a diagnosis for Alzheimer's disease prescribed an anticholinergic drug

Dates are month/year. CPRD=Clinical Practice Research Datalink.

dementia but not in anxiolytics (figure 6). Although the use of hypnotics decreased from 2805 (14.3%) of 19635 to 2475 (9.5%) of 25925, the use of antidepressants increased from 5494 (28.0%) to 9498 (36.6%).

Discussion

This large sample of people with dementia drawn from general practices that participate in the CPRD shows that the number and proportion of patients diagnosed with dementia in the UK rose steadily between 2005 and 2015, reflecting both the ageing population and greater clinical awareness, in line with national policies and guidelines. Nevertheless, many individuals never receive a diagnosis of dementia^{7,8} and might therefore be denied the possibility, for either themselves or their family, of making choices or gaining appropriate help. There are differences across the four countries of the UK (with a higher prevalence of

diagnoses in Scotland and Northern Ireland than in England and Wales), but the trends are common to all.

Our study is in line with, and extends the findings of, another study considering the effect of the National Dementia Strategy,⁸ which tested the validity of the Quality and Outcomes Framework data in dementia and found it to be highly correlated with prescription of acetylcholinesterase inhibitors. The proportion of people with a diagnosis of dementia increased each quarter before and after the National Dementia Strategy was launched in 2009. This study shows the numbers continuing to increase until the end of 2015.

The proportion of people with a diagnosis of dementia who received drugs for Alzheimer's disease has increased by a factor of more than two in the study period. This might partly be because of the change in National Institute for Health and Care Excellence (NICE) guidelines in

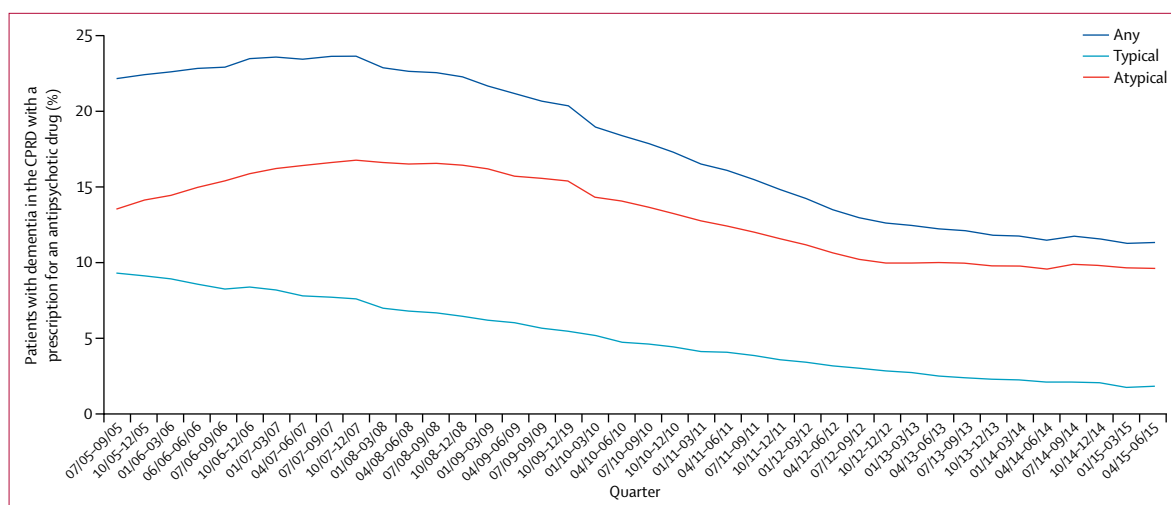


Figure 5: Proportion of patients with a diagnosis for dementia prescribed an antipsychotic drug
 Dates are month/year. CPRD=Clinical Practice Research Datalink.

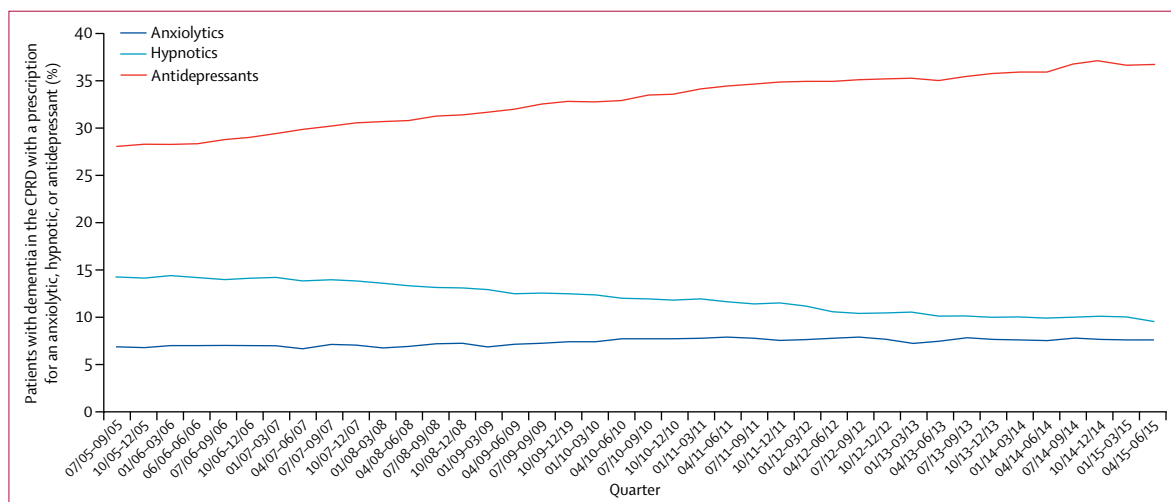


Figure 6: Proportion of patients with a diagnosis for dementia prescribed an anxiolytic, hypnotic, or antidepressant
 Dates are month/year. CPRD=Clinical Practice Research Datalink.

August, 2009, so that those with mild dementia were allowed prescription of acetylcholinesterase inhibitors. However, the use of Read codes probably underestimates the proportion of patients with Alzheimer's disease, which is the most common cause of dementia and accounts for 60–70% of cases,¹ as non-specific Read codes are often used in primary care for dementia.¹⁸ Even so, only around 50% of those who were recorded as having a diagnosis of Alzheimer's disease were prescribed acetylcholinesterase inhibitors or memantine. Although some patients and their families will not want or be able to tolerate these drugs, the figures suggest they are still under-prescribed, despite evidence showing that continued use both improves cognitive outcomes and delays care home admission.²⁰

There is a large increase in the proportion of people with Alzheimer's disease who receive both a acetylcholinesterase

inhibitor and memantine over the study period. This proportion remained largely steady until 2011 but has increased greatly since then, without a change in policy or new evidence to suggest that this is cost-effective. Individuals with a prescription for both drugs in the same period might, however, have been switching from one to another because of side-effects or increasing dementia severity.

Conversely, a proportion of patients are receiving medication for dementia but are not recorded as having a diagnosis of dementia. Some of these individuals without a diagnosis of dementia might be receiving acetylcholinesterase inhibitors for mild cognitive impairment. In view of the evidence that acetylcholinesterase inhibitors do not help those with mild cognitive impairment and might be harmful, this would be of concern.²¹ However, many of these individuals

might have a diagnosis of dementia or Alzheimer's disease made in secondary care but not recorded in the general practitioner database, despite policy initiatives. Hence, the true number of people with a diagnosis and who have received care in a memory clinic and other dementia pathways might be higher than Quality and Outcomes Framework figures.¹⁸

There have been concerns about the harms associated with the use of antipsychotics in dementia that pre-date the period covered by this report. There has been, and continues to be, a policy that there should be a reduction in the prescription of antipsychotic medications which, aside from risperidone, are not licensed for the treatment of dementia and indeed we observed a downward trend in the use of antipsychotics in this study. It is appropriate that the prescribing rate of typical antipsychotics, which are more harmful, has decreased more than that of atypical antipsychotics and is evidence of an understanding of the greater risks of older antipsychotics. There are differences across the four countries of the UK, but the trends in the use of antipsychotics are common to all. Further data have emerged immediately before and after the study period, and there have been a number of initiatives and guidelines aimed at reducing inappropriate use. Particularly important for UK prescribing was the guidance from the Committee on Safety of Medicines issued in 2004 that drew attention to the increased risk of cerebrovascular adverse events and greater mortality and the Time for Change¹⁴ report in 2009 that quantified the excess 1800 deaths attributable to the use of these drugs in dementia in the UK at that time.

As those who have a pre-existing psychosis are not protected from dementia and some individuals with dementia have psychotic and other neuropsychiatric symptoms that cause them great distress, there cannot be a zero level of prescription of these drugs in dementia. This is supported by a recent trial finding¹⁷ that reduction of antipsychotics after review in care homes led to increasing neuropsychiatric symptoms and that it is important that there are other management strategies to take the place of antipsychotics.^{22,23} One of the possible strategies that professionals might have used is the substitution of other psychotropic medications for antipsychotics. To our knowledge, this is the first study to address whether an increase in prescribing of antidepressants has occurred and this seems possible, despite evidence that they are ineffective and potentially harmful in depression associated with dementia.²⁴

The strengths of this study include the large sample size and the fact that in the UK, most dementia diagnosis and treatment is made by the NHS hence the stability of the methods through a longitudinal study across a decade. Although CPRD is a valuable resource, it does have limitations as it includes only a sample of practices which might not be wholly representative of national clinical practice, diagnoses are dependent on Read codes and have not been validated, and the database only holds data for

prescriptions with no information about whether the medication has been dispensed or adhered to. As only the primary care data has been used, diagnoses and prescriptions made in specialised care and not recorded in the primary care record will be missing. This leads to the already discussed difficulties in estimating the number of people in the population with dementia with and without a diagnosis. Finally, this observational study cannot confidently attribute the changes or trends observed to any specific initiative. For example, communications and recommendations from the Medicines and Healthcare products Regulatory Agency and other organisations such as NICE will also have contributed to changes in practice. The interrupted time series shown should be interpreted with caution for this reason, as well as because the implementation of the National Dementia Strategy will have occurred over some time.

These limitations in inference notwithstanding, it is encouraging that there are increasing diagnosis rates and decreasing use of antipsychotic drugs in dementia and that the national quality improvement initiatives taken in the UK appear to be associated, at least temporally, with improvements in the key indicators presented here. The value of decreasing the use of antipsychotic medication is driven by the avoidance of the morbidity and mortality associated with their prescription to people with dementia. The estimates of these harms are derived from multiple randomised controlled trials.¹⁴ In terms of the value of increasing diagnosis rates, there is no evidence from randomised controlled trials that receiving a diagnosis (compared with having dementia but not being given that diagnosis) is associated with improved quality of life and some have raised the possible harms of early diagnosis.²⁵ However, the evidence from observational studies is encouraging. Statistically significant improvements in health-related quality of life (HRQoL) in the first 6 months after diagnosis were reported in the evaluation of the Croydon Memory Service Model²⁶ and more recently in a national evaluation of Memory Assessment Services.²⁷ Weighing the available evidence for diagnosis in dementia in a series of systematic reviews, the 2011 World Alzheimer Report concluded that there was value for people with dementia themselves, their carers, and society as a whole in clinical and economic terms²⁸ on the basis of optimisation of medical management; the relief gained from better understanding of symptoms; maximising decision-making autonomy; access to services; risk reduction; planning for the future; improving clinical outcomes; avoiding or reducing future costs; and diagnosis as a human right.

There is still some way to go, and further exploration of prescribing practices (eg, the duration of treatment) might be of value in informing future direction, but these data present evidence of a sustained change for the better in dementia diagnosis and treatment in the UK and support the development and delivery of national policies to improve care for people with dementia.

Contributors

AB, NF, and KD designed the study. KD conducted the analysis. All authors contributed to the interpretation of the data and the writing of the manuscript.

Declaration of interests

KD is employed by the Medicines and Healthcare products Regulatory Agency, which is an Executive Agency of the UK Department of Health. NF reports fees from Janssen Alzheimer's Immunotherapy, Eli Lilly, personal fees from Novartis, Sanofi, Roche/Genentech, GSK, and other fees Aducanumab/Biogen, outside the submitted work. SB reports grants and personal fees from Abbvie, personal fees and non-financial support from Lilly, personal fees from Eleusis, Daval International, Boehringer Ingelheim, Axovant, Lundbeck, Nutricia, outside the submitted work; and has been employed by the Department of Health for England. AB is the national Clinical Director for dementia at NHS England. NB and GL declare no competing interests.

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