

The burden of psychotropic drug prescribing in people with dementia: a population database study

BRUCE GUTHRIE¹, STELLA ANNE CLARK², COLIN MCCOWAN¹

¹Quality, Safety and Informatics Research Group, University of Dundee, Mackenzie Building, Kirsty Semple Way, Dundee DD2 4BF, UK

²Old Age Psychiatry, NHS Fife, Kirkcaldy, UK

Address correspondence to: B. Guthrie. Tel: +44 (0)1382 420000; Fax: +44 (0)1382 420010. Email: b.guthrie@chs.dundee.ac.uk

Abstract

Objective: to compare psychotropic prescribing in older people with dementia and the general elderly population.

Design and setting: retrospective population database study in 315 General Practices.

Subjects: there were 271,365 patients aged ≥ 65 , of which 10,058 (3.7%) recorded as having dementia.

Methods: epidemiology of psychotropic prescribing in older people with and without dementia; multilevel modelling of patient and practice characteristics associated with antipsychotic prescribing.

Results: people with dementia were currently prescribed an antipsychotic drug (17.7%), an antidepressant (28.7%) and a hypnotic/anxiolytic (16.7%). Compared to the general elderly population, antipsychotic prescribing was 17.4 [95% confidence interval (CI) 16.4–18.4], antidepressant prescribing 2.7 (95% CI 2.6–1.8) and hypnotic/anxiolytics 2.2 (95% 2.1–2.3) times more likely in people with dementia. Most antipsychotic prescribing in people with dementia was prolonged (> 16 weeks). Patients living in more deprived areas and registered with larger and more remote practices were more likely to be prescribed prolonged antipsychotics.

Conclusions: over one in six patients are currently prescribed antipsychotic drugs known to be of little benefit and causing significant harm, with other psychotropics equally commonly used. Changing this will require investment in services to support alternative management strategies for people with behavioural and psychological disturbance associated with dementia.

Keywords: antipsychotic drugs, dementia, elderly, family practice, patient safety, quality of healthcare

Introduction

Increasing dementia prevalence poses significant challenges to health and social care services [1]. An important issue is how to best manage behavioural and psychological disturbance in dementia (BPSD), which is experienced by the majority of people with dementia at some point, and is frequently distressing to patients, carers and professional caregivers in residential or healthcare settings [2–5]. A common response to BPSD is to prescribe psychotropic drugs including antipsychotics, for which there is strong evidence of a weak-to-moderate effect on behaviour, although trials are based on typically short (< 12 week) follow-up, and impact largely relates to reductions in aggression rather than the full range of symptoms experienced [4].

There is significant evidence that psychotropic drugs are associated with harm in older people with dementia, especially antipsychotics. Initial guidance in 2004 focused on risperidone and olanzapine which were found to triple the risk of stroke [6] with a small but significant increase in mortality [4, 7]. Typical antipsychotics have since been shown to have similar risks [8–10], and the European Medicines Agency concluded that a class effect was likely [11]. Subsequently, Ballard *et al.* have shown that people with dementia resident in nursing homes and prescribed antipsychotics could have these drugs stopped with no increase in behavioural disturbance [12]. Although limited by small numbers, follow-up of this trial beyond the period of randomisation found a large mortality benefit for stopping antipsychotics [13]. In 2009 the UK Medicines Healthcare products Regu-

latory Agency amended its guidance, now stating that risperidone is the only antipsychotic licensed in people with dementia, for the short-term (<6 weeks) treatment of severe aggression in people with Alzheimer's disease [14].

Despite these warnings, and National Institute for Health and Clinical Excellence (NICE) guidance that antipsychotics have only a limited place in managing 'severe distress' or 'immediate risk of harm to the person or others' [3], there is persistent concern about overuse of antipsychotics and other sedative drugs as a form of chemical restraint, particularly in nursing homes [15], although acknowledging that this may often reflect a lack of alternative service provision. However, regulatory warnings alone have not been shown to decrease antipsychotic use in people with dementia [16]. In November 2009 an expert review commissioned by the English Department of Health called for urgent action, estimating that up to 180,000 people with dementia were being prescribed antipsychotics and up to two-thirds of these prescriptions were unnecessary and likely to be harmful [17]. Based on limited data of likely prevalence, current prescribing patterns were estimated to cause 1,620 cerebrovascular events and 1,800 fatalities annually in people with dementia [17]. It recommended that new services be commissioned to support more appropriate initiation and regular review of antipsychotics and to provide lay and professional carers access to alternatives for the management of BPSD.

However, data on the proportion of people with dementia prescribed antipsychotics is remarkably sparse. Two small studies in UK nursing homes found rates of prescribing of 31% in 1997 [18] and 48% in 2006 [19], which is similar to larger US studies [20]. This study therefore had two aims: first, to use a large population database to assess the total burden of psychotropic drug prescribing to older people with dementia compared to the general elderly population; second, to examine antipsychotic use in older people with dementia and associations of prolonged antipsychotic prescribing with patient and practice characteristics.

Methods

Data was extracted from 315 General Practices participating in the Scottish Programme for Improving Clinical Effectiveness - Primary Care (SPICE-PC) programme, with analysis based on complete data on 31 March 2007. Thirty-one percent of Scottish practices contributed data covering a population that is representative of Scotland as a whole [21]. Analysis used fully anonymised data compliant with the Primary Care Clinical Informatics Unit research governance process, and National Health Service (NHS) Research Ethics Committee review was therefore not required. Initial analysis was carried out in SPSS v17.0 and multilevel logistic regression in MLwiN 2.0 (Centre for Multilevel Modelling, University of Bristol, UK).

Data was extracted for all patients aged 65 and over on 1 April 2006, including age, sex, postcode-assigned deprivation, the presence of a dementia diagnosis and psychotic

illness defined using Quality and Outcomes Framework (QOF) register Read Codes [22], prescription of acetylcholinesterase inhibiting drugs and psychotropic drug prescribing. Antipsychotics were defined as oral drugs listed in the British National Formulary (BNF) chapter 4.2.1, antidepressants as those listed in BNF 4.3 and hypnotics and anxiolytic drugs as those listed in BNF 4.1.1 and 4.1.2 [23]. Patients were defined as having dementia if they had a QOF dementia register Read Code or if they had ever had a prescription for an acetylcholinesterase inhibiting drug. Current prescribing was defined as a prescription issued in the previous 12 weeks. Since prolonged prescribing of antipsychotics was of particular interest, all analyses only included patients registered with the practice for at least 6 months.

Prevalence of current prescription for oral antipsychotics, antidepressants and hypnotics/anxiolytics and the extent of co-prescription were calculated for patients with and without dementia. The relative risk and 95% confidence interval for patients with dementia compared to those without were calculated. Duration of antipsychotic prescribing for people with dementia was defined as the interval between the first and last recorded prescriptions for the drug currently being prescribed, with prolonged antipsychotic prescribing defined as the current drug having been prescribed for more than either 16 or 24 weeks before the most recent prescription. Multilevel logistic regression was used to examine how prolonged antipsychotic prescribing varied between practices, and associations with patient and practice characteristics. Univariate and adjusted odds ratios were calculated for patient and practice variables, and variation between practices was examined using multilevel residuals from the fully adjusted model. All models were fitted with second order penalised quasi-likelihood estimation, and assumptions of normality of level 2 residuals were checked graphically.

Results

There were 271,365 patients aged 65 and over who had been registered for at least 6 months. Patients [10,058; 3.7% prevalence in over 65 year olds, 95% confidence interval (CI) 3.6–3.8] either had a dementia Read Code (9,736 patients) or had been prescribed an acetylcholinesterase inhibitor without a relevant Read Code being recorded (322 patients). One percent of patients aged 65–74 years were recorded as having dementia, 5.1% of those aged 75–84 and 13.0% of those aged 85 and over. A total of 7,067 (70.3%, 95% CI 70.1–70.5) of people with dementia were female. Two hundred seventy-four patients (2.7%, 95% CI 2.4–3.0) also had a psychosis diagnosis ever recorded, but since excluding these patients did not significantly alter the results, all data presented is for all patients with dementia irrespective of psychosis diagnosis.

Five thousand four hundred and fifty (2.00%, 95% CI 1.96–2.06) of all patients aged 65 and over had been prescribed an antipsychotic in the previous year, and 4,450 (1.64%, 95% CI 1.59–1.69) were currently being prescribed.

Table 1. Prevalence of current psychotropic drug prescribing in people aged 65 and over with and without dementia

	No. (%) of patients with dementia <i>n</i> = 10,058	No. (%) of patients without dementia <i>n</i> = 261,307	Relative risk (95% CI)
Currently prescribed			
Any antipsychotic	1,785 (17.7)	2,665 (1.0)	17.40 (16.44–18.41)
Any antidepressant	2,888 (28.7)	28,105 (10.8)	2.67 (2.58–2.76)
Any hypnotic/anxiolytic	1,643 (16.3)	19,525 (7.5)	2.19 (2.09–2.29)
Currently prescribed			
None	5,351 (53.2)	218,705 (83.7)	0.64 (0.62–0.65)
Antipsychotic only	801 (8.0)	1,137 (0.4)	18.30 (16.76–19.99)
Antidepressant only	1,779 (17.7)	21,200 (8.1)	2.18 (2.09–2.28)
Hypnotic/anxiolytic only	665 (6.6)	12,988 (5.0)	1.33 (1.24–1.43)
Antipsychotic + antidepressant	476 (4.7)	740 (0.3)	16.71 (14.92–18.72)
Antipsychotic + hypnotic/anxiolytic	295 (2.9)	372 (0.1)	20.62 (17.71–23.97)
Antidepressant + hypnotic/anxiolytic	478 (4.8)	5,749 (2.2)	2.16 (1.97–2.37)
All three drug classes	213 (2.1)	416 (0.2)	13.30 (11.29–15.67)

Patients with dementia were currently being prescribed an oral antipsychotic (17.7%), an antidepressant (28.7%) and a hypnotic/anxiolytic (16.7%) (Table 1). People with dementia were more than twice as likely to be prescribed antidepressants and hypnotics/anxiolytics, but most strikingly, were 17.4 times more likely to be prescribed antipsychotics. Prescription of more than one drug class was common, and people with dementia were more likely to be prescribed combinations than the general elderly population.

Sixty-eight percent of current antipsychotic prescribing was for atypical drugs, the commonest prescribed atypicals being quetiapine (33.0% of current prescriptions), haloperidol (17.5%), amisulpiride (12.7%), risperidone (12.0%), chlorpromazine (7.3%) and olanzapine (6.6%). The most frequently prescribed antidepressants were citalopram (27.2% of current prescriptions), trazodone (18.8%), mirtazapine (14.8%), fluoxetine (9.8%), amitriptyline (8.4%) and paroxetine (5.8%). Notably, 3.7% of people with dementia were currently being prescribed tricyclic antidepressants, which significantly worsen cognition because of their anticholinergic effects [24].

Table 2. Prevalence of prolonged prescribing of antipsychotic drugs in people with dementia

	No. of patients with dementia <i>n</i> = 10,058	% (95% CI)
Prescribed antipsychotic in last year	2,202	21.9 (21.1–22.7)
Current antipsychotic (prescribed in last 84 days)	1,785	17.7 (17.0–18.5)
Current antipsychotic and same drug prescribed for >16 weeks ^a	1,417	14.1 (13.4–14.8)
Current antipsychotic and same drug prescribed for >24 weeks ^a	1,285	12.8 (12.1–13.4)

^aDuration defined as number of weeks between most recent and first prescription for the currently prescribed drug in the calendar year 1 April 2006 to 31 March 2007.

Table 2 shows the duration of antipsychotic prescribing in people with dementia. There were 21.9% of patients that had been prescribed an antipsychotic at least once in the previous year, the majority of whom were current users and taking prolonged treatment. Median duration of prescription for people with dementia currently prescribed an antipsychotic was 293 days, and 91% of these prescriptions were coded as ‘repeat prescriptions’ (i.e. could be ordered by phone without clinical review). The majority of people with dementia prescribed antipsychotics therefore received prolonged treatment.

Prolonged (>16 weeks) antipsychotic prescribing was further examined using multilevel logistic regression (Table 3). In univariate analysis, no patient variables were significantly associated with prolonged antipsychotic prescribing. Practices located in accessible areas (settlement size <10,000, within 30 min drive time of a city or urban area) were more likely to prescribe prolonged antipsychotics. In the adjusted model, patients living in the most deprived 40% of postcodes were significantly more likely to be prescribed prolonged antipsychotics, although this should be interpreted cautiously since a large proportion of people with dementia are likely to be living in nursing homes which makes postcode-assigned deprivation scores problematic. Accounting for patient variables, practices in the largest quartile of list size (>7,690) and those located outside primary cities were more likely to prescribe. However, absolute differences and odds ratios for all fixed effects are relatively small. The plot for residual practice variation after accounting for patient and practice variables is shown in Appendix 1 (see Supplementary data available in *Age and Ageing* online). Eighteen (5.7%) practices were identified as having higher than average prolonged antipsychotic prescribing and one lower than average. Compared to the average, the odds ratio for a patient with dementia being prescribed a prolonged antipsychotic prescription in the highest prescribing practice was 3.00 (95% CI 1.71–5.29) and in the lowest prescribing practice 0.33 (95% CI 0.18–0.58).

Table 3. Multilevel logistic regression results for prolonged (>16 weeks) antipsychotic prescribing in people with dementia

Variable	No. (%) of patients with prolonged (>16 weeks) antipsychotic prescription	Multilevel univariate odds ratio (95% CI)	Multilevel adjusted odds ratio (95% CI)
Patient level fixed effects			
Aged 65–74 (<i>n</i> = 1,470)	203 (13.8)	1	1
Aged 75–84 (<i>n</i> = 4,646)	673 (14.5)	1.05 (0.89–1.26)	1.05 (0.88–1.25)
Aged 85 and over (<i>n</i> = 3,942)	541 (13.7)	1.01 (0.84–1.21)	1.00 (0.83–1.20)
Female (<i>n</i> = 7,067)	1,015 (14.4)	1	1
Male (<i>n</i> = 2,991)	402 (13.4)	0.93 (0.82–1.06)	0.90 (0.73–1.11)
Carstairs quintile 1 (affluent <i>n</i> = 2,030)	257 (12.7)	1	1
Carstairs quintile 2 (<i>n</i> = 2,360)	285 (12.1)	0.94 (0.76–1.16)	0.99 (0.80–1.22)
Carstairs quintile 3 (<i>n</i> = 2,321)	335 (14.4)	1.03 (0.83–1.27)	1.15 (0.93–1.44)
Carstairs quintile 4 (<i>n</i> = 1,742)	275 (15.8)	1.16 (0.93–1.44)	1.31 (1.05–1.63)
Carstairs quintile 5 (deprived <i>n</i> = 1,605)	265 (16.5)	1.21 (0.96–1.53)	1.29 (1.03–1.63)
Practice level fixed effects			
List size quartile 1 (small) (<i>n</i> = 760)	108 (14.2)	1	1
List size quartile 2 (<i>n</i> = 997)	153 (15.3)	1.23 (0.89–1.70)	1.18 (0.85–1.63)
List size quartile 3 (<i>n</i> = 3,584)	537 (15.0)	1.16 (0.85–1.59)	1.05 (0.76–1.45)
List size quartile 4 (large) (<i>n</i> = 4,717)	619 (13.1)	1.07 (0.79–1.45)	1.29 (1.03–1.63)
Primary city (<i>n</i> = 3,656)	432 (11.8)	1	1
Urban area (<i>n</i> = 3,533)	537 (15.2)	1.24 (1.00–1.54)	1.31 (1.05–1.63)
Accessible area (<i>n</i> = 1,744)	275 (15.8)	1.40 (1.09–1.81)	1.54 (1.19–1.99)
Remote area (<i>n</i> = 1,125)	173 (15.4)	1.26 (0.95–1.68)	1.44 (1.07–1.95)
Intra-cluster correlation co-efficient (empty model)	–	–	7.45%

Discussion

This study has shown that people aged 65 and older with dementia were much more likely to be prescribed psychotropic drugs than the general elderly population. The percentage of older people with dementia that were currently prescribed one or more psychotropic agents was 46.8%. Contrary to current guidance, 17.7% were currently prescribed antipsychotics, the majority for prolonged periods and as repeat prescriptions. Compared to previous UK research in nursing homes, rates of antipsychotic prescribing in people with dementia found are (unsurprisingly) lower but still substantial [18, 19]. In the multilevel regression model, there was evidence that patients living in more deprived postcodes were more likely to be prescribed antipsychotics, as were those registered with larger practices and those located outside primary cities. However, the absolute differences between these groups, and the odds ratios were not large. More strikingly, there was considerable unexplained variation between practices, although any large change in use of antipsychotics will require change across the board rather than simply focusing on high prescribers.

The strength of this study is that it is a large population-based study of all people with dementia recorded in General Practice clinical IT systems. However, the prevalence of dementia based on general practitioner (GP) registers in this study is only about half that found in epidemiological studies, with under-recording in older age groups in particular [25]. Psychosis without dementia in the elderly is relatively rare with a prevalence of approximately 0.1% for schizophrenia and paranoid psychosis and 0.1% for psychotic depression with delusion and hallucination [26], so it is likely that much

of the antipsychotic prescribing in older patients without a recorded diagnosis of dementia is actually also to people with dementia and cognitive impairment. With a relatively conservative assumption that a quarter of antipsychotic prescribing to patients with no recorded diagnosis of dementia is actually to people with dementia, then a further 666 patients will be at risk from this prescribing in addition to the 1,785 identified from GP dementia registers. The analysis is therefore likely to underestimate the relative risk of psychotropic prescribing in people with dementia compared to the general population.

A weakness is that the dataset does not reliably record whether patients are resident in a nursing home, which is strongly related to use of antipsychotics, and may explain some of the variation between practices. Additionally, the availability of psychogeriatric services varies and may explain the higher rates of prescribing in practices outside of primary cities. Finally, it is important to note that guidelines for antipsychotic use in older people with dementia have changed rapidly, and this analysis compares prescribing practice in 2007 with guidance issued in early 2009. The prescribing being measured was therefore not clearly defined as inappropriate at the time (although approximately one-fifth of antipsychotic prescribing was for risperidone and olanzapine which guidance in 2007 said should not be used). However, these findings do identify the scale of change in practice needed to implement current guidelines [3, 14] and recent policy [17, 27].

Antipsychotic prescribing to people with dementia in the United Kingdom is therefore common and much of it is likely to have little benefit and cause harm [4]. Stopping antipsychotics is not associated with significant increase in behavioural and psychological symptoms in dementia (although this may

not hold for people with high levels of symptoms at baseline) [12] and reduces mortality [13]. Given likely under-recording of dementia on GP registers, patient review should focus on all older people prescribed antipsychotics rather than just on those with recorded dementia. Although antipsychotic prescribing is higher in nursing home residents, focusing on nursing homes may also miss many patients who need review. Similarly, only focusing on practices with higher than average prescribing will not in itself drive large reductions in antipsychotic use. However, achieving the two-thirds reduction in prescribing that recent policy calls for will not be straightforward, since it will require investment in training and services to provide an alternative to prescription [2, 17, 19]. Without such investment, it is likely that other sedative drugs (which are already commonly prescribed to people with dementia) may be substituted for antipsychotics, or existing specialist services that are inadequately resourced will be swamped.

There remains uncertainty over the appropriate place of psychotropic drugs in people with dementia, the risk of harm of different drugs across the full spectrum of dementia and the effectiveness of non-pharmacological interventions for BPSD [2, 3, 17]. However, further research should not delay improvement. The 2008 report of the All-Party Parliamentary Group on Dementia concluded that ‘the widespread inappropriate prescribing of antipsychotic drugs is an unacceptable abuse of the human rights of people with dementia’ [15] and the ‘time for action’ [17] is therefore now. From the perspective of improving current care, we lack detailed information on patterns of antipsychotic use to help target interventions. To our knowledge, there is no published data on who initiates antipsychotic prescribing in people with dementia, or the balance of secondary vs primary care initiation, making it difficult to know where to focus intervention to reduce initiation or ensure that there are clear goals to measure any change against. However, continued prescribing will virtually always be the responsibility of the GP, and therefore medication review and stopping prescribing will only routinely happen if GPs do it, ideally with ready access to specialist support for themselves and for lay and professional carers. At a minimum, GPs should not prescribe antipsychotics to people with dementia as a repeat prescription and should regularly review the need for continuing prescription.

Key points

- Psychotropic drugs including antipsychotics are of limited use in managing behavioural problems in dementia, and are risky.
- People with dementia are 17.7 times more likely to be prescribed antipsychotics than the general elderly population.
- Reducing antipsychotics and other psychotropics will require collaboration between GPs and adequately funded specialist services.

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Conflicts of interest

None declared.

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Supplementary data

Supplementary data mentioned in the text is available to subscribers in *Age and Ageing* online.

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