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# Inequalities in receipt of mental and physical healthcare in people with dementia in the UK

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## Abstract

**Background:** UK Dementia Strategies prioritise fair access to mental and physical healthcare. We investigated whether there are inequalities by deprivation or gender in healthcare received by people with dementia, and compared healthcare received by people with and without dementia.

**Methods:** we investigated primary care records of 68,061 community dwelling dementia patients and 259,337 people without dementia (2002–13). We tested hypotheses that people with dementia from more deprived areas, and who are women receive more psychotropic medication, fewer surgery consultations, are less likely to receive annual blood pressure, weight monitoring and an annual review, compared with those from less deprived areas and men.

**Results:** only half of people with dementia received a documented annual review. Deprivation was not associated with healthcare received. Compared to men with dementia, women with dementia had lower rates of surgery consultations (adjusted incidence rate ratio (IRR) 0.90, 95% CI 0.90–0.91), of annual blood pressure monitoring (adjusted IRR 0.96, 95% CI 0.95–0.97) and of annual weight monitoring (adjusted IRR 0.91, 95% CI 0.90–0.93). Men with dementia were less likely to be taking psychotropic medication than women with dementia. People with dementia had fewer surgery consultations and were less likely to have their weight and blood pressure monitored at least annually, compared to the non-dementia group.

**Conclusions:** people with dementia, in particular women, appear to receive less primary healthcare, but take more psychotropic medication that may negatively impact their physical health. Reducing these inequalities and improving access of people with dementia to preventative healthcare could improve the health of people with dementia.

**Keywords:** dementia, healthcare disparities, deprivation, psychotropic drugs, equalities, medication, older people

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## Introduction

People with dementia have high rates of physical ill-health, most commonly hypertension and diabetes [1] and of neuropsychiatric symptoms, that may be treated with psychotropic medication, including antipsychotics [2–4]. Mental and physical well-being are key determinants of life quality and

independent living in dementia [5]. Improving physical health may slow cognitive decline, by reducing cardiovascular pathology or functional impairment and improving diabetic control [6].

In dementia, antipsychotic prescribing is associated with cognitive decline [7], mortality [8], side effects, somnolence and falls [9] and hypnotics and anxiolytics with cognitive

decline [10, 11] and falls [9]. In 2009, the UK Medicines and Healthcare products Regulatory Agency (MHRA) highlighted risks of stroke and death with antipsychotics [12], and a UK government-commissioned review prioritised reducing their use in dementia [13]; UK usage has fallen since these publications [14–16].

People with dementia may be at increased risk of social inequalities. The reduced access to healthcare typical of the oldest old, women and those with fewer socio-economic resources may compound communication difficulties and social isolation in people with dementia [17]. Socio-economic factors may be implicated in dementia aetiology [1]. Lower levels of education and worse physical health, which are strongly linked to deprivation, are associated with a greater dementia risk [2, 3]. Among people with dementia those from more deprived areas, women and older people are relatively less likely to receive anti-dementia drugs [18]. We aimed to investigate whether there are also social inequalities in physical preventative healthcare provision and psychotropic drug prescribing among people with dementia, and to compare these outcomes in people with and without dementia. We hypothesised, based on previous findings, that women and people from more deprived areas would access physical and mental healthcare less than their counterparts [4, 5]. We selected variables from The Health Improvement Network (THIN) primary care database to test these hypotheses, constrained by data availability. We judged that people with reduced healthcare access would be less likely to receive a dementia review, and more likely to be taking psychotropic medication, because medication for short-term treatments of challenging behaviour would be less frequently reviewed. We tested our hypotheses that people with dementia from more deprived areas, and women receive [1] more psychotropic medication [2], fewer surgery consultations [3], are less likely to have had blood pressure and weight monitoring and [4] an annual dementia review recorded in the last year, compared with those from less deprived areas and men.

## Methods

### Data

THIN primary care database contains anonymised information on twelve million patients from over 500 participating UK general practices (<http://www.csdmruk.imshealth.com>). General Practitioners (GPs) record information on symptoms and medical diagnoses using the Read hierarchical classification system [19], and information on prescriptions is entered onto the system automatically. Demographic information recorded for each patient includes sex, year of birth and Townsend deprivation score quintiles (see details below).

### Study population

Individuals included in the study were under follow-up while aged 50 years or over during the period 2002–13, and had dementia, defined as a Read code for dementia

(see Appendix 1 for code list) or an anti-dementia drug prescription (galantamine, rivastigmine, donepezil or memantine). We excluded individuals for whom deprivation score quintile data were not available (2%). For each practice, only data from the date of acceptable levels of computer usage and death recording were included, as inadequate recording of events before these dates may lead to incidence being underestimated [20, 21].

In this study, our focus was on people who were living outside long-term care facilities. We identified and excluded individuals who were likely to be resident in a long-term care facility, based on the assumption that households with five or more residents aged 70 or over on 1 January 2010 were such facilities. For the psychotropic drug prescribing prevalence and healthcare contact outcomes, patient data were additionally required to contain at least 6 months of follow-up. For each patient in the dementia cohort, we used a frequency matching approach to randomly select up to five patients not in the dementia cohort who were in the same practice, age group and the same sex at the start of follow-up.

### Measurements

A list of Read codes for dementia diagnoses was developed using a published method [22]. We studied deprivation using Townsend score quintiles [23]. This area-level deprivation measure is calculated at the level of UK postcodes, using 2001 census data on unemployment, car ownership, home ownership and home overcrowding: quintiles are based on the whole UK population. Prescription data were used to determine initiation of antipsychotics, hypnotics and anxiolytics. Healthcare contact outcomes were, over a year: (i) number of surgery consultations; (ii) whether blood pressure and weight had been measured; (iii) whether there was a record that an annual dementia review (as required for the Quality Outcome Framework (QOF) payment [24]) had occurred. Reviews involve assessment of physical and mental health. Prevalence of an outcome was defined for each 1-year period as the proportion of those under follow-up during that period who had the outcome during that year. Covariates included sex, UK country, age, and, for the healthcare contact outcomes, a prescribing index as a measure of comorbidity (see details below). Age was analysed in 10-year categories. The prescribing index indicates the number of British National Formulary chapters from which patients received prescriptions (excluding anti-dementia drugs, vaccines and anaesthetics). This is a good measure for comorbidity [25].

### Analysis

We analysed data using Stata version 13.1 (Stata Corp, College Station, Texas). For the period 2002–13, we estimated overall rates of initiation and prescribing prevalence of antipsychotics, hypnotics and anxiolytics; surgery consultations, annual blood pressure monitoring, annual weight monitoring and annual dementia review. We used

multivariable Poisson regression to investigate the relationship between deprivation, gender and these outcomes. Random effects for general practices were included in models to account for variation in individual practices. Comparisons were made to the cohort of patients without dementia. Stratifying by Townsend quintile, incidence rate ratios were calculated for outcomes comparing the dementia cohort to the comparator non-dementia cohort.

**Results**

**Included patients**

A cohort of 68,061 patients was identified who had a record of dementia while aged 50 or over during the period 2002–13 (Supplementary data, Figure S1, available in *Age and Ageing* online); these patients were included in the analyses on psychotropic drug initiation. Of these, data were available from 54,721 (80%) for at least 6 months of follow-up, and so were included in the analyses on psychotropic drug prescribing prevalence and healthcare contact outcomes (Table 1). We included 259,337 people in our control population without dementia.

**Prescribing of psychotropic medication**

The proportion of the 54,721 patients receiving at least one prescription in a calendar year increased up to 2009, but

declined thereafter for antipsychotics, hypnotics and anxiolytics (Supplementary data, Figure S2(a)–(c) available in *Age and Ageing*). During 2013, 3.1% of the 21,716 under follow-up were prescribed antipsychotics, 2.4% were prescribed hypnotics and 2.6% were prescribed anxiolytics. During 2009, when the psychotropic drug prescribing prevalence was highest, 14.1% of the 16,043 then under follow-up were prescribed antipsychotics, 10.6% were prescribed hypnotics and 7.5% were prescribed anxiolytics. The proportion prescribed antipsychotics ranged from 6.8% to 8.0% in the deprivation groups; however, there was no systematic relationship between Townsend quintile and current prescribing of antipsychotics (Table 2). Women with dementia were more likely to be currently prescribed psychotropic medication than men with dementia. For example, 6.3% of men were currently receiving antipsychotics, compared to 7.7% of women, with an adjusted IRR (95% CI) of 1.18 (1.13–1.23).

**Initiation of psychotropic medication**

Overall, there was no systematic association between social deprivation and the initiation of antipsychotics, hypnotics or anxiolytics (Supplementary data, Table S1 available in *Age and Ageing*). Men with dementia were more likely to initiate all types of psychotropic medication than women with dementia.

**Consultations and healthcare monitoring in people with dementia**

The overall rate of surgery consultations was 6.8 visits per year, with no systematic change over time (Supplementary data, Figure S2(g) available in *Age and Ageing*). Annual blood pressure and weight monitoring both increased over time, and of the 21,716 patients who were under follow-up during 2013, blood pressure was recorded in 17,201 (79%) and weight was recorded in 10,118 (47%) (Supplementary data, Figure S2(d)–(e) available in *Age and Ageing*). From introduction in 2006, consistently around half of patients had a record of receiving an annual dementia review (Supplementary data, Figure S2(f) available in *Age and Ageing*). The crude rates and proportions of these outcomes were similar across deprivation score quintiles (Supplementary data, Figure S2 available in *Age and Ageing*; Table 3). Of the 11,273 patients with a dementia review during 2013, 5,657 (50%) had both weight and blood pressure recorded during that year: of the 10,443 patients under follow-up in 2013 who did not have a dementia review, 3,832 (37%) had both weight and blood pressure recorded during that year.

Compared to men, women had lower rates of surgery consultations (6.5 per person-year in women and 7.3 per person-year in men; adjusted IRR 0.90, 95% CI 0.90–0.91), of annual blood pressure monitoring (72% in women and 75% in men; adjusted IRR 0.96, 95% CI 0.95–0.97) and of annual weight monitoring (36% in women and 41% in men; adjusted IRR 0.91, 95% CI 0.90–0.93).

**Table 1.** Characteristics of the included patients at first record of dementia

Characteristic	Number (%)
Patients	68,061
<b>Sex</b>	
Male	25,226 (37%)
Female	42,835 (63%)
<b>Age (years)</b>	
50–59	1,344 (2%)
60–69	5,664 (8%)
70–79	20,678 (30%)
80–84	17,724 (26%)
85–89	14,652 (22%)
90+	7,999 (12%)
<b>Country</b>	
England	52,087 (77%)
Scotland	9,576 (14%)
Wales	4,260 (6%)
Northern Ireland	2,138 (3%)
<b>Calendar year</b>	
2002–05	16,320 (24%)
2006–09	22,851 (34%)
2010–13	28,890 (42%)
<b>Townsend quintile</b>	
1 (least deprived)	16,242 (24%)
2	15,366 (23%)
3	15,091 (22%)
4	12,976 (19%)
5 (most deprived)	8,386 (12%)
<b>Prescribing index</b>	
Median (IQR)	4 (2–6)

**Table 2.** IRRs for prescribing prevalence of antipsychotics, hypnotics and anxiolytics in 54,721 people with dementia, obtained from Poisson regression models with GP practice fitted as a random effect<sup>a,b</sup>

Covariate	Antipsychotics			Hypnotics			Anxiolytics		
	%	Univariable IRR (95% CI)	Multivariable IRR (95% CI)	%	Univariable IRR (95% CI)	Multivariable IRR (95% CI)	%	Univariable IRR (95% CI)	Multivariable IRR (95% CI)
<b>Townsend quintile</b>									
<b>(least deprived)</b>									
1	7.0	1	1	5.5	1	1	3.9	1	1
2	7.1	0.98 (0.92–1.03)	0.97 (0.92–1.03)	5.8	1.04 (0.98–1.11)	1.03 (0.97–1.10)	4.6	1.07 (0.99–1.15)	1.06 (0.99–1.14)
3	8.0	1.07 (1.01–1.13)	1.07 (1.01–1.13)	5.5	0.96 (0.90–1.03)	0.96 (0.90–1.03)	4.6	1.08 (1.00–1.16)	1.07 (1.00–1.16)
4	6.8	0.95 (0.89–1.02)	0.95 (0.89–1.01)	5.2	0.96 (0.90–1.04)	0.96 (0.89–1.03)	3.8	0.92 (0.85–1.01)	0.92 (0.85–1.00)
<b>(most deprived)</b>									
5	7.2	0.93 (0.87–1.00)	0.93 (0.87–1.00)	5.5	1.00 (0.92–1.08)	0.99 (0.91–1.07)	4.5	1.03 (0.94–1.13)	1.02 (0.93–1.12)
<b>Sex</b>									
Male	6.3	1	1	5.1	1	1	3.9	1	1
Female	7.7	1.17 (1.13–1.22)	1.18 (1.13–1.23)	5.7	1.08 (1.04–1.13)	1.06 (1.02–1.12)	4.5	1.11 (1.05–1.16)	1.13 (1.07–1.19)
<b>Age</b>									
50–69	4.7	0.61 (0.56–0.66)	0.61 (0.56–0.67)	2.9	0.52 (0.47–0.58)	0.52 (0.47–0.58)	3.0	0.64 (0.58–0.72)	0.64 (0.58–0.72)
70–79	7.9	1	1	5.8	1	1	4.7	1	1
80–84	7.3	0.89 (0.85–0.94)	0.89 (0.84–0.93)	5.7	0.95 (0.90–1.01)	0.95 (0.90–1.01)	4.3	0.88 (0.83–0.94)	0.87 (0.82–0.93)
85–89	7.2	0.87 (0.83–0.92)	0.83 (0.79–0.88)	5.8	0.96 (0.91–1.02)	0.94 (0.88–0.99)	4.2	0.86 (0.80–0.92)	0.82 (0.76–0.87)
90+	7.2	0.86 (0.81–0.91)	0.82 (0.77–0.87)	5.9	0.98 (0.92–1.05)	0.96 (0.90–1.03)	4.2	0.84 (0.77–0.90)	0.79 (0.73–0.85)
<b>Current year</b>									
2002–05	2.9	0.43 (0.39–0.46)	0.42 (0.39–0.46)	2.4	0.46 (0.42–0.50)	0.46 (0.42–0.50)	1.3	0.29 (0.25–0.32)	0.28 (0.25–0.32)
2006–09	9.4	1.33 (1.28–1.38)	1.32 (1.27–1.38)	7.1	1.32 (1.26–1.38)	1.32 (1.26–1.38)	4.8	0.99 (0.94–1.04)	0.98 (0.93–1.03)
2010–13	6.9	1	1	5.3	1	1	4.7	1	1

<sup>a</sup>Rate per 100 person-years.

<sup>b</sup>Estimates from multivariable models adjusted for all other covariates, as well as for country.

**Table 3.** IRRs for each of the four healthcare contact outcomes in 54,721 people with dementia, from Poisson regression models with GP practice fitted as a random effect

Covariate	Surgery consultations			Blood pressure monitoring			Weight monitoring			Annual dementia review (for follow-up 2006 onwards)		
	Rate <sup>a</sup>	Univariable IRR (95% CI)	Multivariable <sup>b</sup> IRR (95% CI)	%	Univariable IRR (95% CI)	Multivariable <sup>b</sup> IRR (95% CI)	%	Univariable IRR (95% CI)	Multivariable <sup>b</sup> IRR (95% CI)	%	Univariable IRR (95% CI)	Multivariable <sup>b</sup> IRR (95% CI)
<b>Townsend quintile</b>												
<b>(least deprived)</b>												
1	6.8	1	1	72	1	1	37	1	1	46	1	1
2	6.8	1.00 (1.00–1.01)	1.00 (0.99–1.00)	72	1.00 (0.98–1.01)	0.99 (0.98–1.01)	37	0.99 (0.96–1.01)	0.99 (0.96–1.01)	47	0.99 (0.97–1.02)	0.99 (0.97–1.01)
3	6.8	1.01 (1.00–1.02)	1.00 (1.00–1.01)	73	1.01 (0.99–1.03)	1.01 (1.00–1.02)	38	0.99 (0.97–1.02)	1.00 (0.97–1.03)	46	0.98 (0.96–1.01)	0.98 (0.95–1.00)
4	6.8	1.03 (1.03–1.04)	1.02 (1.01–1.02)	74	1.02 (1.00–1.04)	1.01 (0.99–1.03)	39	1.02 (0.99–1.04)	1.01 (0.99–1.04)	47	0.97 (0.94–0.99)	0.96 (0.94–0.99)
<b>(most deprived)</b>												
5	6.5	1.02 (1.01–1.03)	1.00 (0.99–1.01)	75	1.03 (1.01–1.05)	1.02 (1.00–1.04)	40	1.02 (0.99–1.06)	1.02 (0.99–1.05)	48	0.97 (0.94–1.00)	0.97 (0.94–1.00)
<b>Sex</b>												
Male	7.3	1	1	75	1	1	41	1	1	46	1	1
Female	6.5	0.89 (0.89–0.89)	0.90 (0.90–0.91)	72	0.97 (0.96–0.98)	0.96 (0.95–0.97)	36	0.87 (0.86–0.89)	0.91 (0.90–0.93)	47	1.02 (1.00–1.03)	1.01 (0.99–1.03)
<b>Age</b>												
50–59	6.7	0.94 (0.93–0.96)	0.99 (0.97–1.00)	61	0.83 (0.78–0.87)	0.84 (0.80–0.89)	41	0.96 (0.90–1.03)	0.97 (0.91–1.04)	38	0.84 (0.78–0.90)	0.84 (0.78–0.91)
60–69	6.6	0.94 (0.94–0.95)	0.99 (0.98–0.99)	67	0.91 (0.89–0.94)	0.93 (0.90–0.95)	42	0.99 (0.96–1.03)	1.00 (0.97–1.03)	39	0.93 (0.90–0.96)	0.94 (0.90–0.97)
70–79	7.2	1	1	73	1	1	42	1	1	44	1	1
80–84	7.1	0.97 (0.96–0.97)	0.96 (0.95–0.96)	75	1.02 (1.00–1.04)	1.01 (1.00–1.03)	39	0.91 (0.89–0.93)	0.91 (0.89–0.93)	48	1.03 (1.01–1.05)	1.02 (1.00–1.04)
85–89	6.6	0.90 (0.90–0.91)	0.88 (0.88–0.89)	74	1.01 (1.00–1.03)	1.00 (0.98–1.01)	34	0.81 (0.79–0.83)	0.79 (0.77–0.81)	49	1.05 (1.03–1.07)	1.04 (1.02–1.06)
90+	5.9	0.81 (0.80–0.81)	0.79 (0.78–0.79)	72	0.99 (0.97–1.01)	0.97 (0.95–0.99)	30	0.70 (0.68–0.72)	0.68 (0.66–0.70)	50	1.06 (1.03–1.08)	1.04 (1.01–1.06)
<b>Current year</b>												
2002–05	6.7	0.96 (0.95–0.97)	1.03 (1.02–1.03)	64	0.83 (0.81–0.84)	0.85 (0.84–0.87)	24	0.56 (0.55–0.58)	0.57 (0.55–0.59)	–	–	–
2006–09	6.6	0.96 (0.96–0.97)	1.00 (1.00–1.01)	72	0.93 (0.92–0.94)	0.95 (0.94–0.96)	35	0.80 (0.79–0.82)	0.81 (0.80–0.83)	41	0.80 (0.78–0.81)	0.80 (0.79–0.82)
2010–13	6.9	1	1	77	1	1	43	1	1	50	1	1

<sup>a</sup>Rate per person-year.

<sup>b</sup>Estimates from multivariable models adjusted for all other covariates, as well as for country and prescribing index.



### Comparator cohort of patients without dementia

Rates of initiation of antipsychotics, hypnotics and anxiolytics were higher overall in the dementia cohort compared to the non-dementia cohort (Supplementary data, Table S2 available in *Age and Ageing*). People with dementia had fewer surgery consultations and were less likely to have their weight and blood pressure monitored at least annually, compared to the non-dementia group, with similar differences in each of the Townsend quintile strata (Supplementary data, Table S2 available in *Age and Ageing*).

### Discussion

Area-level deprivation was not associated with healthcare or psychotropic medication receipt in people with dementia. Only half of people with dementia received an annual review as reimbursed by QOF. Among people with dementia, female gender was associated with receiving fewer primary care surgery consultations and less health monitoring. Men with dementia were more likely to be initiated on psychotropic drugs, but less likely to be currently taking them. Compared with our control population, people with dementia had fewer primary care consultations and were less likely to have weight and blood pressure monitored annually, despite the association of dementia with vascular risk factors, frailty and malnutrition [1], and were more likely to receive psychotropic medications.

Our findings differ from general population studies that found higher psychotropic prescribing levels in more deprived areas in people without dementia [26]. Perhaps government policies in the past decade, including targets incentivising GPs to identify and review annually people with dementia may have reduced inequities. One interpretation of our findings is that people with dementia, not having a family or friend carer to facilitate appointments may be the most important barrier to care, rather than socio-economic constraints *per se*. Interventions to increase understanding of dementia carers about the importance of maintaining physical health and treating co-morbidities may therefore be an important public health intervention.

Socio-economic prescribing inequalities often arise because patients or carers from less deprived groups better negotiate healthcare systems to seek out more desirable treatments. Socio-economic gradients in psychotropic prescribing have been attributed to differential access to alternate services such as psychological therapies, or different patient or carer expectations [26]. Perhaps this did not happen in people with dementia because there are few psychological, evidence based, routinely available treatments for behavioural and psychological symptoms of dementia [27], or because of the serious risks of initiating psychotropic drugs in dementia, although we did not find inequity before the MHRA warnings in 2009 [12]. In a previous study exploring the likelihood of patients with physical health complaints being referred to secondary care, inequalities associated with socio-economic circumstances occurred more in the absence of explicit

guidance, whereas inequalities with older age and female gender were evident for all conditions [28].

Having a dementia diagnosis predicted receipt of fewer physical health checks and primary care contacts, despite the National Dementia Strategies prioritising healthcare access in this group. People with dementia often experience difficulties arranging, remembering and attending appointments. Women with dementia are reported to have more disability and disease than men with dementia [29], so it is concerning that they receive less health monitoring. Despite this, women were no less likely to receive an annual dementia review, suggesting that the content of reviews should be investigated, as preventative health monitoring should be an important component. Women more often live alone, due to their greater longevity [30]. The lesser likelihood of having a co-resident carer might explain why women with dementia access healthcare less.

Compared to men, women with dementia were less likely to be initiated on psychotropic medication, but overall more of these medications were prescribed to women indicating they took them for longer. More regular medication review could reduce unnecessary psychotropic prescribing. As we found that men accessed healthcare more frequently, there may have been more opportunities for review and reduction where possible in line with current guidelines [13]. In the general population, women are also more likely than men to be prescribed psychotropic medication [31, 32].

### Limitations

Surgery contacts might be lower in people with dementia because they receive more home visits. We did not include home visits in analyses as there is uncertainty about how well they are recorded. Measures other than weight might be used to assess malnutrition on home visits. We could not identify people with undiagnosed dementia or control for dementia severity. As area-level deprivation can reduce access to secondary care where most dementia is diagnosed, there may have been more undiagnosed dementia in deprived areas; if this were so, it is likely that early-stage dementia would be most frequently missed due to symptom misattribution and delayed help-seeking [33]. This could mean that the people in more deprived areas had, on average, more severe dementia, but we did not find higher rates of psychotropic prescribing in these areas that might have suggested this. Women are more likely to move to a care home [34]. Those who remain at home might therefore have dementia which is on average less severe than men living at home. This could explain the lower rate of surgery consultations by women. The use of an area-level deprivation measure is a limitation, as individual deprivation level will sometimes be at odds to the deprivation level of the area in which a person lives.

### Conclusion

Only half of people with dementia have an annual dementia review recorded, as recommended in UK guidelines and

QOF. The QOF review for dementia has been associated with fewer unplanned hospital admissions, so increasing the proportion of patients who receive this may improve health outcomes [6]. In people with dementia, women received less physical healthcare monitoring, surgery visits and prescriptions for psychotropic drugs. A greater likelihood of women living alone without a family carer to help them access healthcare probably explains some of these findings. Enabling variables, such as having a carer to facilitate attending appointments have also been shown to be important determinants of people with dementias' healthcare access in findings from other developed countries [7]. Interventions to improve access to physical healthcare and reduce psychotropic use in people with dementia, especially women, could benefit people with dementia, their families and society by enabling them to live well with dementia for longer.

### Key points

- People with dementia received less primary, preventative healthcare than people without dementia.
- Women with dementia received less primary, preventative healthcare than men with dementia.
- Women with dementia were more likely to be taking psychotropic medication than men with dementia.

### Supplementary data

Supplementary data are available at *Age and Ageing* online.

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### Authors' contributions

All authors devised the study; R.L. undertook all analyses and R.L. and C.C. drafted the paper. All authors were part of the Steering group that managed the study, of which C.C. was Principal Investigator. All authors revised the manuscript critically for intellectual content and approved the final version.

### Conflicts of interest

None declared.

### Ethics approval

The data provider of THIN (CSD Medical Research UK) has obtained overall ethical approval from the South East MREC. As we used anonymised routinely collected data in this study, we did not require further ethics approval, but

we obtained approval by the THIN Scientific Review Committee. We did not recruit, approach or interview individual patients.

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