Comorbidity and polypharmacy in people with dementia

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Co-morbidity and polypharmacy in people with dementia: insights from a large, population-based cross-sectional analysis of primary care data

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Competing interests

We declare the following interests: BG and GM report grants from the Chief Scientist Office ARPG 07/01 during the conduct of the study.

Authors' Contributions

BG and SWM conceived the idea of the study. GMcL carried out statistical analysis and drafting of the results and methodology with BG. FC drafted literature review and interpretation of findings with BG, ER and SWM. All authors contributed to draft revisions. All authors approved the final version before submission. SWM is the guarantor for this study.

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Key words:

Co-morbidity, Multimorbidity, Dementia, Alzheimer's disease, Polypharmacy

Key points:

This paper reports a large cross sectional study of polypharmacy and physical comorbidity among older people with dementia.

People with dementia had more physical conditions and were also prescribed more medications than those without dementia.

This data highlights the importance of integrating specialist and non-specialist care to support complex symptom management.

Abstract

Background

The care of older people with dementia is often complicated by physical comorbidity and polypharmacy, but the extent and patterns of these have not been well described. This paper reports analysis of these factors within a large, cross sectional primary care dataset.

Methods

Data was extracted for 291,169 people aged 65 years or over registered with 314 general practices in Scotland, of whom 10,258 had an electronically recorded dementia diagnosis. Differences in the number and type of 32 physical conditions, and the number of repeat prescriptions in those with and without dementia were examined. Age-gender standardised rates were used to calculate odds ratio (ORs) of physical comorbidity and polypharmacy.

Results

People with dementia, after controlling for age and sex had on average more physical conditions than controls (mean number of conditions 2.9 vs. 2.4; $p<0.001$) and were on more repeat medication (mean number of repeats 5.4 vs. 4.2; $p<0.001$). Those with dementia were more likely to have five or more physical conditions (age-sex standardised OR [sOR] 1.42, 95% CI 1.35 to 1.50; $p<0.001$) and were also more likely to be on five or more (sOR 1.46; 95% CI 1.40 to 1.52; $p<0.001$) or ten or more repeat prescriptions (sOR 2.01; 95% CI 1.90 to 2.12; $p<0.001$).

Conclusions

People with dementia have a higher burden of co-morbid physical disease and polypharmacy than those without dementia, even after accounting for age and sex differences. Such complex needs

require an integrated response from general health professionals and multi-disciplinary dementia specialists.

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Background

Ageing populations are driving large increases in the prevalence of dementia, posing major challenges to healthcare systems internationally [1]. However, dementia and the healthcare of people living with dementia is often viewed in isolation by policymakers and healthcare providers. Health services are typically organised around single conditions, leading to people with multiple conditions often receiving uncoordinated or fragmented care. This is particularly true for people with physical-mental health comorbidity, since physical and mental health services in most countries are not well integrated [2,]. For people with dementia, older people's mental health teams focus almost exclusively on mental health care, and there may be a range of physical specialists involved in care in addition to geriatricians and primary care physicians.

A number of studies have reported the prevalence of co-morbidity in older people with dementia, but the evidence base is inconsistent due to limited sample size and selection bias (e.g. specialist or inpatient cohorts, specific dementia types) and the way in which comorbidity is measured [3-9]. The extent of multiple medication use (polypharmacy) in dementia has been little studied. To our knowledge, only one population-based study has examined polypharmacy, which reported that people with Alzheimer's disease took statistically significantly higher numbers of medication compared to controls when adjusted for gender and age (5.1 vs. 2.9) [10].

Comorbidity and polypharmacy are both associated with worsening effects on cognition, functional ability and survival of individuals with dementia [11, 12]. This paper examines a large population sample of people aged 65 years and over, examining prevalence of physical co-morbidity and polypharmacy in people with and without dementia. We have used similar methods to explore comorbidity and polypharmacy in schizophrenia [13] and bipolar disorder [14] in the same population dataset.

Methods

Data for this cross sectional study was provided by the Primary Care Clinical Informatics Unit at the University of Aberdeen for all registered patients who were alive and permanently registered with 314 general practices on March 31st 2007. The 1,751,841 people registered with these practices are a representative sample of approximately one-third of the Scottish population, and 291,169 people aged 65 years and over are included in this analysis.

People were identified as having dementia based on recording at any point of a relevant Read Code (the standard clinical coding system in use in UK primary care) including Alzheimer's disease, vascular dementia, Lewy Body dementia, dementia associated with other conditions such as Parkinson's Disease, and unspecified dementia . The two outcomes examined were measures of physical co-morbidity and number of repeat prescriptions. Data on the presence of 32 chronic physical health conditions were extracted (see Table 1). A more detailed explanation of how these conditions were selected and defined is available elsewhere[15].

Data on the number of drugs authorised for repeat prescription and issued to the patient in the previous 84 days was extracted. The count of number of repeat prescription drugs includes all pharmacologically active drugs, but excludes devices, dressings and topical preparations without significant systemic effects. Deprivation status was measured using the Carstairs' deprivation score which is widely used in healthcare research and was grouped into quintiles [16]. Age was categorised into five year bands from age 65-69 years to age 95 years and over.

Differences between individuals with dementia and all other individuals (controls) were calculated for age, deprivation status, number of physical conditions and number of repeat prescriptions as defined above. T-tests were used to analyse differences between groups and one-way ANOVA for differences across age groups and deprivation quintiles. As with previous papers, to control for differences between the two populations in age, gender and deprivation levels, we generated

standardised prevalence rates by age group (65 to 69 years; 70 to 74; 75 to 79; 80 to 84; and 85 and older), gender and deprivation quintile using the direct method [17]. These age-gender standardised rates were then used to calculate odds ratio (ORs) and 95% confidence intervals in those with dementia compared with those without for the prevalence of all 32 physical conditions, as well as no physical condition, one physical condition, two physical conditions, three, four and five or more physical conditions. Age-gender standardised rates were calculated in a similar fashion for the number of repeat prescriptions. All quoted odds ratios in the results are age-sex standardised. The NHS National Research Ethics Service had previously approved the use of these data for research purposes, therefore this study did not need individual ethical approval.

Results

There were 10,528 people with dementia recorded in the GP electronic medical record, 3.6% (95% CI 3.5 to 3.7) of those aged 65 and over (Table 1). People with dementia were more likely to be women (70.6% versus 56.7% of controls; p<0.001) and were on average older (mean age 82.6 years vs. 74.7 years; p<0.001). Only 14.9% of people with dementia were aged between 65 and 74 compared to 54.8% of those without, while 42.6% of people with dementia were 85 and over compared to 11.4% (difference 31.2%;p<0.001). No substantial or consistent differences were found by deprivation.

Physical co-morbidity in people with dementia versus controls

People with dementia had on average 2.9 physical conditions compared to 2.4 for controls (p<0.001) (Table 1). Only 8.7% of those with dementia had no physical condition compared to 15.9% of controls (OR 0.62, 95% CI 0.58 to 0.66) while 19% with dementia had five or more physical conditions compared to 13.4% of controls (OR 1.42, 95% CI 1.35 to 1.50).

Table 2 shows that the most commonly diagnosed condition for individuals with dementia was hypertension with a prevalence rate of 43.2% followed by constipation (25.9%), coronary heart

disease (CHD) (22.8%), stroke (19.4%) and pain (16.0%). For each of the 32 individual physical conditions assessed, age-sex standardised prevalence was significantly higher for dementia for 16 conditions, lower for three conditions and no difference was found for the remaining 13 conditions (table 2). Relative prevalence was highest for dementia versus controls for Parkinson's disease (OR 4.32, 95% CI 3.84-4.29), epilepsy (OR 3.26, 95% CI 2.90-3.67) and constipation (OR 2.65, 95% CI 2.52-2.79). The three physical conditions in which the prevalence for dementia patients was significantly lower following standardisation were cancer (OR 0.88, 95% CI 0.82 to 0.95), hypertension (OR 0.81, 95% CI 0.78 to 0.85) and asthma (OR 0.73, 95% CI 0.67 to 0.80).

Polypharmacy in people with dementia versus controls

People with dementia were on average on more active repeat prescriptions (mean number of repeats 5.4 vs. 4.2; p<0.001). Table 3 shows that only 10.9% of those with dementia were not on a repeat prescription compared to 18.3% of controls (OR 0.54; 95% CI 0.51 to 0.58; p<0.001). Over half of those with dementia were on five or more repeat prescriptions with 43.2% on five to nine repeat prescriptions compared to 32.4% of controls (OR 1.46; 95% CI 1.40 to 1.52; p<0.001) and 14% on ten or more compared to 8.4% of controls (OR 2.01; 95% CI 1.90 to 2.12; p<0.001). Apparent differences were reduced after standardising for number of physical conditions. For example, the odds ratios for those on five to nine repeat prescriptions fell to 1.23 (1.18-1.29) and 1.47 (1.38-1.58) for ten or more.

Discussion

Main Findings

This study of a large, non-selected general practice population sample shows that older people with dementia had more physical co-morbidity and polypharmacy than those without dementia. Those with dementia were more likely to have five or more physical conditions (not including dementia)

and to be on five or more repeat prescriptions. The age-sex standardised prevalence of individual physical conditions was significantly higher in dementia for 16 conditions, lower for three conditions and not different from the controls for the remaining 13 conditions.

Limitations

One of the strengths of this study is the large sample size (291,691 community living people aged 65 years and over), which is representative of the wider population in terms of age, sex and deprivation and avoids the biases that are inevitable in clinic or hospital based cohorts. However, the study relies on routine clinical recording of dementia diagnosis, which is known to be lower than expected, although recording in Scotland has historically been better than elsewhere in the UK [18]. Dementia diagnosis appeared to be under-recorded compared to the expected prevalence in the over 65s. Given known difficulties with early dementia identification and recording in general practice [19], this sample may therefore be more likely to describe co-morbidity among "diagnosed" patients with moderate to severe dementia. Thus the data may under specify the comorbidity patterns present among patients with earlier stage disease or among undiagnosed patients in residential care, with potentially higher comorbidity burden.

Comparison with related work

Other studies have also shown high rates of physical comorbidity and medication use in people with dementia, [3-5, 9, 23] although not all studies find this, [6-8] and the current sample is more representative than many of those studied previously. Disease stage and the care setting from which patients are recruited are likely to influence the prevalence of and identification of physical conditions across different study populations [4, 6-8]. For co-morbidity these results broadly agree with the findings of the only other large routine heath dataset published to date, which described administrative claims data and recorded higher comorbid conditions among people with dementia than their matched controls [9]. The same authors note that even when illness burden is controlled

for, the care costs of patients with dementia may be up to 34% higher than those of aged matched controls, with outpatient pharmaceuticals being the key driver of cost difference [20]. A recent Spanish primary care based study found increased rates of Parkinson's disease and cerebrovascular disease, consistent with this dataset,[21] but additionally reported higher rates of thyroid conditions, heart disease, retinal disorder and prostatic hypertrophy. This sample of 3,971 people with dementia was however, considerably smaller than the population reported here. Other studies report variation in condition prevalence between populations with or without dementia, suggestive of additional moderating factors. In a cross-sectional study of seven US primary care centres by Schubert and colleagues, medical co-morbidity was equally common in people with and without dementia[6]. Lyketsos and colleagues, however, reported more comorbidity among people with cognitive impairment and no dementia and individuals with dementia compared to those without these conditions in a population based study [5]. Equivalent comorbidity was similarly found in an inpatient study comparing very old (mean age 85.2 years) people with and without cognitive impairment,[8] but this, like other inpatient studies, is unlikely to be representative of the whole population of older people with and without dementia [22]. Similar issues apply to studies in specialist clinics, such as an earlier report in 1988 examining outpatients with Alzheimer's disease, which concluded that this patient group were healthier than those without dementia [7]. Bunn and colleagues review the dementia comorbidity literature with a focused exploration of disease prevalence in stroke, diabetes and visual impairment [23]. They note studies reporting both elevated and equivalent prevalence of stroke and diabetes relative to controls, suggestive of some data variability related to population selection and representativeness.

This study found that polypharmacy is more common among people with dementia, even after age, gender and comorbidity adjustment, similar to other studies which have found polypharmacy to be common in people with dementia. A large Swedish dataset reported that 33.5% of patients were receiving five or more regular medications [24]. In a study of nursing home residents with advanced

cognitive impairment, 13.9% of the population were on ten or more regular prescribed medications [12]. Another study in Norway reported that participants with Alzheimer's Disease were treated with a significantly higher number of medications as compared to controls (5.1 vs. 2.9 respectively), even after adjustment for co-morbidity [10]. In particular, previous work using the same dataset as this analysis has shown that people with dementia are seventeen times more likely to be prescribed an antipsychotic and twice as likely to be prescribed an antidepressant or a hypnotic/anxiolytic than older people without dementia [25].

Relevance to practice and policy

These findings have a number of implications for the development of policy and dementia care pathways. Both co-morbidity and polypharmacy may individually have a detrimental effect on outcomes of people with dementia. Research indicates that co-morbidity may have a direct negative effect on the clinical manifestation of dementia [12, 25-27] including the potential to increase rate of cognitive decline and accelerate functional decline, up to two years before patients without co-morbidity [27, 28]. Polypharmacy has also been shown to be associated with negative outcomes in people with dementia. In the SHELTER study, in patients with severe dementia, polypharmacy (defined as 10 medications or more) was associated with increased mortality[12].

Emergent evidence indicates that multidisciplinary treatment strategies may have the potential to reduce rates of antipsychotic prescription. Approaches that have been evaluated include timely screening of short term health conditions, systematic pain management protocols, and appropriately targeted psychosocial intervention [29]. Clodomiro and colleagues explore the possibility of applying risk benefit approaches to prescription according to factors such as frailty and multi-morbidity, highlighting in particular the incompatibility of anti-cholinergic treatments with many other medications commonly prescribed in elderly care settings [30].

Conclusions

This analysis, describing one of the largest population samples described to date, has shown high rates of physical comorbidity and polypharmacy in older people with dementia, which are both increased compared to the age-sex standardised control population. Given increasingly evidenced indications of the detrimental impact of comorbidity and polypharmacy, these findings highlight the need to re-evaluate and improve multidisciplinary integration of physical and mental health across a wide spectrum of care provision. Future research might usefully evaluate strategies for the active management of comorbidity and medication review to see whether it slows decline or improves function in people with dementia.

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Tables and Captions

Table 1. Age, gender, deprivation and number of conditions with confidence intervals and odds ratios shown

	People with dementia N=10,528 No. (%) unless stated	People without dementia N=280,641 No. (%) unless stated	Difference 95% CI (p<t)
Female	7428 (70.6)	159,028 (56.7)	13.9 (p<0.001)
Mean age (SD)	82.6 (7.4)	74.7 (7.2)	7.9 (p<0.001)
Age group			
65 to 69	579 (5.5)	83,023 (29.6)	-24.1 (p<0.001)
70 to 74	986 (9.4)	70,692 (25.2)	-15.8 (p<0.001)
75 to 79	1,832 (17.4)	56,369 (20.1)	-2.7 (p<0.001)
80 to 84	2,650 (25.2)	38,469 (13.7)	11.5 (p<0.001)
85 to 89	2,575(24.5)	21,985(7.8)	16.6 (p<0.001)
90 to 94	1,417 (13.5)	7,864 (2.8)	10.7 (p<0.001)
95 and above	489 (4.6)	2,239 (0.8)	3.8 (p<0.001)
Deprivation Quintile			
1 (least deprived)	2,130 (20.2)	52,978 (18.9)	1.3 (p<0.001)
2	2,400 (22.8)	65,255 (23.3)	-0.5 (p=0.27)
3	2,459 (23.4)	64,634 (23.0)	0.4 (p=0.43)
4	1,815 (17.2)	51,936 (18.5)	-1.3 (p=0.01)
5 (most deprived)	1,724 (16.4)	45,838 (16.3)	0.01 (p=0.98)
			Odds ratio (95% CI) Directly standardised for age and sex
No Physical	912 (8.7)	44,654 (15.9)	0.62 (0.58 to 0.66) p<0.001
One Physical	1,894 (18.0)	60,596 (21.6)	0.83 (0.79 to 0.87) p<0.001
Two Physical	2,202 (20.9)	59,922 (21.4)	0.92 (0.88 to 0.97) p=0.01
Three Physical	2,010 (19.1)	46,638 (16.6)	1.19 (1.14 to 1.25) p<0.001
Four Physical	1,508 (14.3)	31,278 (11.2)	1.20 (1.13 to 1.27) p<0.001
Five or more Physical	2,005 (19.0)	37,553 (13.4)	1.42 (1.35 to 1.50) p<0.001

Table 2 Prevalence and odds ratios for individual conditions, standardised by age and gender

Individual Conditions	People with dementia No.(%) N=10,528	People without dementia No. (%) N=280,641	Odds ratio (95% CI) Directly standardised for age and sex
Parkinson's Disease/Parkinsonism	310 (2.9)	2,022 (0.7)	4.32 (3.84 to 4.29) p<0.001
Epilepsy	226 (2.1)	2,704 (1.0)	3.26 (2.90 to 3.67) p<0.001
Constipation	2,728 (25.9)	22,788 (8.1)	2.65 (2.52 to 2.79) p<0.001
Inflammatory arthritis, connective tissue disorders and gout	1,433 (13.6)	27,442 (9.8)	2.23 (2.12 to 2.34) p<0.001
Stroke/TIA	2,038 (19.4)	25,634 (9.1)	2.13 (2.02 to 2.13) p<0.001
Multiple sclerosis	23 (0.2)	702 (0.3)	2.07 (1.57 to 2.74) p<0.001
Liver Disease	25 (0.2)	769 (0.3)	1.80 (1.35 to 2.39) p<0.001
Viral Hepatitis	2 (0.0)	46 (0.0)	1.77 (0.55 to 5.72) p=0.33
Psoriasis or eczema	131 (1.2)	2,882 (1.0)	1.69 (1.46 to 1.97) p<0.001
Inflammatory bowel disease	98 (0.9)	2,659 (1.0)	1.50 (1.27 to 1.77)) p<0.001
Blindness or low vision	418 (4.0)	4,930 (1.8)	1.48 (1.31 to 1.68) p<0.001
Pain	1,684 (16.0)	53,590 (19.1)	1.16 (1.10 to 1.21) p<0.001
Atrial fibrillation	1,124 (10.7)	18,583 (6.6)	1.13 (1.05 to 1.22) p=0.01
Thyroid Disorders	1,526 (14.5)	30,955 (11.0)	1.14 (1.07 to 1.21) p<0.001
Diabetes	1,397 (13.3)	37,347 (13.3)	1.14 (1.08 to 1.21) p<0.001
Hearing Loss	1,454 (13.8)	26,122 (9.3)	1.11 (1.04 to 1.18) p=0.01
Peripheral vascular disease	547 (5.2)	14,108 (5.0)	1.07 (0.98 to 1.17) p=0.10
CHD	2,399 (22.8)	57,303 (20.4)	1.06 (1.01 to 1.11) p=0.01
Prostate	357 (3.4)	10,069 (3.6)	1.06 (0.96 to 1.17) p=0.23
Diverticular	1,196 (11.4)	23,521 (8.4)	1.04 (0.97 to 1.11) p=0.21
Bronchiectasis	51 (0.5)	1,560 (0.6)	1.04 (0.80 to 1.35) p=0.72
COPD	976 (9.3)	28,562 (10.2)	1.03 (0.96 to 1.10) p=0.33
Chronic kidney disease	1,304 (12.4)	27,108 (9.7)	1.03 (0.96 to 1.10) p=0.34
Irritable bowel syndrome	361 (3.4)	11,332 (4.0)	0.99 (0.89 to 1.09) p=0.98
Glaucoma	590 (5.6)	11,127 (4.0)	0.99 (0.90 to 1.10) p=0.99
Heart Failure	727 (6.9)	14,041 (5.0)	0.98 (0.89 to 1.07) p=0.68
Dyspepsia	1,225 (11.6)	32,352 (11.5)	0.96 (0.90 to 1.02) p=0.09
Chronic sinusitis	55 (0.5)	2,097 (0.8)	0.89 (0.70 to 1.13) p=0.36
Any cancer last 5 years	863 (8.2)	23,353 (8.3)	0.88 (0.82 to 0.95) p<0.001
Migraine	20 (0.2)	1,203 (0.4)	0.83 (0.59 to 1.15) p=0.27
Hypertension	4,548 (43.2)	131,853 (47.0)	0.81 (0.78 to 0.85) p<0.001
Asthma	363 (3.5)	18,639 (6.6)	0.73 (0.67 to 0.80) p<0.001

Table 3 Prevalence and odds ratios for repeat prescribing, standardised by age gender and number of physical conditions

Number of active repeat medications*	People with dementia No. (%) N=10,528	People without dementia No. (%) N=280,641	Odds ratio (95% CI) Directly standardised for age and sex	Odds ratio (95% CI) Directly standardised for age, sex, and number of physical conditions
No Repeats	1,145 (10.9)	51,209 (18.3)	0.54 (0.51 to 0.58) p<0.001	0.74 (0.69 to 0.74)p<0.001
One Repeats	542 (5.2)	25,345 (9.0)	0.59 (0.54 to 0.64) p<0.001	0.73 (0.67 to 0.80)p<0.001
Two Repeats	759 (7.2)	29,477 (10.5)	0.77 (0.71 to 0.82) p<0.001	0.77 (0.71 to 0.83) p<0.001
Three Repeats	971 (9.2)	30,431 (10.8)	0.79 (0.74 to 0.85) p<0.001	0.87 (0.82 to 0.93) p<0.001
Four repeats	1,098 (10.4)	29,782 (10.6)	0.88 (0.82 to 0.94) p<0.001	0.94 (0.88 to 1.01)p=0.10
Five to nine repeats	4,544 (43.2)	90,896 (32.4)	1.46 (1.40 to 1.52) p<0.001	1.23 (1.18 to 1.29)p<0.001
Ten or more repeats	1,469 (14.0)	23,501 (8.4)	2.01 (1.90 to 2.12) p<0.001	1.47 (1.38 to 1.58)p<0.001

* Authorised for repeat issue without a consultation *and* issued in the last 84 days