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Association of cardiovascular system medications with cognitive function and dementia in older adults living in nursing homes in Australia

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Abstract

Objective To examine associations between cardiovascular system medication use with cognition function and diagnosis of dementia in older adults living in nursing homes in Australia. **Methods** As part of a cross-sectional study of 17 Australian nursing homes examining quality of life and resource use, we examined the association between cognitive impairment and cardiovascular medication use (identified using the Anatomical Therapeutic Classification System) using general linear regression and logistic regression models. People who were receiving end of life care were excluded. **Results** Participants included 541 residents with a mean age of 85.5 years (± 8.5), a mean Psychogeriatric Assessment Scale–Cognitive Impairment (PAS-Cog) score of 13.3 (± 7.7), a prevalence of cardiovascular diseases of 44% and of hypertension of 47%. Sixty-four percent of participants had been diagnosed with dementia and 72% had received cardiovascular system medications within the previous 12 months. Regression models demonstrated the use of cardiovascular medications was associated with lower (better) PAS-Cog scores [Coefficient (β) = –3.7; 95% CI: –5.2 to –2.2; $P < 0.0001$] and a lower probability of a dementia diagnosis (OR = 0.44; 95% CI: 0.26 to 0.75, $P = 0.0022$). Analysis by subgroups of medications showed cardiac therapy medications (C01), beta blocking agents (C07), and renin-angiotensin system agents (C09) were associated with lower PAS-Cog scores (better cognition) and lower dementia diagnosis probability. **Conclusions** This analysis has demonstrated an association between greater cardiovascular system medication use and better cognitive status among older adults living in nursing homes. In this population, there may be differential access to health care and treatment of cardiovascular risk factors. This association warrants further investigation in large cohort studies.

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Keywords: Cardiovascular agents; Cognitive dysfunction; Dementia; Residential facilities

1 Introduction

Dementia is a condition that has a number of causes, most commonly Alzheimer's disease, and is characterised by a gradual decline in cognitive function. Cognitive functions that may be affected include memory, orientation, learning, problem-solving, attention, language and the ability to perform activities of daily living.[1] It has been estimated that worldwide there are 47 million people living with dementia and the number of people living with dementia is expected to be more than 131 million by 2050 and the total estimated cost of dementia is about $US818 billion in 2015.[2]

Whilst Alzheimer's disease is the most common type of dementia, there is increasing awareness that dementia of mixed pathology is more common than dementia of discrete types.[3] Neurodegeneration and cerebrovascular damage to the brain are the two main causes of age-related cognitive decline and dementia.[4–6] Cardiovascular and cerebrovascular diseases share many pathophysiological traits and risk factors and even heart disease itself could be a risk factor for

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dementia.[7–10] Many classes of cardiovascular drugs have demonstrated effectiveness in the primary prevention, acute treatment and secondary prevention of stroke which is a risk factor for cognitive impairment and dementia.[11] In addition, in some trials of cardiovascular medications a protective effect against cognitive decline and dementia has been demonstrated, in particular with lipid lowering agents, although findings are inconsistent.[12–18] People in nursing homes have high prevalence of cardiovascular disease (CVD) risk factors and high use of CVD mediations.[19] For these reasons, the high rate of use of these medications in aged care may have associations with cognitive status.

There is often a lengthy delay between the appearance of symptoms of dementia and it's diagnosis.[20] Diagnosis is based upon clinical criteria following assessment of the patient's history, cognitive and mental state assessment, physical examination and medication review.[21] A large proportion of dementia is undetected in community and institutional settings and it is estimated that approximately half of people living with dementia in nursing homes are not diagnosed.[22] In Australian nursing home settings, cognitive function is routinely assessed using the Psychogeriatric Assessment Scale–Cognitive Impairment (PAS-Cog) instrument.[23] The PAS-Cog consists of nine questions to test the subject's memory and other cognitive functions, with higher scores indicating greater impairment. The aim of this analysis is to examine associations of cardiovascular system medications with cognitive function and diagnosis of dementia in older adults living in nursing homes in Australia.

2 Methods

2.1 Design, settings and participants

The Investigating Services Provided in the Residential Environment for Dementia (INSPIRED) Study is a cross-sectional study designed to determine and compare the quality of life, quality of care, utilisation of healthcare resources and costs of various residential care facilities that provide alternative models of dementia care for people with cognitive impairment and dementia. We collected data from 17 not-for profit nursing homes across 4 Australian states between January 2015 and February 2016. The inclusion criteria for INSPIRED were: (1) being permanent residents of the facility; (2) residing in the facility for 12 months or more; (3) not in immediate palliative care; (4) if not able to self-consent, have family who are able to provide proxy consent and/or participate on the resident's behalf; and (5) no other complex medical or family issues that would prevent participation. Written informed consents were obtained from participants or their legal guardians. Ethics approval for the study was obtained from the Flinders University social and behavioural research ethics committee. As part of this study we collected comprehensive data on medication use.

2.2 Cognitive and comorbidities measures

We collected the most recent (within three months) PAS-Cog scale data from nursing home records. If a participant had a PAS-Cog score older than three months and that score was higher than 18 (of a possible 21) points we retained that score as the most recent score based on an assumption that an additional PAS-Cog score would not substantially improve. If there was a PAS-Cog score older than three months but less than 18 points, a trained research nurse conducted a face-to-face interview to obtain the PAS-Cog data. A diagnosis of dementia was collected from the residential facility's medical records. In Australia, the Aged Care Act 1997 requires that all nursing homes must keep records about a resident's medical conditions, the treatment they are receiving and the type of care that is being provided under a resident's care plan.[24] Data on participants' comorbidities were also collected from residential facility medical records.

2.3 Cardiovascular medication use

The exposure variable for this analysis was whether a subject had been using medications active on the cardiovascular system within the last 12 months. We classified medication use according to the Anatomical Therapeutic Chemical (ATC) classification system.[25] Cardiovascular (C-class) medications that are considered predominantly to be used to manage cardiovascular risk factors were examined. Cardiovascular system medications are coded as follows: C01: cardiac therapy (cardiac glycosides, antiarrhythmics and vasodilators and other preparations used in cardiac diseases), C02: antihypertensives (antiadrenergics, agents acting on areolar smooth muscle), C03: diuretics, C04: peripheral vasodilators, C05: vasoprotective agents, C07: beta blocking agents, C08: calcium channel blockers, C09: agents acting on the renin-angiotensin system and C10: lipid modifying agents.[25]

Medication use information was obtained from three possible sources: (1) Pharmaceutical Benefits Scheme (PBS) data,[26] with the federal Department of Human Services of Australia providing details of the service records for consenting participants; (2) Pharmacy data records from nursing home-contracted pharmacists, or (3) Facility-based medication charts when pharmacy data could not be obtained.

For this analysis a participant was considered to have

been exposed if they had been prescribed cardiovascular system medications at any point during the previous 12 months.

2.4 Statistical methods

Means, standard deviations and percentages were used to describe the sample. Analysis of variance (ANOVA), Chi-square test and Fisher exact test were used to compare the means and proportions across PAS-Cog categories corresponding to no (score 0 to 4), mild (score 5 to 9), moderate (score 10 to 15) or severe (score 16 to 21) cognitive impairment and whether or not participants had a dementia diagnosis. We used general linear regression models to test the associations between cognitive impairment (measured by the continuous PAS-Cog score) and cardiovascular medications. Logistic regression models were used to test associations between diagnosis of dementia (yes *vs.* no) and cardiovascular medications. Unadjusted analyses were initially conducted and adjusted analyses controlling for potential confounding factors were performed. For multivariable general linear regression and multivariable logistic regression, adjustments were made for residents' age and gender, comorbidities related to cognition, dementia and cardiovascular disease, total number of comorbidities and the use of agents predominantly used for secondary prevention of cardiovascular disease, i.e. antithrombotic agents (B01) and antihemorrhagics (B02). Further analysis to investigate associations between the subgroups of the cardiovascular system medications and cognitive impairment and dementia were also performed using the same models.

3 Results

In total, 1323 residents from the facilities were assessed and 901 were eligible to participate, of these 541 consented to be part of the INSPIRED study. The mean age was 85.5 years (± 8.5); 74.5% were female; the average PAS-Cog score was 13.3 (± 7.7); 83% (448) of the participants had some level of cognitive impairment based on the PAS-Cog score, and 64.6% had been diagnosed with dementia. There was a high prevalence of cardiovascular disease in the study sample; 44% had a history of cardiovascular disease (including angina, congestive cardiac failure, atrial fibrillation, ischaemic heart disease, or stroke) and 47% a history of hypertension (Table 1). Seventy-two percent (390) of the participants had been prescribed medications acting on the cardiovascular system during the previous 12 months. Table 1 summarises the use of individual classes of medications. Table 2 and Table 3 summarise the distributions of considered covariates according to PAS-Cog score and dementia diagnosis. These include ATC code B level 2 medications considered likely to be used to treat existing cardiovascular disease and comorbidities associated with cardiovascular disease and cognition that may confound the analysis. Significant differences in the distribution of age, cardiovascular medication use, the use of antithrombotic agents, the total number of comorbidities and a history of congestive heart failure, ischaemic heart disease and cardiovascular disease were noted by PAS-Cog category. Significant differences in the use of cardiovascular medication use, the use of antithrombotic agents, the total number of comorbidities and a medical history of hypertension, congestive heart failure, ischaemic heart disease, stroke and diabetes between those diagnosed with dementia or not were observed.

Table 1. Characteristics of INSPIRED study sample.

Characteristic	Total sample size (n = 541)
Age, yrs	85.5 ± 8.5
Female	403 (74.5%)
Cardiovascular disease history*	239 (44.2%)
Hypertension history	254 (47.1%)
Hypercholesterolemia history	120 (22.3%)
DVT history	5 (0.93%)
PAS-Cog score	13.3 ± 7.7
PAS-Cog score 0–4, no cognitive impairment	93 (17.2%)
PAS-Cog score 5–9, mild cognitive impairment	100 (18.5%)
PAS-Cog score 10–15, moderate cognitive impairment	82 (15.2%)
PAS-Cog 16–21, severe cognitive impairment	266 (49.2%)
Dementia	348 (64.6%)
Use of any ATC C-class Cardiovascular System Medication	390 (72.1%)
C01 Cardiac therapy	95 (17.6%)
C02 Antihypertensives	16 (3.0%)
C03 Diuretics	161 (29.8%)
C04 Peripheral vasodilators	4 (0.74%)
C05 Vasoprotectives	15 (2.8%)
C07 Beta blocking agents	114 (21.1%)
C08 Calcium channel blockers	81 (15.0%)
C09 Agents acting on the renin-angiotensin system	193 (35.7%)
C10 Lipid modifying agents	169 (31.2%)
Other considered drug use	
B01 Antithrombotic agents	131 (24.2%)
B02 Antihemorrhagics	3 (0.56%)

Data were presented as mean ± SD or n (%). *Including those with a history of angina, congestive cardiac failure, atrial fibrillation, ischaemic heart disease and stroke. ATC: Anatomical Therapeutic Chemical Classification System, DVT: deep vein thrombosis, PAS-Cog: Psychogeriatric Assessment Scale–Cognitive Impairment.

Unadjusted general linear regression models on PAS-Cog score and unadjusted logistic regression models on diagnosis

Table 2. Characteristics and comorbidities of study sample by PAS-Cog score.

Characteristic	No cognitive impairment (PAS-Cog 0–4) *n* = 93	Mild cognitive impairment (PAS-Cog 5–9) *n* = 93	Moderate cognitive impairment (PAS-Cog 10–15) *n* = 93	Severe cognitive impairment (PAS-Cog 16–21) *n* = 93	*P* values
Age, yrs	85.1 ± 8.6	86.8 ± 8.6	87.3 ± 7.3	84.5 ± 8.7	0.0200
Female	68 (73.1%)	68 (68.0%)	64 (78.1%)	203 (76.3%)	0.3446
Any ATC C-class Cardiovascular System Medication	84 (90.3%)	81 (81.0%)	60 (73.2%)	165 (62.0%)	< 0.0001
C01 Cardiac therapy	30 (32.3%)	27 (27.0%)	13 (15.9%)	29 (10.9%)	< 0.0001
C02 Antihypertensives	5 (5.4%)	4 (4.0%)	3 (3.7%)	6 (2.3%)	0.5063
C03 Diuretics	37 (39.8%)	38 (38.0%)	26 (31.7%)	61 (22.9%)	0.0033
C04 Peripheral vasodilators	0 (0.0%)	1 (1.0%)	0 (0.0%)	3 (1.1%)	0.5843
C05 Vasoprotectives	0 (0.0%)	4 (4.0%)	4 (4.9%)	7 (2.6%)	0.2054
C07 Beta blocking agents	29 (31.2%)	26 (26.0%)	21 (25.6%)	42 (15.8%)	0.0068
C08 Calcium channel blockers	24 (25.8%)	17 (17.0%)	14 (17.1%)	28 (10.5%)	0.0047
C09 Agents acting on the renin-angiotensin system	51 (54.8%)	45 (45.0%)	37 (37.8%)	75 (28.2%)	< 0.0001
C10 Lipid modifying agents	44 (47.3%)	32 (32.0%)	27 (32.9%)	74 (27.8%)	0.0077
ATC B-class Anticoagulant Medications					
B01 Antithrombotic agents	27 (29.03%)	29 (29.0%)	13 (15.9%)	36 (13.5%)	0.0005
B02 Antihemorrhagics	1 (1.1%)	2 (2.0%)	0 (0.0%)	9 (3.4%)	0.2501
Comorbidities – medical history					
Hypertension	53 (57.0%)	44 (44.0%)	43 (52.4%)	114 (43.2%)	0.0858
Hypercholesterolaemia	26 (28.0%)	23 (23.0%)	16 (19.5%)	55 (20.8%)	0.4855
Angina	6 (6.5%)	6 (6.0%)	6 (7.3%)	8 (3.0%)	0.2841
Congestive Cardiac failure	10 (10.8%)	14 (14.0%)	6 (7.3%)	13 (4.9%)	0.0254
Atrial Fibrillation	12 (12.9%)	10 (10.0%)	9 (11.0%)	22 (8.3%)	0.6188
Ischaemic Heart Disease	24 (25.8%)	28 (28.0%)	16 (19.5%)	39 (14.8%)	0.0145
Stroke	21 (22.6%)	23 (23.0%)	11 (13.4%)	45 (17.1%)	0.2471
Deep Vein Thrombosis	3 (3.2%)	0 (0.0%)	0 (0.0%)	2 (0.8%)	0.1311
Diabetes Mellitus	22 (23.7%)	26 (26.0%)	17 (20.7%)	48 (18.2%)	0.3657
Depression	44 (47.3%)	42 (42.0%)	36 (43.9%)	109 (41.3%)	0.7805
Parkinson's disease	9 (9.7%)	4 (4.0%)	3 (3.7%)	9 (3.4%)	0.1239
Number of comorbidities	4.0 ± 1.4	3.8 ± 1.3	3.8 ± 1.5	3.5 ± 1.5	0.0204

Data were presented as mean ± SD or *n* (%). ATC: Anatomical Therapeutic Chemical Classification System; PAS-Cog: Psychogeriatric Assessment Scale–Cognitive Impairment.

of dementia showed that using any cardiovascular medications during the previous 12 months was associated with lower PAS-Cog scores (better cognitive function) and lower probability of dementia diagnosis (Table 4). When analysing subgroups of cardiovascular medications, cardiac therapy, diuretics, beta blocking agents, calcium channel blockers, agents acting on the renin-angiotensin system and lipid lowering agents were associated with both lower (better) PAS- Cog scores and a lower probability of dementia diagnosis (Table 4). There were no significant associations between antihypertensive use, peripheral vasodilators and vasoprotective agents with PAS-Cog scores or dementia diagnosis (Table 4).

Multivariable general linear regression models and multivariable logistic regression models controlling for age, gender, hypertension, angina, congestive cardiac failure, atrial fibrillation, ischaemic heart disease, stroke, deep vein thrombosis, diabetes mellitis, hypercholesterolaemia, depression, Parkinson's disease and the use of antithrombotic agents and antihemorrhagics demonstrated associations that were largely consistent with the unadjusted variable regression models (Figure 1), with the exception of diuretic and lipid modifying agents. Following adjustment for these potential confounding factors, the use of diuretic, calcium channel blockers, and lipid modifying agents were associated with lower PAS-Cog scores but were not significantly associated with dementia diagnosis (Figure 1).

4 Discussion

We found that the use of cardiovascular system medica-

Table 3. Characteristics and comorbidities of study sample by dementia status.

Characteristic	Non-dementia (*n* = 185)	Dementia (*n* = 348)	*P* value
Age, yrs	86.0 ± 9.2	85.1 ± 8.1	0.2809
Female	139 (75.1%)	256 (73.6%)	0.6933
Any ATC C-class Cardiovascular System Medication	155 (83.8%)	227 (65.2%)	< 0.0001
C01 Cardiac therapy	53 (28.7%)	44 (12.6%)	< 0.0001
C02 Antihypertensives	5 (2.7%)	13 (3.7%)	0.6216
C03 Diuretics	70 (37.8%)	87 (25.0%)	0.002
C04 Peripheral vasodilators	1 (0.5%)	3 (0.9%)	0.6882
C05 Vasoprotectives	7 (3.8%)	8 (2.3%)	0.3237
C07 Beta blocking agents	64 (34.5%)	52 (14.9%)	< 0.0001
C08 Calcium channel blockers	40 (21.6%)	43 (12.4%)	0.005
C09 Agents acting on the renin-angiotensin system	97 (52.4%)	102 (29.3%)	< 0.0001
C10 Lipid modifying agents	74 (40.0%)	99 (28.5%)	0.0067
ATC B-class Anticoagulant Medications			
B01 Antithrombotic agents	47 (25.4%)	57 (16.4%)	0.0123
B02 Antihemorrhagics	2 (1.1%)	10 (2.9%)	0.2321
Comorbidities			
Number of comorbidities	4.0 (1.3%)	3.5 (1.4%)	< 0.0001
Hypertension	109 (58.9%)	144 (41.4%)	0.0001
Angina	14 (7.6%)	12 (3.5%)	0.0356
Congestive Cardiac failure	24 (13.0%)	18 (5.2%)	0.0015
Atrial Fibrillation	26 (14.1%)	26 (7.5%)	0.0148
Ischaemic Heart Disease	46 (24.9%)	60 (17.2%)	0.0358
Stroke	49 (26.5%)	51 (14.5%)	0.0009
Deep Vein Thrombosis	3 (1.6%)	2 (0.57%)	0.3472
Diabetes Mellitus	53 (28.7%)	59 (17.0%)	0.0016
Hypercholesterolaemia	48 (26.0%)	69 (19.8%)	0.1043
Depression	88 (47.6%)	142 (40.8%)	0.1334
Parkinson's Disease	12 (6.5%)	13 (3.7%)	0.1527

Data were presented as mean ± SD or *n* (%). ATC: Anatomical Therapeutic Chemical Classification System.

Table 4. Unadjusted linear regression and logistic regression on PAS-Cog score and diagnosis of dementia.

Medications on Cardiovascular System	PAS-Cog score		Dementia Diagnosis (Yes *vs.* No)	
	Coefficient β (95% CI)	*P* value	Odds Ratio (95% CI)	*P* value
C Any Cardiovascular system medications	–4.8 (–6.2, –3.4)	< 0.0001	0.29 (0.18, –0.47)	< 0.0001
C01 Cardiac therapy	–4.0 (–5.6, –2.3)	< 0.0001	0.41 (0.26, 0.64)	< 0.0001
C02 Antihypertensive	–3.7 (–7.5, 0.14)	0.0588	1.20 (0.41, 3.5)	0.7432
C03 Diuretics	–3.3 (–4.7, –1.9)	< 0.0001	0.53 (0.36, 0.77)	0.0009
C04 Peripheral vasodilators	2.9 (–4.6, 10.5)	0.4471	1.6 (0.17, 15.6)	0.6715
C05 Vasoprotectives	–0.17 (–4.1, 3.8)	0.9333	0.46 (0.16, 1.3)	0.1339
C07 Beta blocking agents	–3.5 (–5.3, –1.9)	< 0.0001	0.31 (0.20, 0.47)	< 0.0001
C08 Calcium channel blockers	–2.8 (–4.6, –1.0)	0.0021	0.55 (0.34, 0.89)	0.0144
C09 Agents acting on the renin-angiotensin system	–4.1 (–5.4, –2.8)	< 0.0001	0.32 (0.22, 0.46)	< 0.0001
C10 Lipid modifying agents	–2.7 (–4.1, –1.3)	0.0001	0.56 (0.39, 0.82)	0.0026

ATC: Anatomical Therapeutic Chemical Classification System, CI: confidence interval, PAS-Cog = Psychogeriatric Assessment Scale-Cognitive Impairment

tions was associated with less cognitive impairment and a lower probability of having a dementia diagnosis in a population residing in a nursing home for a least one year, who had a high prevalence of cardiovascular diseases. Residents who had been using cardiovascular system medications over a 12-month period were 3.7 (β = –3.7) points lower in

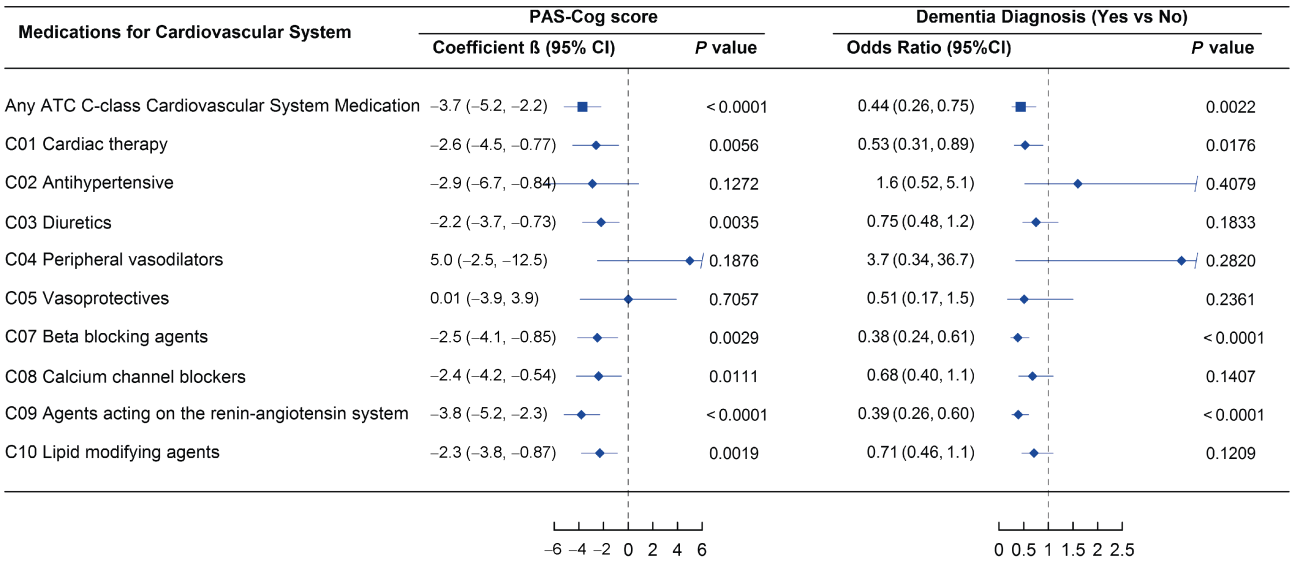

Figure 1. Multivariable linear regression of PASCog score and logistic regression of diagnosis of dementia. All models were adjusted for age, gender, antithrombotic agents (ATC code B01), antihemorrhagics (ATC code B02), number of comorbidities and specific comorbidities listed in Table 2. ATC: Anatomical Therapeutic Chemical Classification System; CI: confidence interval; PAS-Cog: Psychogeriatric Assessment Scale-Cognitive Impairment.

PAS-Cog score and 56% (OR = 0.44) less likely to be diagnosed with dementia than those who did not use any such medications. This association existed for cardiac therapy, beta-blockers, and agents acting on the renin-angiotensin system as classified by the ATC.

Similar associations between cardiovascular medication use and cognitive status have been reported in other studies. An association of reduced cardiovascular medications with dementia has been demonstrated in a community setting.[27] A similar, but smaller, association of cardiovascular medication use with better cognitive status within dementia patients has been shown in an analysis of a Swedish Registry data.[28] A three-year prospective cohort study from a Spanish register demonstrated that while total pharmaceutical consumption increased over the three-year period in people with dementia, the consumption of cardiovascular system drugs decreased.[29]

There are several possible explanations for the observed association. People living with cognitive impairment or dementia are likely to experience barriers to the access and prescription of medications for the management of cardiovascular disease and its risk factors. People living with cognitive impairment or dementia are less likely to be aware of or to effectively communicate their symptoms[30] and may also have a lower rate of presentation for investigation of symptoms or preventative health management.[31,32] Thus, this population may be less likely to receive management and prescriptions for non-symptomatic cardiovascular disease.

The balance of the benefits and harms of prescribing medications to manage cardiovascular risk factors are different in this population to a population without cognitive impairment. As dementia is a non-remitting progressive condition, associated with a reduced life expectancy for many, it may be reasonable that management of risk factors that are only likely to lead to a direct impact on health in the longer term is reduced.

However, in some people diagnosed with dementia or cognitive impairment there may be instances of under-treatment of cardiovascular symptoms.[33] In a Canadian study, it was demonstrated that patients with severe dementia were under-treated for stroke and hypertension.[34,35] Additionally, optimising prescribing and deprescribing medications for people with dementia is complicated by diminished decision making capacity and difficulties with comprehension and communication by the patient and the lack of clinical practice guidelines to guide deprescribing for healthcare practitioners; therefore these factors may affect the prescription or cessation of medications for management of cardiovascular risk factors.[33]

Limited life expectancy and cognitive impairment are important drivers of deprescribing amongst geriatricians.[36] Considering reducing or ceasing antihypertensive medications in frail elderly patients has been recommended, however patients in the palliative treatment stages of disease were excluded from the INSPIRED study.[37,38] Nevertheless, if there is inadequate management of cardiovascular disease risk factors in some individuals this could lead to greater

comorbidities and potentially an increase in any vascular component to cognitive impairment.[39] Hence, the decision to prescribe cardiovascular medications to residents of nursing homes must be balanced against the risk of increasing polypharmacy.[40] In a registry study of people with dementia, there was higher use of drugs to control vascular risk factors at baseline in those with non-degenerative vascular dementia.[29]

There may also be interactions between medications used for treating cardiovascular disease and dementia. In the case of beta-blockers, there is a known precaution to their use for people with dementia prescribed acetylcholinesterase inhibitors as a cognitive enhancing agent, due to concerns about possible additive bradyarrhythmic events such as syncope, bradycardia, arrhythmia and cardiac arrest.[41] In addition, centrally acting alpha-blockers, such as prazosin, have anticholinergic properties that may worsen neurological symptoms in those with cognitive impairment or dementia. No association with cognitive status was seen with the class of medicines that includes these medications (antihypertensives, ATC code C02) in this analysis. However, the lack of association of the 'antihypertensive' group of medicines may be because this class also includes anti-adrenergics. Anti-adrenergics are considered potentially inappropriate for prescription in older adults broadly, rather than specifically those with cognitive impairment.[42]

It is also possible that the observed association is due to a lower prevalence of risk factors associated with cardiovascular disease in those with worsening cognition. A cohort study of nursing home residents in the United States of America found that those with more severe dementia had fewer comorbidities, less hypertension and diabetes than those with no cognitive impairment.[43] Although the current analysis has adjusted for cardiovascular disease and risk factor history, our dataset does not capture all possible risk factors and it is possible that other confounders which were not measured and hence could not be adjusted for (such as Body Mass Index or smoking status) may explain the associations.

Finally, as some cardiovascular medications may have a cognitive protective effect, those who are taking these agents may be less likely to develop dementia. We observed better cognitive status and a lower probability of dementia associated with taking agents acting on the renin-angiotensin system and these agents have been demonstrated to prevent cognitive impairment and dementia.[15,17,44] Furthermore, calcium channel blockers were associated with better cognitive function in this analysis which is in line with the findings of a previous study which showed a longitudinal association between calcium channel clockers and a lower rate of cognitive decline in very old individuals.[45] Treating vascular risk factors may offer a secondary prevention strategy towards disease progression in people with dementia.[46] However, further evidence of this is needed before encouraging the use of cardiovascular medications in nursing homes as older people with dementia are already at risk of polypharmacy. In the current study, it is not possible to determine causation or to examine the direction of any effect.

The strengths of the current analysis were the access to detailed medication prescribing information for all subjects for 12 months from multiple sources. Therefore, the data on medication prescribing is considered highly accurate. Tests of cognitive function were conducted when no recent cognitive assessment was available and access to a diagnosis of dementia from medical records also suggests our measures of cognitive status for the individual participants are reliable. The participants were from 17 different nursing homes across four Australian states. The distributions of the age, gender, marital status and type of dementia were similar in the INSPIRED study sample to the latest available Australian population estimates (data not shown) and are therefore likely to be representative of Australians living in nursing homes nationwide.

The limitations of the current analysis are those inherent to the design of a cross-sectional study; it is not possible to know the direction of any effect, i.e. whether cognitive decline, dementia diagnosis, or prescription of cardiovascular medications occurred first, thus it is not possible to investigate causality. It is also possible confounders exist which have not been adjusted for but that may explain the association; although we have adjusted for history of cardiovascular diseases and risk factors for which data were available. As the captured pharmaceutical use data is retrospective, it represents medication use in nursing home residents that survived for 12 months or longer. Further, although the overall sample size for this analysis was relatively large, for some subgroups of medications the sample size was small which would decrease the statistical power to find associations with cognitive status.

In summary, this analysis has demonstrated consistent associations between the use of cardiovascular system medications and cognitive status among older adults living in nursing homes in Australia for 12 months or longer. The likely explanation for this cannot be determined, and warrants further investigation in longitudinal cohort studies. However, this finding may reflect a pattern of reduced access to or management of cardiovascular risk disease or its risk factors in nursing home residents with worse cognitive function.

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