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Featured Article

Longitudinal patterns of potentially inappropriate medication use following incident dementia diagnosis

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Abstract

Introduction: Potentially inappropriate medication (PIM) use in older adults with dementia is an understudied area. We assessed longitudinal changes in PIM exposure by dementia type following dementia diagnosis.

Methods: We followed 2448 participants aged ≥ 65 years (52% women, 85.5% Caucasian, mean age 80.9 ± 7.5 years) diagnosed with dementia after enrollment in the National Alzheimer's Coordinating Center (2005–2014). We estimated the association between dementia type and PIM annually for 2 years after diagnosis, using Generalized Estimating Equations.

Results: Participants with Lewy body dementia had more PIM use, and participants with frontotemporal dementia had less PIM use than participants with Alzheimer's disease. In the first year following diagnosis, total number of medications increased, on average, by 10% for Alzheimer's disease and 15% for Lewy body dementia ($P < .05$ for both).

Discussion: A tailored approach aimed at optimizing drug therapy is needed to mitigate PIM exposure to improve medical care for individuals with dementia.

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Keywords:

Dementia; Inappropriate medication use; National Alzheimer's Disease Coordinating Center; Beers' Criteria; Polypharmacy

1. Introduction

Optimal drug therapy aimed at avoiding the prescription of potentially inappropriate medications (PIMs), prescribing beneficial medications, and minimizing total number of medications is a challenge for clinicians treating older adults with dementia. For one, older adults with dementia have more physical and mental health conditions and take

more medications to treat these conditions than older adults without dementia [1–4]. In addition, older adults with multiple diseases, including dementia, are often excluded from drug trials, limiting the available evidence to guide prescribing practices [5–8]. Furthermore, some studies suggest that older adults with dementia experience increased sensitivity to the side effects of medications [8,9]. In addition, older adults with dementia experience cognitive, affective, and behavioral changes that present additional challenges to medication management [10–12].

A key component of optimal drug therapy is identifying and deprescribing unnecessary and PIMs. Inappropriate

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prescribing in older adults is most commonly assessed by indicators including the Beers' Criteria [13], scales measuring anticholinergic burden [14,15], and overall number of medications [16–20]. Studies of PIM use in older adults have found associations with increased risk of adverse drug reactions [21], hospitalization and mortality [22], and cognitive decline [23]. Studies of older adults with dementia have found that exposure to polypharmacy (≥ 5 medications) leads to worsening cognitive and functional abilities and greater mortality [24,25]. Polypharmacy has also been found to be associated with increased risk of dementia [26,27] and PIM use among older adults with and without dementia [16]. Recent attempts have been made to develop a consensus list of inappropriate medication for people with advanced dementia [28].

Despite these known risks, the prevalence of PIM use among individuals with dementia remains a clinical and public health concern [16,20]. A recent review of PIM use among individuals with cognitive impairment and dementia reported a prevalence of 10.2%–56.4% across different samples in Europe, Australia, and the United States [11]. Although there is a growing body of evidence suggesting a high prevalence of PIM use in individuals with dementia [11], there is limited research evaluating changes in PIM use in the years following dementia diagnosis [29]. In addition, given the differences in etiology, clinical manifestation, and comorbidities associated with different types of dementia, it would be expected that prescribing practices should differ among individuals diagnosed with different types of dementia [30–33]. In fact, previous studies suggested that risk factors and medications' effects may differ by the type of dementia [34,35]. However, most studies to date are either limited to a single type of dementia (i.e., Alzheimer's disease [AD]) or do not distinguish between different types of dementia. Therefore, the aim of this study was to examine (1) differences in PIM use by type of dementia diagnosis and (2) longitudinal changes in PIM use in the 2 years following diagnosis of common types of dementia.

2. Methods

2.1. Data source

The data for this study were obtained from the National Alzheimer's Disease Coordinating Center (NACC). A description of the NACC cohort, its eligibility criteria, and data collection are available elsewhere [36–39]. In summary, NACC was established in 1999 with the purpose of facilitating research related to AD. This cohort includes participants with AD and related disorders, participants with mild cognitive impairment, and cognitively normal participants. Participants are enrolled through National Institute on Aging-funded Alzheimer's Disease Centers (ADC) based in university medical centers and other institutes, mostly in urban areas throughout the United States. Participants undergo a comprehensive cognitive, behavioral, and functional assessment at their initial study visit and at annual follow-up

visits until they are deceased or decline further participation in the study. Beginning in 2005, Uniform Data Set (UDS) data were collected through standardized evaluations of enrollees from National Institute on Aging-funded ADCs.

2.2. Sample

Our study included participants aged ≥ 65 years, diagnosed with dementia after enrollment in the NACC cohort. Participants were excluded if they: (1) enrolled after 2014 ($n = 1180$); (2) had a diagnosis of dementia at their initial visit (prevalent dementia; $n = 12,046$); (3) had only one NACC assessment ($n = 1065$); (4) were not diagnosed with dementia during the follow-up ($n = 17,012$); (5) were < 65 years at the visit in which incident dementia diagnosis occurred ($n = 204$); (6) had a Clinical Dementia Rating (CDR) global score indicating normal cognition at the visit of incident dementia diagnosis ($n = 7$); or (7) had a primary dementia diagnosis of "other" ($n = 143$). As the aim of this study was to evaluate PIM use among individuals with progressive dementias, we sought to exclude those whose dementia may have been related to treatable/reversible conditions or for whom etiology was unknown [40,41]. The analytic sample for this study includes 2448 participants who enrolled in NACC between 2005 and 2014 and had an incident diagnosis of Alzheimer's dementia (AD: $n = 2090$), vascular dementia (VD: $n = 136$), Lewy body dementia (LBD: $n = 144$), or frontotemporal dementia (FTD: $n = 78$) after their initial visit (Fig. 1).

2.3. Measures

2.3.1. Dementia diagnosis

All participants in our study were deemed to have dementia if they met the standard criteria for dementia of the Alzheimer's type or for other non-Alzheimer's-related dementias based on comprehensive neuropsychiatric battery and cognitive assessment with a trained ADC clinician [37,42,43]. Our analyses only included incident dementia cases, specifically those that were identified as such after enrollment in the NACC cohort.

For our study, participants were grouped into mutually exclusive groups based on the clinician's determination of their primary etiology of dementia at the visit of their incident dementia diagnosis.

1. Alzheimer's disease [44] ($n = 2090$). Participants were considered to have AD if they met the criteria for dementia and had probable AD as the primary clinical diagnosis based on the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association criteria.
2. Vascular dementia ($n = 136$). Included participants identified with stroke, probable VD, possible VD, or any significant vascular brain injury as the primary cause of dementia.

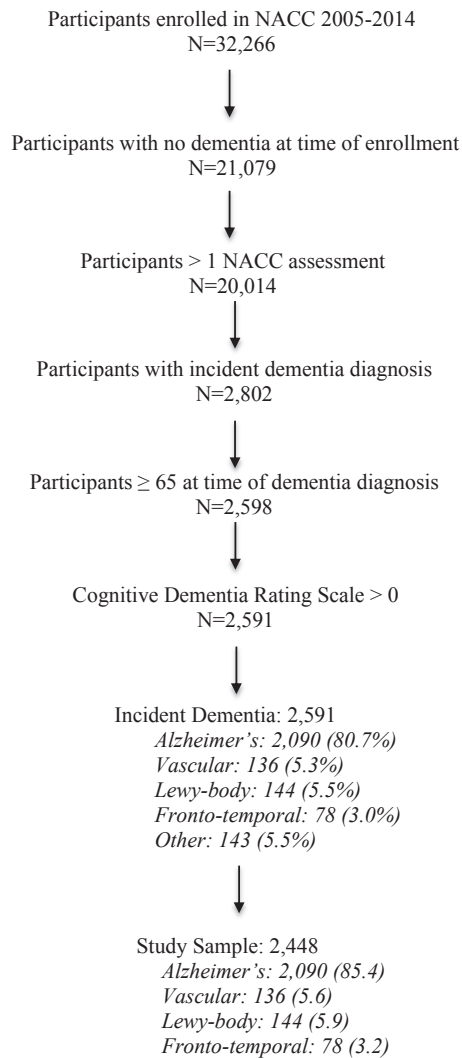


Fig. 1. Study flow chart for sample of 2380 NACC participants, 2005–2014. Abbreviation: NACC, National Alzheimer's Disease Coordinating Center.

3. Lewy body dementia (n = 144). Included participants with LBD listed as the primary etiologic diagnosis on the UDS clinician diagnosis form.
4. Frontotemporal dementia (n = 78). Included participants with FTD as their primary cause of dementia on the UDS clinician diagnosis form.

2.3.2. Potentially inappropriate medication use

Medication use was assessed based on the information provided by the participant and/or the caregiver/legally authorized representative (LAR) who accompanies them for visits. Participants were asked to bring all medications (or their medication list) they had taken in the past 2 weeks. Medication use assessment included all prescription and over-the-counter medications and was conducted using the "brown bag" medication review approach [37]. Based on these medication records, the following outcome variables were created.

2.3.2.1. Beers' Medication Criteria [13]

We used the 2015 updated Beers' Criteria to identify participants using PIM independent of diseases. We created a count of the total number of 2015 Beers' Criteria medications a participant reported taking at each annual visit, independent of participants' specific dementia diagnosis.

2.3.2.2. Anticholinergic Drug Scale score [14,15]

The Anticholinergic Drug Scale score (ADS) ranks anticholinergic effects of medicines with a score between 0 and 3. A score of 0 is given to medicines with no known anticholinergic activity, score 1 for medicines that have potential anticholinergic effects based on receptor binding studies, score 2 for medicines with reported anticholinergic adverse events, usually at excessive doses, and score 3 for medicines with profound anticholinergic properties. Each individual's score is the sum of the individual medication rankings and was calculated for each annual visit.

2.3.2.3. Total number of medications

A count of all medications a participant reported taking at each annual visit, including over-the-counter medications, supplements, and vitamins.

2.3.3. Other covariates

The following measures were recorded in the NACC-UDS data set at each annual visit. Information was obtained from the participant and/or the caregiver/LAR who accompanies them for visits.

2.3.3.1. Sociodemographic characteristics

Sociodemographic characteristics include age, gender, race/ethnicity (Caucasian, African American, or other), education level (high school or less, college, or graduate), living situation (lives alone, lives with a spouse or partner, or other living situation), type of residence (single family residence, retirement community, assisted living, or other), and level of independence (able to live independently, requires assistance, or completely dependent).

2.3.3.2. Health characteristics

We used the information recorded in the UDS Health History form at the time of dementia diagnosis in the cohort. For our analyses, we considered the following: cardiovascular disease (myocardial infarction, atrial fibrillation, angioplasty, coronary artery bypass graft surgery, pace maker, congestive heart failure, or other cardiovascular disease), stroke, diabetes (type 1 or type 2), and psychiatric diagnoses. Body mass index was calculated from measures of the participants' height and weight. Smoking history (number of years the participant has smoked) was obtained by self-report/LAR report.

2.3.3.3. CDR Global Score [45]

Dementia severity was assessed using this 5-point scale to assess domains of cognitive and functional performance and determine the level of impairment (none, questionable, mild, moderate, or severe). The rating was obtained

through a semi-structured interview by the ADC clinician with the participant and his/her LAR. Our study excluded individuals with no impairment as determined by the CDR score.

2.3.3.4. Geriatric Depression Scale [46,47]

The 15-item Geriatric Depression Scale was used to assess participants' depressive symptoms at the visit.

2.4. Statistical analysis

For participants with different dementia diagnoses types, we compared sociodemographic characteristics, comorbidities, and medication use at the visit they were diagnosed with incident dementia during cohort participation (hereafter referred to as baseline). For categorical variables, we used chi-squared tests to identify overall differences across subtypes of dementia. When a significant difference was identified at a level of $P < .05$, we conducted pairwise chi-squared tests to identify differences between pairs of dementia subtypes, applying a Bonferroni correction for multiple comparisons. For continuous variables, we conducted an analysis of variance, applying a Bonferroni correction for multiple comparisons. All analyses were conducted using SAS[®] software, version 9.4 [48].

2.4.1. Modeling medication outcomes

To estimate each of the PIM use measures over the 2 years following incident dementia diagnosis, we used generalized estimating equations. This approach allows for the flexibility to model correlation of within-subject repeated measurements. Poisson distribution was applied to model count outcomes. To account for the large number of participants who were not taking any Beers' Criteria medications (24.8%) or had an ADS score 0 (41.0%), we modeled these outcomes using only participants who had a Beers' Criteria medication count or ADS score ≥ 1 for at least one of the time points in the respective models. A suitable working correlation structure for each model was selected based on quasi-information criterion fit-statistic. Models were adjusted for sociodemographic and health characteristics as described above (see *Measures*: other covariates). Finally, differences in marginal means of PIM use by (1) type of dementia diagnosis (compared to AD) and (2) time-by-type of dementia interactions were estimated as least squares means (LSMs).

2.4.2. Attrition and sensitivity analysis

We examined attrition from the study due to death, loss to follow-up and declined participation, and due to censoring (some participants who were diagnosed with dementia in 2014 were only able to contribute 1 year of data during this study period). To determine the impact of attrition on the results of this study, we compared the estimates obtained from the full sample to a subset of participants ($n = 833$) who participated in all three assessment points in this study.

3. Results

3.1. Baseline characteristics

Overall, participants were 52% women, 85.5% Caucasian, mean age was 80.9 ± 7.8 years, and 74% completed education beyond high school (Table 1). Participants with FTD were younger, and participants with VD were older than participants with other dementias. More participants with LBD were male (74.3%) compared to other dementias (all $P < .05$). Fewer participants with LBD (20.2%) and VD (30.9%) were able to live independently than participants with AD (35.0%, $P < .01$ for both). Participants with AD and VD were more likely to live alone or have "other living arrangements," and participants with LBD and FTD were more likely to be living with a spouse/partner (all $P < .05$).

More participants with VD had cardiovascular diseases and history of stroke than participants with other dementias ($P < .01$). Participants with LBD and FTD had fewer depressive symptoms than participants with AD ($P < .05$). Participants with AD had lower CDR scores (less impairment) compared to VD and LBD ($P < .05$ for both).

In unadjusted analyses at baseline, there were no differences in the number of Beers' Criteria medications by type of dementia. ADS scores were higher among participants with LBD compared to AD and FTD ($P < .05$ for both). Participants with FTD reported taking fewer total medications (mean: 5.9, SD: 3.3) compared to AD (mean: 7.2, SD: 4.1), VD (mean: 8.3, SD = 4.3), or LBD (mean: 8.0, SD: 3.8) (all $P < .05$).

3.2. Longitudinal trends in PIM use by type of dementia

3.2.1. Differences in PIM use by type of dementia diagnosis

Participants with LBD had more PIM use than those with AD, indicated by more Beers' Criteria medications, higher ADS scores, and higher total number of medications. Compared to participants with AD, on average, over the follow-up, participants with LBD were taking 21% more Beers' Criteria medications (LSM estimate: 1.21, 95% CI: 1.02–1.42; Fig. 2A displays by year), had ADS scores 32% higher (LSM: 1.32, 95% CI: 1.10–1.58; Fig. 2B displays by year), and 12% more total medications (LSM: 1.12, 95% CI: 1.03–1.21; Fig. 2C displays by year).

Participants with FTD reported less PIM use than AD, indicated by fewer Beers' Criteria medications and lower count of total medications (Figs. 2A–2C). Participants with FTD were taking 24% fewer Beers' Criteria medications (LSM: 0.76, 95% CI: 0.57–0.95) and 21% fewer total medications (LSM: 0.79, 95% CI: 0.69–0.90) over the follow-up than those with AD. Participants with VD did not differ from participants with AD on any measure of PIM use over the follow-up.

3.2.2. Changes in PIM use in the 2 years following diagnosis

Number of Beers' Criteria medications did not change significantly over the follow-up for any type of dementia

Table 1
Baseline sociodemographic, health, and medication characteristics according to dementia diagnosis

Characteristics	Alzheimer's disease N = 2090 (85.4%)	Vascular dementia N = 136 (5.6%)	Lewy body dementia N = 144 (5.8%)	Frontotemporal dementia N = 78 (3.2%)	All dementias N = 2448
Age in years mean (SD)	80.8 (7.7)	84.7 (7.6) ¹	78.0 (7.2) ^{1,2}	73.7 (6.4) ¹⁻³	80.5 (7.8)
Female, N (%)	1118 (53.5)	75 (55.2)	37 (25.7) ^{1,2}	38 (48.7) ³	1268 (51.8)
Race, N (%)					
White	1776 (85.0)	109 (80.2)	133 (92.4) ²	72 (92.3)	2090 (85.5)
Black	228 (10.9)	22 (16.2)	7 (4.9)	2 (2.6)	259 (10.6)
Other	86 (4.1)	5 (3.7)	4 (2.8)	4 (5.1)	99 (3.9)
Education, N (%)					
High school or less	543 (26.0)	37 (27.2)	36 (25.0)	13 (16.7)	629 (25.7)
College	857 (41.0)	59 (43.4)	55 (38.2)	39 (50.0)	1010 (41.4)
Graduate	684 (32.7)	40 (29.4)	53 (36.8)	25 (32.1)	802 (32.6)
Living situation, N (%)					
Lives alone	525 (25.1)	34 (25.0) ¹	14 (9.7) ^{1,2}	10 (12.8) ^{1,2}	583 (23.8)
Lives with spouse or partner	1221 (58.4)	60 (44.1)	105 (72.9)	62 (79.5)	1448 (59.2)
Other living arrangements	344 (16.5)	42 (30.9)	25 (17.4)	6 (7.7)	417 (17.0)
Independence					
Able to live independently	732 (35.0)	42 (30.9) ¹	32 (22.2) ¹	27 (34.6)	833 (34.0)
Requires assistance	1304 (62.3)	79 (58.1)	105 (72.9)	48 (61.5)	1536 (62.7)
Completely dependent	45 (2.2)	15 (11.0)	7 (4.9)	1 (1.3)	68 (2.8)
Type of residence, N (%)					
Single family residence	1709 (81.8)	90 (66.2) ¹	118 (81.9)	73 (93.6) ²	1990 (81.3)
Retirement community	200 (9.6)	17 (12.5)	9 (6.3)	3 (3.9)	229 (9.4)
Assisted living	149 (7.1)	23 (16.9)	13 (9.0)	1 (1.3)	186 (7.6)
Other/unknown	32 (1.5)	6 (4.4)	4 (2.8)	1 (1.3)	43 (1.7)
Comorbidities, N (%) [*]					
Psychiatric disorders	167 (8.0)	10 (7.4)	14 (9.7)	8 (10.3)	199 (8.1)
Cardiovascular disease [†]	1479 (70.8)	119 (87.5) ¹	102 (70.8) ²	49 (62.8) ²	1749 (71.4)
Stroke	166 (7.9)	83 (61.0) ¹	9 (6.3) ²	2 (2.6) ²	260 (10.6)
Diabetes (type 1 or type 2)	297 (14.2)	29 (21.3)	11 (7.6) ²	9 (11.5)	346 (14.1)
BMI (kg m ⁻²)	25.3 (4.5)	25.8 (4.8)	25.7 (4.1)	25.8 (5.0)	25.3 (4.5)
Years smoked cigarettes, mean (SD)	11.1 (16.1)	14.8 (19.7) ¹	11.5 (15.0)	9.1 (13.9)	11.2 (16.2)
Global Clinical Dementia Rating, N (%)					
Questionable impairment	1167 (55.8)	63 (46.3) ¹	68 (47.2) ¹	44 (56.4)	1342 (54.8)
Mild impairment	832 (39.8)	54 (39.7)	63 (43.8)	29 (37.2)	978 (40.0)
Moderate impairment	74 (3.5)	12 (8.8)	8 (5.6)	4 (5.1)	98 (4.0)
Severe impairment	17 (0.8)	7 (5.2)	5 (3.5)	1 (1.3)	30 (1.2)
Total Geriatric Depression Scale					
0-4	1569 (82.5)	84 (77.1)	82 (62.6) ¹	42 (71.2) ¹	1777 (72.6)
5-9	292 (15.3)	21 (19.3)	38 (29.0)	10 (17.0)	361 (14.7)
10-15	32 (1.7)	4 (3.7)	9 (7.1)	6 (9.8)	51 (2.1)
Medication exposures					
Number of medications, mean (SD)	7.2 (4.1)	8.3 (4.3) ¹	8.0 (3.8)	5.9 (3.3) ¹⁻³	7.3 (4.1)
Anticholinergic Drug Scale score, N (%)					
0	1126 (53.9)	60 (44.1)	54 (37.5) ¹	45 (57.7) ³	1285 (52.5)
1	488 (23.4)	38 (27.9)	40 (27.8)	19 (24.4)	585 (23.9)
2	140 (6.7)	12 (8.8)	17 (11.8)	3 (3.4)	172 (7.0)
≥3	336 (16.1)	26 (19.1)	33 (22.9)	11 (14.1)	406 (16.6)
Number of Beers' Criteria medications, N (%)					
0	763 (36.5)	48 (35.3)	51 (35.4)	34 (43.6)	896 (36.6)
1	824 (39.4)	51 (37.5)	48 (33.3)	31 (39.7)	954 (39.0)
2	357 (17.1)	23 (16.9)	27 (18.8)	10 (12.8)	417 (17.0)
≥3	146 (7.0)	14 (10.3)	18 (12.5)	3 (3.9)	181 (7.4)

Abbreviations: BMI, body mass index; SD, standard deviation.

NOTE. ¹⁻³ indicates a pairwise difference ($P < .05$) with: ¹Alzheimer's disease, ²vascular dementia, and ³Lewy body dementia.

^{*}Based on self-report of participant or informant.

[†]Myocardial infarction, atrial fibrillation, angioplasty, coronary artery bypass graft surgery, pace maker, congestive heart failure, or other cardiovascular disease.

(Fig. 3A). Among participants with LBD, ADS scores increased by 39% (LSM: 1.39, 95% CI: 1.17–1.66) in the first year following dementia diagnosis and decreased in the second year, such that there was no difference in ADS scores be-

tween and baseline and 2-year follow-up (LSM: 1.05, 95% CI: 0.81–1.37) (Fig. 3B). ADS scores did not change significantly over the follow-up for other dementias (Fig. 3B). In the first year after diagnosis, total number of medications

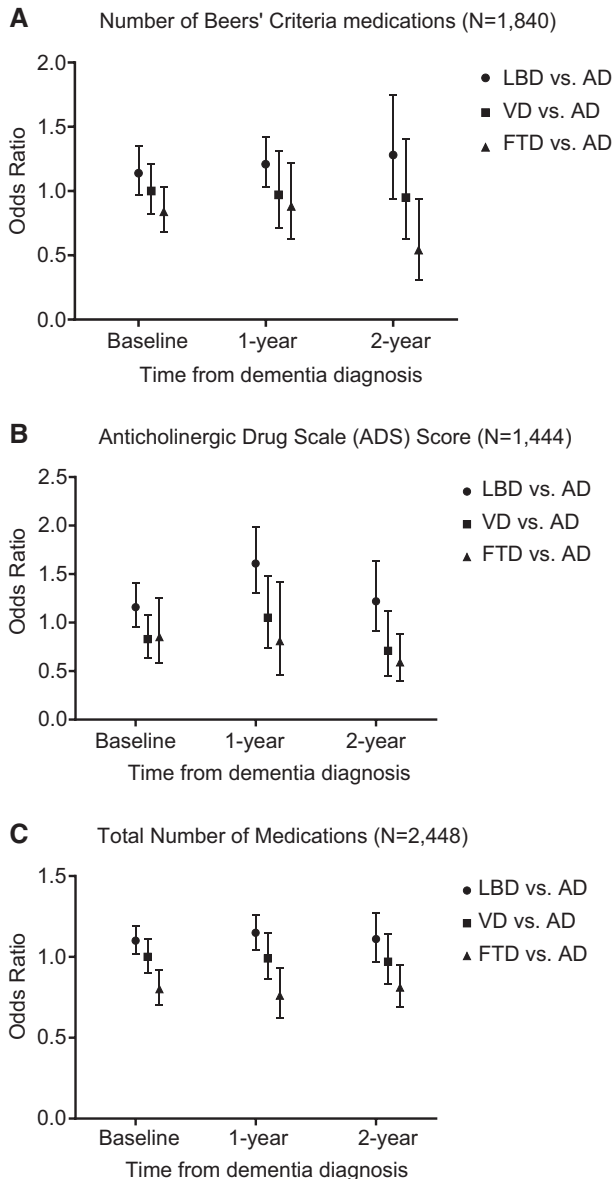


Fig. 2. Adjusted odds ratios for use of Beers' Criteria medications among ever-users (A), ADS score among ever-users (B), and total medications in non-Alzheimer's related dementias compared to Alzheimer's disease (C) over 2 years following dementia diagnosis. Abbreviations: LBD, Lewy body dementia; AD, Alzheimer's disease; VD, vascular dementia; FTD, frontotemporal dementia.

increased by 10% for AD (LSM: 1.10, 95% CI: 1.07–1.13) and 15% for LBD (LSM: 1.15, 95% CI: 1.04–1.26) (Fig. 3C); however, there was no change in the second year after diagnosis for either type of dementia.

3.3. Attrition and sensitivity analysis

We examined differential attrition by type of dementia (Table 2). At 1 year following dementia diagnosis, 38.2% of participants with VD, 24.5% with AD, 27.1% with LBD, and 20.5% with FTD were dead or lost to follow-up. At 2 years, 44.1% of AD, 38.9% of LBD, 29.4% of VD,

and 30.8% of FTD participants were still active in the study. A sensitivity analysis indicated that although point estimates differed between the study sample ($n = 2448$) and the sample with complete data ($n = 833$), overall significance and direction of the estimates between the two samples were similar (results available upon request).

4. Discussion and conclusions

This is the first study to longitudinally investigate PIM use according to dementia types following incident dementia diagnosis. Our results suggest that PIM use in the first 2 years following diagnosis differs by type of dementia. Older adults diagnosed with LBD reported higher PIM use compared with adults diagnosed with AD. Moreover, adults with FTD reported lower PIM use compared with adults with AD, whereas adults with AD and VD did not differ in PIM use.

Our findings are consistent with a previous cross-sectional study, which found that individuals with LBD were receiving more PIM medication including psychotropics compared to individuals with other types of dementia [49]. In our study, adults with LBD were less independent, had more cognitive impairment, and more symptoms of depression at baseline than participants with AD. This could indicate a greater overall medical burden and a need for specific, and PIMs.

Similarly, our finding of less overall medication use in FTD could be attributed to lower overall disease burden in this younger subset of participants. However, baseline prevalence of health conditions other than depression did not differ between participants and FTD and AD in our sample. A previous study has suggested that language deficits in FTD could interfere with the expression of some behavioural and psychological symptoms that lead to pharmacological treatment [49]. Although participants with FTD did not differ from those with AD on overall levels of cognitive impairment at baseline, we did not examine specific subsets of behavioural and psychological symptoms in this study.

Given the additional cardiovascular disease burden and associated depression that characterize VD, we expected more PIM use in this subgroup. Although we did observe less independence; more cardiovascular, cerebrovascular, and metabolic risk factors; and more cognitive impairment at baseline, there were no differences between VD and AD in PIM use over the follow-up when we adjusted for these risk factors. However, 27.9% of participants with VD died in the first year following their dementia diagnosis while only 8.4% of participants with AD were deceased by 1 year. Therefore, it is possible that VD represents an older and sicker subtype of dementia, and future studies of PIM use should examine death as a competing risk.

This study also examined changes in PIM use in the 2 years following diagnosis of different types of dementia. Overall, there was some evidence to suggest an increase in PIM use following diagnosis of LBD and AD. On average, the total

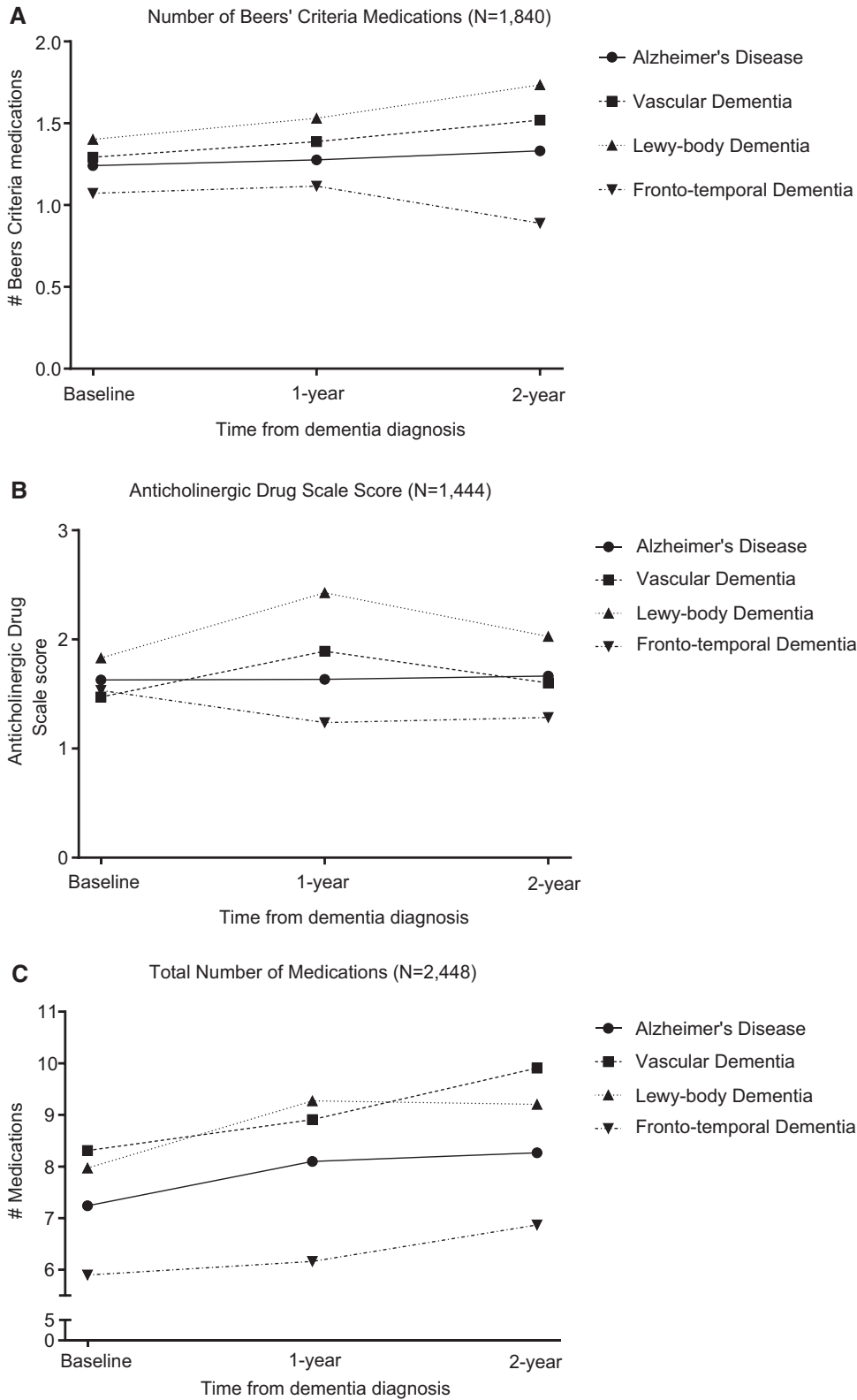


Fig. 3. Adjusted marginal means (least squares mean estimates) for Beers' Criteria medications among ever-users (A), Anticholinergic Drug Scale score among ever-users (B), and total medications by dementia type over 2 years following diagnosis (C).

Table 2
Study participation and causes of attrition over 3 years following dementia diagnosis

Dementia type follow-up status	Baseline	1 year	2 years
	N (%)	N (%)	N (%)
Alzheimer's			
Active*	2090 (100)	1578 (75.5)	921 (44.1)
Lost/Inactive†		336 (16.1)	166 (24.0)
Dead†		176 (8.4)	124 (14.4)
Censoring†			367 (17.5)
Vascular			
Active*	136 (100)	84 (61.8)	40 (29.4)
Lost/Inactive†		14 (10.3)	5 (14.0)
Dead†		38 (27.9)	17 (40.4)
Censoring†			22 (16.2)
Lewy body			
Active*	144 (100)	105 (72.9)	56 (38.9)
Lost/Inactive†		18 (12.5)	14 (22.2)
Dead†		21 (14.8)	13 (23.6)
Censoring†			22 (15.3)
Frontotemporal			
Active*	78 (100)	62 (79.5)	24 (30.8)
Lost/Inactive†		11 (14.1)	5 (20.5)
Dead†		5 (6.4)	9 (17.9)
Censoring†			24 (30.8)

*% reflects proportion of the visit 1 active sample for each type of dementia.

†% reflects cumulative proportion of the visit 1 active sample for each type of dementia.

number of medications increased following diagnosis of dementia for participants with AD and LBD. For both diagnoses, total number of medications increased in the first year after diagnosis and did not change in the second year. Participants diagnosed with LBD also had a significant increase in their ADS scores in the first year following diagnosis followed by a return to baseline levels in the second year.

From a clinical perspective, the fact that we did not find an increase in Beers' Criteria medications or a sustained increase ADS scores following any type of dementia diagnosis suggests that prescribers are aware of the potential harms of these medications. However, nearly two-thirds of participants were taking ≥ 1 Beers' Criteria medication at the time of their dementia diagnosis, and 75.2% reported taking ≥ 1 Beers' Criteria medications at some point over the follow-up. Similarly, nearly half of participants had an ADS score ≥ 1 at baseline, and 59% had an ADS score ≥ 1 for at least one assessment point. Given the additional risk of PIM use among persons with dementia [1,11] that we did not find a reduction in use of Beers' Criteria medications or ADS scores following dementia diagnosis is concerning.

This study had several limitations to consider when evaluating the implications of our findings. First, participants in the NACC cohort tend to be more educated, have higher income; therefore, results may not generalize to other populations. Second, given the advanced age and comorbidities of participants, the rate of attrition over the 2-year follow-up was high, and we cannot rule out a potential healthy survivor effect. Although we conducted a sensitivity

analysis to examine the potential impact of attrition on our outcomes, examining the relationships between type of dementia, PIM use, and mortality is an important area of future study. Third, assessments occur at 1-year intervals and do not capture changes between visits. Hence, dementia diagnosis does not indicate the actual date of dementia onset, and medications may be started and stopped between annual visits. Given that medication use asked about current medications, participants may have been misclassified as not exposed to any PIMs in the situation in which they started and stopped treatment between two consecutive study visits. Fourth, we were not able to assess specific indication for the PIMS examined in this study (i.e., the used of antipsychotic medications to treat hallucinations in participants with LBD). Finally, although this study is strengthened by the inclusion of participants with LBD and other non-Alzheimer's dementias, the number of participants with non-AD dementias was low (a limitation of most large-scale dementia cohort studies), particularly by the 2-year follow-up. Despite these limitations, this is the first study to examine PIM use longitudinally following a dementia diagnosis and to compare four different types of dementia. Our study is further strengthened by standardized data collection methods, extensive neurocognitive assessments and clinical evaluations that support dementia diagnoses for study participants, and the ability to assess both prescription and over-the-counter medications.

Studying the use of PIMs over time will improve our ability to treat and care for individuals with different types of dementia. The results of our study further confirm evidence from cross-sectional studies of the high prevalence of PIM use among individuals with dementia [11]. Our study does not provide evidence of deprescribing, even in a high-risk sample of participants following a dementia diagnosis. Our findings of differences in PIM use by type of dementia and a lack of deprescribing following dementia diagnosis suggests a need for a closer look at PIM use and interventions aimed at optimal drug therapy to balance the risks and benefits in older patients diagnosed with different types of dementia.

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RESEARCH IN CONTEXT

1. Systematic review: The authors reviewed the literature using traditional sources such as PubMed. While longitudinal trends in use of potentially inappropriate medication (PIM) following diagnosis of different types of dementia has not been investigated, PIM use in older adults with dementia has been studied cross-sectionally. These recent studies are appropriately cited.
2. Interpretation: Our findings suggest that PIM use differs by type of dementia and that there is little evidence of deprescribing of PIMs following a dementia diagnosis.
3. Future directions: Further research is needed to better understand long-term prescribing practices, risk factors, and clinical outcomes according to types of dementia.

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