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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.

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 enrolees 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.