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Abstract

Background: Inappropriate polypharmacy may negatively impact quality of life of residents in aged care facilities, but it remains unclear which medications may influence this reduced quality of life.

Objective: The objective was to examine whether the Drug Burden Index (DBI) and potentially inappropriate medications (PIMs), were associated with quality of life in older adults living in residential care with a high prevalence of cognitive impairment and dementia.

Methods: Cross-sectional analyses of 541individuals recruited from 17 residential aged care facilities in Australia in the Investigating Services Provided in the Residential Environment for Dementia (INSPIRED) study. Quality of life was measured using the EQ-5D-5L (a measure of generic quality of life) and the DEMQOL (a measure developed for use in dementia) completed by the participant or a proxy.

Results: In the 100 days prior to recruitment, 83.1% of the participants received at least one anticholinergic or sedative medication included in the DBI and 82.7% received at least one PIM according to the Beers Criteria. Multi-level linear models showed there was a significant association between higher DBI and lower quality of life according to the EQ-5D-5L (β (SE): -0.034 (0.012), p=0.006) after adjustment for potential confounding factors. Increasing numbers of PIMs were also associated with lower EQ-5D-5L scores (-0.030 (0.010), p=0.003) and DEMQOL-Self-Report-Utility scores (-0.020 (0.009), p=0.029). Exposure to both DBI-associated medications and PIMs was associated with lower DEMQOL-Self-Report-Utility scores (-0.034 (0.017), p=0.049).

Conclusion: Exposure to anticholinergic and sedative medications and PIMs occurred in over three-quarters of a population of older adults in residential care and was associated with a lower quality of life.

Key Points

- Potentially inappropriate medications, according to the Beers Criteria, and anticholinergic and sedative medications, described in the Drug Burden Index, were highly prevalent in residential aged care (82.7% and 73.0%).
- Higher exposure to anticholinergic and sedative medications and higher exposure to potentially inappropriate medications were associated with lower quality of life in residents of aged care.
- This study provides evidence to support that there is a need for greater adherence to recommendations for appropriate medication use in residential aged care.

1 Introduction

It is important to explore factors which influence quality of life in older adults living in long-term residential care in order to identify intervention strategies to improve their quality of life. A lower quality of life is associated with a decline in activities of daily living and also mortality in this population [1]. Polypharmacy may negatively impact the quality of life of individuals living in aged care facilities, but it remains unclear which medications may lead to this reduction in quality of life [2]. Medications should be appropriately prescribed for the individual where the benefits of the medication outweigh its potential harms.

Quality of life for older adults living in residential care has been described as the "degree to which an individual resident's overall well-being meets their personal expectations, the expectations of their carers or the expectations of the community" [3]. Many factors can impact the quality of life of older adults such as health status (including co-morbidities), social engagement, cognitive function and medication use [4]. However, these associations are less clear in people living in residential aged care facilities and those living with dementia [5]. Therefore, as more than half of people living in residential aged care are living with

dementia [6], it is difficult for policy-makers to determine where to focus efforts to improve quality of life for the residents.

Potentially inappropriate medications (PIMs) are often identified using validated measures such as the Beers Criteria for older adults [7]. Previously, the Beers Criteria have been shown to be associated with an increased risk of hospitalization and mortality in older adults living in residential care [8]. The criteria were updated in 2015 by the American Geriatrics Society and the statement includes lists of PIMs which are strongly recommended to be avoided in all older adults and additional medications which should be avoided in those with cognitive impairment and dementia. PIMs according to the Beers Criteria have been shown to be commonly used in older adults in residential care settings, but other measures of drug burden may be more useful in this population for predicting certain clinical outcomes [9].

The Drug Burden Index (DBI) is a measure to determine exposure to anticholinergic and sedative medications [10-12]. The DBI has been associated with falls and worse functional outcomes in older adults in residential facilities; however, associations with mortality in different populations and settings remain unclear [9, 13-15]. The DBI may be more strongly associated with functional impairment than the Beers Criteria in an Australian retirement village setting [9], but further exploration of the DBI compared to the Beers Criteria in different populations is needed.

Determining if the DBI or PIMs are associated with quality of life for individuals living in residential aged care is important in order to develop targeted intervention strategies to improve quality of life for these individuals. The main objective of this study was to examine whether the DBI and PIMs according to the Beers Criteria were associated with quality of life in older adults living in residential care facilities with a high prevalence of cognitive impairment and dementia.

2 Methods

2.1 Study participants

The participants were those included in the Investigating Services Provided in the Residential Environment for Dementia (INSPIRED) study, a cross-sectional study of residential aged care facilities in Australia. In Australia, when a person applies for aged care they complete an aged care assessment to determine what level of care they require. Residential care services provide accommodation and support for people who can no longer live at home. Some individuals may be referred to an aged care facility specific to their needs (such as dementia-specific facilities), however, admission to residential aged care facilities is often based on availability at the time of need.

The INSPIRED study was specifically designed to allow the inclusion of those living with cognitive impairment and dementia. The INSPIRED study received ethical approval from the Flinders Social and Behavioural Research Ethics Committee. The study aimed to include facilities from areas representing different socioeconomic backgrounds, geographic locations (e.g. rural vs metropolitan locations) and different states of Australia. In total, 17 facilities, from 5 different not-for profit organisations, in South Australia, New South Wales, Western Australia and Queensland participated in the study. Consent for the participants to be involved in the study was either by self-consent or, when the participant had severe cognitive impairment, informed consent and data collection was undertaken with a proxy, i.e. usually a close family member (76% of the participants). Participants were able to take part if they (a) had been a permanent resident in the facility for 12 months or more, (b) were not in immediate palliative care, (c) had no complex medical or family issues which would impede their participation and (d) had a family member available and willing to participate on behalf of the participant if the participant was severely cognitively impaired.

A total of 1323 residents of the participating facilities were assessed for eligibility; 901 were eligible to participate and 60% of these (n=541) consented to be part of the study. Data collection was completed between January 2015 and February 2016.

2.2 Determination of medication use of the participants

Medication use was primarily based on dispensing records obtained from the appropriate pharmacy. The data collected included the name, dose, dosing instructions and dispensed dates of all the medications dispensed 100 days prior to the start date of the study at each facility. Of the study participants, 3.5% (n=19) did not have available pharmacy records and reviews of their medication charts were undertaken instead. Exposure to a PIM or DBI medication was defined as exposure to an affected medication during the 100 days.

2.3 Drug Burden Index and potentially inappropriate medications by the Beers Criteria

DBI exposure for all resident records was calculated as the sum of exposure to each anticholinergic or sedative medication using the equation below [10]:

$$\text{DBI} = \sum \frac{D}{D+\partial}$$

where D represents the daily dose taken by the subject and ∂ the minimum recommended daily dose registered by the Therapeutic Goods Administration of Australia, as an estimate of the DR50 (dose required for 50% of the maximal therapeutic effect). The Australian product information was used to identify medications with clinically significant anticholinergic and/or sedative effects. Complementary medications and medications prescribed as “when required” were excluded from DBI calculations.

The average daily dose was calculated using the following equation:

$$\text{D} = \frac{(Q\ x\ d)x\ I}{100}$$

where *Q* represents the quantity dispensed, *d* represents the daily dose dispensed, and *I* the number of times the medication was dispensed over the 100 days. If dosing instructions were missing or incomplete, the initial starting dose according to the Australian Product Information was used.

PIMs were identified using the 2015 updated Beers Criteria for all older adults, independent of diagnosis. We also completed a subgroup analysis to examine the separate Beers Criteria list specific for people with cognitive impairment and dementia in addition to the Beers Criteria for all older adults. The Beers Criteria were developed in an American setting and therefore some medications were added to the PIMs lists by research pharmacists to allow for the Australian Register of Therapeutic Goods; these medications were in the same classes as medications that were included in the Beers Criteria lists (Electronic Supplementary Material Table S1).

2.4 Quality of life measures

In the INSPIRED study, quality of life was measured after participant enrolment into the study at the time of data collection. The quality of life of the participants was determined using three different measurement tools (a) a measure of generic health-related quality of life: the EuroQol five dimensions questionnaire (EQ-5D-5L, self-completed or completed by a proxy) [16], (b) the DEMQOL a dementia specific measure of health-related quality of life assessment (self-reported) and (c) the DEMQOL-Proxy (completed by a proxy on behalf of the participant). The EQ-5D-5L covers five dimensions influencing health-related quality of life: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. The EQ-5D-5L has a maximum score of 1 with higher scores indicating a better quality of life. DEMQOL-Utility scores are based on five different dimensions (positive emotion, negative emotion, memory, relationships and loneliness), while DEMQOL-Proxy-Utility scores are

based on four dimensions (positive emotion, negative emotion, memory and appearance). The range for the DEMQOL-Utility scores is from 0.243 to 0.986 and for the DEMQOL-Proxy-Utility scores is from 0.363 to 0.937; higher scores indicating a better quality of life. Utility scores were determined from the DEMQOL, DEMQOL-Proxy and EQ-5D-5L assessments by applying preference-weights based on the preferences of members of the UK general population [17, 18].

2.5 Covariates

The INSPIRED dataset included participant-level characteristic measures for cognitive function (the Psychogeriatric Assessment Scales-Cognitive Impairment Scale (PAS-Cog) score; higher scores indicate worse cognitive function), activities of daily living (the Barthel Index) and behaviour (the Neuropsychiatric Inventory, NPI). Social interaction was based on self-report of whether the participant had interaction with close social ties (relatives and friends) at least once per week. Medical histories from the facilities were used to determine if the participants had a clinical diagnosis of dementia. Comorbidities were extracted from the medical records of the participants and grouped into one of ten disease categories (excluding dementia) as used by Cohen-Mansfield and colleagues [19]. Facility-level characteristics were determined from information collected in a standardised questionnaire which has been validated in an older residential care population [20]. This included 33 questions and the facility-level covariates used in this study were location, number of direct care hours per resident and size of facility. The age, sex and marital status of the participant were also considered as covariates in this study.

2.6 Statistical analysis

Multi-level linear models were used to examine associations between (a) DBI (continuous variable), (b) exposure to a PIM according to the Beers Criteria (yes or no), (c) number of

different PIMs (continuous variable) or (d) having a DBI>0 and exposure to a PIM and quality of life measures. As the participants were clustered in 17 different residential aged care facilities, the data had a two-level hierarchal structure; therefore, two-level multi-level models with random intercepts and independent variance components were used to perform the data analyses. The models were adjusted for both the participant-level characteristics and facility-level characteristics as described in Section 2.5. Adjustments for education level were not undertaken due to a high level of missing data (26.2%). The level of statistical significance was set at $p<0.05$. All analyses were completed using Stata v.14.0 (Stata Corp LP, College Station, TX, USA).

3 Results

3.1 Characteristics of the participants

Of the total participants of the INSPIRED study, 82.8% (n=448) had mild to severe levels of cognitive impairment based on their PAS-Cog score and 64.3% (n=348) had received a clinical diagnosis of dementia. The mean age of the participants was 85.5 (±SD 8.5) years old and 74.5% (n=403) were female. The participants had a mean number of 3.7 (±1.4) co-morbid conditions. The median (IQR) total number of different medications a participant was exposed to was 10 (7-13); 38.2% of participants were exposed to 5-9 medications and 52.3% of participants were exposed to ≥10 medications. Further characteristics are shown in Table 1.

3.2 Drug Burden Index and Beers Criteria for the total study population

No medication data were available for four of the participants, therefore, the effective sample analysed was 537 participants (99.3%) (Figure 1). Of the 537 participants, 83.1% (n=446) had been exposed to at least one medication which contributed to their DBI, therefore the remaining 16.9% (n=91) participants were recorded as having a DBI of 0. The median (IQR)

DBI for all participants was 0.86 (0.36-1.52). According to the Beers Criteria for all older adults, 73.0% (n=392) of the participants had been exposed to a PIM (number of PIMs ranged from 0 to 6). Those exposed to a PIM were more likely to also be exposed to a DBI-associated medication ($p<0.001$). Of the 392 participants exposed to a PIM according to the Beers Criteria, 89.3% (n=350) were also exposed to a DBI-associated medication. Of the 145 participants not exposed to a PIM, 33.8% (n=49) were also not exposed to a DBI-associated medication.

The most common PIMs according to the Beers Criteria for all older adults were proton-pump inhibitors for more than 8 weeks (41.5%), benzodiazepines (30.5%) and antipsychotics (24.8%). The prevalence of the remaining PIMs was relatively small (all <10%). The most prevalent medication classes contributing to the DBI were antidepressants (mirtazapine, 17.1%, sertraline, 9.5%, escitalopram, 8.6% and citalopram, 7.1%) and opioid analgesics (buprenorphine, 14.3%, fentanyl, 9.7% and oxycodone, 8.2%). The most frequently identified benzodiazepine was temazepam (9.9%) and the most common antipsychotic was risperidone (12.7%).

3.3 Drug Burden Index, potentially inappropriate medications and quality of life

Table 2 shows the associations of the DBI and PIMs according to the Beers Criteria for all older adults with the different quality of life outcomes included in the INSPIRED study. Adjusted linear mixed models showed that higher DBI scores were associated with lower EQ-5D-5L utility scores, but not DEMQOL-Proxy-Utility or DEMQOL-Self-Report-Utility scores. For every unit increase in DBI, the EQ-5D-5L utility scores decreased by 0.034 ($p=0.006$).

Being exposed to at least one PIM according to the Beers Criteria for all older adults was not significantly associated with any of the quality of life measures when compared to not being

exposed to a PIM. However, when analysing the number of PIMs a person was exposed to, for every additional PIM a participant was exposed to the DEMQOL-Self-Report-Utility scores decreased by 0.020 (p=0.029) and the EQ-5D-5L decreased by 0.030 (p=0.003). Having a DBI>0 and being exposed to at least one PIM was associated with a decrease in DEMQOL-Self-Report-Utility scores by 0.034 (p=0.049).

3.4 Potentially inappropriate medications for dementia and cognitive impairment and quality of life: subgroup analysis

Of the participants, 86.5% (n=465) had a diagnosis of dementia or cognitive impairment according to their PAS-Cog score (PAS-Cog ≥4) and were included in this subgroup analysis. Of those with cognitive impairment or a diagnosis of dementia, 72.5% (n=337) were identified as being exposed to a PIM that is not recommended for older adults and/or contraindicated in dementia or cognitive impairment. Similar to the results for PIMs for all participants, exposure to a PIM (yes vs. no) was not associated with any quality of life measures after adjusting for confounding factors (Table 3). An increasing number of PIMs was associated with two of the measures of quality of life in this subgroup. For every additional PIM a participant was exposed to the DEMQOL-Self-Report-Utility scores decreased by 0.024 (p=0.003) and the EQ-5D-5L utility scores decreased by 0.027 (p=0.004).

4 Discussion

In this study, higher exposure to anticholinergic and sedative medications as identified in the DBI and higher exposure to PIMs according to the Beers Criteria were both associated with lower quality of life in a population of older adults with a high prevalence of cognitive impairment and dementia. Increasing numbers of PIMs according to the Beers Criteria were associated with both lower EQ-5D-5L and DEMQOL utility scores after adjusting for a wide-range of potential confounding factors, whereas the DBI was associated with lower EQ-5D-

5L utility scores only. Both DBI-associated medications and PIMs according to the Beers criteria were highly prevalent in this population (>80%).

There is external validity in the association between DBI and the EQ-5D-5L, but not the DEMQOL. The DBI was developed to measure the functional burden of medications [10, 11] and the EQ-5D-5L captures physical function (mobility, self-care and usual activities) while the DEMQOL does not. A previous cross-sectional study also found an association between DBI and lower health-related quality of life in older adults with dementia living in residential settings, but did not find an association with PIMs according to the Beers Criteria [21]. This result is consistent with the current findings as in this analysis we also found no significant association of exposure to PIMs according to the Beers Criteria (when analysed as a dichotomous measure) with quality of life. However, we extended this analysis by also examining the degree of exposure to PIMs according to the Beers Criteria, considering it as a continuous measure, and this was associated with lower quality of life in this population. Due to the high prevalence of PIMs in this population, it is considered appropriate to consider the extent of PIMs use and to conduct the analysis as a continuous measure in this setting.

The associations between DBI and number of PIMs according to the Beers Criteria and lower quality of life, although statistically significant, all had a relatively small effect on the different utility scores. The largest difference seen was a 1-unit increase in the DBI (e.g. exposure to two drugs with anticholinergic or sedative effects at their minimum efficacious doses) resulting in a decrease of 0.034 according to the EQ-5D-5L. Similarly, being exposed to a DBI medication and a PIM was associated with a decrease of 0.034 DEMQOL-Self-Report-Utility score compared to not being exposed to a DBI medication or PIM. The precise clinically meaningful difference in the quality of life scores used in this study population remains unclear, but previous literature has suggested a clinically meaningful difference in such utility measures may be in the range of 0.03 to 0.10 depending on the population being

studied [22-24]. This would suggest that many of the associations seen in this study between the number of PIMs a participant was exposed to and quality of life utility measures may not be clinically meaningful (between 0.020 and 0.030 difference in quality of life with exposure to an additional PIM); however, the cumulative impact of multiple PIMs may be clinically significant. Studies powered to detect a smaller change in quality of life measures may be able to detect differences, or it may be useful to explore associations between other criteria for inappropriate medications and quality of life in older populations living in residential aged care if further information is collected regarding their indication and medical conditions, such as the Basger's criteria [25].

Polypharmacy (5-9 medications) and hyperpolypharmacy (≥10 medications) were highly prevalent in this population. Deprescribing has been suggested as a potential method to reduce inappropriate polypharmacy in residential aged care settings. Deprescribing involves a completion of a review of an individual's current medications and subsequent withdrawal of inappropriate medications with supervision from a healthcare professional after careful consideration of the likelihood of adverse events with a goal of improving clinical outcomes [26, 27]. Interventions for deprescribing have been trialled in residential aged care facilities, however the effects of these interventions as shown in randomised controlled trials (RCTs) have been mixed and further studies are required [28-33, 26]. The high prevalence of DBI-associated medications and PIMs according to the Beers Criteria in the current study suggests that current recommendations for appropriate medication use in older adults may need to be better implemented in residential aged care settings. Further studies could examine if deprescribing of medications included in the DBI or Beers Criteria may improve quality of life outcomes for these individuals as well as improve other outcomes associated with reduced exposure to these medications, such as reduced hospitalization and mortality [34, 35].

The INSPIRED study is a large study in this setting and this study was designed to allow the inclusion of individuals with cognitive impairment and dementia. Further, a thorough examination of quality of life in this population was completed which is uncommon in this population. Although the cross-sectional nature of the data in the study could leave the findings open to the effects of confounding, we were able to reduce this risk by adjusting for a wide-range of potential confounding factors due to the comprehensive data collected in this study. Although it is more usual to examine medication use from medication charts, the majority of the dispensing data used were collected from electronic records held by the individual pharmacies associated with the residential aged care facilities. This approach has some advantages as these records are inclusive of all of the medications dispensed to the individuals whilst at the facility. A particular strength of the study is that we were able to compare two established measures for identifying potentially inappropriate medications in this study. Furthermore, within this population, as only a minority of participants did not receive PIMs and a large number of different PIMs were prescribed, examining the number of PIMs prescribed was also feasible. An inherent limitation of the cross-sectional design of the study is the inability to assess causality or the direction of any observed association. It is possible that the lower quality of life with increasing exposure to PIMs or DBI-associated medications seen in this study may be leading to exposure to the medications rather than the medications causing the lower quality of life. As a high proportion of people in the study were not able to self-complete assessments, proxy measures were used and, although this meant that these people could be included in the study, there may be differences between what the proxy reports and what the individual would report if they were able. Even so, the EQ-5D-5L by proxy has been previously validated in residents living in aged care facilities with dementia [36].

5 Conclusions

In this population of older adults living in residential aged care facilities with a high prevalence of cognitive impairment and dementia, exposures to anticholinergic and sedative medications, as measured with the DBI, and exposure to PIMs, according to the Beers Criteria, were highly prevalent. Exposure to increasing DBI and increasing numbers of PIMs, according to the Beers Criteria, were both associated with a lower quality of life.

Compliance with Ethical Standards

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Conflicts of Interest

Suzanne Dyer was employed in the development of Clinical Practice Guidelines for Dementia in Australia which includes recommendations relating to the use of pharmaceuticals in dementia. Stephanie Harrison, Lisa Kouladjian O'Donnell, Clare Bradley, Rachel Milte, Emmanuel Gnanamanickam, Enwu Liu, Sarah Hilmer and Maria Crotty declare that they have no potential conflicts of interest relevant to the content of this article.

Ethical Approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional committee (Flinders Social and Behavioural Research Ethics Committee: Approval numbers 6732 and 6753). Informed consent was obtained from all individual participants included in the study (self-consent or proxy) as approved by the Ethics Committee.

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Tables

Table 1. Characteristics of the participants of the INSPIRED Study (n=541).

Characteristic	Value
Age (y), mean (SD)	85.5 (8.5)
Female, n (%)	403 (74.5)
Married, n (%)	137 (25.3)
Barthel Index, median (IQR)	35 (9-71)
DEMQOL proxy, median (IQR)	0.67 (0.60-0.82)
DEMQOL resident, median (IQR)	0.88 (0.79-0.94)
EQ-5D-5L resident or proxy, median (IQR)	0.54 (0.28-0.78)
NPI, median (IQR)	7 (3-12)
PAS-Cog, median (IQR)	15 (6-21)
Dementia diagnosis, n (%)	348 (64.3)
Number of co-morbid conditions, mean (SD)	3.7 (1.4)
Total number of medications, median (IQR)	10 (7-13)
DBI>0, n (%)	446 (82.4)
DBI, median (IQR)	0.86 (0.36-1.52)
Exposed to a PIM, n (%)	392 (73.0)
Total number of PIMs, median (IQR)	1 (0-2)
Resided in a large residential facility (>90 beds), n (%)	288 (53.2)

Abbreviations: DBI, Drug Burden Index; DEMQOL, Dementia quality of life questionnaire; EQ-5D-5L, EuroQol 5 Dimensions 5 Levels; IQR, Inter-quartile range; NPI, Neuropsychiatric Inventory; PAS-Cog, Psychogeriatric Assessment Scales-Cognitive Impairment Scale; PIM, potentially inappropriate medication.

Table 2. Associations between the Drug Burden Index and potentially inappropriate medications as listed by the Beers Criteria for all older adults and quality of life of the participants.

Quality of life measures	DBI, β (SE), P value	PIM, β (SE), P value	Increasing number of PIMs, β (SE), P value	DBI and PIMs, β (SE), P value
Unadjusted models				
DEMQOL-Proxy-Utility scores	-0.001 (0.006), 0.841	-0.010 (0.013), 0.436	-0.007 (0.005), 0.207	-0.016 (0.012), 0.189
DEMQOL-Self-Report-Utility scores[a]	-0.015 (0.009), 0.093	-0.016 (0.023), 0.500	-0.017 (0.007), 0.046	-0.038 (0.017), 0.028
EQ-5D-5L scores (self-report or proxy)	-0.048 (0.014), 0.001	-0.021 (0.030), 0.491	-0.031 (0.011), 0.009	-0.057 (0.027), 0.03
Adjusted models[b]				
DEMQOL-Proxy-Utility scores	-0.006 (0.007), 0.397	-0.016 (0.014), 0.246	-0.009 (0.005), 0.116	-0.022 (0.012), 0.07
DEMQOL-Self-Report-Utility scores[a]	-0.012 (0.009), 0.181	-0.015 (0.023), 0.510	-0.020 (0.009), 0.029	-0.034 (0.017), 0.049
EQ-5D-5L scores (self-report or proxy)	-0.034 (0.012), 0.006	-0.029 (0.026), 0.254	-0.030 (0.010), 0.003	-0.040 (0.023), 0.08

Abbreviations: DBI, Drug Burden Index; DEMQOL, Dementia quality of life questionnaire; EQ-5D-5L, EuroQol five dimensions questionnaire; PIM, potentially inappropriate medication. [a]Only includes those who could self-consent (n=228). [b]The models are adjusted for resident-level characteristics (age, sex, marital status, PAS-Cog scores, Neuropsychiatric Inventory, dementia diagnosis, number of co-morbid conditions, social ties and Barthel Index) and facility-level characteristics (size of residential facility, number of direct care hours and location).

Table 3. Associations between potentially inappropriate medications as listed by the Beers Criteria for people with cognitive and dementia and quality of life of participants with cognitive impairment and dementia.

Quality of life measures	**PIM for cognitive impairment and dementia, β (SE), P value**	**Increasing number of PIMs for cognitive impairment and dementia, β (SE), P value**
Unadjusted models		
DEMQOL-Proxy-Utility scores	-0.017 (0.014), 0.204	-0.006 (0.005), 0.200
DEMQOL-Self-Report-Utility scores[a]	-0.031 (0.024), 0.201	-0.019 (0.008), 0.022
EQ-5D-5L scores (self-report or proxy)	-0.017 (0.031), 0.573	-0.026 (0.011), 0.022
Adjusted models[b]		
DEMQOL-Proxy-Utility scores	-0.021 (0.014), 0.130	-0.007 (0.005), 0.142
DEMQOL-Self-Report-Utility scores[a]	-0.034 (0.023), 0.145	-0.024 (0.008), 0.003
EQ-5D-5L scores (self-report or proxy)	-0.032 (0.026), 0.219	-0.027 (0.009), 0.004

PIMs included the PIMs for all older adults and the additional PIMs for adults with cognitive impairment and dementia. Abbreviations: DEMQOL, Dementia quality of life questionnaire; EQ-5D-5L, EuroQol five dimensions questionnaire; PIM, potentially inappropriate medication. [a]Only includes those who could self-consent (n=160). [b]The models are adjusted for resident-level characteristics (age, sex, marital status, PAS-Cog scores, Neuropsychiatric Inventory, dementia diagnosis, number of co-morbid conditions, social ties and Barthel Index) and facility-level characteristics (size of residential facility, number of direct care hours and location).

Electronic Supplementary Material Table S1. Complete list of medications considered potentially inappropriate, according to the Beers Criteria, and adapted for an Australian setting.

PIMs for all older adults	**Additional PIMs for adults with cognitive impairment or dementia**
First generation antihistamines	*Antihistamines*
Brompheniramine	Carbinoxamine
Chlorpheniramine	Cetirizine*
Cyproheptadine*	Clemastine
Dexchlorpheniramine	Cyclizine
Diphenhydramine (oral)	Desloratadine*
Doxylamine	Dexbrompheniramine
Promethazine*	Fexofenadine*
Triprolidine	Hydroxyzine
	Loratadine*
Antiparkinsonian agents	Pheniramine
Benzatropine*	Trimeprazine
Biperiden	
Trihexyphenidyl	*Antimuscarinics (urinary incontinence)*
	Darifenacin
Antispasmodics	Fesoterodine
Atropine (excludes ophthalmic)	Flavoxate
Belladonna alkaloids	Oxybutynin*
Hyoscyamine	Propantheline
Propantheline*	Solifenacin*
Scopolamine*	Tolterodine
	Trospium
Antithrombotics	
Dipyridamole, oral short-acting*	*Antiemetic*
Ticlopidine	Domperidone*
	Droperidol
Anti-infective	Prochlorperazine
Nitrofurantoin*	Promethazine*
Peripheral alpha-1 blockers	*H2-receptor antagonists*
Prazosin*	Cimetidine
Terazosin	Famotidine
	Nizatidine*
Central alpha blockers	Ranitidine*
Clonidine	
Disopyramide	
Methyldopa*	
Moxonidine*	
Other cardiovascular medications	
Amiodarone*	
Digoxin*	
Nifedipine, immediate release*	
Antidepressants, alone or in combination	
Amitriptyline*	
Clomipramine	
Doxepin (>6mg/day)*	
Imipramine	
Nortriptyline*	
Paroxetine*	

Antipsychotics (first and second generation) Amisulpride Aripiprazole* Asenapine Chlorpromazine* Clozapine Droperidol Flupentixol* Fluphenazine Haloperidol* Lurasidone Olanzapine* Paliperidone Periciazine* Quetiapine* Risperidone* Trifluoperazine Ziprasidone Zuclopenthixol *Barbiturates* Phenobarbital Primidone *Benzodiazepines (short and immediate acting)* Alprazolam* Bromazepam* Clobazam Flunitrazepam* Lorazepam* Midazolam* Nitrazepam* Oxazepam* Temazepam* Triazolam *Benzodiazepines (immediate acting)* Clonazepam* Diazepam* *Non benzodiazepine receptor agonist hypnotics* Zolpidem *Endocrine* Testosterone* Estrogens with or without progestins (not vaginal creams) Progestogens and estrogens, fixed combinations (not vaginal creams) Glibenclamide Gliclazide* Glimepiride* Glipizide* Growth hormone Insulin, sliding scale* Megestrol *Gastrointestinal* Metoclopramide* Mineral oil, given orally	

Proton-pump inhibitors >8 weeks Esomeprazole* Lansoprazole* Omeprazole* Pantoprazole* Rabeprazole*	
Pain medications Aspirin >325mg/day Celecoxib* Etoricoxib Ibuprofen Indomethacin Ketoprofen Ketorolac, includes parenteral Mefenamic acid Meloxicam* Naproxen Parecoxib Pentazocine Pethidine Piroxicam Sulindac	
Skeletal muscle relaxants Orphenadrine	
Genitourinary Desmopressin	

Medications were added to the list including medications that are in the same classes as medications that were listed in the Beers Criteria and are available in Australia. Medications that are no longer available in Australia are not listed here.

*Dispensed to participants of the INSPIRED study.