Use of Potentially Harmful Medications and Health-Related Quality of Life among People with Dementia Living in Residential Aged Care Facilities

Pascalle R. Bosboom\textsuperscript{a,b} Helman Alfonso\textsuperscript{a,b} Osvaldo P. Almeida\textsuperscript{a,b,d} Christopher Beer\textsuperscript{a–c}

\textsuperscript{a}Western Australia Centre for Health and Ageing, Centre for Medical Research, \textsuperscript{b}School of Psychiatry and Clinical Neurosciences, and \textsuperscript{d}School of Medicine and Pharmacology, University of Western Australia, and \textsuperscript{c}Department of Psychiatry, Royal Perth Hospital, Perth, W.A., Australia

Key Words

Quality of Life – Alzheimer's disease questionnaire \cdot Potentially harmful medication \cdot Potentially inappropriate medication \cdot Modified Beers criteria \cdot Drug Burden Index \cdot Polypharmacy

Abstract

\textbf{Background:} Use of potentially harmful medications (PHMs) is common in people with dementia living in Residential Aged Care Facilities (RACFs) and increases the risk of adverse health outcomes. Debate persists as to how PHM use and its association with quality of life should be measured. We designed this study to determine the association of exposure to PHM, operationalized by three different measures, with self-reported Health-Related Quality of Life among people with dementia residing in RACFs. \textbf{Methods:} Cross-sectional study of 351 people aged \textgreater{}65 years diagnosed with dementia residing in RACFs and with MMSE \textless{}24. The primary outcome measure was the self-rated Quality of Life – Alzheimer’s disease questionnaire (QoL-AD). We collected data on patients’ medications, age, gender, MMSE total score, Neuropsychiatric Inventory total score, and comorbidities. Using regression analyses, we calculated crude and adjusted mean differences between groups exposed and not exposed to PHM according to potentially inappropriate medications (PIMs; identified by Modified Beers criteria), Drug Burden Index (DBI) \textgreater{}0 and polypharmacy (i.e. \textgeq{}5 medications). \textbf{Results:} Of 226 participants able to rate their QoL-AD, 56.41\% were exposed to at least one PIM, 82.05\% were exposed to at least one medication contributing to DBI \textgreater{}0, and 91.74\% to polypharmacy. Exposure to PIMs was not associated with self-reported
QoL-AD ratings, while exposure to DBI >0 and polypharmacy were (also after adjustment); exposure to DBI >0 tripled the odds of lower QoL-AD ratings. **Conclusion:** Exposure to PHM, as identified by DBI >0 and by polypharmacy (i.e., ≥5 medications), but not by PIMs (Modified Beers criteria), is inversely associated with self-reported health-related quality of life for people with dementia living in RACFs.

**Introduction**

The use of potentially harmful medications (PHMs) is common in later life and is associated with an increased risk of unfavourable health outcomes, including adverse drug events, morbidity, mortality and increased healthcare use [1–6]. Use of medication in older age is complicated by several factors, including changes in pharmacokinetics and the presence of multiple comorbidities [7–9]. Consequently, use of PHM is a source of concern that is likely to become more prevalent in the future as the world’s population ages [10, 11].

Observational studies have found use of PHM among Australians, with a worryingly high prevalence of the use of antipsychotics, antidepressants, and sedative-hypnotic drugs [12]. In a recent study we also found evidence that people with dementia (PWD) living in Residential Aged Care Facilities (RACFs) in Western Australia continue to be frequently exposed to polypharmacy, prescription of contraindicated medications, antipsychotics, medications with high anticholinergic burden, and combinations of potentially inappropriate medications (PIMs) [13]. These patterns of prescribing are not always in agreement with existing evidence-based guidelines [12, 14, 15]. Thus, there is a pressing need to know more about the epidemiology and sociology of medication use by older adults in Australia that in many cases may be unnecessary, costly and potentially harmful.

Despite its importance, there is still debate as how to identify the use of PHM and several methods or clinical tools have been proposed. A common approach is the use of the Beers criteria [16]. The Beers criteria comprise a list of PIMs that should be avoided altogether, as well as doses, frequencies and duration of other medications that should be avoided in older adults. Use of PIMs has been associated with higher medical costs, increased rates of adverse drug events and poorer health outcomes [16, 17]. A more recently developed tool is the Drug Burden Index (DBI), a measure of total exposure to anticholinergic and sedative medications that incorporates the principle of dose-response and maximal effect [18]. DBI has been independently associated with poorer performances in physical and cognitive function in a population of well-functioning community-dwelling older people in the USA [19]. Similar associations have been reported by Cao et al. [20]. Recently, Gnjidic et al. [21] compared the DBI with the Beers criteria in older adults in low-level residential aged care. They found that the Beers criteria did not predict functional outcome, but the DBI did. Another measure to identify the use of PHM, which could assist healthcare practitioners, is polypharmacy (e.g., quantified as ≥5 medications at one time). Polypharmacy per se also appears to be a risk factor for PIM use and adverse outcomes [22, 23]. However, this apparent relationship may be confounded by the burden of multiple chronic diseases in the older population [24]. Consequently, it is still unclear which of the proposed measures to identify use of PHM best predicts health outcomes of older people.

The use of PHM has been associated with lower quality of life [25], but this area has been thus far neglected. Health-related quality of life (HRQoL) measures have been identified as important multidimensional outcome measures for the treatment of chronic conditions and are increasingly valued to assess the effect of any intervention on recipients’ interpretation of outcomes [26–28]. Surprisingly, the potential association of the use of PHM – by different measures – with HRQoL in older adults has only been studied to a limited extent [2, 29].
Franic and Jiang [2] found that PIM use was not a significant predictor of HRQoL in a cohort of community-dwelling older adults, while polypharmacy was a significant predictor of HRQoL. The latter association was also reported by Henderson et al. [29]. The identification of robust PHM indicators may be useful for clinicians in their decisions on choosing interventions supporting the improvement of HRQoL of PWD living in RACFs.

This study aimed to determine the association between self-reported HRQoL ratings (as measured with a widely used HRQoL measure, the Quality of Life – Alzheimer’s disease questionnaire, QoL-AD) of PWD living in RACFs and use of PHM, as identified by three different measures, i.e. the PIMs by Modified Beers criteria, DBI and polypharmacy. We hypothesized that self-reported HRQoL ratings would be inversely associated with the PIMs by Beers criteria, the presence of a DBI (i.e. ≥0) and polypharmacy (i.e. number of medications ≥5).

**Methods**

**Study Design and Setting**

The observational data for this cross-sectional study were obtained from the Dementia in residential care: education intervention trial (DIRECT) conducted by the Western Australia Centre for Health and Ageing. The DIRECT study is a prospective randomised controlled trial of educational interventions aiming to improve QoL of PWD living in RACFs, conducted in the metropolitan area of Perth, Western Australia. All RACFs in the Perth Metropolitan area were sent information (n = 184) regarding the DIRECT study and of those, 36 RACFs agreed to participate. Participating RACFs compiled a list of residents to be screened for study participation. General practitioners (GPs) working at the facility and residents meeting the inclusion criteria were invited to take part. The protocol of this trial has been described in detail elsewhere [30].

**Participants**

All participants of the DIRECT study (n = 351) were permanent residents of a low-level or high-level RACF, aged ≥65 years, with a clinical diagnosis of dementia and a Mini Mental State Examination (MMSE) total score of ≤24. The exclusion criteria included: (1) subject is identified by facility as medically unstable or as suffering from delirium, or in the terminal stages of a comorbid illness; and (2) subject is unable to participate in assessment instruments in English [30].

The Human Research Ethics Committee at the University of Western Australia approved this study (RA 4/1/1685). All GPs and RACFs provided written agreement to participate. Research staff applied structured written and verbal consent procedures when the residents of the RACFs with cognitive impairment were approached. The assent of the ‘next of kin’ was required for participation of people with cognitive impairment deemed unable to provide informed consent. This trial was registered (ACTRN12607000417482) on 17/08/2007.

**Outcome of Interest**

The QoL-AD was the primary outcome measure of this study [31, 32]. The QoL-AD is a short, easy to administer, widely used HRQoL instrument that was designed specifically to assess PWD, with well-established psychometric properties [32, 33]. The scale is composed of 13 items that measure different areas of functioning, selected to reflect relevant areas of the QoL of older adults. Each item offers 4 possible answers that range from 1 (‘poor’) to 4 (‘excellent’), producing a total score where higher scores indicate better QoL. Patient and carer versions are available. The QoL-AD has been modified to produce a 15-item scale.
(maximum score 60) to assess the QoL of PWD living in RACFs according to a standard set of instructions [34, 35].

We have previously shown that QoL-AD ratings of patients and carers show acceptable agreement but are driven by different factors [36], and provide valuable information when used separately, not as a composite score. For this reason we used only the ratings provided by patients in this study (n = 226). Similarly to the study of Bosboom et al. [36], item 7 (‘marriage’) of the QoL-AD did not apply to this population. For that reason this item was not included in the total score. For further comparison possibilities, we calculated the percentage of the maximum QoL-AD score (%MaxSc) by dividing the total raw score by the number of items and multiplying this figure by 100.

**Exposure Variables**

Research staff audited participants’ clinical records to compile a list of all medicines the participants were prescribed at the time of data collection, either as a regular or pro re nata (PRN or ‘as required’) medication. Data on all medications was collected, including conventional medications as well as herbal medications, vitamins and minerals. The drug database was cleaned by removing duplicate drugs, correcting spelling errors, and by converting all drugs to generic names. Medications (including all ‘as required’ medications) were coded according to the World Health Organization Anatomical, Therapeutic, and Chemical Classification System [37]. To identify the use of PHM, the following measures were used:

Firstly, we identified PIMs by the Modified Beers criteria [16]. These definitions and the corresponding data sources have been described elsewhere [1]. Participants taking at least one PIM were classified as exposed to PIM according to the Modified Beers criteria.

Secondly, we calculated the DBI. The DBI is an evidence-based tool that utilizes pharmacologic principles to calculate an individual’s total exposure to anticholinergic and sedative medications [18]. The DBI for each participant was calculated as the sum of exposure to each anticholinergic or sedative drug using the equation described by Hilmer et al. [18] and applied by Gnjidic et al. [38, 39]. Participants taking at least one anticholinergic or one sedative medication were classified as exposed to DBI.

Thirdly, we counted the number of medicines for every participant to determine the number of medicines and subsequently the prevalence of participants exposed to polypharmacy, i.e. defined as ≥5 medicines [40].

**Other Study Measures**

We collected demographic and clinical information from participants, including age (in years), gender and prevalent comorbidities. Comorbidity was classified according to the following groups: cardiovascular diseases (including angina, history of heart attack, hypertension), cerebrovascular diseases (including history of stroke), respiratory diseases (including asthma, chronic bronchitis, lung emphysema), heart failure, arthritis or osteoarthritis, other musculoskeletal disorders (including osteoporosis), malignancies, mental health disorders other than dementia (including depression, anxiety), metabolic disorders (including diabetes I or II, thyroid disorders), neurological disorders (including epilepsy) and others (including allergies).

In addition, we assessed participants’ cognitive abilities with the MMSE [41] and behavioural and psychological symptoms associated with dementia using the Neuropsychiatric Inventory (NPI) [42], which was rated by staff informants. The NPI total score was calculated by the sum of the frequency rating times the severity rating for all items. Staff informants were required to have known the resident for at least 2 weeks, and to have observed that resident at least 10 times, for a minimum of 1 h in total during the previous 2 weeks.
**Procedures**

Research assistants were trained in the standard administration of the assessment tools (including the QoL-AD, MMSE and NPI) and adequate inter-rater reliability was established [43]. In face-to-face interviews, participants (PWD) were handed their own copy of the questionnaire that they could follow, if able to. Participants were able to indicate responses verbally or by circling the response. If a participant was unable to offer responses to more than two items, they were considered unable to complete the measure and their results were excluded from the analyses.

**Statistical Methods**

This project was originally designed as a hypothesis-driven study. We hypothesized that HRQoL ratings would be inversely associated with the Beers criteria for PIMs, the presence of a DBI (i.e. > 0) and polypharmacy (i.e. ≥ 5 medications). Continuous variables were described by their mean and standard deviations, and categorical variables by their count and proportions.

Initially, we treated the primary outcome (QoL-AD %MaxSc) as a continuous variable and, using linear regression modelling, we calculated the crude mean differences between the groups that were exposed to PHM according to the different definitions (i.e. Modified Beers criteria, DBI and polypharmacy). We calculated the adjusted mean differences, firstly adjusted for age, gender, MMSE total score and NPI total score, and later added the number of prevalent morbidities. Trying to identify nonlinear relationships, we subsequently treated the outcome (HRQoL %MaxSc) as a categorical variable by dividing it in tertiles to investigate possible threshold effects, and performed logistic regression to investigate the association between the outcome and the Modified Beers criteria, DBI and polypharmacy. Two models were used: the first contained no adjustments (crude model), the second model was adjusted for age, gender, MMSE total score, NPI total score and number of comorbidities. Results are presented with their associated 95% confidence intervals. We declared as significant alpha values <0.05 and all statistical tests were two-tailed. Data were managed and analysed using the statistical package STATA (version 10, StataCorp, 2009).

**Results**

**Demographic and Clinical Characteristics**

Table 1 summarizes the demographic and clinical characteristics of the 226 participants that were included in this study. The mean age of the selected participants was 85.9 ± 7.7 years (range 58–100), 74.8% were women, and the mean MMSE total score was 15.9 ± 5.9 (interquartile range, IQR, 21–12). The mean NPI total score was 19.8 ± 23.7 and the mean burden-of-care subscore of the NPI was 6.9 ± 9.3. The average number of comorbidities was 3.2 ± 1.6 (range 0–8).

**Prevalence of PHM Use**

The prevalence of PHM according to the Modified Beers criteria, DBI, and polypharmacy is also presented in table 1.

One hundred and twenty-four participants were exposed to at least one PIM (56.9%); 76 of those 124 used only 1 PIM (61.3%), 41 used 2 PIMs (33.1%) and 7 used 3 PIMs (5.6%). The most common PIMs by Modified Beers criteria in this sample were temazepam (n = 46, 37.1% of the 124 participants exposed to PIM), bisacodyl (n = 12, 9.7%), oxazepam (n = 12, 9.7%), digoxin (n = 11, 8.9%), diazepam (n = 6, 4.8%), dipyriramole (n = 5, 4.0%), and amitriptyline (n = 4, 3.2%).
A total of 178 (78.8%) participants were exposed to medications leading to a DBI of $\geq 0$: 82 participants (46.1%) were taking an anticholinergic medication and 96 (53.9%) were taking sedative medications.

All participants were using at least one medication. A total of 18 of the participants (7.9%) were exposed to 1 to 4 medications at the time of the study; 208 (92.0%) of the participants were identified with polypharmacy (i.e. using $\geq 5$ medications at one point in time). The mean number of medications was $10.2 \pm 4.04$ (median 10, range 1–21).

**Association of PHM with HRQoL**

The mean QoL-AD total score by self-rating was $41.5 \pm 5.9$ (range 26–58), corresponding to a mean QoL-AD %MaxSc of $69.2 \pm 9.9$ (range 43.3–96.7).

Table 2 shows the differences in self-reported QoL-AD ratings according to the use of PHM. The use of $\geq 1$ PIM(s) was not associated with the self-reported QoL-AD in this group of PWD living in RACFs, but both DBI $\geq 0$ and polypharmacy were, including after adjust-
ments were made for other measured factors. Similarly, a logistic regression analysis using QoL-AD %MaxSc tertiles showed that DBI >0 tripled the odds of participants being in the middle or lowest tertile of QoL ratings (table 3).

Table 2. Differences in self-reported QoL-AD ratings (i.e. %MaxSc on the QoL-AD) according to exposure to PHM

| Measure                        | No exposure | Exposure                                      | Crude mean difference (95% CI) | p     | Adjusted¹ mean difference (95% CI) | p     | Adjusted² mean difference (95% CI) | p     |
|-------------------------------|-------------|-----------------------------------------------|--------------------------------|-------|-----------------------------------|-------|-----------------------------------|-------|
| PIM(s) by Beers criteria      | 102         | 124                                           | -1.79 (-4.40 to 0.81)          | 0.175 | -1.68 (-4.04 to 0.68)            | 0.163 | -1.49 (-3.86 to 0.88)            | 0.217 |
| DBI >0                        | 48          | 178                                           | -4.82 (-7.94 to -1.70)         | 0.003 | -4.38 (-7.51 to -1.24)           | 0.006 | -4.07 (-7.25 to -0.89)           | 0.012 |
| Polypharmacy³                 | 18          | 208                                           | -5.37 (-10.12 to -0.61)        | 0.027 | -5.54 (-10.26 to -0.82)          | 0.022 | -4.96 (-9.79 to -0.12)           | 0.045 |

¹ Adjusted for age, gender, MMSE total score and NPI total score using linear regression modeling. ² Adjusted for age, gender, MMSE total score, NPI total score and number of comorbidities using linear regression modeling. ³ Number of medications consumed per day ≥5.

Table 3. Odds ratios (95% CI) of self-reported QoL-AD ratings (i.e. %MaxSc on the QoL-AD) according to exposure to PHM

| Measure                        | Tertile QoL-AD %MaxSc¹ | Crude OR 95% CI p | Adjusted² OR 95% CI p |
|-------------------------------|------------------------|-------------------|----------------------|
| PIM(s) by Beers criteria      | Highest tertile 71     | 35 (49.3) 1       | 1                    |
|                               | Middle tertile 81      | 46 (56.8) 1.35 (0.71–2.56) 0.356 | 1.35 (0.70–2.58) 0.370 |
|                               | Lowest tertile 74      | 43 (58.1) 1.43 (0.74–2.75) 0.288 | 1.28 (0.65–2.53) 0.475 |
| DBI >0                        | Highest tertile 71     | 46 (64.8) 1       | 1                    |
|                               | Middle tertile 81      | 69 (85.2) 3.13 (1.43–6.84) 0.004 | 3.47 (1.54–7.83) 0.003 |
|                               | Lowest tertile 74      | 63 (85.1) 3.11 (1.39–6.96) 0.006 | 2.75 (1.18–6.42) 0.019 |
| Polypharmacy (≥5)             | Highest tertile 71     | 62 (87.3) 1       | 1                    |
|                               | Middle tertile 81      | 76 (93.8) 2.21 (0.70–6.92) 0.175 | 2.43 (0.73–8.10) 0.150 |
|                               | Lowest tertile 74      | 70 (94.6) 2.54 (0.75–8.66) 0.136 | 2.64 (0.71–9.83) 0.148 |

¹ Tertiles QoL-AD %MaxSc as follows: highest tertile 73.34–96.67; middle tertile 66.517–73.33; lowest tertile 43.33–66.516. ² Adjusted for age, gender, MMSE total score, NPI total score and number of comorbidities.

Discussion

Our study indicates that the relevance of PHM in modulating QoL for PWD living in RACFs depends on how this concept is defined. We found that more than half of the PWD living in RACFs were exposed to at least one PIM (by Modified Beers criteria), over 80% were using medications that contributed to a DBI >0, and over 90% were exposed to polypharmacy (i.e. using ≥5 medications). Our data show that QoL ratings were lower in PWD living in RACFs exposed to DBI >0 or polypharmacy.

Interpretation of the results should be considered in light of design of the study. Its cross-sectional nature does not allow us to infer that the use of PHM causes a decline in the QoL of patients, and the possibility of reverse causality (low QoL leading to an increase in the prescription of medications) cannot be ruled out. Secondly, this study only included PWD
living in Western Australian RACFs who were aged 65 years or older. Therefore, the findings may not be generalizable to the wider population of older PWD living in the community or in other settings. Thirdly, we did not include data regarding characteristics of the RACFs from where participants were recruited. In addition, the sample of participating RACFs is likely to be subject to volunteer bias, which might have reduced the power of the study to detect relevant associations (type II error). Also, data on depression was partly retrieved from the NPI, but information on insight was not available, and this might have limited our ability to adjust the analyses for these known confounders associated with self-reported QoL [36]. Finally, we did not validate the quality of care provided, which may be an important consideration given that factors such as use of restraints and the incidence of falls may be influenced by facility and staff-related factors [30].

We also acknowledge that we might have introduced a bias by only including PWD living in RACFs who were able to self-rate QoL-AD. Although we have previously shown [30] that the majority of PWD living in RACFs can rate their own QoL (64% in the DIRECT study sample), it needs to be noted that PWD able to self-rate the QoL-AD have higher MMSE (median 17; IQR 12–21) compared with less able people (median 5; IQR 0–11). Therefore, the interpretations of our findings are restricted to PWD with moderate or mild dementia living in RACFs.

Another issue to bear in mind involves the exposure to ‘potentially’, not ‘definitely’, harmful medications. Although the risks associated with polypharmacy have been widely reported [22] so are the potential benefits of therapies that lead to cure (e.g. antibiotics) or mitigate distressing symptoms (e.g. pain relief). The development of sound evidence-based strategies that lead to the appropriate use of multiple medications and, at the same time, avoid the undesirable consequences of polypharmacy are urgently needed.

Our study has the merit of having used three different operationalisations to identify the use of PHM in PWD living in RACFs in a moderately large sample (n = 226), which as far as we are aware, has not been done before. Despite its importance, there is still debate as to how to identify the use of PHM and while several methods and clinical tools have been proposed, we are not aware of another study which included simultaneously PIM, DBI and polypharmacy as exposures of interest. In this regard, our study is of clinical relevance and the findings suggest that DBI and polypharmacy can assist healthcare practitioners identify PHM that may compromise the QoL of PWD living in RACFs.

Importantly, the differences that we found were subtle and their clinical relevance uncertain. That is, being exposed to polypharmacy or to drugs contributing to a DBI >0 is associated with 5% lower self-ratings on a widely used HRQoL questionnaire (also after adjustment for possible confounding variables including the number of comorbidities and neuropsychiatric symptoms). At this point, we are unable to state whether such a difference is of immediate or future clinical relevance, but these results suggest a possible intervention opportunity for healthcare practitioners through quality use of medicines.

The prevalence of PIM in our group of participants was high, i.e. more than half of the participants were exposed to ≥ 1 PIM(s). It was unexpected that use of PIM (by Modified Beers criteria) would not be associated with the self-reported QoL-AD in this group of PWD living in RACFs given that the use of PIMs has been associated with increased rate of adverse drug events and poorer health outcomes [16, 17]. However, our results are consistent with the finding of Franic and Jiang [2], who reported that PIM use was not a significant predictor of HRQoL in a cohort of community-dwelling older adults. Our finding that the use of PIM (by Modified Beers criteria) was not associated with HRQoL while the DBI and polypharmacy were, suggests an advantage of the DBI and polypharmacy over PIMs by Modified Beers criteria as predictors of self-reported HRQoL for this population. Furthermore, the lack of reliable information regarding the dosage of certain medications used by our participants (such
as hypnotic benzodiazepines) may have led to some misclassification and dilution of the association between PIM and QoL ratings.

The mechanisms that explain the observed association of DBI and polypharmacy with self-rated QoL in this population are uncertain and might be confounded by factors we did not include in our study. It is well known that polypharmacy is a risk factor for adverse health outcomes [22]. But this apparent relationship may be confounded by the burden of multiple chronic diseases [24]. In our study the number of multiple comorbidities did not affect the association between BDI or polypharmacy with HRQoL. A similar comparison could be made for the possible influence of neuropsychiatric symptoms, which one might expect to increase the risk of exposure to medications, but adjustment for this (with the NPI) had no obvious effect on the association between HRQoL and BDI or polypharmacy. The longitudinal implications of our findings should be explored by future studies.

In conclusion, use of PHM is common and is inversely associated with the self-reported HRQoL in PWD living in RACFs. With regards to clinical tools, our data suggest that DBI and polypharmacy may be better predictors of HRQoL than PIMs by Modified Beers criteria. This study supports the recommendation that, with the overall aim of improving QoL as outcome of care for PWD in RACFs, efforts should be made to avoid the use of PHM through quality use of medicine initiatives.

**Acknowledgements**

We sincerely thank all participants, clinical staff and research staff for their generous contribution to this study. This study was funded by the National Health and Medical Research Council (NHMRC) Dementia Research Grant Program Strategic Award (No. 458797). This trial was registered (ACTRN12607000417482) on 17/08/2007.

**Disclosure Statement**

There is no conflict of interest.

**References**

1. Beer C, Hyde Z, Almeida OP, Norman P, Hankey GJ, Yeap BB, Flicker L: Quality use of medicines and health outcomes among a cohort of community dwelling older men: an observational study. Br J Clin Pharmacol 2011; 71:592–599.
2. Franic DM, Jiang JZ: Potentially inappropriate drug use and health-related quality of life in the elderly. Pharmacotherapy 2006; 26:768–778.
3. Gurwitz JH, Field TS, Avorn J, McCormick D, Jain S, Eckler M, Benser M, Edmondson AC, Bates DW: Incidence and preventability of adverse drug events in nursing homes. Am J Med 2000; 209: 87–94.
4. Klarin I, Wimo A, Fastbom J: The association of inappropriate drug use with hospitalisation and mortality: a population based study of the very old. Drugs Aging 2005; 22:69–82.
5. Lau DT, Kasper JD, Potter DE, Lyles A, Bennett RG: Hospitalization and death associated with potentially inappropriate medication prescriptions among elderly nursing home residents. Arch Intern Med 2005; 165:68–74.
6. Lindley CM, Tully MP, Paramsothy V, Tallis RC: Inappropriate medication is a major cause of adverse drug reactions in elderly patients. Age Ageing 1992; 21:294–300.
7 Basger B, Chen TF, Moles R: Inappropriate medication use and prescribing indicators in elderly Australians: development of a prescribing indicators tool. Drugs Aging 2008;25:777–793.
8 Elmstahl S, Stenberg I, Annerstedt L, Ingvad B: Behavioural disturbances and pharmacological treatment of patients with dementia in family care giving: a 2 year follow-up. Int Psychogeriatr 1998;10:239–252.
9 Gallagher P, Barry P, Ryan C, Hartigan I, O’Mahony D: Inappropriate prescribing in an acutely ill population of elderly patients as determined by Beers’ criteria. Age Ageing 2008;37:96–101.
10 Hamilton HJ, Gallagher PF, O’Mahony D: Inappropriate prescribing and adverse drug events in older people. BMC Geriatr 2009;9:5.
11 Spinewine A, Schmader KE, Barber N, Hughes C, Lapane KL, Swine C, Hanlon JT: Appropriate prescribing in elderly people: how well can it be measured and optimised? Lancet 2007;370:173–184.
12 Hollingworth SA, Lie DC, Siskind DJ, Byrne GJ, Hall WD, Whiteford HA: Psychiatric drug prescribing in elderly Australians: time for action. Aust N Z J Psychiatry 2001;45:705–708.
13 Somers M, Rose E, Simmonds D, Whitelaw C, Calver J, Beer C: Quality use of medicines in residential aged care. Aust Fam Physician 2010;39:413–416.
14 Ballard C, Howard R: Neuroleptic drugs in dementia: benefits and harm. Nat Rev Neurosci 2006;7:492–500.
15 Burke AD, Tariot PN: Atypical antipsychotics in the elderly: a review of therapeutic trends and clinical outcomes. Expert Opin Pharmacother 2009;10:2407–2414.
16 Fick DM, Cooper JW, Wade WE, Waller JL, Maclean JR, Beers MH: Updating the Beers criteria for potentially inappropriate medication use in older adults: results of a US consensus panel of experts. Arch Intern Med 2003;163:2716–2724.
17 Roughhead EE, Anderson B, Gilbert AL: Potentially inappropriate prescribing among Australian veterans and war widows/widowers. Intern Med J 2007;37:402–405.
18 Hilmer SN, Mager DE, Simonsick EM, et al: A drug burden index to define the functional burden of medications in older people. Arch Intern Med 2007;167:781–787.
19 Hilmer SN, Mager DE, Simonsick EM, et al: Drug burden index score and functional decline in older people. Am J Med 2009;122:1142–1149.
20 Cao YJ, Mager DE, Simonsick EM, et al: Physical and cognitive performance and burden of anticholinergics, sedatives, and ACE inhibitors in older women. Clin Pharmacol Ther 2008;83:422–429.
21 Gnjidic D, Le Couteur DG, Abernethy DR, Hilmer SN: Drug Burden Index and Beers Criteria: Impact on Functional Outcomes in Older People Living in Self-Care Retirement Villages. J Clin Pharmacol 2012;52:258–265.
22 Frazier SC: Health outcomes and polypharmacy in elderly individuals: an integrated literature review. J Gerontol Nurs 2005;31:4–11.
23 LeCouteur DG, Hilmer SN, Glasgow N, Naganathan V, Cumming RG: Prescribing in older people. Aust Fam Physician 2004;33:777–781.
24 Lawlor DA, Patel R, Ebrahim S: Association between falls in elderly women and chronic diseases and drug use: cross sectional study. BMJ 2003;327:712–717.
25 Olsson IN, Runnamo R, Engfeldt P: Medication quality and quality of life in the elderly, a cohort study. Health Qual Life Outcomes 2001;9:95.
26 Banerjee S, Samsi K, Petriec CD, Alvir J, Treglia M, Schwam E, del Valle M: What do we know about quality of life in dementia? A review of the emerging evidence on the predictive and explanatory value of disease specific measures of health related quality of life in people with dementia. Int J Geriatr Psychiatry 2009;24:15–24.
27 Baumeister H, Balke K, Härter M: Psychiatric and somatic comorbidities are negatively associated with quality of life in physically ill patients. J Clin Epidemiol 2005;58:1090–1100.
28 Norris S, High K, Gill TM, Hennessy S, Kutner JS, Reuben DB, Unützer J, Landefeld CS: Health care for older Americans with multiple chronic conditions: a research agenda. J Am Geriatr Soc 2008;56:149–159.
29 Henderson JA, Dedra Buchwald D, Manson SM: Relationship of Medication Use to Health-Related Quality of Life Among a Group of Older American Indians. J Appl Gerontol 2006;25:895–1045.
30 Beer C, Horner B, Almeida OP, Scherer S, Lautenschlager NT, Bretland N, Fleet P, Schaper F, Flicker L: Dementia in residential care: education intervention trial (DIRECT); protocol for a randomised controlled trial. Trials 2010;11:63.
31 Logsdon RG, Gibbons LE, McCurry SM, Teri L: Quality of life in Alzheimer’s disease: patient and caregiver reports. J Mental Health Aging 1999;5:21–32.
32 Logsdon RG, et al: Assessing quality of life in older adults with cognitive impairment. Psychosom Med 2002;64:510–519.
33 Thorgrimsen L, Selwood A, Spector A, et al: Whose quality of life is it anyway? The validity and reliability of the Quality of Life-Alzheimer’s Disease (QoL-AD) scale. Alzheimer Dis Assoc Disord 2003;17:201–208.
34 Edelman P, Fulton BR, Kuhn D, Chang CH: A comparison of three methods of measuring dementia-specific quality of life: perspectives of residents, staff, and observers. Gerontologist 2005;45:27–36.
35 Sloane PD, Zimmerman S, Williams CS, Reed PS, Gill KS, et al: Evaluating the quality of life of long-term care residents with dementia. Gerontologist 2005;45:37–49.
36 Bosboom PR, Alfonso H, Eaton J, Almeida OP: Quality of life in Alzheimer’s disease: different factors associated with complementary ratings by patients and family carers. Int Psychogeriatr 2012;24:708–721.
37 World Health Organisation: The Anatomical Therapeutic Chemical Classification System with Defined Daily Doses (ATC/DDD). http://www.who.int/classifications/atcddd/(accessed 2012).
38 Gnjidic D, Cumming RG, Le Couteur DG, et al: Drug Burden Index and physical function in older Australian men. Br J Clin Pharmacol 2009;68:97–105.
39 Gnjidic D, Le Couteur DG, Abernethy DR, Hilmer SN: A pilot randomized clinical trial utilizing the drug burden index to reduce exposure to anticholinergic and sedative medications in older people. Ann Pharmacother 2010;44:1725–1732.
40 Gnjidic D, Hilmer SN, Blyth FM, Naganathan V, Handelsman DJ, Cumming RG, et al: Polypharmacy and adverse outcomes: determining the best cut-off for polypharmacy associated with geriatric syndromes, functional outcomes and mortality in older adults. J Clin Epidemiol 2012, in press.
41 Folstein MF, Folstein SE, McHugh PR: Mini-mental state; a practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;12:189–198.
42 Cummings JL: The Neuropsychiatric Inventory: assessing psychopathology in dementia patients. Neurology 1997;48(5 suppl 6):S10–S16.
43 Beer C, Bosboom PR, Almeida OP, Flicker L: Rating the quality of life of people with dementia living in residential care facilities in routine research practice. Age Ageing 2009;38:343–346.