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ORIGINAL RESEARCH ARTICLE

# Associations of Potentially Inappropriate Medicine Use with Fall-Related Hospitalisations and Primary Care Visits in Older New Zealanders: A Population-Level Study Using the Updated 2012 Beers Criteria

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## Abstract

*Background*   Identifying potentially inappropriate medicines (PIMs) leading to adverse drug events may reduce the risk of morbidity and mortality in older people.

*Objective*   The aim of this study was to examine the relationship between exposure to PIMs and risk of Fall-related hospitalisations (FRH) and frequency of primary care visits in older New Zealanders.

*Methods*   Pharmaceutical collections (2011), diagnostic (2007–2011) and events (2012) information derived from the National Minimum Datasets were used to extract demographics, medication and diagnostic information for 537,387 individuals aged ≥65 years. Prescription and diagnostic information were matched through unique National Health Index numbers. The updated Beers 2012 criteria were used to identify PIMs. Polypharmacy was defined as five or more medicines dispensed concurrently for ≥90 days.

*Results*   Individuals exposed to one or more PIMs had an increased risk of FRH with an incidence rate ratio (IRR) of 1.45 (95 % confidence interval [CI] 1.37–1.52) and a greater number of primary care visits (IRR 1.15; 95 % CI 1.15–1.16). Individuals exposed to polypharmacy had an IRR of 1.41 (95 % CI 1.33–1.50) for FRH and an IRR of 1.14 (95 % CI 1.13–1.15) for primary care visits.

*Conclusion*   PIMs identified by the 2012 Beers criteria showed an increased risk of FRH and a greater number of primary care visits. Age ≥85 years and female sex were identified as significant predictors of FRH and primary care visits.

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### Key Points

Prevention of adverse drug events such as falls, fractures and hospitalisations are clinically important outcomes in people aged 65 years and older.

Potentially inappropriate medicines (PIMs) identified by the 2012 Beers criteria showed an increased risk of Fall-related hospitalisations (FRH) and a greater number of primary care visits in people aged ≥65 years living in New Zealand.

On a population level, Beers criteria can be a useful screening tool to guide prescribing in older people.

## 1 Introduction

Prevention of adverse drug events (ADEs) including falls, fractures and hospitalisations are important clinical outcomes in people aged 65 years and older. Polypharmacy (concomitant use of five or more medicines) is an indicator for potentially inappropriate medicine use and has been associated with adverse clinical outcomes in older people [1]. Identifying exposures to potentially inappropriate medicines (PIMs) that can lead to ADEs can be examined by the use of criterion-based explicit screening tools [2, 3].

Beers criteria are a universally accepted explicit tool for screening for PIMs in older people [2]. The Beers criteria

△ Adis

have been updated since it was first developed in 1991, and applied in various settings including residential care facilities, acute care and ambulatory care to identify high-risk prescribing in older adults [2, 4–6]. Exposure to PIMs determined by the Beers criteria has shown to be associated with an increased risk of mortality, functional impairment, hospitalisations, delirium, falls, fractures and adverse drug events [7–10]. On the contrary, studies have disaffirmed findings of adverse outcomes to exposure to PIMs listed in the Beers criteria [11, 12]. Despite recognition of the aforementioned limitations associated with Beers criteria, including not considering drug–drug interactions, dose and duration (overtreatment) and partial applicability internationally (prescribing patterns and drug availability), it still remains one of the widely accepted criterion-based tools for identifying high-risk prescribing in older people.

Corresponding to global trends, the New Zealand population is aging and the total population will comprise of approximately 22–30 % of people aged 65 years and older by 2061 [13]. Prior studies have shown that a high proportion of older people are prescribed multiple medicines, increasing the risk of exposure to PIMs and potentially leading to ADEs and consequently an increase in healthcare expenditure [9, 14]. These studies have examined PIMs use in older people; however, outcomes data at a population level is limited [15]. Hence, the primary objective of this population-level study was to examine the risk of fall-related hospitalisations and primary care visits associated with PIMs use in people aged 65 years and older in New Zealand.

## 2 Design and Methods

Approval to conduct this study was obtained by the Human Ethics Committee at the University of Otago, New Zealand, ethical approval number 12/147.

### 2.1 Study Population and Data Source

Anonymous data on all older individuals aged 65 years and above who were dispensed at least one prescription medicine between January 1, 2011 through to December 31, 2011 were identified from the Pharmaceutical Claims Data Mart (Pharms) dataset. The prescriptions data for 559,625 individuals representing approximately 98 % of the total population of older New Zealanders was extracted. For these individuals, demographic information such as sex, date of birth and ethnicity, and prescription details such as date of dispensing, medicine name, medicine dose, dosing frequency and quantity supplied were extracted. The diagnoses were coded using the International Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification (ICD-10-AM). The diagnostic

information for 180,978 out of the 559,625 individuals was either missing or unknown.

The following extracts were obtained from the Ministry of Health to undertake this study:

1. Pharms extract files for 2011 contained information on sex, date of birth, medicine, daily dose, frequency, quantity, prioritised ethnicity and District Health Board (DHB) of domicile.
2. National Minimum Data set (2007–2011): information on hospitalisations, event start date (2012), event end date (2012), diagnosis code (ICD-10), accident codes (ICD-10), and procedure codes (ICD-10).
3. General Practitioner (primary care) visits (2012): date of visit/s.

Pharms is used by the Pharmaceutical Management Agency (PHARMAC) and the Ministry of Health of New Zealand to administer payment to pharmacists for dispensing medicines, as well as to assist PHARMAC in its management of the national medicines budget. Pharms extracts are supplied by the Ministry of Health with individual-level prescription data with an encrypted National Health Index (NHI) code which enables individual records to be linked between the various national health data collections whilst still protecting the identity of the individuals. The encryption is an algorithm of the actual NHI. There is only a unique encrypted version of each NHI, which is never changed, allowing linking of new data with datasets previously extracted.

### 2.2 Potentially Inappropriate Medicines (PIMs) Exposure

The updated Beers 2012 criteria were used to identify PIMs, both independent of diagnosis and taking diagnosis or dose into consideration. If an individual was dispensed one or more medicine for any duration, at any given time, the individual was said to have an exposure to PIMs. For this study, criterions related to identifying PIMs in lower urinary tract infections and peptic ulcer diseases were modified. To categorise medicines inappropriate for use in individuals with lower urinary tract symptoms and benign prostatic hyperplasia (BPH), only BPH was used as a diagnosis rather than both the symptoms. Additionally, ICD-10 codes for peptic and gastrojejunal ulcers were included with history of gastric or duodenal ulcers.

### 2.3 Chronic Disease Score

Chronic Disease Score (CDS) is a risk-adjustment metric established on patient demographics (age and sex) and account of dispensed medicines [16]. The CDS was used to compute scores for comorbidities as diagnostic information was unavailable for approximately 33.7 % of the study

population. The CDS was included as a covariate in the regression model.

## 2.4 Polypharmacy

Polypharmacy in individuals was identified as the use of more than five medicines dispensed concurrently for more than or equal to a period of 90 days.

## 2.5 Assessing Clinical Outcomes (Falls-Related Hospitalisation [FRH] and Primary Care Visits)

Anonymous linkages via encrypted NHI numbers were used to match prescription data with FRH and primary care visits data between January 1, 2012 and December 31, 2012.

## 2.6 Statistical Analyses

Means and standard deviations were reported for age and number of medicines in the study population. Proportions were reported for sex and ethnicity. The frequency of primary care visits and FRH were found to be over-dispersed with the variance exceeding the mean. The Pearson goodness-of-fit tests confirmed the distribution of primary care visits and falls significantly differed for a Poisson distribution, distribution, $p$ value of $<0.001$ (Prob $> \chi^2$ [537,385]). Hence, a negative binomial regression was used to model the frequency of primary care visits and FRH. Covariates including age, sex, chronic disease scores were common to all regression models. These covariates have been previously shown to be associated with falls and adverse outcomes in older people [3]. The goodness-of-fit for negative binomial regression models of FRH and primary care visits was analysed. The McFadden's adjusted $R^2$ for FRH and primary care visits were 0.074 and 0.023, respectively. The maximum likelihood (Cox-Snell) $R^2$ for FRH and primary care visits were 0.010 and 0.114, respectively. All statistical analyses were conducted using Stata® Corp Release 12. A $p < 0.05$ was regarded as statistically significant.

## 3 Results

A total of 537,387 individuals 65 years and older were included in the study, of which 54.9 % were females with a mean age of 74.7 years ($\pm$7.6). The prevalence of PIMs dispensed was 40.39 % with 78.5 % of individuals dispensed at least one PIM and 21.5 % dispensed two or more PIMs in 2011. The most common PIMs dispensed to the study population were diclofenac (6.0 %) and amitriptyline (4.9 %), followed by ibuprofen (4.6 %), zopiclone (3.2 %) and naproxen (3.0 %). The mean number of medicines dispensed was 5.6 ($\pm$3.9) (Table 1).

**Table 1** Characteristics of the study population ($n = 537,387$)

| Characteristic | Value | PIMs exposure OR (95 % CI) |
|---|---|---|
| Age (mean $\pm$ SD) | | 74.72 $\pm$ 7.60 |
| Age (years) | | |
| 65–74[a] | 55.10 % | 1 |
| 75–84 | 32.10 % | 1.24 (1.23–1.26) |
| $\geq$85 | 12.80 % | 1.42 (1.39–1.44) |
| Female sex | 54.91 % | 0.88 (0.87–0.89) |
| Ethnicity | | |
| European[a] | 79.11 % | 1 |
| Māori | 4.70 % | 0.85 (0.82–0.87) |
| Asian | 3.76 % | 0.49 (0.47–0.51) |
| Pacific | 2.64 % | 0.63 (0.61–0.65) |
| MELAA | 0.30 % | 0.65 (0.53–0.81) |
| Others/unknown | 9.49 % | 0.72 (0.70–0.73) |
| Individuals exposed to PIMs $\geq$1 | 40.39 % | |
| Mean total number of dispensed medicines | 5.64 $\pm$ 3.91 | |
| Chronic Disease Score (CDS) | 6.04 $\pm$ 4.97 | 1.06 (1.06–1.06) |
| Individuals exposed to polypharmacy | 33.20 % | 2.23 (2.21–2.26) |
| Individuals admitted with falls (6 months after study period) | 2.75 % | 1.54 (1.49–1.60) |
| GP visits (12 months after study period) | 64.66 % | 1.25 (1.24–1.27) |

*CI* confidence interval, *GP* general practitioner, *MELAA* Middle Eastern/Latin American/African, *OR* odds ratio, *PIMs* potentially inappropriate medicine

[a] Reference category

The events (FRH) data for 2012 showed that 2.75 % (14,804) of these individuals had had a FRH in 2012. Of these individuals, 50.8 % (7525/14,804) had an exposure to at least one PIM in 2011. Similarly, data for primary care visits (2012) was matched for all individuals ($n = 537,387$) showing that 64.7 % ($n = 347,452$) of individuals visited their general practitioner one or more times during 2012. Of these individuals, 40.5 % (140,720/347,452) had potentially been exposed to at least one PIM in 2011.

On univariate analysis, PIMs exposure, defined as a categorical variable, was lower in males than in females (odds ratio [OR] 0.88; 95 % CI 0.87–0.89) and was greater in Europeans (OR 1.39; 95 % CI 1.37–1.42) in comparison with any other ethnic group. Approximately 30.90 % of individuals were exposed to polypharmacy (OR 2.23; 95 % CI 2.21–2.26).

Table 2 summarises the negative binomial regression models used to demonstrate associations of FRH and primary care visits after adjusting for age, sex, CDS scores, and exposure to PIMs. Exposure to PIMs was included in

**Table 2** Regression models demonstrating the associations with exposure to PIMs predicting the risks of Fall-related hospitalisations and primary care visits

|  | NBR model IRR (95 % CI) | |
| --- | --- | --- |
|  | FRH | Primary care visits |
| Age (years) | | |
| 65–74[a] | 1 | 1 |
| 75–84 | 2.90 (2.72–3.11) | 1.15 (1.15–1.16) |
| ≥85 | 7.27 (6.79–7.80) | 1.30 (1.30–1.31) |
| Male[a] | 1 | 1 |
| Female | 1.27 (1.20–1.34) | 1.06 (1.06–1.07) |
| Chronic Disease Score | 1.05 (1.05–1.06) | 1.02 (1.03–1.03) |
| No polypharmacy (0–4)[a] | 1 | 1 |
| Polypharmacy ≥5 | 1.41 (1.33–1.50) | 1.14 (1.13–1.15) |
| No exposure to PIMs[a] | 1 | 1 |
| Exposure to PIMs ≥1 | 1.45 (1.37–1.52) | 1.15 (1.15–1.16) |

*CI* confidence interval, *FRH* Fall-related hospitalisations, *IRR* incidence rate ratio, *NBR* negative binomial regression, *PIMS* potentially inappropriate medicine

[a] Reference category

these models as a covariate. Demographic predictors such as female sex (incidence rate ratio [IRR] 1.27; 95 % CI 1.20–1.34) and age ≥85 years (IRR 7.27; 95 % CI 6.78–7.79) were significant predictors of FRH. Individuals having an increased chronic disease score also predicted an increased risk of FRH and primary care visits.

Exposure to one or more PIMs showed an increased risk of FRH (IRR 1.45; 95 % CI 1.37–1.53) and primary care visits (IRR 1.15; 95 % CI 1.15–1.16). Individuals exposed to polypharmacy had an IRR of 1.41 (95 % CI 1.37–1.52) for FRH and IRR of 1.14 (95 % CI 1.15–1.16) for primary care visits.

## 4 Discussion

This population-level study of older New Zealanders identified that approximately 41 % of individuals aged 65 years and older were dispensed at least one PIM in 2011 and over 50 % of individuals with FRH in 2012 were exposed to at least one PIM in 2011. Additionally, 40.5 % of individuals with at least one primary care visit in 2012 were also exposed to one PIM in 2011. Age, sex, CDS, polypharmacy and exposure to PIMs were all predictors of FRH and the frequency of primary care visits in 2012. Three of the top five PIMs dispensed were non-steroidal anti-inflammatory drugs and it is well established that these medicines have a potential to increase the risk of cardiovascular, renal and haematological adverse events in older people [17, 18].

There are limitations to this study. Similar to other global studies using the Beers criteria, not all medicines listed were available in New Zealand or funded by PHARMAC. In addition, only the first twenty diagnoses were accessible from the minimum data set obtained from the Ministry of Health. Additionally, medicines not funded by PHARMAC and over-the-counter medicines not captured by Pharms may have underestimated the exposure to PIMs in this study population. Furthermore, a retrospective study design limits causal relationships between PIMs exposure and adverse outcomes.

Our study showed an increased risk of FRH and primary care visits associated with exposure to PIMs. This result is consistent with findings that have linked exposure to PIMs and polypharmacy to adverse health outcomes [10, 19, 20]. Klarin et al. [10] reported that community-dwelling older people exposed to PIMs had an increased risk of hospitalisation. Previous studies have demonstrated the utility of administrative health data to examine appropriateness of prescribing [21–24].

The charge for fully subsidised medicines at the time of this study was NZ$3, and very few prescriptions would cost more than $3. Hence, a large proportion of dispensing in this age group was captured by Pharms. Selection bias may have been eliminated given that almost the entire older population of New Zealand is captured in the Pharms dataset. Another major strength was the availability of ICD-10 codes which enabled linkage of prescription, diagnosis and events datasets.

This study is the first in New Zealand to examine the relationship between exposure to PIMs and FRH and primary care visits at a population level. Congruent to the findings from previous research, exposure to PIMs is associated with an increased risk of hospitalisations and poor health outcomes [10, 25–27]. Use of such criteria can enable improved prescribing by flagging alerts into the physician dispensing software or into electronic prescribing software or into decision support systems maintained by healthcare organisations.

## 5 Conclusion

Using the updated Beers 2012 criteria, exposure to PIMs showed an association with FRH and frequency of primary care visits. Age ≥85 years and female sex were identified as significant predictors of FRH and primary care visits. On a population level, Beers criteria may be a useful screening tool to identify high-risk prescribing and reduce adverse outcomes in older people.

prescription data extracted from the Pharms database. There are no conflicts of interest that are directly relevant to the content of the study. The manuscript does not contain clinical studies and all patient data are de-identified.

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# References

1. Haider SI, Johnell K, Weitoft GR, Thorslund M, Fastbom J. The influence of educational level on polypharmacy and inappropriate drug use: a register-based study of more than 600,000 older people. J Am Geriatr Soc. 2009;57(1):62–9.

2. American Geriatrics Society Beers Criteria Update Expert P. American Geriatrics Society updated Beers Criteria for potentially inappropriate medication use in older adults. J Am Geriatr Soc. 2012;60(4):616–31.

3. Nishtala PS, Narayan SW, Wang T, Hilmer SN. Associations of drug burden index with falls, general practitioner visits, and mortality in older people. Pharmacoepidemiol Drug Saf. 2014;23(7):753–8.

4. Castelino RL, Hilmer SN, Bajorek BV, Nishtala P, Chen TF. Drug Burden Index and potentially inappropriate medications in community-dwelling older people: the impact of Home Medicines Review. Drugs Aging. 2010;27(2):135–48.

5. Roughead EE, Anderson B, Gilbert AL. Potentially inappropriate prescribing among Australian veterans and war widows/widowers. Int Med J. 2007;37(6):402–5.

6. Beer C, Hyde Z, Almeida OP, Norman P, Hankey GJ, Yeap BB, et al. Quality use of medicines and health outcomes among a cohort of community dwelling older men: an observational study. Br J Clin Pharmacol. 2011;71(4):592–9.

7. Zhan C, Correa-de-Araujo R, Bierman AS, Sangl J, Miller MR, Wickizer SW, et al. Suboptimal prescribing in elderly outpatients: potentially harmful drug–drug and drug–disease combinations. J Am Geriatr Soc. 2005;53(2):262–7.

8. Lane CJ, Bronskill SE, Sykora K, Dhalla IA, Anderson GM, Mamdani MM, et al. Potentially inappropriate prescribing in Ontario community-dwelling older adults and nursing home residents. J Am Geriatr Soc. 2004;52(6):861–6.

9. Jano E, Aparasu RR. Healthcare outcomes associated with Beers' criteria: a systematic review. Ann Pharmacother. 2007;41(3):438–47.

10. 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(1):69–82.

11. Onder G, Landi F, Liperoti R, Fialova D, Gambassi G, Bernabei R. Impact of inappropriate drug use among hospitalized older adults. Eur J Clin Pharmacol. 2005;61(5–6):453–9.

12. Laroche ML, Charmes JP, Nouaille Y, Picard N, Merle L. Is inappropriate medication use a major cause of adverse drug reactions in the elderly? Br J Clin Pharmacol. 2007;63(2):177–86.

13. Wager-Smith K, Markou A. Depression: A repair response to stress-induced neuronal microdamage that can grade into a chronic neuroinflammatory condition? Neurosci Biobehav Rev. 2011;35(3):742–64.

14. Lin HY, Liao CC, Cheng SH, Wang PC, Hsueh YS. Association of potentially inappropriate medication use with adverse outcomes in ambulatory elderly patients with chronic diseases: experience in a Taiwanese medical setting. Drugs Aging. 2008;25(1):49–59.

15. Nishtala PS, Bagge ML, Campbell AJ, Tordoff JM. Potentially inappropriate medicines in a cohort of community-dwelling older people in New Zealand. Geriatr Gerontol Int. 2014;14(1):89–93.

16. Clark DO, Von Korff M, Saunders K, Baluch WM, Simon GE. A chronic disease score with empirically derived weights. Med Care. 1995;33(8):783–95.

17. Barkin RL, Beckerman M, Blum SL, Clark FM, Koh EK, Wu DS. Should nonsteroidal anti-inflammatory drugs (NSAIDs) be prescribed to the older adult? Drugs Aging. 2010;27(10):775–89.

18. Barkin RL, Buvanendran A. Focus on the COX-1 and COX-2 agents: renal events of nonsteroidal and anti-inflammatory drugs-NSAIDs. Am J Ther. 2004;11(2):124–9.

19. Pan HH, Li CY, Chen TJ, Su TP, Wang KY. Association of polypharmacy with fall-related fractures in older Taiwanese people: age- and gender-specific analyses. BMJ Open. 2014;4(3):e004428.

20. Kojima T, Akishita M, Nakamura T, Nomura K, Ogawa S, Iijima K, et al. Association of polypharmacy with fall risk among geriatric outpatients. Geriatr Gerontol Int. 2011;11(4):438–44.

21. Price SD, Holman CD, Sanfilippo FM, Emery JD. Does ongoing general practitioner care in elderly patients help reduce the risk of unplanned hospitalization related to Beers potentially inappropriate medications? Geriatr Gerontol Int. 2014. doi:10.1111/ggi.12400

22. Walker AM. Pattern recognition in health insurance claims databases. Pharmacoepidemiol Drug Saf. 2001;10(5):393–7.

23. Ndukwe HC, Tordoff JM, Wang T, Nishtala PS. Psychotropic medicine utilization in older people in New Zealand from 2005 to 2013. Drugs Aging. 2014;31(10):755–68.

24. Reich O, Rosemann T, Rapold R, Blozik E, Senn O. Potentially inappropriate medication use in older patients in Swiss managed care plans: prevalence, determinants and association with hospitalization. PLoS One. 2014;9(8):e105425.

25. Page RL 2nd, Linnebur SA, Bryant LL, Ruscin JM. Inappropriate prescribing in the hospitalized elderly patient: defining the problem, evaluation tools, and possible solutions. Clin Interv Aging. 2010;5:75–87.

26. Chang CM, Liu PY, Yang YH, Yang YC, Wu CF, Lu FH. Use of the Beers criteria to predict adverse drug reactions among first-visit elderly outpatients. Pharmacotherapy. 2005;25(6):831–8.

27. 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(1):68–74.