

**Are high-care nursing home residents at greater risk of unplanned hospital admission than other elderly patients when exposed to Beers potentially inappropriate medications?**

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**Running title:** Nursing home elderly, PIMs & admissions

**Word count** (including abstract, excluding refs, tables and figures): 3,111

## Abstract

**Aim:** To compare the risk of unplanned hospitalization in high-care nursing home residents taking Beers potentially inappropriate medications (PIMs) against that of other elderly.

**Methods:** Using an enhanced case-time-control design and conditional logistic regression applied to the pharmaceutical claims and other linked data of 245,436 Western Australians aged  $\geq 65$  years (1993-2005), the study derived odds ratios for unplanned hospitalization in each group, from which attributable fractions, numbers, proportions and rates of PIM-related admissions were derived.

**Results:** Overall, 383,150 unplanned hospitalizations were identified. PIM exposure was associated with a similar proportional increase in unplanned hospitalizations in high-care nursing home residents as in other older people; adjusted OR 1.21 (95% CI 1.10-1.34; attributable fraction 17.5%) vs. 1.19 (1.16-1.21; 15.7%). However, high-care nursing home residents had much higher estimated rates of hospitalizations attributed to Beers medications than other elderly (3,951 vs. 1,394 per 100,000 person-years). The relative risk of unplanned hospitalization rose similarly in both groups with increasing numbers of different PIMs taken (OR 5.1 for 10 vs. 0 PIMs), but was affected more markedly by three-month PIM consumption in nursing home residents (OR 4.85 (2.40-9.83) for 900 vs. 0 PIM daily doses) than in other seniors (2.10 (1.73-2.55)).

**Conclusions:** High-care nursing home residents do not appear to have a greater relative risk of unplanned hospitalization when given PIMs, but do incur a higher absolute burden than other elderly. Physicians should exert caution with Beers medications in all older patients, restricting the number of different PIMs and PIM quantity prescribed whenever possible.

**Keywords:** Aged, hospitalization, inappropriate prescribing, nursing homes, pharmacoepidemiology

## Introduction

Older people are generally more susceptible to adverse drug events due to physiological deterioration, polypharmacy and other age-related factors.<sup>1-3</sup> This has led to the development of lists of 'potentially inappropriate medications' (PIMs) to be avoided in the elderly, such as the Beers Criteria.<sup>4</sup>

Numerous studies have examined the prevalence of PIMs in elderly populations, while others have concentrated on the association between PIMs and adverse health outcomes. However, little is known on whether nursing home residents are at greater risk of PIM-related adverse events than other elderly people. Due to poor health, nursing home residents may have a greater predisposition to medication exposure (including PIMs) and to serious outcomes such as unplanned hospitalizations. However, close monitoring by aged care staff may help protect nursing home residents from serious PIM-related harm.

Our large population-based study (1993-2005) examined the association between exposure to Beers medications<sup>4</sup> and unplanned hospitalizations in Western Australian (WA) residents aged  $\geq 65$  years. It compared estimates applicable to high-care nursing home residents with those of other WA elderly based on exposure to general PIMs upon hospitalization (dichotomous measure), number of different PIMs taken, and overall PIM quantity consumed over three months.

## Methods

### *Data linkage and cohort selection*

This study linked Australian Pharmaceutical Benefits Scheme (PBS),<sup>5,6</sup> Medicare<sup>7,8</sup> and residential aged care<sup>9</sup> data with inpatient, death and electoral roll records from the WA Data Linkage System<sup>10</sup> through probabilistic linkage. The study protocol was approved by The University of Western Australia's Human Research Ethics Committee.

The cohort was restricted to people aged  $\geq 65$  years by the end of 2004, who continuously resided in WA during 1993-2005 (until death) and had  $\geq 1$  pharmaceutical claim during that time, thus ensuring that study participants had ascertainable drug exposures. Eight percent were subsequently excluded due

to problem data (e.g. records post-death, no gender on any record). The resulting cohort captured 80-85% of WA elderly residents.

### ***Drug reference database***

Details of all PBS items from available schedules (August 1991-June 2007)<sup>11</sup> were assembled into a reference database, retaining the last published entry for each item. Anatomical Therapeutic Chemical (ATC) codes were reconciled with the 2007 World Health Organization (WHO) ATC drug classification.<sup>12</sup> Since the prescribed dose was not recorded on PBS claims, average prescribed daily doses from the Australian Bettering the Evaluation and Care of Health (BEACH)<sup>13</sup> general practice data, MIMS Australia<sup>14</sup> registered drug information, and 2008 WHO ATC Defined Daily Doses (DDDs)<sup>15</sup> were compared to derive average daily doses for each item, based on drug form, route and strength. Furthermore, each drug's elimination half-life was obtained (predominantly from MIMS),<sup>14</sup> from which the period of drug effect, defined as five times the drug's half-life,<sup>16,17</sup> was estimated.

### ***Drug groups and domains***

Each item from the 2003 Beers list<sup>4</sup> was defined according to the 2007 ATC classification.<sup>12</sup> Following integration of patient and drug reference variables with the PBS master data file for 1993-2005, the ATC code list for 'general' PIMs (i.e. excluding disease-specific criteria) was applied to determine which of these PIMs were supplied to WA residents aged  $\geq 65$  years during the study period. This process identified 43 individual PIMs, which were grouped into 20 broad drug classes (i.e. drug domains), each class consisting of medications used to treat similar conditions to those treated by related PIMs.

### ***Case-time-control design***

The relationship between PIM exposure and unplanned hospitalizations was expressed as an odds ratio (OR) obtained from an enhanced case-time-control design.<sup>18,19</sup> This involved index subjects acting both as cases and as their own historical controls, while background time trends in predisposition to exposure were adjusted using similarly constructed case and control observation windows in a reference group drawn from the same general domain of patients as the

index subjects. The patient domain in this instance consisted of everyone in the study cohort who had ever been prescribed a drug from any of the 20 broad medication classes associated with PIMs during 1993-2005.

Index subjects were patients within the drug domain who had experienced an unplanned (i.e. emergency) hospital admission between 1 July 1994 and 31 December 2005 whilst aged  $\geq 67$  years, thus ensuring sufficient lead-up time for the control observation period. Many individuals were included in the analysis as multiple index subjects, although a few ( $\leq 0.1\%$ ) with  $>50$  index admissions were excluded. Two records were created for each index subject, one representing the 'case time' (i.e. the admission date) and the other the 'control time' (usually 365 days prior but, if the patient was in hospital at this preferred control time, the admission date of that earlier hospitalization was used instead).

Each index subject was matched by gender, aged care status and year of birth to a randomly selected reference subject from the study's domain. The aged care status was a dichotomous variable that identified whether the person was receiving high-level residential aged care in a nursing home at 30 June of the index admission year. If the person was alive at index admission but dead by mid-year, the aged care status from the previous calendar year was used instead. Subjects born prior to 1900 were allocated a birth year of 1900 for matching purposes only. 'Case time' and 'control time' records were created for each reference subject as per the corresponding index subjects, matching the case and control dates as closely as possible.

Once created, the case and control time records for index and reference subjects were populated with variables required to control for potential confounding, including nursing home status at the specific time stated on the record (i.e. case or control time); hospital days, overall Charlson comorbidity index<sup>20</sup> and 'general practitioner (GP) coverage' percentage, all for the previous year; and a drug consumption profile for the preceding 90 days (plus the case or control date), which included the number of broad medication categories involved, the overall number of daily doses consumed (for any drug) and a

count of daily doses for each broad drug category. To determine the GP coverage percentage, each GP visit identified in the Medicare dataset was allocated a 'coverage' period of 61 days (overlapping periods merged together), from which coverage proportions were calculated for the period of interest. This measure provided a general indicator of patients' ongoing GP monitoring.

Additionally, PBS records were checked to ascertain exposure status at each case and control date. If a prescription was found for a PIM and the time period bound by its supply date and exposure effect end date overlapped with the case or control time, the PIM exposure status was set to 'exposed'. The end date was calculated by adding the prescription's number of drug consumption days (i.e. script's drug quantity / average daily dose) to the supply date (-1) plus the period of drug effect (up to seven days) and a seven-day latency period. Thus, the exposure status indicated the potential for a hospital admission at the case or control time to have resulted from the effects of PIM exposure.

Once the case and control details were finalized, conditional logistic regression models with robust analysis of variance were applied using the SAS 9.2 PHREG procedure, with the COVS option and stratification based on a unique identifier for each subject. The OR of primary interest was derived from the coefficient of the cross-product between exposure and the binary index/reference indicator.<sup>18</sup> The adjusted model controlled for all health and drug consumption indicators mentioned earlier.

This analysis was performed separately for each aged care group (i.e. high-level nursing home residents versus other elderly). The initial models used a dichotomous variable as the PIM exposure measure, but subsequent analyses substituted this variable with the number of different PIMs and the number of PIM daily doses taken in the three-month period prior to the case or control time to enable the examination of associations related to PIM polypharmacy and dose-response, respectively.

### ***PIM-related unplanned hospitalizations***

Using the OR derived from the interaction between PIM exposure and the index/reference indicator, the attributable fraction (AF) of unplanned

hospitalizations associated with PIMs within the exposed was calculated, where  $AF = (OR - 1) / OR$ . An estimate of the number of unplanned hospital admissions attributed to PIMs was then derived as  $AF \times \text{count of exposed index subjects}$ .<sup>21-</sup>

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To further compare the unplanned hospitalization profile in the two groups (high-level aged care versus other elderly), crude rates were computed. This was achieved by first generating the study cohort's person-year follow-up time for each group (based on high-level aged care status at 30 June of each calendar year), including those with a predominant age  $\geq 67$  years for each year, and restricting the time period to July 1994-December 2005, as per the index admissions. Rates were then calculated (per 100,000 person-years) using counts of unplanned admissions attributed to PIMs in exposed patients; those not attributed to PIMs in the exposed; and those occurring in unexposed patients.

## Results

In our population of 251,305 elderly people, 245,436 (97.7%) had either taken a PIM from the 'general' Beers list during 1993-2005 or a drug used to treat conditions similar to the indications for prescribing these PIMs. Of these, 187,616 (76.4%) had actually been prescribed a PIM, and 120,332 (49.0%) had hospital admissions that met the criteria for inclusion as 'index subjects'.

Table 1 summarizes overall study results for both high-care nursing home residents and other elderly. Overall, 383,150 unplanned admissions ('index subjects') were included, 20,525 (5.4%) of which involved high-care nursing home residents. The proportion of male index subjects was much lower, the mean age higher, and the proportion exposed to a PIM at the time of admission higher in the high-level aged care group than in other WA elderly. For a detailed comparison between the two groups regarding exposure to specific PIMs upon admission, please refer to Table 2.

Exposure to a PIM was associated with a significant increase in unplanned hospitalizations in both groups. Unadjusted results suggested a lower relative risk of PIM-related unplanned hospitalization in the high-care group. However,

after adjusting for patients' health profile and medication intake over time, this difference was no longer evident (adjusted OR 1.21 (1.10-1.34) versus 1.19; (1.16-1.21)). Corresponding estimates of the proportion of unplanned hospitalizations attributed to PIMs in exposed index subjects were also similar in both groups (Table 1).

The relative risk of unplanned hospitalization also rose in a similar manner in both groups with increasing counts of different PIMs taken over three months, ORs for both suggesting a risk in those taking 10 different PIMs 5.1 times that of PIM-unexposed counterparts (Figure 1). However, high-care nursing home residents seemed affected to a greater extent by increasing PIM quantities than other elderly. For instance, high-level aged care residents taking 900 PIM daily doses over three months had a relative risk of unplanned hospitalization 4.85 (2.40-9.83) times that of high-care residents unexposed to PIMs, whereas the corresponding OR in other elderly was 2.10 (1.73-2.55) (Figure 2).

Finally, nursing home residents receiving high-level care not only had higher overall rates of unplanned hospitalizations and of unplanned hospitalizations while exposed to PIMs than other WA elderly, they also had considerably higher rates of unplanned hospital admissions attributed to PIM exposure (3,951 versus 1,394 per 100,000 person-years) (Figure 3).

## **Discussion**

This study examined the association between PIM exposure and unplanned hospitalizations in a large WA population aged  $\geq 65$  years, comparing high-care nursing home residents with all other elderly people. Data linkage facilitated the establishment of a fairly comprehensive health profile for each individual, permitted extensive cross-validation of demographic details, and allowed the ascertainment of patients' drug exposure status upon admission.

### ***Major findings***

After adjusting for confounding factors (including health and medication profiles), the association between exposure to general Beers medications and unplanned hospitalizations was similar in both the high-care nursing home

residents and other WA elderly. Our adjusted ORs for both groups suggested a likely increase in unplanned admissions around 20% in subjects exposed to PIMs. These results were similar to or slightly lower than those obtained in other comparable studies involving older people in nursing home (OR 1.27)<sup>24</sup> and community settings (OR range 1.62-1.78).<sup>25-27</sup> From our ORs, we deduced that 17.5% (8.9-25.2%) of unplanned hospitalizations in high-care nursing home residents were attributed to PIMs in exposed subjects, and 15.7% (13.7-17.6%) in other elderly.

Our results also suggested that the likelihood of unplanned hospitalization increases with the number of different PIMs and overall PIM quantity taken, in both groups of elderly. This is not surprising, given that polypharmacy and high medication intake are linked to an increased risk of adverse drug events.<sup>1-3</sup> In both groups, the risk of unplanned hospitalization increased five-fold when taking 10 different PIMs compared to none. However, the impact of PIM quantity on unplanned hospitalizations in nursing home residents seemed to be greater than in other elderly. For example, high-level aged care residents taking the equivalent of ten average daily doses of PIMs every day over three months (~900 daily doses) appeared to have nearly five times the risk of unplanned hospitalization of PIM-unexposed nursing home residents, whereas a similar comparison in other elderly yielded only a two-fold risk increase. One may speculate that perhaps nursing home residents were particularly sensitive to higher doses of PIMs due to their increased levels of physiological deterioration, which increased their susceptibility to adverse drug effects when taking high doses. More in-depth investigations beyond the scope of our study would be required to gain a better understanding of this apparent difference.

Despite similar overall relative risks of PIM-related unplanned hospitalizations in both groups of elderly, high-care nursing home residents had substantially higher rates of unplanned hospitalizations attributed to PIMs than other older people. This is likely due to their poorer health and thus, greater requirement for medications (including PIMs) and susceptibility to hospitalization. Our nursing home subjects' much higher rates of unplanned admissions, overall and while exposed to PIMs, support this premise.

Given the much smaller size of the high care group, the expectation that exposure to most individual PIMs would be low, and limitations in resources, we concentrated on associations that were related to overall PIM exposure in this study. However, the PIM exposure statistics from Table 2 suggest that further comparative analysis may be warranted for some individual PIMs in future, especially temazepam (sedative), digoxin (cardiac glycoside), and oxazepam (anxiolytic). These PIMs were highly prevalent in our index population, especially in subjects who were high-care nursing home residents.

### ***Limitations***

Despite an extensive clean-up and cross-validation process, made possible through data linkage, our research was subject to some data quality and availability issues, as per other studies involving administrative health data. In particular, our PBS data had some coverage limitations. It excluded drugs prescribed in public hospitals, over-the-counter medications, and prescriptions for which a pharmaceutical claim could not be made.<sup>28</sup> However, in our elderly population, most of whom would have had very low co-payment requirements, these coverage issues unlikely impacted on study results to any great extent, as most non-hospital scripts for medications of interest would have been recorded in this age group.

Furthermore, difficulties in the ascertainment of drug exposure at the specific times of interest were of concern, as no information was available on the daily dose specifically prescribed for each dispensed drug. Much attention was devoted to the derivation of exposure status from average recommended daily doses, but this could not have been completely accurate for every subject. Assuming similar levels of exposure misclassification at both case and control times for each subject (i.e. non-differential measurement error), our estimated ORs may possibly have been attenuated slightly (i.e. pushed towards null) as a result.<sup>29</sup>

This OR attenuation may, however, have been counter-balanced to some extent by an opposite effect stemming from residual time trend bias related to the case-time-control design.<sup>18,19,30</sup> To address this problem, we adjusted for

each subject's health status and overall drug consumption over time using a number of relevant variables, in addition to the inclusion of matched reference subjects. Our prior work suggests that this approach improves internal validity.<sup>31</sup> Nonetheless, data limitations may have prevented us from fully adjusting for time-dependent confounders.

We also acknowledge that the aged care status criteria used to match index and reference subjects were imperfect. Since this variable changed over time, we used people's status at 30 June of the index admission year for matching purposes. Although we did control further in the analysis for aged care status at the specific case and control times, our results may have been affected slightly by associated misclassification.

### ***Conclusions***

Our study not only provides further evidence in support of an increased risk of serious harm resulting from exposure to Beers medications in older people, but also refutes the hypothesis that high-level aged care residents have a higher relative risk of unplanned hospitalization in relation to PIM exposure than other elderly people. However, high-care nursing home residents appear to have a substantially higher rate of unplanned hospitalizations attributed to PIMs than other elderly, likely due to their frailty and predisposition to both medication exposure and hospitalization. Given an apparent 20% increase in unplanned hospitalizations among PIM elderly users residing in nursing homes and elsewhere, physicians should continue to exert caution when prescribing Beers medications in all patients aged  $\geq 65$  years, restricting the number of different PIMs and PIM quantity prescribed whenever possible.

**Acknowledgments**

We thank the Australian National Health and Medical Research Council for funding the research; the Western Australian Department of Health (DoH) and Australian Department of Health and Ageing for supplying the project data; and the Data Linkage Branch (DoH) for undertaking the record linkage.

**Disclosure statement**

No potential conflicts of interest were disclosed.

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## Figure legends

**Figure 1.** Potentially inappropriate medications (PIMS) in Western Australians aged  $\geq 65$  years (1993-2005)<sup>†</sup>: association between number of different PIMS taken<sup>‡</sup> and unplanned hospitalizations (adjusted odds ratios and 95% confidence intervals) in high-level aged care residents versus other elderly<sup>§</sup>

<sup>†</sup> Although the study period covered 1993-2005 in this population, index cases related to unplanned hospital admissions between July 1994 and December 2005 only, in patients aged  $\geq 67$  years upon admission; these additional constraints were required to ensure sufficient lead-up time for the control observation period.

<sup>‡</sup> Number of different PIMs taken was determined based on drug consumption during the three-month period preceding the case and control times (including the case/control dates).

<sup>§</sup> High care subjects were those who were receiving high-level aged care services in a nursing home at 30 June of the index admission year; other subjects included all other elderly (i.e. those receiving low-level hostel or community aged care services and those living in a private home without any aged care support at that time).

**Figure 2.** Potentially inappropriate medications (PIMS) in Western Australians aged  $\geq 65$  years (1993-2005)<sup>†</sup>: association between three-month PIM consumption<sup>‡</sup> and unplanned hospitalizations (adjusted odds ratios and 95% confidence intervals) in high-level aged care residents versus other elderly<sup>§</sup>

<sup>†</sup> Although the study period covered 1993-2005 in this population, index cases related to unplanned hospital admissions between July 1994 and December 2005 only, in patients aged  $\geq 67$  years upon admission; these additional constraints were required to ensure sufficient lead-up time for the control observation period.

<sup>‡</sup> PIM consumption was determined based on total count of daily doses taken during the three-month period preceding the case and control times (including the case/control dates) Each daily dose represented exposure to one medication for one day, where the quantity taken was the average dose recommended per day, based on drug form, route and strength.

<sup>§</sup> High-level aged care residents were those who were receiving high-care services in a nursing home at 30 June of the index admission year; other elderly included all other subjects (i.e. those receiving low-level hostel or community aged care services and those living in a private home without any aged care support at that time).

**Figure 3.** Potentially inappropriate medications (PIMS) in Western Australians aged  $\geq 67$  years (July 1994-December 2005)<sup>†</sup>: estimates of unplanned hospital admissions per 100,000 person-years in high-level aged care residents versus other elderly<sup>‡</sup>, broken down by PIM exposure status

<sup>†</sup> Although the study period covered 1993-2005 in a population aged  $\geq 65$  years, index cases related to unplanned hospital admissions between July 1994 and December 2005 in patients aged  $\geq 67$  years upon admission, to ensure sufficient lead-up time for the control observation period. Consequently, rates were calculated for this time period and age group.

<sup>‡</sup> High care subjects were those who were receiving high-level aged care services in a nursing home at 30 June of each calendar year; other subjects included all other elderly (i.e. those receiving low-level hostel or community aged care services and those living in a private home without any aged care support at that time).

## Tables

**Table 1. Potentially inappropriate medications (PIMs) in Western Australians aged  $\geq 65$  years (1993-2005)<sup>†</sup>: association between exposure to any PIM and unplanned hospitalizations in high-level aged care residents versus other elderly**

Statistics	High-level aged care status <sup>‡</sup>	
	High care	Other
Number of index subjects (i.e. unplanned admission cases)	20,525	362,625
Number/proportion of male index subjects	6,893 (33.6%)	167,560 (46.2%)
Index subjects' mean age at admission (years) <sup>¶</sup>	83.5 (83.4-83.6)	78.1 (78.0-78.1)
Number of exposed index subjects (Exp Idx) & proportion <sup>§</sup>	10,336 (52.9%)	138,953 (38.3%)
Unadjusted odds ratio (Unadj OR) <sup>¶</sup>	1.19 (1.11-1.28)	1.33 (1.30-1.35)
Unadjusted odds ratio p-value	<0.001	<0.001
Adjusted odds ratio (OR) <sup>¶</sup>	1.21 (1.10-1.34)	1.19 (1.16-1.21)
Adjusted odds ratio p-value	<0.001	<0.001
Attributable fraction: AF = (OR-1) / OR (%) <sup>¶</sup>	17.5% (8.9-25.2%)	15.7% (13.7-17.6%)
Estimate of index admissions attributed to PIM (AF x Exp Idx) <sup>¶</sup>	1,808 (923-2,605)	21,792 (19,063-24,494)

<sup>†</sup> Although the study period covered 1993-2005 in this population, index cases related to unplanned hospital admissions between July 1994 and December 2005 only, in patients aged  $\geq 67$  years upon admission; these additional constraints were required to ensure sufficient lead-up time for the control observation period.

<sup>‡</sup> High care subjects were those who were receiving high-level aged care services in a nursing home at 30 June of the index admission year; other subjects included all other elderly (i.e. those receiving low-level hostel or community aged care services and those living in a private home without any aged care support at that time).

<sup>§</sup> Exposed index subjects were those who were taking  $\geq 1$  PIM immediately prior to hospital admission.

<sup>¶</sup> 95% confidence interval shown in parentheses.

**Table 2. Potentially inappropriate medications (PIMs) in Western Australians aged  $\geq 65$  years (1993-2005)<sup>†</sup>: number and proportion of index subjects exposed to individual PIMs<sup>‡</sup> immediately prior to hospital admission by high-level residential aged care status**

Medication class	PIM	High-level aged care status <sup>§</sup>	
		High care (n=20,525)	Other (n=362,625)
Antirheumatics	Indomethacin	88 (0.4%)	3,587 (1.0%)
	Naproxen	240 (1.2%)	6,501 (1.8%)
	Piroxicam	182 (0.9%)	5,305 (1.5%)
Analgesics	Dextropropoxyphene	8 (<0.1%)	203 (0.1%)
	Meperidine/pethidine	17 (0.1%)	151 (<0.1%)
Antihistamines (systemic)	Cyproheptadine	110 (0.5%)	1,382 (0.4%)
	Promethazine	45 (0.2%)	841 (0.2%)
Antipsychotics	Thioridazine	235 (1.1%)	823 (0.2%)
Anxiolytics, hypnotics/sedatives	Oxazepam	1,391 (6.8%)	13,597 (3.7%)
	Alprazolam	53 (0.3%)	1,176 (0.3%)
	Diazepam	787 (3.8%)	10,176 (2.8%)
Antidepressants	Temazepam	4,767 (23.2%)	40,268 (11.1%)
	Amitriptyline	501 (2.4%)	8,421 (2.3%)
	Doxepin	214 (1.0%)	4,744 (1.3%)
Cardiac rhythm regulators	Fluoxetine	304 (1.5%)	2,566 (0.7%)
	Digoxin	2,009 (9.8%)	32,113 (8.9%)
	Amiodarone	439 (2.1%)	11,193 (3.1%)
Hypertension drugs	Methyldopa	42 (0.2%)	1,996 (0.6%)
	Nifedipine	329 (1.6%)	11,370 (3.1%)
	Clonidine	13 (0.1%)	248 (0.1%)
High ceiling diuretics	Ethacrinic acid	9 (<0.1%)	218 (0.1%)
Antithrombotics	Dipyridamole	325 (1.6%)	3,223 (0.9%)
Iron preparations	Ferrous sulphate	995 (4.8%)	10,264 (2.8%)
Peptic ulcer/GORD <sup>¶</sup> drugs	Cimetidine	118 (0.6%)	2,871 (0.8%)
Laxatives	Bisacodyl	688 (3.4%)	3,817 (1.1%)
Bowel disorder drugs/ belladonna & derivatives	Belladonna alkaloids	32 (0.2%)	474 (0.1%)
	Propantheline	112 (0.5%)	975 (0.3%)
Urinary antispasmodics	Oxybutynin	350 (1.7%)	3,147 (0.9%)
Urinary tract antibacterials	Nitrofurantoin	237 (1.2%)	1,743 (0.5%)
Oestrogens <sup>‡</sup>	Oestrogens-all	169 (0.8%)	7,302 (2.0%)

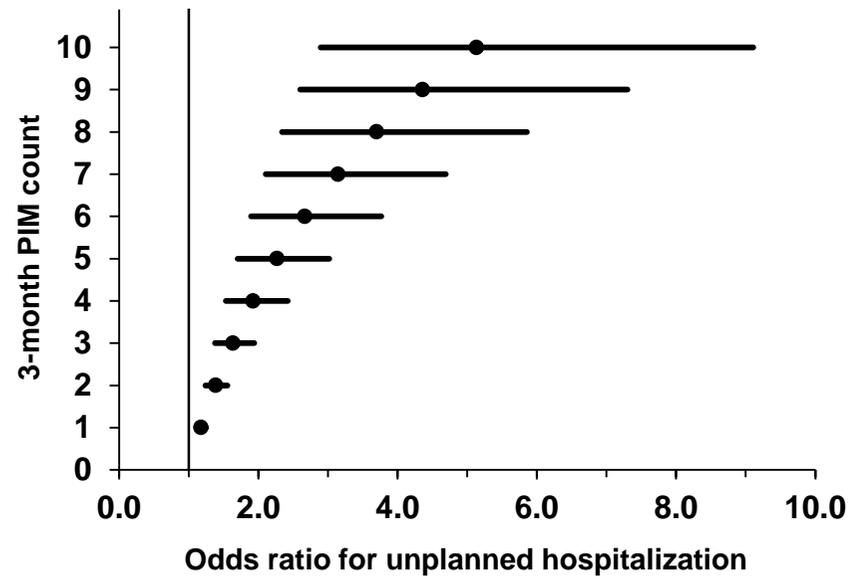
<sup>†</sup> Although the study period covered 1993-2005 in this population, index cases related to unplanned hospital admissions between July 1994 and December 2005 only, in patients aged  $\geq 67$  years upon admission; these additional constraints were required to ensure sufficient lead-up time for the control observation period.

‡ Forty-three PIMs were included in the study. However, the six oestrogens (ethinyloestradiol, oestradiol, oestriol, oestrone, conjugated oestrogens and fosfestriol sodium) are combined into one entry in this table and the following PIMs are omitted: orphenadrine, diphenhydramine, hydroxyzine, dexamphetamine, disopyramide, ticlopidine, chlorpropamide, and dicyclomine. This was required due to low cell counts, in order to protect patient confidentiality.

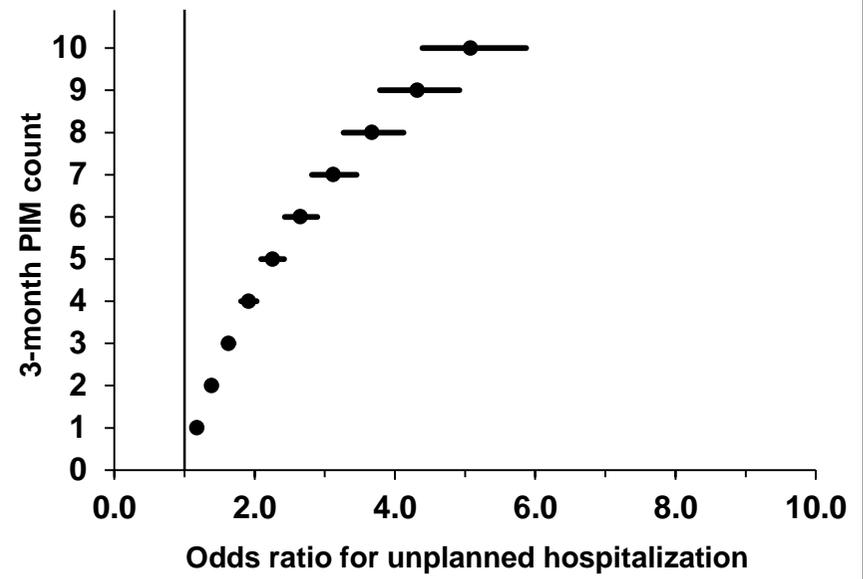
§ High care subjects were those who were receiving high-level aged care services in a nursing home at 30 June of the index admission year; other subjects included all other elderly (i.e. those receiving low-level hostel or community aged care services and those living in a private home without any aged care support at that time).

¶ GORD refers to gastro-oesophageal reflux disease.

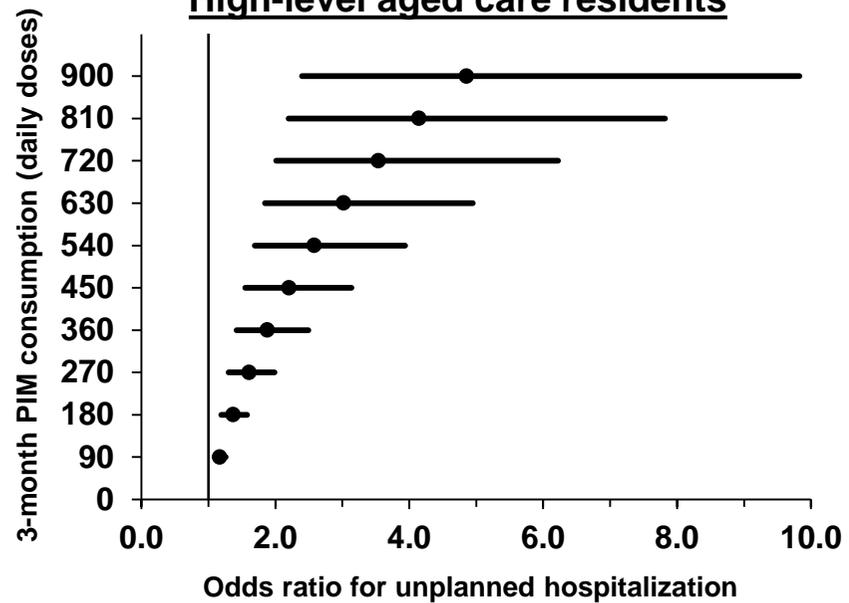
### High-level aged care residents



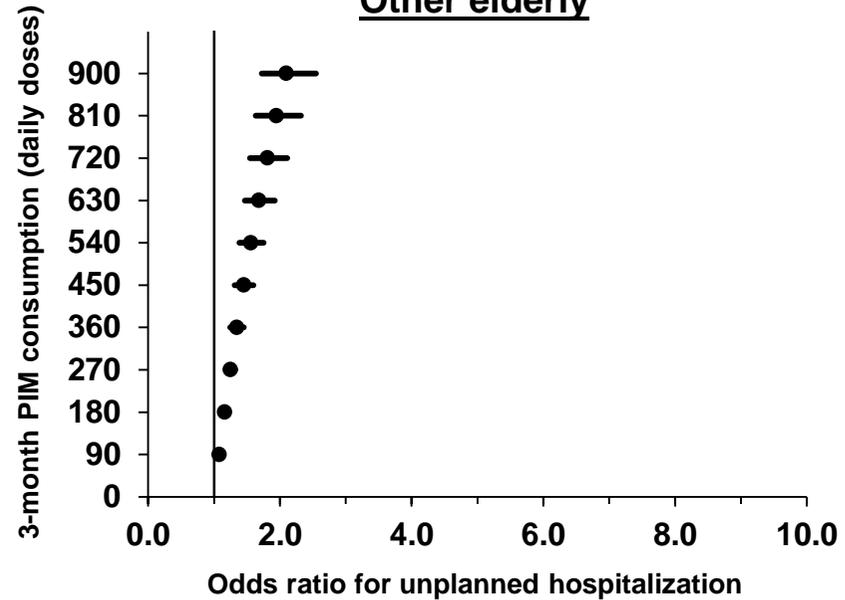
### Other elderly



### High-level aged care residents



### Other elderly



High-level aged care status

High care

3 951 (8.8%)

18 636 (41.5%)

22 265 (49.6%)

Other

1 394 (6.0%)

7 495 (32.3%)

14 310 (61.7%)

0 5 000 10 000 15 000 20 000 25 000 30 000 35 000 40 000 45 000

Annual estimates of unplanned hospital admissions per 100 000 persons aged  $\geq 67$  years

■ Exposed - admission attributed to PIM ■ Exposed - admission not attributed to PIM □ Unexposed to PIMs at time of admission

