

Does ongoing GP care in elderly patients help reduce the risk of unplanned hospitalization related to Beers potentially inappropriate medications?

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Abstract

Aim: To compare estimates of unplanned hospitalizations associated with exposure to Beers potentially inappropriate medications (PIMs) in elderly people receiving different levels of ongoing general practitioner (GP) care.

Methods: Using the pharmaceutical claims and other linked health data of 245,436 Western Australians aged ≥ 65 years with ≥ 1 claim for a medication from a PIM-related drug class (1993-2005), we applied an enhanced case-time-control design to obtain odds ratios (ORs) for unplanned hospitalization, from which attributable fractions, numbers, proportions and rates of admissions related to PIM exposure were derived.

Results: Overall, 383,150 unplanned hospitalizations ('index subjects') were identified. PIM exposure was associated with a similar relative risk of unplanned hospitalization in elderly people receiving the lowest and highest levels of ongoing GP care, but with a decreasing risk in the three highest tiers; adjusted ORs (95% CIs; attributable fractions) were 1.15 (1.09-1.21; 12.9%), 1.36 (1.27-1.46; 26.6%), 1.20 (1.15-1.26; 16.9%) and 1.13 (1.09-1.17; 11.4%), for groups from the lowest to highest levels. However, those with higher GP coverage had higher rates of PIM-related hospitalization. Similar patterns were demonstrated for commonly used high-risk PIMs (temazepam, diazepam, oxazepam, naproxen and digoxin).

Conclusions: Increased requirement for ongoing GP contact in less healthy elderly people appears to help minimize their risk of unplanned hospitalization due to PIM-related harm. GPs should continue to avoid Beers medications in older patients where possible, given their greater predisposition to medication exposure (including PIMs) and adverse drug events. Nonetheless, close monitoring of elderly patients who need to use PIMs should prove beneficial.

Key words: Aged, general practice, hospitalization, inappropriate prescribing, pharmacoepidemiology

Introduction

The prescribing of medications in older people is very complex due to physiological deterioration, multiple comorbidities, polypharmacy, and other age-related factors. As a result, elderly patients are more susceptible to inappropriate drug use and adverse drug events.¹ This susceptibility has led to the development of lists of 'potentially inappropriate medications' (PIMs) to be avoided in the elderly, such as the Beers Criteria.²

Numerous studies have examined the prevalence of drugs from the Beers list in elderly populations, while others have concentrated on the association between Beers medications and adverse health outcomes. For example, our own previous work in this field suggests that Western Australians aged ≥ 65 years were prescribed 6-7 different types of drugs annually (on average) during 1993-2005 and that 40-47% were exposed to Beers medications every year.³ Furthermore, older people were 18% more likely to have an unplanned hospitalization when exposed to these drugs.⁴

To our knowledge, no one has compared the risk of PIM-related adverse outcomes in older patients receiving varying levels of ongoing general practitioner (GP) care. Older patients who see their GP very regularly may often do so because of declining health, which is associated with increased medication use (including PIMs) and susceptibility to hospitalization. Conversely, extensive GP follow-up might also protect these patients from serious harm due to PIM exposure, through close monitoring for adverse drug effects.¹

In Australia, quality, safety and efficacy of medications is regulated through the Therapeutic Goods Administration (TGA). However, most therapeutic drugs prescribed outside public hospitals are accessed through the Pharmaceutical Benefits Scheme (PBS), a government-subsidized universal system of pharmaceutical provision established in 1950.^{5,6} Although a maximum number of allowable repeat prescriptions is specified for each therapeutic item listed on the PBS, multiple repeats covering up to 4-6 months of therapy are permissible for most medications used in the treatment of chronic conditions.⁷ Furthermore,

no specific list of medications considered potentially inappropriate in the elderly has been endorsed nationwide. Medical practitioners (including GPs) prescribe medications according to TGA and PBS regulations, but must use their own judgment to minimize the risk of adverse drug events, through appropriate prescribing and adequate patient monitoring.

In this large linked-data study (1993-2005), we compared estimates of unplanned hospitalizations associated with exposure to Beers medications in Western Australian (WA) residents aged ≥ 65 years receiving different levels of ongoing GP care. We present our results for all PIMs from the general Beers list (combined) and for individual high-risk PIMs most commonly used in this population.

Methods

Selection criteria and data preparation

This study linked Australian PBS,⁵⁻⁷ Medicare⁸ and residential aged care⁹ data with inpatient, death and electoral roll records from the WA Data Linkage System¹⁰ through probabilistic linkage. The study protocol was approved by The University of WA's Human Research Ethics Committee.

The study methodology has been described elsewhere.^{4,11} To summarize, the cohort consisted of people who were ≥ 65 years old by the end of 2004, continuously lived in WA during 1993-2005 (until death) and had ≥ 1 pharmaceutical claim during that time. About 80-85% of WA elderly residents were captured annually.

Details for all PBS drug items were assembled into a large reference database, which included 2007 Anatomical Therapeutic Chemical (ATC) codes,¹² average daily doses ascertained from three sources,¹³⁻¹⁵ and period of drug effect (defined as five times the drug's elimination half-life).^{16,17} This information was merged to the PBS master file for 1993-2005.

Each item from the 2003 Beers list² was then defined according to the 2007 ATC classification,¹² and the ATC code list for 'general' PIMs (i.e. excluding disease-specific criteria, but including PIMs with dosage and duration

constraints) applied to the PBS dataset. Forty-three individual PIMs were identified through this process and 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

Associations between PIM exposure and unplanned hospitalizations were expressed as odds ratios (ORs) obtained from a case-time-control design.^{18,19} Hence, identified index subjects acted both as cases and as their own historical controls, while background time trends in exposure were adjusted using matched reference subjects drawn from the same drug-defined patient domain as the index subjects.

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 ≥ 67 years, thus ensuring sufficient lead-up time for the control observation period. Individuals could be included multiple times as index subjects, but patients with >50 index admissions ($\leq 0.1\%$) were excluded. Each index subject was matched by gender, overall 'GP coverage' category and year of birth to a randomly selected reference subject from the drug-defined domain. To determine the level of GP coverage, each GP visit identified in the Medicare dataset was allocated a 'coverage' period of 61 days (adjacent and overlapping periods being merged together), from which overall and annual coverage proportions were calculated. Derived quartiles helped define GP coverage categories, which provided a general indicator of ongoing GP monitoring for each patient.

For each index and reference subject, 'case-time' and 'control-time' records were created, where the case time was the index subject's admission date and the control time usually 365 days prior. If the preferred times were within a hospital stay, the admission date of the overlapping hospitalization was used instead. These records included nursing home status at the specified time; hospital days, overall Charlson comorbidity index²⁰ and 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 daily dose count for each broad drug category. Additionally, PBS claims were checked to ascertain the PIM exposure status, which was set to 'exposed' if the period bound by the supply date and exposure effect end date for a relevant prescription overlapped with the case or control time. The end date was calculated by adding the number of drug consumption days associated with the script to the supply date (-1) plus the period of drug effect (up to 7 days) and a 7-day latency period.

For each PIM sub-study, conditional logistic regression models with robust analysis of variance (COVS option) were applied using the SAS 9.2 PHREG procedure. The OR of primary interest was derived from the coefficient of the cross-product between exposure and the binary index/reference indicator,¹⁸ adjusted models controlling for all health and drug consumption indicators mentioned earlier. This analysis was performed separately for each GP coverage group, and repeated for all PIMs combined and for individual PIMs.

Estimation of PIM-related unplanned hospitalizations

Using the OR derived from the interaction term in the adjusted models described above, we calculated the attributable fraction (AF) of unplanned hospitalizations associated with PIMs of interest within the exposed, where $AF = (OR - 1) / OR$. An estimate of the number of unplanned hospitalizations attributed to PIMs was then derived as $AF \times \text{number of exposed index subjects}$.²¹

To further compare the unplanned hospitalization outcomes in different GP coverage groups, crude rates were estimated. This was achieved by first generating the study cohort's person-year follow-up time for each GP coverage group, including those with a predominant age ≥ 67 years for each calendar 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 hospitalizations attributed to PIMs in exposed patients;

those not attributed to PIMs in the exposed; and those occurring in unexposed patients.

Results

From an initial cohort of 251,305 participants, 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. They comprised the patient domain for this study. Of these, 187,616 (76.4%) had actually been prescribed a PIM.

Overall, 383,150 unplanned admissions ('index subjects') were included, which involved 120,332 patients. Although the number of participants in each GP coverage group loosely reflected a quartile distribution, those in the highest level of GP care were clearly over-represented in terms of number of unplanned admissions, reflecting their likely poorer health. The proportion of male index subjects decreased considerably with increasing GP coverage (from 62.4% to 35.8%), although the mean age was around the overall average of 78 years in all groups. The proportion of subjects exposed to a PIM at the time of admission was similar for the lowest and third tier of GP coverage (~34%), but increased from 28.3% to 48.6% in the three highest tiers (Table 1).

For the health and drug intake profiles of index subjects in each GP coverage group (at case and control times), please refer to Table 2. This information suggests a trend of declining health over time in all groups. It also reveals rising levels of health care service and medication use with increasing GP care for the three highest tiers of GP coverage. Levels for the lowest GP coverage tier deviated from this pattern though, generally being much higher than expected for that group.

Similar patterns were detected for corresponding reference subjects (statistics not shown). However, since most reference subjects were not hospitalized at case time, they were less likely to have accessed health care services or taken medication than their index counterparts. All of this was expected, and demonstrates the need to include known time-dependent variables representing potential confounders in regression analysis models, where possible, thus

reserving the inclusion of reference subjects for the additional adjustment of time trends associated with unknown time-dependent factors.

Exposure to a PIM was associated with a significant increase in unplanned hospitalizations in all groups. Furthermore, a decreasing OR trend was apparent in the three highest tiers of GP coverage, both before and after adjustment for patients' health profile and medication intake over time. For the lowest GP coverage tier, the adjusted OR was similar to that of the highest tier (Table 1/Figure 1).

Corresponding estimates of the proportion of unplanned hospitalizations attributed to PIMs in exposed index subjects followed a similar pattern to the one described for ORs. However, despite their lower relative risk, those in the upper tier of GP coverage were associated with the highest estimates of unplanned hospitalizations attributable to PIM exposure.

The patterns described above applied to both males and females independently, as well as overall. Additionally, results for the individual high-risk PIMs most commonly used in our population (e.g. temazepam, diazepam, oxazepam, naproxen and digoxin) mirrored those presented for overall PIM exposure (Table 3).

In terms of unplanned hospitalization rates (Figure 2), the lowest tier of GP coverage had the lowest number and proportion of unplanned hospitalizations attributed to PIMs annually. For the other three groups, the annual count of PIM-related admissions rose, but the proportion fell with increasing levels of GP coverage.

Discussion

This study applied a case-time-control design to linked health data from a large WA elderly population to compare the association between Beers medications and unplanned hospitalizations in elderly people with different levels of ongoing GP care. No other study has specifically concentrated on differences between groups with varying patterns of GP contact in relation to PIMs and adverse health outcomes. A strength of our study is its large sample sizes, which

produced narrow confidence intervals even for individual GP coverage groups. Furthermore, our study applied three levels of defence against confounding: a crossover configuration to control for fixed confounders; matched reference subjects to control for unmeasured time-variant confounders; and regression modelling to adjust for measured patient-specific time-variant confounders (e.g. general health and drug consumption indicators).

Major findings

PIM exposure was associated with an increased risk of unplanned hospitalizations at all levels of GP coverage. Our adjusted ORs, which estimated a 13-36% increase in unplanned hospitalizations in elderly people exposed to Beers' PIMs (depending upon the GP coverage group), were similar to or slightly lower than those obtained in other comparable studies in a community setting (OR range 1.27-1.78).²²⁻²⁵ From these ORs, we deduced that 11.4-26.6% of unplanned hospitalizations were attributed to PIMs in exposed subjects.

The relative risk of unplanned admission associated with PIM exposure decreased in elderly people with increasingly higher levels of GP coverage, suggesting that better ongoing GP monitoring may have a protective effect against PIM-related hospitalizations. However, because of the rising levels of PIM use and unplanned hospitalization in older patients receiving increasing levels of ongoing GP care (see Tables 1 and 2), likely due to declining health, the absolute burden of hospitalizations attributed to PIMs increased with each higher tier of GP coverage.

This pattern did not apply to elderly people with the lowest level of ongoing GP care though. People in this group had a higher than expected level of PIM use and unplanned hospitalization, but a low relative risk of hospitalization associated with PIM exposure. We suspect this GP coverage group may have consisted of a heterogeneous elderly population, one possibly involving two distinct sub-groups. One sub-group likely included fairly healthy elderly, with low exposure to medication overall, few hospital admissions, and a low need for frequent GP contact. Because of their good physiological condition, they were

probably less prone to potential harm from PIMs. Consequently, they would get minimal benefit from the protective effect of frequent GP visits against PIM-related hospitalizations, even though physicians might be less cautious in prescribing PIMs to them.

The other sub-group would have been less healthy, with high levels of medication use and unplanned hospitalizations, which would explain the inflated rate of unplanned hospitalization for the group as a whole. Despite benefitting from ongoing GP monitoring, this second sub-group may have experienced fewer GP visits due to various health care access issues. Elderly people from this sub-group were likely at high risk of PIM-related hospitalization (for those taking PIMs), this fact being masked in our group-level results by the healthy sub-group's much lower relative risk. Alternatively, some older people from this sub-group may have paid regular visits to a specialist physician rather than a GP (thus benefitting from ongoing medical practitioner monitoring despite their allocation to a low-level GP coverage category), which may also partially account for the low relative risk of PIM-related hospitalization in the lowest GP coverage tier.

These explanations are in line with our other results, which support a decline in the relative risk of unplanned hospitalization with increasing GP coverage in relation to PIM exposure. Unfortunately, data and resource limitations have prevented us from exploring these theories any further.

Our study also suggests that GP coverage patterns related to unplanned hospitalizations and overall PIM exposure likely apply to individual PIMs as well. This was apparent for several commonly used high-risk PIMs, including various benzodiazepines, naproxen and digoxin. Admittedly, OR confidence intervals between adjacent GP coverage groups overlapped to a greater degree for individual PIMs. Thus, additional research is required to confirm these results.

Limitations

Despite the rigorous measures applied in this study to control for confounding effects, we are mindful of the potential for time-trend bias, which has been associated with the case-time-control design in some circumstances.^{18,19,26}

Although sensitivity and other comparative analyses applied in our earlier work suggest that our approach is fairly robust,¹¹ some residual confounding is likely reflected in our results, given the limitations of our administrative data.

Difficulties in the ascertainment of drug exposure at the specific times of interest were also of concern, as derivation of exposure status from average recommended daily doses could not have been completely accurate for every subject. Assuming non-differential measurement error at both case and control time for each subject, our estimated ORs may possibly have been attenuated slightly (i.e. pushed towards null) as a result,²⁷ perhaps counter-balancing some of the potential OR inflation stemming from unadjusted time-trend bias.

Furthermore, our PBS datasets did have coverage limitations, excluding drugs prescribed in public hospitals, over-the-counter medications, and prescriptions for which a claim could not be made.²⁸ However, given the very low co-payment thresholds in most elderly people, these coverage issues unlikely had much impact on study results.

We also acknowledge that our grouping of elderly people according to level of ongoing GP care were not perfect. As already mentioned, it appears people with the lowest level of GP coverage may have been a hybrid group. Furthermore, we used patients' overall average GP coverage percentages for grouping and matching purposes. Although we did control further in the analysis for GP coverage in the year immediately preceding the case and control times, our results may have been affected slightly by potential misclassification in the allocation of subjects to the appropriate GP coverage group.

Conclusions

Our study provides further evidence in support of an elevated risk of serious harm resulting from exposure to Beers medications in older people, suggesting that this risk is evident in most elderly, with some variations depending upon their level of ongoing GP care. Older people may choose to visit their GP more regularly because of their declining health but, thankfully, persistent continuity of

care in elderly patients who need it most appears to help minimize their risk of greater medication-related harm.

Physicians should continue to avoid Beers medications in the elderly where possible, especially in less healthy older patients, due to the latter's greater predisposition to medication exposure (including PIMs) and adverse drug events. However, in situations where PIM use is judged to be clinically appropriate, close monitoring in older patients should prove beneficial.

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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 ≥ 65 years (1993-2005):[†] association between PIM exposure and unplanned hospitalizations (adjusted[‡] odds ratios and 95% confidence intervals) for groups with varying levels of general practitioner coverage[§]

[†] 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 ≥ 67 years upon admission; these additional constraints were required to ensure sufficient lead-up time for the control observation period.

[‡] Conditional logistic regression models were adjusted for the following time-dependent variables: nursing home status at the case or control time; hospital days, overall Charlson comorbidity index²⁰ and 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.

[§] Average annual general practitioner (GP) coverage was obtained from patients' proportion of GP coverage over 1993-2005, where each GP visit was allocated a 61-day coverage period (adjacent and overlapping periods being merged together). GP coverage categories were then derived from approximate quartiles, providing a general indicator for the level of ongoing GP monitoring.

Figure 2. Potentially inappropriate medications (PIMs) in Western Australians aged ≥ 67 years (July 1994-December 2005):[†] estimates of unplanned hospital admissions per 100,000 person-years for groups with varying levels of general practitioner coverage,[‡] broken down by PIM exposure status

[†] Although the study period covered 1993-2005 in a population aged ≥ 65 years, index cases related to unplanned hospital admissions between July 1994 and December 2005 in patients aged ≥ 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.

[‡] Average annual general practitioner (GP) coverage was obtained from patients' proportion of GP coverage over 1993-2005, where each GP visit was allocated a 61-day coverage period (adjacent and overlapping periods merged together). GP coverage categories were then derived from approximate quartiles, providing a general indicator for the level of ongoing GP monitoring.

Tables

Table 1. Potentially inappropriate medications (PIMs) in Western Australians aged ≥ 65 years (1993-2005):[†] association between exposure to any PIM and unplanned hospitalizations for groups with varying levels of general practitioner coverage

Statistics	Average annual general practitioner coverage ^{††} (1993-2005)				
	0-6 months	>6-8 months	>8-10 months	>10 months	Overall
Domain participants [‡] (number of people in PIM study cohort)	67,553	50,122	59,645	68,116	245,436
Number/proportion of participants contributing as index subjects	30,140 (44.6%)	20,051 (40.0%)	29,576 (49.6%)	40,565 (59.6%)	120,332 (49.0%)
Number of index subjects (i.e. unplanned admission cases)	92,397	52,324	87,070	151,359	383,150
Number/proportion of male index subjects	57,662 (62.4%)	25,189 (48.1%)	37,454 (43.0%)	54,148 (35.8%)	174,453 (45.5%)
Index subjects' mean age at admission (years)	78.7	77.6	77.9	78.6	78.4
Number of index subjects exposed to PIMs (Exp Idx) & proportion	31,019 (33.6%)	14,789 (28.3%)	29,939 (34.4%)	73,542 (48.6%)	149,289 (39.0%)
Unadjusted odds ratio (Unadj OR) [§]	1.30 (1.24-1.36)	1.59 (1.50-1.69)	1.35 (1.29-1.41)	1.21 (1.18-1.25)	1.31 (1.28-1.33)
Unadjusted odds ratio p-value	<0.001	<0.001	<0.001	<0.001	<0.001
Adjusted [¶] odds ratio (OR) [§]	1.15 (1.09-1.21)	1.36 (1.27-1.46)	1.20 (1.15-1.26)	1.13 (1.09-1.17)	1.18 (1.15-1.21)
Adjusted odds ratio p-value	<0.001	<0.001	<0.001	<0.001	<0.001
Attributable fraction: AF = (OR-1) / OR (%) [§]	12.9% (8.3-17.2%)	26.6% (21.4-31.5%)	16.9% (13.0-20.8%)	11.4% (8.6-14.2%)	15.3% (13.3-17.1%)
Estimate of index admissions attributed to PIM (AF x Exp Idx) [§]	3,998 (2,587-5,320)	3,938 (3,172-4,653)	5,072 (3,883-6,215)	8,406 (6,317-10,414)	22,773 (19,922-25,500)

[†] 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 ≥ 67 years upon admission; these additional constraints were required to ensure sufficient lead-up time for the control observation period.

[‡] Domain participants were those who took medications used to treat similar conditions to those indicated for any of the PIMs included in the study (i.e. medications from the same broad drug classes); these people were considered to be part of the study's population at risk.

[§] 95% confidence interval shown in parentheses.

- ¶ Conditional logistic regression models were adjusted for the following time-dependent variables: nursing home status at the case or control time; hospital days, overall Charlson comorbidity index²⁰ and 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.
- †† Average annual general practitioner (GP) coverage was obtained from patients' proportion of GP coverage over 1993-2005, where each GP visit was allocated a 61-day coverage period (adjacent and overlapping periods being merged together). GP coverage categories were then derived from approximate quartiles, providing a general indicator for the level of ongoing GP monitoring.

Table 2. Potentially inappropriate medications (PIMs) in Western Australians aged ≥65 years (1993-2005):[†] Index subjects' health status and medication intake profiles at case time (admission date) and control time (one year prior to admission date) for groups with varying levels of general practitioner coverage

Health status/medication intake indicator	Average annual general practitioner coverage ^{ss} (1993-2005) ^{†††}				
	0-6 months	>6-8 months	>8-10 months	>10 months	Overall
High-level aged care at case time	3,917 (4.2%)	2,238 (4.3%)	4,458 (5.1%)	9,056 (6.0%)	19,669 (5.1%)
High-level aged care at control time	1,755 (1.9%)	1,016 (1.9%)	2,171 (2.5%)	4,795 (3.2%)	9,737 (2.5%)
Hospitalised in year prior to case time	60,061 (65.0%)	30,578 (58.4%)	54,063 (62.1%)	105,824 (69.9%)	250,526 (65.4%)
Hospitalised in year prior to control time	46,663 (50.5%)	22,346 (42.7%)	41,412 (47.6%)	87,856 (58.0%)	198,277 (51.7%)
Mean count of hospital days in year prior to case time	15.2 (15.1-15.4)	12.2 (11.9-12.4)	12.3 (12.1-12.5)	14.4 (14.3-14.5)	13.8 (13.7-13.9)
Mean count of hospital days in year prior to control time	8.8 (8.7-9.0)	6.7 (6.5-6.8)	7.0 (6.9-7.2)	9.1 (9.0-9.2)	8.2 (8.2-8.3)
Charlson index [‡] > 0 for year prior to case time (incl. case date)	64,132 (69.4%)	33,629 (64.3%)	58,870 (67.6%)	111,616 (73.7%)	268,247 (70.0%)
Charlson index [‡] > 0 for year prior to control time (incl. control date)	27,411 (29.7%)	11,989 (22.9%)	23,228 (26.7%)	54,485 (36.0%)	117,113 (30.6%)
Mean Charlson index [‡] for year prior to case time (incl. case date)	2.00 (1.98-2.02)	1.80 (1.78-1.82)	1.86 (1.84-1.87)	2.08 (2.07-2.09)	1.97 (1.97-1.98)
Mean Charlson index [‡] for year prior to control time (incl. control date)	0.71 (0.70-0.72)	0.54 (0.53-0.55)	0.62 (0.61-0.63)	0.85 (0.85-0.86)	0.72 (0.72-0.73)
Mean GP coverage % in year prior to case time [§]	22.6 (22.5-22.8)	65.4 (65.2-65.6)	80.5 (80.3-80.6)	94.3 (94.3-94.4)	69.9 (69.8-70.1)
Mean GP coverage % in year prior to control time [§]	24.8 (24.7-25.0)	68.0 (67.8-68.2)	81.9 (81.8-82.0)	94.6 (94.5-94.6)	71.3 (71.2-71.4)
Any PBS drug use [¶] in 90 days prior to case time (plus case date)	79,527 (86.1%)	45,943 (87.8%)	80,001 (91.9%)	143,234 (94.6%)	348,705 (91.0%)
Any PBS drug use [¶] in 90 days prior to control time (plus control date)	73,768 (79.8%)	42,950 (82.1%)	77,033 (88.5%)	140,932 (93.1%)	334,683 (87.4%)
Mean count of broad drug categories ^{††} in 90 days prior to case time	3.7 (3.7-3.7)	3.2 (3.2-3.2)	3.8 (3.8-3.8)	4.9 (4.9-4.9)	4.1 (4.1-4.1)
Mean count of broad drug categories ^{††} in 90 days prior to control time	3.2 (3.1-3.2)	2.6 (2.5-2.6)	3.2 (3.2-3.2)	4.4 (4.4-4.4)	3.6 (3.6-3.6)
Mean drug daily doses ^{††} in 90 days prior to case time	371.2 (368.8-373.7)	291.8 (289.3-294.3)	370.5 (368.4-372.6)	540.6 (538.5-542.7)	427.1 (425.9-428.3)
Mean drug daily doses ^{††} in 90 days prior to control time	325.5 (323.1-327.9)	241.5 (239.2-243.9)	316.9 (314.9-318.9)	490.8 (488.8-492.8)	377.4 (376.2-378.6)
Exposed to any PIM in 90 days prior to case time	40,778 (44.1%)	19,936 (38.1%)	39,957 (45.9%)	93,245 (61.6%)	193,916 (50.6%)
Exposed to any PIM in 90 days prior to control time	35,691 (38.6%)	16,393 (31.3%)	35,006 (40.2%)	87,628 (57.9%)	174,718 (45.6%)
Mean count of different PIMs in 90 days prior to case time	0.69 (0.68-0.70)	0.53 (0.53-0.54)	0.67 (0.66-0.67)	1.02 (1.01-1.03)	0.79 (0.79-0.80)
Mean count of different PIMs in 90 days prior to control time	0.59 (0.59-0.60)	0.42 (0.41-0.43)	0.56 (0.56-0.57)	0.93 (0.93-0.94)	0.70 (0.69-0.70)
Mean PIM daily doses ^{††} in 90 days prior to case time	40.4 (39.9-40.8)	30.1 (29.6-30.6)	38.4 (37.9-38.8)	64.4 (64.0-64.8)	48.0 (47.8-48.2)
Mean PIM daily doses ^{††} in 90 days prior to control time	36.8 (36.4-37.2)	25.4 (24.9-25.9)	34.4 (34.0-34.8)	61.5 (61.0-61.9)	44.4 (44.2-44.7)
Exposed to any PIM at case time	31,019 (33.6%)	14,789 (28.3%)	29,939 (34.4%)	73,542 (48.6%)	149,289 (39.0%)
Exposed to any PIM at control time	26,573 (28.8%)	11,715 (22.4%)	25,442 (29.2%)	67,980 (44.9%)	131,710 (34.4%)

- † 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 ≥ 67 years upon admission; these additional constraints were required to ensure sufficient lead-up time for the control observation period.
- ‡ Charlson comorbidity index was derived using methods described in *Quan et al, 2005*.²⁰
- § Percentage of general practitioner (GP) coverage was obtained from patients' proportion of GP coverage in the year prior to the case or control time, where each GP visit was allocated a 61-day coverage period (adjacent and overlapping periods being merged together).
- ¶ 'Any PBS drug use' indicates whether the patient took any medications for which a claim was recorded on the Australian Pharmaceutical Benefits Scheme in the specified period.
- †† 'Count of broad drug categories' refers to the number of broad drug classes (out of 22) included in the patient's medication regimen in the specified period.
- ‡‡ Average daily doses for each PBS drug item were determined based on information extracted from the following sources: average prescribed daily doses derived from the Australian Bettering the Evaluation and Care of Health (BEACH) general practice database;¹³ MIMS Australia's registered drug information;¹⁴ and the World Health Organization's Anatomical Therapeutic Chemical (ATC) defined daily doses (DDDs).¹⁵
- §§ Overall average annual general practitioner (GP) coverage was obtained from patients' proportion of GP coverage over 1993-2005, where each GP visit was allocated a 61-day coverage period (adjacent and overlapping periods being merged together). GP coverage categories were then derived from approximate quartiles, providing a general indicator for the level of ongoing GP monitoring.
- ¶¶ For all statistics, either the 95% confidence interval (for means) or percentage (%) is shown in parentheses.

Table 3. Potentially inappropriate medications (PIMs) in Western Australians aged ≥ 65 years (1993-2005):[†] association between exposure to individual PIMs and unplanned hospitalizations (adjusted[‡] odds ratios and 95% confidence intervals) for groups with varying levels of general practitioner coverage

PIM [§]	Average annual general practitioner coverage [¶] (1993-2005)				Overall
	0-6 months	>6-8 months	>8-10 months	>10 months	
Temazepam	1.27 (1.13-1.42)	1.44 (1.18-1.77)	1.39 (1.23-1.58)	1.23 (1.15-1.31)	1.27 (1.21-1.34)
Diazepam	1.23 (1.07-1.42)	1.67 (1.32-2.10)	1.51 (1.30-1.75)	1.15 (1.06-1.25)	1.26 (1.18-1.34)
Oxazepam	1.24 (1.08-1.43)	1.30 (1.02-1.65)	1.30 (1.12-1.51)	1.18 (1.09-1.28)	1.22 (1.15-1.30)
Naproxen	1.15 (0.99-1.33)	1.37 (1.11-1.68)	1.29 (1.11-1.48)	1.15 (1.04-1.27)	1.20 (1.12-1.29)
Digoxin	1.10 (1.00-1.21)	1.14 (0.99-1.30)	1.13 (1.03-1.25)	1.02 (0.97-1.08)	1.07 (1.03-1.11)

[†] 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 ≥ 67 years upon admission; these additional constraints were required to ensure sufficient lead-up time for the control observation period.

[‡] Conditional logistic regression models were adjusted for the following time-dependent variables: nursing home status at the case or control time; hospital days, overall Charlson comorbidity index²⁰ and 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.

[§] The overall prevalence of each PIM in the study population has been reported in a separate publication.³

[¶] Average annual general practitioner (GP) coverage was obtained from patients' proportion of GP coverage over 1993-2005, where each GP visit was allocated a 61-day coverage period (adjacent and overlapping periods being merged together). GP coverage categories were then derived from approximate quartiles, providing a general indicator for the level of ongoing GP monitoring.



