Are older Western Australians exposed to potentially inappropriate medications according to the Beers Criteria? A 13-year prevalence study

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Abstract

Objective: To examine time trends and factors associated with exposure to Beers potentially inappropriate medications (PIMs).

Methods: PIM consumption days accumulated from the pharmaceutical claims of 251,305 Western Australians aged ≥ 65 years (1993-2005) and person follow-up times produced counts/rates. Logistic/Poisson regression generated odds/rate ratios.

Results: 187,616 participants (74.7%) took ≥ 1 PIM (1993-2005), the cohort consuming 109,415 PIM daily doses/1000 person-years. Annual exposure decreased from 45-47% to 40%, and annual consumption rate declined from 117,836 to 90,364 daily doses/1000 person-years. Temazepam had the highest exposures ($>17,000$ daily doses/1000 person-years). Number of medications taken (OR 35.03; 95% CI 34.37-35.71 for ≥ 10 vs. 0-2 drugs), annual drug intake (2.08; 2.04-2.12 for highest vs. lowest quartile), and high-level residential aged care (1.96; 1.91-2.01) were most predictive of PIM exposure.

Conclusions: PIM exposure remains high in older Western Australians. Our findings identify patients most at risk and medications to consider on Australia-specific PIM lists.

Key words: Inappropriate prescribing, prevalence, risk factors, aged, Western Australia

Key Points

- Three-quarters of Western Australians aged ≥ 65 years (40-47% each year) were exposed to Beers potentially inappropriate medications (PIMs) to be avoided in older people during 1993-2005, annual consumption rate decreasing over that time.
- Temazepam was the most commonly prescribed PIM, whereas number of medications prescribed, annual drug intake and high-level residential aged care were factors associated with the highest risks of PIM exposure.
- Our findings identify Beers medications that are available and most frequently used in Australia for potential inclusion on Australia-specific PIM lists.

Introduction

Adults generally become more susceptible to adverse drug events with advancing age due to physiological deterioration, increasing comorbidities and other age-related factors.[1] This has led to the development of lists of 'potentially inappropriate medications' (PIMs) to be avoided in older people. Among them, the Beers Criteria[2] are by far the most commonly used.

Beers medication prevalence studies have reported the number/proportion of exposed older patients, but not utilisation rates. Most have been restricted to short time periods and very few have involved Australians.

The aim of this comprehensive study was to examine time trends in exposure to Beers medications in older Western Australians over a 13-year period (1993-2005), by estimating not only the number/proportion of people exposed but also daily doses/1000 person-years (PY) for both overall and individual PIMs. Furthermore, this study identified factors associated with PIM exposure.

Methods

Data preparation

The study protocol was approved by The University of Western Australia's Human Research Ethics Committee. As only de-identified records were accessed, participants' informed consent was not required.

People aged ≥ 65 years by 31 December 2004, who continuously lived in Western Australia (WA) and had ≥ 1 prescription claim during 1993-2005 were included, thus ensuring all had ascertainable drug exposures. Further details of the cohort selection are presented elsewhere.[3] The ultimate cohort captured 80-85% of older WA residents.

Participants' Pharmaceutical Benefits Scheme (PBS), Medicare and residential aged care data were linked with their inpatient, death and electoral roll records from the WA Data Linkage System[4] through probabilistic linkage. For each person, a record registered reconciled demographic details, date of death, follow-up time estimates and other characteristics. Socio-economic disadvantage was derived based on place of residence from WA quartiles (1996/2001) for Socio-Economic Indexes for Areas (SEIFA).[5,6] Similarly, remoteness was determined using Accessibility/Remoteness Index of Australia (ARIA+) definitions.[7]

Overall follow-up time was calculated as the count of days from the start of follow-up (1 January 1993 or person's 65th birthday if within study period) to the follow-up end date (31 December 2005 or date of death). Follow-up days by calendar year and five-year age group were also computed.

Additionally, patients' general practitioner (GP) visits (identified from Medicare records) were each allocated a 'coverage' period of 61 days (merging overlapping periods together), from which overall and annual coverage proportions were calculated. Derived quartiles helped define GP coverage categories, providing a general indicator of ongoing GP monitoring for each patient. Using aged care records, participants' mid-year aged care status for each calendar year was also determined.

Furthermore, details of all PBS items from available schedules (August 1991-June 2007) were assembled, retaining the last published entry for each item and reconciling Anatomical Therapeutic Chemical (ATC) codes with the 2007 World Health Organization (WHO) ATC drug classification.[8] Average daily doses for each item were estimated using average prescribed daily doses from the BEACH[9] general practice data, MIMS[10] registered drug information, and 2008 WHO ATC Defined Daily Doses (DDDs).[11] Estimates were allocated per drug strength, consumption statistics reflecting exposure days per medication rather than a specific drug quantity.

Statistical analysis

Each item from the 2003 Beers list[2] was defined according to the 2007 ATC classification.[8] Once patient and drug reference variables had been merged to the PBS master file, the ATC code list for 'general' PIMs (i.e. excluding disease-specific criteria but including PIMs with dosage or duration constraints irrespective of the dose/duration likely prescribed) was applied to identify relevant prescriptions supplied to participants.

For each selected PBS record, the drug consumption period was determined as follows: start date = supply date and end date = supply date + (quantity prescribed / drug item's average daily dose) - 1 (excluding time post-death and beyond 2005). Consumption days were then allocated for each record to the relevant calendar year(s) and overall. Thereafter, patient-level and population-level drug consumption

statistics (overall and annual) were generated for each PIM and for all PIMs combined using SAS 9.2.

Subsequently, summary follow-up statistics derived from the patient master file and PIM consumption sums (daily doses) were imported into Microsoft Excel® 2003, from which corresponding drug consumption rates were calculated as follows: PIM daily doses/1000PY = (total PIM daily doses consumed / total follow-up person-days) x 1000 persons x days per calendar year.

Rate ratios were computed using univariate Poisson regression on grouped data (SAS 9.3 GENMOD); ordinal analysis was used for time trends. To determine which factors predicted PIM exposure, univariate and multivariate logistic regressions were performed (SAS 9.3 LOGISTIC). All variables shown in Table 3 were included in the multivariate model. Since several covariates were time-dependent, multiple entries per participant were included, one for each calendar year in which the person contributed follow-up time. To obtain patients' overall drug intake, all PBS records were checked (i.e. not just PIMs), from which counts of consumption days by calendar year were accumulated for each person, as per computations for PIMs only. The number of different generic drugs contributing to each annual drug consumption count was also retained for each person, based on the number of different ATC codes involved.

Results

The study involved 251,305 participants and 2,076,176 PY of follow-up (1993-2005). Annual follow-up time increased from 128,262 to 185,816 PY (1993-2004) before decreasing to 185,776 (2005). Exclusion of WA residents whose 65th birthday occurred in 2005 (for logistical reasons) predominantly explains the lower 2005 figure.

As indicated in Table 1, 187,616 participants (74.7%) were prescribed ≥1 general PIM during 1993-2005, the cohort taking 109,415 PIM daily doses/1000PY. Older Western Australians who were female, born in earlier years, from more disadvantaged areas, living less remotely, and with more ongoing GP monitoring appeared more likely to have been exposed to PIMs and had higher PIM consumption rates than their counterparts. High-level aged care residents had a PIM consumption rate more than double that of other older people.

Until 2001, 45-47% of participants took ≥ 1 PIM annually, this proportion decreasing to 40% by 2005. The PIM consumption rate fluctuated during 1993-2000 between 117,836 and 110,477/1000PY, but then declined to 90,364/1000PY in 2005. Female figures were consistently higher than males' (Table 2).

Although PIM consumption rates remained higher in older age groups throughout 1993-2005, age-specific rates decreased more substantially over time in the oldest age groups. For example, in people aged ≥ 90 years, annual rates declined from 215,808 to 149,350 daily doses/1000PY between 1993 and 2005 (3.4%/year, $p < 0.0001$) compared with 84,133 to 65,238 daily doses (1.8%/year, $p < 0.0001$) in 65-69 year-olds.

On average, each person took 2.2 different PIMs during 1993-2005 (males 2.0; females 2.5). Annually, participants initially averaged 0.8 different PIMs (1993-2000), this figure decreasing to 0.6 by 2005. The highest number of different PIMs taken by an individual over the 13-year study period was 20 (8-13 annually).

Table 3 shows the results of univariate and multivariate logistic regression performed on participants' annual data to determine PIM exposure risk factors. Regression models included 1,860,630 entries, after excluding 311,312 (14.3%) with missing SEIFA/ARIA+ details. Univariate findings reflected the relative proportions of exposed participants from Table 1. For time-dependent characteristics, they also suggested that higher PIM use was associated with increasing age, high-level aged care, annual quantity of medications, number of different drugs taken, and year of death.

In multivariate results, many of these associations remained, but were generally weaker than those from the univariate model. PIM use still increased with age, although participants aged 65-69 years had higher odds of PIM exposure than 70-74 and 75-79 year-olds. A decreasing trend by calendar year became more apparent, whereas the association between PIM exposure and birth year virtually disappeared, and the effects of socio-economic status and remoteness of residence were reversed in direction. Moreover, only those in the highest tier of ongoing GP contact had higher PIM exposure than those with the lowest GP coverage. The annual count of different drugs taken had the strongest association with PIM exposure.

Table 4 presents counts of patients (1993-2005) taking each of the 43 individual drugs from the general PIMs list for which claims were recorded in our PBS dataset. These relate to 31 of Beers' 49 general PIM categories (30 shown in table, as diphenhydramine applied to two categories). Table 5 provides corresponding rates of daily doses for each drug.

The medications consistently used by the most people and with the highest consumption rates, both overall and in 2005, included: temazepam, digoxin, nifedipine, oxazepam, diazepam, amitriptyline, naproxen and piroxicam. The consumption rate of these drugs generally decreased over time, especially for digoxin, piroxicam and naproxen. However, it increased for both amitriptyline and temazepam. Temazepam was by far the most commonly used (Figure 1).

Among other PIMs, indomethacin and bisacodyl were prescribed to a high number of participants throughout but this was not reflected in terms of daily doses consumed, suggesting that these drugs were usually not prescribed for long-term use. From a trend perspective, dipyridamole, amiodarone and oxybutynin intake increased over time, whereas cimetidine, oestrone, ferrous sulphate, methyldopa, doxepin and indomethacin use declined.

Discussion

This comprehensive study assessed older Western Australians' exposure to Beers' medications over time (1993-2005) and identified predictors of PIM exposure. Our linked data improved the accuracy of demographic details and follow-up time estimates, and permitted the generation of person-level statistics for a broader range of characteristics. Furthermore, comparison of daily dosage information from three different sources (two of which were Australian) and the allocation of separate average daily dose estimates for different drug strengths ensured a more precise assessment of drug intake duration for each prescription.

Overall prevalence

Our results suggest a very high level of exposure to Beers' general PIMs in our cohort. Three-quarters of participants (nearly 80% of females) were prescribed ≥ 1 PIM over the study period, each exposed to an average of 2.2 (up to 20) different PIMs during that time. Annually, $\geq 40\%$ of older patients were exposed, double the 21% reported by Roughead et al.[12] in Australian war veteran beneficiaries (≥ 70

years) but similar to the 35-50% estimates from Australian nursing home[13,14] and retirement village sub-populations.[15] However, Roughead's study was based on a 6-month period only and excluded PIMs associated with dosage/duration criteria, whereas the other Australian results were based on drug use at a specific point in time and also had different Beers inclusions. Similar variations are noted in international studies, which have generally reported 10-40% PIM prevalence in older people.[16,17] Our study also estimated PIM consumption rates but comparable statistics were not available in the literature.

Despite remaining high, PIM exposure has decreased over time in older Western Australians, as per several other studies.[18-20] Hopefully this reflects a greater awareness of PIMs, and replacement of Beers medications with more appropriate treatment options. Nonetheless, we project from our data that $\geq 30\%$ of WA residents aged ≥ 65 years were prescribed ≥ 1 PIM in 2012, which is still quite high as each PIM prescription could lead to potentially preventable adverse effects.

Predictors of PIM exposure

Medication intake was strongly associated with PIM exposure in our cohort. However, the number of different drugs taken was a much greater predictor than overall drug quantity, suggesting that polypharmacy predisposes to increased PIM use in older people.

Additionally, female gender was an independent predictor of PIM exposure, as per other studies.[18,19,21-24] Our multivariate results also linked increasing PIM exposure with advancing age, but only from ≥ 70 years. It is unclear why 70-79 year-olds were less likely to be exposed than those aged 65-69 years. Clinicians may perhaps consider their 'younger' aged patients still too healthy to concern themselves with possible adverse PIM effects. Mixed results are reported in the literature in relation to age as a predictor of PIM exposure.

Residing in a high-level aged care facility was also an independent factor predicting PIM exposure after adjustments. Two other studies initially identified living in residential care as a risk factor for PIMs, but this association no longer existed once other factors, including polypharmacy, were taken into account.[18,24]

The associations of socio-economic status and remoteness of residence with PIM exposure were reversed after confounding adjustments. Although varying

demographic profiles in these sub-groups may have played a part, medication intake was likely the main confounder. If so, it is somewhat reassuring to find that the apparent increase in PIM exposure in the lower socio-economic tiers is probably due to a greater need for medications overall than to sub-standard prescribing practices. The increased likelihood of prescribing PIMs to those living in remote areas (all other factors being equal) is of greater concern, however, as potential GP monitoring restrictions would make these patients more vulnerable to PIM-related adverse events.

In our multivariate model, only those with extensive GP coverage had a higher level of PIM exposure than those with the least coverage, whilst those from intermediate levels were the least likely to be exposed to PIMs. It could be that many patients with little GP contact are generally very healthy, such that clinicians are less concerned about possible adverse PIM effects in this sub-group compared with those from the intermediate sub-groups. In contrast, patients receiving extensive GP coverage may be deliberately monitored very closely due to their increased comorbidities and polypharmacy. Clinicians may feel it is justified to prescribe specific PIMs in some of these patients, but compensate through extensive monitoring in these circumstances.

Study participants were also 54% more likely to take PIMs during their year of death than at other times. Thus, palliative treatment may be a higher priority than potential harm from PIMs as patients approach death.

Most common PIMs

Temazepam was by far the most common PIM in our study. This is particularly alarming as intake of this sedative, which was given a Beers 'high severity' rating, increased over time and was still >17,000 daily doses/1000PY in 2005, whereas consumption of most other drugs of concern declined. Some may contest that these patients unlikely exceeded the Beers 2003 upper daily limit of 15 mg. However, since the latest Beers Criteria update[25] recommends avoidance of short-acting benzodiazepines in older people regardless of dosage, alternative treatment of insomnia is advised in this age group.

By comparison, digoxin, a cardiac glycoside with a 1993 consumption rate similar to temazepam's, saw its rate decrease to 11,000 daily doses/1000PY by 2005. Similarly, consumption of naproxen and piroxicam, two non-steroidal anti-

inflammatory drugs (NSAIDs), decreased considerably during the study period. The NSAID decline likely related to increased prescribing of cyclooxygenase-2 inhibitors though, some of which were eventually withdrawn due to potential adverse effects.[26]

Diazepam, oxazepam and amitriptyline were also among the most commonly prescribed PIMs, which is not surprising given the high intake of anxiety and depression medication in older people,[27] as was nifedipine, an anti-hypertensive.

Although not highly prevalent during 1993-2005, dipyridamole, amiodarone and oxybutynin may require particular attention in future PIM prevalence studies, due to their upward consumption trends. Conversely, it is reassuring that exposure to cimetidine, oestrone, ferrous sulphate, methyldopa, doxepin, and indomethacin has declined considerably, likely due to safer alternatives becoming available. In the case of cimetidine, once the preferred drug for treating peptic ulcers and reflux, better understanding of disease aetiology has largely removed the need for this drug.[28] Similar developments from ongoing medical research will hopefully promote the decline of other risky drug prescribing practices in older people.

Study limitations

Despite extensive cross-validations between data sources, our results were constrained by some data limitations. For instance, no data were available on the daily dose specifically prescribed or on patient compliance. We used average recommended daily doses to estimate individual drug consumption, but this could not have been completely accurate in every case. Nevertheless, given our large cohort, average dosages likely yielded adequate population-level PIM consumption estimates.

Additionally, our PBS dataset excluded drugs prescribed within public hospitals, over-the-counter medications, and prescriptions for which a PBS claim cannot be made. However, most PIMs prescribed in a community setting would have been recorded for our older cohort, which mostly involved concession cardholders with very low co-payment requirements. Moreover, our study excluded older people with no PBS record during 1993-2005 and only included those who resided in WA for the entire period (until death). As the excluded seniors were probably younger, healthier and wealthier than the study population average, our overall results may have slightly

overestimated PIM exposure rates based on PBS scripts compared with those applicable to the entire population of older Western Australians.

Impact of recent developments

An inventory of the latest Australian PBS schedule indicates that only five individual PIMs from our study have been removed from the PBS since 2005. Of those, propoxyphene and meperidine (pethidine) had extremely low consumption rates by 2005 and the other three were 'oestrogen only' medications, which could readily have been substituted with oestradiol, a PIM that remains on the current PBS. Consequently, it seems unlikely that current PIM consumption patterns would be much different from those suggested by time trends derived from our study.

Furthermore, five individual drugs from our study have been removed from the latest Beers Criteria update.[25] Two (propoxyphene and ethacrynic acid) are no longer or seldom prescribed (in America and Australia) and two others (ferrous sulphate and fluoxetine) were omitted because related concerns are not restricted to older patients. Bisacodyl was the only one excluded due to insufficient evidence.[29] The revised Beers Criteria also include a number of new medications, although many are not yet available in Australia.

Conclusions

Our study has demonstrated a high level of exposure over time to temazepam and many other Beers medications in older WA residents, and identified patients at highest risk of exposure. Clinicians are urged to exert caution when treating vulnerable older patients, particularly those who require multiple drugs, have a high drug intake or reside in nursing homes, avoiding Beers medications when possible.

Given this high prevalence, it may be beneficial to use the Beers medications as a starting point to establish general lists of PIMs to be avoided in older Australians. Our research has identified which PIMs are on the Australian PBS and are most frequently prescribed in older Australians. Common Australian medications that are unavailable elsewhere and drugs appearing on non-Beers PIM lists should also be considered, as well as relevant medications from Basger's prescribing appropriateness criteria for older Australians.[30]

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Figure Legend

Figure 1. Potentially inappropriate medications in Western Australian residents aged ≥ 65 years (1993-2005) - rate of consumption (daily doses/1000 person-years) by calendar year for most commonly prescribed PIMs

PIM = Potentially inappropriate medication

Tables

Table 1. Potentially inappropriate medications in Western Australian residents aged ≥65 years (1993-2005) - cohort participants, number/proportion exposed and rate of consumption (daily doses/1000 person-years)

Population	Cohort participants	Number/proportion taking PIMs (%) ^{††}	Daily doses/1000 PY ^{‡‡}
Persons	251,305	187,616 (74.7%)	109,415
Gender			
Male	114,146	79,417 (69.6%)	88,381
Female	137,159	108,199 (78.9%)	125,745
Year of birth			
<1910	12,426	10,757 (86.6%)	198,115
1910-1919	41,852	36,957 (88.3%)	154,267
1920-1929	91,131	76,892 (84.4%)	106,354
1930-1939	105,896	63,010 (59.5%)	78,408
Socio-economic disadvantage[†]			
Most disadvantaged	54,002	44,097 (81.7%)	126,629
Moderately disadvantaged	53,739	43,183 (80.4%)	118,460
Slightly disadvantaged	47,629	37,793 (79.3%)	115,579
Least disadvantaged	55,240	42,761 (77.4%)	106,724
Unknown	40,695	19,782 (48.6%)	56,438
Remoteness of residence[‡]			
Major city	152,169	122,467 (80.5%)	118,914
Inner regional area	29,448	23,494 (79.8%)	112,600
Outer regional area	18,165	14,033 (77.3%)	112,937
Remote/very remote area	5,496	4,062 (73.9%)	104,288
Unknown	46,027	23,560 (51.2%)	62,666
Aged care status[§]			
High-level residential aged care	N/A	N/A	236,106
Other	N/A	N/A	106,324
GP coverage (overall)[¶]			
0-6 months/year (average)	71,864	42,973 (59.8%)	69,053
>6-8 months/year (average)	51,065	34,855 (68.3%)	65,113
>8-10 months/year (average)	60,004	48,245 (80.4%)	100,855
>10 months/year (average)	68,372	61,543 (90.0%)	197,073

† Derived based on place of residence from Western Australian quartiles (1996 and 2001) for Socio-Economic Indexes for Areas (SEIFA) - disadvantage component;[5,6] reflects most common quartile over time

‡ Derived from place of residence using Accessibility/Remoteness Index of Australia (ARIA+) definitions;[7] reflects most common level of accessibility/remoteness over time

§ Identifies person's high-level residential aged care status at 30 June of calendar year associated with drug supply date; patient counts available by calendar year but not really relevant for 1993-2005 as a whole

¶ Based on 61-day coverage per general practitioner visit and derived from proportion of coverage for 1993-2005

†† Corresponding overall λ^2 tests and univariate logistic regression analysis comparing proportions of people taking PIMs against first (reference) category defining each characteristic all yielded p-values <0.0001

‡‡ Corresponding univariate Poisson regression analysis for all comparisons of daily dose rates against first (reference) category defining each characteristic yielded p-values <0.0001

GP = General practitioner **PIMs** = Potentially inappropriate medications **PY** = Person-years

N/A = Not applicable

Table 2. Potentially inappropriate medications in Western Australian residents aged ≥65 years (1993-2005) - cohort participants, number/proportion exposed and rate of consumption (daily doses/1000 person-years) by gender and calendar year

Population	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	1993-2005
Males														
Cohort participants	57,123	60,206	63,215	66,053	68,624	71,154	73,678	76,447	79,518	82,217	84,716	87,250	84,262	114,146
Number taking PIMs	22,177	23,507	24,970	27,219	27,718	28,542	30,367	31,501	31,246	29,193	29,080	29,536	29,006	79,417
% taking PIMs ^{†,§}	38.8%	39.0%	39.5%	41.2%	40.4%	40.1%	41.2%	41.2%	39.3%	35.5%	34.3%	33.9%	34.4%	69.6%
Daily doses/1000 PY ^{‡,§}	95,269	95,078	91,660	98,370	96,137	95,094	92,199	94,797	78,243	78,902	75,275	73,508	70,758	88,381
Females														
Cohort participants	78,013	81,131	84,103	86,564	88,884	91,237	93,819	96,366	99,264	101,906	104,471	107,323	104,398	137,159
Number taking PIMs	38,768	40,505	41,212	43,206	43,623	44,098	48,129	48,833	49,460	50,410	48,790	48,573	47,279	108,199
% taking PIMs ^{†,§}	49.7%	49.9%	49.0%	49.9%	49.1%	48.3%	51.3%	50.7%	49.8%	49.5%	46.7%	45.3%	45.3%	78.9%
Daily doses/1000 PY ^{‡,§}	133,599	134,499	124,434	132,317	128,700	125,431	133,960	129,261	114,552	127,082	116,106	111,446	106,123	125,745
Persons														
Cohort participants	135,136	141,337	147,318	152,617	157,508	162,391	167,497	172,813	178,782	184,123	189,187	194,573	188,660	251,305
Number taking PIMs	60,945	64,012	66,182	70,425	71,341	72,640	78,496	80,334	80,706	79,603	77,870	78,109	76,285	187,616
% taking PIMs ^{†,§}	45.1%	45.3%	44.9%	46.1%	45.3%	44.7%	46.9%	46.5%	45.1%	43.2%	41.2%	40.1%	40.4%	74.7%
Daily doses/1000 PY ^{‡,§}	117,520	117,836	110,477	117,725	114,594	112,208	115,661	114,088	98,474	105,664	97,910	94,515	90,364	109,415

† Estimated 1.1%, 0.2% and 0.7% decreases in proportions exposed per year for males, females and persons, respectively, based on univariate logistic regression

‡ Estimated 2.7%, 1.6% and 2.1% decreases in daily dose rates per year for males, females and persons, respectively, based on univariate Poisson regression

§ All ordinal unadjusted time trend analysis (males, females, persons) for both proportions exposed and daily dose rates yielded $p \leq 0.0001$

Table 3. Factors associated with exposure to potentially inappropriate medications in Western Australian residents aged ≥65 years (1993-2005) - odds ratios

Factor/characteristic	Unadjusted		Adjusted	
	Odds ratio (95% CI)	P-value	Odds ratio (95% CI)	P-value
Male [†] - Gender	-	-	-	-
Female	1.54 (1.53, 1.55)	<0.01	1.36 (1.35, 1.37)	<0.01
<1910 [†] - Year of birth	-	-	-	-
1910-1919	0.75 (0.74, 0.77)	<0.01	1.02 (0.99, 1.04)	0.25
1920-1929	0.52 (0.51, 0.53)	<0.01	0.99 (0.96, 1.02)	0.49
1930-1939	0.39 (0.38, 0.40)	<0.01	1.03 (0.99, 1.07)	0.21
65-69 years [†] - Age group	-	-	-	-
70-74 years	1.27 (1.26, 1.28)	<0.01	0.93 (0.92, 0.94)	<0.01
75-79 years	1.55 (1.54, 1.56)	<0.01	0.95 (0.94, 0.97)	<0.01
80-84 years	1.88 (1.86, 1.90)	<0.01	1.02 (1.00, 1.05)	0.02
85-89 years	2.22 (2.19, 2.25)	<0.01	1.11 (1.08, 1.14)	<0.01
≥90 years	2.49 (2.45, 2.54)	<0.01	1.20 (1.16, 1.25)	<0.01
Most disadvantaged [‡] - Disadvantage [‡]	-	-	-	-
Moderately disadvantaged	0.94 (0.93, 0.95)	<0.01	1.00 (0.99, 1.01)	0.95
Slightly disadvantaged	0.91 (0.90, 0.92)	<0.01	1.03 (1.02, 1.04)	<0.01
Least disadvantaged	0.82 (0.82, 0.83)	<0.01	1.10 (1.09, 1.11)	<0.01
Major city [‡] - Remoteness [§]	-	-	-	-
Inner regional area	0.95 (0.94, 0.96)	<0.01	1.06 (1.05, 1.07)	<0.01
Outer regional area	0.89 (0.88, 0.90)	<0.01	1.06 (1.05, 1.08)	<0.01
Remote/very remote area	0.79 (0.77, 0.80)	<0.01	1.10 (1.07, 1.12)	<0.01
Not high-level aged care [¶] - Aged care [¶]	-	-	-	-
High-level residential aged care	3.36 (3.29, 3.43)	<0.01	1.96 (1.91, 2.01)	<0.01
0-4 months/year ^{††} - Annual GP coverage ^{††}	-	-	-	-
>4-8 months/year	0.88 (0.87, 0.88)	<0.01	0.97 (0.96, 0.98)	<0.01
>8-11 months/year	1.69 (1.67, 1.70)	<0.01	0.96 (0.95, 0.97)	<0.01
>11 months/year	3.56 (3.53, 3.59)	<0.01	1.16 (1.15, 1.18)	<0.01
0-166 daily doses [†] - Annual drug intake ^{‡‡}	-	-	-	-
>166-643 daily doses	5.99 (5.93, 6.06)	<0.01	1.79 (1.77, 1.82)	<0.01
>643-1330 daily doses	10.22 (10.12, 10.34)	<0.01	1.73 (1.71, 1.76)	<0.01
>1330 daily doses	21.88 (21.64, 22.12)	<0.01	2.08 (2.04, 2.12)	<0.01
0-2 drugs [†] - Annual drug count ^{§§}	-	-	-	-
3-5 drugs	7.61 (7.51, 7.70)	<0.01	5.97 (5.88, 6.07)	<0.01
6-9 drugs	18.10 (17.87, 18.32)	<0.01	12.71 (12.50, 12.93)	<0.01
10+ drugs	54.05 (53.35, 54.77)	<0.01	35.03 (34.37, 35.71)	<0.01
Not year of death [†] - Death year	-	-	-	-
Year of death	2.13 (2.09, 2.16)	<0.01	1.54 (1.51, 1.58)	<0.01
1993 [†] - Calendar year	-	-	-	-
1994	1.02 (1.00, 1.03)	0.04	0.93 (0.91, 0.95)	<0.01
1995	1.01 (0.99, 1.02)	0.30	0.88 (0.86, 0.90)	<0.01
1996	1.07 (1.05, 1.08)	<0.01	0.81 (0.80, 0.83)	<0.01
1997	1.04 (1.02, 1.05)	<0.01	0.74 (0.73, 0.76)	<0.01
1998	1.02 (1.01, 1.04)	<0.01	0.67 (0.66, 0.68)	<0.01
1999	1.12 (1.11, 1.14)	<0.01	0.76 (0.75, 0.78)	<0.01
2000	1.12 (1.10, 1.14)	<0.01	0.66 (0.65, 0.68)	<0.01
2001	1.08 (1.06, 1.09)	<0.01	0.54 (0.53, 0.55)	<0.01
2002	1.01 (0.99, 1.02)	0.36	0.45 (0.44, 0.46)	<0.01
2003	0.94 (0.93, 0.96)	<0.01	0.40 (0.39, 0.41)	<0.01
2004	0.93 (0.92, 0.94)	<0.01	0.36 (0.35, 0.36)	<0.01
2005	0.94 (0.92, 0.95)	<0.01	0.35 (0.34, 0.36)	<0.01

† The first category listed for each factor was used as reference for odds ratio comparisons

‡ Derived based on place of residence from Western Australian quartiles (1996 and 2001) for Socio-Economic Indexes for Areas (SEIFA) - disadvantage component;[5,6] reflects person's most common quartile over time

§ Derived from place of residence using Accessibility/Remoteness Index of Australia (ARIA+) definitions;[7] reflects most common level of accessibility/remoteness over time

¶ Identifies person's high-level residential aged care status at 30 June of calendar year

†† Based on 61-day coverage per general practitioner (GP) visit and derived from proportion of coverage for calendar year

‡‡ Derived from study population quartiles for the overall quantity of medication consumed annually; the daily dose units estimate the cumulative number of days of exposure per drug during the calendar year of interest

§§ Number of different generic drugs taken during the calendar year of interest

GP = General practitioner CI = Confidence interval

Table 4. Potentially inappropriate medications in Western Australian residents aged ≥65 years (1993-2005) - number of participants exposed by PIM and calendar year[†]

Medication class	PIM	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	1993-2005 (%)
Antirheumatics	Indomethacin	4,212	4,534	4,538	4,841	4,796	4,743	4,821	4,266	3,476	3,385	3,445	3,384	3,376	24,846 (9.9%)
	Naproxen	8,808	9,302	9,544	10,243	10,188	10,395	10,848	9,264	6,900	6,530	5,539	5,695	6,341	48,513 (19.3%)
	Piroxicam	8,253	8,664	8,659	9,428	9,281	9,422	9,494	7,623	5,011	4,197	3,761	3,649	3,940	38,332 (15.3%)
Analgesics	Dextropropoxyphene	202	170	168	214	201	205	218	217	149	109	105	77	83	1,115 (0.4%)
	Meperidine/pethidine	132	144	152	170	175	173	150	118	125	113	113	100	68	1,180 (0.5%)
Anti-Parkinson drugs	Orphenadrine	79	73	70	75	63	49								171 (0.1%)
Antihistamines (systemic)	Diphenhydramine	22	23	21	33	32	<5								76 (0.0%)
	Hydroxyzine	30	24	26	38	71	57	64							206 (0.1%)
	Cyproheptadine	1,008	1,152	1,233	1,296	1,183	1,279	1,498	1,610	1,753	1,796	1,739	1,747	1,527	10,121 (4.0%)
	Promethazine	1,925	2,385	2,385	2,618	2,297	232	289	293	303	340	339	325	327	9,128 (3.6%)
Antipsychotics	Thioridazine	980	1,019	1,023	1,026	1,035	1,045	1,008	850	359	118	85	49	39	3,673 (1.5%)
Anxiolytics, hypnotics/sedatives (benzodiazepines)	Oxazepam	7,215	7,480	7,433	7,722	7,564	7,592	8,153	8,314	8,225	8,128	8,303	8,146	8,031	30,985 (12.3%)
	Alprazolam	<5	182	296	360	419	481	551	660	756	777	823	862	917	2,786 (1.1%)
	Diazepam	6,212	6,554	6,658	7,361	7,262	7,439	7,900	8,001	7,967	8,364	8,291	8,474	8,383	37,556 (14.9%)
	Temazepam	16,229	17,425	18,460	20,213	20,656	21,446	23,532	24,570	25,118	25,740	25,729	26,244	26,021	87,602 (34.9%)
Antidepressants	Amitriptyline	2,862	3,043	3,149	3,513	3,770	4,190	5,013	5,774	6,282	6,379	6,848	7,462	7,676	26,672 (10.6%)
	Doxepin	3,267	3,355	3,140	3,121	2,933	2,934	3,050	2,945	2,908	2,484	2,325	2,250	2,116	12,252 (4.9%)
	Fluoxetine	916	1,565	1,220	1,466	1,564	1,505	1,522	1,502	1,556	1,352	1,480	1,538	1,468	7,870 (3.1%)
Psychostimulants	Dexamphetamine	7	15	26	35	34	36	44	63	79	61	60	71	63	194 (0.1%)
Cardiac rhythm regulators	Disopyramide	162	152	135	125	113	104	90	89	84	79	57	49	42	297 (0.1%)
	Digoxin	9,288	10,040	9,913	10,175	10,127	10,289	10,625	10,555	10,391	9,676	9,426	9,343	9,048	32,302 (12.9%)
	Amiodarone	763	1,001	1,296	1,659	2,019	2,463	2,977	3,435	3,974	3,854	3,867	3,853	3,761	12,351 (4.9%)
Hypertension drugs	Methyldopa	2,505	2,276	1,919	1,711	1,539	1,408	1,303	1,108	1,013	841	749	703	690	4,738 (1.9%)
	Nifedipine	6,532	6,698	6,860	6,937	6,716	7,262	7,345	7,354	7,416	6,416	6,170	6,140	5,947	23,527 (9.4%)
	Clonidine	145	156	171	225	229	268	293	303	284	285	303	325	277	1,477 (0.6%)
High ceiling diuretics	Ethacrinic acid	104	111	102	81	83	82	93	84	84	78	94	9	21	467 (0.2%)
Antithrombotics	Dipyridamole							752	1,965	2,757	2,635	2,493	2,298	2,202	5,914 (2.4%)
	Ticlopidine	5	8	27	57	63	70	58	47	38	23	22	24	17	234 (0.1%)
Diabetes drugs	Chlorpropamide	204	206	174	152	135	87	<5							340 (0.1%)
Iron preparations	Ferrous sulphate	5,461	5,272	5,776	6,300	6,171	6,103	6,582	7,032	5,165	4,103	4,788	5,291	3,396	32,500 (12.9%)
Peptic ulcer/reflux drugs	Cimetidine	6,741	5,932	4,784	4,067	3,240	2,736	2,286	1,875	1,486	1,031	754	604	469	13,102 (5.2%)
Laxatives	Bisacodyl	2,227	2,546	2,798	2,998	3,037	3,028	3,195	3,264	3,175	3,371	3,314	3,178	3,123	18,657 (7.4%)
Bowel disorder drugs/ belladonna & derivatives	Belladonna alkaloids	1,493	1,717	1,726	1,845	1,557	25	22	15	36	78	89	86	46	5,791 (2.3%)
	Dicyclomine	11	13	11	7	16	23	20	23	22	19	14	14	<5	97 (0.0%)
	Propantheline	781	865	792	915	896	884	958	972	779	686	576	508	530	5,649 (2.2%)
Urinary antispasmodics	Oxybutynin				345	759	1,067	1,447	2,052	2,517	2,848	2,989	3,194	3,279	9,798 (3.9%)
Urinary tract antibacterials	Nitrofurantoin	1,135	1,183	1,341	1,328	1,391	1,393	1,349	1,388	1,453	1,493	1,586	1,580	1,781	10,452 (4.2%)
Oestrogen-only medication	Ethinylloestradiol	426	450	436	510	214									874 (0.3%)
	Oestradiol	1,566	1,781	2,246	2,612	2,952	3,175	3,611	3,965	4,058	3,261	2,624	2,174	1,833	10,047 (4.0%)
	Oestril	7	11	6	12	26	27	25	39	37	48	36	34	33	148 (0.1%)
	Oestrone	2,082	2,614	3,041	3,520	3,997	4,356	4,885	5,188	5,261	4,333	2,887	2,126	1,782	11,450 (4.6%)
	Oestrogens-conjugated	2,371	2,852	3,356	3,878	4,601	5,016	5,602	6,238	6,341	5,211	3,564	2,789	2,450	14,971 (6.0%)
	Fosfestrol sodium	57	45	29	25	48	62	74	73	72	67	29			258 (0.1%)

[†] To derive percentages of exposed participants for individual PIMs by calendar year, please use person counts (i.e. 'Cohort participants') from Table 2 as denominators.

PIM = Potentially inappropriate medication

Table 5. Potentially inappropriate medications in Western Australian residents aged ≥65 years (1993-2005) - rate of consumption (daily doses/1000 person-years) by PIM and calendar year

Medication class	PIM	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	1993-2005
Antirheumatics	Indomethacin	3,653	3,363	3,094	3,179	3,019	2,827	2,705	2,273	1,641	1,773	1,726	1,637	1,607	2,417
	Naproxen	7,110	6,743	6,345	6,847	6,431	6,462	6,365	5,199	3,437	3,668	3,065	3,012	3,395	5,065
	Piroxicam	7,853	7,525	6,666	7,012	6,535	6,342	6,072	4,809	2,857	2,832	2,469	2,337	2,563	4,834
Analgesics	Dextropropoxyphene	29	26	23	27	26	25	24	22	15	12	11	10	9	19
	Meperidine/pethidine	33	55	54	49	49	46	66	40	25	24	21	16	13	36
Anti-Parkinson drugs	Orphenadrine	109	97	73	71	66	55								77
Antihistamines (systemic)	Diphenhydramine	16	21	20	21	20	4								20
	Hydroxyzine	26	22	23	23	34	28	36							27
	Cyproheptadine	667	708	722	761	699	699	818	870	878	990	950	928	856	822
	Promethazine	977	1,108	1,133	1,307	1,085	122	134	136	136	147	136	140	146	469
Antipsychotics	Thioridazine	1,159	1,166	1,169	1,140	1,137	1,144	1,043	872	245	124	103	58	55	672
Anxiolytics, hypnotics/sedatives (benzodiazepines)	Oxazepam	8,625	8,398	7,700	7,874	7,509	7,375	7,539	7,284	6,475	6,924	6,872	6,699	6,573	7,302
	Alprazolam		119	264	374	444	499	535	606	631	794	842	902	932	604
	Diazepam	5,053	5,116	4,853	5,215	5,006	4,942	5,026	4,871	4,359	4,876	4,704	4,708	4,625	4,855
	Temazepam	16,474	17,048	16,528	17,891	17,901	17,821	18,426	18,651	17,273	18,615	17,680	17,542	17,321	17,664
Antidepressants	Amitriptyline	3,891	3,908	3,708	3,992	3,940	4,163	4,522	4,928	4,837	5,629	5,803	6,176	6,531	4,874
	Doxepin	4,879	4,604	4,060	4,099	3,838	3,725	3,666	3,476	2,986	3,079	2,823	2,654	2,504	3,486
	Fluoxetine	725	1,281	1,119	1,297	1,534	1,490	1,546	1,515	1,404	1,585	1,638	1,740	1,735	1,458
Psychostimulants	Dexamphetamine	11	19	31	51	50	48	53	63	65	70	72	83	79	56
Cardiac rhythm regulators	Disopyramide	264	232	187	174	160	138	125	114	102	104	91	76	57	134
	Digoxin	16,060	17,440	15,678	15,976	15,501	14,955	14,885	14,354	12,447	13,385	12,651	11,833	11,022	14,119
	Amiodarone	1,047	1,245	1,525	2,066	2,453	2,910	3,373	3,824	3,991	4,716	4,618	4,683	4,582	3,309
Hypertension drugs	Methyldopa	4,580	3,907	3,014	2,754	2,425	2,137	1,936	1,644	1,261	1,209	1,081	1,004	996	2,025
	Nifedipine	10,064	9,690	9,322	10,071	9,954	10,082	10,304	10,108	9,127	9,671	9,153	9,003	8,958	9,622
	Clonidine	177	186	175	207	206	209	231	241	204	216	235	235	223	213
High ceiling diuretics	Ethacrinic acid	136	149	121	75	68	59	69	69	58	56	63	5	11	68
Antithrombotics	Dipyridamole							711	1,513	2,393	3,099	3,029	2,886	2,708	2,622
	Ticlopidine	5	11	19	39	47	52	54	42	30	27	25	22	17	32
Diabetes drugs	Chlorpropamide	370	349	268	238	209	168								283
Iron preparations	Ferrous sulphate	4,935	4,362	4,597	4,997	4,750	4,670	4,791	4,999	2,329	2,868	3,275	3,706	1,077	3,851
Peptic ulcer/reflux drugs	Cimetidine	8,151	6,953	5,337	4,699	3,543	2,906	2,338	1,927	1,358	1,055	765	592	443	2,807
Laxatives	Bisacodyl	1,395	1,643	1,679	1,697	1,695	1,670	1,588	1,645	1,474	1,631	1,581	1,489	1,372	1,577
Bowel disorder drugs/belladonna & derivatives	Belladonna alkaloids	961	1,011	988	1,054	850	1	1	1	1	2	2	2	2	327
	Dicyclomine	12	11	7	8	10	14	12	12	13	11	11	7	1	11
	Propantheline	748	738	639	656	602	556	603	576	434	419	346	324	299	517
Urinary antispasmodics	Oxybutynin				282	534	796	1,079	1,488	1,653	2,109	2,199	2,328	2,496	1,680
Urinary tract antibacterials	Nitrofurantoin	759	711	750	804	763	726	736	778	714	818	823	732	878	771
Oestrogen-only medication	Ethinylloestradiol	265	264	238	280	126									262
	Oestradiol	1,791	2,104	2,386	3,037	3,297	3,624	4,186	4,462	4,047	4,110	3,200	2,566	2,355	3,205
	Oestrinol	7	6	2	6	12	16	19	25	23	26	23	22	23	17
	Oestrone	2,702	3,429	3,726	4,601	4,950	5,319	6,148	6,456	5,704	5,381	3,408	2,479	2,202	4,343
	Oestrogens-conjugated	1,743	2,027	2,204	2,750	3,085	3,336	3,835	4,137	3,796	3,549	2,373	1,876	1,702	2,815
	Fosfestrol sodium	60	41	28	22	33	46	61	59	52	60	43			47

PIM = Potentially inappropriate medication