Benzodiazepine Use in Older Adults in the United States, Ontario, and Australia from 2010 to 2016

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OBJECTIVES: To detail annual trends in benzodiazepine incidence and prevalence in older adults between 2010 and 2016 in three countries.

DESIGN: Observational multicountry cohort study with harmonized study protocol.

SETTING: The United States (veteran population); Ontario, Canada; and Australia.

PARTICIPANTS: All people aged 65 and older (8,270,000 people).

MEASUREMENTS: Annual incidence and prevalence of benzodiazepine use stratified according to age group (65–74, 75–84, ≥85) and sex. We performed multiple regression analyses to assess whether rates of incident and prevalent use changed significantly over time.

RESULTS: Over the study period, we observed a significant decrease in incident benzodiazepine use in the United States (2.6% to 1.7%) and Ontario (6.0% to 4.4%) but not Australia (7.0% to 6.7%). We found significant declines in prevalent use in all countries (United States: 9.2% to 7.3%; Ontario: 18.2% to 13.4%; Australia: 20.2% to 16.8%). Although incidence and prevalence increased with age in Ontario and Australia, they decreased with age in the United States. Incidence and prevalence were higher in women in all countries.

CONCLUSION: Consistent with other international studies, there have been small but significant reductions in the incidence and prevalence of benzodiazepine use in older adults in all three countries, with the exception of incidence in Australia, although use remains inappropriately high— particularly in those aged 85 and older—which warrants further attention from clinicians and policy-makers. **J Am Geriatr Soc 66:1180–1185, 2018.**

Key words: benzodiazepines; older adults; Choosing Wisely; Australia; Ontario; United States

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Benzodiazepine use in older adults has been associated with a number of harms, including greater risk of falls, hip fracture, impaired cognition, all-cause mortality, overdose, and substance use disorder.[1–5] As a result, the American Geriatrics Society Beers Criteria and Screening Tool of Older Person's Prescriptions and Screening Tool to Alert doctors to Right Treatment Screening Tools for Geriatric Medicine advise avoiding benzodiazepine use in older adults.[6,7] Most recently, the Choosing Wisely (CW) International campaign,[8] as well as country-specific CW programs in the United States, Canada, and Australia,[9–12] have addressed this potentially inappropriate prescribing. Despite this, rates of new and continuing benzodiazepine use in older adults remain higher than in younger age groups.[13,14]

Benzodiazepine use in older adults has been previously described in the United States, Canada, and Australia,[13–16] as well as in several European countries,[17] but differing data sources, methods, and time periods make comparisons of studies challenging. Moreover, most studies have not been population based or have used episode- rather than person-level data, impeding analysis of patterns of individual use. In addition, there have been no studies detailing the extent of benzodiazepine use in older adults in multiple countries since the start of the CW Campaign.

The aim of this study is to detail trends in annual benzodiazepine incidence and prevalence in older adults from

2010 to 2016 using a common methodology in three jurisdictions: the United States, (veteran population) Ontario, and Australia.

METHODS

Study settings and data

We used prescription claims data from three countries for this observational study: the Veterans Health Administration of the U.S. Department of Veterans Affairs (VA), the Ontario Drug Benefit (ODB) program, and the Australian Pharmaceutical Benefits Scheme (PBS). All of these systems capture prescription claims for enrolled beneficiaries and have been used previously to describe changes in medication use in their respective countries.[18–20] Although each of these three countries provide access to subsidized medicines for a wide age range of people, we limited our analysis to beneficiaries aged 65 and older, because older adults are the focus of the CW benzodiazepine recommendations.[9–12] This study was based on a common protocol, and analyses were harmonized across all three individual databases.

Study population

The study population consisted of all people aged 65 and older in each of the three countries from January 1, 2010, to December 31, 2016, except for the United States, for which data was available only until December 8, 2016. The study denominator for each year included any individual that was alive for part of the year and had at least one prescription claim for any medicine. We restricted all analyses to people for whom we had complete capture of prescription claims over the study period; in the Australian cohort, this meant restricting the population to people who were concession card holders for the entire period.[18]

Medicines of interest

We identified benzodiazepine derivatives—as defined according to the Anatomical Therapeutic Chemical classification system (classes N03AE, N05BA, and N05CD)—subsidized in each country. The specific benzodiazepines available in each country varied (Supplementary Table S1); we excluded intravenous formulations.

Measures and statistical analysis

Characteristics of the study populations. We determined the sex and age group (65–74, 75–84, ≥85) of all people aged 65 and older with at least one prescription claim between 2010 and 2016 according to country. We also determined these characteristics for people aged 65 with at least one benzodiazepine claim over this study period.

Annual incidence and prevalence. We determined yearly incident and prevalent benzodiazepine use in each country from 2010 to 2016 (Supplementary Figure S1). We estimated incident (new) use by identifying persons with a benzodiazepine prescription claim during a given calendar year and no prescription claims for a

benzodiazepine during the previous 12 months. We estimated prevalent use by identifying persons with at least one prescription claim for a benzodiazepine within a given calendar year. We present incidence and prevalence in each country overall and stratified according to age (65–74, 75–84, ≥85) and sex. The denominator for each country was the number of people in the corresponding age or sex category who had a prescription claim for any medication during a given year. Incidence and prevalence were expressed per 1,000 population.

To determine whether annual incidence and prevalence changed from one year to the next in each country, we used multiple Poisson regressions to model the number of people with new or prevalent benzodiazepine use each year. Along with study year, we adjusted the model for age group, sex, and the log of the denominator (total number of people) as an offset term. We reported fixed effects as rate ratios with 95% confidence intervals. Because of significant overdispersion, as assessed using the Lagrange multiplier test, a negative binomial distribution was used to produce more accurate parameter estimates.

All analyses were performed using SAS version 9.3 (SAS Institute Inc., Cary, NC) and Stata version 12 (Stata-Corp, College Station, TX).

Ethics and data access approval

The Institutional Review Board of the VA Ann Arbor Healthcare System, the Research Ethics Board at Sunnybrook Health Sciences Centre, and the New South Wales Population and Health Services Research Ethics Committee and Department of Human Services approved the analyses for this study. The data remained in each country.

RESULTS

There were differences in age and sex strata between the three study populations (Table 1). There were proportionally more people in the older age groups (75–84, ≥85) in the Australian study population than in the other countries. Although the Australian and Canadian study populations had similar proportions of men and women, the U.S. VA population was almost entirely male.

Annual incidence and prevalence. Our estimates of annual incidence and prevalence are presented according to country in Figure 1 (data available in Supplementary Table S2). We observed a significant linear decline in incident benzodiazepine use in the United States (2.6% in 2010 to 1.7% in 2016). The decline in incident benzodiazepine use in Ontario (from 6.0% in 2010 to 4.4% in 2016) was also significant over the entire study period, but there was a greater decline between 2011 and 2012 than in prior and subsequent years. We did not observe a statistically significant change in incident benzodiazepine use in Australia over the study period from (7.0% in 2010 to 6.7% in 2016) (Figure 1, Supplementary Table S3).

There was a significant decline in prevalent benzodiazepine use in all countries between 2010 and 2016, decreasing from 9.2% to 7.3% in the United States, 18.2% to 13.4% in Ontario, and 20.2% to 16.8% in

Table 1. Characteristics of the Three Study Populations (2010–2016) Expressed Per 1000 People

Characteristic	United States, 3,888	Ontario, n=2,595	Australia, n=1,787
Study population, n	3,888	2,595	1,787
Age, n (%)			
65–74	2,442 (62.8)	1,736 (66.9)	888 (49.7)
75–84	1,049 (27.0)	626 (24.1)	646 (36.1)
≥85	398 (10.2)	234 (9.0)	254 (14.2)
Sex, n (%)			
Female	78 (2.0)	1,420 (54.7)	1,010 (56.5)
Male	3,810 (98.0)	1,175 (45.3)	777 (43.5)
≥1 benzodiazepine dispensed, n (%)	527 (13.6)	686 (26.4)	332 (18.6)
Age, n (%)			
65–74	360 (68.3)	357 (52.0)	141 (42.5)
75–84	125 (23.6)	221 (32.3)	128 (38.7)
≥85	43 (8.1)	108 (15.7)	62 (18.8)
Sex, n (%)			
Female	14 (2.6)	439 (64.0)	221 (66.7)
Male	513 (97.4)	247 (36.0)	111 (33.3)

Australia. The rate of this decline was relatively linear for all countries.

In general, age-stratified trends followed similar trajectories within countries (Figure 1b). For Ontario and Australia, people aged 85 and older had the highest prevalence, followed by those aged 75 to 84 (Figure 1c) and then by those aged 65 to 74 (Figure 1d). In the United States, this pattern was reversed, with individuals aged 65 to 74 having the greatest prevalence. Annual incidence was similar across age groups for Ontario and Australia, whereas individuals aged 65 to 74 consistently had the highest incident use in the United States. Multiple regression analyses supported differences between age groups in incidence and prevalence within each country (Supplementary Table S3).

Women had the highest incident and prevalent benzodiazepine use over the study period in all three countries, and trends for men and women followed similar trajectories (Supplementary Figure S2). This observation was supported in our multiple regression analyses, with female sex significantly associated with greater rates of incident and prevalent benzodiazepine prescriptions, irrespective of country (Supplementary Table S3).

DISCUSSION

The United States, Canada, and Australia were early adopters of CW (in 2012, 2014, and 2015, respectively), and all emphasize that benzodiazepines should not be prescribed to older persons. In order to compare trends we have used a standardized methodology to measure annual incident and prevalent benzodiazepine use between 2010 and 2016 in these countries. Although using a standardized methodology facilitates comparison of annual trends between countries, differences in underlying study populations make direct comparison of absolute incidence and prevalence challenging. Nevertheless, we found small but

statistically significant decreases in benzodiazepine incidence and prevalence in all three countries, with the exception of incidence in Australia, which did not reach statistical significance. In addition, incidence and prevalence were highest in those aged 85 and older in Ontario and Australia but decreased with advancing age in the U.S. VA population.

It is unclear whether the decrease in benzodiazepine use observed in the U.S. VA population in this study applies more broadly to the general U.S. population. Prevalence figures in this study are similar to those of the general U.S. population in 2008 based on a national prescription database covering approximately 60% of all retail pharmacy prescriptions,[14] although the decreasing use over time found here is in contrast to recent non-VA U.S. studies demonstrating stable or increasing use. Analysis of the nationally representative Medical Expenditure Panel Survey suggested an increase in the prevalence of benzodiazepine use in older adults between 1996 and 2013 (from 4.1% to 5.6% of older adults), although this increase appeared to plateau in the last 3 years of the study.[21] A separate analysis of U.S. ambulatory clinic visits to primary care providers found an increase in visits in which benzodiazepines were prescribed to older adults between 2003 and 2012 (from 5.6% to 8.7% of visits).[22] Although overall prevalence in the VA would be expected to be lower than in the general population because the population is predominantly male and fewer men are prescribed benzodiazepines,[14] our observed trends persisted after stratification according to sex. There have been a number of VA-specific policy and education initiatives focused on safe psychotropic prescribing, as well as treatment guidelines (e.g., for posttraumatic stress disorder) that may have all contributed to the observed reductions in benzodiazepine prescribing within the VA system.[23] It is also conceivable that prescribing has declined more recently in the non-VA U.S. population, but this has not been demonstrated.

Our findings of decreasing benzodiazepine use in Australia and Canada are consistent with previous studies in these countries[15,24] and may also be the result of recent initiatives in each country to address this practice.[20,25]

The decreases in benzodiazepine use in older adults generally described worldwide are likely to be in response to safety concerns and lack of evidence of effectiveness. Benzodiazepine-related "Z-drugs" such as zopiclone and zolpidem were not measured in this study, but there are concerns that they are being used instead of conventional benzodiazepines, putatively because of perceptions of a superior safety profile, and this warrants further investigation.[26]

Despite the modest decreases in benzodiazepine incidence and prevalence seen in our study and in spite of consistent messaging about the hazards of using benzodiazepines in this population, the rates of benzodiazepine use in older adults remain high. Ongoing use may be related to providers' tendency to minimize the risks of prescribing to older adults,[27] which older adults may do as well.[28] Limited access to nonpharmacological alternatives such as psychotherapy[29] and limited physician time[14] are other factors associated with ongoing benzodiazepine initiation.
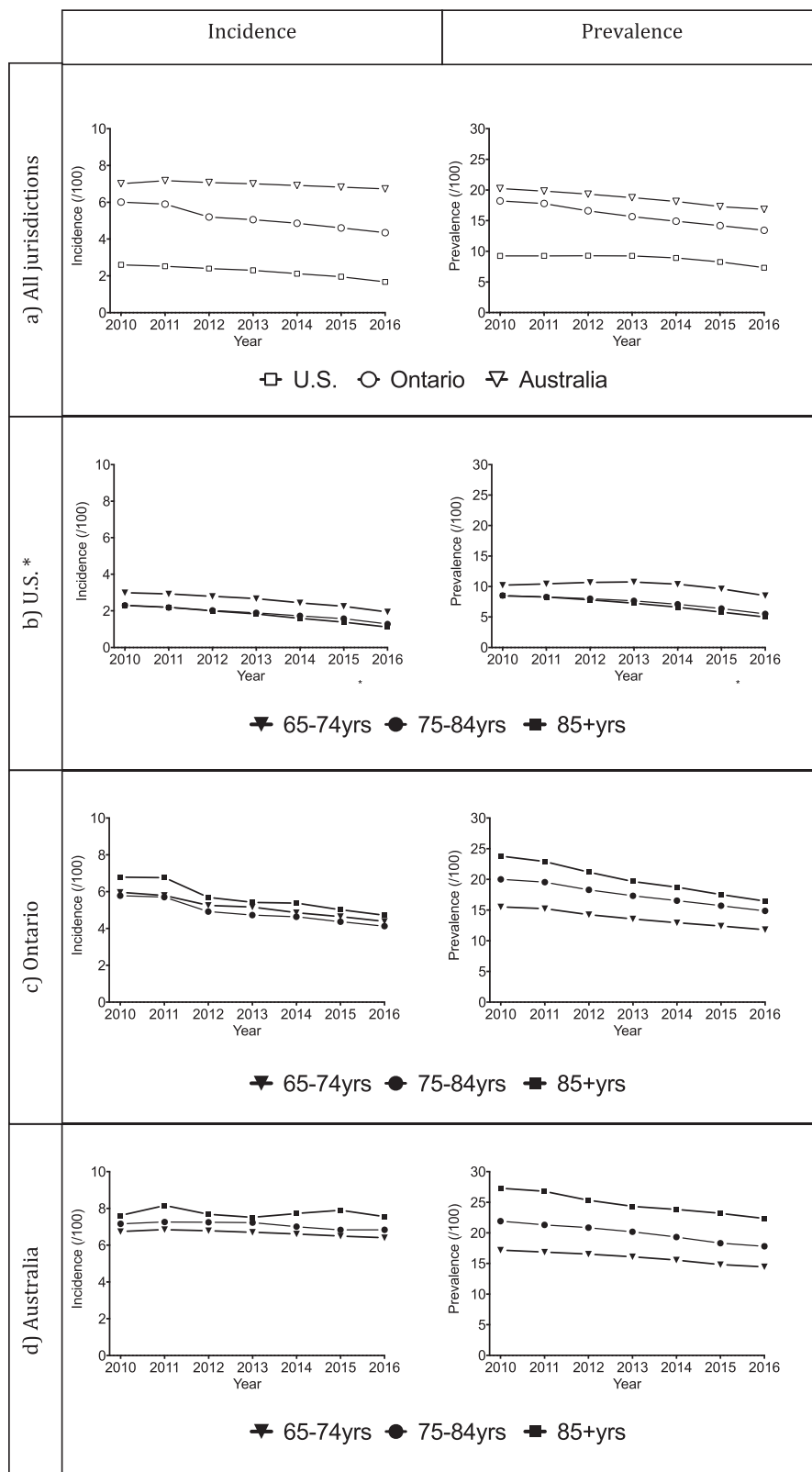
Figure 1. Incidence and prevalence of benzodiazepine dispensing in (a) all countries, (b) United States, (c) Ontario, and (d) Australia. U.S. data available through December 8, 2016; incidence and prevalence calculated accordingly.

As demonstrated previously in the general U.S. population,[14] as well as for Australia and Ontario in this study, benzodiazepine use typically increases with age, so rates are highest in the oldest individuals. This is particularly troubling because potential harms may be even greater in individuals aged 85 and older. It is unusual that, in the U.S. VA population, the group aged 65 to 74 had the highest rates of use. This may be related

to the aging of Vietnam-era veterans, who have more diagnosed depression and anxiety than earlier veteran cohorts.

In Ontario, there was a marked decline in incidence between 2011 and 2012. This may be a result of implementation of the province's Narcotics Safety and Awareness Act (November 2011) and Narcotics Monitoring System program (May 2012), a two-pronged approach to limit potentially inappropriate benzodiazepine use.[20] Similar real-time prescription drug monitoring programs are becoming increasingly prevalent in the United States in an effort to limit prescription drug abuse and potentially reduce overdose risk.[30] Despite their benefits, prescription drug monitoring programs are unlikely to be nuanced enough to pinpoint potentially inappropriate use as opposed to abuse.[5] Australia has not implemented national prescription drug monitoring or other similar dedicated policy efforts, which might partially explain the lack of change in new use of benzodiazepines in elderly adults. At a clinical level, limiting the conversion of new use to chronic use may be the most effective initial step in reducing the prevalence of benzodiazepine use, because ceasing chronic use can be more challenging. This could be achieved by explicitly limiting the duration of new prescriptions and not routinely providing repeat prescriptions. For people who have been using benzodiazepines for a long time, a discussion about the risks and benefits of continued therapy and attempts to reduce the dose gradually might be the best strategy.[31]

LIMITATIONS

Only subsidized medicines were captured in this study, meaning that the prevalence of benzodiazepine use may be underestimated if people obtain prescriptions outside of the subsidizing program. In Australia, unrecorded private prescribing accounts for up to 10% of all benzodiazepine prescriptions[32] and this may also be an issue for the Ontarian and U.S. VA programs. In addition, restricting the Australian study cohort to people who were continuous concession cardholders may limit the generalizability of the results, because this population tends to be older and have greater comorbidity than the general population. Similarly, although the U.S. study cohort was the largest population in this analysis, it was limited to older adults receiving care in the VA healthcare system. Although it was not the intention of this study to identify "true" new use (first ever use), the 12-month look-back used to classify incident use might have overestimated "true" new use. We did not measure benzodiazepine-related Z-drugs because these were not consistently subsidized in all three countries. There were significant differences in the age and sex strata of the three populations and benzodiazepine subpopulations, reflecting differences in organizational structures, although these were accounted for in our regression models of trends over time. Finally, information on other factors such as treatment duration, clinical indication, and comorbidity was not available consistently from all three countries, so it was not possible to compare and adjust for these differences between populations.

CONCLUSION

In this analysis of three countries, incident and prevalent benzodiazepine use in older adults has decreased in Ontario and in the VA system in the United States, and prevalent use has decreased in Australia. Our findings are generally consistent with separate international studies that have used varying methods, although use in the respective older adult populations remains high and warrants further attention from clinicians and policy-makers. A detailed description of the methodology used to measure low-value prescribing practices, as well as a description of historical trends for this practice, facilitates harmonization of methodologies across countries to allow other countries to benchmark this practice using the same methodology. This also paves the way for future internationally coordinated efforts to decrease low-value care by investigating the motivations for prescribing and the effectiveness of initiatives used to limit benzodiazepine use using criterion standard methods such as interrupted time series analyses.

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Author Contributions: JB performed Australian analyses and all regression analyses and drafted the manuscript. DM managed U.S. data analysis and reviewed the manuscript. RVI performed U.S. data analysis. ZB managed Ontarian data analysis and reviewed the manuscript. GM performed Ontarian data analysis. EK, SB, and AE assisted in drafting the manuscript. SP reviewed all drafts of the manuscript and took overall responsibility for the project direction.

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SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article.

Table S1: List of benzodiazepines available in each country
Figure S1: Flow chart outlining incidence and preva-lence calculation
Figure S2: Incidence and prevalence in each country stratified by sex
Table S2: Raw incidence and prevalence data in each country
Table S3: Results of multivariable negative binomial regression modelling