ORIGINAL ARTICLE

Long-term benzodiazepines and z-drug prescribing in Australian general practice between 2011 and 2018: A national study

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Abstract

Despite reducing benzodiazepine prescribing, benzodiazepine-involving deaths have substantially increased in Australia. This study aimed to explore patterns in long-term prescribing of medications (benzodiazepine and z-drugs [BZD]) used for sleep-issues/insomnia in Australia to better understand these changes. Open cohort study using de-identified electronic health records of 1 414 593 adult patients regularly attending 404 Australian general practices from 2011 to 2018 (MedicineInsight). We used logistic regression adjusted for patient and practice characteristics to; (1) estimate long-term BZD prescribing prevalence (≥3 prescriptions in 6 months) and the associated sociodemographic factors, and (2) Poisson regression to compute annual changes in prescribing rates. Long-term BZD prescribing changed from 4.4% in 2011 to 5.8% in 2015, remaining relatively stable until 2018 (annual increase +2.5% [95% CI +2.0%;+3.0%]). Long-term BZD prescribing in any year was up to six times more likely in elderly rather than in younger patients and 30%–43% more prevalent in females, or patients living in or attending a practice located in more disadvantaged areas. The increase was more pronounced among males, adults aged 35–49 years, and individuals living in advantaged areas. The median duration among incident cases decreased from 1183 to 322 days between 2011 and 2017, and was up to 197 days longer among elderly females than males. Despite a slight increase and recent stability in long-term BZD prescribing, the higher rates and durations among elderly patients, women, or those living in more disadvantaged areas are concerning and highlights the need for interventions that reduce the potential harms of long-term BZD use in vulnerable groups.

KEYWORDS
benzodiazepine, electronic health records, longitudinal data, long-term, primary care, z-drugs

1 | INTRODUCTION

Over the last 30 years, harms caused by benzodiazepines and z-drugs (BZD) use have been widely reported in the literature. These include cognitive impairment, falls and hip fractures, traffic accidents, physical dependence, Alzheimer's disease, drug-related hospitalizations, and all-cause mortality.[1-4] In fact, despite a decline in the prescription of benzodiazepine in Australia in recent years,[5,6] deaths that had benzodiazepine listed as underlying cause or one of the multiple causes of deaths increased from 2.4 per 100 000 population in 2011 to 3.8 per 100 000 population in 2018,[7] probably due to the long-term use of these medications and/or in combination with other drugs (opioid and alcohol). As a result of the adverse effects related to long-term BZD use, international guidelines recommend restricting the use of BZD and similar drugs to a maximum of 4–12 weeks for the management of most conditions.[8,9] Despite this, and limited evidence of the clinical benefit, the prescription of BZD for long-term management of conditions such as insomnia persists.[6,10,11]

Recent studies have reported the prevalence of long-term BZD prescribing among the adult population to be 0.7% in the United Kingdom (survey of general practice [GP] surgeries in Bradford, 2014–15),[12] and 3.6% in Finland (Finnish Prescription Register 2014).[13] Long-term benzodiazepine prescribing ranged from 1.4% in the United States (National Health and Nutrition Examination Survey 1999–2014),[14] to 2.8%–3.8% in France (drug reimbursement data 2015),[15] in recent studies. In Japan, 9.0% of new BZD users were prescribed BZD for ≥8 months (health insurance data, 2015)[16]; similarly in Australia, 9.5% of people received ≥3 benzodiazepine prescriptions within 90 days after benzodiazepine initiation (dispensing data 2014–2017).[17] The wide variation in these estimations across countries is mainly a consequence of the variations in the definitions used for long-term prescribing or dispensing, as well as the study design, and data sources.[18] Most of these existing studies used dispensing data,[17,18] which has limited, if any, information about the sociodemographic characteristics of patients receiving these prescriptions.

Consequently, most studies in this field either lack information about the distribution of long-term BZD use according to sociodemographic characteristics or have results that are contradictory to each other. Among those studies that were investigating these relationships, long-term BZD use was more common in the elderly, but the association with gender or socioeconomic position was mixed.[11,13,15,18-20] For example, studies from Canada, France, and Finland showed that low education, low occupation grade, not being at work, low household income, and receiving social benefit were linked with increased long-term BZD use.[11,15,19] A Danish study demonstrated that the use of z-drugs for >4 weeks was more common among advantaged groups (high education and high income), and more than 6 months use of z-drugs was higher among disadvantaged groups.[20] Studies from Canada, France, and Finland indicated the long-term BZD use was higher among females.[11,13,15] However, two recent studies from Australia and Japan showed that although

What is already known about this subject

- Previous studies have shown recent reductions in BZD prescribing; however, little is known about sociodemographic characteristics and trends of long-term BZD prescribing in Australia.
- Most studies report a high proportion of long-term BZD prescribing/dispensing among elderly people; however, evidence about long-term BZD use by gender and socioeconomic position is inconsistent.

What this study adds

- Long-term BZD prescription rates increased from 4.4% in 2011 to 5.8% in 2015, remaining relatively stable until 2018.
- Long-term BZD prescribing was more common and for longer periods among elderly women
- People living in or attending general practices located in disadvantaged areas were more likely to receive long-term BZD prescriptions.

females were more likely to start BZD treatment, men were more likely to become long-term users.[16,17]

There were also differences among the few international studies reporting recent trends of long-term use of BZD, with a slight increase reported in Canada (2004–2013)[11] and a decrease observed in Finland (2006–2014),[13,21] while benzodiazepines alone have been decreased in Korea (2009–2013).[22] In studies where benzodiazepines and z-drugs were analyzed separately, a Canadian linked data study (2004–2013) reported a slight decline in long-term benzodiazepine and an increase in long-term z-drug use,[11] whereas a US study using National Health and Nutrition Examination Survey data (1999–2014) reported an increase in long-term use of both, benzodiazepines and z-drugs.[14]

In recent years, national databases containing primary care electronic health records (EHR) have been used to explore long-term prescription trends of medications such as benzodiazepines and opioids.[18,23,24] These EHR databases overcome some of the limitations of using dispensing data, such as the availability of more comprehensive data on sociodemographic variables, clinical information, and laboratory findings, as well as the possibility of tracking the same patient over time.[25]

Australia has a publicly funded universal health insurance scheme called Medicare,[26] which covers visits to GPs through the Medical Benefits Scheme and the cost of many medications through the Pharmaceutical Benefits Scheme. Although most general practices are privately owned and operated in Australia, the cost of GP consultations is either fully or partially subsidized by Medicare. Moreover, up to 83% of individuals in Australia visit a GP every year.[27] Therefore, the use of a nationwide general practice database

could assist in the analysis of prescription patterns and early identification of patients at higher risk of long-term BZD use.[28]

This study aimed to explore sociodemographic patterns in the long-term prescribing medications commonly used for managing sleep issues in Australia (benzodiazepines and z-drugs), from 2011 to 2018 by using an Australian general practice database.

2 | MATERIALS AND METHODS

2.1 | Setting, study design, and data source

In this open cohort study, we used a national primary care database (MedicineInsight) that includes routinely collected/recorded data from 2700 general practitioners (GPs) and 662 general practices across Australia (8% of all practices in Australia).[25] The characteristics of the general practices included in the MedicineInsight database are reflective of all Australian practices.[25] De-identified EHRs are extracted every month, and each patient is allocated a unique identification number used for long-term follow-up within the practice.

2.2 | Study population

Practices with inconsistent data provision (gaps in data provision ≥6 weeks in the last 2 years, a ratio between the minimum and maximum number of annual consultations between 2011 and 2018 higher than five) were excluded to minimize information bias.[25] Moreover, patients in Australia can visit multiple general practices, and some may attend a practice only once. These "non-regular" can introduce bias and lead to underestimated results due to the unavailability of all diagnoses and prescriptions in the EHRs.[29] Therefore, each year was treated as a different cohort, and "regular" patients in a specific year were defined as those who had at least three consultations between that year and the previous year, and at least one consultation in each of these 2 years (e.g., a patient was considered "regular" in 2018 if they had 3+ consultations between 2017 and 2018, with at least one in each of these 2 years, irrespective of whether they attended or not the practice in other years).[25] The final sample included de-identified EHRs from 1 414 593 "regular" patients aged 18+ years attending 404 general practices between January 01, 2011 and December 31, 2018.

2.3 | Data on medication and definition of long-term BZD

Information on the prescribed medications was extracted from the database using the commercial brand name and active ingredient of the prescribed drugs. All prescriptions of benzodiazepines (temazepam, diazepam, nitrazepam, oxazepam, lorazepam, clonazepam, alprazolam, flunitrazepam, midazolam, clobazam, bromazepam) or Z-drugs (zopiclone and zolpidem) approved for use in Australia[9,30]

and prescribed between January 2011 and December 2018 were extracted. Long-term BZD prescribing was defined as three or more benzodiazepines or z-drugs scripts provided to the same patient within 180 days (or 6 months). This definition was supported by a recent systematic review, which showed that 6 months was the most common period used in other studies to characterize long-term BZD use.[18] Considering that Australian guidelines recommend the use of BZD for no more than 4 weeks,[9] we added the criterion that the second script of any benzodiazepine or z-drug should have been received any time after 28 days from the first recorded script, but within 180 days.

An episode of long-term BZD prescribing ended when the patient had not received any new prescription for benzodiazepine or z-drug for 6 or more months. The "end date" of an episode of long-term BZD prescribing was considered as being 28 days after the last provided script in that episode.[9] The total duration of a long-term BZD episode was calculated as the difference between the date of the first script and the "end date" of that episode. For example, a patient starting BZD prescribing on 1-Jan-2011 and receiving a new BZD prescription every 2 months with the last script provided on December 31, 2013 (i.e., no further BZD prescriptions or gap higher than 180 days until the next BZD script) would have January 28, 2014 as the "end date" of that episode. Therefore, the total duration of that long-term BZD prescribing would be 1123 days. That patient would be considered an "incident" case in 2011 but not in further years, even if they experienced new episodes of long-term BZD prescribing over time.

2.4 | Sociodemographic variables

The practice-level sociodemographic characteristics included the Index of Relative Socioeconomic Advantage and Disadvantage (IRSAD) score (i.e., most-disadvantaged, middle, most-advantaged) and remoteness/location of the practice (i.e., major cities, inner regional, outer/remote/very remote). IRSAD is an area-level measure of socioeconomic advantage and disadvantage developed by the Australian Bureau of Statistics and based on indicators that combine household income, education level, working status, and age distribution.[31] Although IRSAD is often reported in quintiles, we combined the upper two quintiles (as "most-advantaged") and the lower two quintiles ("most-disadvantaged"), because of similar estimates in those groups. Both IRSAD and remoteness scores were assigned to patients and practice by MedicineInsight based on postcode data. Patient-level characteristics included age (categorized into groups of 18–34 years, 35–49 years, 50–64 years, 65–75 years, and ≥75 years), sex (male, female), and patient's IRSAD.

2.5 | Statistical analysis

The annual period prevalence of long-term BZD prescribing for each year from 2011 to 2018 was computed by dividing the number of patients prescribed long-term BZD by the total number of

patients in the corresponding year and presented as a percentage (%). Practice-level estimates were only adjusted for practice characteristics (IRSAD and remoteness), while patient-level estimates were adjusted for both individual (sex, age, remoteness, and IRSAD) and practice characteristics. Logistic regression was used to obtain the marginal adjusted prevalence of long-term BZD prescriptions (overall and according to sociodemographic characteristics). The average annual change in the prescription of long-term BZD was analyzed using Poisson regression and presented as percentual annual change.

The median duration (in days) and interquartile range (IQR) of the of "incident" long-term BZD episodes among regular patients (i.e., first episode of long-term BZD prescribing for any patient) was estimated for all years. Information on the median use for 2018 was omitted as insufficient follow-up data could underestimate these figures. Quantile regression models were used to investigate if the median duration (in days) of the long-term BZD prescription among incident cases varied according to sex and age (i.e., 18–64 or 65+ years). These results were presented graphically with the corresponding 95% confidence intervals (95% CI).

All analyses were conducted on Stata MP15.1 (StataCorp), considering practice as a cluster, conditioned to the patient's number of visits to the practice in that year, and using robust standard errors. There was <1% of missing data for each variable included in this paper.

3 | RESULTS

There were total 1 414 593 regular adult patients in the MedicineInsight database across the whole period. The number of these patients each year ranged from 614 940 (number of patients prescribed long-term BZD = 30 327) in 2011 to 1 066 039 (number of patients prescribed long-term BZD = 74 116) in 2018. Of the 13 BZDs we investigated for long-term prescription between 2011 and 2018; diazepam was most frequently prescribed (29.5%), followed by temazepam (28.8%), oxazepam (14.7%), zolpidem (6.5%), nitrazepam (5.3%), alprazolam (4.8%), zopiclone (4.2%), clonazepam (2.5%), lorazepam (2.2%), and each of the remaining drugs were prescribed less than 0.5%. Among those receiving long-term BZD prescriptions, there was a higher proportion of women, individuals aged ≥65 years, and living in or attending practices in more disadvantaged areas than those not prescribed long-term BZD (Table 1). The distribution according to the remoteness of location of the practice was similar in both groups in any year.

The adjusted estimates presented in Table 2 show that the proportion of patients receiving long-term BZD prescriptions increased from 4.4% in 2011 to 5.8% in 2015 and then remained relatively steady until 2018 (overall annual increase +2.5% [95% CI +2.0%; +3.0%]). Long-term BZD prescriptions in any year were more common among patients who were attending practices from more disadvantaged areas, female or living in areas with a lower socioeconomic (IRSAD) score. For example, 5.0% of female patients were prescribed long-term BZD, which increased to 6.2% in 2018 (annual increase

+1.6% [95% CI +1.2% to +2.0%]). Among men who visited a GP in 2011, 3.5% were prescribed long-term BZD, which increased to 4.8% in 2018 (annual increase +2.7% [95% CI 2.1% to 3.3%]).

Although the number of long-term BZD prescriptions were similar among those living in urban or rural settings, the prevalence was 5–6 times higher among those aged ≥75 years compared to younger adults (i.e., 18–34-year-olds) and between 30% and 43% more prevalent in females or patients living in or attending a practice located in more disadvantaged areas. For example, of all ≥75-year old patients who attended a GP in 2011, 10.1% were prescribed long-term BZD, which increased to 11.9% in 2018 (annual change +1.7% [95% CI +1.2% to +2.2%]). Among those aged 18–34 years, 1.5% were prescribed long-term BZD in 2011 and 1.7% in 2018 (annual change +0.5% [95% CI −0.6% to +1.7%]).

There was a monotonic increase of long-term BZD prescriptions across the investigated sociodemographic variables, but it was slightly more pronounced in outer/remote/very remote Australia, males, adults aged 35–49 years, and those living in more advantaged areas. Crude estimates of long-term BZD prescribing showed similar patterns (Table S1).

The median duration of "incident" long-term BZD prescribing episodes among regular patients decreased over time: 1183 days in 2011 (IQR = 363;2260), 1112 days in 2012 (IQR = 341;2006), 976 days in 2013 (IQR = 314;1762), 806 days in 2014 (280;1445), 666 days in 2015 (IQR = 245;1136), 499 days in 2016 (IQR = 204;805), and 322 days in 2017 (IQR = 181;481). Figure 1 shows the median duration of the long-term episodes and their reduction over time was similar among men and females aged 18–64 years. Among elderly patients (i.e., ≥65 years), the median duration was 118–197 days longer in females than males between 2011 and 2015, decreasing to 99 days in 2016 and 23 days in 2017. The difference between age groups (i.e., longer median duration in the elderly) also reduced from 336 days in 2011 to 26 days in 2017.

4 | DISCUSSION

In this study, we used a large national general practice data set to examine trends in long-term BZD prescribing in Australia from 2011 to 2018. Three main findings can be highlighted from our results. First, the number of patients receiving long-term BZD prescriptions increased between 2011 and 2015, remaining thereafter relatively steady until 2018. Moreover, despite the observed decrease in the duration of these episodes, they still lasted at least 11 months among new users in 2017. Second, rates and duration of long-term BZD prescribing were higher among females and elderly patients, with a prevalence 5–6 times higher among those aged ≥75 years compared to younger adults (i.e., 18–34 years old). Finally, long-term BZD prescriptions in any year were up to 43% more common among patients attending practices located in more disadvantaged areas or those living in areas with a lower IRSAD score (disadvantaged), but prescribing was similar for those living in urban or rural settings.

TABLE 1 Characteristics of regular adult patients (≥18 years) who attended MedcineInsight general practices in 2011 and 2018

	Regular patients[a] who visited a GP in 2011				Regular patients who visited a GP in 2018			
	(n = 614 940)				(n = 1 066 039)			
	No long-term BZD prescription		Long-term BZD prescription[b]		No long-term BZD prescription		Long-term BZD prescription	
	n	%	n	%	n	%	n	%
Overall	584 613	95.1	30 327	4.9	991 923	93.1	74 116	7.0
Practice characteristics								
Remoteness	584 613		30 327		991 923		**74 116**	
Major Cities	341 441	58.4	17 317	57.1	591 360	59.6	42 292	57.1
Inner Regional	165 658	28.3	9273	30.6	268 086	27.0	21 932	29.6
Outer/Remote/Very Remote	77 514	13.3	3737	12.3	132 477	13.4	9892	13.4
IRSAD	582 380		30 297		987 939		**73 930**	
Advantaged	244 643	42.0	11 604	38.3	423 849	42.9	29 364	39.7
Middle	142 253	24.4	7283	24.0	230 656	23.4	17 668	23.9
Disadvantaged	195 484	33.6	11 410	37.7	333 434	33.8	26 898	36.4
Patient characteristics								
Sex	584 549		30 323		991 394		**74 105**	
Male	234 107	40.0	10 065	33.2	412 455	41.6	27 098	36.6
Female	350 442	60.0	20 258	66.8	578 939	58.4	47 007	63.4
Age	584 506		30 324		991 792		**74 113**	
18–34 years	93 637	16.0	1792	5.9	184 447	18.6	4385	5.9
35–49 years	145 386	24.9	5488	18.1	208 307	21.0	12 240	16.5
50–64 years	186 509	31.9	9278	30.6	258 847	26.1	17 964	24.2
65–74 years	101 007	17.3	6940	22.9	183 303	18.5	15 662	21.1
75+ years	57 967	9.9	6826	22.5	156 888	15.8	23 862	32.2
IRSAD	580 395		30 173		984 524		**73 656**	
Advantaged	238 924	41.2	10 830	35.9	411 195	41.8	27 407	37.2
Middle	138 876	23.9	7305	24.2	228 895	23.3	17 934	24.4
Disadvantaged	202 595	34.9	12 038	39.9	344 434	35.0	28 315	38.4

Note: BZD, benzodiazepines; IRSAD, index of relative socioeconomic advantage and disadvantage.

[a]Individuals aged 18+ years with at least three visits in two consecutive years, and at least one consultation in each of these 2 years.

[b]Long-term BZD: a patient receiving at least three scripts of benzodiazepines or Z-drugs (BZDs) within 180 days, with the second script prescribed after 28 days of the initial script (then no more than 180 days without a new script to define the end of the episode).

Although previous Australian studies have suggested a reduction in the total number of BZD prescriptions,[5,6] our figures showed a 2.5% annual increase in long-term prescribing between 2011 and 2018. These results may be an underestimation of the real magnitude of the problem, given that prescriptions to patients included in our study by GPs and other health professionals who are not part of MedicineInsight, are not captured. Also, we did not consider repeats for the investigated BZD prescriptions (approximately 10% of all BZD scripts provided in general practice between 2011 and 2018 had one or more repeats).[6]

Our findings are consistent with results from other high-income countries, such as the US and Canada.[11,14] The odds of benzodiazapine use in the US between 1999 and 2014 increased for medium-term (Odds Ratio [OR] = 1.45) and for long-term use (OR = 2.17).[14]

In Canada, a study from British Columbia reported that there was 10% increase in long-term sedative prescribing among adult women (from 4.1% to 4.5%), and 14% among men (from 2.5% to 2.9%) between 2004 and 2013.[11] However, a study from Finland reported an opposite trend, showing the prevalence of long-term BZD prescribing decreased from 5.3% to 3.6% from 2006 to 2014 (prescription register data).[13] In our study, long-term BZD prescribing remained stable in recent years (2015–2018), perhaps influenced by the latest guidelines for accountable prescribing of BZD released in 2015 by The Royal Australian College of General Practitioners (RACGP), the peak professional body for GPs in Australia.[9]

Our findings demonstrating a small increase in long-term BZD prescriptions could be explained by a rise in the prevalence of the mental health conditions in Australia in recent years. Data from

TABLE 2 Adjusted prevalence (%) of "regular" adult patients[a] on long-term BZD prescriptions[b] and average annual change according to sociodemographic characteristics. MedicineInsight, 2011–2018

	Prevalence of long-term BZD prescriptions[b]								
	2011	2012	2013	2014	2015	2016	2017	2018	Annual change (%)
Total number of patients	614 940	675 710	742 503	815 267	892 176	974 648	1 064 153	1 066 039	
Overall prevalence (95% CI)	4.4% 4.2, 4.6	5.0% 4.8, 5.3	5.4% 5.1, 5.7	5.6% 5.4, 5.9	5.8% 5.5, 6.0	5.8% 5.5, 6.0	5.7% 5.4, 6.0	5.6% 5.3, 5.9	+2.5 (2.0, 3.0)
Practice characteristics[1]									
Remoteness									
Major cities	4.5	5.1	5.5	5.6	5.7	5.7	5.6	5.4	+2.0 (1.4, 2.6)
Inner regional	4.5	5.1	5.5	5.8	6.0	6.1	6.1	6.0	+2.9 (1.9, 3.9)
Outer/remote/ very remote	3.7	4.5	4.9	5.2	5.4	5.5	5.5	5.4	+3.5 (2.2, 4.9)
IRSAD[c]									
Advantaged	3.9	4.6	4.9	5.1	5.3	5.3	5.3	5.3	+2.5 (1.9, 3.2)
Middle	4.3	5.0	5.4	5.6	5.7	5.8	5.7	5.7	+3.1 (2.1, 4.2)
Disadvantaged	5.0*	5.7*	6.1*	6.3*	6.4*	6.3*	6.2*	5.9*	+2.0 (1.0, 2.9)
Patient characteristics[1,2]									
Gender									
Male	3.5	4.1	4.4	4.7	4.8	4.9	4.8	4.8	+2.7 (2.1, 3.3)
Female	5.0*	5.7*	6.1*	6.3*	6.4*	6.4*	6.3*	6.2*	+1.6 (1.2, 2.0)
Age									
18–34 years	1.5	1.7	1.9	2.0	1.9	1.9	1.8	1.7	+0.5 (−0.6, 1.7)
35–49 years	3.1	3.7	4.1	4.2	4.4	4.4	4.4	4.4	+3.7 (2.8, 4.5)
50–64 years	4.4	4.9	5.2	5.3	5.5	5.5	5.4	5.4	+2.4 (1.9, 3.0)
65–74 years	6.2	6.9	7.3	7.4	7.5	7.4	7.3	6.9	+0.9 (0.4, 1.5)
75+ years	10.1*	11.1*	11.8*	12.2*	12.4*	12.6*	12.5*	11.9*	+1.7 (1.2, 2.2)
IRSAD									
Advantaged	3.8	4.4	4.7	5.0	5.1	5.1	5.1	5.0	+2.5 (2.0, 2.9)
Middle	4.5	5.2	5.5	5.8	5.9	6.0	6.0	5.9	+2.4 (1.7, 3.1)
Disadvantaged	5.0*	5.7*	6.1*	6.3*	6.4*	6.4*	6.2*	6.1*	+1.3 (0.6, 2.1)

Note: Results on the prevalence of long-term BZDs prescriptions are adjusted for (1) practice characteristics; (2) patient characteristics.

Additional information on total number of patients in each category and number of patients prescribed long-term BZD in 2011 and 2018 are provided in Table S1.

[a]Individuals aged 18+ years with at least three visits in two consecutive years.

[b]Long-term BZD: a patient receiving at least three scripts of benzodiazepines or Z-drugs (BZDs) within 180 days, with the second script prescribed after 28 days of the initial script (then no more than 180 days without a new script to define the end of the episode).

[c]IRSAD: The Index of Relative Socioeconomic advantage and disadvantage.

*Difference between categories with a p-value <0.01.

[1]Represents practice characteristics, and it shows that the practice related estimates were adjusted for practice characteristics.

[2]Indicates the estimates were adjusted for both patient and practice characteristics

the National Health survey shows that mental or behavioral conditions in Australia increased from 17.5% in 2014–2015 to 20.1% in 2017–2018 (anxiety-related condition increased from 11.2% to 13.1%, and depression/depressive symptoms increased from 8.9% to 10.4%).[32] A previous study using MedicineInsight data also showed that despite a decrease in total BZD and related drugs, there has been an increased proportion of patients with a clinical history of insomnia or sleep problems receiving these

medications.[6] These findings are consistent with evidence of a recent qualitative paper examining GPs perceptions on managing insomnia. The 2020 study highlighted the challenges faced by GPs when they treat patients with long-term medication dependence, especially given that support services and referral pathways can be difficult to access.[33]

The increase in long-term BZD prescribing in this study may partly help us understand why the number of Australian deaths
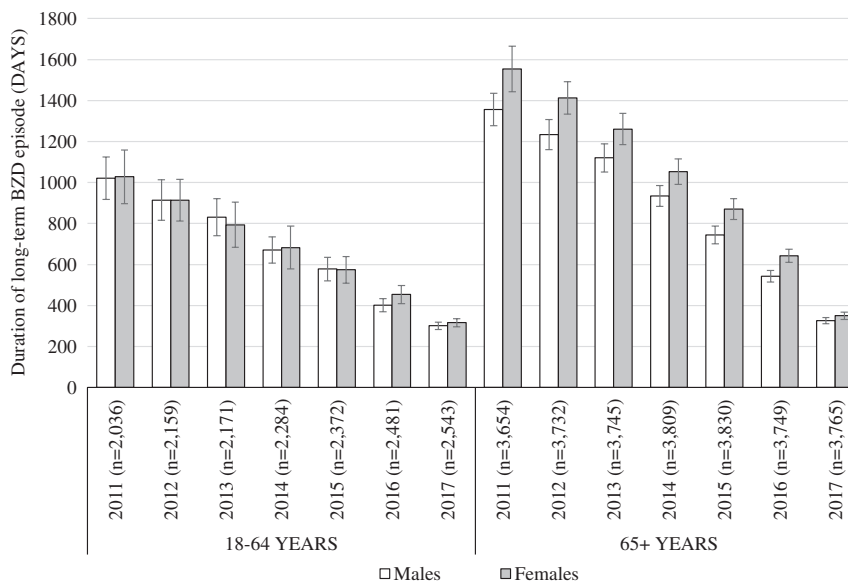
FIGURE 1 Median duration (days) of "incident" long-term BZD prescribing among adults in any year, stratified by age, and sex. An episode of long-term BZD prescribing was defined as three or more benzodiazepines or z-drugs scripts provided to the same patient within 180 days. The "end date" of an episode was defined as 28 days after the last provided script in that episode (i.e., no further BZD prescriptions or gap higher than 180 days until the next BZD script). The total duration of a long-term BZD episode was calculated as the difference between the date of the first script and the "end date" of that episode. Considering that some patients could have multiple episodes of long-term BZD prescribing over time, only the first episode of long-term BZD prescribing (i.e., "incident" episode) is presented in this figure. Results for 2018 were excluded from analysis to allow enough follow-up time for these episodes. Vertical lines represent the 95% confidence interval of the median duration

involving benzodiazapine use rose by 70% between 2009 and 2018 (from 518 to 883 deaths),[34] as well as why there was an increase in benzodiazepine-related hospital separations (completion of hospital care by discharge, deaths, or transfer) in the same period,[34] despite a decrease in overall benzodiazepine prescribing.[5] A comparison with z-drugs cannot be drawn, as the report looking at hospital separations did not examine z-drugs, stating that they make up a very small proportion of sedative/hypnotics issued in Australia.[34,35] The increase in mortality involving benzodiazepine has been found not only just in Australia, but also overseas.[36] In addition, long-term prescribing of benzodiazepines may also increase the risk of co-administration with other drugs such as opioids or alcohol, or increase the risk of non-medical use, further potentiating the possibility of adverse health outcomes. Indeed, 97% of drug-induced deaths in 2019 in Australia, where benzodiazepines were present, involved other drugs such as alcohol.[7] Similarly, benzodiazepine was involved in 55% of the opioid-induced deaths in 2019.[7,37] This indicates the importance of strategies such as real-time prescription monitoring to help prevent harm.

Consistent with our study, a number of previous papers have also reported an increase in long-term BZD prescribing among disadvantaged groups[11,15] and among elderly people.[11,13,17] The higher prevalence and longer duration of long-term prescriptions of BZDs in the ≥65-year-old age group is of particular concern given the substantial risk of adverse effects in the elderly.[4,9] This finding could be explained by an increase in the frequency of sleeping disorders[38,39] and anxiety[40] in the elderly. For example, an Australian study reported that sleep issues such as waking

overnight, waking early, and not being able to get back to sleep was almost twice as high in the elderly compared with younger people.[41] However, it is important to note that BZD use is not recommended for the older age group in particular given the higher rates of adverse events.[4,9]

The finding that the majority of long-term BZD users were female is consistent with much of the literature published internationally.[11,13,15] However, two recent studies that looked at the factors associated with new BZD users progressing to long-term use found that male sex was a risk factor.[16,17] Although men may be more likely to become long-term BZD users, according to our findings women are more likely to remain long-term users, which would explain our findings of a higher prevalence in females (i.e., incidence-prevalence bias). Such findings are important to understanding where to target interventions to reduce long-term BZD prescribing rates.

The duration of a long-term BZD episode in our study estimates GPs prescription behavior rather than BZD use. It does not mean that the patient filled the prescription or used BZD daily for that entire period, but that the patient received BZD scripts consecutively for at least 180 days. It is difficult to directly compare our findings with the available literature, as other studies in this field are mostly based on different data sources. However, an Irish study using a national pharmacy claims database found similar results on the duration of long-term BZD prescribing episodes. The authors reported that about 20% of patients aged ≥16 years receiving BZD between 2006 and 2015 used these medications consecutively for more than 180 days.[42]

Despite the strengths of the study, such as the use of a large national database and routinely collected information, some limitations should be recognized. Indications for BZD prescriptions (starting or continuing) are not commonly recorded as a reason for prescription and their link to other fields in the dataset is susceptible to information bias (i.e., not recorded, recorded on a different date, recall from a previous diagnosis, information recorded in the EHR but not extracted by MedicineInsight). It should also be noted the completeness and accuracy of recorded information may vary between GPs and that the nature of our data also means we cannot account for any variation in the quantity of tablets provided in each prescription. However, research looking at patients initiating benzodiazepines has found that the majority were dispensed as full-packs,[17] so this is unlikely to have a significant impact on our findings.

5 | CONCLUSION

Long-term prescribing of BZD's in Australian general practice increased in the initial years of our study and more recently showed an apparent plateau, probably influenced by recent guidelines.[9] Nonetheless, the median duration of these episodes (322 days in 2017) is still 11 times higher than current recommendations.[9] These findings coincide with a higher number of hospitalizations and deaths associated with BZD use in Australia,[34] despite an overall decline in their prescribing.[6] Long-term use of BZD is a particular problem especially among elderly women and could potentially be linked to the increased prevalence of chronic mental health issues and use for insomnia management. To reduce harm, especially in the elderly, there should be availability of non-pharmacological approaches to help avoid BZD initiation, as well as access to programs to help with cessation of long-term BZD use.

ETHICS APPROVAL STATEMENT

The independent MedicineInsight Data Governance Committee approved this study (protocol 2019–029) and the Human Research Ethics Committee of The University of Adelaide exempted it from ethical review because of the use of non-identifiable data.

DISCLOSURE

There is no competing interest to declare.

AUTHORSHIP

AW prepared the draft and MB conducted the analyses and helped in preparing the draft. NS and DGC acquired the data and contributed in conceptualizing and design, analyses, interpreting the findings, reviewing, and editing the drafts. All other authors equally contributed to interpretation, critical review, and editing of the drafts.

DATA AVAILABILITY STATEMENT

MedicineInsight data are not publicly available and not owned by the researchers. To access and use this database, an application can be lodged the MedicineInsight data governance office.

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