

BMJ Open Pattern and probability of dispensing of prescription opioids and benzodiazepines among the new users in Australia: a retrospective cohort study

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ABSTRACT

Objective Opioids and benzodiazepines are recommended to use for a short duration. Clinicians face a challenge to appraise the risk of new users to become long-term users. This study examined the pattern and probability of opioids and benzodiazepines dispensing among the new users.

Design A unit-record data of an incident and a point-incident cohort of new users, who were not dispensed in the previous 2 years, was examined and retrospectively followed up for 24 months.

Setting Australia.

Participants A random 10% national sample.

Primary and secondary outcome measures Distribution of total dispensing in calendar months. Probability of staying in the cohort in each successive month. Effect of first month's dispensing pattern on the total duration of dispensing during 2nd–24th month in total number of calendar months the dispensing was recorded.

Results In the incident cohort, 68.24% were dispensed opioids, 23.96% were dispensed benzodiazepines and 7.80% were dispensed both medicines. Over 70% in the incident cohort and 50% in the point-incident cohort were dispensed for a month only. Codeine was the most prevalent opioid, dispensed to 52% of opioid users; and diazepam was the most prevalent benzodiazepines, dispensed to 45.34% of benzodiazepine users. The probability of staying in the cohort and hence receiving further dispensing continued to be very high if dispensing did not end in the first month. The quantity (in defined daily dose) and the total number of dispensing episodes in the first month were significant predictors of the total duration of dispensing in the later period.

Conclusions Since harms from long-term use of these medicines may outweigh the benefits, and since the probability of further dispensing was high for those who were dispensed for more than a month, clinicians should endeavour to keep the dispensing duration and quantity as small as possible while initiating a prescription for the new users.

INTRODUCTION

Opioids and benzodiazepines are two of the most frequently misused prescription medicines in the world.¹ Opioids are widely used in the treatment of pain² and benzodiazepines in anxiety and sleep problems.³

Strengths and limitations of this study

- In this study, participants were taken randomly from the dispensing database for prescription opioids and benzodiazepines, and followed them retrospectively for 24 months.
- The study used a detailed analysis to assess the pattern of dispensing and calculated the population-level probability of dispensing of two important medicines: opioid and benzodiazepine.
- The dataset had limited number of variables to use for adjusting the multivariable regression models.
- Opioids and benzodiazepines that were dispensed in hospitals and through private prescriptions were not captured in this dataset.

An ageing population and increasing prevalence of conditions that are treated with these medicines put pressure on healthcare professionals to increase the prescribing and dispensing of these medicines. However, both medicines cause tolerance, dependence and addiction and may have serious adverse health outcomes.^{4 5} There is now growing scientific evidence that at the population level, negative health outcomes from long-term use of these medicines may outweigh the benefits.^{6 7} Their increasing level of utilisation and associated adverse health outcomes attracted substantial public health interest.⁸ Thus, on one hand, there is a growing demand for these medicines to treat pain, anxiety and insomnia, and on the other hand, there is pressure from public health point to reduce the prescription and dispensing of these medicines due to associated harms.

Recent studies in Australia found that at a population level, opioids and benzodiazepines are more commonly dispensed only for a quarter of a year than a longer duration.^{9 10} However, despite a relatively small proportion being dispensed for a longer duration,^{9 11 12} the largest volume of opioids and benzodiazepines

is being dispensed for that smaller proportion of patients.^{10–12} Due to adverse health outcomes from long-term use, it is strongly recommended to take necessary precautions prior to prescribing or dispensing these medicines so that potential adverse effects can be reduced without diminishing legitimate access.¹³ However, clinicians strive to speculate the possibility of a new user to continue using for a longer duration. While, to a large extent, this depends on individual patient's circumstances, population-level and longitudinal data can help to understand the progression from initial to long-term use, inform an appropriate decision while providers prescribe/dispense and optimise the use of these medicines. However, there are very few longitudinal studies that examine patients who are initially prescribed opioids or benzodiazepines. Using a 10% random sample of unit-record dispensing data, this study examines: (1) the pattern of dispensing of opioids and benzodiazepines among the new users during 2 years after commencing use and (2) the effect of dispensing pattern in the first month on the total duration of dispensing in the later period.

METHOD

Dataset

According to the subsidy scheme of medicine, all prescription medicines dispensed through community pharmacies in Australia can be categorised into the following four types: Pharmaceutical Benefits Schemes (PBS), Repatriation PBS (RPBS), under copayment and private. The PBS subsidises prescribed medicines for Australian residents and visitors from other countries that have reciprocal healthcare agreements with Australia. The RPBS is available to eligible war veterans and their families and includes all PBS-listed medicines and some additional items.¹⁴ The price of some medicine items is below the general patient copayment and hence known as under copayment items. As the subsidy is not required for under copayment items, patients pay the full price. Some medicines are not listed on the PBS or RPBS, and thus, patients pay the full price for those items as a private prescription. Overall, around 80% of all prescription medicines dispensed are covered by the PBS/RPBS.¹⁵

A 10% random sample of a longitudinal and unit-record extract of Australians who were dispensed prescription opioids and or benzodiazepines from community pharmacies was collected from the Australian Government Department of Human Services. The department usually offers a 10% random sample. The dataset covered PBS, RPBS and under copayment data dispensed in all states and territories of Australia. Medicines were recorded according to WHO Anatomical and Therapeutic Chemical classification¹⁶ and the time variable was recorded based on the date of supply. The names of the opioids and benzodiazepines used in the analysis and their corresponding Anatomical Therapeutic Classification codes were presented in the appendix (online supplementary table S1). This study analysed dispensing data from January 2013 to December 2016. Since the frequency for

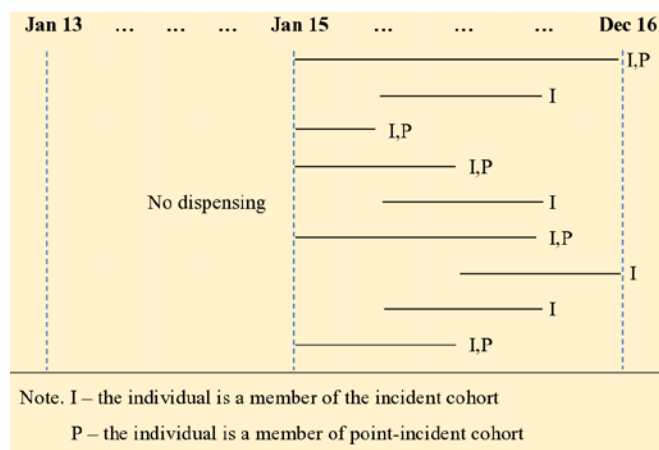


Figure 1 Demonstrating incident and point-incident cohorts of new users.

clients of age group <10 years had a very low count, to ensure confidentiality and minimise the risk of identification, dispensing records of the clients of age group <10 years were excluded/suppressed.

Incident and point-incident cohorts

To classify the new users, two cohorts —(1) incident cohort and (2) point-incident cohort—were identified separately for opioids and benzodiazepines. To identify the incident cohort, a subset of users was extracted who were not dispensed any opioids or benzodiazepines during the first 2 years (ie, 2013 and 2014). The incident cohort had a record of at least one episode of opioids and or benzodiazepines dispensing between 1 January 2015 and 31 December 2016. Given that many participants in the incident cohort commenced opioids or benzodiazepines at various time points, to have a better understanding of the pattern of dispensing during the follow-up period, two point-incident cohorts—one for opioids and the other for benzodiazepines—were also extracted with participants who commenced only in the first month of 2015 (figure 1). Thus, the point-incident cohort was a subset of incident cohort with users for whom dispensing commenced in the first month of 2015.

Thus, a person was classified as a new user of opioids if he/she was not dispensed any opioids between January 2013 and December 2015. Similarly, new users of benzodiazepines were not dispensed any benzodiazepines during these 2 years. Therefore, all individuals of the incident and the point-incident cohorts were new users; and as can be seen from figure 1, there were two types of new users: one that belongs to the point-incident cohort and the other that belongs to the incident cohort.

Analysis

Descriptive analysis was conducted to compute the duration and amount of dispensing separately for both medicines across age group and sex. The duration was computed in terms of the number of individual calendar months the dispensing was recorded. The total number of users ceased receiving dispensing in each month,

and a number of potential participants staying in the cohort during the remaining follow-up period were also computed. An actuarial life table method was used to estimate the probability of staying in the cohort in each month of the follow-up period based on the number of potential candidate users and those who ceased receiving any further dispensing. Here ‘cessation’ indicates the last episode of dispensing in the entire study period remaining. For instance, if N_1 was the total number of users in the first month, and M_1 was the number of users ceased at the end of the first month (meaning that M_1 were dispensed only during the first month and they were never dispensed during the follow-up period), then at the end of the first month the potential candidate users (R_1) staying in the study and who were at risk of further dispensing during the remaining follow-up period were equal to $N_1 - M_1$. Therefore, the proportion of at-risk users staying in the cohort after the i^{th} month was computed as $P_i = (R_i - M_i)/R_i$, where i is month number. In fact, these participants were at risk of further dispensing during the remaining period of the follow-up. The sensitivity test for the pattern of dispensing was performed by using a different cohort of users for whom the dispensing commenced in February 2015.

Finally, the effect of dispensing pattern in the first month on the total duration of dispensing in terms of number of individual calendar months in the later period (ie, duration of dispensing from 2nd month to the end of the 24th month) was examined by using the multivariable regression model. Using the point-incident cohort, the following two sets of regression models were developed: (1) the association between total dispensing episodes (ie, the total number of times dispensing was recorded) in the first month and the duration of opioid dispensing during the 2nd–24th month, and (2) the association between total quantity of dispensing in the first month and the duration of benzodiazepine dispensing during the 2nd–24th month. The quantity dispensed in the first month was computed in defined daily dose (DDD), which corresponds to the estimated daily dose of a drug when used for its main indication in adults. This metric was introduced by WHO Collaborating Centre.¹⁶ DDD brings both quantity and potency into consideration. Since, the dependent variable, that is, durations of dispensing during the 2nd–24th month were highly positively skewed, the Poisson regression with robust variance estimate was used.^{17 18}

All analyses were performed using Stata V.13 (Stata Corp LP, College Station, Texas, USA, 2011),¹⁹ Microsoft Excel programme was used to develop the figures.²⁰

Patient and public involvement

As this study used de-identified data, there was no scope of involving patients in setting the research questions, study design or outcome measures. Thus, there are no plans to disseminate the results of this research to study participants.

RESULTS

The incident cohort had 312 324 participants, 47% were male and 53% female users. The mean age was 47.38 years (SD 19.42). In this cohort, 68.24% were dispensed opioids and 23.96% were dispensed benzodiazepines, 7.80% were dispensed both medicines. During 2 years, 71.92% of the opioid users were dispensed in 1 month only and the rest (28.08%) in two or more months. Similarly, among the benzodiazepine users, 70.67% were dispensed in 1 month only and the rest (29.33%) in 2 or more months. The durations of dispensing, frequency and respective percentages of the incident cohort are presented in [table 1](#). The median duration of opioid dispensing was higher (2.1 months) for the users who used both opioids and benzodiazepines than for opioid only users (1.6 months). The median duration of benzodiazepines dispensing was similar (1.7 months) for those who used both drugs and those who used benzodiazepines only.

In the incident cohort, codeine (and derivatives) was the most prevalent item, which was dispensed to 52% of all opioid users. Oxycodone and derivatives (31.3%) and tramadol (13.1%) were the next two prevalent items. Diazepam was the most prevalent benzodiazepine item, which was dispensed to 45.34% users, followed by temazepam (42.80%) and oxazepam (8.66%). These trends in dispensing of individual items were similar to that of the point-incident cohort.

The durations of dispensing, frequency and respective percentages of the point-incident cohort are presented in [table 2](#). In this cohort, 58.16% of the opioid users were dispensed in 1 month only and the rest (41.84%) in 2 or more months. Similarly, among the benzodiazepine users, 56.80% were dispensed in 1 month only and the rest (43.20%) in 2 or more months. Similar to the incident cohort, more women (52.2%) were dispensed opioids and benzodiazepines (56.94%) than men (47.8% and 43.1%, respectively). Overall, the number of users being dispensed opioids or benzodiazepines in terms of the total number of calendar months exhibit an exponential decay type trend—decreases rapidly at first, and then more slowly as time went on.

As can be seen from [table 3](#), at the end of the first month, 6207 of 10672 participants in point-incident cohort ceased receiving opioids dispensing, meaning that they were not dispensed opioids in the next 23 months of the follow-up period. In other words, at the end of the first month, some 4465 participants were still at risk for further dispensing of opioids. Therefore, at the end of the first month, the probability of at-risk users staying in the cohort was $(10672 - 6207)/10672 = 0.42$. This means, number-wise, at the end of the first month, 42% of participants ($n=4465$) were potential candidates to further dispensing of opioids during the next 23 months follow-up period. Similarly, at the end of the second month, 399 of 4465 participants ceased receiving dispensing, leaving 4066 potential candidates to further dispensing. As only a few (ie, $n=399$) ceased, at the end of the second month,

Table 1 The distribution of users of the incident cohort in terms of total number of calendar months the dispensing was recorded

Total no of calendar months	Opioids				Benzodiazepines			
	Overall	% of overall	Men %	Women %	Overall	% of overall	Men %	Women %
1	170797	71.92	48.40	51.60	70101	70.67	42.40	57.60
2	39791	16.75	48.50	51.50	15549	15.68	42.18	57.82
3	12457	5.25	47.45	52.55	5565	5.61	42.86	57.14
4	5336	2.25	47.56	52.44	2744	2.77	45.08	54.92
5	2692	1.13	50.11	49.89	1577	1.59	48.07	51.93
6	1708	0.72	49.82	50.18	922	0.93	46.75	53.25
7	1062	0.45	51.22	48.78	658	0.66	48.18	51.82
8	741	0.31	52.77	47.23	477	0.48	46.75	53.25
9	570	0.24	50.18	49.82	341	0.34	52.49	47.51
10	448	0.19	46.88	53.13	251	0.25	46.61	53.39
11	365	0.15	47.12	52.88	220	0.22	48.64	51.36
12	272	0.11	51.47	48.53	155	0.16	45.16	54.84
13	212	0.09	51.89	48.11	131	0.13	54.96	45.04
14	189	0.08	44.97	55.03	96	0.10	42.71	57.29
15	195	0.08	46.67	53.33	80	0.08	46.25	53.75
16	139	0.06	41.73	58.27	63	0.06	39.68	60.32
17	141	0.06	55.32	44.68	65	0.07	44.62	55.38
18	100	0.04	46.00	54.00	47	0.05	42.55	57.45
19	78	0.03	43.59	56.41	46	0.05	50.00	50.00
20	74	0.03	58.11	41.89	34	0.03	50.00	50.00
21	43	0.02	53.49	46.51	25	0.03	52.00	48.00
22	45	0.02	48.89	51.11	29	0.03	34.48	65.52
23	28	0.01	46.43	53.57	15	0.02	33.33	66.67
24	10	0.00	40.00	60.00	4	0.00	50.00	50.00
Total	237493		48.41	51.59	99195		42.75	57.25

the probability of staying in the cohort was relatively high (0.91). As [table 3](#) and [figure 2](#) demonstrate, commencing from the second month the probability of at-risk users staying in the cohort remains relatively high, as the number of clients ceased receiving dispensing continued to remain low. Following this approach, the probability of at-risk users staying in the cohort was calculated up to the end of 21 months. As the follow-up period after the 21st month came down to less than 3 months, the probability was not computed after this point of time.

The probability of at-risk users staying in the cohort and their probability of receiving further dispensing during the follow-up period remained very high if dispensing did not end in the first month ([table 3](#)). The trends in the number of users dispensed, ceased receiving benzodiazepines on each month, and those who were at risk of further dispensing were similar to that for opioids (ie, similar to [figure 2](#)). However, the declining slope of the probability of further dispensing was higher for opioids than benzodiazepines.

The average number of calendar months the users were dispensed opioids or benzodiazepines increased with their average age ([figure 3](#)). The increments across the age range were positive both for opioid and benzodiazepines dispensing. The trends were similar both for male and female users.

The number of episodes and the quantity of dispensing (in DDD) during the first month were associated with the overall duration of dispensing during the 2nd–24th month ([table 4](#)). These relationships hold for both opioids and benzodiazepines dispensing. Users' age was found marginally significant but not users' sex.

DISCUSSION

Prescription opioids and benzodiazepines are the important medicines. The findings of this study do not suggest to drastically reduce the dispensing of these medicines, rather they highlight the population-level trend in utilisation or dispensing of these medicines among the

Table 2 The distribution of users of the point-incident cohort in terms of total number of calendar months the dispensing was recorded

Total number of calendar months	Opioids				Benzodiazepines			
	Overall	% of overall	Men %	Women %	Overall	% of overall	Men %	Women %
1	6207	58.16	47.95	52.05	2440	56.80	42.87	57.13
2	2345	21.97	47.16	52.84	831	19.34	41.28	58.72
3	894	8.38	47.20	52.80	373	8.68	41.02	58.98
4	433	4.06	46.42	53.58	215	5.00	46.51	53.49
5	218	2.04	46.33	53.67	101	2.35	51.49	48.51
6	138	1.29	45.65	54.35	76	1.77	39.47	60.53
7	87	0.82	57.47	42.53	54	1.26	50.00	50.00
8	46	0.43	54.35	45.65	32	0.74	43.75	56.25
9	55	0.52	58.18	41.82	24	0.56	62.50	37.50
10	38	0.36	26.32	73.68	15	0.35	53.33	46.67
11	24	0.22	54.17	45.83	19	0.44	57.89	42.11
12	20	0.19	65.00	35.00	14	0.33	35.71	64.29
13	17	0.16	58.82	41.18	14	0.33	57.14	42.86
14	22	0.21	40.91	59.09	13	0.30	46.15	53.85
15	18	0.17	50.00	50.00	11	0.26	45.45	54.55
16	15	0.14	53.33	46.67	6	0.14	50.00	50.00
17	18	0.17	50.00	50.00	9	0.21	55.56	44.44
18	10	0.09	20.00	80.00	6	0.14	33.33	66.67
19	12	0.11	75.00	25.00	5	0.12	20.00	80.00
20	9	0.08	66.67	33.33	5	0.12	80.00	20.00
21	10	0.09	50.00	50.00	8	0.19	50.00	50.00
22	13	0.12	53.85	46.15	13	0.30	30.77	69.23
23	13	0.12	53.85	46.15	8	0.19	25.00	75.00
24	10	0.09	40.00	60.00	4	0.09	50.00	50.00
Total	10672		47.76	52.24	4296		43.06	56.94

new users. Using a random and population-level sample with 2 years of administrative data of all states and territories of the country, this study provides detailed information about the pattern of dispensing of opioids and benzodiazepines among the new users of a large cohort. One of the central findings of this study is that around half of the new users of the point-incident cohort and 70% of the incident cohort were dispensed a month only. However, if dispensing was not ceased in the second month, the probability of staying thereafter in the cohort was more than 90%. This probability of at-risk users staying in the cohort after each successive month decreased slowly after the first month and remained over 80%. This observation was consistent for both opioid and benzodiazepine users. The average duration of dispensing increased with the average age of the participants.

Findings of this study also suggest that the number of users being dispensed opioids or benzodiazepines in total number of calendar months exhibit an exponential decay type distribution. Also, the total quantity and episodes of dispensing during the first month were significant

predictors for the overall duration of dispensing. Together these observations warrant prescribers to better assess the implication of initiating and then continue prescribing these medicines. Dependence or addiction associated with these medicines is now well documented.^{21 22} For instance, a systematic review found that average rates of addiction were 8%–10% among pain patients with long-term opioid use.²³ Also, there is a substantial risk of overdose, particularly from the concurrent use of opioids and benzodiazepines.²⁴ Literature suggests the most important risk factor for opioid analgesic-related dependence or overdose involves receiving a prescription for opioids. For example, patients with a history of preoperative opioid use²⁵ or newly prescribed opioids after short-stay surgery are associated with a substantially increased risk of becoming a long-term opioid user.²⁶ Similarly, the over-riding determinant for benzodiazepine use is its previous use. In a recent study of a sample of the senior citizen, Gerlach *et al* found that nearly one-third of patients went on to long-term use.²⁷ Some users may have a genetic predisposition to opioid dependence.



Table 3 Pattern of dispensing, discontinuing and the probability of remaining in the cohort over the months in the point-incident cohort

i^{th} Month	Benzodiazepine users											
	Dispensed	At risk	Probability of at-risk users staying in the cohort after the i^{th} month	Cumulative probability of staying i years in the cohort	Dispersed	At risk	Probability of at-risk users staying in the cohort after the i^{th} month	Cumulative probability of staying i years in the cohort	Dispersed	At risk	Probability of at-risk users staying in the cohort after the i^{th} month	Cumulative probability of staying i years in the cohort
	N_i	R_i	$P_i=(R_i-M_i)/R_i$	CP_i	N_i	R_i	$P_i=(R_i-M_i)/R_i$	CP_i	N_i	R_i	$P_i=(R_i-M_i)/R_i$	CP_i
1	10672	10672	0.42	0.42	4296	4296	0.42	0.42	4296	4296	0.43	0.43
2	1149	4465	0.91	0.38	388	1856	0.91	0.38	101	1755	0.95	0.41
3	793	4066	0.94	0.36	374	1664	0.94	0.36	91	1593	0.96	0.39
4	606	3825	0.96	0.34	300	1535	0.96	0.34	71	1473	0.96	0.37
5	567	3654	0.96	0.33	302	1415	0.96	0.33	58	1355	0.96	0.36
6	546	3492	0.96	0.32	252	1307	0.96	0.32	62	1243	0.96	0.34
7	555	3358	0.95	0.30	281	1211	0.95	0.30	58	1156	0.96	0.33
8	508	3188	0.96	0.29	254	1097	0.96	0.29	60	1035	0.96	0.31
9	517	3057	0.95	0.28	238	960	0.95	0.28	48	960	0.96	0.30
10	477	2903	0.95	0.26	257	875	0.95	0.26	64	875	0.95	0.29
11	465	2749	0.95	0.25	216	800	0.95	0.25	32	795	0.97	0.28
12	448	2602	0.94	0.23	243	719	0.94	0.23	55	719	0.95	0.27
13	413	2446	0.94	0.22	242	641	0.94	0.22	59	641	0.95	0.25
14	412	2304	0.94	0.21	236	548	0.94	0.21	62	548	0.94	0.24
15	454	2171	0.92	0.19	269	462	0.92	0.19	75	462	0.93	0.22
16	435	2006	0.92	0.17	270	388	0.92	0.17	85	388	0.91	0.20
17	441	1850	0.91	0.16	249	300	0.91	0.16	80	300	0.91	0.18
18	447	1678	0.89	0.14	234	245	0.89	0.14	76	245	0.90	0.17
19	452	1497	0.88	0.12	231	197	0.88	0.12	78	197	0.89	0.15
20	450	1310	0.86	0.11	245	186	0.86	0.11	93	186	0.85	0.13
21	407	1124	0.83	0.09	218	186	0.83	0.09	87	186	0.84	0.11
22	423	-	-	-	218	-	-	-	-	-	-	-
23	454	-	-	-	224	-	-	-	-	-	-	-
24	462	-	-	-	197	-	-	-	-	-	-	-

*That is, after the i^{th} month, these users were never dispensed during the study period.

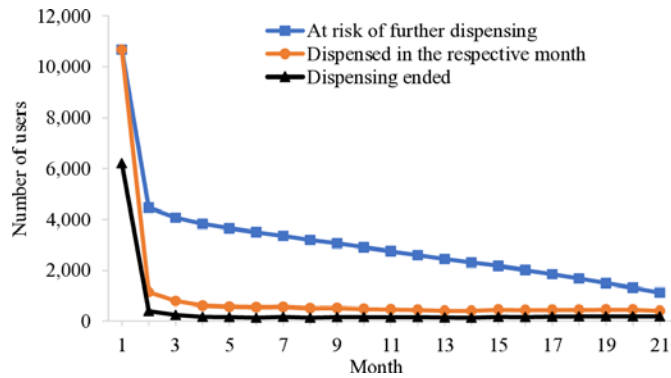


Figure 2 Trends in number of users dispensed, discontinued and at risk of further dispensing of opioids during the follow-up period.

However, often this is difficult to ascertain in day-to-day clinical practice.²⁸

This study did not examine the reason as to why the initial dispensing pattern in the first month was associated with the longer duration of dispensing during the rest of the period. A possible explanation is that the patients with more persistent and severe pain get more prescription and hence more dispensing episodes and higher quantities. Part of this association could be explained by the fact that patients at higher risk of long-term use (eg, substance abuse or history of depression) are more likely to receive prescriptions than patients with lower risk, despite recommendations to the contrary.²⁹ Further study is recommended to precisely examine the cause. Deyo *et al* in their study in the USA found that for most patients initiating opioids, the intention was a short-term use and observed that the probability of long-term use could be minimised by initiation with a single prescription of a short-acting opioid, with no refills, and a cumulative dose less than 120 morphine equivalents.²⁹ Similar studies are warranted in Australia with a particular focus on assessing the contribution of the initial pattern of dispensing that could be reasonably reduced to avert the risk of long-term use driven by dependence. Gerlach *et al*'s²⁷ recommendation for prescribers to 'begin with the end in mind' while

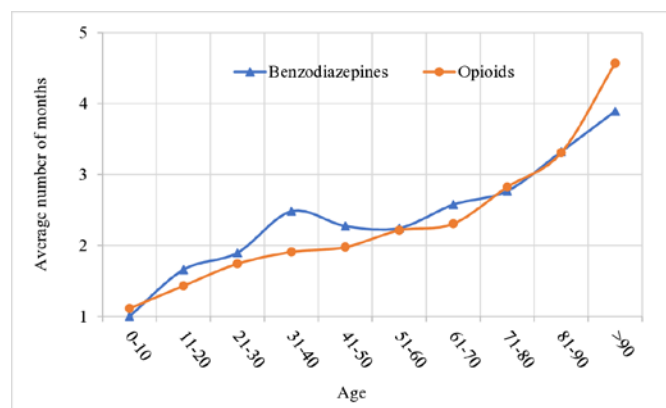


Figure 3 Average number of months prescriptions for opioids and benzodiazepines were dispensed across various age groups.

initiating a prescription for the new users and immediate discussion about the expected (brief) length of treatment is a reasonable clinical strategy.

Due to adverse health risks associated with the misuse of low-dose codeine-containing medicines in Australia, starting from February 2018, all codeine-containing over-the-counter products became a prescription-only medicine. The early results show that this rescheduling had substantially reduced the dispensing of codeine-containing products.³⁰ However, it is not yet clear as to whether this reduction in dispensing had any impact on the misuse of codeine-containing medicines. It should be noted that the literature largely suggests that the upscheduling in 2010 did not reduce the misuse of these medicines.³¹ Also, research is needed to examine if this reduction in overall use had any impact on the dispensing of other opioid items.

The quantity and/or duration of dispensing could partly be influenced by doctor shoppers.³² Their number could have drastically be reduced with the introduction of a real-time prescription drug monitoring programme, which was not available during the study period in most states/territories.^{33 34} In the absence of such a programme, clinicians and dispensers are mostly reliant on the information they receive from the patients. In such a situation, it is not unlikely that some unnecessary prescription and dispensing took place. A real-time prescription drug monitoring programme, which is now being implemented in most jurisdictions in Australia, may help to reduce such unnecessary or undue dispensing of these addictive medicines.

Limitations

This study has some limitations. First, the dataset had a limited number of variables to use for adjusting the multivariable regression models. For instance, information, such as multimorbidity and socioeconomic status of the individual patients, was not available. Second, opioids and benzodiazepines that were dispensed in hospitals, through private prescriptions, and the drugs sourced online or diverted from other sources were not captured in this dataset. As a result, a subset of new users may have used opioids during the previous 2 years of incident dispensing and may not have been truly new users. However, this dataset covers around 80% of all dispensing.¹⁵ Also, the dataset did not have information about the indications for dispensing or the number of prescribers, and it was beyond the scope of the study to ascertain as to whether or to what extent the dispensing was inappropriate. Moreover, the quantity of medicine dispensed was not taken into consideration when estimated the population-level dispensing pattern during the follow-up period. Future research should aim to examine these aspects. Finally, the results of this study may not be generalisable in other settings, as the dispensing/utilisation of opioids and benzodiazepines are influenced by a range of factors that may differ across settings.

**Table 4** Outputs of Poisson regression assessing the effect of dispensing episode and quantity in the first month on dispensing duration in the remaining follow-up period

Variable	Opioids users (n=10672)		Benzodiazepines users (n=4296)	
	IRR	95% CI	IRR	95% CI
Total dispensing episodes in the first month	1.26	1.19 to 1.33	1.75	1.49 to 2.06
Total quantity of dispensing in DDD in the first month	1.02	1.01 to 1.02	1.01	1.00 to 1.01
Age	1.02	1.02 to 1.02	1.01	1.01 to 1.02
Male (ref. female)	1.01	0.92 to 1.10	1.04	0.92 to 1.18
Constant	0.28	0.25 to 0.32	0.34	0.27 to 0.43

IRR, Incidence Rate Ratio.

Conclusion

More than half of the new users in the point-incident cohort were dispensed opioids and benzodiazepines for a month, during the 2-year follow-up period. The probability of further dispensing during the follow-up period remained very high if dispensing did not end in the first month. The quantity and the number of episodes of dispensing in the first month were significant predictors of the total duration of dispensing in the later period. Given that long-term use of these medicines may cause substantial adverse health outcomes, the results of this study echo the most guidelines that the prescription and dispensing of opioids and benzodiazepines should be carefully assessed before initiation, and dispensing duration and quantity should be kept as small as possible if these medicines are deemed necessary.

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Data availability statement Data may be obtained from a third party and are not publicly available. The author is not allowed to share the dataset. However, data of recent 5 years could be accessed on approval of the Australian Government Department of Human Services.

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