Prescription opioid dispensing and prescription opioid poisoning: Population data from Victoria, Australia 2006 to 2013

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Abstract

Objective: To describe recent trends in opioid prescribing and prescription opioid poisoning resulting in hospitalisation or death in Victoria, Australia.

Method: This is a population-based ecological study of residents of Victoria, 2006 -14. Australian Bureau of Statistics residential population data were combined with Pharmaceutical Benefits Scheme (PBS) opioid prescription data, Victorian Admitted Episodes Data (VAED) and cause of death data.

Results: Annual opioid dispensings increased by 78% in 2006 -13, from 0.33 to 0.58 per population. Opioid use increased with age: in 2013, 14% of Victorian residents aged ≥65 years filled at least one oxycodone prescription. In 2006 -14, prescription opioid related hospital admissions increased by 6.8% per year, from 107 to 187 /1,000,000 person-years; 56% were due to intentional self-poisoning. Annual deaths increased from 21 to 28 /1,000,000 persons, in 2007 -11. Admissions and deaths peaked at 25-44 years.

Conclusions: Although both opioid prescribing and poisoning have increased, there is discrepancy between the exposed group (dispensings increased with age) and those with adverse consequences (rates peaked at ages 25-44 years).

Implications: A better understanding is needed of drivers of prescribing and adverse consequences. Together with monitoring of prescribing and poisoning, this will facilitate early detection and prevention of a public health problem.

Key words: prescription opioids, drug overdose, pharmacoepidemiology

Prescription opioid-related harm has been referred to as epidemic in the United States (US).[1] Between 2001 and 2014 there was a three-fold increase in deaths from this cause, plateauing in 2011 at about 17,000 deaths annually.[2-4] US health agencies have recognised the national increase in opioid prescriptions as a key driver of the increase in prescription drug overdose deaths; particularly the prescribing of long-term opioids for chronic non-cancer pain.[5-9] A number of US states have implemented a series of policy responses focused on restriction of prescription opioid supply and increased availability of the opioid antagonist drug naloxone.[10,11] While there has been a plateau in the non-fentanyl prescription opioid epidemic curve that has coincided with the constraints on prescription supply, heroin deaths in the US since 2011 have tripled, with consequent ongoing escalation of the overall opioid-related public health problem.[2,3,12,13] Fentanyl can be obtained on prescription or manufactured illicitly: on the death certificate, deaths involving prescription fentanyl cannot be distinguished from deaths involving illicitly manufactured fentanyl. The availability of illicitly manufactured fentanyl has increased in the US.[14]In the US, the relationship between opioid prescriptions and opioid deaths has been explored in some detail. Regular opioid use in the US is more commonly reported among women than men, with women more likely to use opioids chronically at higher doses and to increase their use with age.[15] Deaths are more frequent among men than women, although women are hospitalised for opioid overdose more frequently and currently have a death rate that is increasing more quickly than among men.[15] The highest rate of deaths in both sexes is in the 45-55 age group.[16] Individuals at highest risk of opioid related harm are those being prescribed long term, high Morphine Equivalent Doses and those obtaining concurrent prescriptions from different sources.[17,18]There are three key lessons to be learned from the US experience. First, there is a substantial period between the beginning of the epidemic and the point at which a national response can be mobilised. Second, the increase in opioid deaths appears to be related to an increase in the amount of opioids prescribed, both at a population level and in relation to the group for whom prescriptions are intended. Third, the problem appears somewhat resistant to intervention. There are early indications that Australia has a prescription opioid problem. Annual opioid analgesic use has increased in Australia 2002-2009, from 13 to 16 defined daily dosages (DDD) per 1,000 population per day.[19] A study of opioid prescribing and adverse outcomes in Australia reported a 15-fold increase in opioid prescribing between 1992 and 2012, but with an apparently small effect on opioid related harm.[20] Oxycodone and fentanyl prescribing have both increased since 2000, but unlike the US, the rate of increased prescribing was not shown to match the rate of increase in deaths.[21-23] Fentanyl prescribing in Australia has increased in recent years, particularly among persons aged over

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80 years, and fentanyl deaths have also increased; however, deaths from this cause are still uncommon and mainly (75%) involve persons aged less than 47 years.[22] Results from a study in the Australian state of Victoria report a nine-fold increase in oxycodone prescriptions between 2000 and 2009 that is more than matched by an increase in deaths involving oxycodone.[24] Codeine use in Australia is difficult to capture because codeine can (to date) be obtained without prescription; furthermore, codeine is relatively inexpensive and is frequently obtained below the Australian Pharmaceutical Benefits Scheme co-payment threshold.[19] Codeine-related harm in Australia has increased: in 2000-09, accidental codeine overdose deaths increased from 1.8 to 5.1 deaths annually per million persons.[25] Of accidental codeine related deaths in 2000-13, the majority (84%) involved multiple drug toxicity.[25]

The sparse and inconsistent findings of previous research are insufficient to support an informed response to the problem of prescription opioid-related harm in Australia. Specifically, there is little information on age and gender differences in opioid use in Australia, and none on the relationship between the population being prescribed opioids and those most susceptible to opioid-related harm.

More detailed understanding of the current trends in opioid prescribing and opioid poisoning related hospital admissions and deaths in Australia by demographic groups is needed to adequately monitor the nature and extent of the public health consequences. To address this need our study aimed to (1) describe the population exposure to prescription opioids, and (2) describe the frequency and distribution of opioid-related hospital admissions and deaths, by age and gender. The analysis is limited to the State of Victoria, Australia, to provide population-based results for a defined population.

Methods

The study was reviewed by the Monash University Human Research Ethics committee and was granted exemption for ethical review. The research proposal satisfies section 5.1.22 of the National Statement on Ethical Conduct in Human Research ('institutions may choose to exempt from ethical review research that is negligible risk research, and involves the use of existing collections of data or records that contain only non-identifiable data about human beings').[26]

Pharmaceutical Benefits Scheme (PBS)

The Australian Government subsidises medicines through the PBS, which is available to citizens and permanent residents.[27] There is an out-of-pocket cost: for general patients this was set at $29.50 in 2006; this increased annually and reached $36.10 in 2013. For concession patients (e.g. pension card holders), this was $4.70 and $5.90, respectively.

Pharmaceutical prescription data

Prescription drugs that were PBS-listed and subsidised through a PBS co-payment were captured. Prescriptions purchased at a price below the PBS co-payment threshold were not included. All dispensings for concessional beneficiaries are captured in these data as all drugs are priced above their co-payment, but dispensings for general beneficiaries are not complete as some opioids are priced below the higher co-payment. PBS-listed medications were provided with a unique PBS code specific to the drug type, form, dosage and pack size. Summary PBS opioid prescription data were requested from the Australian Government Department of Human Services; availability and interpretation of PBS data for research is outlined in a recent publication by Mellish et al (2015).[28] The requested datasets were stratified by age (<25 years, 25-44; 45-64 and ≥65 years) and gender, and prescription dispensing year. PBS items were grouped by opioid type, based on anatomical therapeutic chemical classification (ATC) coding.[29] Methadone and buprenorphine dispensings coded as drugs used in opioid dependence (N07BC02 and N07BC01, respectively) were not included. Results were provided in terms of the number of prescriptions as well as the number of persons receiving a prescription in each stratum.

Hospital admissions data

Hospital admissions (2006 -14) related to opioid poisoning were determined from the Victorian Admitted Episodes Dataset (VAED). The VAED, in de-identified unit record format, is provided annually to the Victorian Injury Surveillance Unit by the Victorian Department of Health and Human Services and is coded according to the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modifications (ICD-10-AM). Hospital admissions related to opioid poisoning were identified as those with one or more of the following ICD-10-AM diagnostic codes: T40.2: Other opioids (codeine, morphine), T40.3: Methadone, and T40.4: Other synthetic narcotics (pethidine). For the purposes of this study, drugs that are potentially available on prescription are considered prescription drugs, even though these drugs could also be obtained over the counter or illegitimately. Opium and heroin are not available via prescription in Australia; however, heroin (T40.1) or opium (T40.0) ICD-10-AM codes occurring in the study sample, i.e. in combination with a T40.2, T40.3 or T40.4 code, were identified and reported in the study results. Codeine combinations are (currently) available over the counter as well as on prescription and are included in this study.

Only incident admissions were selected: transfers within and between hospitals were excluded. Admissions that took place in the ED only, i.e. the patient received care in the ED only, throughout the recorded admission, were identified and excluded. Aggregate tables were created by summing admissions by admission year, age group and gender. Intentional self-harm was identified as cases with cause coded as (ICD-10-AM external causes of morbidity and mortality: X60 through to X69: Intentional self-poisoning). Other causes were grouped as 'Unintentional poisoning' (X40-X49), 'Other unintentional' (X00-X39, X50-X59, W00-W46, W49-W81, W83-W94, W99), 'Other intentional self-harm' (X70 - X84), 'Assault' (X85- X99, Y00- Y09), 'Poisoning - other and undetermined intent' (Y10-Y19), and 'Other – other and undetermined intent' (Y20-Y36, Y40-Y89).

Death data

Deaths in 2007-12 associated with opioid poisoning were determined from the Cause of Death Unit Record file, provided to the Victorian Injury Surveillance Unit by the Australian Coordinating Registry. These data are based on the death unit record files coded by the Australian Bureau of Statistics and are coded using the International Statistical Classification of Diseases and Related Health Problems tenth revision (ICD-10). Death data is lagged and subject to revision pending coronial investigation: in this study, the death data from 2007-10 was final, data from 2011 was revised and data from 2012 was preliminary. Deaths related to opioid poisoning were identified as those with an external cause *and* one of the following ICD10 codes in the record axis data (which contain codes for all causes of death): T40.2: Other opioids (codeine, morphine),

T40.3: Methadone, and T40.4: Other synthetic narcotics (pethidine). Deaths were categorised according to year of registration, age group and gender. Intentional self-harm was identified as cases with cause coded as 'Intentional self-poisoning' (ICD-10 external causes of morbidity and mortality: X60 through to X69: Intentional self-poisoning).

Residential population

The population of Victoria from 2006 to 2013 was based on estimated resident population data available from the Australian Bureau of Statistics.[30] Residential population data were stratified by year, age group and gender.

Analysis

Data were analysed using SAS 9.4. Population-based dispensing rates were calculated by combining the pharmaceutical records with population data. Prescription opioid dispensing was calculated in terms of annual prescriptions and annual prescriptions per residential population. Where relevant, the statistical significance of differences in proportions was calculated with 2-tailed z-tests. The statistical significance of trends in annual dispensings per population over time were modelled using Poisson models (proc genmod in SAS), as trends in the annual number of dispensings, with the log of the annual Victorian residential population as offset.

Deaths and hospital admissions were combined with residential population data and presented as frequencies and rates. Population based rates were calculated as the number of events (deaths, admissions) per residential population per year, and presented as events per 1,000,000 person-years, with 95% confidence intervals. Rates were calculated per age group, gender and year, for hospital admissions and for deaths. Rates were also calculated separately for each of the relevant ICD codes (T40.2, T40.3, T40.4) and for intentional self-poisoning. For event counts below n=10, frequencies were suppressed and rates were not calculated. Time trends in the rate of admissions were modelled using Poisson models, as the annual number of events as a function of time in years (continuous), age group and gender, with the log of the annual Victorian residential population as offset. Trends in the rate of deaths were not calculated because only five years of final data were available.

Time trend results are presented as the modelled percentage change in rate per year, calculated as: *percentage change*=$[e^{\alpha}-1]\times 100\%$ where α is the parameter estimate of *year*, in the Poisson model. The analyses were conducted using the PROC GENMOD procedure in SAS V9.4.

Prescription data, hospital data and death data were not linked at a unit level: this study is therefore a report of observed rates rather than a cohort with follow-up/outcomes study.

Results

Prescription opioid dispensings: overall

Between 2006 and 2013, the annual number of PBS prescription opioid dispensings more than doubled, from 1.64 million in 2006 to 3.32 million in 2013 (Table 1). During this time, the residential population of Victoria increased 13%, from 5.06 to 5.74 million. Accounting for population growth, the annual number of prescription opioid dispensings increased from 0.33 to 0.58 per resident: a 78% increase between 2006 and 2013.

The annual prescription opioid dispensings per gender and age group are shown in Figure 1. Annual dispensings per population increased statistically significantly from 0.38 in 2006 to 0.68 in 2013 (76% increase) among women, and from 0.26 in 2006 to 0.48 in 2013 among men (81% increase). Annual dispensings per population also increased in each of the age groups during this time period: from 0.02 to 0.07 in the age group of under 24 years (204% increase); 0.24 to 0.42 at ages 25-44 years (78% increase), 0.43 to 0.79 at ages 45-64 years (86% increase), 1.00 to 1.41 at ages 65-84 years (42% increase), and 1.61 to 3.07 at ages 85 years and over (90% increase). Of all prescription opioid dispensings in 2006, 8.1% were received by persons age 85 years or over; in 2013 this increased to 10.6%.

To determine whether the high rates of opioid dispensings among women are due to overrepresentation of women among older persons, the female: male ratio in annual dispensings per population for each age group is shown in Figure 1 (bottom). From 2006 to 2013, in every age group, the annual rate was higher among women than men.

Table 1: Trends in population size and opioid dispensings in Victoria, Australia 2006 -13.

Year	Residents[a]	Annual opioid dispensings[b]	Annual opioid dispensings per population[b]
	x 1000,000	x 1,000	
2006	5.1	1,643	0.325
2007	5.2	1,784	0.346
2008	5.3	1,921	0.365
2009	5.4	2,022	0.376
2010	5.5	2,166	0.397
2011	5.5	2,256	0.407
2012	5.6	2,937	0.521
2013	5.7	3,322	0.579

a: Based in Australian Bureau of Statistics data.

b: Results are limited to prescribing according to the Pharmaceutical Benefits Scheme.

Prescription opioid dispensings: drug types

Of all captured opioid prescriptions, 29% were for codeine with paracetamol, 27% for oxycodone, 20% for tramadol, 10% for buprenorphine, 7.7% for morphine, 4.1% for fentanyl, 1.3% for oxycodone with naloxone, 0.6% for methadone, 0.5% for hydromorphone, 0.05% for pethidine hydrochloride and 0.003% for codeine with aspirin. The trends in use of the seven most commonly prescribed opioids, and relative use, are shown in Figure 2. In terms of dispensings per 100 residents per year, each of the opioid types increased in use with the exception of morphine. Between 2006 and 2013, there was a relative increase in oxycodone from 6.1 to 17.3 dispensings per 100 residents per year (an average annual increase of 16%), fentanyl from 0.5 to 2.3 (an average annual increase of 27%), codeine combinations from 11.8 to 15.7 (an average annual increase of 5.2%), tramadol from 8.7 to 10.1 (an average annual increase of 2.7%), and oxycodone combinations emerged in 2011. Buprenorphine dispensing increased from 0.9 to 6.0 dispensings per 100 residents per year (an average annual increase of 38%), methadone dispensings increased from 0.22 to 0.31 (an average annual increase of 5.5%) and morphine decreased by 6.4% per year on average, from 4.1 to 2.5 dispensings per 100 residents per year.

Age and gender trends in exposure to the strongest five opioids that were commonly prescribed are shown in Tables 2-3. In terms of the number of persons receiving prescriptions at least once in the relevant year, the number of oxycodone, fentanyl and buprenorphine recipients increased between 2006 and 2013, both in the <65 years and the ≥65 years age groups. The most commonly used strong opioid was oxycodone: in 2013, 14% of Victorian residents aged ≥65 years filled at least one oxycodone prescription. The most pronounced gender difference in exposure to strong opioids was observed for buprenorphine: by 2013 women were 2.2 times as likely as men to receive buprenorphine (1.44% vs. 0.65%; p<0.0002).

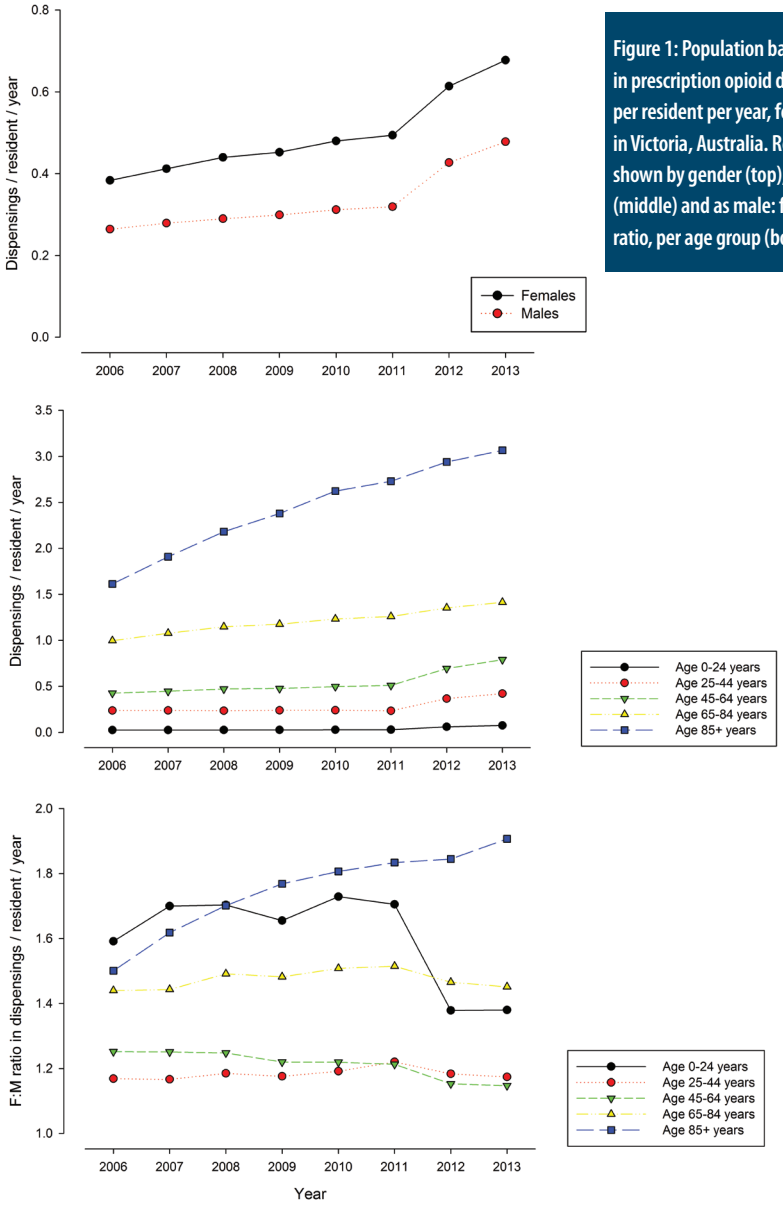

Figure 1: Population based trends in prescription opioid dispensings per resident per year, for 2006 -13 in Victoria, Australia. Results are shown by gender (top), age group (middle) and as male: female ratio, per age group (bottom).

Opioid-related harm: hospital admissions

Prescription opioid poisoning related hospital admissions in Victoria 2006 -14 are summarised in Table 4: there were 7287 prescription-opioid related admissions during this time period. The most commonly assigned ICD-10-AM-coded diagnoses (n=5874, 81%) were: 'Other opioids: codeine; morphine' (T40.2), followed by: 'Other synthetic narcotics: pethidine' (ICD-10-AM: T40.4) (n=1208, 17%), and: 'Methadone' (T40.3) (n=486, 7%). In 67 cases (1%), the diagnostic code for heroin poisoning (T40.1) was listed as well as a prescription opioid poisoning code.

Of all prescription opioid poisoning related admissions in Victoria 2006 -13, 4050 (56%) admissions were considered to be intentional self-poisoning; 1764 (24%) unintentional poisoning; 1102 (15%) poisoning of other and undetermined intent; 154 (2%) other unintentional, 31 (0.4%) other intentional self-harm and 14 admissions (0.2%) were due to assault. Among the admissions coded as intentional self-poisoning, the distribution of ICD-10-AM diagnostic codes was similar to that in the overall prescription opioid poisoning admissions: in most cases (n=3435, 86%) the diagnostic code was: 'Other opioids: codeine; morphine'. Next most common (n=628, 15%) were: 'Other synthetic narcotics: pethidine' and 'Methadone' (n=169, 4%). In 18 intentional self-poisoning cases (0.4%), the diagnostic code for heroin poisoning (T40.1) was listed as well as a prescription opioid poisoning code.

During the study period (2006-14), the hospital admission rate among women was 1.68 times higher than men (Table 4). The rate of intentional self-poisoning by opioids among women was 2.15 that of men. Admissions rates were highest in the 25-44 year age groups, and lowest in the ≥85 year age groups, which is a strikingly different pattern to that observed for opioid prescription use. There was a gradual increase in the rate of hospital admissions, from 107 admissions per 1,000,000 person years in 2006 to 187 in 2014. Adjusted for age and gender, the rate increased by 6.8% per year. The rate of admissions related to 'Other opioids – codeine, morphine' increased by 6.5% per year; the rate of methadone related admissions increased by 11.7% per year, and the rate of 'Other synthetic narcotics' increased by 8.0% per year. The rate of opioid-related admissions that were considered to be due to self-harm increased by 8.4% per year (Table 4).

Opioid-related harm: deaths

Deaths associated with prescription opioid poisoning in Victoria, 2007-12, are summarised in Table 5. The most commonly occurring diagnosis was 'other opioids – codeine, morphine' (n=640, 73.1%), followed by methadone (n=254, 29.0%), followed by 'other synthetic narcotics' (n=76, 8.7%). Of all prescription opioid poisoning related deaths, 143 cases (16.3%) were considered to be intentional self-poisoning. Contrary to the patterns observed for hospital admissions, the rate of death related to prescription opioid poisoning was 1.90 times higher among men than women. This was true for each of the drug type categories. There were, however, no statistically significant gender differences in intentional self-poisoning death rates. The highest opioid poisoning related death rate occurred the 25-44 year group; the 45-64 year group had the highest rate of *self-poisoning deaths*. Cell counts of <10 deaths have been suppressed: for the ≥85 year age group, the death rate was therefore below 11.1 deaths per 1,000,000 person-years (the rate corresponding with 10 deaths in this age group); which is less than a third of the recorded death rate for the 25-44 year age group. Overall, the rate of opioid related deaths increased from 21 deaths per 1,000,000 person years in 2007 to 28-29 in 2008-11, followed by a drop to 26.5 in 2012, possibly due to the preliminary data for that year (which is to be revised in the coming year).

Discussion

Our research findings in Victoria between 2006-07 and 2011-14 show a clear increase in the frequency of prescription opioid

dispensings, particularly an increase in potent opioids such as oxycodone and fentanyl. Opioid-related harm also increased in this population. However, the problem of prescription opioid dispensing and related harm in this population is not yet as severe as has been described in the US. Furthermore, the population-based relationship between exposure (high rates of prescription opioid dispensings) and adverse outcomes (overdose, death) was not linear: there was an overrepresentation of adverse outcomes in younger people, relative to exposure. Few conclusions about the nature of the relationship between prescribing and harm can be drawn from the descriptive information presented, indicating a critical area where further studies are required. However, the increasing number of deaths associated with opioid poisoning and the recent steep increase in prescribing of certain types of opioids, makes this further research a necessity.

Prescription opioid dispensing in Victoria increased by 78% over the period 2006 to 2013. Opioid use increased with increasing age, with highest rates of use among those aged ≥85 years. Opioid poisoning related hospital admission (2006 -14) and death rates (2007 -11) increased; opioid poisoning was most common among those aged 25-44 years. The overrepresentation of poisonings in younger people relative to dispensings suggests that in Victoria, increased numbers of the population being treated with prescription opioids does not fully correlate with prescription opioid poisoning rates.

Overall, the rate of opioid dispensings in Victoria was greater among women than men in every age group; prescription opioid hospital admissions were also more common among women than men, but opioid poisoning deaths were more common among men. This pattern is not dissimilar to that observed in the US, where drug overdose deaths are more common among men.[15] In the US, the gender gap is closing: death rates are increasing more rapidly among women than men[15] and prescription opioid overdose hospitalisations have also increased

Figure 2: Trends in the seven most commonly prescribed opioids in dispensings per opioid type.

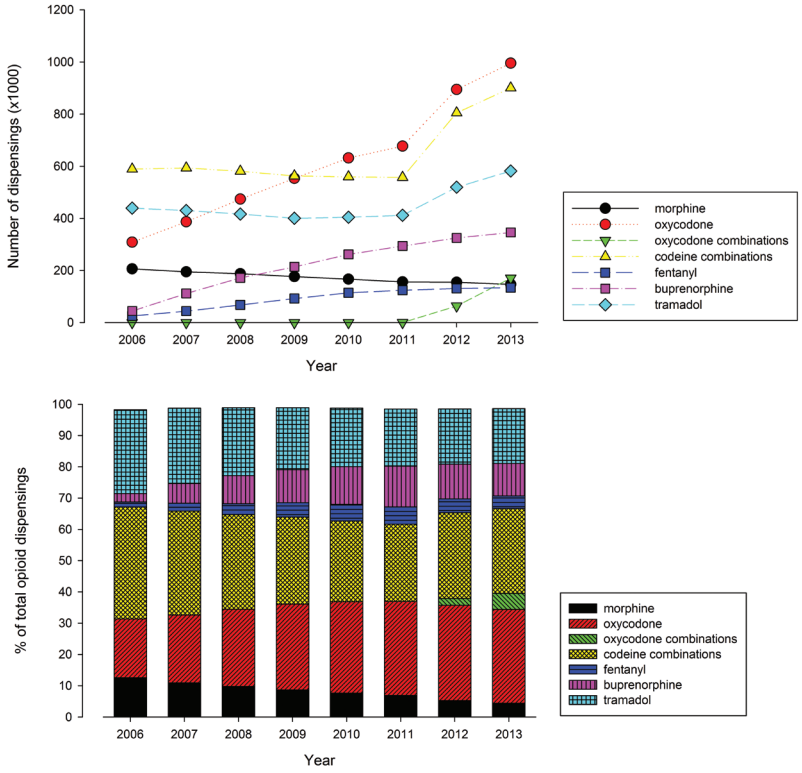

Table 2: Trends in the number of persons receiving prescriptions for the five most commonly prescribed strong opioids, by age group.

Year	Morphine		Oxycodone		Oxycodone combinations		Fentanyl		Buprenorphine	
	Persons aged <65 years N (%)[a]	Persons aged ≥65 years N (%)	Persons aged <65 years N (%)	Persons aged ≥65 years N (%)	Persons aged <65 years N (%)	Persons aged ≥65 years N (%)	Persons aged <65 years N (%)	Persons aged ≥65 years N (%)	Persons aged <65 years N (%)	Persons aged ≥65 years N (%)
2006	16,924 (0.4)	22,411 (3.3)	33,861 (0.8)	38,395 (5.7)	-	-	3,556 (0.1)	5,800 (0.9)	5,085 (0.1)	10,750 (1.6)
2007	15,090 (0.3)	21,609 (3.1)	43,194 (1.0)	50,850 (7.3)	-	-	5,096 (0.1)	8,435 (1.2)	7,702 (0.2)	21,432 (3.1)
2008	14,205 (0.3)	20,440 (2.9)	53,388 (1.2)	62,644 (8.8)	-	-	7,332 (0.2)	11,873 (1.7)	9,914 (0.2)	28,700 (4.0)
2009	13,558 (0.3)	20,027 (2.7)	64,380 (1.4)	75,055 (10.3)	-	-	9,110 (0.2)	14,587 (2.0)	11,066 (0.2)	32,599 (4.5)
2010	13,011 (0.3)	20,990 (2.8)	74,324 (1.6)	88,950 (11.8)	-	-	10,098 (0.2)	16,871 (2.2)	12,839 (0.3)	38,492 (5.1)
2011	12,617 (0.3)	22,932 (3.0)	83,003 (1.7)	98,627 (12.7)	221 (0.0)	252 (0.0)	10,389 (0.2)	17,971 (2.3)	13,532 (0.3)	41,691 (5.4)
2012	13,521 (0.3)	23,830 (3.0)	187,493 (3.9)	114,090 (14.1)	10,011 (0.2)	14,590 (1.8)	10,677 (0.2)	20,084 (2.5)	15,342 (0.3)	44,216 (5.5)
2013	13,225 (0.3)	22,972 (2.7)	234,805 (4.9)	117,994 (14.1)	23,729 (0.5)	31,575 (3.8)	9,900 (0.2)	19,279 (2.3)	15,193 (0.3)	45,067 (5.4)

a: The number of persons who filled at least one prescription for the opioid type in the given year is presented as absolute number as well as percentage of the residential population in that age group

Table 3: Trends in the number of persons receiving prescriptions for the five most commonly prescribed strong opioids, by gender.

Year	Morphine		Oxycodone		Oxycodone combinations		Fentanyl		Buprenorphine	
	Women N (%)[a]	Men N (%)	Women N (%)	Men N (%)	Women N (%)	Men N (%)	Women N (%)	Men N (%)	Women N (%)	Men N (%)
2006	21,018 (0.8)	18,317 (0.7)	40,774 (1.6)	31,482 (1.3)	-	-	5,209 (0.2)	4,147 (0.2)	10,950 (0.4)	4,885 (0.2)
2007	19,577 (0.8)	17,122 (0.7)	52,950 (2.0)	41,094 (1.6)	-	-	7,794 (0.3)	5,737 (0.2)	20,124 (0.8)	9,010 (0.4)
2008	18,596 (0.7)	16,049 (0.6)	65,939 (2.5)	50,093 (1.9)	-	-	11,515 (0.4)	7,690 (0.3)	26,887 (1.0)	11,727 (0.5)
2009	17,976 (0.7)	15,609 (0.6)	79,248 (2.9)	60,187 (2.3)	-	-	14,225 (0.5)	9,472 (0.4)	30,260 (1.1)	13,405 (0.5)
2010	18,224 (0.7)	15,777 (0.6)	93,405 (3.4)	69,869 (2.6)	-	-	16,401 (0.6)	10,568 (0.4)	35,816 (1.3)	15,515 (0.6)
2011	19,078 (0.7)	16,471 (0.6)	104,212 (3.7)	77,418 (2.8)	272 (0.0)	201 (0.0)	17,660 (0.6)	10,700 (0.4)	38,567 (1.4)	16,656 (0.6)
2012	19,943 (0.7)	17,408 (0.6)	164,933 (5.8)	136,650 (4.9)	14,515 (0.5)	10,086 (0.4)	19,509 (0.7)	11,252 (0.4)	41,437 (1.5)	18,121 (0.7)
2013	19,158 (0.7)	17,039 (0.6)	191,935 (6.6)	160,864 (5.7)	32,381 (1.1)	22,923 (0.8)	18,667 (0.6)	10,512 (0.4)	41,874 (1.4)	18,386 (0.6)

a: The number of persons who filled at least one prescription for the opioid type in the given year is presented as absolute number as well as percentage of the population

more rapidly among women than men.[31] For a better understanding of how trends in exposure impact on drug overdose and fatality rates among men versus women, a population based data linkage study of prescription drug dispensing, hospital admissions and deaths is needed. This will provide insight into potential risk factors, in terms of age and gender and other sociodemographic factors, comorbidity, and prescribing history including opioid strength, type and prescription repeats. A population-based data linkage study could also provide insight into potential drug diversion pathways.

Table 4: Prescription opioid poisoning related hospital admissions in Victoria, 2006 -13.

	Prescription opioid poisoning admissions, n=7,287		Diagnosis (ICD10)			Intentional self-poisoning, n=4,050
			Other opioids – codeine, morphine (T40.2), n=5,874	Methadone (T40.3), n=486	Other synthetic – narcotics (T40.4), n=1,208	
	N[a]	Rate (95% CI)[b]	Rate (95% CI)[b]	Rate (95% CI)[b]	Rate (95% CI)[b]	Rate (95% CI)[b]
Gender						
M	2,684	111 (106–115)	83 (79–87)	11.2 (9.8–12.5)	21 (19–22)	52 (50–55)
F	4,603	186 (180–191)	156 (151–161)	8.7 (7.5–9.8)	29 (27–31)	112 (108–116)
Age group						
0-24	1,429	90 (85–95)	72 (68–77)	4.7 (3.7–5.8)	16 (14–18)	59 (55–62)
25-44	2,912	204 (196–211)	157 (150–163)	20.7 (18.3–23.0)	35 (32–38)	125 (119–131)
45-64	2,001	166 (159–174)	140 (134–147)	8.9 (7.2–10.6)	25 (22–27)	94 (88–99)
65-84	769	129 (120–138)	110 (102–119)	–	20 (16–24)	31 (27–36)
85+	176	195 (167–224)	153 (128–179)	–	44 (31–58)	28 (17–39)
Year						
2006	544	107 (98–117)	91 (83–99)	4.7 (2.8–6.6)	14 (11–18)	56 (49–62)
2007	645	125 (115–135)	101 (93–110)	6.2 (4.1–8.4)	22 (18–26)	67 (60–74)
2008	694	132 (122–142)	107 (98–116)	8.9 (6.4–11.5)	20 (16–24)	72 (65–79)
2009	732	136 (126–146)	110 (101–119)	8.6 (6.1–11.0)	22 (18–26)	75 (68–82)
2010	722	132 (123–142)	106 (97–114)	10.3 (7.6–12.9)	21 (18–25)	73 (65–80)
2011	833	150 (140–161)	118 (109–128)	10.5 (7.8–13.2)	29 (24–33)	81 (73–88)
2012	994	176 (166–187)	143 (133–152)	11.9 (9.0–14.7)	29 (24–33)	98 (90–106)
2013	1,029	179 (168–190)	144 (134–153)	13.4 (10.4–16.4)	30 (26–35)	105 (96–113)
2014	1,094	187 (176–198)	151 (141–161)	13.5 (10.5–16.5)	31 (27–36)	111 (102–119)
Average % change per year[c]		+6.8% (5.2–8.4%)	+6.5% (4.7–8.2%)	+11.7% (7.4–16.2%)	+8.0% (5.6–10.5%)	+8.4% (6.4–10.5%)

a: Number of hospital admissions 2006 -14; transfers and in-hospital deaths excluded.

b: Rate of hospital admissions related to opioid poisoning, per 1,000,000 person-years 2006 -14.

c: Calculated using a Poisson model of admissions per year, adjusted for age and gender; offset by population size.

CI = confidence interval.

Table 5: Prescription opioid poisoning related deaths in Victoria 2007–2012.

	Prescription opioid poisoning deaths, n=876		Diagnosis (ICD10)			Intentional self–poisoning, n=143
			Other opioids – codeine, morphine (T40.2), n=640	Methadone (T40.3), n=254	Other synthetic – narcotics (T40.4), n=76	
	N[a]	Rate (95% CI)[b]	Rate (95% CI)[b]	Rate (95% CI)[b]	Rate (95% CI)[b]	Rate (95% CI)[b]
Gender						
M	570	23.5 (21.5–25.4)	16.9 (15.3–18.5)	7.0 (6.0–8.1)	1.9 (1.4–2.5)	3.1 (2.4–3.8)
F	306	12.4 (11.0–13.7)	9.3 (8.1–10.5)	3.4 (2.6–4.1)	1.2 (0.7–1.6)	2.7 (2.1–3.4)
Age group						
0–24	60	3.8 (2.8–4.7)	2.5 (1.7–3.3)	1.4 (0.8–2.0)	–	
25–44	501	35.1 (32.0–38.1)	24.9 (22.3–27.4)	11.8 (10.0–13.5)	2.4 (1.6–3.2)	3.3 (2.3–4.2)
45–64	281	23.3 (20.6–26.1)	18.1 (15.7–20.5)	5.2 (3.9–6.4)	2.5 (1.6–3.4)	5.9 (4.5–7.3)
65–84	25–35[d]	5.2 (3.4–7.0)	4.4 (2.7–6.0)			2.9 (1.5–4.2)
85+	<10[d]					
Year						
2007	109	21.2 (17.2–25.1)	16.3 (12.8–19.8)	5.4 (3.4–7.4)	–	2.9 (1.4–4.4)
2008	151	28.7 (24.1–33.3)	24.2 (20.0–28.4)	7.2 (4.9–9.5)	–	3.2 (1.7–4.8)
2009	154	28.7 (24.1–33.2)	22.7 (18.7–26.7)	6.9 (4.7–9.1)	–	6.3 (4.2–8.5)
2010	155	28.4 (23.9–32.9)	19.0 (15.4–22.7)	8.8 (6.3–11.3)	2.7 (1.4–4.1)	4.8 (2.9–6.6)
2011	158	28.5 (24.1–33.0)	18.8 (15.2–22.4)	10.1 (7.5–12.8)	3.1 (1.6–4.5)	4.5 (2.7–6.3)
2012[c]	149	26.5 (22.2–30.7)	17.6 (14.1–21.0)	8.3 (6.0–10.7)	4.3 (2.6–6.0)	4.6 (2.8–6.4)

a: Number of deaths in 2007-12.

b: Deaths per 1,000,000 person-years

c: 2007-10 death data are final; 2011 death data has been revised, and the 2012 deaths are provided as preliminary data: these numbers are likely to change when the 2012 revised and final data are released.

d: Exact number is not given to prevent recalculation of the low cell count for the ≥85 year age group.

CI = confidence interval.

Prescription opioid dispensing among persons aged 85 years and over increased by 90% between 2006 and 2013; particularly oxycodone use. The deaths and hospital admission analysis, however, did not show relatively high rates of opioid poisoning among older persons. These findings support earlier reports showing that older persons are underrepresented among oxycodone-related fatalities.[24] The rapid increase in prescription opioid use among older persons, however, warrants active monitoring of oxycodone-related hospitalisations and deaths, particularly as older persons are likely to take multiple medications and are therefore at risk of multiple drug toxicity. This will facilitate early identification of a trend following the opioid mortality observed in the US. Potential early interventions include revising dosing guidelines and regulations regarding potentially harmful drug combinations.

Prescription opioid poisoning may not be a direct consequence of increased prescription opioid use in the population: a more complex conceptual model, including drug diversion, tampering and other non-recommended use, is required to fully understand how prescribing trends and population-based exposure affect opioid poisoning trends. The high proportion of hospital admissions that were coded as intentional self-poisoning suggests that mental health should also be taken into account. Future research to provide more insight into the trends and potential for prevention and intervention could include analysis of coronial data to establish comorbidity, substances involved and drug source, and circumstances of the opioid poisoning. Data linkage studies of drug prescription data, hospital admissions data and death data will further contribute to knowledge of how drug prescribing trends affect adverse consequences.

This study's main limitation relates to incompleteness in the prescription data. The following prescriptions are not captured: 'private' prescriptions; prescriptions dispensed in some hospital settings; prescriptions obtained through the Repatriation Pharmaceutical Benefits Scheme (RPBS) and prescriptions that are below the co-payment threshold and paid out of pocket. These omissions may affect the described use per age groups: drugs that are below the co-payment threshold for regular patients may appear in the PBS data for concession patients such as pension card holders. In a study of prescription opioid analgesics in

Australia, 5.7% of oxycodone dispensings in 2008 were reported to be below the co-payment threshold, and 2.8% were private prescriptions.[19] Of morphine dispensings, 2.7% were under the co-payment threshold and 3.4% were private prescriptions. Tramadol and codeine had higher proportions of non-co-payment dispensings: 12.8% and 20.1%, respectively, and 4.3% and 6.7% were private prescriptions.[19] In another recent study, the overall capture of prescription opioids in the PBS and RPBS in the period 1992 -11 were reported to be lower (68%); 17% were reported to be obtained through private prescriptions and 15% were below the co-payment threshold[32] (although these are Australia-wide findings that may not accurately reflect the situation in Victoria). Furthermore, over-the-counter codeine was not captured in this study: in Australia, 55.8% of codeine packs sold in 2013 were over-the-counter; for Victoria, this was 55.4%.[33] In other words, the current report under-estimates actual opioid prescription filling. This inaccuracy is greater for younger persons than for older persons, as older persons are more likely to receive prescriptions at concessional rates (i.e. for older persons, dispensings captured in the co-payment PBS records better reflect the total numbers of dispensings). Age-differences in prescription filling are therefore likely to be overestimated in this study. Another limitation is that this study is based on separate data sources that were not linked: access to unit level prescription data and linkage with hospital and death data were not possible at the time of the study, but this will be the direction of future research in this area.

Victoria is the second-most populous state of Australia. In a recent study of opioid dispensing in Australia, high-to-low ranking of opioid dispensed through the PBS/RPBS per state in 2013 shows Victoria as ranking fifth out of the eight jurisdictions.[32] Victoria ranked fourth in oxycodone dispensings, fifth in tramadol dispensings and sixth in morphine dispensings.[32] The results presented in this study, although limited to Victoria, do not misrepresent prescription opioid dispensing in Australia.

Conclusion and implications

Overall prescription opioid consumption has increased rapidly in Victoria in 2006-13. Increase in prescription opioid dispensing has been most pronounced among women and older Australians; particularly oxycodone use among older persons has increased. Hospital admissions (2006-14) and deaths (2007-12) related to prescription opioid poisoning also increased, but these were most common in the 25-44 year age group. Furthermore, the majority of hospital admissions were due to intentional self-poisoning. The results emphasise the need for more in-depth research on opioid-related hospital admissions and deaths in Australia, and a better understanding of the drivers of prescribing and adverse consequences of prescribing. Drug diversion, drug tampering as well as physical and mental comorbidity need to be taken into account. In combination with monitoring of opioid prescribing and opioid poisoning, this will facilitate early detection and prevention of a potential opioid epidemic.

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