The POPPY Research Programme protocol: investigating opioid utilisation, costs and patterns of extramedical use in Australia

Louisa Degenhardt, Bianca Blanch, Natasa Gisev, Briony Larance, Sallie Pearson

ABSTRACT

Introduction: Opioid prescribing is increasing in many countries. In Australia, there is limited research on patterns of prescribing and access, or the outcomes associated with this use. The aim of this research programme is to use national dispensing data to estimate opioid use and costs, including problematic or extramedical use in the Australian population.

Methods and analysis: In a cohort of persons dispensed at least one opioid in 2013, we will estimate monthly utilisation and costs of prescribed opioids, overall and according to individual opioid formulations and strengths. In a cohort of new opioid users, commencing therapy between 1 July 2009 and 31 December 2013, we will examine patterns of opioid use including initiation of therapy, duration of treatment and concomitant use of opioids and other prescribed medicines. We will also examine patterns of extramedical opioid use based on indicators including excess dosing, use of more than one opioid concomitantly, doctor/pharmacy shopping and accelerated time to prescription refill.

Ethics and dissemination: This protocol was approved by the NSW Population and Health Services Ethics Committee (March 2014) and data access approved by the Department of Human Services External Review Evaluation Committee (June 2014). This will be one of the first comprehensive Australian studies with the capability to investigate individual patterns of use and track extramedical use. In the first instance our analysis will be based on 5 years of dispensing data but will be expanded with ongoing annual data updates. This research has the capability to contribute significantly to pharmaceutical policy within Australia and globally. In particular, the trajectory of extramedical prescription-opioid use has been the subject of limited research to date. The results of this research will be published widely in general medical, pharmacoepidemiology, addiction and psychiatry journals.

BACKGROUND

The global increase in prescribed opioid use over the past 30 years has been well documented. In Australia, between 1992 and 2007, there was a 300% increase in the number of opioid prescriptions dispensed in the community. In 2012, 7.4 million opioid prescriptions were dispensed via the Pharmaceutical Benefits Scheme (PBS), costing the Australian government approximately $A271 million. In the 20-year period 1992–2012, the Commonwealth of Australia subsidised over $A2 billion in...
prescribed opioids, with oxycodone and morphine accounting for $A1.1 billion. Europe and the USA have seen even larger increases in opioid dispensing than Australia. Despite the Australian government’s significant investment in these medicines, we know little about the way they are used in routine clinical care.

The observed global increase in opioid use can be attributed, in part, to the broadening of regulatory and subsidy approval of opioids to manage chronic non-cancer pain; previously use was restricted to the management of cancer pain. As opioid use has increased, so too has the concern from healthcare professionals and the public in relation to the harms of prolonged medical use, including concerns about the appropriateness of prescribing opioids long term and the risk of iatrogenic dependence. The most serious risk associated with opioid use is the harm related to opioid overdose. In the USA, prescribed medicines account for more fatal and non-fatal overdoses than illicit drugs. People dying from opioid overdoses often use other medicines concomitantly such as benzodiazepines, antidepressants, antipsychotics and psychostimulants, which may further contribute to the risk of an adverse outcome. In Australia, notable increases in reported opioid prescriptions have occurred. This has been associated with hospital separations for opioid poisoning, treatment episodes and deaths attributed to pharmaceutical opioids such as oxycodone.

’Extramedical use’ is defined as use not as directed by a doctor. Among other things, it may include using more than directed by the doctor; asking for escalating doses; obtaining prescriptions from multiple doctors without their knowledge; tampering with opioids and taking opioids via routes other than intended (eg, snorting or injecting). A 2010 Australian national survey reported a 7.4% lifetime prevalence and 4.2% 12-month prevalence of using medicines such as analgesics, sedatives/hypnotics, methadone, other opioids and steroids when not medically indicated, equating to approximately 1 in 14 Australians engaging in extramedical use of a prescribed medicine in their lifetime (with a higher prevalence in younger age groups).

Observational cohort studies from the USA and Europe have examined the natural history of opioid analgesic use for chronic non-cancer pain. Small retrospective cohort studies have examined treatment duration, pain reduction, adverse drug events and aberrant behaviours. Larger retrospective cohort studies have examined the risk of overdose, the impact on disability, non-medical use, conditions treated in older adults, and rates of adverse events.

However, in Australia, few studies have examined person-level behaviours of people prescribed opioids, prescribing patterns, patterns of use, or the outcomes and costs associated with this use. In order to gain a comprehensive understanding of these issues, we have started a programme of research examining the patterns and costs of PBS-subsidised opioid use, including extramedical use in the Australian population. This protocol summarises the scope of our programme.

Aims
The overall objective of this research programme is to evaluate the patterns and costs of opioid use in Australia. Specifically, we aim to:
1. Estimate monthly and annual utilisation and costs of prescribed opioids, overall and according to individual opioid formulations and strengths.
2. Examine patterns of opioid use including initiation of therapy, duration of treatment, concomitant use of opioids and other therapy.
3. Examine patterns of extramedical opioid use based on indicators including excess dosing, use of more than one opioid concomitantly, doctor/pharmacy shopping, and accelerated time to prescription refill.

METHODS AND ANALYSIS
Setting
Australia has a publically funded universal healthcare system entitling all Australian citizens and permanent residents to a range of subsidised health services. This includes free treatment in public hospitals (funded jointly by Commonwealth and State/Territory governments), subsidised outpatient services including consultations with medical and selected healthcare professionals (funded by the Commonwealth’s Medicare Benefits Scheme) and medicines prescribed in the community and private hospitals (funded by the PBS). Medicines prescribed to public hospital inpatients are covered primarily by hospital budgets.

Opioids of interest
The prescribed opioids of interest in this study include opioid medicines belonging to the WHO’s Anatomical Therapeutic Chemical classification system (http://www.who.int/classifications/atcddd/en/) categories N02A, N07B and R05D (table 1). We requested data for all formulations of these medicines (individual PBS item numbers). Methadone or buprenorphine may be prescribed for the indication of opioid addiction or pain. For the indication of opiate addiction, these medicines are listed under the S100 Highly Specialised Drug Program administered by the individual Australian states rather than under the national funding system. We listed these indications for completeness, however, the Department of Human Services (DHS) do not record dispensings for opioids dispensed under the state-based S100 program. All records we obtain will be for the indication of pain.

Data of interest
Our research programme will be underpinned by access to dispensing claims processed by the DHS, the PBS administering body. Until recently, DHS only recorded dispensing claims submitted for the payment of a PBS-subsidy. As such, medicines costing less than the patient copayment...
threshold were not ascertained in the collection. In effect, low-cost medicines dispensed to beneficiaries with the highest patient copayment threshold (referred to as general beneficiaries) have been underascertained; this issue does not impact on medicines dispensed to beneficiaries with lower copayment thresholds (PBS concessional parts as described below:

copayment prescriptions.

Our PBS-data requests have been structured in two parts as described below:

Prevalent user cohort: comprising Australians dispensed at least one opioid. This is a national cohort of all persons (of any age) prescribed at least one opioid of interest in a given calendar year (with the first year of data being 2013). The cohort will provide contemporary information about the prevalence of monthly and annual prescribed opioid use across the Australian population, including data from under copayment opioid prescriptions. Data will be updated annually.

Incident user cohort: comprising Australians starting new opioid therapy. This is a national cohort focusing on persons dispensed at least one opioid in the period 1 July 2009 to 31 December 2013. Our observation period was chosen as the DHS holds PBS data for a period of only 4 years and 6 months. The data set is updated daily and when each additional day is added, the earliest date in the data set is deleted. Therefore, our exact study period is dependent on the date of extraction. This cohort will be used to examine patterns of prescribed opioid use, including extramedical use. Inclusion criteria are as follows: (1) opioid naïve for at least 3 months prior to the index prescription (see online supplementary appendix A of details on the way in which this was operationalised); (2) aged ≥18 years at the index prescription. We chose a 3-month wash-out period for cohort inclusion because it was considered sufficient time to ensure that any new, index prescriptions reflected a new ‘course’ of treatment for a new or recurrent indication. It is possible that some individuals will receive a new prescription under this definition for an indication for which they have been treated previously. However, we will also undertake sensitivity analyses by extending the period of non-use to 6 months. This cohort will also be updated annually.

Tables 2 and 3 detail the variables requested from DHS for the prevalent and incident user cohorts.

Statistical analysis

We will use best-practice pharmacoepidemiological methods to explore prescribed opioid medicines use in the two cohorts. The general approaches are detailed below:

### Table 2 Variables requested regarding cohort demographics

| Variables                                      | Justification                                                                 |
|------------------------------------------------|-------------------------------------------------------------------------------|
| Scrambled patient ID                           | A unique sequence number enabling person-level analysis and linkage to PBS data set |
| Month and year of birth                        | To report demographics of cohort and used to stratify analyses according to age group |
| Sex                                            | To report demographics of cohort and used to stratify analyses                  |
| Month and year of death (mm/yy)                 | Date of death, in order to censor the follow-up time for each individual in the cohort |
| Postcode of residence mapped to Statistical Local Area | Used to identify location of residence and map to indices of socioeconomic disadvantage (ie, the Socio-Economic Indexes for Areas (SEIFA)† and remoteness (ie, the Accessibility/Remoteness Index of Australia (ARIA)†) |
| Geographic location of residence according to the SA2 | Used to identify geographic location of residence to map prescription rates and to evaluate prescription rates according to key demographic characteristics |

†ATC classification system is an internationally established methodology endorsed by the WHO that is used to classify medicines based on the organ or system on which they act, or their therapeutic and chemical characteristics. Details of the ATC classification system are found online at: http://www.who.int/classifications/atcddd/en/.

‡Single ingredient codeine 30 mg tablets (opium alkaloids and derivatives) are ATC coded to the respiratory system R05D and not the nervous system N02A.

| Medicine | ATC code† |
|----------|-----------|
| Oxycodeone | N02AA05, N02AA55 |
| Tramadol | N02AX02 |
| Buprenorphine | N02AE01, N07BC01, N07BC51 |
| Fentanyl | N02AB03 |
| Morphine | N02AA01 |
| Hydromorphone | N02AA03 |
| Methadone | N02AC52, N07BC02 |
| Codeine | N02BE51, N02AA59, N02AA79, R05DA04‡ |
| Tapentadol* | N02AX06 |

*Tapentadol PBS-listed from 2014.

†ATC classification system from an internationally established methodology endorsed by the WHO that is used to classify medicines based on the organ or system on which they act, or their therapeutic and chemical characteristics. Details of the ATC classification system are found online at: http://www.who.int/classifications/atcddd/en/.

‡Single ingredient codeine 30 mg tablets (opium alkaloids and derivatives) are ATC coded to the respiratory system R05D and not the nervous system N02A.

ATC, Anatomical Therapeutic Chemical; PBS, Pharmaceutical Benefits Scheme.
1. **Utilisation and costs**: we estimate the monthly and annual prevalence and costs of opioid use overall and according to individual opioid formulations and strengths. Utilisation estimates will be based on number of prescriptions, Defined Daily Dose (DDD) per 1000 population per day or in oral morphine equivalent mg. Analyses will be stratified according to patient age, gender, location of residence and indices of socioeconomic disadvantage. Data from the Australian Bureau of Statistics will determine population estimates for each subgroup of interest. Estimates will also be presented using ESRI ArcGIS (a mapping software programme). This will show overall national patterns of use by geographical area of patient, prescriber or dispensing pharmacy (eg, Statistical Local Area, jurisdictionally), as well as graphical presentation of variations in levels of use. Publicly available data on the demographic characteristics of geographical areas will be obtained from the Australian Bureau of Statistics (age distribution, income, education and unemployment).

2. **Patterns of opioid use**: we will examine patterns of use in the following ways:
   A. **Median duration of opioid treatment**: defined as the time from the first opioid dispensing record to the last dispensing record plus 30 days. These estimates can also detail different courses of opioid therapy by accounting for breaks in treatment of more than 60 days.
   B. **Dose escalation**: we will estimate the average daily dose of each opioid prescription dispensed using the internationally recognised DDD unit. At the individual level, we will calculate the changes in average DDDs by prescription and report the number of patients in whom doses are increasing, and by what level, over time.
   C. **Concomitant opioid and other concomitant medicines use**: we will investigate the concomitant use of multiple opioids, in addition to the use of opioids with other prescribed medicines, such as benzodiazepines, antidepressants and antipsychotics. Concomitant use will generally be defined as the observation of at least two dispensing records from different medicines within a specific time-frame of each other. The rules will vary according to the therapy of interest. Furthermore, we will identify individuals at risk of potentially harmful drug–drug interactions deemed to be clinically relevant in the

---

**Table 3** Pharmaceutical Benefits Scheme (PBS) data on opioid dispensing (and other medication dispensing) history

| Variables                | Description                                                                 | Justification                                                                 |
|--------------------------|----------------------------------------------------------------------------|--------------------------------------------------------------------------------|
| Scrambled patient ID     | A unique sequence number                                                   | Enable person-level analysis and linkage to sociodemographic data set          |
| Month and year of birth  | Month and year when each person was born                                   | Determine age at time of dispensing. Also used as cross-check with data in demographic file |
| Sex                      | Sex                                                                        | Cross-check with data in demographic file                                      |
| Date of supply           | Date medicine is dispensed                                                 | Establish temporal relationship in dispensing records                          |
| Item code                | A unique number which represents the dose form and strength of the pharmaceutical item patients receive | Identify medicines of different forms and strengths                            |
| ATC code                 | Anatomical Therapeutic Chemical classification code                         | Delineate between medicine types                                               |
| Generic name             | Generic medication name                                                    | Delineate between medicine types                                               |
| Quantity dispensed       | Quantity of medicine dispensed                                             | Calculate defined daily dose and durations of treatment                         |
| Original or repeat       | A variable to distinguish between repeat or new prescription               | Understand pattern of treatment                                                |
| prescription             |                                                                            |                                                                                |
| Beneficiary level        | General beneficiary±safety net; concession card holder±safety net           | Identify level of entitlement and determine comprehensiveness of data capture |
| PBS benefit              | Amount paid by the Australian government                                   | Determine the total cost incurred by the Australian government to supply opioids in a given calendar year |
| Prescriber scrambled ID  | A unique sequence number given to each prescriber                          | Delineate between scripts written by different doctors                         |
| Prescriber location      | Postcode mapped to Statistical Local Area                                  | Establish location of practice                                                  |
| Prescriber type          | Identifies primary specialty of the prescribing doctor                     | Identify what type of doctors prescribe medicines of interest                   |
| Pharmacy scrambled ID    | A unique sequence number given to each dispensing pharmacy                 | Delineate between scripts dispensed at different pharmacies                     |
| Pharmacy location        | Postcode mapped to Statistical Local Area                                  | Establish location of pharmacy                                                  |
literature and common drug information resources. These will be examined using a previously published approach overall, and for specific population subgroups such as older adults.

3. Extramedical use indicators of extramedical opioid use—we will adopt measures of extramedical use described previously in the literature and report on the rates of these patterns of extramedical use:

   A. Excess dosing: defined as average daily dosing outside guideline recommendations.
   B. Concomitant opioid use: as described above.
   C. Doctor shopping: opioid prescriptions written by more than one doctor and dispensed within a specific time-frame.
   D. Pharmacy shopping: dispensing opioid prescriptions at more than one pharmacy within a specified time-frame.
   E. Accelerated prescription refill: repeated dispensing of opioid prescriptions earlier than the estimate of when the prescription is complete.

The medication possession ratio and refill compliance rate are measures which use administrative data to assess adherence to medicines. We have included accelerated prescription refill as one of our measures of extramedical use.

We may restrict some of our analyses to concession card-holding populations only, as not all opioid medicines of interest are above the general beneficiary copayment amount. Other medicines of interest including benzodiazepines and psychotropic medicines such as antidepressants, antipsychotics and central nervous system stimulants, also fall below the general beneficiary copayment. We will also undertake analyses with and without persons dispensed cancer medicines to establish how the inclusion of patients with cancer (who generally receive significantly higher opioid doses than patients without cancer) impacts on our estimates.

Data access approval
Data access has been approved by the DHS External Review Evaluation Committee (MI0166). However, DHS have recently advised that it may be necessary to restrict our cohorts due to the considerable amount of data they will be required to provide to us. For example, to access the entire dispensing history of all people dispensed an opioid in our incident user cohort, it has been estimated that we would be provided with 40% of the entire DHS data holdings. As such, our cohorts may be restricted to a 10% random sample of the national opioid user cohort.

Consent and privacy considerations
Use and Disclosure of Information: Commonwealth data are governed under the Privacy Act 1988. Information Privacy Principle (IPP) 2 under the Privacy Act 1988 provides that personal information should not be used or disclosed for any purpose other than the primary purpose of the collection. We have obtained approval for the use of data for a secondary purpose: that of research involving access to person-level information. Under IPP2.1(d), use or disclosure for another purpose is allowed if (A) it is necessary for research and it is impracticable to gain consent AND (B) the use is in accordance with the Section 95A guidelines (which provides a process to resolve the conflict that may arise between the public interest in privacy and the public interest in medical research).

Consent: The waiver for individual consent was approved by the Population and Health Services Research Ethics Committee in accordance with Section 95A of the Commonwealth Privacy Act 1988. This was because:

- There were hundreds of thousands of people in the cohort, so it was not possible or practical to obtain consent because of the large study population.
- Obtaining consent would prejudice the scientific value of the research due to the high participation rates required for unbiased samples (at least 90%).
- The Australian evidence about the sociodemographic differences between participants who consent to data linkage research and those who do not is impracticable to gain consent AND (B) the use is in accordance with the Section 95A guidelines (which provides a process to resolve the conflict that may arise between the public interest in privacy and the public interest in medical research).

We have minimised the risk to personal privacy by ensuring:

- Only researchers involved in data analysis will have access to the data.
- Data will be securely stored at both sites (see below).
- The research team will not be in possession of any personally identifying information. The files released to the research team will not contain patients’ name, rather a unique patient number will be generated by the DHS staff.

Finally, all data will be presented in aggregated form only and potentially identifiable information will not be published. We will suppress data with small cell sizes.

Confidentiality of data and record retention
This is a collaborative project involving two research teams, one based at the National Drug and Alcohol Research Centre, The University of New South Wales, Australia, and one based at the Faculty of Pharmacy, The University of Sydney. To ensure consistency between the analyses and research teams, decision rules will be developed in group meetings and all analyses will be conducted in SAS so all relevant code can easily be shared where necessary. The confidentiality of records will be ensured by strict adherence to the study protocol in relation to access to, transfer and storage of study data.
DISCUSSION
The rate of pharmaceutical opioid use is increasing across the globe. However, the actual extent of such use and extramedical use, is currently unknown. The research programme outlined in this protocol will be the first large-scale and nationally representative Australian study to examine patterns of opioid use, including extramedical use, and the costs associated with this use. Previously, PBS opioid dispensing data has typically been analysed using aggregated data.\textsuperscript{5-9} This research will also form the foundation of additional studies that can examine the medical consequences of excessive prescription opioid use. This type of research will be possible by access to emergency department and hospitalisation plus cause of death data.

From a clinical perspective, we will investigate common opioid utilisation patterns and identify behaviour indicative of extramedical use of opioids. Furthermore, we will investigate the prevalence of potentially inappropriate combinations of medicines prescribed with opioids, estimating the number of individuals at risk of adverse drug events due to potentially harmful drug–drug interactions. Together, this information could provide a strong evidence base for targeted future intervention programmes to identify and treat high-risk individuals across Australia, as well as forming the basis of developing appropriate harm-reduction strategies.

From a public health perspective, this research programme will serve as an important first step to understanding and monitoring prescription opioid use, costs and extramedical use of opioids, now and into the future. Regulators across jurisdictions currently use different criteria for authorising long-term opioid therapy, identifying at-risk patients and measuring potentially problematic opioid use. Valid indicators are required to identify the emergence of problems and provide information that will allow the extent of the problem to be monitored. Therefore, through the development of robust proxies or indicators of extramedical opioid use, this study will yield a useful surveillance tool for public health authorities. Currently no universally accepted indicators exist,\textsuperscript{5,2} and given the growing problem of opioid use in Australia and globally, the indicators have many potentially useful future applications.

Limitations
It is important to acknowledge several limitations of these data. The first relates to the extent to which these data reflect total opioid consumption in Australia. As noted earlier, until 2012 only medicines reimbursed under the PBS appear in the PBS collection. Items costing less than the general beneficiary contribution did not receive a PBS benefit and was not captured in the collection. This is particularly problematic for selected opioids. Private prescriptions are also not included in the PBS collection, which account for an unknown but potentially substantial number of opioid prescriptions in Australia. Finally, these data do not include opioids that are available in pharmacies without a prescription (over-the-counter opioids), which in Australia includes codeine, the unit sales of which were more than 15 million in 2013 (personal communication, Gisev N, Nielsen S, Bruno R, et al, 2014). Notwithstanding these limitations, the data we will use will certainly comprise the most detailed information to hand about person-level patterns of opioid consumption in Australia, permitting detailed estimates of clinical issues that are of increasing community concern and great public health importance.

Second, dispensing claims do not detail clinical information, particularly that relating to indication for use. This poses particular challenges given opioids are prescribed at different doses depending on the nature of the pain being managed; dosing for cancer and non-cancer pain are likely to differ significantly. Given we will be provided with the PBS dispensing history of all opioid-treated patients, we have the capacity to undertake sensitivity analyses excluding patients with a cancer treatment history. However, this approach will not be definitive as cancer medicines dispensing history is likely to be a specific but not sensitive proxy for a cancer diagnosis.

The final limitation relates to the extent to which indicators of extramedical use accurately reflect the problem. However, we will develop our proxies through a process of consultation of the extant literature,\textsuperscript{53} and ongoing discussion with and feedback from expert clinicians in the fields of pain, cancer and addiction. We will make ongoing efforts to generate valid indicators to the fullest extent possible. Our use of sensitivity analyses to check whether our conclusions are affected by variations in definitions will also be a feature of our analyses.

Conclusions
This is a novel Australian research programme of opioid use, costs and extramedical use at an individual level, and with ongoing updates over time. This research has the capability to contribute significantly to pharmacological policy within Australia and globally.

Author affiliations
1National Drug and Alcohol Research Centre, UNSW Medicine, UNSW Australia, Sydney, New South Wales, Australia
2Faculty of Pharmacy, Pharmacoeconomics and Pharmaceutical Policy Research Group, University of Sydney, Sydney, New South Wales, Australia
3School of Public Health, Sydney Medical School, University of Sydney, Sydney, New South Wales, Australia

Contributors All authors had involvement in development of the original protocol document on which this manuscript was based. LD, SP, BB, NG and BL contributed to the design of the study and revision to the manuscript. LD and SP drafted the first iteration of the manuscript. NG led the preparation of applications to relevant ethics committees, with input from SP, LD, BB and BL. All authors edited the manuscript and approved the final draft.

Funding This research is supported, in part, by a National Health and Medical Research Council Health (NHMRC) Centre of Research Excellence in Medicines and Ageing (ID: 1060407), and by funding from the Australian National Health and Medical Research Council (NHMRC, #1005668). LD and BL are supported by NHMRC research fellowships (#1041472, #1073858). SP is supported by a Cancer Institute New South Wales Career Development Fellowship (ID: 12/CD/2-25) and BB is supported by a University of Sydney Degenhardt L, et al. BMJ Open 2015;4:e007030. doi:10.1136/bmjopen-2014-007030
Postgraduate Award (2013–2016). The National Drug and Alcohol Research Centre at UNSW Australia is supported by funding from the Australian Government under the Substance Misuse Prevention and Service Improvements Grant Fund.

Competing interests LD and BL have received untied educational grants from Reckitt Benckiser and Mundipharma to conduct postmarketing surveillance of new opioid medications in Australia.

Ethics approval This research programme has been approved by the NSW Population and Health Services Ethics Committee (HREC/13/CIPHS/50) and data access approved by the Department of Human Services External Review Evaluation Committee (MI016).

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement No data are publicly available.

Open Access This is an Open Access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/

REFERENCES

1. Bell JR. Australian trends in opioid prescribing for chronic non-cancer pain, 1986–1996. Med J Aust 1997;167:26–9.
2. Berbatis CG, Sunderland VB, Bulsara M, et al. Trends in licit opioid use in Australia, 1984–1998: comparative analysis of international and jurisdictional data. Med J Aust 2000;173:524–7.
3. Roxburgh A, Bruno R, Larance B, et al. Prescription of opioid analgesics and related harms in Australia. Med J Aust 2011;195:280–4.
4. Roxburgh A, Burns L, Drummer OH, et al. Trends in fentanyl prescriptions and fentanyl-related mortality in Australia. Drug Alcohol Rev 2013;32:269–75.
5. Leong M, Murison B, Haber P. Examination of opioid prescribing in Australia from 1992 to 2007. Intern Med J 2009;39:676–81.
6. Huyczko R, Tisonova J, Bozekova L, et al. Trends in consumption of opioid analgesics in Slovak Republic during 1998–2002. Eur J Clin Pharmacol 2004;60:445–8.
7. Garcia del Pozo J, Carvajal A, Villoria JM, et al. Trends in the consumption of opioid analgesics in Spain. Higher increases as fentanyl replaces morphine. Eur J Clin Pharmacol 2008;64:411–16.
8. Eisenberg E, Adler R. Consumption of opioids in a hospital setting—what can we learn from a 10 year follow-up? Isr Med Assoc J 2004;6:19–23.
9. Blanch B, Pearson S, Haber P. An overview of the patterns of prescription and costs related in harms in Australia. Br J Clin Pharmacol 2014;78:1159–66.
10. Dhalla IA, Mamdani MM, Sivivoli ML, et al. Prescribing of opioid analgesics and related mortality before and after the introduction of long-acting oxycodone. CMAJ 2009;181:891–6.
11. Compton WM, Volkow ND. Abuse of prescription drugs and the risk of addiction. Drug Alcohol Depend 2006;83(Suppl 1):S4–7.
12. Compton WM, Volkow ND. Major increases in opioid analgesic abuse in the United States: concerns and strategies. Drug Alcohol Depend 2006;81:103–7.
13. Rintoul AC, Dobbin M, Nielsen S, et al. Recent increase in detection of alprazolam in Victorian heroin-related deaths. Med J Aust 2013;198:206–9.
14. Martyes RF, Cleave D, Burns JM. Seeking drugs or seeking help? Escalation of “doctor shopping” by young heroin users before fatal overdose. Med J Aust 2004;180:211–14.
15. Rintoul AC, Dobbin MD, Drummer OH, et al. Increasing deaths involving oxycodone, Victoria, Australia, 2000–09. Inj Prev 2011;17:254–9.
16. Larance B, Degenhardt L, Lintzeris N, et al. Definitions related to the use of pharmaceutical opioids: extra-medical use, diversion, non-adherence and aberrant medication-related behaviours. Drug Alcohol Rev 2011;30:236–45.
17. Australian Institute of Health and Welfare. Drugs in Australia 2010: tobacco, alcohol and other drugs. Canberra: Australian Institute of Health and Welfare, 2011:73–83.
18. Sjogren P, Gronbaek M, Peuckmann V, et al. A population-based cohort study on chronic pain: the role of opioids. Clin J Pain 2010;26:763–9.
19. Reid MC, Henderson CR Jr, Papaleontiou M, et al. Characteristics of older adults receiving opioids in primary care: treatment duration and outcomes. Pain Med 2010;11:1063–71.
20. Hanifah J, Lamb GC, Neumer JM. Long-term opioid contract use for chronic pain management in primary care practice. A five year experience. J Gen Intern Med 2007;22:485–90.
21. Dunn KM, Saunders KW, Rutter CM, et al. Opioid prescriptions for chronic pain and overdose: a cohort study. Ann Intern Med 2010;152:85–92.
22. Franklin GM, Stover BD, Turner JA, et al. Disability Risk Identification Study Cohort. Early opioid prescription and subsequent disability among workers with back injuries: the Disability Risk Identification Study Cohort. Spine (Phila Pa 1976) 2008;33:199–204.
23. Pletcher MJ, Kertesz SG, Sidney S, et al. Incidence and antecedents of non-medical prescription opioid use in four US communities. The Coronary Artery Risk Development in Young Adults (CARDIA) prospective cohort study. Drug Alcohol Depend 2006;85:171–6.
24. Reid MC, Engles-Horton LL, Weaver MB, et al. Use of opioid medications for chronic noncancer pain syndromes in primary care. J Gen Intern Med 2002;17:173–9.
25. Hartung DM, Middleton L, Haxby DG, et al. Rates of adverse events of long-acting opioids in a state Medicaid program. Ann Pharmacother 2007;41:1047–51.
26. Campbell G, Nielsen S, Bruno R, et al. The Pain and Opioids IN Treatment (POINT) study: Characteristics of a cohort using opioids to manage chronic non-cancer pain. Pain 2015. http://dx.doi.org/ 10.1016/j.pain.2015.03.031.
27. Gadzhanova S, Bell JS, Roughhead EE. What analgesics do older people use prior to initiating oxycodone for non-cancer pain? A retrospective database study. Drugs Aging 2013;30:921–6.
28. Rogers KD, Kemp A, McLachlan AJ, et al. Adverse selection? A multi-dimensional profile of people dispensed opioid analgesics for persistent non-cancer pain. PloS ONE 2013;8:e80096.
29. Nielsen S, Degenhardt L, Loban B, et al. Comparing opioids: a guide to estimating oral morphine equivalents (OME) in research. NDARC Technical Report No. 329. Sydney: National Drug and Alcohol Research Centre, UNSW Australia, 2014.
30. World Health Organisation. WHO Collaborating Centre for Drug Statistics Methodology. Oslo: Norwegian Institute of Public Health, 2008.
31. MIMS Australia: MIMS Online Drug Interactions. 2014.
32. Australian Medicines Handbook Pty Ltd. Australian Medicines Handbook: Adelaide: Australian Medicines Handbook Pty Ltd, 2014.
33. Baxter K, Preston CL eds. Stockley's Drug Interactions, 10th edn. London: Pharmaceutical Press, 2015.
34. Ringland C, Mant A, McGettigan P, et al. Uncovering the potential risk of serotonin toxicity from long-acting opioids. Drug Alcohol Depend 2010;106:682–8.
35. Bachs LC, Bramness JG, Engeland A, et al. Repeated dispensing of codeine is associated with high consumption of benzodiazepines. Norsk Epidemiol 2008;18:185–90.
36. Logan J, Liu Y, Parekh H, et al. Opioid prescribing in emergency departments: the prevalence of potentially inappropriate prescribing and misuse. Med Care 2013;51:846–53.
37. White AG, Birnbaum HG, Schiller M, et al. Analytic models to identify patients at risk for prescription opioid abuse. Am J Manag Care 2009;15:987–906.
38. Bramness JG, Furu K, Engeland A, et al. Carisoprodol use and prescribing in Norway: a pharmacoepidemiological study. Br J Clin Pharmacol 2007;64:210–18.
39. Wilsey BL, Fishman SM, Gilson AM, et al. Profiling multiple provider prescribing of opioids, benzodiazepines, stimulants, and anorectics. Drug Alcohol Depend 2010;109:98–106.
40. Han H, Kass PH, Wilsey BL, et al. Individual and county-level factors associated with use of multiple prescribers and multiple pharmacies to obtain opioid prescriptions in California. PloS ONE 2012;7:e46246.
41. Cepeda MS, Fife D, Chow W, et al. Opioid shopping behaviour: how often, how soon, which drugs and what payment method. J Clin Pharmacol 2012;53:112–17.
42. Cepeda MS, Fife D, Vyas Y, et al. Distance traveled and frequency of interstate opioid dispensing in opioid shoppers and nonshoppers. J Pain 2013;14:1158–61.
43. Cepeda MS, Fife D, Chow W, et al. Assessing opioid shopping behaviour: a large cohort study from a medication dispensing database in the US. Drug Saf 2012;35:325–34.
44. Peirce GL, Smith MJ, Abate MA, et al. Doctor and pharmacy shopping for controlled substances. Med Care 2012;50:494–500.
45. Pradel V, Thirion X, Ronfle E, et al. Assessment of doctor-shopping for high dosage buprenorphine maintenance treatment in a French
region: development of a new method for prescription database. 

Pharmacoepidemiol Drug Saf 2004;13:473–81.

46. Braker LS, Reese AE, Card RO, et al. Screening for potential prescription opioid misuse in a Michigan Medicaid population. Fam Med 2009;41:729–34.

47. Katz N, Panas L, Kim M, et al. Usefulness of prescription monitoring programs for surveillance—analysis of Schedule II opioid prescription data in Massachusetts, 1996–2006. Pharmacoepidemiol Drug Saf 2010;19:115–23.

48. Rice JB, White AG, Bimbaum HG, et al. A model to identify patients at risk for prescription opioid abuse, dependence, and misuse. Pain Med 2012;13:1162–73.

49. Seal KH, Shi Y, Cohen G, et al. Association of mental health disorders with prescription opioids and high-risk opioid use in US veterans of Iraq and Afghanistan. JAMA 2012;307:940–7.

50. Holman CD. The impracticable nature of consent for research use of linked administrative health records. Aust N Z J Public Health 2001;25:421–2.

51. Young AF, Dobson AJ, Byles JE. Health services research using linked records: who consents and what is the gain? Aust N Z J Public Health 2001;25:417–20.

52. Secora AM, Dormitzer CM, Staffa JA, et al. Measures to quantify the abuse of prescription opioids: a review of data sources and metrics. Pharmacoepidemiol Drug Saf 2014;23:1227–37.

53. Blanch B, Mellish L, Buckley N, et al. How is prescription opioid misuse measured, and what is the extent of opioid misuse globally? A systematic review of observational studies using routinely collected dispensing data (2000–2013). In: Global Addiction Conference. Rio de Janeiro, Brazil, 10–12 November, 2014.

54. Australian Bureau of Statistics. 1216.0.15.003—Australian Standard Geographical Classification (ASGC) Remoteness Area Correspondences, 2006. Canberra: Australian Bureau of Statistics, 2006.

55. Australian Bureau of Statistics. 1216.0—Australian Standard Geographical Classification (ASGC), July 2006. Canberra: Australian Bureau of Statistics, 2006.
Author/s:
Degenhardt, L; Blanch, B; Gisev, N; Larance, B; Pearson, S

Title:
The POPPY Research Programme protocol: investigating opioid utilisation, costs and patterns of extramedical use in Australia

Date:
2015-01-01

Citation:
Degenhardt, L., Blanch, B., Gisev, N., Larance, B. & Pearson, S. (2015). The POPPY Research Programme protocol: investigating opioid utilisation, costs and patterns of extramedical use in Australia. BMJ OPEN, 5 (1), https://doi.org/10.1136/bmjopen-2014-007030.

Persistent Link:
http://hdl.handle.net/11343/260652

File Description:
Published version

License:
CC BY-NC