The changing face of Australian data reforms: impact on pharmacoepidemiology research

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Abstract

Objective
A wealth of data is generated through Australia’s universal health care arrangements. However, use of these data has been hampered by different federal and state legislation, privacy concerns and challenges in linking data across jurisdictions. A series of data reforms have been touted to increase population health research capacity in Australia, including pharmacoepidemiology research. Here we catalogued research leveraging Australia’s Pharmaceutical Benefits Scheme (PBS) data (2014–2018) and discussed these outputs in the context of previously implemented and new data reforms.

Methods
We conducted a systematic review of population-based studies using PBS dispensing claims. Independent reviewers screened abstracts of 4,996 articles and 310 full-text manuscripts. We characterised publications according to study population, analytical approach, data sources used, aims and medicines focus.

Results
We identified 180 studies; 133 used individual-level data, 70 linked PBS dispensing claims with other health data (66 across jurisdictions). Studies using individual-level data focussed on Australians receiving government benefits (87 studies) rather than all PBS-eligible persons. 63 studies examined clinician or patient practices and 33 examined exposure-outcome relationships (27 evaluated medicines safety, 6 evaluated effectiveness). Medicines acting on the nervous and cardiovascular system account for the greatest volume of PBS medicines dispensed and were the most commonly studied (67 and 40 studies, respectively). Antineoplastic and immunomodulating agents account for approximately one third of PBS expenditure but represented only 10% of studies in this review.

Conclusions
The studies in this review represent more than a third of all population-based pharmacoepidemiology research published in the last three decades in Australia. Recent data reforms have contributed to this escalating output. However, studies are concentrated among specific subpopulations and medicines classes, and there remains a limited understanding of population benefits and harms derived from medicines use. The current draft Data Availability and Transparency legislation should further bolster efforts in population health research.

Keywords
medical record linkage; drug prescriptions; observational study; pharmacoepidemiology

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Highlights

- Australia has the potential to undertake whole-of-health care and whole-of-population research using data from its universal health care system.
- Reforms related to data availability and use in Australia have facilitated linkage of Australian Government and state health data, such as the Pharmaceutical Benefits Scheme (PBS) dispensing claims, hospitalisations, and deaths.
- Encouragingly, in the past 5 years research output in population-based pharmacoepidemiology research increased substantially. The studies catalogued in this review represent more than a third of all population-based pharmacoepidemiology studies published in the last 30 years in Australia.
- The majority of studies published in recent years used individual-level data (n = 133), 70 linked PBS dispensing claims with other health data (66 across jurisdictions). Evidence derived from these studies is concentrated among subpopulations and on medicines acting on the nervous system and cardiovascular system.
- There is still very limited evidence on the real-world safety and effectiveness of medicines in Australia.
- New legislative reform, particularly the Data Availability and Transparency Act will be formalised in the near future and will accelerate population-based research efforts in Australia, including pharmacoepidemiology.

Introduction

Worldwide population-based health administrative data are being mobilised to evaluate the quality and outcomes of care. The data collected through Australia’s universal health care arrangements have the potential to advance knowledge in population health and generate timely, comprehensive clinical and policy insights. However, population-based research has been hampered by the heterogeneity in legislation, regulations and guidelines at national and state levels plus privacy concerns and the ability to link person-level data across jurisdictional boundaries [1].

The Western Australia Data Linkage System pioneered cross-jurisdictional data linkage in the late 90s, supporting a broad range of population-based research [2–6]. However, it wasn’t until the mid-2000s that key initiatives enhanced the entire country’s capability to leverage population-based health data for research. These include the establishment of: Australian Government approved Integrating Authorities that probabilistically link person-level data across jurisdictional boundaries (using best-practice privacy preserving protocols); data safe havens where sensitive data can be accessed and analysed by approved researchers [7]. More recently, the 2017 Australian Productivity Commission’s Data Availability and Use inquiry recommended sweeping reform to drive efficiency, safety and support decision-making [1]. The Federal government’s response to the Inquiry [8] led to the establishment of the Office of the National Data Commissioner (ONDC) and the development of a legislative package to streamline the sharing of government data for service provision, policy evaluation and research, while preserving strict data privacy and confidentiality provisions. Together, these initiatives are expected to bolster Australian population health research, including the field of pharmacoepidemiology, the foundation of medicines policy research.

In Australia, it is estimated that more than 27 million individual Pharmaceutical Benefits Scheme (PBS) prescriptions are in use on any given day; more than nine million people are taking at least one prescribed medicine daily and two million are taking five or more daily [9]. PBS data linked to other administrative claims are a powerful tool to examine real-world medicines use, safety, effectiveness, and value for money in populations not typically represented in clinical trials [10, 11]. Importantly, to assess these outcomes, PBS data, under the custodianship of the Australian Government, needs to be linked at the individual-level with outcomes data such as hospitalisations, which are under the custodianship of the States and Territories. This situation has led researchers in this field to rely on publicly available aggregated data and/or stand-alone, bespoke data collections with individual-level data as the primary sources for evidence generation [1].

Our previous systematic review of population-based research leveraging PBS data over a 25 year period to 2013, documented relatively few published studies, especially compared to the pharmacoepidemiology output in the Nordic countries over a period of six years (228 versus 515 studies) [12]. We also demonstrated that output had increased substantially from 2007 to 2013, pointing to the benefits of infrastructure development in the mid-2000s and the use of Department of Veterans Affair’s data collections (DVA). As a single payer, the DVA has data on a broad range of health services used by their clients that can be leveraged for quality use of medicines and outcomes research. However, we also highlighted significant blind spots in our understanding of medicine use and outcomes in Australia. In particular, we reported a paucity of published literature examining specific population sub-groups (including children and pregnant women), specific medicines (including high-cost therapies prescribed by specialists) and studies linking individual-level medicines exposure and outcomes to quantify benefits and harms [13].

Here we catalogue contemporary population-based medicines policy research leveraging Australia’s PBS and other data in the period 2014–2018 and discuss these outputs in the context of Australia’s data reforms.

Methods

Setting and data of interest

Australia has a universal health care system providing access to subsidised prescription medicines to citizens and eligible residents and clients of the DVA via the PBS and the Repatriation Pharmaceutical Benefits Scheme (RPBS), respectively. People contribute a co-payment towards the cost of their medicines, which varies depending on their
entitlements. Our review focusses on studies using routinely collected data on medicines dispensed through PBS and RPBS. These dispensing claims are processed by Services Australia (previously the Department of Human Services and Medicare Australia) and are provided to the Australian Government Department of Health and the DVA for monitoring, evaluation, and health service planning. These data are available to third parties, publicly or by request, for monitoring, evaluation, and research (see Supplementary Table 1).

Study identification

We searched Medline and Embase from January 2013 through December 2018 using a combination of keywords and search terms describing medicines use (e.g. prescription drugs, drug therapy, drug utilisation) with PBS dispensing data sources (see Supplementary Appendix A for search strategy). We also conducted searches on key researchers in the field of medicines policy research in Australia and screened the reference lists of all included studies (Figure 1).

Study eligibility criteria

We included full-text English-language studies using PBS and/or RPBS dispensing claims data to measure patterns of medicines use or using medicines as a proxy of a health condition or an outcome. We excluded studies: focussing exclusively on medicine expenditure or modelling; using dispensing data obtained directly from pharmacies; requiring individual informed consent to access dispensing data; or using data derived from state-based registries.

Study selection and data extraction

Two reviewers (CB, SP) screened a random 20% sample of titles and abstracts independently to identify potentially relevant studies for inclusion; one reviewer (CB) screened the remainder. Two reviewers (JOC, CB) extracted data independently from all included studies and disagreements were resolved by discussion. We extracted the following key features of each study (Box 1):

Box 1: Features extracted from included studies

| Study characteristics | Publication year, journal, study aims, funding source, and setting |
|-----------------------|-------------------------------------------------------------------|
| Study period          | Difference between the earliest and latest month and year of observation |
| Publication lag        | The earliest month and year of publication minus last month and year of study observation |
| Age profile of study population | No age restrictions (entire eligible population), elderly (≥ 65 years), adults (≥ 18 years), women of childbearing age, or children |
| Beneficiary status of study population | All PBS beneficiaries, people receiving government benefits and eligible to pay lower PBS co-payments (concessional beneficiaries) or clients of the DVA |
| Analytical approach   | Individual-level studies (track patients and/or providers over time) or claims-level studies. Studies using both approaches were classified as ‘individual-level’ |
| Data source(s)        | Primary dispensing claims dataset (e.g. PBS 10% sample, RPBS data), geographic coverage (e.g. national or state level), the inclusion of other dispensing claims or data sources and individual-level linkage to other data sources |

Classification of studies

We classified the broad study focus into six themes; (1) Medicine utilisation: examined trends and patterns of dispensing overall or stratified by gender, age, and medicine or additional variables; (2) Clinician practices: used individual-level data to study prescribing patterns (e.g. concomitant or inappropriate prescribing); (3) Patient practices: used individual-level data to examine patient behaviour around medicines use, such as medicine persistence or adherence; (4) Exposure and outcomes: 4A) investigated the relationship between medicine use and at least one outcome, such as death or hospital admission (‘medicine use and outcomes’), OR 4B) investigated the relationship between other exposures (e.g. device use) and at least one outcome but used dispensing claims to define a cohort, comorbidities or an outcome (‘other exposure and outcomes’); (5) Intervention impacts: examined the effect of one or more population-level interventions on prescribing or another outcome, classified as educational (e.g. prescriber feedback and education), policy (e.g. subsidy changes and restrictions), media (e.g. advertising campaigns), or multi-faceted (combination of the above); (6) Methods: used dispensing data to develop and refine pharmacoepidemiological techniques (e.g. validation of prescribing indicators) or study protocols reporting data based on dispensing claims.

Medicines focus of studies

We assigned WHO Anatomical Therapeutic Chemical (ATC) classifications to the medicine focus of each study [14]. We also report the proportion of studies according to their medicine focus relative to the proportion of PBS volume and spend for these classes by ATC code.

Reporting

Due to the heterogeneity of study methodology, we did not assess individual study quality. However, we extracted 23 items pertaining to the REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) checklist [15] to describe areas of underreporting. Two reviewers (JOC, CB) independently reviewed all articles published in the most recent year (2018); disagreements in extraction were resolved by discussion. For each item (see
We report the results of this review according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [16].

Results
We identified 4,996 studies through electronic searches and 14 through manual searches. After excluding duplicate records, we screened titles and abstracts of 4,362 articles and assessed 310 full-text manuscripts for eligibility. This review included 180 eligible studies (Figure 1) (see Supplementary Appendix C for the bibliography of included studies and Supplementary Appendix D for details of study features).

Study characteristics (Table 1 and Supplementary Figure 1)
We observed a steady increase in the number of studies published annually and a sharp rise in 2018; this last observation year accounting for nearly one-third of all studies published in the period. Most studies used individual-level data (133 studies, 74%). The time between the study observation end date and publication was up to 2-years for 58% of studies; 16% of studies had a publication lag of more than 5 years. The median lag time for claims-level studies was 29 months and for individual-level studies, 34 months.
Age profile and beneficiary status of the study population (Table 1)

Approximately half of the 180 studies did not place age restrictions on their study cohorts (91 studies, 51%). The remaining studies restricted cohorts to people aged 65 years or older (55 studies, 31%) or people aged 18 years or older (26 studies, 14%). Five studies focussed on women of childbearing age and two on children. Approximately half of the studies restricted their populations to concessional beneficiaries or DVA clients (91 studies, 51%). Approximately 90% of studies using claims-level analyses used the entire PBS-eligible population. In contrast, approximately 65% of studies using individual-level analyses restricted their cohorts to the elderly, DVA clients or concessional beneficiaries.

Data sources (Table 1, Figure 2)

Approximately two-thirds of studies leveraged dispensing claims and other health data (118 studies, 66%). Approximately 20% of studies used publicly available dispensing claims and 78% used data available by request, with a marked increase in the use of the PBS 10% sample and PBS ad hoc extracts over time.

Two-thirds of claims-level studies used publicly available data; 62% of these also included other unlinked health data. Individual-level studies used RPBS data (42%), the PBS 10% sample (29%) or ad hoc data extracts (22%). These individual-level studies were Australian-wide or restricted to residents of Western Australia and/or New South Wales. Seventy of these studies linked individual-level dispensing claims to other health data such as hospitalisation data, medical services claims, residential aged care claims, emergency department data, or cancer and perinatal registries; 66 were linked across jurisdictions (data not shown in table).

Study focus (Table 1 and Figure 3)

Approximately one-third of all studies used individual-level data to examine clinician or patient practices (47 and 16 studies, respectively). Individual and claims-level exposure-outcomes studies accounted for 21% of all studies, 27 of the 38 studies evaluated medicine safety and 6 evaluated medicine effectiveness. One-fifth of all studies used claim-level data to investigate medicine utilisation (36 studies); methodological studies and those evaluating intervention impacts each accounted for around 24% of all studies (25 and 18 studies, respectively).

Medicines focus (Table 2)

The most commonly studied medicines were those acting on the nervous system (38%) and cardiovascular system (23%), followed by those acting on the alimentary tract and metabolism (14%). In general, the most commonly studied medicines groups were also the medicines groups accounting for the greatest proportion of PBS dispensing in 2018. However, this medicine focus does not align with the proportion of PBS expenditure. For example, PBS expenditure with antineoplastic and immunomodulating agents represented 32% of the PBS spend in 2018 but less than 10% of the studies published in this review.

Reporting of the included studies – RECORD (Supplementary Figure 2)

Of the 55 studies published in 2018, we excluded seven methodological studies for which most of the RECORD items would not be applicable. From the 48 studies evaluated, the median RECORD score was 95% (interquartile range 90–100%); 13 (27%) studies scored 100%. The most underreported items were: study design, either by not reporting this item in the abstract (14 studies, 30%) or in the methods (9 studies, 19%), followed by the type of data used (14 studies, 30%), and methods of population selection (8 studies, 17%). Moreover, two-thirds of studies using linked data did not report the use of linked data in the abstract.

Discussion

The exponential growth and availability of health data has created new opportunities to generate high-quality real-world evidence in many jurisdictions across the globe, contributing to the growth in pharmacoepidemiology research. We observed a marked increase in Australian output in this field; studies identified in this 5-year systematic review represented more than one-third of all population-based pharmacoepidemiology publications in the last three decades in Australia (Supplementary Figure 3). [13] In the current review period, we also observed an increase in the use of individual-level data and studies linking dispensing claims with other data collections. These studies represented more than half of individual-level and data linkage studies in pharmacoepidemiology in the last 30 years in Australia.

There is little doubt that several initiatives, including significant investment in data linkage infrastructure in Australia, have been pivotal in the growth in data availability and pharmacoepidemiology research. Here, we highlight those initiatives specific to the PBS data collection addressing the creation and accessibility of datasets, and challenges related to data ascertainment and interpretation. We further discuss the pharmacoepidemiology outputs in the context of Australia’s data current and future reforms.

Initiatives improving availability and ascertainment of dispensing claims data

First, the availability of a standardised data collection of person-level dispensing claims for a 10% sample of PBS-eligible people (“PBS 10%”) has contributed to the rapid increase in the number of studies using individual-level dispensing claims over time. The PBS 10% sample dataset, established in 2005, contains the entire PBS-claims history for a 10% random selection of PBS-eligible Australians. To minimise the risk of re-identification, the data is limited to a population sample, offset dates of dispensing by up to 14 days (but identically for each person), and it is not permitted to be linked to any other dataset. The collection is provided to approved third parties on a fee-for-service basis, has a streamlined governance process and approved organisations
Table 1: Study characteristics

| Characteristic                                               | All studies, n (%) | Claims-level studies, n (%) | Individual-level studies, n (%) |
|--------------------------------------------------------------|--------------------|-----------------------------|---------------------------------|
|                                                              | N = 180            | n = 47                      | n = 133                         |
| Publication Year                                             |                    |                             |                                 |
| 2014²                                                        | 20 (11.1)          | 4 (8.5)                     | 16 (12.1)                       |
| 2015                                                         | 33 (18.3)          | 10 (21.3)                   | 23 (17.3)                       |
| 2016                                                         | 35 (19.4)          | 11 (23.4)                   | 24 (18.0)                       |
| 2017                                                         | 37 (20.6)          | 9 (19.1)                    | 28 (21.1)                       |
| 2018                                                         | 55 (30.6)          | 13 (27.7)                   | 42 (31.6)                       |
| Publication lag (time between last observation year and publication year) |                    |                             |                                 |
| <1 year                                                      | 18 (10.0)          | 5 (10.6)                    | 13 (9.8)                        |
| 1–2 years                                                    | 86 (47.8)          | 28 (59.6)                   | 58 (43.6)                       |
| 3–5 years                                                    | 47 (26.1)          | 10 (21.3)                   | 37 (27.8)                       |
| >5 years                                                     | 29 (16.1)          | 4 (8.5)                     | 25 (18.8)                       |
| Median publication lag, months (IQR)                         | 32.5 (22.0; 49.0)  | 29.0 (19.0; 40.0)           | 34.0 (23.0; 50.0)               |
| Study Population: Age profile                                |                    |                             |                                 |
| No age restrictions                                          | 91 (50.6)          | 44 (93.6)                   | 47 (35.3)                       |
| Elderly (≥ 65 years)                                        | 55 (30.6)          | 0 (0.0)                     | 55 (41.4)                       |
| Adults (≥ 18 years)                                         | 26 (14.4)          | 1 (2.1)                     | 25 (18.8)                       |
| Women of childbearing age                                   | 6 (3.3)            | 2 (4.3)                     | 4 (3.0)                         |
| Children                                                    | 2 (1.1)            | 0 (0.0)                     | 2 (1.5)                         |
| Study population: Beneficiary status                        |                    |                             |                                 |
| All PBS beneficiaries                                       | 89 (49.5)          | 43 (91.5)                   | 46 (34.6)                       |
| Concessional PBS beneficiaries†                             | 35 (19.4)          | 4 (8.5)                     | 31 (23.3)                       |
| Clients of the DVA                                          | 56 (31.1)          | 0 (0.0)                     | 56 (42.1)                       |
| Data sources                                                |                    |                             |                                 |
| Dispensing claims only                                      | 62 (34.4)          | 18 (38.3)                   | 44 (33.1)                       |
| Dispensing claims & other health data                       | 118 (65.6)         | 29 (61.7)                   | 89 (66.9)                       |
| Primary dispensing claims data                              |                    |                             |                                 |
| Publicly available                                          | 30 (16.7)          | 29 (61.7)                   | 1 (0.8)                         |
| Medicare Statistics Online                                  | 18 (10.0)          | 18 (38.3)                   | 0 (0.0)                         |
| Australian Statistics on Medicines                          | 9 (5.0)            | 9 (19.1)                    | 0 (0.0)                         |
| Section 85 extract                                          | 2 (1.1)            | 2 (4.3)                     | 0 (0.0)                         |
| 10% MBS-PBS sample                                         | 1 (0.6)            | 0 (0.0)                     | 1 (0.8)                         |
| Available by request                                        | 141 (78.3)         | 14 (29.8)                   | 127 (95.5)                      |
| PBS ad hoc extracts                                         | 38 (21.1)          | 8 (17.0)                    | 30 (21.8)                       |
| RPBS                                                        | 56 (31.1)          | 0 (0.0)                     | 56 (42.1)                       |
| PBS 10% sample                                              | 39 (21.7)          | 1 (2.1)                     | 38 (28.6)                       |
| DUSC                                                        | 8 (4.4)            | 5 (10.6)                    | 3 (2.3)                         |
| Not specified                                               | 9 (5.0)            | 4 (8.5)                     | 5 (3.7)                         |
| Geographic coverage of primary dispensing data*             |                    |                             |                                 |
| National                                                    | 153 (85.0)         | 41 (87.2)                   | 111 (83.5)                      |
| Western Australia                                           | 12 (6.7)           | 0 (0.0)                     | 12 (9.0)                        |
| New South Wales                                             | 14 (7.8)           | 2 (4.3)                     | 12 (9.0)                        |
| Other states/territories                                   | 5 (2.8)            | 5 (10.6)                    | 0 (0.0)                         |
| Study focus                                                 |                    |                             |                                 |
| Medicine utilisation                                       | 36 (20.0)          | 36 (76.6)                   | 0 (0.0)                         |
| Clinician practices                                         | 47 (26.1)          | 0 (0.0)                     | 47 (35.3)                       |
| Patient practices                                           | 16 (8.9)           | 0 (0.0)                     | 16 (12.0)                       |
| Intervention impacts                                       | 18 (10.0)          | 5 (10.6)                    | 13 (9.8)                        |
| Exposure and outcomes                                       | 38 (21.1)          | 5 (10.6)                    | 33 (24.8)                       |
| Medicine use and outcomes                                  | 33 (18.3)          | 4 (8.5)                     | 29 (21.8)                       |
| Other exposures and outcomes                                | 5 (2.8)            | 1 (2.1)                     | 4 (3.0)                         |
| Methods                                                     | 25 (13.9)          | 1 (2.1)                     | 24 (18.0)                       |
| Funding*                                                    |                    |                             |                                 |
| No funding                                                  | 23 (12.8)          | 17 (36.2)                   | 6 (4.5)                         |

Continued
Table 1: Continued

| Characteristic | All studies, n (%) | Claims-level studies, n (%) | Individual-level studies, n (%) |
|---------------|--------------------|----------------------------|-------------------------------|
|               | N = 180            | n = 47                      | n = 133                        |
| Not reported  | 18 (10.0)          | 11 (23.4)                   | 7 (5.2)                        |
| One or more   |                    |                            |                               |
| Government    | 122 (67.8)         | 12 (25.5)                   | 110 (82.7)                     |
| University    | 22 (12.2)          | 4 (8.5)                     | 18 (13.5)                      |
| Industry      | 14 (7.8)           | 1 (2.1)                     | 13 (9.8)                       |
| Other         | 25 (13.9)          | 8 (17.0)                    | 17 (12.8)                      |

*N = interquartile range.

†Includes 3 studies not identified in the previous review.

‡People receiving government benefits and eligible to pay lower PBS co-payment thresholds.

*Percentages may not add up to 100% (studies could report multiple options).

can hold longitudinal data that is updated at least quarterly. The earliest research studies using this collection were published between 2008–2013 [17–22]. In the period of the current review, 39 studies have been published using this collection. The governance arrangements allow relatively rapid turnaround for approval of studies using contemporary data. This is a model that should be replicated across other data collections, including those with PBS dispensing claims linked to other health datasets.

Second, individual-level studies using PBS data prior to 2012 were often restricted to people receiving government entitlements to ensure complete capture of dispensing records [23]. The 2012 reform allowing the capture of all PBS dispensings (irrespective of whether they attracted

Figure 2: Number of publications (cumulative) according to primary dispensing claims data
Figure 3: Number of studies according to study focus and analytical approach

With respect to undertaking exposure-outcomes studies, the Australian Institute of Health and Welfare’s development of multi-source enduring linked data assets (MELDAs) comprising continuing cross-jurisdictional, person-level linkages of medicines exposure with hospitalisation and mortality data show strong potential to further accelerate national population-based research capacity [25, 26]. At the time of writing, there were no formal policies around third-party access (including to academic researchers) to the current suite of MELDAs; this should be considered an immediate priority to realise this significant investment in public money [27].

Future directions

In July 2019, quality use of medicines and medicines safety was announced as Australia’s tenth national health priority [28, 29]. Studies catalogued in this systematic review provide contemporary evidence assessing quality use of medicines including the impact of medicines policy interventions, [30–32] medicine use in populations not always represented in clinical trials, [33, 34] and adherence with current treatment guidelines [35–37]. However, there is a need for greater focus on outcomes studies, especially pertaining to medicine safety, and with greater attention to vulnerable population sub-groups [38].

Despite advances, studies examining clinician and patient practices, as well as medicines utilisation studies, still represented a large proportion of the body of literature (Supplementary Figure 3) [13]. Further, the evidence base is still dominated by studies on cardiovascular medicines and a government subsidy) led to an increase in individual-level studies conducted across the entire eligible Australian population, not just in people receiving government benefits [13]. However, the collection does not contain information on private prescriptions, has limited capture of highly specialised medicines dispensed in public hospitals prior to 2013 and no information on prescription indication, prescribed daily dosage, and treatment duration. These limitations are not uncommon in community-based dispensing claims data, but it is important to consider these in pharmacoepidemiological study designs [23, 24].
those acting on the nervous system and in elderly Australians. Significant blind spots remain in our understanding of real-world medicine effectiveness and safety, particularly in Australians who do not receive government benefits and in populations consistently excluded from clinical trials, such as women of childbearing age and children. In this context, individual-level dispensing claims linked to health outcomes data, would provide a deeper understanding of the benefits and harms derived from medicine use, including indications for prescribing, clinical diagnoses, and other patient risk factors.

Historically, researchers have faced trade-offs between the ease of using readily available individual-level data, such as stand-alone PBS dispensing claims with limited clinical information (comprising the majority of individual-level studies in our review) or investing in the long process of gaining approvals and access to linked data [39, 40]. Encouragingly, we observed an increasing number of studies based on dispensing claims linked at the individual level to other data sources and we anticipate a further upswing in these types of studies in light of the major reforms underway in Australia. Particularly the new Data Availability and Transparency legislation, designed to maximise the value of Australian Government public sector data for service delivery and research. The legislation creates roles and responsibilities to data sharing. It adopts a guidance package to allow consistent practices across jurisdictions and safe sharing of data for public good purposes, including research and development, overriding secrecy provisions [41].

Other Commonwealth countries with similar health care systems and political structures, such as Canada and the United Kingdom, have bolstered their research capability by establishing independent centres serving the specific needs of the research community and closing the gap between linkage and analysis [42, 43]. Australia would benefit from adopting a similar model to harness data from its health care system covering over 25 million citizens and residents.

Limitations of this review

Our systematic review is not without limitations. We have focussed on studies using only routinely collected data and did not include studies using PBS data that required specific individual consent. We developed an arbitrary classification to classify studies by their main focus and given the high degree of variability both within and across studies, many could have been classified under alternative categories. Finally, we only addressed the reporting quality of studies published in 2018, identifying key elements that future studies should consider increasing their transparency and reproducibility and did not assess the methodological quality or relevance of included studies.

Conclusion

Here we used pharmacoepidemiology research as an exemplar to demonstrate the way in which data reforms have supported population health research in Australia. While our findings are encouraging in that we have observed significant growth in output in a five-year period, there is still some way to go before we realise the full potential of Australia’s administrative data in population-based research. Major legislative reform currently in place is likely to further break down barriers to facilitate more timely and comprehensive research to support clinical and policy decision-making.

Conflicts of interest

The authors report no actual, potential, or perceived conflict of interest with regard to the submission of this manuscript. The Centre for Big Data Research in Health, UNSW Sydney has received funding from AbbVie to conduct research, unrelated

Table 2: Number and proportion of studies by pharmacological group compared to PBS volume and PBS expenditure (2014–2018). Study could be classified under more than one pharmacological group (N = 176∗)

| Anatomical therapeutic classification first level grouping | Claims-level studies n | Individual-level studies n | All studies n | PBS volume 2018 % | PBS cost 2018 % |
|----------------------------------------------------------|------------------------|---------------------------|---------------|------------------|----------------|
| A Alimentary tract and metabolism                         | 7                      | 17                        | 24            | 13.6             | 15.5           |
| B Blood and blood forming organs                          | –                      | 17                        | 17            | 9.7              | 4.6            |
| C Cardiovascular system                                   | 6                      | 34                        | 40            | 22.7             | 31.5           |
| D Dermatologicals                                          | 3                      | 9                         | 12            | 6.8              | 1.9            |
| E Endocrine system                                        | 1                      | 4                         | 5             | 2.8              | 1.8            |
| F Eyes                                                    | 5                      | 6                         | 11            | 6.3              | 6.3            |
| G Genito-urinary system and sex hormones                  | 1                      | 14                        | 17            | 9.7              | 1.9            |
| H Systemic hormonal preparations                          | 1                      | 14                        | 15            | 8.5              | 3.4            |
| I Anti-infectives for systemic use                        | 2                      | 14                        | 21            | 12.5             | –              |
| J Anti-neoplastic & immunomodulating agents               | 5                      | 6                         | 11            | 6.3              | 6.3            |
| K Respiratory system                                      | 20                     | 47                        | 67            | 38.1             | 22.1           |
| L Musculoskeletal system                                  | 1                      | 14                        | 15            | 8.5              | 3.4            |
| M Nervous system                                          | 10                     | 24                        | 34            | 19.6             | 3.7            |
| N Cardiovascular system                                   | 10                     | 24                        | 34            | 19.6             | 3.7            |
| O Other ATC groups                                        | 10                     | 24                        | 34            | 19.6             | 3.7            |
| P All ATC groupings                                       | 10                     | 24                        | 34            | 19.6             | 3.7            |

∗4 studies were removed from the analysis. These studies used individual-level drug data to define their cohort, only.

∗∗Other ATC groups: D, dermatologicals; S, sensory organs; V, various.

#Data derived from the PBS: Expenditure and prescriptions twelve months to 30 June 2018. Canberra; 2013. http://www.pbs.gov.au/info/statistics/expenditure-prescriptions/expenditure-prescriptions-twelve-months-to-30-june-2018. The figures include prescriptions on the general Section 85 and Section 100; excluding under co-payment prescriptions.
to the present study. AbbVie did not have any knowledge of, or involvement in, this study.

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Ethics statement

This study used only published data and did not require Ethics Approval.

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Supplementary Table 1: Sources of dispensing claims data available to third parties for monitoring, surveillance, and research

| Data source                  | Description                                                                                                                                                                                                 | PBS data | RPBS data | Level of data | Data custodian          |
|------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------|-----------|---------------|-------------------------|
| **Publicly available**       |                                                                                                                                                                                                            |          |           |               |                         |
| Medicare Statistics Online¹  | Reports by PBS Item and Group. Reports do not include data on under co-payment (i.e., PBS-medicines priced below the co-payment threshold) or private prescriptions                                                                 | ✓        |           | Aggregated claims | Services Australia      |
| Section 85 extract²          | Reports on PBS and RPBS claims updated monthly and only available for most recent 5 years. Includes under co-payment medicines                                                                                                                                       | ✓        | ✓        | Aggregated claims | Department of Health    |
| Australian Statistics on Medicines (ASM)³ | Annual publication produced by the Drug Utilisation Sub-Committee (DUSC) of the Pharmaceutical Benefits Advisory Committee, Combining PBS/RPBS data with estimates of non-subsidised (under co-payment and private) prescription medicines use obtained from a panel survey of Australian pharmacies. | ✓        | ✓        | Aggregated claims | Department of Health    |
| Under co-payment extract⁴    | Extract of both PBS and RPBS under co-payment data. Available from July 2012-onward.                                                                                                                        | ✓        | ✓        | Aggregated claims | Department of Health    |
| 10% Medicare Benefits Scheme (MBS)/PBS dataset⁵ | 10% random sample of people claiming Medicare Benefits since 1984, or Pharmaceutical Benefits since 2003. Included individual-level linked PBS-MBS data (2003–2014). Data was withdrawn from the public domain in 2016. | ✓        |           | Individual-level, unit record data | Department of Health |
| **Available to third parties by request** |                                                                                                                                                                                                            |          |           |               |                         |
| PBS 10% sample                | Standardised, longitudinal, unit-record extract containing all PBS medicine dispensing data for a random 10% sample of PBS-eligible persons.                                                                        | ✓        |           | Individual-level, unit record data | Services Australia      |
| PBS ad hoc extracts           | Longitudinal data for all PBS-eligible Australians to address specific questions.                                                                                                                             | ✓        |           | Individual-level, unit record data or aggregated claims | Services Australia, Department of Health |
| RPBS                         | Longitudinal data for all eligible veterans and dependents to address specific questions.                                                                                                                  |           | ✓        | Individual-level, unit record data | Department of Veteran’s Affairs |
| DUSC                         | Customised extracts from data underlying the ASM (see above) since 1987.                                                                                                                                     |           | ✓        | Aggregated claims | Department of Health    |

Source: Adapted from Mellish L, Karanges EA, Litchfield MJ, Schaffer AL, Blanch B, Daniels BJ, et al. The Australian Pharmaceutical Benefits Scheme data collection: a practical guide for researchers. BMC Research Notes. 2015;8:634.

¹ [http://medicarestatistics.humanservices.gov.au/statistics/pbs_item.jsp](http://medicarestatistics.humanservices.gov.au/statistics/pbs_item.jsp)
² [http://www.pbs.gov.au/info/statistics/dos-and-dop/dos-and-dop](http://www.pbs.gov.au/info/statistics/dos-and-dop/dos-and-dop)
³ [http://www.pbs.gov.au/info/statistics/asm/australian-statistics-on-medicines](http://www.pbs.gov.au/info/statistics/asm/australian-statistics-on-medicines)
⁴ [http://www.pbs.gov.au/info/statistics/under-co-payment/ucp-data-report](http://www.pbs.gov.au/info/statistics/under-co-payment/ucp-data-report)
⁵ [www.data.gov.au](http://www.data.gov.au)
Supplementary Figure 1: Number of publications (cumulative) according to analytical approach (n = 180)
Supplementary Figure 2: RECORD classification of studies published in 2018 per evaluated item (n = 48)
Supplementary Figure 3: Number of publications (cumulative) according to study focus (1987–2018)
Supplementary Appendix A: Search strategy

Medline search

Database: OVID MEDLINE 1946 to May Week 4 2019

Search strategy:

| S. No. | Search terms |
|--------|--------------|
| 1      | drug utilization/ |
| 2      | drug utilisation.mp. |
| 3      | drug utilization.mp. |
| 4      | drug prescriptions/ |
| 5      | prescription drugs/ |
| 6      | drug therapy/ |
| 7      | pharmaceutical preparations/ |
| 8      | health insurance commission.mp. |
| 9      | pharmaceutical benefits scheme.mp. |
| 10     | pbs.mp. |
| 11     | pharmacoepidemiolog$.mp. |
| 12     | dispens$.mp. |
| 13     | 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 Australia?.mp. |
| 14     | 13 and 14 |
| 15     | mcmanus p.au. |
| 16     | roughead ee.au. |
| 17     | colvin l.au. |
| 18     | gilbert al.au. |
| 19     | (henry or henry da).au. |
| 20     | preen db.au. |
| 21     | tett se.au. |
| 22     | ortiz m.au. |
| 23     | 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 |
| 24     | 15 or 24 |
| 25     | limit 25 to yr="2013–2018" |
| 26     | remove duplicates from 26 |
EMBASE search

Database: EMBASE 1974 to 2019 June 03
Search Strategy:

| S. No. | Search terms |
|--------|--------------|
| 1      | drug utilization/ |
| 2      | drug utilisation.mp. |
| 3      | drug utilization.mp. |
| 4      | drug prescriptions/ |
| 5      | prescription drugs/ |
| 6      | drug therapy/ |
| 7      | pharmaceutical preparations/ |
| 8      | health insurance commission.mp. |
| 9      | pharmaceutical benefits scheme.mp. |
| 10     | pbs.mp. |
| 11     | pharmacoepidemiology$.mp. |
| 12     | dispens$.mp. |
| 13     | 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 |
| 14     | Australia?.mp. |
| 15     | 13 and 14 |
| 16     | mcmanus p.au. |
| 17     | roughead ee.au. |
| 18     | colvin l.au. |
| 19     | gilbert al.au. |
| 20     | (henry or henry da).au. |
| 21     | preen db.au. |
| 22     | tett se.au |
| 23     | ortiz m.au. |
| 24     | 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 |
| 25     | 15 or 24 |
| 26     | limit 25 to yr="2013–2018" |
| 27     | remove duplicates from 26 |
| Item No. | STROBE items | RECORD items |
|---------|--------------|--------------|
| **Title and abstract** | (a) Indicate the study’s design with a commonly used term in the title or the abstract  
(b) Provide in the abstract an informative and balanced summary of what was done and what was found | RECORD 1.1: The type of data used should be specified in the title or abstract. When possible, the name of the databases used should be included.  
RECORD 1.2: If applicable, the geographic region and timeframe within which the study took place should be reported in the title or abstract.  
RECORD 1.3: If linkage between databases was conducted for the study, this should be clearly stated in the title or abstract. |

**Introduction**

- Background rationale

- Objectives

**Methods**

- Study Design

- Setting

- Participants

- Variables

**Data sources/measurement**

- For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group

**Study size**

- Explain how the study size was arrived at

**Quantitative variables**

- Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why

**Results**

- Participants

- Descriptive data

Continued
| Item No. | STROBE items | RECORD items |
|---------|--------------|--------------|
| Outcome data | 15 | *Cohort study* - Report numbers of outcome events or summary measures over time  
*Case-control study* - Report numbers in each exposure category, or summary measures of exposure  
*Cross-sectional study* - Report numbers of outcome events or summary measures |

**Discussion**

| Item No. | STROBE items | RECORD items |
|---------|--------------|--------------|
| Key results | 18 | Summarise key results with reference to study objectives |
| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias  
RECORD 19.1: Discuss the implications of using data that were not created or collected to answer the specific research question(s). Include discussion of misclassification bias, unmeasured confounding, missing data, and changing eligibility over time, as they pertain to the study being reported. |

**Other Information**

| Item No. | STROBE items | RECORD items |
|---------|--------------|--------------|
| Funding | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based |

Source: Benchimol EI, Smeeth L, Guttmann A, Harron K, Moher D, Petersen I, Sørensen HT, von Elm E, Langan SM, the RECORD Working Committee. The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) Statement. *PLoS Medicine* 2015; in press.  
*Checklist is protected under Creative Commons Attribution (CCBY) license.*
Supplementary Appendix C: List of studies included in the systematic review

1. Acar M, Juneja P, Handel M. Treatment persistence of subcutaneous TNF inhibitors among Australian patients with immune-mediated rheumatic disease (IMRD). Open Access Rheumatology: Research and Reviews. 2018; Volume 10:151–60. https://doi.org/10.2147/oarrr.s179704
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| First author, year of publication | Study aim | Data source | Study period (duration) | Primary outcome measure |
|----------------------------------|-----------|-------------|-------------------------|-------------------------|
| **Drug Utilisation by drug, age and gender**<br>Claims-level (14 studies) |
| Bingham, 2018 [12] | Levonorgestrel-releasing intra-uterine device prescribing | PBS ad hoc extracts (DHS) ABS | 2008–2012 (4 years and 10 months) | Annual prescription rates per 1000 women by age and location |
| Gisev, 2018 [49] | Quantify the extent in which subsidised medicine data underestimate prescription-only and total opioid utilisation | DUSC IMS Health | 2010–2014 (5 years) | Difference (%) in opioid utilisation in PBS/RPBS and IMS Health data, calculated using OME |
| Karanges, 2018 [92] | Opioid prescribing according to three volume-based metrics and a person-based metric | PBS 10% sample, DUSC | 2006–2015 (10 years) | Annual opioid use (DDD/1000 pop/day OME/1000 pop/day No. opioid dispensings/1000 pop No. persons dispensed opioids/1000 pop No. (%) of prescriptions of antiarrhythmic drugs and atrial fibrillation ablations/pop/year No. (%) of quetiapine poisonings and% of overdoses No. (%) of quetiapine mortality cases No. prescriptions (DDDs) |
| Khan, 2018 [97] | Trends in rhythm control for atrial fibrillation | PBS Online (ASM) MBS Online | 1997–2016 (20 years) | |
| Lee, 2018 [110] | Determine current trends in quetiapine overdose, misuse and mortality. | PBS Online (ASM) VIC Poisonings Information Centre | 2000–2015 (16 years) | No. of calls for quetiapine poisonings and% of overdoses No. (%) of quetiapine mortality cases No. prescriptions (DDDs) |
| Perera, 2018 [130] | Intravesical bacille Calmette–Guérin prescribing in Australia during fluctuations in global availability | PBS Online (Medicare) ABS | 2006–2016 (11 years) | No. prescriptions per month per clinical indication |
| Eyre, 2017 [37] | Triptan derivatives prescribing compared with available international data | PBS Online (Medicare, Section 85 DoS/DoP Centrelink Income Assistance data | 1997–2015 (19 years) | Annual DDD/1000 concessional beneficiaries/day |
| Ford, 2017 [39] | Antimicrobial medicines prescribing by dental practitioners (concession) | PBS Online (Medicare) ABS Centrelink Income Assistance data | 2001–2012 (12 years) | DDD/1000 concessional beneficiaries/day by medicine and year |
| Hollingworth, 2017 [61] | Non-antimicrobial medicines prescribing by dental practitioners (concession) | PBS Online (Medicare) ABS Centrelink Income Assistance data | 2001–2012 (12 years) | Yearly % change in utilisation rates |
| Turkstra, 2017 [173] | Examine submissions made to the Pharmaceutical Benefits Advisory Committee and assess whether the predicted financial impact and utilisation was associated with a recommendation | PBS Online (Medicare) ABS | 2012–2014 (3 years) | No. submissions accepted, rejected, or deferred No. predicted vs observed prescriptions $AUD and e EUR predicted vs observed expenditure |
| Hopkins, 2016 [65] | Trends in biological disease-modifying antirheumatic drug use and expenditure for rheumatoid arthritis | PBS Online (Medicare) ABS | 2000–2014 (15 years) | Annual DDD/1000 pop/day by drug group Annual PBS expenditure |
| Thai, 2016 [169] | Influence of policies and drivers affecting PBS statin utilisation and expenditure | PBS Online (Medicare) ABS | 1992–2013 (22 years) | Monthly expenditure/prescription Annual DDD/1000 pop/day |
| Barozzi, 2015 [6] | Change in COX-2 inhibitors dispensing after rofecoxib withdrawal and bisphosphonates dispensing | PBS Online (Medicare) ABS Centrelink Pharmaceutical Industry Marketing Expenditure | 2000–2012 (13 years) | Annual, quarterly and/or monthly DDD/1000 pop/day of COX-2 inhibitors and bisphosphonates by drug |
| Hasan, 2015 [58] | Diabetes prevalence and anti-diabetic medication dispensing (Australia and Malaysia) | PBS Online (ASM) Other international dispensing data | 2004–2008 (5 years) | Annual antidiabetic use (DDD/1000 pop/day), overall, by drug and country |
### Extended drug utilisation

#### Claims (22 studies)

| First author, year of publication | Study aim | Data source | Study period (duration) | Primary outcome measure |
|-----------------------------------|-----------|-------------|-------------------------|-------------------------|
| **De Graaff, 2018 [35]**          | Uptake and financial impact of direct-acting antiviral agents | PBS Online (Medicare) ABS NNDSS | 2016–2017 (1 year and 6 months) | Total no. of prescriptions Prescriptions per 100000 pop by jurisdiction Expenditure costs ($AUD per medicine) DDD/1000 pop/day |
| **Islam, 2018 [77]**              | Relationship between opioid dispensings and neighbourhood disadvantage-index, and standardised doses | PBS ad hoc extracts (VIC only) ABS | 2013–2015 (3 years) | % of persons dispensed opioids No. of prescriptions over time in DDD/1000 pop/day |
| **Islam, 2018 [79]**              | Trends in prescription opioid dispensing, identified high dispensing areas and factors associated with the doses dispensed | PBS ad hoc extracts (NSW, ACT only) ABS | 2013–2015 (3 years) | % of persons dispensed opioids No. of prescriptions over time in DDD/1000 pop/day |
| **Thai, 2018 [171]**              | Compare the prices and utilisation of statins with three international countries | PBS Online (Section 85 DoS) Other international dispensing data | 2011–2013 (3 years) | Statin DDD/1000/day per year by country Weighted average strengths per year by country |
| **Islam, 2016 [80]**              | Trends and types of opioid prescribing and geographic variations | PBS Online (ASM, not specified) ABS | 1992–2011 (20 years) | Annual DDD/1000 pop/day by state Trends in dispensing and seasonal variations Differences between states in dispensing trends |
| **Bericki-Gisolf, 2017 [10]**     | Trends in opioid prescribing and poisoning resulting in hospitalisation or death in Victoria, Australia | PBS ad hoc extracts (VIC only) ABS, VIC Admitted Episodes Data Cause of Death Unit Record File | 2006–2013 (8 years) | No. events (deaths, admissions) per 1,000,000 person-years by age group, gender and year % change in rates per year |
| **Hollingworth, 2017 [64]**       | Ezetimibe use and reported adverse events | PBS Online (Medicare) ABS DAEN | 2004–2015 (12 years) | % of annually increased in utilisation No. (%) adverse events by organ class system |
| **Wagemaakers, 2017 [176]**       | Compare the use of opioids in two countries | PBS Online (ASM) International dispensing data | 2000–2014 (15 years) | Annual DDD/1000 pops/day Annual % change in prescribing |
| **Berling, 2016 [11]**            | Compare trends in prescriptions and overdoses of antipsychotic medicines in Hunter, NSW region | PBS Online (ASM) (NSW only) Hunter Toxicology Admissions | 1990–2011 (22 years) | Rates of antipsychotic overdose by class and subclass No. overdoses per 100,000/pop/year Annual DDD/1000/day Annual rate of prescription per 1000 women by age group, remoteness, no. of Aboriginal medical services and family planning clinic Average annual % change Calls due to ADHD by demographics, no. of exposures, coingestants, route and disposition Annual DDD/1000 pop/day by medicine No. packs sold (%) and dispensing by medicine type and location No. packs sold per person by location and medicine Annual OME mg per person by location and medicine |
| **Bingham, 2016 [13]**            | Trends in etonogestrel-releasing subdermal implant prescribing and associated factors | PBS ad hoc extracts (DHS) | 2008–2012 (4 years and 10 months) | No. packs sold per person by location and medicine |
| **Cairns, 2016 [24]**             | Trends in overdoses with medications used to treat attention deficit hyperactivity disorder | PBS Online (not specified) NSW Poisonings Information Centre | 2004–2014 (11 years) | No. packs sold per person by location and medicine |
| **Degenhardt, 2016 [36]**         | Total opioid utilisation (PBS subsidized and over the counter) and sociodemographic correlates of use | PBS Online (Section 85 DoS) IMS Health ABS | 2013 (12 months) | Annual DDD/1000 pop/day by medicine No. packs sold (%) and dispensing by medicine type and location No. packs sold per person by location and medicine Annual OME mg per person by location and medicine |
| **Gardiner, 2016 [45]**           | Immunosuppressants in transplant recipients compared to European countries | PBS Online (Medicare) ABS HSD Expenditure Reports Other international drug and population datasets | 2007–2013 (7 years) | Annual DDD/1000 pop/day |
| First author, year of publication | Study aim | Data source | Study period (duration) | Primary outcome measure |
|-----------------------------------|-----------|-------------|-------------------------|-------------------------|
| Hawke, 2016 [59]                 | Trends in consumer help-seeking about antibiotics in relation to age and antibiotic utilisation | PBS Online (ASM) Medicine call centre data BEACH-GP Survey ABS | 2002–2010 (7 years and 10 months) | Calls per 100,000 people/population by medicine and other characteristics No of calls per 100,000 ASM prescriptions Ratio of the % of Medicines Line calls to the % of BEACH prescriptions for a specific antibiotic |
| Thai, 2016 [170]                 | Community and hospital differences in proton pump inhibitor utilisation and pricing | PBS Online (Medicare) Hospital Sales data | 2011–2012 (2 years) | Average weighted price per DDD DDD/1000 persons/day |
| Forrester, 2015 [40]             | Trends in community and hospital clozapine use | PBS Online (Medicare) (QLD only) QLD Hospital data, ABS | 2004–2013 (10 years) | Number of clozapine dispensings, by year and data source Prevalence of initiators (people/100,000 pop/year) Median duration of treatment and % ceasing treatment |
| Hollingworth, 2015 [62]          | Trends in opioids dispensings | DUSC | 2002–2009 (8 years) | DDD/1000 pop/day and yearly % change in dispensings by overall, drug, prescription type (PBS-subsidised, under general co-payment and private), gender,10-year age groups, and medicine strength |
| Kelly, 2015 [95]                 | Trends in use of endocrine therapies for breast cancer in nine countries | PBS Online (Medicare) Other international dispensing and population databases | 2001–2012 (12 years) | Total and age-adjusted DDD/1000 population/day DDD/1000 new breast cancer cases/day by year, country and medicine (overall and by individual drug) |
| Macintyre, 2015 [112]            | Trends in herpes zoster and post-herpetic neuralgia incidence and associated healthcare utilisation pre- and post- varicella vaccination introduction | PBS ad hoc extracts (DHS) NHMD, NSW, VIC; Emergency Department Data BEACH GP survey ABS | 1998–2013 (16 years and 6 months) | Incidence of herpes zoster/post-herpetic neuralgia (defined by the number of GP visits, antiviral dispensings, hospital separations, emergency department admissions) by age group, dataset and year |
| Meumann, 2015 [114]              | Trends in E. Coli antimicrobial resistance and antibiotic use | PBS Online (Medicare) (TAS only) Laboratory data ABS | 2010–2012 (3 years) | Antibiotic use (DDD/1000 pop/day) by drug and time period (month, season) % of E.coli samples with antimicrobial susceptibility by drug and overall Odds of antimicrobial resistance following increased antibiotic use by time lag (same month, 1m, 2m, 3m and season prior) |
| Karanges, 2014 [93]              | Anti-depressant, antipsychotic and ADHD medication prescribing Benzodiazepine dispensing | PBS ad hoc extracts DUSC | 2009–2012 (4 years) 1992–2011 (20 years) | No. and % change in prescriptions by drug, age, gender, prescriber specialty and year DDD/1000 pop/day by drug, script type, state/territory, and year No. prescriptions and Ashton diazepam equivalent dose/1000 pop/day by drug, script type and year DDD/script by script type and year |

Note: ABS = Australian Bureau of Statistics, ACT = Australian Capital Territory, ADHD = attention deficit hyperactivity disorder, ASM = Australian Statistics on Medicines, ATC = Anatomical Therapeutic Class, BEACH-GP Survey = Bettering the Evaluation and Care of Health in General Practice Survey, DDD = Defined Daily Dose, DHS = Department of Human Services, DoH = Department of Health, DoP = Date of Processing, Dos = Date of Supply, DUSC = Drug Utilisation Sub-Committee, DVA = Department of Veterans’ Affairs, HSD = Highly specialised drugs, MBS = Medicare Benefits Schedule, NNDSS = National Notifiable Diseases Surveillance System, NSW = New South Wales, OME = Oral Morphine Equivalent, PBS = Pharmaceutical Benefits Scheme, QLD = Queensland, RPBS = Repatriation Pharmaceutical Benefits Scheme, VIC = Victoria, TAS = Tasmania.
| First author, year of publication | Study aim | Data source | Study period (duration) | Primary outcome measure |
|-----------------------------------|-----------|-------------|------------------------|------------------------|
| Brett, 2018 [22]                  | Quantify the extent of low value psychotropic prescribing practices | PBS 10% sample | 2010 – 2016 (7 years) | Annual rate of low-value prescribing practice indicators (/100 persons) |
| Brett, 2018 [20]                  | Detail annual trends in benzodiazepine incidence and prevalence in older adults in three countries | Not specified (concession) | 2010 – 2016 (7 years) | Annual incidence and prevalence of use (per 1000) by age and sex |
| Daniels, 2018 [30]                | Examine the treatment of women receiving trastuzumab for HER2-positive metastatic breast cancer and adherence to national prescribing restrictions | PBS ad hoc extracts Herceptin Program | 2001–2016 (15 years and 6 months) | % of women prescribed trastuzumab receiving at least one non-adherent HER2-targeted treatment, according to different clusters |
| Hajarizadeh, 2018 [52]           | Estimate levels and patterns of direct-acting antiviral agents treatment uptake | PBS 10% sample | 1997–2016 (20 years) | Monthly no. of persons receiving direct-acting antiviral agents among people living with Hepatitis C |
| Hajati, 2018 [54]                | Examine the extent to which the adult Australian population on lipid-lowering medications receives the level of high-density lipoprotein cholesterol (HDL-C) testing recommended by national guidelines | PBS 10% sample | 2008–2014 (7 years) | % of persons on lipid-lowering treatment who did not receive any HDL-C test in a given year |
| Kalisch Ellett, 2018 [85]        | Prevalence of antipsychotic polypharmacy and the use of medicines to manage adverse events associated with antipsychotics | RPBS (full entitlement) DVA: Health services, Hospitalisations | 2013–2014 (1 year and 4 months) | % of persons dispensed an antipsychotic medicine in the study period, co-dispensed anticholinergic, hyperlactatemia, oral diabetes medicine and those on dual antipsychotics |
| Keen, 2018 [94]                  | Estimate the HIV cascade in 2016 in NSW and describe enhanced data collection methods | PBS 10% sample (NSW only) | 2016 (12 months) | No. of people living with HIV |
| Kemp-Casey, 2018 [96]            | Describe how post-market utilisation analysis informs cost-effectiveness assessment and pricing decisions, through case studies | RPBS (full entitlement) | 2010–2017 (6 years and 1 month) | Monthly no. of alfivirenz and rilpivirine prescriptions dispensed to veterans and non-veterans by demographic and clinical characteristics. |
| Lim, 2018 [111]                  | Compare the use of medicines and health services for chronic obstructive pulmonary disease (COPD) against guideline recommendations | RPBS (full entitlement) MBS DVA: Health services, Hospitalisations | 2014–2016 (2 years and 3 months) | No. (%) of persons on COPD medicines |
| Ofori-Asenso, 2018 [125]         | Trends in statin use among older patients | PBS 10% sample (concession) | 2006–2016 (11 years) | No. (%) of persons with clinical visits for health services by COPD patients in the prior 1–2 years |
| Ofori-Asenso, 2018 [123]         | Evaluate changes in the rate of medication dispensation for multiple chronic conditions among older Australians | PBS 10% sample | 2013 – 2016 (4 years) | Annual prevalence (%) of use |
| Raman, 2018 [144]                | Prevalence of attention-deficit hyperactivity disorder (ADHD) medication use in children and adults in multiple countries | PBS ad hoc extracts (DoH) International dispensing datasets | 2009–2014 (6 years) | Annual incidence (per 1000) of use |
| Brett, 2017 [19]                 | Examine changes in annual patterns of psychotropic medication use | PBS 10% sample (concession) | 2006–2015 (10 years) | % of persons dispensed medications for 22 pre-specified chronic conditions |
| Brett, 2017 [18]                 | Psychotropic polypharmacy prescribing | PBS 10% sample (concession) | 2006–2015 (10 years) | % of persons dispensed medications for multiple chronic conditions within 180-days per year |
| Caughey, 2017 [26]              | Examine the appropriateness of medicine use and potentially high-risk prescribing before and after hospitalisation for diabetes | RPBS (entitlement not specified) DVA: Health services, Hospitalisations | 2007–2013 (5 years and 3 months) | % of persons on non-recommended treatments 4 months after hospitalisations |
| First author, year of publication | Study aim | Data source | Study period (duration) | Primary outcome measure |
|----------------------------------|-----------|-------------|-------------------------|------------------------|
| Finger, 2017 [38]                | Assess disparities in treatment provision and need for treatment for neovascular age-related macular degeneration across Australia | PBS ad hoc extracts ABS Other data | 2010–2014 (4 years and 6 months) | No. (%) of incident cases not treated per year Factors associated with percentage of untreated incident cases |
| Hajarizadeh, 2017 [53]           | Provide updated estimates of chronic hepatitis C infection care cascade and burden | PBS 10% sample and Not specified PBS data NNDOSS Other data | 1997–2014 (18 years) | No. of individuals living with hepatitis C, diagnosed, on treatment, cured and on various clinical stages Increase in the % of persons dispensed hepatitis C treatment |
| Hálfdánarson, 2017 [55]          | International trends in antipsychotic use | PBS 10% sample International datasets | 2006–2014 (9 years) | Overall prevalence of antipsychotic use by year and country |
| Hansen, 2017 [57]                | Characterize the use of opioids in total knee arthroplasty patients before and after surgery and identify risk factors of chronic opioid use | PBS 10% sample (concession) | 2000 – 2013 (14 years) | % of persons prescribed opioids before and after surgery by duration of use (none, some, chronic) % of change by duration of use (none, some, chronic) Factors associated with chronic opioid use after surgery |
| Handelsman, 2017 [56]            | Estimate the impact of the first year of new eligibility criteria for testosterone prescribing | PBS Online (Medicare) PBS ad hoc extracts ABS | 1992 – 2016 (25 years) | Total PBS expenditure $AUD per year No. Prescriptions per year by new, renewed and total, prescriber type, and age |
| Kjosavik, 2017 [99]              | Analyse average treatment duration with antipsychotics, the incidence and prevalence of prescribing and trends over time | PBS 10% sample (concession) | 2005–2013 (9 years) | Annual incidence of antipsychotics use Average duration of antipsychotics use (prevalence/incidence) by age group and year |
| Morley, 2017 [118]               | Explore the pattern of dispensing of pharmacotherapy for alcohol dependence across remote and disadvantaged Australia | PBS ad hoc extracts ABS | 2009 – 2013 (4 years) | Age-standardized mean dispensing ratio (observed vs expected) by remoteness and disadvantage |
| Reeve, 2017 [146]                | Quantify health care use and costs in the last 6 months of life in a cohort of elderly decedents and to examine the factors associated with end-of-life resource use and costs | RPBS (full entitlement, NSW only) DVA: Health services, Hospitalisations, Aged care NSW: RBDM, CCR, APDC, EDDC | 1994–2009 (16 years) | Mean (per person) health service use in 6month before death Mean total costs ($AUD per decadent) by health service by month |
| Whitely, 2017 [178]              | Association of birth month and probability of children being treated for ADHD | Not specified (WA only) | 2013 (12 months) | Prevalence of children prescribed ADHD medicines |
| Baker, 2016 [5]                  | Compare direct oral anticoagulants and other antithrombotic therapy use in patients with Atrial Fibrillation/Flutter within one NSW hospital and national use of these medicines | Not specified (PBS Online) Manning Hospital data | 2013 – 2014 (2 years) | Annual prevalence (% by medicine No. (%) dispensings by medicine |
| Gadzhanova, 2016 [42]            | Current use of medicines in children | PBS 10% sample ABS | 2013 (12 months) | % of dispensions per ATC group Prevalence per 1000 children by medicine group, age group Prevalence of antibiotic per 1000 children by class, age, no. dispensings, sex, comorbidity No. (%) of persons initiating therapy according to demographics and previous non-opioid and weak opioid analgesics use Prevalence of use by year of last admission |
| Gisev, 2016 [48]                 | Characterize individuals initiating strong opioids and factors associated with the type of opioid initiated | PBS 10% sample (concession) ABS | 2009 – 2013 (4 years and 6 months) | Prevalence of opioid and chronic opioid use before and after surgery Factors associated with persistent chronic opioid use before and after surgery |
| Gunnell, 2016 [50]               | Evaluate dispensing patterns in people with acute coronary syndrome by gender and time since hospitalisation | PBS ad hoc extracts (WA only) EDDC HMDCC MBS | 1989 – 2008 (19 years and 7 months) | Prevalence of use by year of last admission |
| Inacio, 2016 [70]                | Determine chronic opioid use pre-THA (total hip arthroplasty) and post-THA, and risk factors for persistent or new chronic opioid use post-THA | RPBS (entitlement not specified) DVA: Health services, Hospitalisations | 2001–2013 (13 years) | Prevalence of opioid and chronic opioid use before and after surgery Factors associated with persistent chronic opioid use before and after surgery |
## First author, year of publication

| Study aim | Data source | Study period (duration) | Primary outcome measure |
|-----------|-------------|-------------------------|-------------------------|
| Kjosavik, 2016 [98] | Analyse the average treatment duration with antidepressants | PBS 10% sample (concession) | 2005 – 2013 (9 years) | No. of prevalent and incident users per year and age group |
| Langton, 2016 [104] | Characterise health service use and associated costs from a health care payer perspective in the last six months of life in a cohort of elderly decedents with a cancer history | RPBS (full entitlement, NSW only) | 1994–2009 (16 years) | Mean duration of treatment % prescriptions issued by prescriber type (GP, psychiatrist, other physicians) |
| Moon, 2016 [115] | Trends in the utilisation of metformin in Australia and the appropriateness of metformin doses in patients attending a teaching hospital | DUSC | 1990–2012 (23 years) | DDDS/1000 pop/day |
| Parkinson, 2016 [127] | Examine differences between clinical trial and real-world setting data characteristics and outcomes using a case study. | PBS ad hoc extracts | 2001–2010 (8 years and 4 months) | No. (%) of persons treated weekly vs. thrice weekly and on concomitant chemotherapies |
| Pratt, 2016 [135] | Evaluate the uptake of oral anticoagulants after PBS listing | RPBS (full entitlement) | 2012–2014 (2 years and 8 months) | Monthly rates of use per 1000 veterans by medicine |
| Schaffer, 2016 [159] | Evaluate the use of first-line antihypertensive drug therapy and the uptake of fixed-dose combinations and its impact on treatment discontinuation | PBS 10% sample (concession) | 2005–2014 (9 years) | No. (%) of persons initiating non-recommended antihypertensive therapy |
| Allard, 2015 [3] | Access to guideline-based clinical care in chronic hepatitis B | PBS ad hoc extracts | 2011–2012 (2 years) | No. and % of patients receiving Hepatitis B Virus DNA tests and anti-viral treatment by state and territory |
| Gadjhanova, 2015 [41] | Use of teratogens and other medicines in women of reproductive age | PBS 10% sample | 2013 (12 months) | Prevalence and % total dispensings by pregnancy risk category and therapeutic class |
| Gadjhanova, 2015 [43] | Anti-dementia medicine initiation and anticholinergic and sedative use | Not specified (Full) | 2008 – 2011 (4 years) | Prevalence of sedative and anticholinergic use among anti-dementia medicine initiators in 6 months pre and post-initiation |
| Pearson, 2015 [128] | Patterns of antidepressant initiation around cancer diagnosis and associated factors | RPBS (full entitlement, NSW only) | 1994–2009 (16 years) | Adjusted hazards ratio for antidepressant initiation in cancer vs non-cancer patients, overall and according to time from cancer diagnosis |
| Schaffer, 2015 [160] | Describe and compare the treatment, health service use and survival of patients with cancer of unknown primary diagnosis | RPBS (entitlement not specified, NSW only) | 1999–2009 (10 years and 6 months) | Median time to initiation/discontinuation by class |
| Sluggett, 2015 [168] | Medicine use after hospitalisation for transient ischaemic attack or ischaemic stroke | RPBS (full entitlement) | 2001–2010 (9 years and 6 months) | Probability of receiving less treatment (medicines, therapy or surgery) one-year post diagnosis |
| Supplemenary Appendix D: Continued | | | | | Incident rate ratio of health service use (primary care consults, emergency department visits, hospitalisation) |
| | | | | | Risk of death within 30 days of diagnosis |
| | | | | | Prevalence of antihypertensive, antithrombotic and lipid lowering medicine use before and after incident hospitalisation by age and medicine class |
| First author, year of publication | Study aim | Data source | Study period (duration) | Primary outcome measure |
|---------------------------------|-----------|-------------|------------------------|------------------------|
| Vajdic, 2015 [174]              | Compare the pathways to diagnosis between people with cancer of unknown primary diagnosis and other cancers | RPBS (full & specific entitlement, NSW only) DVA: Health services, Hospitalisations, Aged care NSW: RBDM, CCR, APDC, EDDC | 1999–2007 (10 years and 6 months) | % of consultations, visits, cancer-related procedures and pathology tests in the 3 months prior and month of diagnosis Predictors of cancer of unknown primary diagnosis |
| Kalisch Ellett, 2014 [84]       | Incident oxybutynin dispensing after initiation of medicines associated with urinary incontinence | RPBS (full entitlement) DVA: Hospitalisations | 2001–2011 (11 years) | No. oxybutynin users Risk of oxybutynin initiation by medicine class |
| Price, 2014 [139]              | Examine time trends and factors associated with exposure to potentially inappropriate medications (PIMs) by the Beers Criteria | PBS ad hoc extracts (WA only) MBS Aged care Electoral roll | 1993–2005 (13 years) | No. (%) of persons exposed to PIMs DDD/1000 person-years for overall and individual PIMs |
| Simons, 2014 [162]             | Use of lipid-lowering drugs according to contemporary guidelines in patients with high coronary risk | PBS 10% sample (concession) | 2006–2013 (7 years and 5 months) | % of persons using lipid-lowering drugs by age, gender and risk status |
| Sluggett, 2014 [167]           | Use of secondary stroke prevention medicines in survivors of transient ischemic attack and ischemic stroke | RPBS (full entitlement) DVA: Hospitalisations | 2000 – 2010 (10 years and 6 months) | Rate of medicine use/100 persons by month % annual change in medicine use |
| Slugget, 2014 [166]            | Estimate the use of anticoagulants among acute ischaemic stroke patients with atrial fibrillation after discharge | RPBS (full entitlement) DVA: Health services, Hospitalisations | 2001 – 2010 (9 years and 6 months) | % of persons using antithrombotic agents in the 4 months after hospitalisation |

**Patient practices**

**Individual-level (16 studies)**

| Acar, 2018 [1] | Describe subcutaneous tumour necrosis factor inhibitors treatment persistence in immune-mediated rheumatic disease | PBS 10% sample | 2010 – 2016 (6 years and 6 months) | Median treatment persistence (time from initiation to switch or discontinuation) by treatment and line of therapy (1st, 2nd, 3rd) |
| Bartlett, 2018 [8] | Compare the persistence rates among people who initiate the combination of amldipine and statin as a fixed-dose combination or separate pill combination and impact of prior medicine exposure on this outcome | PBS ad hoc extracts | 2012 – 2015 (3 years) | Time to cessation of combination therapy (both an antihypertensive and lipid lowering therapy), i.e., persistence of combination therapy, with a minimum of 15 months’ follow-up for each patient. |
| Bartlett, 2018 [9] | Demonstrate the effect of prior medicine experience on persistence in those initiating combinations of cardiovascular medicines | PBS ad hoc extracts | 2012–2014 (2 years and 9 months) | % ceasing combination therapy over 12 months with a minimum of 15 months’ follow-up for each patient. |
| Blanch, 2018 [15] | Examine associations between patient factors and increasing opioid access measured by three metrics | PBS 10% sample (concession) | 2009–2013 (4 years and 6 months) | No. of unique opioid prescribers and dispensing pharmacies No. of opioid dispensings recorded within 1-year after initiating or reinitiating strong opioid treatment |
| Jones, 2018 [82] | Describe the persistence of biologic disease modifying anti-rheumatic drugs according to the use of other concomitant therapy | PBS 10% sample | 2010–2014 (3 years and 11 months) | % persistence at 12 months post-treatment initiation Median time to stopping (months) |
| Lalic, 2018 [102] | Identify patterns of opioid analgesic use and determine predictors of persistent opioid use among people without cancer | PBS 10% sample | 2012–2016 (4 years and 6 months) | % persistence over 12 months following opioid initiation defined by patterns using group-based trajectory modelling |
| Ofori-Asenso, 2018 [124] | Examine the prevalence of statin use and assess long term adherence and persistence among older diabetes patients | PBS 10% sample (concession) | 2006–2016 (11 years) | 1-year prevalence of statin use per year % adherent to therapy at 6 up to 9 years % discontinued therapy in 9 years |

Continued
| First author, year of publication | Study aim | Data source | Study period (duration) | Primary outcome measure |
|----------------------------------|-----------|-------------|-------------------------|------------------------|
| Bartlett, 2017 [7]              | Compare adherence and persistence in patients who add ezetimibe to statin therapy as a separate pill combination or fixed dose combination | PBS ad hoc extracts | 2004–2014 (10 years and 9 months) | Mean medication possession ratio per group after 6 months of initiation (separate or fixed dose) % adherent after 6 months of initiation (separate or fixed dose) Time to discontinuation (persistence) of initial medicines, any lipid-lowering therapy, within 12 months of follow-up |
| Blanch, 2017 [16]               | Benchmark prescriber access patterns for opioids against statins in Australia and British Columbia, Canada | PBS 10% sample (concession) Other international dispensing data | 2011 (12 months) | No. (%) of unique prescribers No. of prescribers visited |
| Schaffer, 2017 [158]             | Compare statin adherence in individuals initiating fixed-dose or free combination | PBS 10% sample (concession) | 2005 – 2015 (11 years) | Patterns of adherence in 24 months following initiation (near perfect, good, declining and early non-adherence) |
| Simons, 2017 [164]              | Examine medium-term persistence in atrial fibrillation patients using a non-vitamin-K antagonist oral anticoagulant drugs (NOACs) | PBS 10% sample (concession) | 2013 – 2016 (2 years and 10 months) | % persistent with NOACs over 12 and 30 months % switching to another NOAC or warfarin |
| Simons, 2017 [163]              | Evaluate treatment persistence and mortality using a single-pill, fixed-dose combination tablet compared with a two-pill combination for hypertension | PBS 10% sample (concession) | 2011–2014 (4 years) | % discontinued within 12 months by single- or two pill Median persistence time (months) by single- or two pill Survival (%) in 48 months of follow up by single- or two pill |
| Gadzhanova, 2016 [44]           | Compare the persistence rates among people using fixed or separate antihypertensive therapy | PBS ad hoc extracts (concession) | 2005–2012 (7 years) | No. (%) of persons dispensed each medicine by age and gender Median days on medication % of patients with 2 and 3 dispenses |
| Morley, 2016 [117]              | Characterise patterns of alcohol pharmacotherapy use and costs | PBS ad hoc extracts (DHS) | 2009–2013 (4 years) | No. of patients and prescriptions dispensed by medicine Analgesic equivalent days ((strength*quantity*number scripts)/DDD) |
| Ortiz, 2016 [126]               | Compare extended-release paracetamol with standard paracetamol use in patients with osteoarthritis | PBS 10% sample (concession) | 2008–2010 (3 years) | Median time on index therapy (persistence) Persistence rate over 4 years |
| Simons, 2016 [165]              | Evaluate the persistence in atrial fibrillation patients using a non-vitamin-K oral anticoagulant | PBS 10% sample (concession) | 2005–2015 (10 years and 3 months) | Median persistence in 2 years by medicine % failing to fill first repeat prescription % discontinued within 12 months |

Note: ABS = Australian Bureau of Statistics, ADHD = attention-deficit hyperactivity disorder, APDC = Admitted Patients Data Collection, CCR = Central Cancer Registry, COPD = chronic obstructive pulmonary disease, DDD = Defined Daily Dose, DoH = Department of Health, DUSC = Drug Utilisation Sub-Committee, DVA = Department of Veterans’ Affairs, EDDC = Emergency Department Data Collection, GP = General Practitioner, HDL-C = high-density lipoprotein cholesterol, HMDC = Hospital Morbidity Data Collection, HSD = Highly Specialised Drugs, MBS = Medicare Benefits Schedule, NNDSS = National Notifiable Diseases Surveillance System, NOAC = non-vitamin-K antagonist oral anticoagulant drugs, NSW = New South Wales, PBS = Pharmaceutical Benefits Scheme, PIM = potentially inappropriate medications, RBDM = Registry of Births, Deaths, and Marriages, RPBS = Repatriation Pharmaceutical Benefits Scheme, THA = total hip arthroplasty, WA = Western Australia.
| First author, year of publication | Study aim | Data source | Study period (duration) | Primary outcome measure |
|----------------------------------|-----------|-------------|------------------------|------------------------|
| **Intervention impacts, policy** | | | | |
| **Claims-level (4 studies)** | | | | |
| Roughhead, 2018 [151] | Impact of the policies for generic medicines on the total prices of atorvastatin therapy | ABS | 2006–2015 (10 years) | Annual price per DDD supplied or sold by country |
| | | PBS Online (ASM) | | % price reduction in 4 years following generic drug entry |
| | | 3 Asia Pacific pharmacy databases | | |
| Hopkins, 2017 [66] | Impact of subsidy restriction changes on the use and expenditure on leflunomide and bDMARDs | PBS Online (Medicare) | 2000–2013 (14 years) | DDD/1000 pop/day by year |
| | | ABS | | Total expenditure per year ($AUD) |
| Karanges, 2016 [91] | Trends in community use of prescribed opioids according to major changes to opioid registration and subsidy | Not specified (DUSC or PBS online) | 2004–2012 (8 years and 5 months) | DDD/1000 persons/day by year |
| | | | | % change in medicine use after warnings |
| Morgan, 2018 [116] | Impact of introduction of non-vitamin K antagonist anticoagulants in anticoagulant use and government expenditure | PBS 10% sample (concession) | 2005–2015 (10 years and 10 months) | Monthly quetiapine dispensing |
| | | PBS Online (Medicare) | | % of persons discontinuing within 90 days and switching quetiapine strength |
| | | | | |
| **Individual-level (6 studies)** | | | | |
| Brett, 2018 [21] | Impact of two subsidy restriction changes on quetiapine dispensing: removal of prior authorisation and repeat prescriptions | Not specified (DUSC or PBS online) | 2004–2012 (8 years and 5 months) | Monthly no. and % of persons discontinuing and switching quetiapine before and after the reformulation |
| | | | | |
| Morgan, 2018 [116] | Impact of introduction of non-vitamin K antagonist anticoagulants in anticoagulant use and government expenditure | NSW Poisons Information Centre | 2012–2016 (4 years and 6 months) | Monthly no. and % of persons discontinuing and switching quetiapine before and after the reformulation |
| | | | | |
| Schaffer, 2018 [156] | Impact of the reformulation of tamper-resistant controlled-release oxycodone on dispensing, switching and poisonings | NSW Poisons Information Centre | 2012–2016 (4 years and 6 months) | Monthly no. and % of persons discontinuing and switching quetiapine before and after the reformulation |
| | | | | |
| Caughey, 2016 [29] | Impact of a general practitioner management plan (GPMP) on the risk of hospitalisation for diabetes | PBS Online (ASM) | 2006–2014 (8 years) | Risk of diabetes-related hospitalisation in the 12 months following GPMP |
| | | RPBS (entitlement not specified) | | |
| | | DVA: Health services, Hospitalisations | | |
| Schaffer, 2016 [155] | Impact of rescheduling alprazolam on benzodiazepine prescribing, dispensing, and intentional poisonings | PBS Online (ASM) | 2010–2015 (5 years and 6 months) | Monthly no. calls about poisoning |
| | | PBS 10% sample (concession) | | Monthly no. people switching |
| Vitry, 2014 [175] | Impact of chronic disease management programme in long-term health outcomes | PBS Online (ASM) | 2004–2012 (8 years) | Time until next potentially preventable hospitalisation for heart failure |
| | | PBS Online (Medicare) | | |
| | | PBS Online (ASM) | | |
| **Intervention impacts, educational** | | | | |
| **Claims-level (1 studies)** | | | | |
| Wu, 2018 [179] | Impact of educational interventions on antimicrobial dispensings | PBS Online (ASM) | 2004–2015 (11 years and 6 months) | Monthly estimated change (%) in dispensing following interventions |
| | | RPBS (entitlement not specified) | | Monthly no. dispensed scripts by health practitioner type |
| | | MBS | | |
| | | DVA: Health services, Hospitalisations, Aged care | | |
| | | | | |
| **Individual-level (6 studies)** | | | | |
| Kalisch Ellett, 2018 [89] | Impact of quality improvement interventions on the uptake of collaborative Home Medicines Reviews (HMR) | RPBS (entitlement not specified) | 2001–2016 (15 years and 2 months) | % of HMR use 9-months after each intervention |
| | | DVA: Health services, Hospitalisations | | Rate of BMD testing in 9-months after the intervention |
| | | | | Rate of initiation of any treatment for osteoporosis in 9-months after the intervention |
| | | 3 Asia Pacific pharmacy databases | |%
| Kalisch Ellett, 2018 [83] | Impact of interventions on hypnotic use among Australian veterans and associated health consequences | RPBS (entitlement not specified) | 2007–2014 (7 years and 3 months) | % of BMD testing in 9-months after the intervention |
| | | DVA: Health services, Hospitalisations | | % of initiation of any treatment for osteoporosis in 9-months after the intervention |
| | | | | |
| Kalisch Ellett, 2017 [90] | Impact of two national quality improvement initiatives on the uptake of bone mineral density (BMD) testing and osteoporosis medicines | RPBS (entitlement not specified) | 2006–2012 (6 years) | |
| | | DVA: Health services, Hospitalisations | | |
| | | | | |

Continued
| First author, year of publication | Study aim | Data source | Study period (duration) | Primary outcome measure |
|----------------------------------|-----------|-------------|------------------------|-------------------------|
| Pratt, 2017 [132]               | Impact of national initiatives on proton pump inhibitors (PPI) use among older Australians | RPBS (entitlement not specified) | 2003–2013 (11 years) | % changes in: the monthly rate of PPI use the monthly rate of low strength PPIs |
| Pratt, 2015 [133]               | Impact of commitment to discuss health issue with GP (via commitment questions) on uptake of targeted health services in Veterans | RPBS (entitlement not specified) DVA: Health services | 2006–2013 (8 years) | Change in health service use (rate/ 1000 targeted patients/month) Commitment question response (yes, no/unsure, no response); Association (rate ratio) between positive response and health service use |
| Roughead, 2013 [150]            | Impact of audit and feedback educational interventions on medicine use in the elderly | RPBS (entitlement not specified) DVA: Health services, Hospitalisations | 2003–2009 (6 years and 7 months) | Rate of medicine use/1000 veterans by month % change in medicine use after each intervention Estimated no. of patients with a sustained change in medicine use 2 years following the intervention |

| Intervention impacts, other Individual-level (1 study) | |
| Schaffer, 2015 [157] | Impact of televised science journalism program on statin use | PBS 10% sample (concession) | 2009–2014 (5 years) | Weekly change (%) in statin dispensings, persons discontinuing statins before and after the program by risk category |

Note: ABS = Australian Bureau of Statistics, bDMARDs = biological Disease-modifying antirheumatic drug use, BMD = bone mineral density, DDD = Defined Daily Dose, DVA = Department of Veterans’ Affairs, HMR = Home Medicines Reviews, MBS = Medicare Benefits Schedule, PBS = Pharmaceutical Benefits Scheme, PPI = proton pump inhibitors, RPBS = Repatriation Pharmaceutical Benefits Scheme.
### Exposure and Outcomes (Other exposure and outcomes)

#### Claims-level (1 study)

**Rowell, 2017** ([153])

**Study aim**: Evaluate the effect of weather on medications prescribed to treat Parkinson’s disease

**Data source**: Not specified

**Study period (duration)**: 1992–2014 (23 years)

**Primary outcome measure**: Aggregate levodopa equivalent dose (LED) for 51 Parkinson’s medications

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#### Individual-level (4 studies)

**Gillam, 2018** ([47])

**Study aim**: Describe the type and frequency of re-hospitalisations for complications and mortality after discharge following pacemaker implantsations

**Data source**: RPBS (full entitlement), DVA: Health services, Hospitalisations

**Study period (duration)**: 2005–2015 (10 years and 6 months)

**Primary outcome measure**: No. and % of re-hospitalisations for each type of complication

**Inacio, 2018** ([75])

**Study aim**: Prevalence and change in analgesic medications use prior to joint replacement in older patients

**Data source**: RPBS (entitlement not specified), DVA: Health services, Hospitalisations

**Study period (duration)**: 2001–2012 (12 years)

**Primary outcome measure**: Prevalence of prescription analgesics, hypnotics and muscle relaxants 1-year period prior to joint replacement

**Caughey, 2017** ([28])

**Study aim**: Identify factors associated with re-hospitalised within 30 days of discharge among older Australians admitted to hospital with diabetes

**Data source**: RPBS (full entitlement), DVA: Health services, Hospitalisations

**Study period (duration)**: 2011–2013 (2 years and 1 month)

**Primary outcome measure**: Causes of re-hospitalisation

**Gillam, 2017** ([46])

**Study aim**: Compare the risk of heart failure in patients with conventional metal-on-metal or metal-on-polyethylene total hip arthroplasty

**Data source**: RPBS (full entitlement), DVA: Health services, Hospitalisations

**Study period (duration)**: 2003–2014 (11 years and 6 months)

**Primary outcome measure**: Incidence of hospitalisation within 30 days of discharge

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### Exposure and Outcomes (Medicine use and outcomes)

#### Claims-level (4 studies)

**Blanch, 2014** ([17])

**Study aim**: Trends in opioid use, costs and outcomes

**Data source**: PBS Online, NHMD, ABS Cause of Death

**Study period (duration)**: 1992–2012 (21 years)

**Primary outcome measure**: No. prescriptions and costs by drug by year

**Hollingworth, 2015** ([63])

**Study aim**: Pattern of reported adverse events for dopamine agonists

**Data source**: Not specified, DAEN

**Study period (duration)**: 1992–2012 (21 years)

**Primary outcome measure**: No. accidental deaths related to illicit drugs and pharmaceutical opioids by year

**Huang, 2015** ([68])

**Study aim**: Evaluate reports and incidence of lactic acidosis cases associated with metformin

**Data source**: PBS Online, DAEN

**Study period (duration)**: 1997–2011 (15 years)

**Primary outcome measure**: Estimated incidence of metformin-associated lactic acidosis

**Jamolowicz, 2015** ([81])

**Study aim**: Association between statin use and memory-related adverse events

**Data source**: PBS Online, DAEN

**Study period (duration)**: 1992–2013 (21 Years and 4 months)

**Primary outcome measure**: No. and incidence rate of memory-related adverse events by drug and type of adverse event

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#### Individual-level (29 studies)

#### Linked (21 studies)

**Ahmed, 2018** ([2])

**Study aim**: Association between 1st trimester exposure to renin-angiotensin system blockers and maternal and perinatal outcomes among women with chronic hypertension

**Data source**: PBS ad hoc extracts (concession, NSW only), ADPC, PDC

**Study period (duration)**: 2005–2012 (8 years)

**Primary outcome measure**: % hypertensive pregnant women exposed to renin-angiotensin system blockers with a record of preterm delivery, caesarean section, baby low birth weight, small for gestational age and Apgar score <7

**Daniels, 2018** ([32])

**Study aim**: Real-world treatment patterns and overall survival for women receiving trastuzumab for metastatic breast cancer compared with results of clinical trials

**Data source**: PBS ad hoc extracts, Herceptin Program

**Study period (duration)**: 2001–2016 (15 years and 6 months)

**Primary outcome measure**: Time on trastuzumab and overall survival from initiation

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**Continued**
| First author, year of publication | Study aim | Data source | Study period (duration) | Primary outcome measure |
|-------------------------------|-----------|-------------|------------------------|-------------------------|
| Daniels, 2018 [33]           | Real-world treatment patterns and overall survival for women surviving five or more years from initiation of trastuzumab for HER2-positive metastatic breast cancer | PBS ad hoc extracts Herceptin Program | 2001–2016 (15 years and 6 months) | % of women initiating trastuzumab surviving ≥ 5 years and conditional probability of surviving an additional 5 years | Time on trastuzumab and other HER2-targeted therapies |
|                               |           |             |                        | Frequency and duration of breaks from trastuzumab and other HER2-targeted therapies | Overall survival from initiation of trastuzumab for metastatic breast cancer |
|                               |           |             |                        | Time from cessation of trastuzumab for early breast cancer until initiation of trastuzumab for metastatic cancer | Duration of trastuzumab in the metastatic setting |
| Daniels, 2018 [31]           | Survival outcomes for patients using (neo)adjuvant trastuzumab who relapse (early breast cancer) and then receive trastuzumab for metastatic breast cancer | PBS ad hoc extracts Herceptin Program | 2001–2014 (13 years and 3 months) |  |  |
| Lai, 2018 [101]              | Risk of gastrointestinal hospitalisation with loxoprofen and mefenamic acid use compared with other nonsteroidal anti-inflammatory use in Asia-Pacific populations | RPBS (entitlement not specified) Other international hospital databases | 2001–2012 (12 years) | No. and incidence of gastrointestinal hospitalization/1,000 person-years in Japan, Taiwan, Korea, Hong Kong and Australia |  |
| Qin, 2018 [142]              | Association between renin-angiotensin system inhibitors and β-blockers dispensed to patients within 60 days post-heart failure hospital discharge and improved 1-year survival | PBS ad hoc extracts (concession, WA only) HMDC Mortality registry | 1983–2011 (28 years and 6 months) | Time from hospital discharge and 60 days later to all-cause mortality censored at 1 year of follow-up | Time to rehospitalisation Composite of all-cause mortality or re-hospitalisation, whichever occurred first |
| Roughead, 2017 [152]         | Assess whether antipsychotic use is a contributing factor in the association between post-traumatic stress disorder and dementia | RPBS (entitlement not specified) DVA: Health services, Hospitalisations | 2001–2014 (13 years and 6 months) | Annual median DDD/person | No. (%) people with dementia |
| Leach, 2017 [109]            | Risk of hip fracture in older people following concurrent use of psychoactive medicines | RPBS (full entitlement) DVA: Health services, Hospitalisations | 2008–2012 (5 years) | Risk of hip fracture associated with each of the individual medicine | Risk of hip fracture as a result of concurrent use of two medicines |
| Leach, 2017 [108]            | Risk of hip fracture due to mirtazapine, and the use of other antidepressants in combination with mirtazapine | RPBS (entitlement not specified) DVA: Health services, Hospitalisations | 2008–2012 (5 years) | Risk of hip fracture due to use of antidepressants alone | Risk of hip fracture due to mirtazapine in combination with other antidepressants |
| Kalisch Ellett, 2016 [88]    | Risk of hospitalisation in older people associated with concurrent use of psychotropics | RPBS (full entitlement) DVA: Health services, Hospitalisations | 2011–2013 (2 years) | Hospitalisation rates by: cumulative number of DDDs no. of central nervous system medicines used |  |
| Kalisch Ellett, 2016 [86]    | Risk of hospital admission for dehydration or other heat-related illness following initiation of medicines | RPBS (entitlement not specified) DVA: Health services, Hospitalisations | 2000–2013 (13 years and 6 months) | No. persons hospitalised for heat-related illness in the 12 months pre and post initiation of medicine |  |
| Caughey, 2015 [27]           | Prevalence of suboptimal medication related care before hospitalisation of older patients | RPBS (entitlement not specified) DVA: Client file, Health services, Hospitalisations | 2007–2012 (5 years) | % and no. of hospitalisations preceded by suboptimal medication-related care by problem/disease state | Odds of hip fracture after psychoactive drug exposure (in intermittent users vs intermittent non-users) by class and individual medicine |
| Leach, 2015 [107]            | Association between psychoactive medicine use and hip fracture in the elderly | RPBS (entitlement not specified) DVA: Health services, Hospitalisations | 2008–2012 (5 years) |  |  |
| Pratt, 2015 [137]            | Association between initiation of ophthalmic timolol and risk of hospitalisation for bradycardia | RPBS (full entitlement) DVA: Health services, Hospitalisations | 2002–2009 (7 years) | Incidence of hospitalisation for bradycardia after 1-30, 31-180 and >180 days of timolol initiation |  |

Continued
| First author, year of publication | Study aim | Data source | Study period (duration) | Primary outcome measure |
|----------------------------------|-----------|-------------|-------------------------|-------------------------|
| Price, 2015 [141]                | Impact of level of GP care on unplanned hospitalisations due to potentially inappropriate prescribing in the elderly | PBS ad hoc extracts (WA only) MBS Aged care Electoral roll | 1993–2005 (13 years) | Odds of unplanned hospitalisation following potentially inappropriate medicine exposure (Beers criteria) by level of GP coverage (<6m, 6-8m, 8-10m, >10m) and medicine (all and individual high-risk) |
| Kalisch Ellett, 2014 [87]       | Association between multiple anticholinergic medication use and risk of hospitalisation for confusion with dementia | RPBS (full entitlement) DVA: Hospitalisations | 2009–2012 (3 years) | Cumulative anticholinergic medicine use Risk of hospitalisation for confusion or dementia |
| Pratt, 2014 [138]               | Association between ranibizumab use and risk of hospitalisation for ischaemic stroke and myocardial infarction | RPBS (full entitlement) DVA: Hospitalisations | 2006–2013 (6 years and 7 months) | Risk of hospitalisation for ischaemic stroke and myocardial infarction |
| Price, 2014 [140]               | Evaluate if potentially inappropriate medications are predictors of adverse events | PBS ad hoc extracts (WA only) MBS Aged care Electoral roll | 1993–2005 (13 years) | Risk of index unplanned hospitalisation by drug class, 'dose' over 3 months |
| Leach, 2013 [106]               | Medicine use associated with falls or hip fracture before hip fracture and whether medicine use changed after hip fracture | RPBS (full entitlement) DVA: Hospitalisations MBS Electoral roll | 2009 (12 months) | Use of medicines associated with greater risk of falls and hip fracture prior to hip fracture % change in medicine use after hospitalisation for hip fracture |
| Ramsay, 2013 [145]             | Association between proton pump inhibitor use and hospitalisation | RPBS (full entitlement) DVA: Hospitalisations | 2007–2011 (4 years and 6 months) | Risk of hospitalisation for pneumonia |
| Ecological (3 studies)          | Trends in heroin and pharmaceutical opioid overdose deaths | DUSC National Coronial Information System ABS | 2001–2012 (12 years) | Annual rate of (heroin) overdose deaths per million persons by age, gender and intent |
| Buckley, 2015 [23]             | Association between in hospital mortality and morbidity and self-poisoning with different drug classes over an extended period | Not specified (ASM) Hunter Area Toxicology Service | 1991–2011 (21 years) | Hospital length of stay, types of drugs ingested, intensive care unit admission, requirement for ventilation, in hospital Deaths (per 1000) Rates of antidepressant drug use (DDD/1000 pop/day) |
| Roughhead, 2015 [149]          | Comparative risk of heart failure and oedema associated with thiazolidinediones across six countries | RPBS (entitlement not specified) DUSC Other international dispensing or hospital databases | 2005–2010 (6 years) | Risk (adjusted sequence ratio) of oedema (i.e. incident furosemide dispensing) or incident heart failure hospitalisation after incident rosiglitazone, pioglitazone or metformin dispensing, by country and ethnic group |
| Only dispensing claims, using medicine as a proxy of outcome (5 studies) | Risk of people on medication for schizophrenia developing different components of the metabolic syndrome and their life expectancy compared with people without schizophrenia | PBS 10% sample | 2006–2015 (10 years) | Time taken from first prescription of schizophrenia treatment to the first prescription for the treatment of comorbidities Median life expectancy |
| Kumar, 2018 [100]             | Factors that predict the need for add-on therapy in patients with type II diabetes in the community | PBS 10% sample (concession) | 2006–2014 (7 years and 9 months) | Median time (years) to add-on therapy in adherent and non-adherent patients |
| Ng, 2018 [120]                | Compare how frequently selected chronic diseases developed in women with breast cancer receiving endocrine therapy, and in women without cancer. | PBS 10% sample (concession) | 2003–2014 (12 years) | Ten-year incidence rates for comorbidities, identified with the RxRisk-V model |
| First author, year of publication | Study aim | Data source | Study period (duration) | Primary outcome measure |
|----------------------------------|-----------|-------------|-------------------------|------------------------|
| Ng, 2018 [119]                   | Patterns of comorbidities among men with prostate cancer treated with androgen deprivation therapy | PBS 10% sample (concession) | 2003–2014 (12 years) | Risk of comorbidities dispensings over time |
| Roughead, 2016 [148]            | Association between proton pump inhibitor use and *Clostridium difficile* infections across multiple countries | PBS ad hoc extracts, RPBS (entitlement not specified), Other international dispensing databases | 2001–2013 (13 years) | No. (%) people dispensed oral vancomycin as a proxy for *Clostridium difficile* infection |

Note: ABS = Australian Bureau of Statistics, ASM = Australian Statistics on Medicines, ADPC = Admitted Patients Data Collection, DAEN = Database of Adverse Event Notifications, DDD = Defined Daily Dose, DUSC = Drug Utilisation Sub-Committee, DVA = Department of Veterans’ Affairs, GP = General Practitioner, MBS = Medicare Benefits Schedule, NHMD = National Hospital Morbidity Database, NSW = New South Wales, OME = Oral Morphine Equivalent, PBS = Pharmaceutical Benefits Scheme, PDC = Perinatal Data Collection, RPBS = Repatriation Pharmaceutical Benefits Scheme, WA = Western Australia.
## Supplementary Appendix D: Continued

### Methods

#### Claims-level (1 study)

**Huang, 2018**

Validate use of a large HIV-positive cohort compared to the PBS 10% sample Sample for surveillance and monitoring purposes

| First author, year of publication | Study aim | Data source | Study period (duration) | Primary outcome measure |
|-----------------------------------|-----------|-------------|-------------------------|------------------------|
| Huang, 2018 [67]                  | Validate use of a large HIV-positive cohort compared to the PBS 10% sample Sample for surveillance and monitoring purposes | PBS 10% sample Australian HIV Observational Database | 2013–2016 (2 years and 9 months) | Distribution of patient demographics, state/territory of residence, and HIV treatment (% use) data in both datasets per year |

#### Individual-level (18 studies)

**Arnet, 2018**

Operationalise and validate new method of adherence, the daily polypharmacy possession ratio compared with medication possession ratio

| First author, year of publication | Study aim | Data source | Study period (duration) | Primary outcome measure |
|-----------------------------------|-----------|-------------|-------------------------|------------------------|
| Arnet, 2018 [4]                   | Operationalise and validate new method of adherence, the daily polypharmacy possession ratio compared with medication possession ratio | PBS ad hoc extracts (concession, WA only) | 2002–2011 (9 years) | Mean adherence values using daily polypharmacy possession ratio and medication possession ratio |

**Hoang, 2018**

Assess the use of supervised machine learning as a signal detection tool for adverse drug reactions

| First author, year of publication | Study aim | Data source | Study period (duration) | Primary outcome measure |
|-----------------------------------|-----------|-------------|-------------------------|------------------------|
| Hoang, 2018 [60]                  | Assess the use of supervised machine learning as a signal detection tool for adverse drug reactions | PBS 10% sample Other data | 2012–2016 (4 years and 6 months) | Performance measures of model: sensitivity, specificity, positive and negative predictive values and area under the receiver operating characteristic curve |

**Langton, 2018 [103]**

Demonstrate the value-add of cross-jurisdictional data and the factors associated with healthcare use towards the end of life

| First author, year of publication | Study aim | Data source | Study period (duration) | Primary outcome measure |
|-----------------------------------|-----------|-------------|-------------------------|------------------------|
| Langton, 2018 [103]               | Demonstrate the value-add of cross-jurisdictional data and the factors associated with healthcare use towards the end of life | RPBS (full entitlement, National and NSW) DVA: Health services, Hospitalisations, Aged care NSW: RBDM, CCR, APDC, EDDC | 2005–2007 (2 years and 6 months) | Associations between cohort characteristics and ≥3 hospitalisations/≥3 emergency department presentations during the last six months of life in the population cohort and DVA cohort |

**Pratt, 2018**

Map ATC Classification System codes to individual Rx-Risk comorbidities and validate the Rx-Risk Comorbidity Index.

| First author, year of publication | Study aim | Data source | Study period (duration) | Primary outcome measure |
|-----------------------------------|-----------|-------------|-------------------------|------------------------|
| Pratt, 2018 [134]                 | Map ATC Classification System codes to individual Rx-Risk comorbidities and validate the Rx-Risk Comorbidity Index. | RPBS (full entitlements), PBS 10% sample DVA: Health services, Hospitalisations | 2013–2015 (2 years and 6 months) | Mortality after 1-year |

**Roper, 2018**

Develop an algorithm and validate it to resolve disparity between the evidence of pharmacotherapy utilisation for smoking cessation and the recording of smoking in pregnancy

| First author, year of publication | Study aim | Data source | Study period (duration) | Primary outcome measure |
|-----------------------------------|-----------|-------------|-------------------------|------------------------|
| Roper, 2018 [147]                 | Develop an algorithm and validate it to resolve disparity between the evidence of pharmacotherapy utilisation for smoking cessation and the recording of smoking in pregnancy | PBS ad hoc extracts (WA, NSW only) | 2003–2012 (10 years) | No. of women dispensed smoking cessation therapy identified by the algorithm |

**Zhan, 2018**

Develop and validate a data-driven method to automatically detect potential adverse drug events from prescription data

| First author, year of publication | Study aim | Data source | Study period (duration) | Primary outcome measure |
|-----------------------------------|-----------|-------------|-------------------------|------------------------|
| Zhan, 2018 [180]                  | Develop and validate a data-driven method to automatically detect potential adverse drug events from prescription data | PBS ad hoc extracts Other data | 2013 – 2014 (2 years) | Prevalence of smoking cessation pharmacotherapy utilisation Estimated frequency and proportion (%) of adverse drug events (validated, suspected and false) Sensitivity, specificity, positive and negative predictive value |

**Tran, 2017**

Present the data cleaning and preparation process for a large-scale linkage study

| First author, year of publication | Study aim | Data source | Study period (duration) | Primary outcome measure |
|-----------------------------------|-----------|-------------|-------------------------|------------------------|
| Tran, 2017 [172]                  | Present the data cleaning and preparation process for a large-scale linkage study | PBS ad hoc extracts (WA, NSW only) | 2002 – 2014 (13 years) | No. of records and persons in each dataset No. and type of corrections made No. of duplicates, excluded persons and likely false positives |

**Inacio, 2016**

Evaluate the predictive ability of co-morbidity measures in total hip arthroplasty and total knee arthroplasty patients

| First author, year of publication | Study aim | Data source | Study period (duration) | Primary outcome measure |
|-----------------------------------|-----------|-------------|-------------------------|------------------------|
| Inacio, 2016 [74]                 | Evaluate the predictive ability of co-morbidity measures in total hip arthroplasty and total knee arthroplasty patients | RPBS (entitlement not specified) DVA: Health services, Hospitalisations | 2001–2013 (13 years) | Prevalence of medication use after total hip arthroplasty surgery % revisions within one and five years |

**Inacio, 2016**

Evaluate the predictive ability of co-morbidity measures in total hip arthroplasty and total knee arthroplasty patients

| First author, year of publication | Study aim | Data source | Study period (duration) | Primary outcome measure |
|-----------------------------------|-----------|-------------|-------------------------|------------------------|
| Inacio, 2016 [76]                 | Evaluate the predictive ability of co-morbidity measures in total hip arthroplasty and total knee arthroplasty patients | RPBS (entitlement) DVA: Health services, Hospitalisations | 2000–2013 (14 years) | Mortality rates within 90 days and 1 year of the surgery Model discrimination ability (c statistic) and calibration ( Hosmer and Lemeshow Goodness of Fit) |

**Wahab, 2016**

Assess the utility of sequence symmetry analysis as a signal detection tool for detecting adverse event signals

| First author, year of publication | Study aim | Data source | Study period (duration) | Primary outcome measure |
|-----------------------------------|-----------|-------------|-------------------------|------------------------|
| Wahab, 2016 [177]                 | Assess the utility of sequence symmetry analysis as a signal detection tool for detecting adverse event signals | RPBS (entitlement not specified) DVA: Health services, Hospitalisations | 2002–2011 (10 years) | No. (%) with heart failure No. (%) using medicines used to treat adverse events |

**Blanch, 2015**

Effect of look-back period length on new user misclassification

| First author, year of publication | Study aim | Data source | Study period (duration) | Primary outcome measure |
|-----------------------------------|-----------|-------------|-------------------------|------------------------|
| Blanch, 2015 [14]                 | Effect of look-back period length on new user misclassification | PBS 10% sample (concession) | 2005–2014 (9 years) | % of persons misclassified as new users of therapy based on 10 different look-back periods (range 1 m–7 y) Cumulative infection incidence by type of arthroplasty and no. of comorbidities Association between the number of comorbidities and infection within 90 days of surgery |

**Inacio, 2015**

Compare the ability of three comorbidity indices to predict infection after total joint arthroplasty.

| First author, year of publication | Study aim | Data source | Study period (duration) | Primary outcome measure |
|-----------------------------------|-----------|-------------|-------------------------|------------------------|
| Inacio, 2015 [73]                 | Compare the ability of three comorbidity indices to predict infection after total joint arthroplasty. | RPBS (full entitlement) DVA: Hospitalisations | 2000 – 2012 (13 years) | Prevalence of smoking cessation pharmacotherapy utilisation Estimated frequency and proportion (%) of adverse drug events (validated, suspected and false) Sensitivity, specificity, positive and negative predictive value |
### Supplementary Appendix D: Continued

| First author, year of publication | Study aim | Data source | Study period (duration) | Primary outcome measure |
|----------------------------------|-----------|-------------|-------------------------|-------------------------|
| Inacio, 2015 [71]               | Compare ability of RxRisk-V, and two other comorbidity indices to predict post-operative revision in joint arthroplasty | RPBS (entitlement not specified) DVA: Hospitalisations | 2000 – 2012 (13 years) | Association between number of comorbidities and post-operative revision 1 and 5 years following total hip or knee arthroplasty |
| Inacio, 2015 [72]               | Compare the prevalence and identity of comorbidities identified using three comorbidity indices | RPBS (full entitlement) DVA: Hospitalisations | 2000–2012 (13 years) | Prevalence of comorbidities, overall and by individual conditions, for each metric and type of arthroplasty Agreement between metrics by comorbidity and type of arthroplasty |
| Nguyen, 2015 [121]             | Assess whether linking pharmaceutical and hospital data can identify medicines associated with drug-induced hospitalisations | RPBS (full entitlement) DVA: Hospitalisations | 2005 – 2012 (7 years and 6 months) | No. (%) of admissions for drug-induced liver toxicity with: causative medicines or medicine classes recorded causative medicines matched to outpatient dispensings other potentially contributory outpatient medicine dispensings |
| Mellish, 2015 [113]            | Overview and guide for researchers using PBS data | PBS Online (Section 85 DoS & DoP, ASM), DUSC | 1998 – 2014 (16 years) | No. of dispensings by month/year of select medicines by date of supply vs processing and script type No. of dispensings, DDD/1000 pop/day and cost to government for psychotropics Temporal association (adjusted sequence ratio) between amiodarone or allopurinol initiation and subsequent thyroxine initiation, by country |
| Pratt, 2015 [131]              | Cross-country consistency of prescription sequence symmetry analysis in assessing the temporal association between medicine dispensings and adverse drug events | RPBS (entitlement not specified) Other international dispensing data | 2001 – 2012 (12 years) | Reported: No. of dispensings by medicine type and type of breast cancer No. persons receiving treatment Intended: Duration of therapy and survival outcomes Extent of resource use of each service type by patient demographics and treatment setting |
| Daniels, 2017 [34]             | Protocol of a programme of work that will provide evidence of prescribing patterns, safety monitoring and outcomes of patients with breast cancer treated with HER2-targeted therapies | PBS ad hoc extracts MBS Herceptin Program | 2001–2014 (13 years and 4 months) | Reported: No. of dispensings by medicine type and type of breast cancer No. persons receiving treatment Intended: Duration of therapy and survival outcomes Extent of resource use of each service type by patient demographics and treatment setting |
| Seaman, 2017 [161]             | Protocol for a whole-of-population study that will evaluate health outcomes and health service utilisation after the consumer co-payment changes | PBS ad hoc extracts (WA Only) MBS HMDC Mortality data | 2000–2010 (11 years) | Reported: No. of dispensings and persons dispensed statins Intended: Risk of hospitalisation, death for each statin group (continuing, reduced, ceased) Health service utilisation, additional medicines, clinical and demographic characteristics for each statin group (continuing, reduced, ceased) |
| Qin, 2016 [143]                | Protocol of a study that will evaluate trends in dispensing of heart failure medicine use, and outcomes following hospitalisation for heart failure | PBS ad hoc extracts (concession, WA only) HMDC Death registry | 2002 – 2014 (12 years and 6 months) | Reported: No. of persons included in the study cohort Intended: Adherence, persistence |
| Langton, 2015 [105]            | Protocol of program that will examine resource use, costs and quality of end-of-life cancer care. | RPBS (full entitlement, NSW only) DVA, Health services, Hospitalisations, Aged care NSW: APDC, EDDC, RBDM, CCR ABS | 1994 – 2009 (16 years) | Reported: Cohort characteristics (No., %) Intended: Resource use (%) and costs ($AUD per decadent) in 6 months end of life |
| First author, year of publication | Study aim | Data source | Study period (duration) | Primary outcome measure |
|----------------------------------|-----------|-------------|-------------------------|-------------------------|
| Gunnell, 2014 [51]               | Protocol of a study that will investigate trends dispensing of medicines for secondary prevention of cardiovascular events | PBS ad hoc extracts (NSW only)  
PBS Online (concession)  
NSW: APDC, EDDC, RBDM, MBS | 1980–2013 (34 years) | Reported: No. of persons in the cohort after linkage and number of records in each data set  
Annual concessional dispensings counts by drug and state  
Intended: dispensed drug trends, drug adherence, all-cause/cardiovascular events, cost-effectiveness of these long-term therapies and the impact of adherence |
| Pearson, 2014 [129]             | Protocol of study that will examine the use and impact of cancer medicines in elderly cancer patients | RPBS (any entitlement, NSW only)  
DVA: Health service, Hospitalisations, Aged care  
NSW: APDC, EDDC, RBDM, CCR, ABS | 2004 – 2012 (19 years) | Reported: Patient demographics, most common medicine, cancer treatments and No. of health service use over a 1-year period  
Intended: Patterns of use of cancer medicines, treatments, and health services prior to diagnosis by patient characteristics  
Predictors and risk of health outcomes by medicine |

Note: ABS = Australian Bureau of Statistics, AIC = Akaike information criterion, ASM = Australian Statistics on Medicines, APDC = Admitted Patients Data Collection, CCR = Central Cancer Registry, DDD = Defined Daily Dose, DoP = Date of Processing, DoS = Date of Supply, DUSC = Drug Utilisation Sub-Committee, DVA = Department of Veterans' Affairs, EDDC = Emergency Department Data Collection, HMDC = Hospital Morbidity Data Collection, MBS = Medicare Benefits Schedule, NSW = New South Wales, PBS = Pharmaceutical Benefits Scheme, RBDM = Registry of Births, Deaths, and Marriages, RPBS = Repatriation Pharmaceutical Benefits Scheme, WA = Western Australia.