

The Medicines Intelligence Centre of Research Excellence: Co-creating real-world evidence to support the evidentiary needs of Australian medicines regulators and payers

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Abstract

Regulators and payers play a pivotal role in facilitating timely and affordable access to safe and efficacious medicines. They use evidence generated from randomised clinical trials (RCTs) to support decisions to register and subsidise medicines. However, at the time of registration and subsidy approval, regulators and payers face uncertainty about how RCT outcomes will translate to real-world clinical practice. In response to this situation, medicines policy agencies worldwide have endorsed the use of real-world data (RWD) to derive novel insights on the use and outcomes of prescribed medicines. Recent reforms around data availability and use in Australia are creating unparalleled data access and opportunities for Australian researchers to undertake large-scale research to generate evidence on the safety and effectiveness of medicines in the real world. Highlighting the critical importance of research in this area, Quality Use of Medicines and Medicine Safety was announced as Australia's 10th National Health Priority in 2019. The National Health and Medical Research Council, Medicines Intelligence Centre of Research Excellence (MI-CRE) has been formed to take advantage of the renewed focus on quality use of medicines and the changing data landscape in Australia. It will generate timely research supporting the evidentiary needs of Australian medicines regulators and payers by accelerating the development and translation of real-world evidence on medicines use and outcomes. MI-CRE is developing a coordinated approach to identify, triage and respond to priority questions where there are significant uncertainties about medicines use, (cost)-effectiveness, and/or safety and creating a data ecosystem that will streamline access to Australian data to enable researchers to generate robust evidence in a timely manner. This paper outlines how MI-CRE will partner with policy makers, clinicians, and consumer advocates to leverage real-world data to co-create real-world evidence, to improve quality use of medicines and reduce medicine-related harm.

Keywords

MI-CRE; quality use of medicines; real world evidence; pharmacovigilance; safety; health policy; knowledge translation; partnership

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Introduction

Prescribing medicines is the most common health intervention worldwide [1]. When used appropriately, medicines offer significant benefits. However, sub-optimal use can lead to significant misadventure and harm [2]. Medicine overuse and misuse results in adverse health outcomes for individuals and populations, and wastes valuable health resources [2].

Medicine regulators and payers play a fundamental role in facilitating timely and affordable access to safe and efficacious medicines. They also monitor the quality use, benefits and safety of medicines once approved for use in the community. Randomised clinical trials (RCTs) are the cornerstone of the evidence base used to support considerations for registration and public subsidy [3, 4]. However, RCTs commonly focus on single medicines and do not necessarily reflect routine practice or typical patients due to their strict inclusion criteria and intensive patient monitoring. RCTs also exclude people with comorbid disease who take multiple medicines and those with complex treatment regimens [5, 6] and due to limited sample sizes are often unable to quantify all possible safety concerns, particularly rare outcomes [5, 6]. Subsequently, at the time of approval, decision-makers face significant uncertainty about whether purported RCT outcomes will translate into real-world settings. As such, there is critical need for comprehensive, fit-for-purpose approaches to generate evidence about medicine use, benefits, and harms outside clinical trial conditions.

Regulators and payers have different evidentiary needs when monitoring the quality use and safety of medicines once they are widely available in the community [7, 8]. Surveillance of medicines quality, safety, and efficacy forms the remit of medicines regulators, whereas payers are interested in patterns of medicine use and costs plus real-world comparative (cost) effectiveness. Regulators have traditionally relied on voluntary adverse event reports from doctors, patients, and manufacturers to identify safety concerns. Quantifying risk across different population sub-groups, however, requires measurement of incidence and strength of association between medicine exposures and outcomes, which is not possible through adverse event reporting alone [3, 4]. In contrast, payers have tracked medicine use and costs using claims data, a by-product of payments to pharmacies for dispensing subsidised medicines [9]. These analyses generally use descriptive approaches to monitor medicine use and costs, but rarely quantify benefits, harms, or other health-system impacts associated with decisions to list or change the conditions under which a medicine is subsidised.

While these traditional approaches remain an important part of the surveillance toolkit for regulators and payers, medicines policy agencies worldwide have endorsed the use of real-world data (RWD) to derive novel insights on the use and outcomes of prescribed medicines [10, 11]. Real-world data [12] allows real-world evidence (RWE) to be generated for all patient populations, including those excluded from clinical trials, and to study the effects and outcomes of medicines in everyday clinical use – precisely the type of evidence missing from clinical trials of single medicines.

The exponential growth and availability of health data has created new opportunities to improve the efficiency and sophistication of RWE generation. Regulatory agencies worldwide – including the US Food and Drug Administration

(FDA) [13], the Canadian Agency for Drugs and Technology in Health (CADTH) [14] and the European Medicines Agency (EMA) [15] – have partnered with academics, health providers, and payers to establish active surveillance systems generating timely RWE about medicine use and harm. Examples of these government-academic partnerships include the US Sentinel Initiative [16] and the Canadian Network of Observational Studies (CNODES) [17]; these partnerships have already delivered high-quality evidence informing medicines policy decisions across the globe [18–22].

Australia's medicines policy landscape

In Australia, the medicines regulator, the Therapeutic Goods Administration (TGA), and national payer, the Pharmaceutical Benefits Advisory Committee (PBAC), play pivotal roles in the quality use and safety of medicines. They facilitate timely and affordable access to safe and efficacious medicines; promote medicines use based on strict evidentiary requirements; and monitor harms once medicines are widely available in the community. They work closely with other policy agencies, health professional societies, not-for-profit organisations, consumer organisations, and the pharmaceutical industry to communicate emerging evidence to prescribers and the general public about medicine harm; they also provide reassurance about medicine safety, effectiveness, and cost-effectiveness.

It is estimated that more than 35% of the Australian population are taking at least one prescribed medicine daily and almost 10% are taking five or more daily [23]. In Australians aged 65 years and over approximately 20–30% of hospital admissions are medicine-related [24], which has been estimated to cost more than \$1.4 billion between 2016–17 [25]. In the past decade, drug-induced deaths in Australia were far more likely to be due to prescription medicines than illicit drugs, and there has been a substantial rise in deaths where prescription medicines were implicated [26]. Yet the true toll of medicine-related harm among Australians is likely to be far greater than these estimates, as many drug-induced events are attributed to underlying conditions and other causes [27].

Highlighting the urgent need to curtail this significant health and system burden, the Australian Government announced Quality Use of Medicines and Medicine Safety as Australia's 10th National Health Priority in 2019 [24, 28]. This 'call to action' shines the spotlight on Australia's National Medicines Policy and Quality Use of Medicines framework [29], emphasising the importance of evidence-informed decisions by individual patients, treating clinicians, and policy agencies whose decisions impact the health of the entire population.

Australia has a federated, universal health system, where the federal (Commonwealth) or State and Territory governments are responsible for the delivery of specific aspects of care. Due to its funding structure, the Australian health system has accumulated some of the most comprehensive, population-wide real-world health and social data globally. However, Australia's federated health system also means these data are under the custodianship of different agencies and held across different jurisdictional boundaries. To undertake pharmacoepidemiologic research on medicine use and outcomes, medicines exposure data held by the Commonwealth must be linked with outcomes data, such as hospitalisations, held by the States and Territories [30]. This

has traditionally been a significant barrier to generating timely and contemporary research output [31–33]. However, recent reforms around data availability and use are paving the way for population-based, public health data to be combined on a scale never before seen in Australia [34–36]. This provides opportunities for researchers to partner with policymakers, clinicians and consumers to ensure these data are analysed in much more nuanced and intelligent ways to improve health outcomes for all Australians.

It is imperative that the impact of health system-specific drivers such as population characteristics, prescribing practices, and policies form part of RWE generation. Historically, a coordinated approach to address these important issues has been lacking in Australia. The Medicines Intelligence Centre of Research Excellence (MI-CRE) was formed to spearhead this activity. MI-CRE is a research program funded by the Australian National Health and Medical Research Council (2020–2025). It is a partnership between government and an inter-disciplinary team of pharmacoepidemiologists and medicines safety researchers from nine universities across five Australian states. Modelled on mature government-academic partnerships [17, 22], MI-CRE builds on many of the existing international collaborative efforts to support the real-world evidentiary requirements of *both* regulators and payers.

MI-CRE's approach

MI-CRE was established to respond to the evidentiary needs of medicines policy makers by simultaneously: (i) generating timely RWE about medicine use and outcomes by creating an enabling data infrastructure; (ii) identifying, triaging and responding to priority questions and breaking down barriers to research translation by fostering engagement with policy makers and other end-users; and (iii) equipping the next generation of medicines researchers in Australia with the skills to co-create evidence with 'medicines intelligence' end-users. Here we describe MI-CRE's implementation approach and achievements to date, with MI-CRE currently in its second year of operation.

Generating timely real-world evidence

To enable timely generation of evidence about medicine use and outcomes, MI-CRE is creating a data ecosystem with the capability of responding rapidly to a comprehensive range of complex questions from evidence end-users. Specifically, we are creating a data ecosystem that comprises several linked data platforms with streamlined data access arrangements coupled with a repository of reproducible analytic code to clean data, create project-specific cohorts, fast-track feasibility queries, and address research questions. MI-CRE researchers will leverage the data and tools available in this ecosystem to generate reliable and timely answers to questions raised by medicines regulators and payers.

The data platforms that will be included in the MI-CRE data ecosystem will contain regularly updated medicines exposure data, linked at the person level with outcomes data (such as death records and hospitalisations). New and existing data platforms will be included, some of which are being

purpose-built for MI-CRE. These data platforms have been selected to support whole-of population medicines research across the entire life course. They relate to populations defined by jurisdiction (e.g., residents of New South Wales and Western Australia), service use (e.g., people dispensed opioids or other drugs of dependence, clients of the Department of Veterans' Affairs), and health events (e.g., women who gave birth, people with cancer, or people who experienced poisonings or substance misuse). A comprehensive review of Australian data collections that can be leveraged for whole-of-population medicines use and outcome studies is detailed in our recently published review [30] Table 1 also describes two of the key data platforms that will underpin MI-CRE's evidence generation. These platforms were funded by a Research Infrastructure Grant from MI-CRE's lead institution and were developed to generate evidence and drive improvements in the health and wellbeing across the life course.

Most of the data platforms MI-CRE will utilise have been established as 'programmatic' data linkages in that they are approved by Human Research Ethics Committees (HRECs) and data custodians for use in a wide range of studies within a specified theme or research program. Depending on the scope of the original HREC approval and the governance arrangements in place, individual studies leveraging these data can be undertaken without further approvals, or by submitting a brief study protocol to the primary HREC as an amendment to the original ethics application; meaning studies can be approved and commenced in a matter of weeks. This approach is in stark contrast to historical data linkages in Australia, which were performed on a project-by-project basis. Each fully defined project required full review by the relevant HREC(s) and data custodians before the linkage process could begin, typically resulting in years of delay between project conception and data delivery.

MI-CRE is employing cloud computing architectures for sensitive large-scale data, to ensure safe and secure access for analyses [37–39] This will support researchers working across different sites to analyse linked data collaboratively, reducing research waste and duplication of effort.

To facilitate the efficient replication of analyses across different jurisdictions, MI-CRE will translate data where feasible into a common data model (CDM) [40, 41] which means that data will be structured in a standardised format and core data elements, such as medicine and diagnosis codes, will use a common internationally recognised standardised vocabulary. This will allow MI-CRE researchers to rapidly conduct systematic analyses across disparate data sources using the same underlying structure, eliminating the current extensive duplication in data preparation. CDMs are being established worldwide and the translation of Australian data to these formats will allow us to replicate findings from previous investigations and pool the outcomes of analyses across multiple databases and health jurisdictions, both across Australia and worldwide. MI-CRE researchers have strong links with international data networks that have already established CDMs in their respective jurisdictions, such as the Asian Network of Pharmaco-epidemiology (AsPEN) [42, 43] and the Observational Health Data Sciences and Informatics (OHDSI) collaborative network [41]. The data held by these international networks will be useful to assess queries when the number of people exposed to a medicine in Australia is

Table 1: Characteristics of two key data platforms that will be leveraged for MI-CRE evidence generation

Platform and purpose	Cohort definition (size)	Datasets linked at person-level
Medicines Platform; generate evidence to drive improvements in quality use of medicines and medicines safety in adults.	All Medicare (universal health insurance in Australia) enrolled persons 18 years and over residing in NSW at any time since 2002 (n ≈ 10 million)	Commonwealth: Medicare consumer directory; pharmaceutical dispensings; medical, procedural, and diagnostic services. State (NSW): hospital; emergency department; cancer; mortality; cause of death.
Early Life Course Platform; generate evidence to drive improvements in the health and wellbeing of mothers and children.	All recorded births (stillbirths, live births) in NSW from 2001 along with their mothers and second parents (n ≈ 5.5 million)	Commonwealth: pharmaceutical dispensings; medical, procedural and diagnostic services; income assistance. State (NSW): perinatal; birth notifications; perinatal death reviews; neonatal intensive care unit; congenital condition notifications; hospital; mental health ambulatory care; cancer; controlled drugs; school enrolment; National Assessment Program Literacy and Numeracy (NAPLAN); Australian Early Development Census; mortality; cause of death.

low, or there is insufficient power to undertake fully adjusted analyses using Australian data alone.

Specifically, we plan to convert data to the Observational Medical Outcomes Partnership (OMOP) CDM [41]. This will allow us to make use of open-source software and analytic code that are available through the large community of practice using the OMOP CDM under the auspices of the OHDSI network. Specifically, MI-CRE is developing a toolkit of fit-for-purpose research designs and a suite of best-practice methodologies to investigate real-world medicines use, comparative (cost) effectiveness, and safety. Even where multi-jurisdictional collaboration is not required, these tools will improve the timeliness and efficiency of our evidence generation, as well as enhancing the reliability and reproducibility of data analytics and outputs.

Alignment with policy and consumer needs

A central tenet of MI-CRE is genuine engagement with consumers, communities, and organisations in developing and conducting medicines safety research, disseminating research findings, and translating research into policy and practice. To this end, the MI-CRE governance model has been modelled after an established framework [44] and designed to facilitate intellectual exchange, enhance collaboration and academic outputs, and align research priorities to major national and international medicines policy issues.

MI-CRE governance model

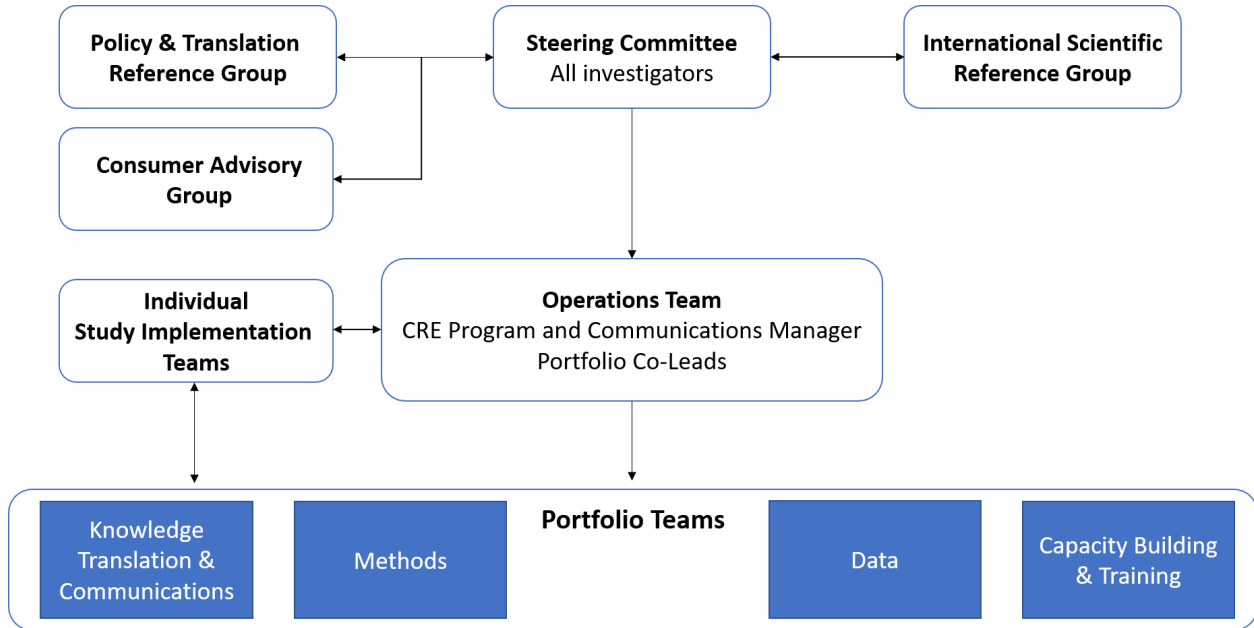
Partnerships generating desired outcomes are underpinned by strong relationships (shared goals) and sound governance [45, 46]. MI-CRE has formalised partnerships by embedding decision makers in its governance structure to facilitate research co-design. This is represented by three key groups: the Policy and Translation Reference Group, the International Scientific Reference Group, and the Consumer Advisory Group (Figure 1). The *Policy and Translation Reference Group* guides strategic direction, provides a sounding board

for new ideas, conceptualises new research projects, and facilitates links with translational partners. Members hold key senior medicines policy roles and are engaged across the research continuum from research priority setting through to knowledge translation. The *International Scientific Reference Group* includes international leaders in pharmacoepidemiology, health services and policy research with formal links and collaborations with medicines policy agencies in Europe, North America and Asia. Additionally, this group acts as a resource from which MI-CRE can seek guidance on specific topics, supports development of state-of-the-art methodology, and provides opportunities for knowledge exchange. The *Consumer Advisory Group* comprises community representatives drawn from peak quality use of medicines committees and advisory groups and provides ongoing strategic advice on how to effectively and sustainably engage with consumers and the community to ensure that all aspects of MI-CRE's work remain relevant to those most impacted by medicines use and policy. Additionally, the *Consumer Advisory Group* will assist in facilitating education and training to MI-CRE researchers on consumer engagement and provide mentorship to new consumer representatives to continually build capacity. Importantly, consumer engagement activities are budgeted, and participants are compensated for their contributions.

All projects conducted within the auspices of MI-CRE establish their own *Study Implementation Team* to provide guidance on project design, interpretation, and dissemination of findings. Members are drawn from MI-CRE's network of expert researchers and key stakeholders, including Chief or Associate Investigators, and/or members of the Reference Groups and Consumer Advisory Group. Each *Study Implementation Team* includes at least one consumer representative from an area relevant to the research.

Underpinning the implementation of MI-CRE, we have established four integrated, cross-cutting portfolios: the Data, Methods, Knowledge Translation and Communications, and Capacity Building and Training portfolios (Table 2). These have been modelled on the successful CNODES structure [17]. The *Methods* and *Data* portfolios support the development

Figure 1: MI-CRE Governance Structure



of fit-for purpose study designs, research-ready ‘big data’ platforms, and cutting-edge analytical methods to increase the timeliness and efficiency of real-world evidence generation. In partnership with medicine regulators, payers, and other key stakeholders, the *Knowledge Translation and Communications* portfolio leads the development of infrastructure to support co-creation of real-world evidence that meets the needs of end-users. Lastly, the *Capacity Building and Training* portfolio provides innovative inter-disciplinary training to foster the next generation of ‘medicines intelligence’ researchers.

MI-CRE operations are coordinated centrally from UNSW Sydney. A *Steering Committee* oversees and prioritises research initiatives, monitors progress, and facilitates training, mentoring, and research exchanges. Membership is comprised of the 20 MI-CRE Chief and Associate Investigators, many of whom sit on a range of key medicines policy committees and have advisory roles in government, including with the PBAC and its sub-committees (payer) as well as the TGA (regulator). Operational activities supporting MI-CRE including communications, secretariat support for the governance groups (*Steering Committee*, *Reference and Advisory Groups*), portfolio leadership, financial allocation, and day-to-day coordination are conducted by the *Operations Team*.

Research – policy pipeline

MI-CRE is collaborating with both the Australian regulator (the TGA) and payer (the PBAC) to co-create a coordinated research program to accelerate the development and translation of evidence about real-world medicine use and outcomes. This research-policy pipeline identifies, triages, and responds to priority questions where there are significant uncertainties about medicines use, (cost)-effectiveness, and/or safety, whilst maintaining the requisite flexibility to support the different evidentiary needs of regulators and payers.

Our pathway for evidence generation expands on a multi-stage approach that was demonstrated to be effective in foundational work preceding the establishment of MI-CRE [47–49]. In our experience, the particular questions posed by medicines policy agencies can be addressed simply through preliminary or descriptive exposure-endpoint feasibility analyses. These are completed in a matter of days or weeks, thereby providing agencies with the evidence they need in a timely manner (first phase). Where required, preliminary findings are followed up by more rigorous, fully controlled analyses (subsequent phase), while still enabling informed decisions to be made during the interim. These analyses are underpinned by the research data infrastructure defined above, and guided by MI-CRE investigators, who have strong track records in generating high-quality, methodologically sound pharmacoepidemiology research [43, 50–56] to support the specific evidentiary needs of regulators and payers.

Although our partnership with policy makers ensures research is relevant to end-users maximising potential for impact [45] MI-CRE is also establishing infrastructure to ensure effective communication of research findings. Leveraging best practice approaches [57], MI-CRE is developing formal structures and activities to promote exchange between researchers, policy makers, health professional groups, and the wider community. Central to this is an annual research symposium and policy forum, which involves MI-CRE investigators, members of the *Policy and Translation Reference Group* and *Consumer Advisory Group*, policy makers, health practitioners, researchers, students, and consumers. Thus far, the meetings have involved a keynote address by an international recognised scientific leader. The meeting also showcases research outputs, identifies priorities for new research, informs participants about the value of research using linked health data, promotes debate on issues arising from the research, and encourages policy responses. The forums serve as vehicles to advocate for enhancements to data resources,

Table 2: MI-CRE portfolios

MI-CRE portfolio's	Goal	Strategy	Assessing value and impact
Data	Develop 'research-ready' data infrastructure leveraging established collections and developing new data linkages	Advocate for and provide strategic leadership on access to and effective use of health data for public benefit	A purpose-built, 'research-ready', enduring big data infrastructure with robust and transparent governance
Methods	Develop a toolkit of fit-for-purpose research designs and a suite of best-practice methodologies for interrogating health data	Develop innovative analytic methodology using fit-for purpose study designs, and cutting-edge analytical methods to increase the timeliness, quality and efficiency of actionable real-world evidence	The use of the shared infrastructure will create efficiencies in data costs, harmonisation of methods and training, transparency and replication of findings
Knowledge Translation	Build effective partnerships with policy makers and other key stakeholders to optimise the utility and timeliness of research findings	Develop Knowledge Translation framework across the life cycle of each project including dissemination and translation plan	A research-policy pipeline that will improve the speed and responsiveness to policy imperatives New knowledge relevant to local and international regulators and payers, translated directly into policy and practice
Capacity Building	Cultivate Australia's 'medicines intelligence' workforce capacity to attract and train new talent and develop research leaders	Leverage MI-CRE investigator experience and stakeholder partnerships to equip the next generation of 'medicine intelligence' researchers with the skills to generate RWE for medicines policymakers	Career opportunity, training and mentorship for highly talented early and mid-career researchers and a suite of training resources for the broader Australian research community

data access and governance, and showcase the research of our early career researchers.

Building workforce capacity

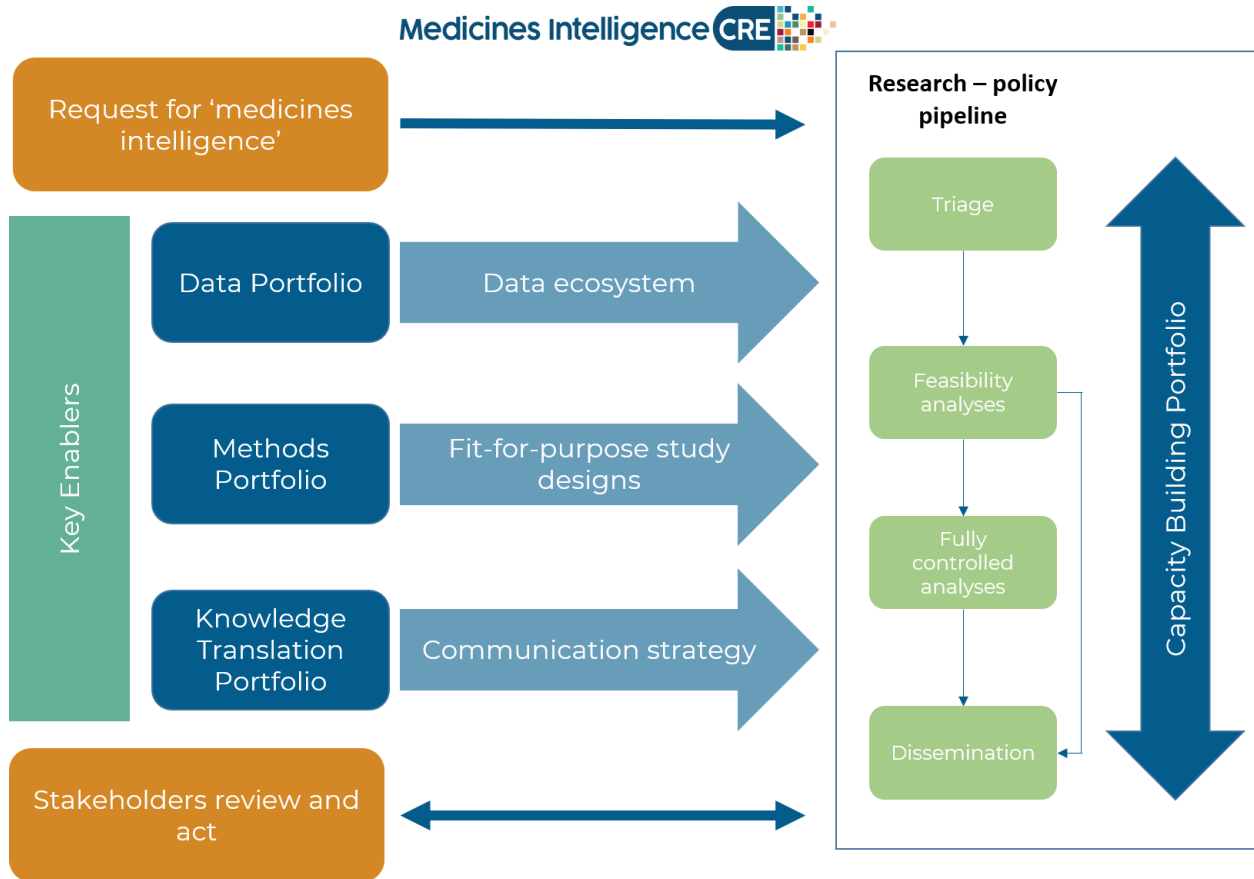
Despite the recent considerable investment in data linkage infrastructure in Australia, there has been no matching investment in expanding Australia's human capacity to lead policy-relevant research using these newly available resources. Traditionally the pharmacoepidemiology workforce has come from a heterogeneous base, including people with backgrounds in biostatistics, epidemiology, clinical medicine, pharmacy, and psychology. But the growth in big data and the potential for application of machine learning and artificial intelligence approaches creates an imperative to build an even broader 'medicines intelligence' workforce, including people with backgrounds in computational statistics, bioinformatics, computer and data science. This diversity creates challenges in ensuring the workforce has high-quality foundational training that will give them the tools to innovate, think creatively, and generate robust RWE and apply that with a policy-influencing lens.

MI-CRE is building the 'medicines intelligence' workforce by equipping a new cohort of independent researchers with the skills to generate real-world evidence that responds to policymakers' needs. To build this capacity, MI-CRE provides opportunities for researchers to undertake formal training (e.g. in data analytics and consumer engagement)

and is developing and/or facilitating access to resources including a suite of tools that support the embedding of evidence translation pathways into research projects from the outset, a pharmacoepidemiology methods library, and a toolkit of fit-for-purpose research designs and best-practice methodologies for medicines-related research. In order to build the research workforce beyond the MI-CRE network, these opportunities and resources will be made available to the research community at large. Within MI-CRE's network of researchers, peer-to-peer learning is facilitated through activities such as a regular journal club, skill-sharing sessions, and our recently established mentoring program. MI-CRE is also delivering the following on-the-job training for early- and mid-career researchers:

- Each MI-CRE portfolio (Data, Methods, Knowledge Translation and Capacity Building) is co-led by a senior investigator and an early- or mid-career researcher, with new leads elected each year. Portfolio co-leads are from different universities and disciplinary backgrounds to foster cross-institutional and interdisciplinary collaboration and skill-sharing.
- MI-CRE's communication with each policy partner is co-led by a senior investigator and an early- or mid-career researcher.
- A project incubator scheme provides a structured opportunity to obtain stakeholder input from project inception and throughout its lifecycle. This scheme

Figure 2: MI-CRE research – policy pipeline and enablers for accelerating RWE development in Australia



is targeted towards early- and mid-career researchers and provides modest funding to cover the expenses associated with end-user engagement or other research costs. A requirement for cross-institutional collaboration in these projects provides another opportunity for interdisciplinary collaboration and skill-sharing.

- Research led by early- and mid-career researchers is showcased at the MI-CRE Annual Research Symposium and Policy Forum.
- Our plans to access existing analytic tools and adapt them for use on MI-CRE data platforms will facilitate the learning of best-practice programming approaches and efficiencies in writing code.

Figure 2 summarises MI-CRE's implementation approach.

Expected outcomes

The achievements of MI-CRE will be measured as the program evolves with a particular focus on four key areas of health service research impact [58]: advancing knowledge, informing policy and decision making of regulators and payers, health service impact, and societal impact. Our success in advancing knowledge will be measured using traditional metrics such as publications and conference presentations and their reach (e.g., citations, social media mentions etc.) as well as metrics based on non-traditional outputs such as open-source protocols and analytic tools that will support the academic

community into the future. We will evaluate the extent to which MI-CRE has informed policy and decision making with both process and outcome measures. Process measures will include metrics such as the number of projects that have been co-designed with evidence end-users, the number of studies that result in policy briefs or other translational outputs, and the time from project initiation to dissemination of these translational outputs. Outcome measures related to our success in informing policy will include whether MI-CRE research had led to changes in the listing/de-listing of a medicine, the conditions under which a medicine can be prescribed, or other regulatory actions. We will measure MI-CRE's health service impact through the citation of our research findings in clinical guidelines and other resources targeting health care professionals and/or consumers, while our societal impact will be measured through follow-up studies reporting the extent to which Australia is achieving quality use of medicines.

Challenges ahead

MI-CRE has embarked on an ambitious program of database and methods development, training and mentorship, and collaborative research projects. The success of this comprehensive program of observational research on medicines use and outcomes will depend on sustained investment in enabling data infrastructure and the workforce with the skills to analyse, interpret and translate study outcomes.

Streamlined access to contemporary, linked Australian data will be critical to MI-CRE's ongoing operations and sustainability. Historically, statutory, privacy, and political barriers have impeded the linkage of and access to these data [33]. However, recent developments in data access, governance, and infrastructure mean that cross-jurisdictional health and social data are increasingly available for linkage. At the time of writing the *Data Availability and Transparency Act 2022* has been enacted. This federal legislation establishes a new, best practice scheme for sharing of Australian Government data, underpinned by strong privacy safeguards and more simplified, efficient access processes. These encouraging developments now require large-scale implementation and cooperation across jurisdictional boundaries. MI-CRE views these developments as an important opportunity to demonstrate the value of data for public benefit. In parallel, we will scale up the implementation of common data models as new data become available, further facilitating the generation of accurate, reproducible, and well-calibrated evidence.

Evidentiary needs of policy makers are varied and shifting, and MI-CRE must have the agility to evolve and respond. We are currently in the early stages of establishing a national collaborative effort that will create the requisite efficiency and flexibility. MI-CRE must also advocate for the importance of RWE and continually innovate methodologies that can overcome inherent limitations in observational data. This will be key to reassuring policy makers of the quality of the evidence and building confidence in using it to inform policy and decision making. Research co-design with medicines agencies is a must. We recognise the pivotal role of open communication; we have built on our long-standing relationships with key stakeholders in Australia and formally integrated medicines agencies representatives in MI-CRE governance, supporting direct pathways for research translation to policy and practice. Our connections with and learning from mature models internationally will not only benefit Australia's national effort but foster Australian contributions to international initiatives.

The primary aim of MI-CRE is to support regulatory decisions about licensing, prescribing restrictions, price negotiations with manufacturers, and further evidence requests. At the same time, we must balance those objectives with the expectations of our funders and investigators, which are to generate impactful academic research outputs. We believe both are achievable; a significant proportion of work undertaken by MI-CRE remains of interest to academic audiences, as we address emerging quality use and medicines safety issues of global interest and use state-of-the-art methods with the most contemporary data available.

Conclusions

Policy agencies generally want answers to their questions quickly – within months, rather than years. Historically, these turn-around times have been difficult to achieve in Australia for several reasons, leading to a paucity of real-world evidence based on the Australian context. By streamlining access to Australian data, tools, and methodology for medicines research, breaking down barriers to translation

of priority research questions, and fostering the next generation of medicines researchers in Australia, MI-CRE will support the real-world evidentiary requirements of both regulators and payers. At the completion of the five-year funding period, MI-CRE will have substantively improved the output, capacity, quality, and policy-relevance of pharmacoepidemiologic research in Australia, supporting quality use of medicines and reducing medicine-related harm.

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Author Contributions

SP and NP conceptualised the paper. NP, XC, AH and SP led the drafting of the manuscript. All authors contributed to the manuscript draft, reviewed and edited the manuscript and approved the final submitted version.

Conflicts of Interest

CEB is a member of the Pharmaceutical Benefits Advisory Committee (PBAC); SP, NP, TL and CEB are members of the Drug-Utilization Sub-Committee of the PBAC; TL is a member of the Economics Sub-Committee of the PBAC; SP is a member of the National Data Advisory Council; CMV is Deputy Chair of the NSW Population Health Service Research Ethics Committee; DP is a member of the Sax Institute Board. The views of authors expressed in this review article are their own and do not represent those of the aforementioned bodies. In 2020, the Centre for Big Data Research in Health received funding from AbbVie Australia to conduct post-market surveillance research. AbbVie did not have any knowledge of, or involvement in, this manuscript.

Ethics statement

No specific ethics was required for this manuscript as no analysis has been performed.

Break out box

Pharmaceutical Benefits Advisory Committee
<ul style="list-style-type: none"> • The Pharmaceutical Benefits Advisory Committee (PBAC) make recommendations for medicines to be listed for subsidised prescribing to the Australian public on the Pharmaceutical Benefits Scheme (PBS) [59]. • Once listed on the PBS, dispensings of those medicines are captured by Services Australia in the PBS dataset. These data can then be used to monitor medicines usage patterns and associated costs, including real-world cost effectiveness [9]. • Medicine utilisation analyses are then used to support PBAC decision making and to evaluate the impact of their decisions. Descriptive approaches are often used to monitor medicine use and costs, but these rarely quantify benefits, harms, or other health-system impacts which limits the information available to make recommendations to either fund or change the conditions under which a medicine is subsidised. • These descriptive approaches are limited by the absence of a consistent and co-ordinated approach to join up national data collections linking medicines utilisation with health outcomes. • MI-CRE will partner with medicine payers to develop more sophisticated and comprehensive ways of generating prospective real-world evidence of medicines use and outcomes for informing judicious funding of medicines within a finite health budget and maximise benefits whilst minimising harms.
Therapeutic Goods Administration
<ul style="list-style-type: none"> • In Australia, surveillance of medicines quality, safety, and efficacy is the remit of the Therapeutic Goods Administration (TGA). • To-date the TGA has relied on voluntary adverse event reports from doctors, patients, and manufacturers to investigate medicines safety concerns in the post-market setting. Although this approach remains an important part of the surveillance toolkit for regulators, evidence of harms from passive reporting is limited by underreporting, lack of timeliness, and an inability to estimate population risk • The exponential growth and availability of health and other public sector data has created new opportunities to improve the efficiency and sophistication of real-world evidence (RWE) generation to support the regulatory activities of the TGA [60]. • MI-CRE will partner with TGA to address this challenge by taking advantage of the growing wealth of real-world data to quantify the risks of adverse drug reactions (ADRs) across different population sub-groups and generate estimates of strength of association between medicine exposure and outcome to support regulatory actions [3, 4].

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