Prescription medications have made a significant and positive contribution to the health and wellbeing of Australians. However, some medications have the potential to cause harm when misused. Pharmacological classes identified as being particularly susceptible to misuse, dependence or subsequent harm are the benzodiazepines and the opioid analgesics. Although these drugs can legitimately be used for the evidence-based short-term treatment of patients with anxiety, insomnia and chronic pain, recent data highlight increasing rates of harm associated with their use. Given the substantial increases in the prescription of opioids and benzodiazepines in Australia, there is a growing challenge for the Federal and the various state and territory governments to increase awareness about the potential misuse of prescription medications, and to implement mechanisms that promote quality use of medicine and minimise harm. This challenge is multifaceted and requires both system level (e.g. policies related to prescribing and dispensing and monitoring systems) and individual level (e.g. screening for appropriate behavioural markers, referral and treatments) actions to succeed.

Benefits and challenges to the implementation of real-time prescription monitoring

Harms linked to prescription drug misuse are rising in tandem with increased prescription availability. Individual practitioners and the healthcare system each have roles in reducing harms associated with pharmaceutical drugs and a real-time prescription monitoring system could help in this process.

KEY POINTS

- Benzodiazepines and opioids are efficacious medications for the short-term management of patients with anxiety, insomnia and pain, but are susceptible to being misused and abused.
- Recent studies have consistently identified increasing morbidity and mortality associated with these drugs in Australia.
- Real-time prescription monitoring (RTPM) has the potential to assist prescribers and dispensers in adhering to the quality use of medicines.
- RTPM also assists in the identification of those patients at risk of misuse or abuse of pharmaceuticals.
- Individual practitioners have an important role in minimising the misuse of pharmaceuticals by devising treatment plans and contracts and conducting ongoing monitoring of patients who are prescribed these medicines.

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Benzodiazepines and opiate analgesics: benefits and risks

Benzodiazepines are widely prescribed and are efficacious in the treatment of patients with anxiety disorders and insomnia in the short term. Benzodiazepines also have significant side effect profiles if they are misused, most notably the development of tolerance and dependence with longer-term use. Chronic use of benzodiazepines is associated with cognitive impairment, falls and a diminished quality of life, especially in the elderly. In addition, short-acting benzodiazepines such as alprazolam, typically prescribed for the management of patients with anxiety, are more likely to be diverted for other uses, and are associated with both drug-related offending and increased utilisation of emergency resources.

Opioids are efficacious analgesics and have legitimate and important treatment indications for the management of patients with pain. Misuse of opioids such as fentanyl, morphine and oxycodone is associated with significant side effects including respiratory depression, which can result in death. The long-term use of opioids for chronic pain is increasing in community settings, and has been associated with higher rates of fatal overdose. This has led to increasing debate about their efficacy and safety in the management of patients with chronic nonmalignant pain.

Pharmaceutical drug use and associated harms in Australia

In 2013, 4.7% of people in Australia aged 14 years and older engaged in nonmedical use of analgesics, sedatives and/or corticosteroids, compared with 3.9% in 2001. This upward trend mirrors international patterns, and is occurring in parallel with rising supplies of commonly misused medications including opioids such as oxycodone and the antipsychotic quetiapine. In Australia, from 1992 to 2012, the number of dispensed PBS opioid prescriptions increased 15-fold (from 500,568 to 7,495,648 prescriptions), with dramatic increases in morphine prescription during the 1990s, oxycodone prescription from 2000 and fentanyl prescription from the mid-2000s. The concordant proliferation in the number of available opioid formulations from 11 preparations in 1992 to 146 preparations in 2013 was predominantly driven by the development of slow-release preparations.

Changing PBS regulations over the past 20 years have precipitated alterations in benzodiazepine prescribing patterns. For example, although the highest number of prescriptions per year in most years from 1992 to 2011 were for diazepam, there were notable shifts from the prescribing of oxazepam, nitrazepam and temazepam towards the prescription of alprazolam. The subsequent popularity of alprazolam and its well-documented harms resulted in its rescheduling to a restricted Schedule 8 drug in 2014.

Greater population-level prescription is not necessarily detrimental. Continued high benzodiazepine and opioid demand is expected as Australia’s ageing population results in a greater prevalence of painful conditions and psychological disorders that peak during the middle and older years. If rising prescriptions reflect quality use of medicines, then people in Australia will profit from the advantageous potential of these drugs. Yet, as more people have engaged in nonmedical use of these medicines concomitant to their greater supply, associated harms have also increased.

Since the late 1990s, inappropriate benzodiazepine use has been involved in more ambulance attendances in Melbourne than any other drug except alcohol (Figure). Over this period, pharmaceutical opioid-related ambulance attendances have increased more than fourfold, whereas heroin-related events have halved. In parallel, hospitalisations in Australia for pharmaceutical opioid (excluding methadone) poisoning substantially increased from 1998 to 2009, these drugs superseding heroin as the leading cause of opioid-poisoning hospitalisations in 2001.

Although hospital separations related to benzodiazepines remained stable, rates were consistently high and these drugs were the second leading drug cause of hospitalisation in Victoria (after alcohol) from 2000/01 to 2010/11. Perhaps most troubling is the growing rate of deaths in Australia involving oxycodone and fentanyl, as well as increased benzodiazepine involvement in heroin-related deaths over the past two decades.

Reducing harms associated with pharmaceutical drug misuse

Pharmaceuticals are often misused by individuals who do not typify those traditionally seeking treatment for alcohol and other drug problems. Pharmaceutical drugs may be conceived of as ‘safe’ and unlikely to lead to addiction by the general public because they have been prescribed by a physician. Currently, information regarding pharmaceutical misuse relies on printed warnings on medication packaging and advice provided to the patient at either the point of prescription (e.g. by a physician) and/or the point of sale (e.g. by a pharmacist). Accompanying this, information on regulation and monitoring of Schedule 8 drugs differs among the countries.
and conducting frequent monitoring and reviews) and by governments (e.g. requiring pharmacy and/or prescriber reports or use of wholesale data to monitor patterns of prescribing). One strategy that has received much interest in Australia is the implementation of real-time prescription monitoring (RTPM). RTPM systems collect information about the prescriber, the dispenser, the patient and relevant drugs. The Royal Australasian College of Physicians and the Royal Australian College of General Practitioners both recommended the adoption of a real-time reporting system to operate nationally, and this is also supported by the Federal Government.

Prescription drug monitoring programs have been introduced in different jurisdictions to help control nonmedical use and/or medical abuse of prescription drugs. In the USA, such systems originated in the early 20th century with the goal of detecting and prosecuting drug diversion and the abuse of controlled substances, with a secondary aim of providing information to prescribers in order to prevent the abuse of prescription medications. A RTPM system has recently been introduced in Tasmania to monitor Schedule 8 drugs prescribed alone or in combination with alprazolam. However, there has been limited data examining the effectiveness of RTPM, with those studies completed focusing primarily on law enforcement rather than health outcomes.

**Benefits, Limitations and Challenges to the Implementation of Real-Time Prescription Monitoring**

**Benefits**
- Can alert prescribers to patient’s prescription history
- Can alert prescribers to current prescriptions the patient has filled
- Has the ability to flag potential drug interactions
- Will make it more difficult for patients to engage in doctor shopping
- May identify patients who initially obtained drugs for genuine need but are at ‘risk’ of misuse or abuse

**Limitations**
- Proposed Australian system will monitor Schedule 8 drugs only
- It is unclear what the best practice is for patients at ‘risk’ of harm or misuse
- It is unclear how doctors and pharmacists will continue their support of individuals who are flagged in the system
- Patients with a genuine need may not be prescribed needed medications (the chilling effect)

**Challenges**
- At what threshold will a response be triggered?
  - Drug dose
  - Frequency of prescription
  - Comorbid use of prescription drugs
  - Comorbid mental health or physical condition
- Who will respond to a potential flag?
  - Prescribers
  - Pharmacists
  - Health services
  - Legal/law enforcement services
- Will the system be able to monitor shifts in drug prescribing?
- How will patient privacy be protected?
- What information about patients will be collected?
- Will the system be ‘proactive’ or ‘reactive’?
- Who will develop and implement the system?
- Who will be responsible for training system users?

Given the large increases in harms associated with pharmaceutical drug misuse and abuse, and the increased number of opioid prescriptions filled in Australia, there has been considerable interest in strategies to minimise harms associated with long-term opioid use. This includes steps that can be taken by individual physicians (e.g. conducting a comprehensive pain and substance use history, devising a treatment plan and contract for those deemed at risk, and conducting frequent monitoring and reviews) and by governments (e.g. requiring pharmacy and/or prescriber reports or use of wholesale data to monitor patterns of prescribing). One strategy that has received much interest in Australia is the implementation of real-time prescription monitoring (RTPM). RTPM systems collect information about the prescriber, the dispenser, the patient and relevant drugs. The Royal Australasian College of Physicians and the Royal Australian College of General Practitioners both recommended the adoption of a real-time reporting system to operate nationally, and this is also supported by the Federal Government.

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**Benefits and challenges to the implementation of RTPM**

Multiple benefits, limitations and challenges will accompany the implementation of national RTPM in Australia (Box). Potential benefits of RTPM include the ability of the system to inform prescribers about a patient’s prescription history and their current filled prescriptions. Such information is important in decreasing the incidence of ‘doctor shopping’, encouraging prescribing that concurs with relevant guidelines and alerting prescribers to potential drug interactions. Collection of this information may also help to identify people who use scheduled drugs for a genuine medical need initially and then go on to misuse or abuse these drugs.

One limitation involves the scope of drugs to be included in the Australian proposal. The monitoring of Schedule 8 drugs means that some opioids (e.g. tramadol, codeine preparations) will be excluded despite their demonstrated roles in morbidity and mortality in Australia. Another limitation concerns what is best practice for patients deemed to be ‘at risk’ of misuse or abuse of these medications. Current treatment pathways for such patients are not well defined, and referral pathways to other services and nondrug alternatives for managing chronic pain are not clear. Addiction and chronic pain are often complex presentations and there is currently limited funding for addiction specialist expertise across Australia. There is also limited practical training opportunities for healthcare professionals in the management of patients with addiction and chronic pain, which means that there are real concerns about increasing stigma and the provision of adequate care to individuals
who are flagged in the system. An additional concern is that patients with a genuine need for prescription medications may not be prescribed them for fear that an individual, or a prescriber, may become ‘flagged’ in the system.

Issues of privacy and confidentiality are clearly paramount to the success of RTPM, with a focus on health outcomes. This includes clear delineation of who will have access to the information, what information will be collected and stored, and how long records will be kept. Finally, it is important to determine whether the system should be ‘proactive’ (e.g. generate reports for clinics or individual prescribers and identify those who may be at risk of dependence or abuse based on information provided to it) or ‘reactive’ (rely on user requests once someone is deemed at risk in order to identify potential problems from a patient or physician perspective).

Conclusion

With evidence of increasing misuse and harms associated with prescription medications, there has been a renewed interest in effective practitioner and system responses to promote quality use of medicines and minimise harm. Quality use of medicines by individual practitioners includes treatment plans, contracts and ongoing monitoring subsequent to a comprehensive pain, mental health and substance use history. In parallel, at the systems level the utility and value of RTPM must balance the needs of individual patients who require treatment with the public health ideal of reducing harm across the population.

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COMPETING INTERESTS: Dr Ogé, Dr Heilbronn and Associate Professor Lloyd: None. Professor Lubman has received speaking honoraria from AstraZeneca and Janssen, and has provided consultancy advice to Lundbeck.