PRESCRIBED DEATHS

LIFE IN THE KILLING ZONE

PATRICK O'CONNOR

Release date July 2020

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Prescribed Deaths – Life in the Killing Zone

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Warning

Do not stop taking a prescribed medication without discussing it with your doctor. Information can also be obtained by calling the NPS Medicines Line on 1300 633 424 or the Adverse Medicines Events Line on 1300 134 237 for advice. If you need support for any medical concern, including mental health matters, please contact your doctor. Lifeline also provides a 24 hour support service on 13 11 14 or www.lifeline.org.au

PRESCRIBED DEATHS

LIFE IN THE KILLING ZONE

PATRICK O'CONNOR

ABOUT THE AUTHOR – PATRICK O'CONNOR

UN. New York – 2019

My name is Patrick O'Connor. Like a million other Australians, I live with severe mental illness. And like most of those people – my people – I also live with other debilitating chronic illnesses.

In 2016, I reached the end of the line when it came to medical treatments in Australia. Based on my condition, statistically I only had three years to live. My physical conditions were destroying my body, my mental illness was torturing me with extreme psychological distress, and the prescribed medication – well, that was killing me too.

I honestly couldn't see myself lasting another 12 months, and I shouldn't have.

BECOMING TREATMENT RESISTANT

Many of the dangerous PBS medications described in this report have been prescribed to me. These medications shorten lives, threaten lives, and can be used to end lives. I know, I have experienced all three.

My life expectancy was comparable to living with a terminal illness, yet I was told that there were no treatments left to try. Doctors described my conditions as 'treatment resistant' – but I felt that the doctors in Australia were the ones being resistant to trying new treatments. Faced with the reality that my doctors could offer nothing to save my life, I made the decision to save myself.

Ketamine Research Institute, Florida, USA – 2018

I researched new advancements in medicine and continually came to the same outcome: I needed to go to the USA. While I had experienced a negative view of the US healthcare system by many Australian doctors, to me, it offered the best chance at life.

For four years, I travelled to the US every few months for treatments that were not available in Australia.

While not everything worked, I could still see how the treatments were helping others. Many treatments did (and still do) work for me and saved my life – as well as thousands of others in the US every day.

EXPLORING OPTIONS

To find the right medical pathway for me, I knocked on the doors of countless medical specialists across America. The whole time, I was tormented with the realisation that unless I could bring these treatments to Australia, my people would continue to suffer and die prematurely. That is what led to this report.

I wrote this report during my battle, not at the end of it. I wanted to provide information to save lives, just in case I wasn't successful in saving my own. I needed to make sure what you are about to read didn't die if I died.

I am proud, very proud, that I have been able to play a role in bringing some of the treatments from the US to Australia. A second report will follow this one to explain that journey.

FORMING THE KILLING ZONE

Severe mental illness is pure evil. It seeks to destroy everything you love, and when it has done that, it comes back to take your life. It's a slow death, torturous and horrific. It impacts everyone around you, it has no mercy or compassion and even after it has taken lives it continues to bring pain to family and friends. You cannot co-exist with evil – it has to be killed and that has always been my goal.

Yale University, School of Medicine, USA – 2019

Before you read the report there is something deeply personal that I want to share with you. In short, I should be dead. Several years ago, I went through a period when I wasn't winning. I was suffering on an unimaginable level and I lost my battle. I simply wanted the suffering to end, so I consumed a large quantity of my medication. It was the worst day of my life, but not my last. The next morning, I woke up in my hotel room. Written on the note pad beside my bed were three words: 'The Killing Zone'. I knew what that meant and what I had to do.

Something happened that night in the period when my body was processing a prescription medication cocktail that should have ended my life. In my heart, I believe that the thousands of 'my people' who lost their battles, sent me back to tell our story. That day I opened my laptop and I started to write this report.

A friend once told me that "depression costs people, people"; for me it cost me the women I loved. There was never any fault, and I always knew this was a battle I had to fight alone. They all loved and supported me, yet losing their smiles from my world made me fight harder to stop the same thing happening to others.

I make no apologies for anything contained in this report. I have written this in the same way that I have lived the last eight years – fighting for change and for a better life.

REMEMBERING THOSE WE HAVE LOST

On one of my visits to the US I visited a cemetery in a region heavily impacted by the Opioid Crisis. Hundreds of thousands of vulnerable people died after seeking help from their doctors, without receiving warning of the risks of the medications prescribed.

While there, I had a brief conversation with a couple about this report. They asked me to publish the names of those who need to be made accountable, no matter the consequences. I hesitated to commit, but they pointed to the recent graves and said, "It's the only way to stop families having to put names here". It was a deeply moving day for me.

I have fulfilled the promise. The report is finished but the fight for change is only just getting started.

Patrick O'Connor

CONTENTS

LIST OF TABLES

LIST OF FIGURES

EXECUTIVE SUMMARY

The greatest barrier to improving the lives of millions of Australians with mental illness is not the illness itself, it is the medications prescribed by our doctors. This report unravels a myriad of systemic issues, and lays bare a healthcare system that is causing more suffering and deaths than the illness it treats. There are multiple safety failures in the medication prescribed to treat mental illness and pain conditions (conditions commonly suffered together). By exposing the indefensible failure to uphold our human right to safe healthcare and the resulting loss of life, this report aims to force urgent changes in the way these conditions are treated.

Severe mental illness rarely exists as a single condition and sufferers typically deal with multiple chronic illnesses. To attempt to improve our afflictions we are managed by multiple doctors, using complex medication prescriptions combined with other treatments. From diagnosis to unconscionable exposure to premature death – this is the reality of Australia's response to mental illness.

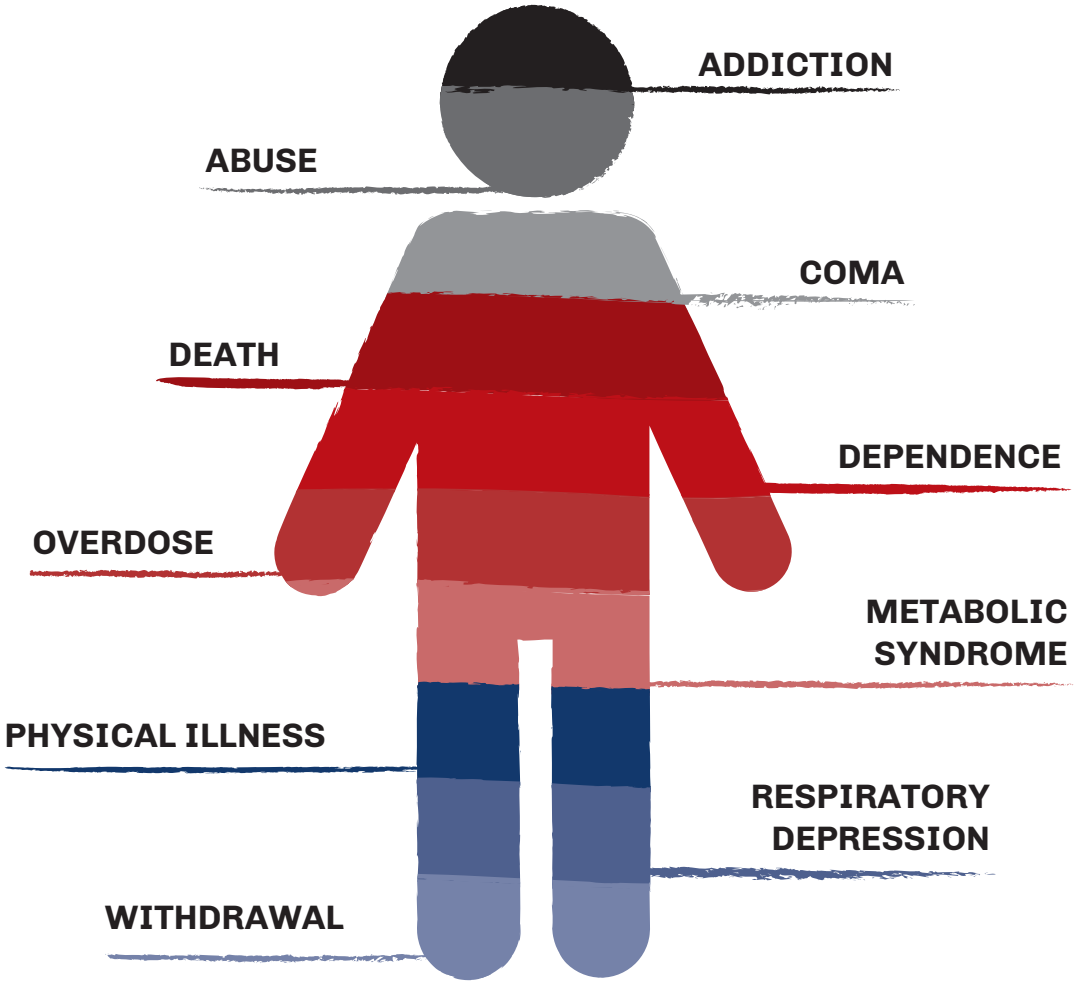
This report is written from the perspective of people who live with severe mental illness. The author has personally experienced treatments in both the Australian and the US mental healthcare systems. Using those experiences, we provide a deeper understanding of what life is like with mental illness, the issues that are not being addressed, and some recommendations to start saving lives today.

Arguably the greatest barrier to fixing many of these systemic problems is getting people in positions of responsibility to acknowledge publicly that the failures exist. This report aims to call attention to how dire the situation really is in this country.

Prescribed Deaths – Life in The Killing Zone provides frightening insights into our endless struggle to survive. Thankfully, there is a path to saving lives, and it starts here.

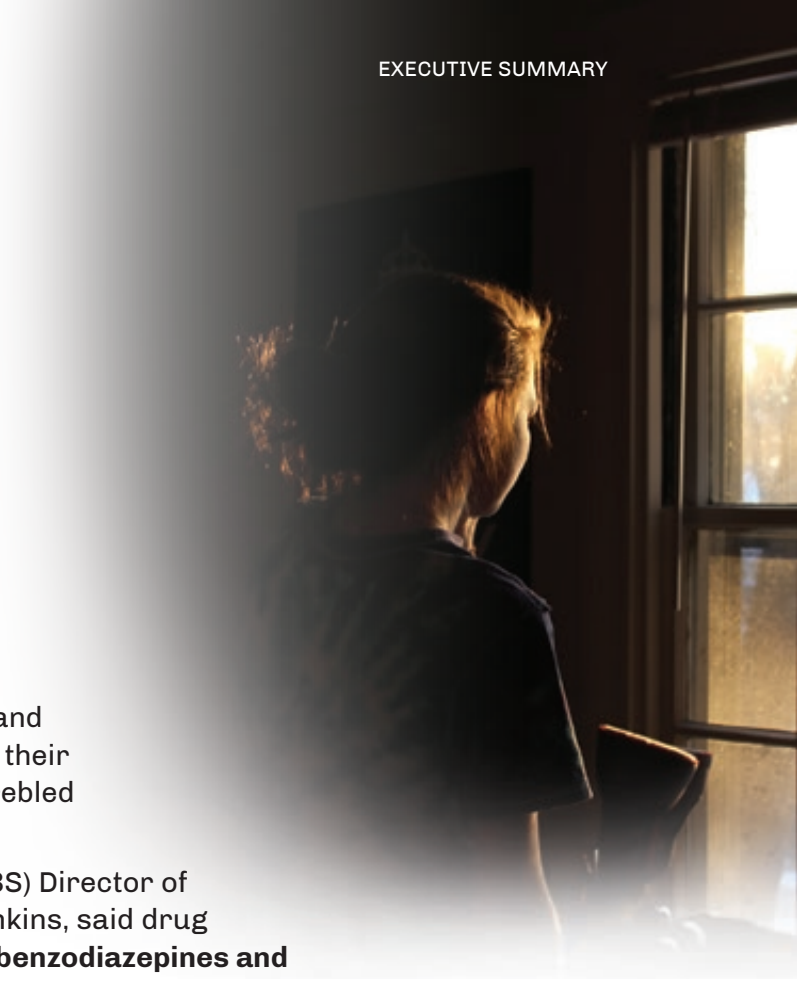
OUR PHARMACEUTICAL COCKTAIL

Medications used as frontline treatments for mental health in Australia include opioids, benzodiazepines, antidepressants and antipsychotics. The life-threatening risks of these medications include:



Due to these high risks, most of these medications are classed as scheduled poisons. Their use is controlled and it is illegal to possess them without a prescription. The risks of these medications, such as addiction, begin from the **first dose** and they are present even when being used as prescribed for a short period of time. Australia places second in the world for prescription drug addiction (the US is first).

On one hand, these drugs are deemed medications for treatment, but due to the dangerous side effects, they are also classed as dangerous poisons. When these medications happen to be used together, the risks multiply – particularly the risk of death. Yet lethal combinations of these medications are prescribed to treat millions of vulnerable people with mental illness and pain conditions in Australia, with the numbers growing each year.



THE HUMAN COST

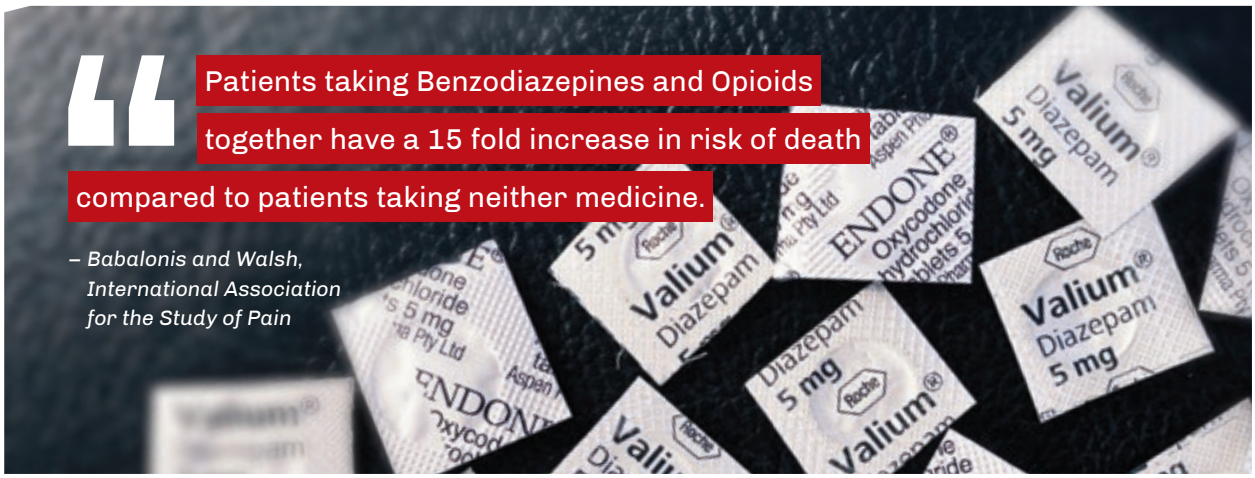
Tragically these medications are also the leading cause of overdose deaths and hospitalisations in Australia. People are dying as a result of the medication that was prescribed to treat them; the greatest failure a healthcare system can make. Drug overdose deaths kill more Australians each year than car accidents, with prescription medications being the most common drug present. The victims are most commonly people who are taking medications that are prescribed by their own doctor, for diagnosed mental illness and pain conditions, with medications dispensed by their usual pharmacist. The number of deaths has trebled since 2007 and it continues to rise each year.

In 2017 the Australian Bureau of Statistics (ABS) Director of Health and Vital Statistics, James Eynstone-Hinkins, said drug deaths were **most commonly associated with benzodiazepines and oxycodone**, noting that, "These are both prescription drugs which are used to manage anxiety and pain respectively".

ABS statistics also tell us that three million people use opioids each year and six million prescriptions are dispensed for benzodiazepines. Between 2001–2017, all opioids deaths totalled 13,269 and benzodiazepines caused 8,061 deaths.

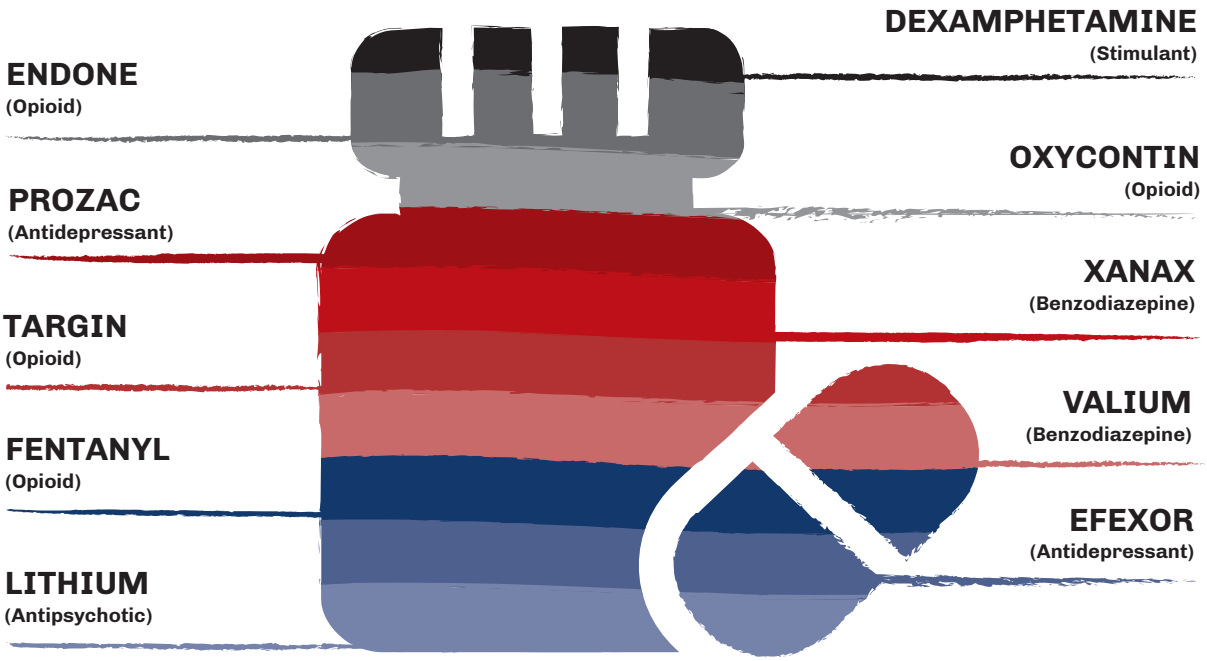
The risks of prescription medication also pose a significant non-fatal impact. There are 250,000 Australians hospitalised each year, with another 400,000 presenting to emergency departments. As with fatalities, the medications identified in people's bodies are opioids, benzodiazepines, antidepressants and antipsychotics.

NSW Health estimates that there may be 750,000 Australians currently dependent on pharmaceutical opiates. Monash University claim 50,000 new people become long-term users of dispensed pain killers each year, putting them at risk of addiction. The prescribing practises of our doctors puts these lethal poisons in our hands, but the consumer warnings are just as deadly.



CONSUMER MEDICATION WARNINGS

This report has undertaken a detailed assessment of 10 medications prescribed in Australia through the Pharmaceutical Benefits Scheme (PBS). The analysis shows that pharmaceutical companies have been producing consumer medication information (CMI) documents that **deliberately include misleading, inaccurate and incomplete information on the life-threatening risks of taking these medications for over 20 years**. These risks include addiction, overdose, coma and death. For the 10 medications analysed, we identified 46 instances where the warnings represent breaches of the *Therapeutic Goods Act 1989*.



This is a sample of the most deadly prescription medications in Australia. These are the treatments prescribed to our most vulnerable people, yet the pharmaceutical companies have ensured they have not been warned of life-threatening risks. The CMIs provide very little information to the person on their exposure to these risks and how to avoid them. For example:

- Valium and Endone are controlled drugs due to the high risk of addiction, yet neither CMI mentions the risk of addiction once.
- Xanax, the benzodiazepine classified as the most dangerous due to the number of deaths recorded, contains no warning on the risk of death.
- OxyContin is responsible for the US opioid epidemic, where deliberately misleading information attributed to the deaths of hundreds of thousands of Americans. This misleading information is present in Australian CMIs.
- The Endone CMI describes the side effect of consuming alcohol whilst taking the medication as dizziness. In a separate document provided to doctors, the side effects listed include profound sedation, coma and death.
- The lethal toxicity of Lithium is dangerous even at prescribed levels, yet the CMI states the opposite.
- The combination of opioid and benzodiazepine medications is the leading cause of overdose deaths, yet none of the CMIs mention the risk of death when these drugs are prescribed together.

> ... these are all very dangerous drugs, reading these Australian warnings, I am very disturbed that patients haven't been warned up front, they haven't been warned adequately, and they haven't been warned enough.
>
> *– Dr Lori Calabrese (US psychiatrist and medication expert)*

When CMI versions from earlier years were analysed, the number of critical warning failures is two to three times greater. Arguably many of these are so incomplete that they do not meet the legal requirement to be classified as a CMI. We asked two leading US medication experts to provide their opinions on the warnings identified in our analysis. Both doctors noted that these side effects have been well known for decades and are clearly explained in US consumer warnings written by the *same companies* – and this presents a real risk to the safety of consumers.

Even for the 'weaker', commonly prescribed codeine opioids like Panadeine Forte, the CMI does not contain a single mention of the risk of death, addiction, dependence, tolerance, withdrawal or abuse. In comparison, the document provided to doctors for Panadeine Forte discloses the risk of death nine times.

This report shows that the **exact risks not disclosed are directly or indirectly linked to the majority of Australia's adverse drug events and deaths**. The cause and effect cannot be any clearer and the people affected are vulnerable people who are prescribed these medications.

INFORMED CONSENT

The rights of vulnerable people – in fact, all people – to safe healthcare is enshrined in the Universal Declaration of Human Rights, the Australian Charter of Healthcare Rights, and the Convention on the Rights of Persons with Disabilities. It is a legal requirement that medical treatment, including taking medication, can only commence after we give our informed consent. For the consent to be valid, it has to be informed, meaning that we have been provided with all the information about potential risks of taking the medication. This includes when multiple medications are prescribed.

The law provides us with the right to full disclosure of all risks – there is no discretion, even for risks that might be deemed rare in occurrence. Our CMI analysis is emphatic in demonstrating dangerous risks have not been disclosed for the most commonly prescribed medications for people with mental illness and pain conditions. Millions of people have given consent, without being informed, and hence their consent is not legally valid. You simply cannot assess a risk that you don't know about. You cannot follow safety advice if it has never been given to you. The resulting impact on human life has been physical illness, dangerous side effects and for many, death. Prescribing medication without informed consent is criminal. It exposes the system to medical negligence claims and it is an unequivocal breach of our fundamental human right to safe healthcare.

> These Australian documents are woefully inadequate, they do not give a person the multiple life-threatening risks of these medications. This doesn't provide them with an understanding of the risks to give **informed consent**.

– Dr Craig Allen (US medical expert)

Global studies have shown that at least one third of people do not get any improvement at all from mental health medications. Benzodiazepines are not recommended to be used for more than a few weeks. Opioids are recommended to be prescribed at the lowest dose, for the shortest period of time. It is impossible to see how the benefits outweigh the risks, especially if the risks are not being acknowledged.

THE HEALTH CARE SYSTEM FAILURE

Medication is the most widely used medical treatment for mental health and pain in Australia. It is funded by the PBS, which is controlled by the Australian Government. Medication is prescribed by doctors and dispensed by pharmacists. It is regulated by the Therapeutic Goods Administration (TGA) and medication safety is also addressed by multiple other government departments. The ABS regularly reports on adverse medication events, including deaths. We have multiple organisations responsible for implementing the national mental health strategy. We also have countless independent mental health organisations and charities. Medication safety goes further than the pharmaceutical companies and the contents of the CMIs; it is the responsibility of all areas of the health care system.

Hence, how has an entire health care system failed to identify and correct the largest systemic failure of consumer health care rights in the last 50 years? Especially considering the resulting deaths are reported every year.

By examining the role of each area in this tragic failure, we uncover multiple systemic issues:

- **DOCTORS** – Mental health treatment is largely managed by General Practitioners (GPs). Mental illness diagnosis is based on self-reported symptoms, with significant potential for human error, misdiagnosis and unnecessary exposure to the wrong medication/s. It is estimated as many as 50% of diagnoses for depression may be incorrect. As with the CMIs, details of many medication risks have not been provided to GPs. For instance, a guideline for GPs on the prescribing of benzodiazepines made no mention of the risk of death. Over the 12-year period it was in use, 84 million prescriptions were dispensed,

and 4,459 people died from adverse side effects caused by benzodiazepines. Examining the time poor process by which GPs make a diagnosis, select medication for treatment, explain the risks and obtain informed consent, raises questions as to how the consent could possibly be valid.

> ... some GPs lack knowledge and skills in mental health and require considerably more training in identifying risks, diagnosing conditions, assessing and recognising the physical health consequences of prescribed treatments, and connecting patients with other services (such as online mental health services and allied health services).

– Productivity Commission report into Mental Health 2019

– **PHARMACISTS** – The stewards of medication safety, pharmacists are remunerated significantly by the PBS for providing medication to Australians. They have an ethical and legal responsibility to deliver the highest level of medication safety to vulnerable people. The code of ethics for pharmacists requires them to ensure patients have information to make an informed decision on medication treatments. The code also requires pharmacists to ensure the information is relevant, and up to date. Pharmacists are responsible for dispensing the CMI leaflets, as part of consumer consultations to ensure safe medication use, and so have failed to identify and address the lack of warnings in the CMIs. A patient may have multiple doctors, but they generally have only one pharmacist. As such, pharmacists have visibility and access to information on a person's multiple prescriptions, as they are the chemist physically dispensing them. Pharmacists have also failed to ensure that vulnerable people with multiple prescriptions have been warned of the dangerous side effects of these combinations, even though they have software to automatically assess these risks.

  There is no legal requirement for a doctor or pharmacist to give a person a CMI when medication is prescribed or dispensed. This is the case even for medication that is strictly controlled due to high risks, for medication that a person has never taken before, when a person is cognitively impaired, and even when **new dangerous warnings are added to a CMI**. A CMI is not even a mandatory provision when the side effects of the medication include sedation, confusion and memory loss, which are common with mental health medications. It is left to the person to ask for the information, or left to the discretion of a doctor or pharmacist. Multiple studies show that CMIs are rarely provided, and pharmacists have resisted any changes to the laws.

> Pharmacy Guild of Australia spokesman Greg Turnbull said the organisation supported "maximum patient empowerment and health literacy" but that making the issuing of a CMI mandatory "for every one of the 300 million-plus PBS scripts per year might not be the best solution".

When it comes to medication safety, this is actually the only solution. It is difficult to understand how consumers can reach a position of 'maximum patient empowerment and health literacy' without the information to read.

In comparison, the provision of consumer warnings with every prescription are mandatory in the US. In an interview with a pharmacist in Connecticut for this report, when asked why he agreed with this process he replied:

> Because the cost of a human life is worth more than the cost of a piece of a paper.

If only the Pharmaceutical Society of Australia (PSA) and the Pharmacy Guild of Australia felt that way too.

Real world experience of pharmacy consultations has been included in this report to show that information that is misleading and inaccurate is commonly provided to vulnerable people, including advice that could increase the risk of death to the consumer. The transcripts of the discussions with 15 pharmacists are simply horrifying.

> If you'd had some Endone and some Valium and two or three beers, you'd be like, 'No, I'm home for the night', because they've all got a sedating thing. I should write it down.

– Pharmacist

> You would have exactly what I have if you Google it up. Type in the name and read, that's exactly what I would give you.

– Pharmacist

> If you overdose, then – let me check. So the [inaudible] I mentioned it may lead to respiratory depression, constipation problem.

– Pharmacist

The PBS even allocates additional fees to be paid to pharmacists for the dispensing of dangerous medications that are scheduled poisons, like opioids and benzodiazepines.

– **THERAPEUTIC GOODS ADMINISTRATION (TGA) –** The TGA regulates consumer warning documents in Australia. In 2019 they admitted that the CMI for opioids do not contain warnings for the dangerous risks identified in this report. Each risk not appropriately disclosed is a breach of the *Therapeutic Goods Act 1989*, however the TGA opted to take no action, other than to request the pharmaceutical companies update the CMIs. Remember, 13,269 lives have been due lost to opioid use between 2001–2017 in Australia, yet the TGA takes **no legal action against the pharmaceutical companies who knowingly misled consumers**, with fatal consequences. Nor did the TGA investigate how broad this issue is or how it came to happen in the first place. The TGA's actions on CMI disclosure are woeful and fail to urgently address the issues. Troublingly they also have made no recommendations to ensure it doesn't happen again.

  Belatedly, some changes to opioid CMIs are slowly taking place. Finally, warnings relating to coma, overdose, addiction, abuse and death are being added. The TGA stated that the "improvements to information for prescribers and patients [are to] encourage best-practice prescribing and help consumers to be better informed about the potential risks and how to mitigate them". Consumers can only give informed consent to taking medication if they have been fully informed. The changes now being made by the TGA are an emphatic admission of the opioid risks that consumers have not been provided within the CMIs for decades.

  And alarmingly, the pharmacists we spoke to were unaware of the recently updated CMIs, and therefore, the critical warnings remain unknown to those filling or re-filling their prescriptions.

GOVERNMENT RESPONSE

When taking action on overdose deaths, the Australian Government goes to great lengths to blame the victims for the situation, even their own deaths. They enforce this narrative of prescription medication 'misuse and abuse' and 'victim blaming' in government policy. It provides a neat cause and effect link that all prescription medication deaths are caused by abuse and misuse, without any serious examination of other alternative reasons for these adverse events. The increase in deaths from prescription medication has increased with the growing prescribing of these medications. Why has there not been more investigation into how vulnerable people became addicted in the first place?

The government endorses the CMI as the information source for accurate medication safety and side effects, including prescription medication interactions. Approving these medications for the PBS provides a further endorsement in the minds of vulnerable people – given the PBS subsidises the cost, it makes the medication more accessible to us. The failure to ensure that vulnerable people are provided with accurate information is not only a breach of our right to safe health care, it also means that the government has full culpability for the resulting health issues we have suffered.

A CMI leaflet gives you information on how to use your medicine safely and properly. For example, it tells you:

- *how to take the medicine*
- *why it may have been prescribed for you*
- *potential side effects*
- *other medicines it may interact with*

There is a significant difference between 'how to take the medicine' instructions and warnings of the 'potential side effects' of taking a medication. Advising to not consume alcohol whilst taking the medication, is a how to take instruction. Advising that the consumption of alcohol with the medication can result in respiratory depression, coma or death, is an explanation of potential side effects. The CMI analysis shows that the focus is on how to use instructions and whilst this is important, it does not provide the information on the potential risks to enable a person to give informed consent.

The role of government is to protect the most vulnerable in our society. The thousands of people who have died and suffered at the hands of medication prescribed to them, without warning them of the risks, deserve a better response than to be blamed for their own deaths. It seems completely lost on all areas of health care that our cognitive ability is diminished due to the conditions we suffer and the medications we are prescribed. When it comes to medication safety, it is easy to see how this tragedy has unfolded.

The Australian healthcare system prescribes lethal poisons as treatments, without telling people the risks that can kill them. Please take a moment to read that again.

This report documents the government response to issues relating to medication safety attributed to doctors, pharmacists and pharmaceutical companies. In these instances, no link is made between the failures and the deaths. The issues are downplayed and handled with soft touch responses, like general warning letters. Overall, the government's response to the range of issues is disjointed, ignoring systemic issues in health care and lacking urgency given the severity of the problems. The introduction of a Real Time Prescription Monitoring (RTPM) system again focuses on the concept of victim blaming, using 'doctor shopping' as the primary reason for such a system. Despite the importance placed on the RTPM by government, it still hasn't been implemented nationally and is years overdue.

This report has also reviewed the recommendations of multiple government mental health plans and inquiries. The recurring outcome is that not only are the issues reported on mental health medication safety deliberately ignored, there is also very little being done to progress new treatments being introduced into Australia. In responding to the draft recommendations of the Productivity Commission report into Mental Health, the Pharmaceutical Society of Australia National President said:

> Unfortunately, what the draft report seems to overlook is the need for improved medicine safety practices and strategies for people with mental ill health and across mental health services.

> We need to ensure we are using medicine as effectively as possible in the treatment of mental ill-health. For this reason, PSA does not think it is possible to look at mental health care without considering the safe and quality use of medicines...

These organisations have also largely ignored the global recognition of the risks of medications and programs to reduce these deaths. The submissions to government from the lead mental health organisations, Beyond Blue, Black Dog Institute and Orygen/Headspace also ignore this issue. The consumer information they produce does not adequately explain the risks. These mental health organisations encourage Australians to seek treatment, so they have a responsibility to make sure the treatment they get is safe and people are informed of the risks.

Despite all the evidence, Australia still refuses to acknowledge and address the issues, urgently adopt safer medicine treatments, or even to warn consumers.

And why is it that a number of the organisations mentioned in this report have significant, and long-term, lobbying power with government? How is this regulated?

THE US AND AUSTRALIAN OPIOID CRISIS

A comparison of the well-documented US Opioid Crisis with trends in Australia's opioid deaths uncovered some brutally obvious consistencies. The same pharmaceutical companies, selling the same medications, withheld the same dangerous consumer warnings – the outcome is thousands of fatal and non-fatal events over the last 20 years. The only difference between the US and Australia is that the US has taken legal action against those companies, whilst in Australia they continue to enjoy the full support of government. In the last 12 months the companies referred to in this report have been forced to pay over USD $14 billion in compensation for the adverse drug events of the medications we analysed. In Australia they haven't paid a cent.

The architect of the US Opioid Crisis, Purdue Pharma, has filed for bankruptcy. Their Australian operation, Mundipharma, which sells OxyContin and Targin, is being sold to finance the compensation settlement to the American people. Purdue is also providing medication to prevent opioid overdoses for free as part of the settlement. Purdue do not provide the same medication for free in Australia; Mundipharma sell it at full price to the PBS.

> Well, we don't want to end up in the place that the United States is in where opioids are a national crisis. Here, we are in a much better position...

– Greg Hunt, transcript of Tyabb Doorstop, 23 June 2018

Tragically the 13,269 people who died from opioid use, are certainly not in a better position.

> It's time to call this what it is: Australia's very own overdose crisis. And make no mistake; it's a crisis that is getting worse.

– John Ryan, Chief Executive Officer of drug policy organisation, Penington Institute

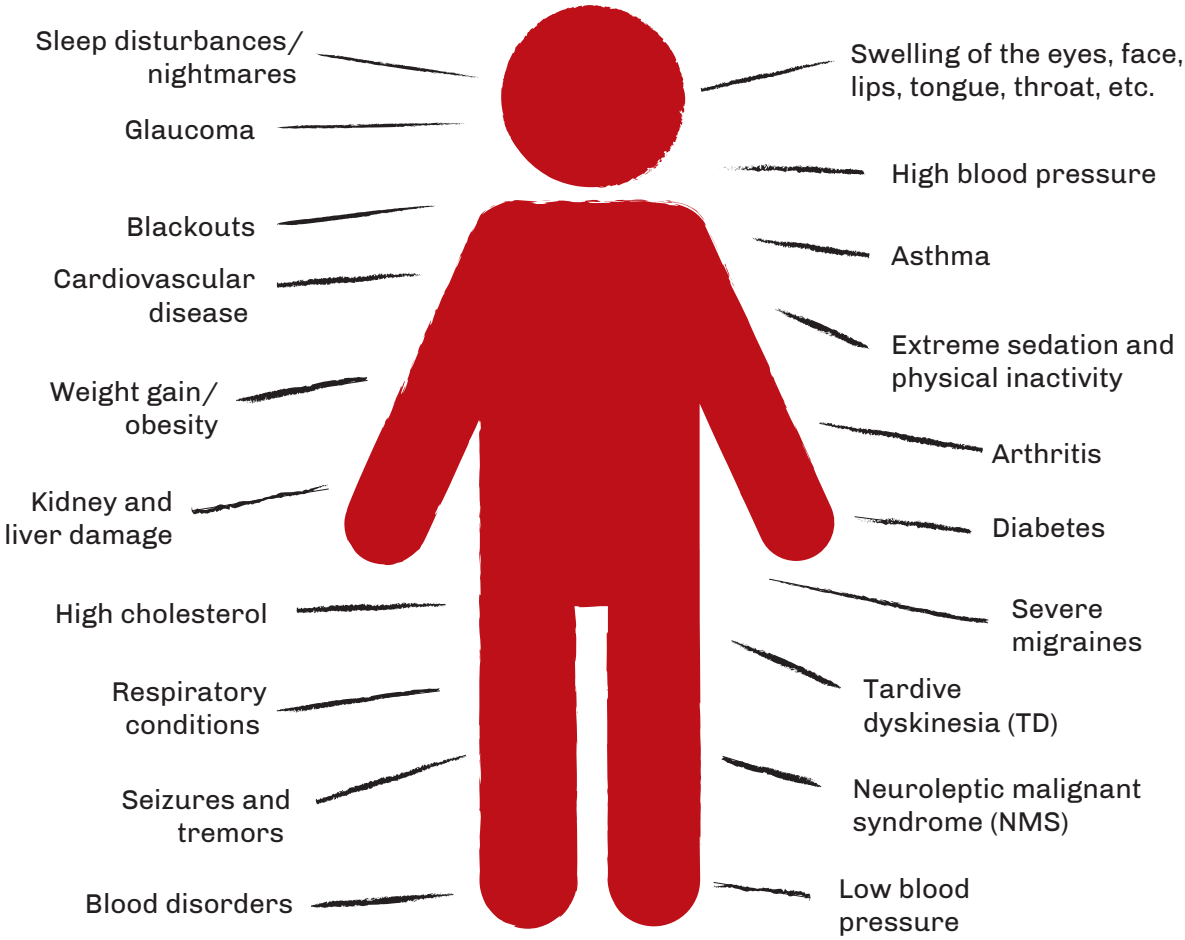
The legal action in the US has been successful based on the lack of consumer warnings that were provided about life-threatening risks. The exact same situation exists in Australia and it is time similar compensation is made payable to the victims.

SEVERE MENTAL ILLNESS – LIFE IN THE KILLING ZONE

> ...people with mental illness typically live between 10 and 32 years less than the general population.

– The Royal Australian and New Zealand College of Psychiatrists (RANZCP)

At least 800,000 Australians suffer from severe mental illness. Many also suffer from other physical conditions like chronic pain and even multiple mental illnesses. One million Australians suffer from both anxiety and depression. In addition to the life-threatening risks already mentioned, the medication prescribed also has many side effects that are described as life shortening; they are the main reason we live 10–32 years less than expected. **The medication prescribed for mental illness actually causes so much damage to our bodies that it shortens our lives. In trying to save people from suicide, we die prematurely due to physical illnesses**. Some of the side effects include:



This is one of the facts actually not disputed by the health care system; the physical damage from side effects has been known for decades. The Australian Government's National Mental Health Commission (NMHC) *2012 National Report Card on Mental Health and Suicide Prevention* confers:

> *"The finding regarding antipsychotic medications is most concerning. Most Australians may not know treatments with prescribed psychiatric drugs may lead to worse physical health. There are increased risks for some specific treatments such as antipsychotics and for those with underlying vulnerabilities such as diabetes. This can mean that the antipsychotic medications that are prescribed to manage severe mental illnesses such as schizophrenia, contribute to the risk of having severe physical illnesses. The decision for people to take medications to improve their mental health, is made often with the knowledge that their physical health and quality of life will suffer."*

People with lived experience will disagree that we have ever been made aware of these risks, and the CMIs provide no information on the trade-off we have made with our mortality.

Unlike other chronic illnesses like cancer, severe mental illness is not an illness that a person is expected to be cured from. Improving to a position of being in remission is rarely achieved or even discussed. We exist, we don't live. Our quality of life is poor and hope for a better life is all many have to hold on to. Unfortunately, hope can only last so long for many of us. The suicide rate among people with a mental illness is at least seven times higher than the general population. It is one of the main causes of our premature deaths.

In addition to the life-threatening and life-shortening risks, the lethal nature of our medications exposes us to risks that are described as life-ending. Prescription medication overdose is a common method of suicide. The same medications prescribed to vulnerable people with mental health and pain conditions are also toxic enough to be used as a means of suicide death, and sadly, they are being used for this purpose.

The statistics from the last 20 years show that opioids, benzodiazepines, antidepressants, and antipsychotics are not only the most common drugs present in accidental drug deaths, but they are also the same medications used in suicide attempts and deaths. Horrifyingly, in some instances, the very medication prescribed to treat the *risk* of suicide is used as a method of poisoning in suicide. Distressingly the increase in prescriptions of these medications to young Australians has resulted in an increase in their deliberate self-poisoning using these medications.

The risk of a person dying by suicide increases if they have access to lethal means of death, like a firearm. Suicide prevention experts classify the medications in this report as lethal means of death, comparable to having a loaded gun in the home. Prescribing medication that can cause death, actually increases the risk of suicide to people with mental illness. No CMI explains this or provides any strategies to reduce this risk.

"Reducing access to lethal means in the home, such as firearms and medication, can determine whether a person at risk for suicide lives or dies.

– Suicide Prevention Resource Center (US)

The medication given to mentally ill people provides us with a method for taking our own lives, funded by the PBS, right in our own homes. How can deadly medications be legally prescribed and PBS-funded, with almost no consumer warnings to help patients and their families protect against the use of these drugs in suicides? Is there a greater failing of any society, or a greater breach of our human rights, than when a health care system deliberately provides vulnerable people with a deadly means of ending their suffering, funded by taxpayers?

The architects of Australia's adult and youth mental health system argue that it is more dangerous to not use these medications to treat mental illness than to use them, which is a view not universally agreed. What is beyond dispute is that all the risks of using medications must be provided to obtain informed consent. This report has found no evidence of any written consumer information in which this occurs.

The tragedy of prescription medications being used in suicides is also not mentioned in our national suicide prevention plans or reports. The World Health Organization (WHO) recommends that national plans have specific objectives to *reduce the number of suicides as a result of overdose of medications*. It seems this doesn't apply to Australia.

The statistics prove that you do not live a long time with severe mental illness. The greater the number and severity of medical conditions, the greater the suffering, the greater the struggle to regain good health and the greater risk of suicide. That is why many of us describe life with severe mental illness as living in The Killing Zone.

> Although psychological strategies are the first-line of treatment, antidepressants and other drugs form an important part of the care provided. But only about half of patients have a positive response from their first medication prescription, and the response diminishes with subsequent alternatives. Current approaches of trialling different medications may result in prolonged episodes of depression, which impacts on quality of life and may increase the risk of suicide.

– Greg Hunt in a statement about pharmacogenomic testing

PRESCRIBED HOPE – A CHANCE FOR LIFE

There is hope for those in The Killing Zone. Several new medications are now available and many more are in the final stages of regulatory approval overseas.

The National Institute of Mental Health (NIMH) is the lead US federal agency for research on mental disorders. With an annual budget of USD $2 billion, it is the largest mental health research centre in the world. They have been the driving force behind a number of medications now in use or in trial stage. Ketamine, administered via an IV drip, is described as having strong, rapid antidepressant effects within hours, even for people who have not responded to previous medications. A nasal spray ketamine version called Spravato was recently launched, as was the first medication for postpartum depression called Brexanolone. Global trials of Psilocybin and MDMA are yielding incredible results in depression treatment, with notable organisations involved including Yale University, John Hopkins University and the Imperial College of London.

Medical cannabis has proven globally to be a life-saving treatment to enable a better quality of life for people with chronic pain and mental illness. Whilst it is available in Australia, the regulatory process and lack of PBS subsidy makes it out of reach to most people.

Unfortunately, the Productivity Commission and NMHC are silent on these new treatments. They are not mentioned in recent reports or recommendations at all. Despite the lobbying of many with lived experience and mental health groups, accessibility of these treatments is far from imminent.

Incredibly, the lead reason given for not embracing these new medications is a belief that they will expose Australians to dangerous side effects. Not only is this position in contrast to their actions on protecting Australians from the dangers of existing medications, it also ignores the current global evidence that these new treatments are actually safer and more effective. So why are they so reluctant to change?

TIME FOR ACCOUNTABILITY

As disgraceful as the actions of the pharmaceutical industry are, vulnerable people have actually never met them. They don't treat patients, they don't diagnose conditions, they don't prescribe medication, they don't dispense medication, they don't review the patient's conditions regularly, they don't know what other medication the patients are taking or even their stage of recovery. Producing a medication with dangerous side effects and an equally dangerous CMI in itself doesn't kill anyone. For that to happen, it has to get in the hands of a patient and there are a lot of critical failures that occur to make that happen.

Many failures have also occurred in response to our prescription medication crisis; that list is even greater.

The RANZCP acknowledges the adverse side effects of mental health medications and the shorter life expectancy they contribute to. However, the *attitude* of psychiatrists in Australia to this matter has long been seen as a barrier to acknowledging the required changes to the prescribing practices of psychiatrists. The RANZCP in a media release (which has since been deleted) said:

> *"Psychiatrists are highly trained medical professionals with expertise in managing both physical and mental health. The prescription of antidepressant or antipsychotic medications is something that a psychiatrist only ever does in partnership with the patient and after due consideration of the risks and benefits."*

The patients of psychiatrists in this country do not share this view. We have been demanding new treatments to kill our mental illnesses because the ones we have now just kill us. These medications are the responsibility of the RANZCP and there is a lot that they need to explain and change.

The Black Dog Institute, Beyond Blue and Orygen/Headspace have received billions in taxpayer funding, yet no independent review of the investment has ever been released. These organisations refer to themselves repeatedly as 'world leading', 'world class' in delivering 'evidence based treatments', yet the real world results tell a different story. The use of medications like fluoxetine (Prozac) in Headspace clinics demands further examination, considering the rise in youth self-harm using fluoxetine and the fact that Orygen/Headspace published guidelines on its use and the lack of warnings in the CMIs.

These organisations have the most noble causes at their heart, but good intentions don't save lives; good medicine does. Encouraging people to talk, to seek help, and to help others, is not a treatment. The frustration of many people with lived experience with these organisations is that we have provided them with decades of stories on the failure of safe medication prescription. Despite this, we are still prescribed ineffective treatments, with horrendous side effects, reduced life expectancy, and no alignment with international human rights. Reviewing the online forum of these organisations shows a litany of messages dating back over years that are cries for help.

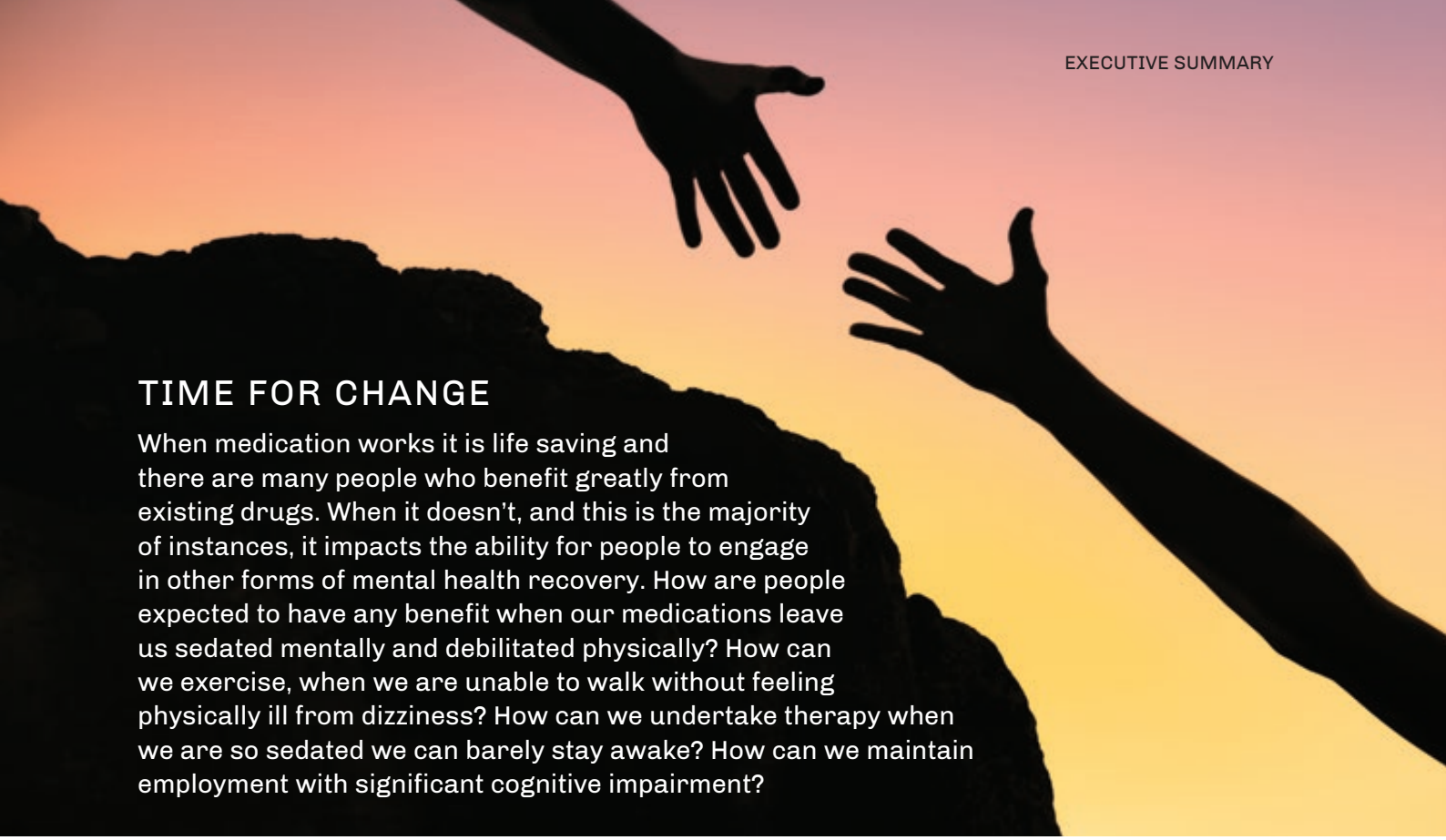
> Many doctors and many psychiatrists – not one talked about side-effects or interactions with other medications.

– online forum Beyond Blue (2013)

These organisations might not be the appropriate areas to implement the changes, but they absolutely have the obligation to fight for us until someone else does. It is not just lived experience that has been dismissed, but also the numerous reports provided by medication safety audits.

> Studies undertaken in the community have shown that people with mental illness who receive a collaborative medicines review have between four and seven medication-related problems per person, including problems with adverse drug reactions and drug interactions.

– Australian Commission on Safety and Quality in Health Care



TIME FOR CHANGE

When medication works it is life saving and there are many people who benefit greatly from existing drugs. When it doesn't, and this is the majority of instances, it impacts the ability for people to engage in other forms of mental health recovery. How are people expected to have any benefit when our medications leave us sedated mentally and debilitated physically? How can we exercise, when we are unable to walk without feeling physically ill from dizziness? How can we undertake therapy when we are so sedated we can barely stay awake? How can we maintain employment with significant cognitive impairment?

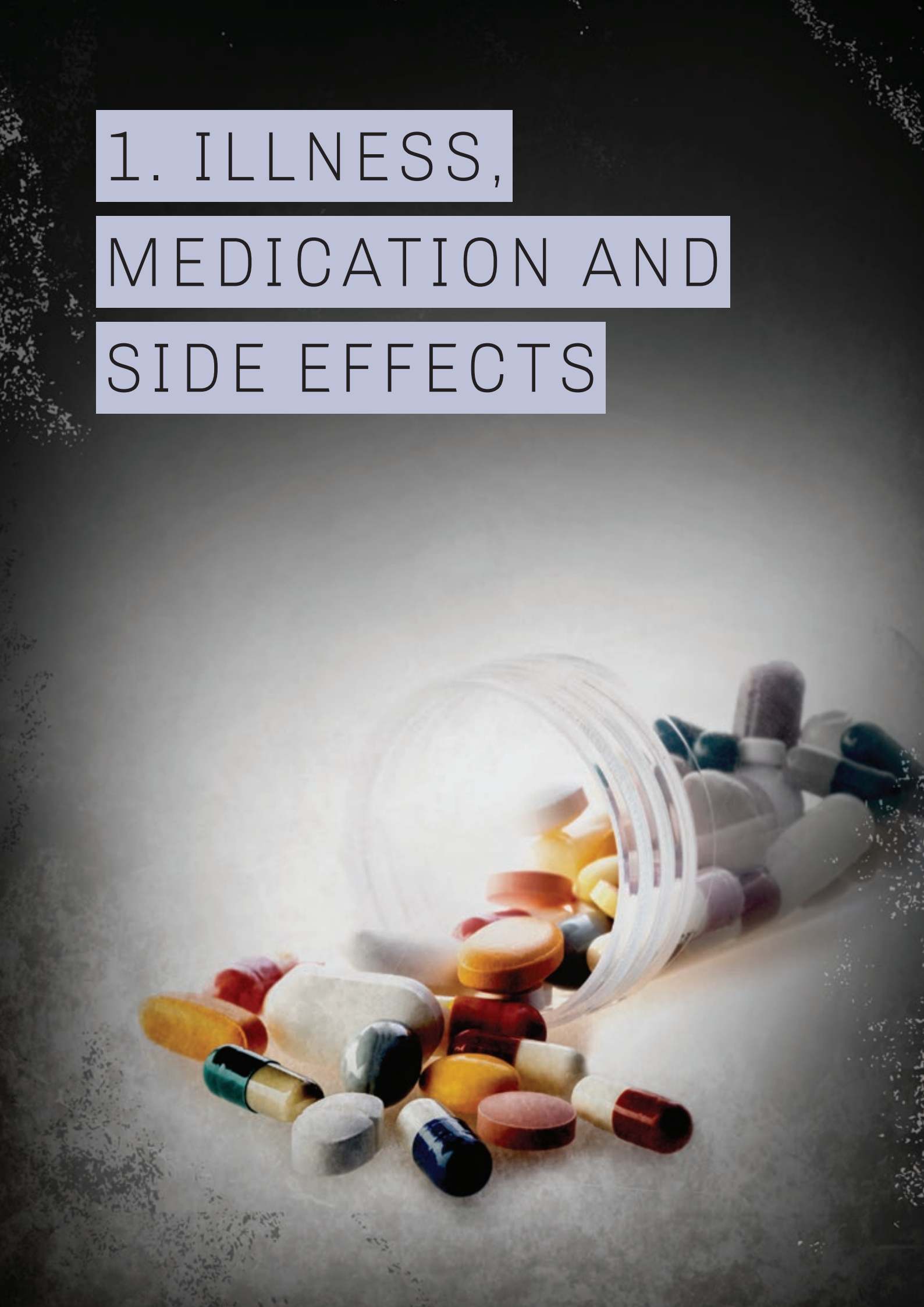
The best pathway to new treatments in all areas of mental health is to force national debate about the failures of the current health care model. We have no hope of a better life when government refuses to acknowledge and remedy the reasons why our life expectancy is 32 years shorter than it should be. We need a broad and all-encompassing Royal Commission into all areas of medication safety. Many aspects of this report demand criminal investigation. Thousands of lives have been lost. It is too easy to say that the system failed these people; **each person who died has a name**. Each person deserved better care from their doctors and those doctors have names. Each person deserved better care from their pharmacists and they have names too. The government officials who failed in their duty of care are easy to identify, as are the pharmaceutical brands they were prescribed.

The government's job is to save vulnerable people from disease and death. Saving vulnerable people from mental illness is no different to saving vulnerable people from COVID-19. Today, COVID-19 has no vaccine and no cure, and neither does mental illness. At the date of publication, COVID-19 has taken 102 Australian lives, and based on previous ABS reports, suicide will have taken over 1500 in the same time period.

Like cancer, the best way to stop mental illnesses is to treat it as soon as the symptoms appear. It is widely commented that people are slow to seek help for mental health conditions. The reason is attributed to a perceived stigma of these conditions. We have a different view. **People are not afraid of seeking help, they are afraid of the help they are going to get.** At all stages of a mental health illness, we need, expect and demand a level of intense focus to save our lives – with the same level of urgency that would be applied for a cancer diagnosis or a coronavirus pandemic. There is no other alternative.

The most important measure of success is actually not the lives that are saved from suicide, it is the quality of the life everyone who is afflicted gets to live. The health care system needs to be judged against delivering this outcome. There is no chance of achieving 'zero suicide' unless people are given a life worth living. More Australians will start talking when they can see a mental health system that saves lives, not reduces the quality and duration of them. Most importantly when this happens, and only then, can we finally start to win this war.

1. ILLNESS, MEDICATION AND SIDE EFFECTS



1. INTRODUCTION

Mental illness is a common health issue in Australia. Prescription medication is a core treatment strategy. These drugs have significant side effects.

Figure 1: Common medications for mental illness

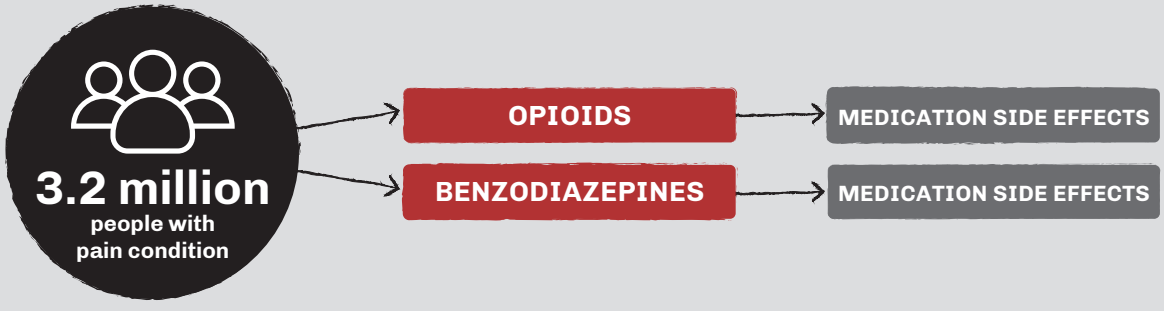
People can suffer from two or more mental illnesses. Those who suffer from multiple conditions (known as comorbidity), are treated with multiple medications (called polydrug use) and are exposed the multiple side effects.

Figure 2: Polydrugs for two or more mental illnesses

*e.g. 1 million people suffering from both depression and anxiety

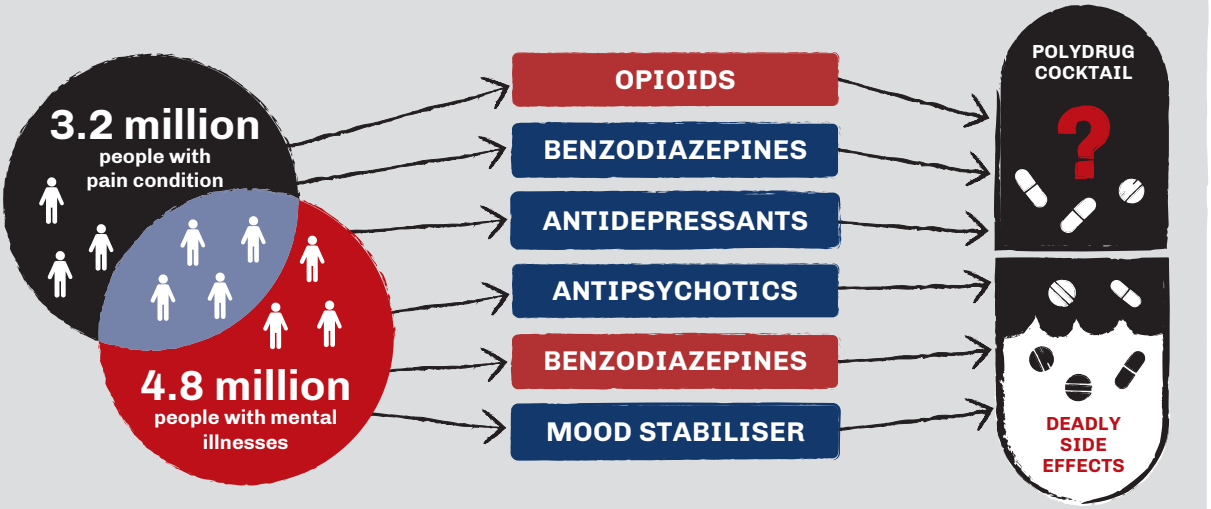
Pain is also a common health issue in Australia, for which prescription medication is also a core treatment strategy. Again, these drugs have significant side effects.

Figure 3: Common medications for pain



Sadly, many people suffer from both pain and mental illness (comorbidity). These are amongst Australia's most vulnerable and sick people because they suffer from **multiple conditions**, are treated with **multiple medications**, and are exposed to the **multiple side effects**.

Figure 4: Comorbidity treatment cocktail



The side effects of these prescription medications is significant. The medication/s prescribed have side effects that adversely impact overall patient health. Dependence on prescription medication is a well-established consequence, as is the evidence for overdose deaths and suicide.

There are three significant and alarming risks associated with the side effects of these medications. They can be:

Life Threatening

Life Shortening

Life Taking

Combined with the effects of chronic disease, the ability to make a recovery and pursue a good quality of life is an incredibly difficult goal. Moreover, the complexity of the treatment model makes adherence to treatment difficult.

2. MENTAL ILLNESS AND CHRONIC PAIN

2.1 MENTAL ILLNESS FOR ALMOST HALF OF ALL AUSTRALIANS

> Supporting mental health and suicide prevention is the Government's highest health priority, and is a central feature of our long-term National Health Plan. It is also a personal priority for the Prime Minister, Scott Morrison, and myself.[1]

– Greg Hunt, Federal Minister for Health, 10 October 2019

In Australia the most commonly reported chronic condition for both males and females in 2017–18 were mental health and behavioural conditions. The Australian Institute of Health and Welfare (AIHW) reported in 2018 that almost half (45%) of Australians aged 16 to 85 will experience a mental disorder such as depression, anxiety or substance use disorder at some stage in their life.[2] The Australian Bureau of Statistics (ABS) National Health Survey for 2017–18 showed that **4.8 million Australians** (20% of the estimated Australian population of 24.6 million) had a mental or behavioural condition in 2017–18.[3]

This figure represented an increase from the previous survey in 2014–15 when 4 million or 17.5% of Australians has a mental of behavioural condition. According to ABS data, this increase was due predominantly to a rise in the number of people with anxiety-related conditions or depression. **Anxiety-related** conditions were the most common mental or behavioural condition, with **13%** of Australians affected in 2017–18.[4]

However mental illness can complicate diagnosis and treatment in a unique and particularly challenging way. Having one mental illness, sadly, does not protect you from having another; in fact, it increases the likelihood of having more than one. An individual can be suffering at the same time from, for example, a major depressive disorder and a generalised anxiety disorder. The most common co-existing mental and behavioural conditions are **anxiety** and **depression.** According to ABS data, **one million** Australians (4.4%) experience both these conditions.[5]

A new study conducted by the University of Queensland, released in January 2019, revealed that people diagnosed with mood disorders like depression have a very high risk of being diagnosed with a neurotic disorder like anxiety in the first six months following diagnosis.[6]

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1 G Hunt (Minister for Health), World Mental Health Day 2019, media release, 10 October 2019.
2 Australian Institute of Health and Welfare (AIHW), Australia's Health 2018, Australia's Health Series no. 16, Canberra, 2018.
3 Australian Bureau of Statistics (ABS), National Health Survey, First Results, Australia 2017–18, 4364.0.55.001, Canberra, 2018.
4 ABS, 2018.
5 Australian Bureau of Statistics (ABS), National Health Survey: Mental Health and Co-existing Physical Health Conditions, Australia, 2014–15, 4329.0.00.004, Canberra, 2015, p6.
6 Professor J McGrath, University of Queensland 'Risk for Developing More Than One Mental Health Disorder Revealed', *Science Daily*, 17 January 2019.

We define mental and behavioural conditions as those where people reported that their condition was current and long-term; that is, it had lasted, or was expected to last, six months or more.[7]

2.2 COMORBIDITY COMPLICATIONS

> For people with mental disorders, comorbidities and their risk factors are the rule rather than the exception.[8]

– Royal Australian and New Zealand College of Psychiatrists

Having two or more co-existing chronic conditions at the same time is known as comorbidity or multi-morbidity.

Comorbidity brings with it a number of added complexities for the sufferer. There is the risk that the *interactions* between these conditions can actually worsen the status of each, and the overall level of health of the individual. There is also the risk the interaction of the side effects of the medical treatments for each condition can have a greater negative impact on a person's health.

Simply put, the greater the number and severity of comorbid conditions, the greater the suffering and the greater the struggle to regain good health. This situation may be unintended, but it can be anticipated and is a possible consequence that is recognised by government.

> At an individual level, Australians diagnosed with one or more chronic conditions often have complex health needs, die prematurely and have poorer overall quality of life.[9]

– AIHW

Mental illness is a chronic condition that appears to almost invite other chronic illnesses to manifest in the sufferer. For example, many people who are undergoing treatment for cancer may also develop a mental health issue like depression or anxiety, as a result of their cancer battle. In terms of mental health and comorbidity, **3.6 million Australians** (15.8% of all Australians), have reported co-existing long-term mental and behavioural, as well as physical health conditions.[10]

7 This definition of mental and behavioural conditions is based on the Australia Bureau of Statistics (ABS) definition in its National Health Survey, First Results, Australia 2017–18, Canberra, p40.

8 The Royal Australian and New Zealand College of Psychiatrists (RANZCP), *The Economic Cost of Serious Mental Illness and Comorbidities in Australia and New Zealand*, Melbourne and Wellington, 2016, p5.

9 AIHW, 2018, p94.

10 ABS, 2015, p1.

2.3 THE CHRONIC PAIN STRUGGLE

> Nowhere do psychiatric and medical pathologies intertwine more prominently than in pain conditions.[11]

– Pain Australia

Of all the chronic illnesses that a person can suffer from, in combination with mental illness, chronic pain is the one that we fear the most. If mental illness is regarded as a disease of the mind, then combining it with a disease of the physical body is nothing short of a living hell.

Unfortunately, this is a reality for millions of Australians.

> 3.2 million Australians live with painful conditions, from arthritis to low back pain, to endometriosis and fibromyalgia.[12]

– Productivity Commission

More than half of Australian adults with chronic pain become anxious or depressed because of their pain.[13] Beyondblue states that research indicates there are strong links between anxiety, depression and chronic physical illness.[14] Similarly, Painaustralia argues that **44.6%** of patients who presented to a pain specialist had comorbidity for chronic pain and depression or anxiety (according to a 2019 Deloitte Access Economics report).[15] Major depression is the most common mental health condition associated with chronic pain, with **30% to 40%** of people with a diagnosed mental health condition also presenting for treatment for chronic pain.[16]

The relationship between pain and mental health conditions may be bi-directional, with pain potentially linked to poorer mental health, and poor mental health increasing vulnerability to pain. There are several ways that pain and major depression may be associated:

- the psychological and physical distress of persistent pain may precipitate an episode of major depression for an individual
- depression may be a precursor to, and contribute to, an individual's experience of pain by lowering their level of pain tolerance
- chronic pain and major depression may both be associated with a common underlying process, such as a neurological illness or fibromyalgia.[17]

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11 R Gatchel, 'Comorbidity of chronic pain and mental health disorders: the biopsychosocial perspective', *Am Psych* 2009, quoted in Painaustralia, *Productivity Commission Inquiry Into the Role of Improving Mental Health to Support Economic Participation and Enhancing Productivity and Economic Growth*, Canberra, 2019, p1.

12 Painaustralia, *Productivity Commission Inquiry Into the Role of Improving Mental Health to Support Economic Participation and Enhancing Productivity and Economic Growth*, Canberra, 2019.

13 Healthdirect, Australian Government, accessed 3 April 2020, see https://www.healthdirect.gov.au/chronic-pain.

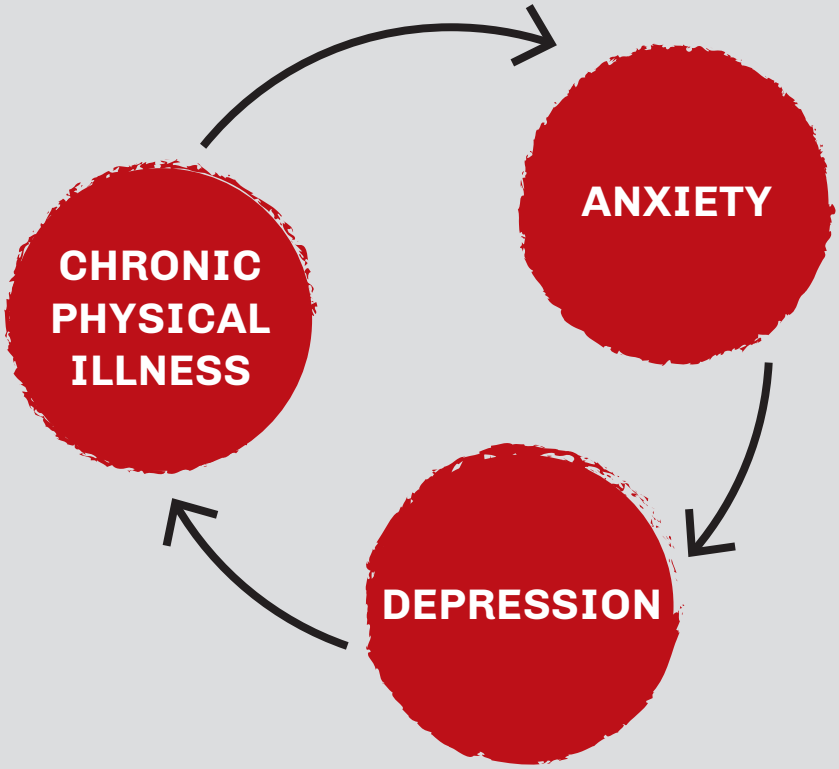
14 Beyondblue, *Chronic physical illness, anxiety and depression*, 2018, p2.

15 Deloitte Access Economics, *The Cost of Pain in Australia*, painaustralia, Canberra, 2019, p13.

16 A Holmes, N Christelis and C Arnold, 'Depression and Chronic Pain', *Medical Journal of Australia*, 199(6 Suppl): S17-S20, doi: 10.5694/mja12.10589, 2013.

17 Deloitte Access Economics, 2019, p13.

Figure 5: Links between mental health and chronic pain (Source: Painaustralia, 2019)



People managing both chronic pain and mental illness epitomise the endless struggle that exists. Patients with chronic pain and depression are more likely to describe increased sadness, reduced self-worth, lack of meaning and suicidality than those with pain alone.[18]

People with two or more mental and behavioural conditions only were five times as likely as the general adult population to report high or very high levels of psychological distress (55.9%). Similarly, those with co-existing mental and behavioural and physical health conditions were almost four times as likely (40.9%) to report high or very high levels of psychological distress as the general adult population.[19]

These higher levels of psychological distress present considerably greater risk of suicide. Another study shows that suicidal behaviour is two to three times higher in people with chronic pain than the general population.[20]

18 A Holmes, 2013.
19 ABS, 2015.
20 N K Tang and C Crane, 'Suicidality in Chronic Pain: A Review of the Prevalence, Risk Factors and Psychological Links', *Psychol. Med* 36:575–86, 2006.

3. PRESCRIPTION MEDICATIONS

The Pharmaceutical Benefits Scheme (PBS) provides Australians with a broad range of medications to treat mental illness and pain conditions. Antidepressants like Prozac are the most commonly used medication class to treat mental illnesses like depression and anxiety. Opioids, like Oxycodone, are the most commonly prescribed medication class for people suffering from chronic pain. Benzodiazepines, like Valium, are sedatives that can be used to treat both chronic pain and mental illness. Antipsychotics like Seroquel are used to treat illnesses with psychotic symptoms. Mood stabilisers like Lithium treat bipolar disorder, but it is also used to treat patients with suicidal ideation. Table 1 provides an overview of common medications prescribed under the PBS.

Table 1: Common PBS medicines to treat mental illness and chronic pain (Sources: Health Direct, Beyondblue, Painaustralia, Sane Australia, PBS)

Medication	Condition	How it helps	PBS examples
Opioids	Chronic pain	Opioid class drugs work by binding to opioid receptors in the brain which control pain and reward to inhibit messages of pain sent to the body.[21]	**Oxycodone** (**Endone, OxyContin, Targin**), **Codeine**, Tramadol, **Fentanyl**, Morphine
Benzodiazepines	Anxiety and chronic pain	Have calming and sedative effects due to their depressive activity on the central nervous system.[22]	**Alprazolam, Diazepam**, Oxazepam, Clonazepam, Temazepam, Oxazepam
Antipsychotics	For illnesses such as schizophrenia	Psychotic symptoms are associated with changes in a particular brain chemical called dopamine. Antipsychotic medications assist the brain to restore its usual chemical balance.[23]	Amilsulpride (Solian) Aripriprazole (Abilify) **Clozapine** (Clozaril, **Clopine**) **Olanzapine** (Zyprexa) Quetiapine (Seroquel) Risperidone (Risperdal)

21 J Le Merrer J Becker, K Befort, B Kieffer, 'Reward Processing by the Opioid System in the Brain', *Physiological Reviews*, Vol. 89, Issue 4, October 2009

22 Australian Institute of Health and Welfare (AIHW), Alcohol, tobacco & other drugs in Australia, cat. no: PHE 221, 2020.

23 Sane Australia, accessed 3 April 2020, see https://www.sane.org/information-stories/facts-and-guides/treatments-for-mental-illness#medication

Medication	Condition	How it helps	PBS examples
Antidepressants	Depression and anxiety	The symptoms of depression are associated with changes in a particular brain chemical called serotonin. Antidepressant medications assist the brain to restore its usual chemical balance.[24]	**Fluoxetine (Prozac)** Sertraline (Zoloft) Citalopram (Cipramil) Fuvoxamine (Luvox, Faverin, Mavox, Voxam) **Venlafaxine (Efexor)** Mirtazapine (Avanza, Mirtazon, Remeron, Axit-30) Paroxetine (Aropax, Oxetine, Paxtine)
Mood Stabilisers	Bipolar disorder	People with bipolar disorder (sometimes called manic depression) experience extremes of mood, ranging from 'highs' of irrational over-excitement to 'lows' of depression and despair. Lithium carbonate can help reduce the frequency of the recurrence of major depression and can also reduce the symptoms of manic or 'high' episodes.[25]	**Lithium carbonate (Lithicarb**, Quilonum)

The commonly prescribed medications of Endone, OxyContin, Fentanyl (Durogesic), and Valium will be analysed in Chapter 2.

These medications are supported by the PBS and for many Australians they provide a significant level of medical assistance in their battle to regain good health. The stigma around the use of the medications is often regarded as a barrier to people seeking help for mental health conditions.

Importantly, for people who ingest these medications on a **daily basis** there exists a far greater problem: the side effects associated with their long-term use.

24 ibid.
25 ibid.

3.1 HARMFUL SIDE EFFECTS

> Medicines are the most common treatment used in health care. Although appropriate use of medicines contributes to substantial improvements in health, medicines can also be associated with harm. Because they are so commonly used, medicines are associated with a higher incidence of errors and adverse events than other healthcare interventions. Some of these events are costly, in terms of morbidity, mortality and resources. Up to 50% are potentially avoidable.

– Australian Commission on Safety and Quality in Healthcare[26]

These are the most significant side effects of the most common classes and types of medications.

It must be understood that the PBS medications commonly prescribed for particular conditions are, in some cases, more detrimental to our health than our illnesses.

3.1.1 Antipsychotic medication

When looking at an example of an antipsychotic medication, *Seroquel*, it may cause serious side effects[27], including:

- risk of suicidal thoughts or actions
- falls
- high blood sugar (hyperglycaemia)
- high fat levels in your blood (increased cholesterol and triglycerides)
- drowsiness
- sudden drop in blood pressure upon standing
- weight gain
- sluggishness
- abnormal liver tests
- upset stomach
- dry mouth
- dizziness
- weakness
- abdominal pain
- constipation
- sore throat
- high fever
- excessive sweating
- rigid muscles
- confusion
- changes in your breathing, heartbeat, and blood pressure
- risk of death in the elderly with dementia
- stroke that can lead to death can happen in elderly people with dementia who take medicines neuroleptic malignant syndrome (NMS)
- movements you cannot control in your face, tongue, or other body parts (tardive dyskinesia)
- increases in blood pressure in children and teenagers
- low white blood cell count
- cataracts
- seizures
- abnormal thyroid tests
- increases in prolactin levels

26 Australian Commission on Safety and Quality in Healthcare, *National Safety and Quality Health Service (NSQHS) Standards*, Medication Safety Standard, accessed on 20 April 2020, see https://www.safetyandquality.gov.au/standards/nsqhs-standards/medication-safety-standard

27 FDA Medication Guide SEROQUEL 2019 ©AstraZeneca.

3.1.2 Antidepressant medication

When looking at an example of an antidepressant medication, *Efexor XR*, it may cause serious side effects[28], including:

- suicidal thoughts or actions
- Serotonin Syndrome (can be life-threatening)
- changes in blood pressure
- manic/hypomanic episodes
- seizures or convulsions
- abnormal bleeding
- elevated cholesterol
- enlarged pupils (mydriasis)
- anxiety and insomnia
- changes in appetite or weight
- low salt (sodium) levels in the blood
- increase in heart rate
- lung disease and pneumonia
- severe allergic reactions
- unusual dreams
- sexual problems
- loss of appetite, constipation, diarrhoea, nausea or vomiting, or dry mouth
- feeling tired, fatigued or overly sleepy
- change in sleep habits, problems sleeping
- yawning
- tremor or shaking
- dizziness, blurred vision
- sweating
- feeling anxious, nervous or jittery
- headache

3.1.3 Benzodiazepines

Benzodiazepines are most commonly prescribed to relieve stress and anxiety and to help people sleep. However, there is increasing concern among medical professionals about the risks of using these drugs, particularly when they are used for a long time.[29]

Benzodiazepines have a muscle relaxant effect.[30] Whilst it is a drug prescribed for mental health conditions, the muscle relaxant effect means that benzodiazepines can also assist with pain management and can be used to treat pain conditions.

Giving up benzodiazepines after using them for a long time is challenging because the body becomes un-used to functioning without them. **Benzodiazepines can cause overdose, particularly when used with alcohol or other drugs. They are also associated with addiction, dependence and withdrawal symptoms, even after a short period of use.**

28 FDA Medication Guide Efexor XR 2017 © Pfizer.

29 Alcohol and Drug Foundation, published on 28 January 2020, see https://adf.org.au/drug-facts/benzodiazepines/

30 National Drug and Alcohol Research Centre for the Department of Health, *Benzodiazepines, What You Need to Know About Sleeping Pills*, Canberra, 2014, p2.

The side effects of benzodiazepines include:

Common side effects	Long-term side effects	Overdose symptoms	Withdrawal
– depression – confusion – feelings of isolation or euphoria – impaired thinking and memory loss – headache – drowsiness, sleepiness and fatigue – dry mouth – slurred speech or stuttering – double or blurred vision – impaired coordination, dizziness and tremors – nausea and loss of appetite – diarrhoea or constipation.	– addiction – impaired thinking or memory loss – anxiety and depression – irritability, paranoia and aggression – personality change – weakness, lethargy and lack of motivation – drowsiness, sleepiness and fatigue – difficulty sleeping or disturbing dreams – headaches – nausea – skin rashes and weight gain.	– over-sedation or sleep – jitteriness and excitability – mood swings and aggression – slow, shallow breathing – unconsciousness or coma – death (more likely when taken with another drug such as alcohol).	– headaches – aching or twitching muscles – dizziness and tremors – nausea, vomiting, stomach pains – bizarre dreams, difficulty sleeping, fatigue – poor concentration – anxiety and irritability – altered perception, heightening of senses – delusions, hallucinations and paranoia – seizures.

3.1.4 Opioids

The AIHW define opioids as:

> *A group of pain-relieving drugs that work by interacting with the brain's opioid receptors and changing how they respond to pain stimuli. As well as relieving pain, opioids can produce euphoria (a sense of profound wellbeing).*
>
> *Opioids can be grouped in several different ways. 'Strong' and 'weak' opioids are defined based on how much is needed to produce the desired pain-relieving effect, often in comparison with morphine. 'Strong' opioids are more potent, so a smaller amount is required to relieve pain compared with a 'weak' opioid. Hydromorphone and oxycodone are more potent than morphine, as is fentanyl, which is considered to be up to 100 times as potent as morphine (Chodoff & Domino 1965). More potent opioids are typically prescribed in smaller doses than morphine.*[31]

31 Australian Institute of Health and Welfare (AIHW), *Opioid Harm in Australia and Comparisons between Australia and Canada*, Canberra, 2018, pp2–3.

The side effects[32] of opioids include:

General side effects	Long-term side effects	If a large dose is consumed, someone may develop	Withdrawal
– extreme relaxation – drowsiness and clumsiness – confusion, slurred speech – slow breathing and heartbeat.	– addiction – increased tolerance – constipation – dependence – damage to vital organs such as the lungs, brain and heart.	– cold, clammy skin – slow breathing – blue lips and fingertips – falling asleep ('going on the nod') – death by respiratory depression.	– craving – anxiety, restlessness and irritability – disturbed sleep – gastrointestinal tract symptoms (for example anorexia, abdominal pain, nausea, vomiting and diarrhoea) – muscle, bone and joint aches and pains, headache, muscle cramps – tremor – lacrimation, rhinorrhoea and sneezing – yawning – hot and cold flushes, sweating and piloerection.

NOTE: International package shown. Australian package contains no warning on the risk of addiction nor is this contained in the CMI.

32 Alcohol and Drug Foundation, published on 28 January 2020, see https://adf.org.au/drug-facts/opioids/

Figure 6: Prescription opioid side effects (Source: Reach for the Facts[33])

For some, longer-term opioid use can lead to tolerance as well as a condition known as opioid-induced hyperalgesia, lowering the body's pain threshold and actually increasing pain.

An example of a 'weak' opioid is Codeine and common brands include Panadeine, Panadeine Forte and Nurofen Plus.[34]

Fentanyl is considered a strong opioid, available in different forms and strengths, including Transdermal patches (Durogesic® and generic versions). It is prescribed for chronic or acute severe pain as a result of cancer, nerve damage, back injury, major trauma and surgery. In Australia, fentanyl is subject to strict legislative controls because it is a **Schedule 8 drug**, which is a classification for drugs known to be **addictive**. It is up to 100 times stronger than morphine.[35]

33 Reach For The Facts, accessed on 3 April 2020, see https://reachforthefacts.com.au/side-effects/
34 Faculty of Pain Medicine, ANZCA, *Opioid Dose Equivalence*, 2019.
35 Alcohol and Drug Foundation, published on 15 August 2019, see https://adf.org.au/drug-facts/fentanyl/

3.1.5 Controlled drugs

According to Health Direct, all medicines and poisons in Australia are categorised by how they are made available to the public. Medicines with a low safety risk are usually less tightly controlled than medicines that have a higher safety risk. This system is called 'scheduling'.[36]

Scheduling is designed to protect public health and safety because some medicines have a higher risk of causing harm than others. Also, some medicines are more likely to be misused, such as medicines that can cause dependence or addiction. Scheduling is a way of sorting out which medicines or poisons need to be more tightly controlled, and which don't.

On the Victorian health website, scheduled medicines are called **poisons** and explained like this:

> ***Schedule 8 poisons***
>
> *Schedule 8 poisons (labelled 'Controlled Drug') are medicines with strict legislative controls, including opioid analgesics – for example, pethidine, fentanyl, morphine (MS-Contin®, Kapanol®), oxycodone (OxyContin®, Endone®), methadone (Physeptone®) and buprenorphine. Two benzodiazepines (flunitrazepam and alprazolam) are also classified as Schedule 8 poisons and ketamine is a Schedule 8 poison, which some nurse practitioners may be authorised to prescribe.*
>
> ***Schedule 4 poisons***
>
> *Schedule 4 poisons (labelled 'Prescription Only Medicine') include most other medicines for which prescriptions are required – for example, local anaesthetics, antibiotics, strong analgesics (such as Panadeine Forte®) – and that are not classified as Schedule 8 poisons. Whereas most benzodiazepines are Schedule 4 poisons; flunitrazepam and alprazolam are classified as Schedule 8 poisons.*
>
> ***Schedule 2 and 3 poisons***
>
> *Schedule 2 and 3 poisons (labelled 'Pharmacy Medicine' or 'Pharmacist Only Medicine', respectively) include some local anaesthetics and analgesics that are commonly referred to as over-the-counter medicines.*
>
> ***Drugs of dependence***
>
> *Drugs of dependence are substances, listed in Schedule 11 of the Act, known to be subject to misuse and trafficking. They include all Schedule 8 poisons, and some Schedule 2, Schedule 3 and Schedule 4 poisons known to be the subject of misuse and trafficking – for example, benzodiazepines, midazolam, Duromine® and anabolic steroids.*[37]

Table 2: Medicine categorisation based on risk

Schedule 8 Poisons	Schedule 4 Poisons
Fentanyl (Durogesic), Oxycodone (OxyContin®, Endone®), Targin, Alprazolam (Xanax)	Benzodiazepines (Valium, Diazepam), Panadeine Forte, Lithium, Efexor, Prozac, Dexamfetamine

36 Healthdirect, Australian Government, accessed on 3 April 2020, see https://www.healthdirect.gov.au/scheduling-of-medicines-and-poisons

37 Victorian Department of Health, accessed on 3 April 2020, see https://www2.health.vic.gov.au/public-health/drugs-and-poisons/scheduled-medicines

3.1.6 Iatrogenic dependence

The risk of addiction is present with a wide range of drugs prescribed to people with mental illness and pain conditions. Many medications prescribed under the PBS have a risk of iatrogenic dependence.

What is iatrogenic dependence?

According to a 2017 report by the AIHW:

> *Iatrogenic dependence occurs when an individual develops a physical dependence to a pharmaceutical drug after using it to treat a legitimate medical issue. In Australia, Schedule 8 drugs — such as **oxycodone, fentanyl and alprazolam** — are intended for therapeutic use. But these drugs have high potential for **abuse and addiction**, and are often the most susceptible to producing iatrogenic dependence. Symptoms of dependence can include difficultly in controlling use, craving, persisting despite adverse consequences, tolerance, and withdrawal (WHO 1993).*
>
> *People with iatrogenic dependence might be consuming pharmaceutical drugs in excessive quantities or frequencies to support their dependence. Importantly, this form of 'misuse' differs to other forms of non-medical use, in that the pharmaceutical drugs are not being deliberately abused to produce certain desired effects, such as euphoria. There are challenges in estimating the prevalence of iatrogenic dependence in Australia, due to variations in definitions of 'dependence'.*
>
> *One study found that **8–25% of people taking opioids for chronic non-cancer pain for more than six weeks met the criteria for some form of dependence**, with variations according to the definition adopted (Campbell et al. 2016). Another study found that 1 in 5 people using long-term opioids met the criteria for substance use disorder, and about half of those met the diagnostic criteria for pharmaceutical opioid dependence (Degenhardt et al. 2015).* [38]

The scale of the problem is also demonstrated by the large number of Australians who are currently dependent on prescription opioids.

> NSW Health estimates that there may be 750,000 Australians currently dependent on pharmaceutical opiates, the overwhelming majority of whom are not recognised as having a dependency problem but who nevertheless receive repeat prescriptions.[39]
>
> *– State Coroner's Court of NSW*

38 Australian Institute of Health and Welfare (AIHW), *Non-medical Use of Pharmaceuticals: Trends, Harms and Treatment, 2006–07 to 2015–16*, Drug treatment series no. 30 Cat. No. HSE 195, Canberra, 2017, p17.

39 State Coroner's Court of NSW, *Inquest into the death of DB 2016/00139604...*, Lidcombe, NSW, 2019, p31.

> It starts innocuously enough. You have your wisdom teeth out and are given an opioid like oxycodone for pain relief. You complain of insomnia and your doctor prescribes you Xanax, Valium or another benzodiazepine. You feel the onset of a migraine and head to the pharmacy for codeine. For most of us it's just a way to manage pain in the short term. But for some people, it's a pathway to addiction, or worse.[40]

– Health Agenda, HCF

The UN's 2014 World Drug Report listed **Australia as second only to the US in prescription drug addiction**.[41]

This is not a recent discovery. Following a formal inquiry, a 2007 report to the Victorian Parliament on the misuse/abuse of benzodiazepines and other forms of pharmaceutical drugs in Victoria identified that abuse of prescription drugs as a result of iatrogenic treatment was 'a serious and to a certain extent **unrecognised** problem'.[42]

The report noted that people might seek pharmaceutical narcotics and benzodiazepines because they have become dependent on a drug they were prescribed through their treatment for a previous or continuing medical condition. A good example of this was chronic pain patients who may become opioid-dependent as a result of long periods of consuming prescribed or over-the-counter analgesics.

Another example provided was long-term users of benzodiazepines. As noted by the support agency TRANX in their submission to the Inquiry, it had been known for many years that use of benzodiazepines at the appropriate prescribed dose for more than a few weeks could result in a dependence syndrome and serious physical complications associated with withdrawal.[43]

Numerous problems can occur when pharmaceutical drugs such as benzodiazepines and narcotic analgesics are used for non-medical purposes. Even when used as prescribed and under the care of a medical practitioner these drugs can have adverse effects. An example of this are the problems associated with long-term use of benzodiazepines. The Inquiry's report drew on a submission by TRANX in this regard:

> *In the case of the benzodiazepines, significant harm has been and continues to be caused to people taking these drugs in prescribed doses, but for inappropriately long periods of time. Many of these people have taken doses within the recommended daily dose limit, have only seen one GP and have taken the drugs as advised by their medical practitioner.* ***It may be more appropriate to describe the drugs as being 'mis-prescribed' rather than 'misused'***.[44]

What can we learn from the US opioid epidemic and class actions? Read Chapter 8.

40 HCF, *Addictive prescription drugs: Understand the risks*, published April 2017, see https://www.hcf.com.au/health-agenda/health-care/treatments-and-procedures/prescription-medications

41 ibid.

42 Parliament of Victoria, Drugs and Crime Prevention Committee (DCPC), *Inquiry into the Misuse/Abuse of Benzodiazepines and Other Forms of Pharmaceutical Drugs in Victoria–Final Report*, Melbourne, 2007, p95.

43 ibid. Submission of Gwenda Cannard, Director, TRANX (Tranquilliser Recovery and New Existence) Inc. to the Inquiry in June 2006. TRANX subsequently changed its name to ReConnexion.

44 Parliament of Victoria, DCPC, 2007, Submission of Gwenda Cannard, Director, TRANX (Tranquilliser Recovery and New Existence) Inc. to the Inquiry in June 2006, p63.

According to an article titled, *Is Australia next in line for an opioid class action?*:

> *To put it another way, 1.9 million Australian adults initiate opioid use, and 3 million use opioids each year.*

> *Samanta Lalic, a clinical pharmacist and PhD candidate at Monash University, says dependant users are often first exposed to prescription painkillers for chronic conditions like back pain. They need stronger doses as the pain persists and they grow accustomed to the medication. If they hit obstacles sourcing legal prescriptions, they might turn to illegal opioids. Heroin is a common progression.*

> *"People assume that the stereotype of a drug user or 'addict' is the depraved, criminal, homeless junkie or druggie," says Lalic. "But what we have actually seen is that it can be anyone who initiates opioid use and becomes dependant. The reality is more mainstream, suburban, white-collar and regional."*[45]

Unfortunately, iatrogenic dependence is a significant issue faced by people with mental illness and pain conditions, however it is one that is rarely included as a factor of prescription medication addiction by government. While the risks and side effects of these medications are well known, when the side effects do occur – even when being taken as prescribed – these side effect consequences are invariably attributed and dismissed as 'misuse and abuse' rather than recognising iatrogenic causes.

The Society of Hospital Pharmacists of Australia (SHPA) report found more than 70% of hospitals send patients home with powerful opioids 'just in case'. More than 60% of hospitals were found to be writing opioid prescriptions even before a decision had been made to discharge the patient.[46]

3.1.7 The genetics mystery

How a person responds to a medication is determined by their biology. This means that the same dose and type of a medication will have different responses for people based purely on the way their body processes it. Wide variations can and do occur.

According to a US Pharmacogenetic Testing and Opioids paper:

> *A majority of medications are metabolized by the liver's CYP450 system. Metabolism of specific pain medications differs among individuals due to pharmacogenetic variation. The CYP450 enzymes, CYP3A4 (fentanyl) and CYP2D6 (codeine, hydrocodone, oxycodone, tramadol) are involved in the metabolism of opioids.*
>
> *Patients with CYP450 pharmacogenetic variations may respond differently to opioids, ranging from drug unresponsiveness to toxicity with elevated serum levels.*[47]

Codeine is an opioid. It is a common analgesic metabolised by CYP2D6 enzymes. A person's response to codeine is determined by their genes, specifically a gene that codes for the enzyme CYP2D6. This enzyme activates codeine by converting it to morphine in the body. So, depending on individual DNA, some people don't get any effect from codeine, some get a 'normal' effect, while others find it toxic at what is normally considered a safe dose (see Figure 7).[48]

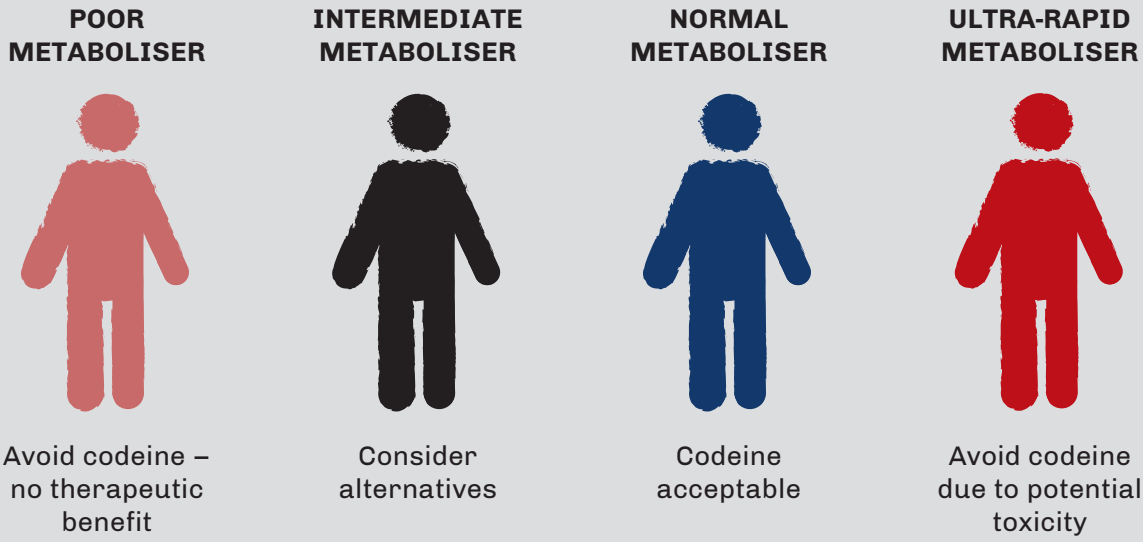
45 K Allman, LSJ Online, 'Is Australia next in line for an opioid class action?', 4 June 2019.

46 Society of Hospital Pharmacists of Australia, *Reducing Opioid-Related Harm: A hospital pharmacy landscape paper*, Collingwood, Victoria, November 2018.

47 T Collins and D Nykamp, Pharmacogenetic Testing and Opioids, sourced from https://www.uspharmacist.com/article/pharmacogenetic-testing-and-opioids,2015.

48 Royal Australian College of General Practitioners (RACGP), accessed on 3 April 2020, see https://www.racgp.org.au/clinical-resources/clinical-guidelines/key-racgp-guidelines/view-all-racgp-guidelines/genomics-in-general-practice/pharmacogenomics-more-information

Figure 7: Codeine has a different affect depending on metabolism (Source: Royal Australian College of General Practitioners)

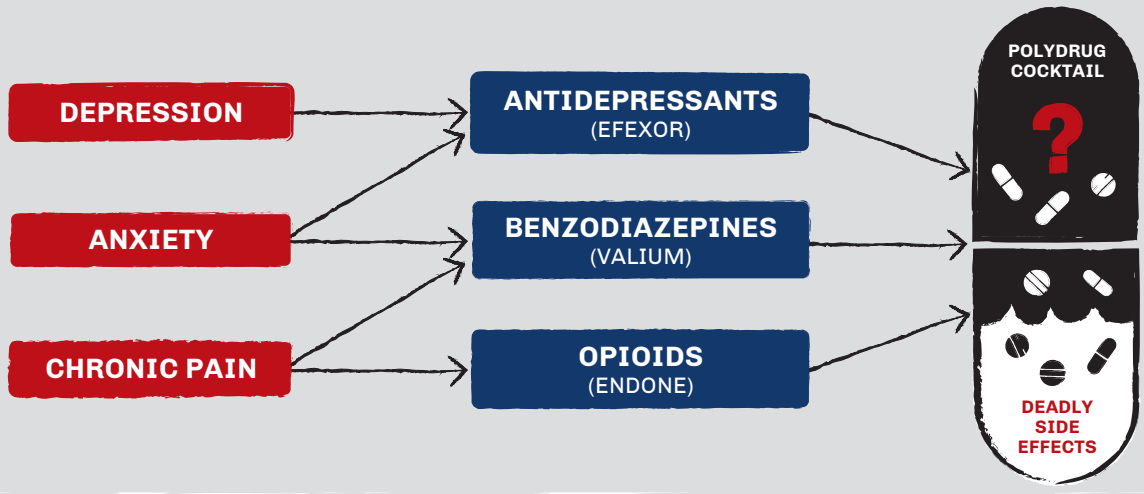


International guidelines exist for different medications and doses, for each metaboliser status, to reduce the likelihood of drug toxicity. **This Codeine example shows that adverse drug events for many people occur are prescribed levels and are completely unrelated to 'misuse and abuse' behaviours.**

3.2 OUR PRESCRIPTION PHARMACEUTICAL COCKTAIL (POLYDRUGS)

Life with comorbid conditions means treatment with multiple prescription medications. Polydrug use or polypharmacy is when a person uses multiple medications, at the same time, to treat one or more conditions. The side effects of the medication prescribed is significant, but when these medications are ingested together, the combined effect on the person can be deadly. Polypharmacy can be associated with multiple side effects, interactions and patient harm.[49]

Figure 8: Drug interactions



49 General Practice Supervisors Australia, accessed 3 April 2020, see https://gpsupervisorsaustralia.org.au/product/polypharmacy-deprescribing/

For example, a person who has depression, anxiety and chronic pain may be prescribed an antidepressant, a benzodiazepine and an opioid medication. The deadly side effect risk of this polydrug combination is outlined in numerous government documents and websites, including on the Alcohol and Drug foundation website:

Using benzodiazepines with other drugs

The effects of taking benzodiazepines with other drugs can be unpredictable and dangerous, and could cause:

Benzodiazepines + alcohol or opiates (such as heroin): breathing difficulties, an increased risk of overdose and death.

Benzodiazepines + some pharmaceutical drugs: strong pain-relievers, antidepressants, anticonvulsants, antipsychotics, some antihistamines and over the counter medications can have an adverse effect when taken with benzodiazepines and lead to breathing difficulties, an increased risk of overdose and death.[50]

Effects of opioids

Many people do not realise that many medications prescribed for pain relief can cause dependence. If they are overused, or combined with other drugs that depress the central nervous system, such as alcohol or benzodiazepines, they may lead to an overdose. Pharmaceutical opioids now account for more drug-related deaths in Australia than any other drug category.[51]

Using opioids with other drugs

The effects of taking opioids with other drugs – including over-the-counter or prescribed medications – can be unpredictable and dangerous, and could cause:

Opioids + alcohol, or benzodiazepines: slow down breathing and brain activity, and increased risk of overdose.[52]

The Penington Institute underscores the risk of benzodiazepines with other drugs, in particular opioids:

> Like opioids, benzodiazepines slow down the central nervous system and consistently rate as one of the most common drug groups detected in drug-induced deaths. When taken alone, benzodiazepines' depressant effect on the respiratory system does not usually result in complete loss of breathing function. However, their effect on respiration is increased when combined with other drugs like alcohol or opioids, making concurrent use of benzodiazepines with alcohol and/or opioids especially dangerous.[53]

50 Alcohol and Drug Foundation, published 28 January 2020, see https://adf.org.au/drug-facts/benzodiazepines/
51 Alcohol and Drug Foundation, published 28 January 2020, see https://adf.org.au/drug-facts/opioids/
52 ibid.
53 Penington Institute, Australia's Annual Overdose Report 2019, Melbourne, 2019, p17.

The Australian Government's National Health and Medical Research Council, in relation to a clinical trial seeking to improve quality use of medicines and outcomes in older hospital patients, has also published:

> *There has been a major increase in polypharmacy (multiple medicines use) in Australia over the past decade and the prevalence continues to rise, especially in older adults.* ***Polypharmacy can lead to medication errors, adverse drug reactions, falls, confusion, frailty, loss of independence, hospitalisation and mortality****.*[54]

And Science Daily stated in June 2019:

> *Common antidepressants interact with the opioid pain medication tramadol to make it less effective for pain relief, according to a study from University Hospitals (UH). These findings have important implications for the opioid epidemic, suggesting that some patients suspected of drug-seeking may in fact be under-medicated and just are seeking more effective pain relief. They also could help explain why some people exceed the prescribed dose of tramadol, increasing their risk of addiction.*[55]

Polydrug prescriptions are one of the greatest dangers to patients. Prescription medication should only be prescribed after assessing the risks and benefits of that medication and all others it will interact with. However, the lethal nature of many polydrug combinations is not being met with an appropriate level of patient safety in Australia. The health care system in Australia is failing.

A study released in 2015, titled the Pain and Opioid IN Treatment (POINT) study, recruited candidates with the assistance of the Pharmacy Guild and pharmacists located around Australia. The study identified patterns of pharmaceutical opioid prescribing, and the risk of adverse events. The 1,500 study participants were all patients that were prescribed opioids for chronic non-cancer pain.[56]

The study found that the most commonly prescribed strong opioid was *oxycodone*. Over half of all participants were currently prescribed an *antidepressant*, and approximately two-thirds were concurrently prescribed a *benzodiazepine*.

The report also noted that two of the three groups studied,

> were also prescribed higher doses of opioids, were more likely to also be prescribed codeine, and were likely to be taking concurrently prescribed benzodiazepines, antidepressants, and antipsychotics. Taken together, these characteristics suggest a very high-risk group, with multiple concomitant risk factors for overdose due to polypharmacy.[57]

54 National Health and Medical Research Council (NHMRC), Australian Clinical Trials, accessed on 3 April 2020, see https://www.australianclinicaltrials.gov.au/anzctr/trial/ACTRN12617000926336

55 University Hospitals Cleveland Medical Center, 'Common antidepressants interact with opioid med to lessen pain relief', *Science Daily*, 2019.

56 G Campbell, et.al., The Pain and Opioids IN Treatment study: characteristics of a cohort using opioids to manage chronic non-cancer pain, *PAIN*, 2015 Feb;156(2):231-42, doi: 10.1097/01.j.pain.0000460303.63948.8e.

57 ibid.

These individuals were all recruited through the nation's network of pharmacies and the report was released in 2015. This is a sizeable study representation of the consumers who access prescription medication from pharmacies nationwide.

Polydrug prescriptions are not only extremely dangerous, they are very common.

See how pharmacists are advising people with lived experience about the health impacts from polydrug side effects in Chapter 4.

4. WHOLE PERSON SIDE EFFECTS

RANZCP has reported alarmingly poor outcomes for people with comorbid mental and physical conditions – and the fact that there are ways to improve these outcomes, including in relation to managing multiple medications.

The report has also addressed that while antipsychotic medications might be effective in managing mental health symptoms, they can have a range of side effects that can undermine overall good health. As the prescribers of these medications, psychiatrists have an added responsibility to screen and intervene to manage the side effects of medication. The report also acknowledges that more needs to be done by psychiatrists and others to ensure that people are not carrying a double burden of mental illness as well as the (mostly preventable) side effects of anti-psychotic medication. The report notes that psychiatrists (and other health professionals) must discuss treatment options with people in a way which ensures that they can make informed decisions about medication and its effects.

The RANZCP report recognised an intrinsically related problem that needs to be addressed: there is a need for further investments by the pharmaceutical industry to **develop medications with less-deleterious side effects**, stating, "The College is disappointed that so little has been done to develop better medication options for people with serious mental illness.[59]

58 The Royal Australian & New Zealand College of Psychiatrists (RANZCP), Keeping Body and Mind Together: Improving the physical health and life expectancy of people with serious mental illness, 2015, p6.

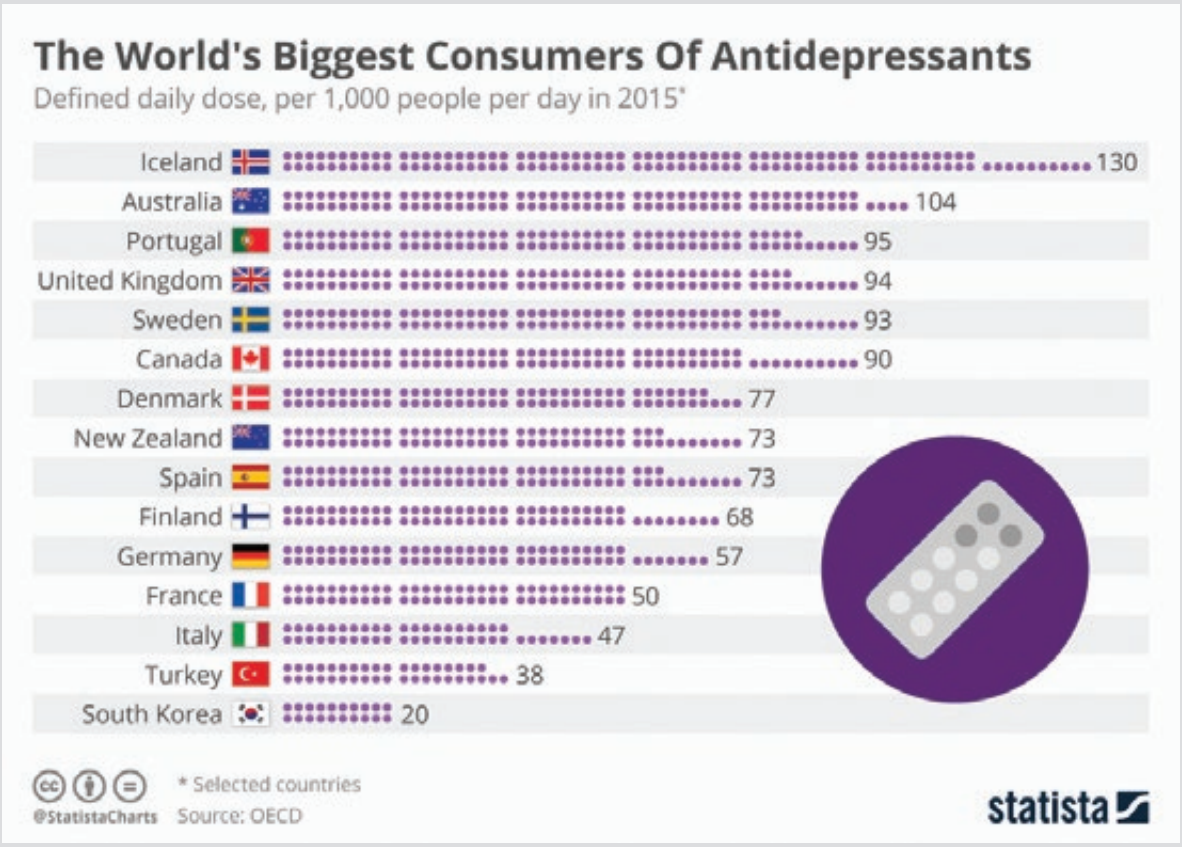
59 ibid.

The Australian Government's National Mental Health Commission (NMHC) *2012 National Report Card on Mental Health and Suicide Prevention* confers:

> *"The finding regarding antipsychotic medications is most concerning. Most Australians may not know treatments with prescribed psychiatric drugs may lead to worse physical health. There are increased risks for some specific treatments such as antipsychotics and for those with underlying vulnerabilities such as diabetes. This can mean that the antipsychotic medications that are prescribed to manage severe mental illnesses such as schizophrenia, contribute to the risk of having severe physical illnesses.* ***The decision for people to take medications to improve their mental health, is made often with the knowledge that their physical health and quality of life will suffer****."*
>
> *"Half have metabolic syndrome, which is associated with an increased risk of cardiovascular disease and diabetes as a side effect of prescribed antipsychotic medications."*[60]

The RANZCP and NMHC both recognise the life shortening effects of many mental health medications. From a lived experience perspective, we have long questioned why the use of these medications is amongst the highest in the world. In fact, Australia's usage has doubled since 2000.[61]

Figure 9: High users of prescription medications such as antidepressants (Source: Statista[62])



60 Australian Government National Mental Health Commission, *2012 National Report Card on Mental Health and Suicide Prevention*, 2012, p29.

61 C Davey and A Chanen, 'The unfulfilled promise of the antidepressant medications', *The Medical Journal of Australia*, 204 (9): 348-350, doi: 10.5694/mja16.00194, 2016.

62 N McCarthy, 'The World's Biggest Consumers of Antidepressants', Statista, 20 August 2019.

An interview with Dr Jon Jureidini in April 2019 says three million Australians are now reliant on antidepressants.

> *New data from the Pharmaceutical Benefits Scheme shows one in every eight Australians are using the drugs, including 100,000 children. The data has prompted concerns Australia is over-diagnosing and over-treating depression.*
>
> *Psychiatrist Dr Jon Jureidini, from the University of Adelaide, said too many doctors are prescribing the drug.*
>
> *"The marketing of antidepressants has been extremely successful, and lots of people have been led to believe they're better off taking the drugs.*
>
> *"The safety of these drugs is often overestimated, the risks are underestimated."*[63]

Similarly, an ABC article published in August 2019 states benzodiazepines were the most common substance in overdose deaths in 2016.

> *Nearly 6 million scripts for the anti-anxiety drug were handed out through the PBS in 2017–18.*
>
> *Patients are regularly prescribed the drug for longer than the recommended 2-4 weeks.*
>
> *The president of the Royal Australian College of General Practitioners, Dr Harry Nespolon, conceded that although GPs are much more aware of the risks of benzodiazepines these days, they are still overprescribed.*[64]

4.1 THE COMPLEX TREATMENT MODEL

A broad network of professionals deliver mental health services to Australians.

Mental health sufferers with comorbid conditions will, in many cases, have additional specialists and service providers to support conditions not related to their mental illness. Whilst the GP is deemed the primary care support, comorbidity means added complexity due to the increase in medical professionals managing a patient's health.

For patients with mental illness and pain conditions, additional professionals like pain specialists, rehabilitation therapists, and surgeons may be involved. Treating multiple conditions generally means being treated by – and obtaining medication from – multiple physicians (see Figure 10).

63 B Fordham, 'Concerns after data reveals three million Australians now using antidepressants', 2GB, 24 April 2019.

64 M Morris, 'Benzodiazepines most common substance in overdose deaths in 2016, ahead of oxycodone and fentanyl', ABCNews, 14 August 2019.

Figure 10: A complex treatment model for multiple conditions

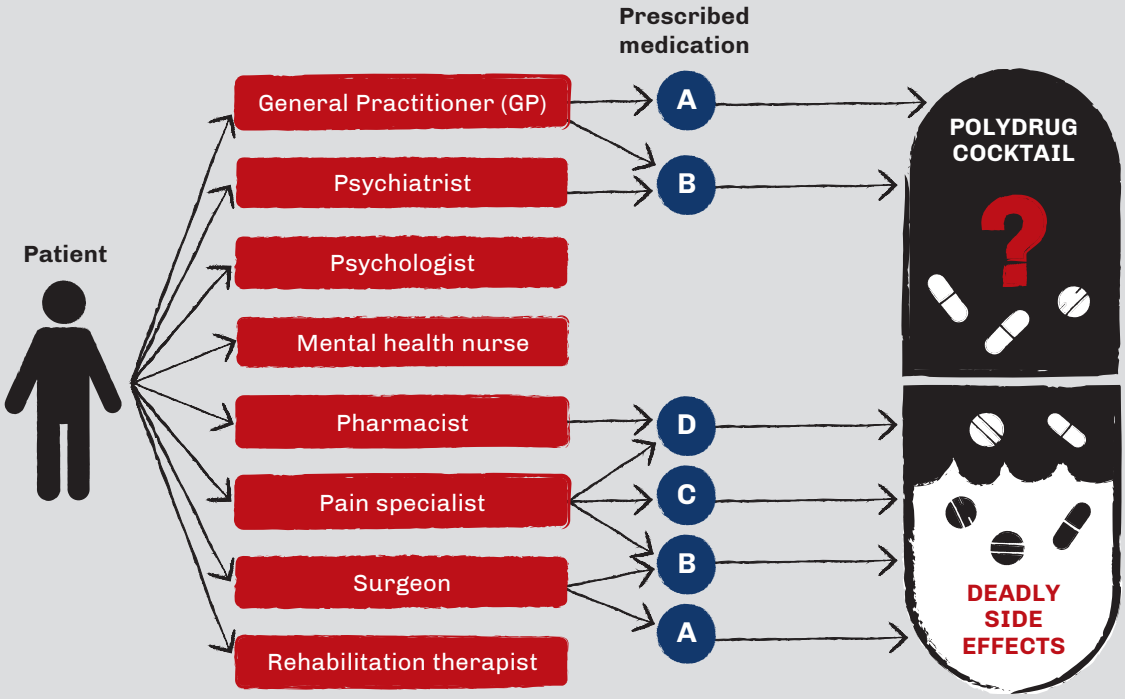


Figure 10 illustrates the systemic issues with the **single disease health care model** that exists in Australia. Multiple physicians, treatment plans, prescribed medications and drug interactions. For a person who already has comorbid chronic illnesses and life-threatening risks, this model allows for limited chances of recovery.

The 2018 Australian Health Policy Collaboration (AHPC) paper[65] describes the current inability of Australia's health care system to cater for multiple chronic diseases, particularly where there is mental illness present.

> *People with multiple conditions currently incur unnecessary costs within a fragmented system with services and providers working in isolation from each other, lack of continuity of care and treatment, and both wasteful duplication and gaps in services. These structural barriers militate against good outcomes for people with complex conditions who require proactive, long-term, coordinated, evidence-based management and team care.*

Figure 11: 2018 Australian Health Policy Collaboration (AHPC) paper

65 B Harris, M Duggan, P Batterham, K Bartlem, T Clinton-McHarg, J Dunbar, C Fehily, D Lawrence, M Morgan & S Rosenbaum, *Australia's Mental and Physical Health Tracker: Background Paper*, Australian Health Policy Collaboration issues paper no. 2018-02, Melbourne, 2018, pp28, 29, 30, 19.

Extensive data suggest some treatments for mental health conditions can adversely affect physical health. Treatments for one disorder can, and often do, affect other systems in the body. People on long-term antipsychotic medicine, for example, can experience a range of metabolic disorders including weight gain, dyslipidaemia (elevated cholesterol) and diabetes.

The management of multi-morbidity with drugs is often complex, resulting in polypharmacy (multiple drugs being prescribed), with its attendant risks. Polypharmacy is known to create problems with adherence to drug regimens due to side effects that decrease quality of life, increased disorganisation, and high costs. Researchers have highlighted opportunities to improve guidelines and support for continuing antidepressants.

Mental and physical health problems together can have a greater effect on functional status and quality of life than physical illness alone. A significant part of the reason for these poorer outcomes is that a co-existing mental health problem may reduce a person's ability to actively manage their other health conditions.

Patients with multimorbidity (comorbidity) have a high treatment burden in terms of understanding and self-managing the conditions, attending multiple appointments and managing complex drug regimes. Qualitative research highlights the "endless struggle" patients experience in managing their conditions.

The lack of understanding and action on comorbid illness is perfectly highlighted in communication from the Department of Health, as explained in a *Sydney Morning Herald* article on 17 February 2020:

Last week the Department of Health sent letters to 341 general practitioners, accusing them of inappropriately claiming Medicare funding for managing both a physical and a psychological issue in one consultation.

Essentially, Medicare will pay for one or the other problem, but not both, and the department was warning these GPs to cut their consultations short, bill the patient privately for one of the matters, or tell the patient to come back another time.

If the government does not understand that our doctors need to treat our conditions as a holistic problem, what chance do we have?

In its 2016 report, RANZCP emphasised that serious mental illnesses are widely recognised as debilitating conditions that are closely associated with suffering, disability and premature mortality. The report noted that:

It is less well understood that these poor outcomes are significantly influenced by the overall poor health of individuals with serious mental illnesses. Increasingly the evidence implicates chronic physical diseases as the major causes of disability and loss of life amongst this group, rather than principally suicide as previously thought.[66]

Two tables from the RANZCP report are included here, because they show the prevalence of common physical comorbidities and common risk factors for people with different types of psychosis in Australia. The rates of all the physical conditions are much higher than in the general population, especially for cardiovascular disease and diabetes (see Table 3). There are similarly very high rates of risk factors such as high blood pressure, elevated cholesterol, smoking, obesity and physical inactivity (see Table 4).[67]

66 RANZCP 2016, p13.

67 ibid, pp21, 37.

Table 3: Prevalence of physical comorbidities in people with psychosis, Australia, 2010 (Source: RANZCP)

	Schizo-phrenia %	Schizo-affective disorder %	Bipolar disorder with psychosis %	Depressive psychosis %	Delusional and other nonorganic psychoses %	Any psychosis %	Australian population %
Asthma	28.0	34.1	32.2	43.0	18.3	30.0	11.3
Cardiovascular disease	11.5	15.9	11.1	17.9	7.8	12.2	9.9
Severe headaches/ migraines	20.1	29.1	32.4	39.1	17.7	24.8	20.6
Diabetes	21.6	22.9	22.4	16.4	15.9	21.4	6.6
Arthritis	18.9	21.4	26.0	37.1	12.3	21.2	5.7
Respiratory conditions	17.9	20.2	16.1	33.2	8.7	18.2	8.0
Anaemia	9.8	16.8	17.0	29.3	6.2	13.2	11.7
Hepatitis	11.7	12.3	11.4	10.9	16.8	12.0	5.5
Epilepsy	7.9	7.4	6.1	7.8	7.0	7.4	0.3

Source: Morgan et al. 2014, IHME 2015), ABS 2015.

Table 4: Risk factors for cardiovascular disease and diabetes in people with psychosis, Australia, 2010 (Source: RANZCP)

	Schizophrenia	Schizo-affective disorder	Bipolar disorder with psychosis	Depressive psychosis	Delusional and other nonorganic psychoses	Any psychosis
	%	%	%	%	%	%
Metabolic syndrome	58.3	63.3	67.4	52.4	62.2	60.8
Reduced high density lipoprotein levels	58.0	59.4	58.1	48.4	64.9	58.1
Elevated triglyceride levels	56.0	54.9	56.0	50.3	55.9	55.5
Elevated glucose levels	35.7	37.4	35.6	31.6	28.2	35.3
Elevated blood pressure	51.7	53.5	59.6	52.4	64.4	54.4
Current smoking	67.0	70.3	59.3	55.8	73.8	65.9
Overweight/obese	75.0	78.1	79.1	77.8	74.8	76.4
Low/very low level of physical activity	96.0	95.1	96.1	98.0	96.2	96.0

Source: Morgan et al. 2014.

4.2 EFFECTIVENESS OF MEDICATIONS

When it comes to the effectiveness of commonly prescribed medications, the results for most people is disturbing.

The STAR*D trial, funded by the NIMH at a cost of $35 million, took six years to conduct. It was touted as the 'largest antidepressant effectiveness trial ever conducted' and was completed in 2006. Some of the findings included:

- One third of patients experienced remission of their symptoms after three months of taking the medication.
- One third of patients had some relief after trying several different types of medications and one third had no improvement at all.

– Many of the patients who responded relapsed after 12 months.
– Follow up research shows that only 7% of subjects in remission remained stable and stayed in the study until the end.[68]

Professor Chris Davey from The University of Melbourne has stated in The Medical Journal of Australia:

> We need more effective treatments for depression, because current treatments avert less than half of the considerable burden caused by the illness.[69]

In 2018, scientists from University College London published a study in The Lancet Psychiatry[70], that was conducted in GP surgeries across England. It was the largest to be conducted without the involvement of the pharmaceutical industry. In an article published on MSN in September 2019[71], Professor Glyn Lewis, who led the research commented that the UK's most commonly-prescribed antidepressant sertraline 'barely works'. He said:

"We were shocked and surprised when we did our analysis...

"Our primary hypothesis was that it would affect those depressive symptoms at six weeks and we didn't find that.

"We definitely need better treatments for depression, and we need more research in this area.

The article went on to say:

He suggested that new, more effective classes of antidepressants could be based on ketamine, psilocybin, the psychedelic in magic mushrooms, and anti-inflammatories.

Researchers looking at the comparative efficacy and acceptability of 21 antidepressant drugs for the acute treatment of adults with major depressive disorder: a systematic review and network meta-analysis, was published in 2018. *The New York Times* reported about the research in March 2018 noting that "The effectiveness of antidepressants was limited for those with moderate depression, and small for those with severe depression." [72]

Many other studies have shown limited effectiveness, including a study by Harvard Medical School[73] and an analysis of the effects of 18 antipsychotics on metabolic function in patients with schizophrenia.[74]

Benzodiazepines are not recommended to be used for longer than a few months, so are meant only to be a short-term strategy to assist patients. Likewise, the long-term use of opioids has shown to have a low rate of efficacy. Both medications are currently the focus of government and medical body campaigns to reduce their use in Australia.

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68 The National Institute of Mental Health Information Resource Center, 'Sequenced Treatment Alternatives to Relieve Depression (STAR*D) Study', 2006.
69 C Davey and A Chanen, 2016.
70 G Lewis, L Duffy, A Ades, R Amos, R Araya, S Brabyn, et.al, 'The clinical effectiveness of sertraline in primary care and the role of depression severity and duration (PANDA): a pragmatic, double-blind, placebo-controlled randomised trial', The Lancet Psychiatry, vol. 6, issue 11, P903-914, 1 November 2019.
71 H Bodkin, 'Most common antidepressant barely helps improve depression symptoms, 'shocking' trial finds', The Telegraph, 19 September 2019.
72 A Carroll, 'Do Antidepressants Work?', *The New York Times*, 12 March 2018.
73 Harvard Medical School, 'What are the real risks of antidepressants', Harvard Health Publishing, published March 2014.
74 T Pillinger, R McCutcheon, L Vano, Y Mizuno, A Arumuham, G Hindley, et.al, 'Comparative effects of 18 antipsychotics on metabolic function in patients with schizophrenia, predictors of metabolic dysregulation, and association with psychopathology: a systematic review and network meta-analysis', *The Lancet Psychiatry*, vol. 7, issue 1, P64-77, 1 January 2020.

There are many people who benefit greatly from existing mental health medication. Unfortunately, there are also many who don't benefit, even after trying several different types of medications.

The scientific evidence is conclusive. The greater the severity of the mental health condition, the lower the effectiveness of the medication. And, we **do not have a cure for mental illness**.

4.3 THE DIAGNOSIS DISASTER

Mental illness is not only a difficult illness to treat, it is also as difficult illness to diagnose. There are generally no blood tests or brain scans that can confirm a mental illness. A diagnosis is made by reviewing the 10 answers of a questionnaire called a K10, which is completed by a patient with the doctor (see Figure 12).

Figure 12: K10 questionnaire (Source: Black Dog Institute)

K10

For all questions, please select the appropriate response.

In the past 4 weeks:	None of the time	A little of the time	Some of the time	Most of the time	All of the time
1. About how often did you feel tired out for no good reason?	☐	☐	☐	☐	☐
2. About how often did you feel nervous?	☐	☐	☐	☐	☐
3. About how often did you feel so nervous that nothing could calm you down?	☐	☐	☐	☐	☐
4. About how often did you feel hopeless?	☐	☐	☐	☐	☐
5 About how often did you feel restless or fidgety?	☐	☐	☐	☐	☐
6. About how often did you feel so restless you could not sit still?	☐	☐	☐	☐	☐
7. About how often did you feel depressed?	☐	☐	☐	☐	☐
8. About how often did you feel that everything was an effort?	☐	☐	☐	☐	☐
9. About how often did you feel so sad that nothing could cheer you up?	☐	☐	☐	☐	☐
10. About how often did you feel worthless?	☐	☐	☐	☐	☐

Today's Date: _ _ / _ _ / _ _ _ _

Black Dog Institute

> *"The K10 uses a five value response option for each question – all of the time, most of the time, some of the time, a little of the time and none of the time which can be scored from five through to one. The maximum score is 50 indicating severe distress, the minimum score is 10 indicating no distress."*[75]

A doctor uses the results from the K10, and may ask further questions of the patient, in order to establish the symptoms.

Mental illnesses are described in the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5), which is published by the American Psychiatric Association. This manual is used by the doctor to diagnose the mental illness.

Following the diagnosis, the doctor will use guidelines on treatments, including medication, which are provided by the RANZCP.

The obvious problem is that this diagnostic tool is significantly exposed to human error. It requires the patient to be able to fully and honestly articulate the symptoms, without leaving anything out. It requires the doctor to correctly understand and interpret the results from the answers given by the patient. If the patient has other health conditions, like chronic pain, the doctor has to decide if the symptoms are independent of that condition.

According to Krista Baker, L.C.P.C., manager of adult outpatient schizophrenia services at Johns Hopkins Medicine:

> *"Diagnostic errors can be devastating for people, particularly the wrong diagnosis of a mental disorder," she adds.* [76]

A 2018 RACGP article titled, *Reducing diagnostic error* stated that, **"It has been estimated that the diagnostic error rate in a general practice setting is 10–15%"** and that "diagnostic error is the underlying cause of approximately half of the medical negligence claims involving Australian GPs."[77] The article identifies cognitive errors as one of the common reasons for diagnostic errors and proposes some techniques to reduce them.

The article ends by stating:

> *"The authors of Improving diagnosis in health care conclude:*
>
> *Diagnostic errors persist throughout all settings of care and continue to harm an unacceptable number of patients.*
>
> *Improving the diagnostic process is not only possible, but also represents a moral, professional, and public health imperative."*[78]

Diabetes is diagnosed through blood tests. Cancer is diagnosed through biopsies and medical imaging. Mental illness is largely diagnosed through a checklist of self-reported symptoms from the patient. Can you imagine trying to diagnose cancer through a questionnaire? Considering that many patients also have physical health conditions and, in some cases, multiple mental health conditions, the challenge in making a correct diagnosis is colossal.

Most mental health conditions are diagnosed and treated by GPs, not psychiatrists, and all of this generally happens in one appointment that lasts between 20–40 minutes.

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75 Black Dog Institute, K10, accessed 20 April 2020, see https://www.blackdoginstitute.org.au/docs/default-source/psychological-toolkit/k10.pdf?sfvrsn=4

76 John Hopkins Medicine, Study suggests overdiagnosis of schizophrenia, *Science Daily*, 22 April 2019.

77 S Bird, 'Reducing diagnostic error', *newsGP*, RACGP, 23 February 2018.

78 ibid.

A 2009 global meta-analysis including Australia, discovered that general practitioners can only correctly identify depression in 47.3 per cent of cases—and many doctors diagnose depression in people who just don't have it.[79]

This is not surprising. Many people with lived experience have vocally advocated these issues, suggesting that it can take years before they are correctly diagnosed. **Misdiagnosis is a wrong diagnosis**. If the diagnosis is wrong then the treatment also has a high chance of failure. With medication being the leading treatment for mental illness, it means patients could be prescribed medication that will not improve their symptoms.

Misdiagnosis also potentially exposes patients to medication that they don't need. The wrong medication can increase the symptoms of a mental illness, expose the patient unnecessarily to side effects, and worse, delay the time to improving a patient's symptoms.

For patients with severe mental illness, this increases the risk of suicide.

For any patient prescribed mental health medication, the doctor has a further factor to consider when reviewing a patient: are the symptoms related to the condition or are they the side effects of the medication?

An example of the scale of the problem was identified by Dr Jon-Paul Khoo who stated that:

> *"Bipolar disorder is a complex and difficult disorder to treat. It is the sixth leading cause of disability worldwide, and the lifetime risk of death by suicide is as high as 19%."*
>
> *"Misdiagnosis is the norm and more than one-third of Australians with bipolar disorder are symptomatic for 10 or more years before diagnosis."*[80]

The Australian Government and many mental health organisations are strong supporters of focusing mental health investment into early diagnosis and treatment. The sensible theory is that like cancer, earlier detection means it can be treated before it becomes deadly. Unfortunately, there has been almost no research into the success of the system in correct diagnosis and even less into appropriate medication selection. If we are ever going to improve the mental health of the nation, it starts with accurate diagnosis. Even the Productivity Commission report into Mental Health states:

> "...some GPs lack knowledge and skills in mental health and require considerably more training in identifying risks, diagnosing conditions, assessing and recognising the physical health consequences of prescribed treatments, and connecting patients with other services (such as online mental health services and allied health services).[81]

79 A Mitchell, A Vaz, S Rao, 'Clinical diagnosis of depression in primary care: a meta-analysis', *Lancet* 2009; 374: 609–19, 28 July 2009.

80 J Khoo, 'Mood stabilisers', *Australian Prescriber*, 2012;35:164-8, 1 October 2012.

81 Australian Government Productivity Commission, *Mental Health Draft Report*, October 2019, 28.

A paper from Yale School of Medicine on detecting diagnostic errors in psychiatry concluded:

> *"The question of diagnostic error in psychiatry involves two intertwined issues, diagnosis and error detection. You cannot detect diagnostic error unless you have a reliable, valid method of making diagnoses. Since the diagnostic process is less certain in psychiatry than in general medicine, that will make the detection of error less confidant."*[82]

In the Australian mental health care system, neither is a priority.

5. SEVERE MENTAL ILLNESS – LIVING IN THE KILLING ZONE

5.1 OUR MENTAL HEALTH MEDICATION HELL

Living with multiple medication prescriptions is life for most people with severe mental illness. This treatment strategy is well explained in the 2015 article *Adult depression: a step-by-step guide to treatment* written by a group of psychiatrists, many from the Black Dog Institute:

> *"For patients with difficult-to-treat depression, an algorithmic management approach with steps that include increasing the antidepressant dose, switching antidepressants, augmenting with a non-antidepressant treatment and combining antidepressants improves the chance of patient recovery."*[83]

82 J Phillips, 'Detecting diagnostic error in psychiatry', *Diagnosis*, Vol 1, Issue 1, 8 January 2014.

83 J Anderson, V Galvez, C K Loo, P B Mitchell, 'Adult depression: a step-by-step guide to treatment', *Medicine Today*, 16(11): 16-24, November 2015.

The 2017 government report, *Medication safety in mental health* also highlighted the issues of polydrug mental illness treatments:

> *"A number of Australian studies have assessed use of multiple antipsychotics, a practice not generally recommended, demonstrating that on average 35% of people with serious or difficult to treat mental illness were prescribed multiple antipsychotics."*[84]
>
> *"Studies undertaken in the community have shown that people with mental illness who receive a collaborative medicines review have between four and seven medication-related problems per person, including problems with adverse drug reactions and drug interactions."*[85]
>
> *"Australian studies show that more than 80% of people with a psychotic illness endure unpleasant side effects from their medicines and one in three live with moderate to severe impairment due to side effects."*[86]
>
> *"The overwhelming majority of consumers and carers expressed a need for more information about their medicines and in particular, a need to be included in the decision-making processes about their medicines."*[87]
>
> *"Confusion over which health professional, the general practitioner, psychiatrist or community mental health centre, was responsible for care decisions, particularly where the problem related to physical health but was a result of medicines prescribed for mental health, was identified as an issue on multiple occasions."*[88]
>
> *"Consumers, carers and healthcare professionals participating in our consultations highlighted the need for more discussion with consumers when commencing a medicine, particularly about side effects."*[89]

5.2 LIVING IN THE KILLING ZONE – OUR WORLD

At least 800,000 Australians suffer from severe mental illness[90]. Our lives are shorter, but our days are also an endless struggle for survival.

Severe mental illness rarely exists as a single condition and we suffer from other chronic illnesses. To attempt to improve our afflictions we are managed by multiple doctors, using complex medication prescriptions combined with other treatments. The side effects of these medications have significant physical implications, including the risk of overdose death. The ineffective nature of these medications for many sufferers is well known.

It seems to be an unrecognised fact that **medication so dangerous to be classified as a poison**, is legally prescribed to a group of the most vulnerable people in society.

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84 L Roughead, N Procter, K Westaway, J Sluggett, C Alderman, Australian Commission on Safety and Quality in Health Care, *Medication safety in mental health*, June 2017, p 6.

85 ibid, p 7.

86 ibid.

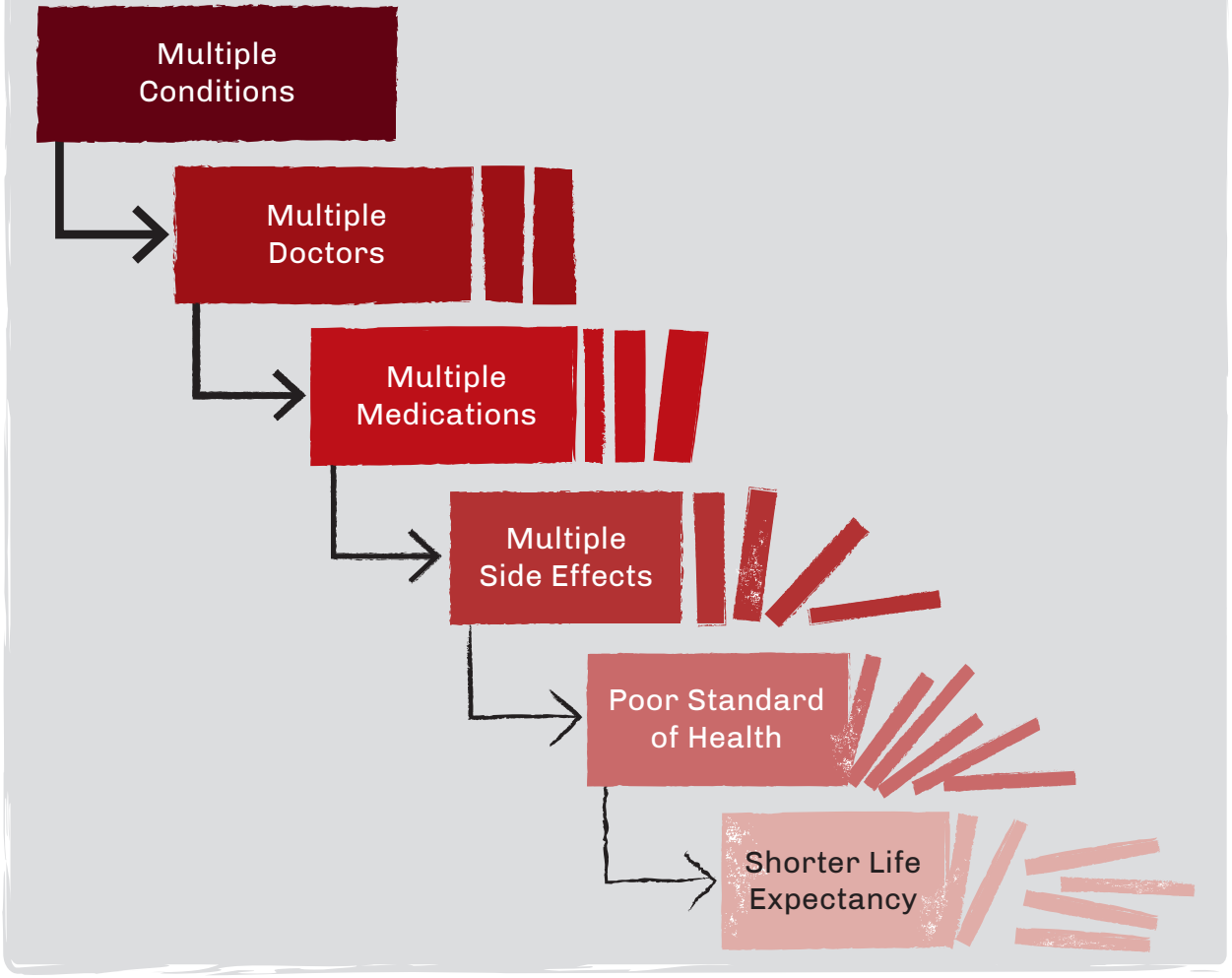
87 ibid.

88 ibid.

89 ibid.

90 Sane Australia, *SANE Australia says Royal Commission into Victoria's Mental Health System must focus on access*, media release, 16 July 2019.

Figure 13: The complications of severe mental illness



> Australia now has the eighth-highest per-capita opioid consumption in the world. Out of 167 countries and territories it's ahead of New Zealand and the UK but still well behind the United States.[91]

– The Age, February 2020

Unlike other chronic illnesses like cancer, severe mental illness is not an illness that a person is expected to be cured from. Improving to a position of being in remission is rarely achieved or even discussed. **We exist, we don't live**. Our quality of life is poor and hope for a better life is all many have to hold on to. Unfortunately, hope can only last so long for many of us. The suicide rate among people with a mental illness is at least seven times higher than the general population. It is one of the main causes of our premature deaths.[92]

The lethal nature of medications exposes us to another risk that is described as **Life Taking**. Prescription medication overdose is a common method of suicide. The medication given to mentally ill people provides us with a method for taking our own lives, funded by the PBS, right in our own homes.

91 F Tomazin, 'Australia's opioid crisis: Deaths rise as companies encourage doctors to prescribe', *The Age*, 4 February 2020.

92 Sane Australia, accessed on 3 April 2020, see https://www.sane.org/information-stories/facts-and-guides/suicidal-behaviour

The statistics prove that you do not live a long time with severe mental illness. That is why life with severe mental illness is described as living in The Killing Zone. This term might be uncomfortable to many people, but we cannot think of a more appropriate one.

Any government program to reduce suicide deaths must acknowledge and address the endless struggle of mental illness and comorbidity. In particular the widely prevalent and equally horrific combination of mental illness and pain conditions. You simply cannot achieve 'zero suicide' when people live in a state of extreme psychological distress. You cannot reduce psychological distress whilst people suffer from multiple chronic illnesses.

5.3 ALTERNATIVE TREATMENTS

There is hope for those of us wanting to escape The Killing Zone. Several new medications are now available and many more are in the final stages of regulatory approval overseas. Unfortunately, many of these have faced significant barriers from the Australian Government. Others have received so little support from mental health organisations that Australians are travelling overseas for treatment. When medication is made available, too often the cost and lack of PBS support makes the treatment out of reach to those who need it most. The situation is clearly evident in the accessibility and cost of medical cannabis. A medication that has proven globally to be a life-saving treatment to enable a better quality of life for people with chronic pain and mental illness.

As reported in February 2020 by the ABC:

> *Seeking cannabis oil for medical purposes has been legal since 2016 when federal laws were changed to allow doctors to prescribe cannabis products to patients suffering an array of conditions.*
>
> *Patients are paying around $600 a month for medicinal cannabis. There is currently no subsidy for cannabis products under the Pharmaceutical Benefits Scheme (PBS).*
>
> *Doctors wishing to prescribe it must first apply to the Therapeutic Goods Administration to seek individual patient approval, a time-consuming process...*[93]

The anaesthetic medication, ketamine, has been used for over 10 years in the USA by doctors to provide fast-acting treatment to acutely depressed, suicidal patients. It is clinically acknowledged as the most effective treatment against mental illness that has ever been produced. A nasal spray version of the medication, to treat depression, is now available in the USA and Europe. University of Sydney's Brain and Mind Centre co-director Professor Ian Hickie said in 2019 this new drug was a "tremendous opportunity" to treat severe depression in Australia, but one the government needs to handle strategically.

> *"We need to get into this early, but do it smart," Professor Hickie said. "Historically, we get into it late and do it dumb. "Waiting five more years – that's the dumb approach."*[94]

Yet 12 months later nothing has been done to fast track its availability. It has very little support from the medical or mental health community, and Australians are travelling to the USA to get access and treatment.

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93 S McCarthy and T Joyner, 'Medicinal cannabis regulation costing patients $600 a month, forcing some to turn to the black market', ABCNews, 20 February 2020.

94 D Maguire, 'US regulatory body approves nasal spray for 'chemical cousin' of ketamine to treat people with depression', ABCNews, 7 March 2019.

Unfortunately, the Productivity Commission and NMHC are silent on these new treatments. **They are not mentioned in recent reports or recommendations at all**. Chapter 12 shows that mental illness medication is completely ignored in our nation's mental health programs. Despite the lobbying of many with lived experience and mental health groups, accessibility of these treatments is far from imminent.

The best pathway to new treatments is to force national debate about the failures of the current health care model. We have no hope of a better life when government refuses to acknowledge and remedy the reasons why our life expectancy is 32 years shorter than it should be.

Warning

Do not stop taking a prescribed medication without discussing it with your doctor. Information can also be obtained by calling the NPS Medicines Line on 1300 633 424 or the Adverse Medicines Events Line on 1300 134 237 for advice. If you need support for any medical concern, including mental health matters, please contact your doctor. Lifeline also provides a 24 hour support service on 13 11 14 or www.lifeline.org.au

2. CONSUMER WARNINGS

1. INTRODUCTION

This chapter exposes the **critical risks that do not exist in Consumer Medicines Information (CMI)** for a large number of medications prescribed to people with mental illness and chronic pain.

The CMI exists to guide and warn consumers about how to use a medication, the risks and side effects. A significant number of side effects and risks are contained in each CMI. However, consumers need to be made aware of the **more significant side effects with life-threatening risks**. If these are not fully identified, consumers are not able to ensure they take the necessary steps to protect their health.

1.1 COMPARING THE INFORMATION PROVIDED TO DOCTORS AND CONSUMERS

The Therapeutic Goods Administration (TGA) regulates these consumer warning documents for prescription medication in Australia. In fact, the Statutory Rules No. 394, 1990 made under the *Therapeutic Goods Act 1989*, Schedule 12—Patient information documents (subregulation 9A(1)) states that:

> *A patient information document about a medicinal product must be:*
> – *written in English*
> – *clearly legible*
> – *written in language that will easily be understood by patients*
> – *consistent with product information about the product.*

The Product Information (PI) is provided to doctors. In a breach of this legislation, most **CMIs DO NOT reflect product information provided to medical practitioners**. This information includes the risk of life-threatening side effects.

1.2 COMPARING THE SAME MEDICINE IN TWO COUNTRIES

The equivalent body in the USA is the USA Food and Drug Administration (FDA) and their Medication Guides (MGs).

We provide a comparison of the content of these documents in Australia and the USA (CMI versus MG) for the prescription medication that is identified as a common cause of death.

As part of our analysis:

– we compare, where possible, the same drugs made by the same companies
– we compare CMIs from different time periods
– we consulted two USA experts to provide analysis on the documents.

Our findings are startling.

Many dangerous risks appear in the USA's MG but not in Australia's CMI – and many of these risks are life-threatening.

The CMI should enable consumers to make a decision about the risks and benefits of taking a medication. Based on the information they receive, they will choose to proceed taking the medication, fully aware of the risks.

In the USA, the FDA mandates what is included in the MG. In Australia it is up to the pharmaceutical companies' discretion to decide what is included. As such they have deliberately not included many of the life-threatening warnings.

2. ABOUT THE TGA

According to the TGA website, the body is part of the Australian Government Department of Health, and is responsible for regulating therapeutic goods including prescription medicines, vaccines, sunscreens, vitamins and minerals, medical devices, blood and blood products.[95]

This includes regulatory oversight of the **medication warnings** provided by pharmaceutical companies.

2.1 PRODUCT INFORMATION – THE SCIENTIFIC GUIDE

The **Product Information (PI)** for all prescription medications:

> *provides health professionals with a summary of the essential scientific information for the safe and effective use of a prescription medicine. The information has been written by the pharmaceutical company responsible for the medicine and has been approved by the TGA. It provides objective information about the medicine's quality, safety and effectiveness, as demonstrated in the data provided to the TGA by the pharmaceutical company.*

2.2 CMIS – THE CONSUMER GUIDE

The document that is designed for consumers is called the **Consumer Medicines Information (CMI)**:

> *The information has been written for consumers by the pharmaceutical company responsible for the medicine. It provides information on the safe and effective use of a prescription medicine. CMIs are important to consumers and those who provide medicines and care, as they provide information aimed at bringing about better health outcomes.*

95 Australian Government Department of Health Therapeutic Goods Administration, accessed on 3 April 2020, see https://www.tga.gov.au/tga-basics

2.3 THE ROLE OF THE CMI

The Australian Government promotes the importance of the CMI as the accurate source of medication information on numerous government websites including healthdirect:

> *"You need to understand the medicines you are taking. The Consumer Medicine Information (CMI) leaflet has information about your medicine. This will help you get the best out of your medicine and know what to do if you miss a dose. It will also help you know what to do if you have any side effects."*

> *"A CMI leaflet gives you information on how to use your medicine safely and properly. For example, it tells you:*
>
> – *how to take the medicine*
> – *why it may have been prescribed for you*
> – *potential side effects*
> – *other medicines it may interact with"*[96]

It states that your medicine's CMI can be found by searching in healthdirect's medicines section. Other advice includes:

> *"Read the CMI of your new medicine, before taking any."*
>
> *"Keep all your CMIs in the one place so you can easily find them. You may also need to re-check some details while using the medicine".*
>
> *"Sometimes one medicine can affect how another medicine works. One medicine can change the side effects of another. This is called an 'interaction'. Interactions can also happen between medicines and certain foods or drink, including alcohol. Known interactions are usually listed in your medicine's CMI."*
>
> *"Speak to your doctor or pharmacist if there's anything in the CMI that worries you."*[97]

Other information provided under Accidental overdose of medicine states that, "More Australians are accidentally overdosing on medicines than ever before. Taking too much of a medicine can be very dangerous, and even fatal. But accidental overdoses can be prevented", and, "You are more at risk of accidental overdose if one or more of the following applies to you" and it specifies that this risk applies if, "You don't follow the instructions of your doctor or pharmacist properly."[98]

2.4 WHO IS RESPONSIBLE FOR THE INFORMATION?

The pharmaceutical company responsible for the medicine (known as the medicine's 'sponsor') provides the **content** of the PI document and the CMI document. The PI is approved by the TGA. It is the responsibility of the sponsor to make the documents available to the TGA.

> While the PI is approved by the TGA, the CMI is not. The content of the CMI is not regulated by the TGA, yet the *Therapeutic Goods Regulations 1990* requires the CMI to be consistent with the PI.

96 Healthdirect, Australian Government, accessed on 3 April 2020, see https://www.healthdirect.gov.au/how-to-read-cmis
97 ibid.
98 Healthdirect, Australian Government, accessed on 3 April 2020, see https://www.healthdirect.gov.au/accidental-overdose-of-medicines

The information in the CMI is currently provided at the discretion of the pharmaceutical company. The TGA does provide a template that must be followed, to include:

- Name of the medicine
- Names of the active and inactive ingredients
- Dosage of the medicine
- What the medicine is used for and how it works
- Warnings and precautions, such as when the medicine should not be taken
- Interactions the medicine might have with food or other medicines
- How to use the medicine properly
- Side effects
- What to do in the case of an overdose
- How to store the medicine properly
- Name and address of the sponsor
- Date the CMI was last updated

And if you need to report a problem with the content of a CMI or PI document?
The TGA suggests you contact the pharmaceutical company responsible for the medicine. The TGA does not offer a complaints process for the content of these documents, meaning a person must complain to the company who is responsible for the problem, not the regulatory body.

3. FDA AND MEDICATION WARNINGS

The US equivalent of the TGA is the FDA. The FDA is responsible for protecting the public health by ensuring the safety, efficacy, and security of human and veterinary drugs, biological products, and medical devices.[99]

The FDA requires multiple documents to be provided for prescription medication. For comparison purposes, we are focusing on the equivalent of Australia's CMI which are the Medication Guides (MG).

The FDA approves the content of all warning labels and documents. This includes consumer warnings, side effects and drug interaction guides. The FDA advises pharmaceutical companies of any changes that need to be made and the final version requires FDA sign off before being used.[100]

> *Patient Package Inserts (PPI), Medication Guides (MG), and Instructions for Use (IFU) are paper handouts that come with many prescription medicines. The guides address issues that are specific to particular drugs and drug classes, and they contain FDA-approved information that can help patients use the medicine safe and effectively and try to avoid serious adverse events.*

99 U.S. Food & Drug Administration (FDA), published on 28 March 2018, see https://www.fda.gov/about-fda/what-we-do

100 Code of Federal Regulations, Part 208 - MEDICATION GUIDES FOR PRESCRIPTION DRUG PRODUCTS, published 1 April 2010, see https://www.govinfo.gov/content/pkg/CFR-2010-title21-vol4/xml/CFR-2010-title21-vol4-part208.xml

According to the FDA:

> ***Medication Guides (MG)*** *are paper handouts that come with many prescription medicines. The guides address issues that are specific to particular drugs and drug classes, and they contain FDA-approved information that can help patients avoid serious adverse events.*
>
> *They offer answers to such crucial questions as:*
>
> – *What is this drug and what does it do?*
> – *What's the most important information that I need to know about the medication?*
> – *What are the risks involved in taking this?*
> – *What are the possible side effects?*
> – *Who shouldn't take the drug?*
> – *What ingredients are in this medication?*[101]

3.1 CONNECTICUT AND THE OPIOID CRISIS

The Opioid Crisis in the USA provides a valuable opportunity for Australia to learn from the horrific failures that contributed to the deaths of over 400,000 people. The responses by both the government and health care system are important considerations for Australia in light of the prescription medication deaths we are currently trying to reduce.

Connecticut is an excellent centre to look to for expertise on both the **cause** and the **solutions** to prescription overdose deaths. Yale Medical School is located in Connecticut, which was one of the lead institutions tasked with combating the crisis. It is also home to many private health institutions like Hartford Healthcare, which is a specialist department treating prescription medication issues. Specialists, Dr Craig Allen and Dr Lori Calabrese, were interviewed multiple times to analyse the differences in Australia's CMIs compared to America's MGs.

3.1.1 Introducing Dr J. Craig Allen

Dr. Allen is the Medical Director of Rushford, Hartford Healthcare's (HHC) substance use and co-occurring disorder treatment center. He Chairs HHC's Opioid Management Committee and Addictions Clinical Council. Dr. Allen is a member of the state Advisory board for the Department of Mental Health and Addiction Services, chairs the Treatment committee for the Alcohol and Drug Policy Council, is on the State Medical Society's Addiction Medicine Committee and Opioid Task Force and is the current President of the Connecticut Chapter of the American Society of Addiction Medicine.

Dr. Allen is Associate Professor of Psychiatry at Quinnipiac University, Frank Netter School of Medicine and has held faculty appointments at Harvard and Yale Medical schools. Currently he trains Addiction Medicine fellows in Rushford's ACGME accredited ADM program, and Child and Adolescent Psychiatry Fellows and Residents from the Institute of Living.

101 U.S. Food & Drug Administration (FDA), published on 3 January 2010, see https://www.fda.gov/consumers/consumer-updates/medication-guides-certain-prescription-products

Dr. Allen lectures and advocates locally and nationally for prevention, screening, early intervention and treatment access for Substance use and other Psychiatric disorders throughout the lifespan. Dr. Allen is board certified in Child, Adolescent and Adult Psychiatry and Addiction Medicine.[102]

3.1.2 Introducing Dr Lori Calabrese

Lori Calabrese, MD is a psychiatrist who specialises in comprehensive and state-of-the-art psychiatric evaluation and innovative psychiatric treatment of adults and adolescents in South Windsor, CT, just minutes from Hartford.

With over 20 years of experience, Dr. Calabrese is a graduate of The Johns Hopkins University School of Medicine, and completed her residency training at Massachusetts General Hospital. She has served as a clinical faculty member at both Harvard Medical School and Yale School of Medicine and is often thought of as "a doctor's doctor," as so many physicians and their families rely on her expertise, treatment, and referrals.

Dr. Calabrese is a specialist among her peers in psychopharmacology and interventional psychiatry, and incorporates the newest scientific information regarding brain health, genetic testing, inflammation and the brain-gut microbiome connection into the care of her patients.

She serves a broad spectrum of patients. Among her areas of expertise are anxiety, depression, bipolar disorder, psychiatric disorders during pregnancy and post-partum, trauma, eating disorders, ADHD, alcohol and substance use disorders co-occurring with other psychiatric disorders, and psychiatric disorders among the medically ill.[103]

4. MEDICATION ANALYSIS

In order to better understand some of the central reasons for the adverse health impacts of prescription medication for people with mental illness and pain conditions in Australia, we will explore the CMI warnings that are available from the manufacturers.

For this purpose, we will focus on a number of PBS medications that are typically prescribed to people with mental illness and pain conditions. The current CMI and MG is compared as at January 2020 in most comparisons.

Where possible, we compare the same medication, made by the same company, or its Australian subsidiary. For some medications, we also compare earlier versions of the CMI. In addition, for some medications we have included extracts from the PI to show the difference in information given to doctors compared to patients.

102 Connecticut Bar Foundation, see https://www.ctbarfdn.org/ctbar/Allen%2C%20J.%20Craig.pdf
103 Lori Calabrese, MD, see https://loricalabresemd.com/meet-lori-calabrese/

For each medication, we assessed the comparable warnings for key areas like side effects. The focus is on identifying differences in material risks between the two consumer versions. We investigated to see if the **dangerous risks disclosed in the USA are also disclosed in Australia**. The risk of death was the focus for the comparisons, however other material risks are compared when the disclosures are significantly different. Information that is similar is excluded.

Table 5: Commonly prescribed medications

Medication	USA Company & Australian trading name	Treating Condition	Medication Class	Controlled Drug
OxyContin	Purdue (USA) Mundipharma (Aust)	Pain	Opioid	Schedule 8
Targin	Purdue (USA) Mundipharma (Aust)	Pain	Opioid	Schedule 8
Endone	Aspen Pharma (Aust)	Pain	Opioid	Schedule 8
Valium	Roche	Mental Illness/ Pain	Benzodiazepine	Schedule 4
Xanax	Pfizer	Mental Illness/ Pain	Benzodiazepine	Schedule 8
Durogesic	Johnson & Johnson (USA) Janssen (Aust)	Pain	Opioid	Schedule 8
Lithium	Aspen Pharma (Aust)	Mental Illness/ Suicidal Ideation	Antipsychotic	Schedule 4
Efexor	Pfizer	Mental Illness	Antidepressant	Schedule 4
Prozac	Eli Lilly	Mental Illness	Antidepressant	Schedule 4
Dexamfetamine	Aspen	Mental Illness	Stimulant	Schedule 8

4.1 EXPERT OPINION ON MEDICATION WARNINGS

"Have a think about the people that take prescription drugs for the first time; they are sick, tired, not thinking straight. Here in the US they receive several pieces of information with every prescription from the pharmacy. The medical guide is a one- to two-page leaflet that has the important information, in simple language. It is really clear and straight to the point. Drugs that carry large risks, drugs that carry risks of death, need a whole different level of respect and a whole different level of fear associated with having them in the home with children, and using them

yourself. I like my patients to have a healthy level of fear of the drugs. When I use the word fear, what I really mean is being afraid that things might happen to help you follow the rules, learn all you can, take it as prescribed. It gives you sort of a healthy awareness that things can go wrong really quickly with some of these medicines. The US has learnt from our mistakes; patients didn't always receive all the risks in the guides, they certainly do now. They are given the information with every prescription. You never want to lose an opportunity to inform someone about the details and the risks of the medicines that they're taking." ***– Dr Lori Calabrese***

"Written medication warnings exist to reduce the chance of dangerous side effects and to assist to get the best possible outcome for the patient. We have seen here in the US what can happen when information is withheld from patients. Patients have a legal right to understand the risks and they can then make a decision to consent to the treatment. However, they have to be easy to understand, accurate, inclusive of all the risks and clearly informed on how to manage medication safety. The risks that are included are the risks we know can and do occur, that's why they are there."
– Dr Craig Allen

4.2 CMI COMPARISONS

At a glance, these snapshot comparisons indicate whether the risk of death is clearly disclosed in CMIs and MGs.

If the item is classified as 'No' it means a warning exists in the document, however the risk of death is not mentioned as a potential side effect. If classifed as 'Yes', it means the risk of death is mentioned as a potential side effect.

Most CMIs have been sourced from the TGA website at www.tga.gov.au/consumer-medicines-information-cmi

4.2.1 OxyContin

OxyContin is an opioid made by Purdue (USA)/Mundipharama (Australia). The disclosed risk of death is summarised in Table 6.

Table 6: Disclosure of risk of death for OxyContin 2019 (an overview)

Does the CMI warning mention the risk of death of using OxyContin in combination with:		
	Australia CMI (2019)[104]	USA MG (2019)[105]
Alcohol	No	Yes
Benzodiazepines	Not mentioned in the CMI	Yes
Other Medications	No	Yes
Sharing Opioids	No	Yes
Addiction	No	Yes
Pregnancy	No	Yes
Taken as prescribed	No	Yes

104 Mundipharma, OxyContin tablets Consumer Medicine Information, December 2019.
105 Purdue, Medication Guide, Oxycodone HCl Extended-release tablets, October 2019.

4.2.2 Targin

Targin is another opioid made by Purdue–Mundipharma. The Targin CMI/MG mirrors OxyContin. The disclosed risk of death is summarised in Table 7.

Table 7: Disclosure of risk of death for Targin 2019 (an overview)

Does the CMI warning mention the risk of death of using Targin in combination with:		
	Australia CMI (2019)[106]	USA MG (2016)[107]
Alcohol	No[108]	Yes
Benzodiazepines	Not mentioned in the CMI	Yes
Other Medications	No	Yes
Sharing Opioids	No	Yes
Addiction	No	Yes
Pregnancy	No	Yes
Taken as prescribed	No	Yes

4.2.3 Endone

Endone does not have a direct comparison product in the USA. In Australia it is used as an alternative to OxyContin. Hence we have compared Endone in Australia with OxyContin in the USA in Table 8. Endone is made by Aspen.

Table 8: Disclosure of risk of death for Endone 2019 (an overview)

Does the CMI warning mention the risk of death of using Endone (Aust) vs OxyContin (USA) in combination with:		
	Australia (2015)[109]	USA (2019)
Alcohol	No	Yes
Benzodiazepines	Not mentioned in the CMI	Yes
Depression Medications	No	Yes
Sharing Opioids	No	Yes
Addiction	No	Yes
Pregnancy	No	Yes
Abuse	No	Yes
Taken as prescribed	No	Yes

106 Mundipharma, TARGIN tablets Consumer Medicine Information, December 2019.
107 Purdue, Medication Guide, TARGINIQ ER, December 2016.
108 Targin is not reviewed in detail in this report. Refer to the relevant CMI for full details.
109 Aspen Pharma, Endone Consumer Medicine Information, July 2015.

4.2.4 Valium

Valium is a benzodiazepine made by Roche. The disclosed risk of death is summarised in Table 9.

Table 9: Disclosure of risk of death for Valium 2019 (an overview)

Does the CMI warning mention the risk of death of using Valium in combination with:		
	Australia (2018)[110]	USA (2016)[111]
Alcohol	No	Yes
Opioids	Not mentioned in the CMI	Yes
Other Medications	No	Yes
Addiction	Not mentioned in the CMI	No
Pregnancy	No	Yes
Overdose	No	No
Suicide	Not mentioned in the CMI	Yes

4.2.5 Durogesic

Durogesic is an opioid made by Johnson & Johnson (USA) and Janssen (Australia). The disclosed risk of death is summarised in Table 10.

Table 10: Disclosure of risk of death for Durogesic 2018 (an overview)

Does the CMI warning mention the risk of death of using Durogesic in combination with:		
	Australia (2018)[112]	USA (2019)[113]
Alcohol	No	Yes
Benzodiazepines	Not mentioned in the CMI	Yes
Sharing Opioids	No	Yes
Addiction	No	Yes
Pregnancy	No	Yes
Overdose	No	Yes
Patch Exposure	No	Yes
Abuse	Not mentioned in the CMI	Yes
Taken as prescribed	No	Yes

Summary

In the comparison of these side effects for the five selected medications, the **USA MG warns of the risk of death 34 times.** For the same list of side effects, the **Australian CMI warns of the risk of death once. These medications are reviewed in more detail in this Chapter, section 4.4.**

110 Roche, Valium Consumer Medicine Information, March 2018.
111 Roche, Medication Guide, VALIUM, December 2016.
112 Janssen, Durogesic Consumer Medicine Information, August 2018.
113 Janssen, Medicine Guide, DURAGESIC, October 2019.

4.2.6 Xanax (discontinued 1991–2013)

Xanax is a benzodiazepine made by Pfizer. Studies identifed increased deaths when used in combination with alcohol or opioid medications. Studies also indicated higher rates of addiciton and abuse in comparison to other benzodiazepines like valium.[114] [115] [116] In response the TGA announced in 2013 that Xanax would be made a Schedule 8 poison.

In December 2013, Pfizer Australia announced they would discontinue Xanax in Australia as it was no longer commercially viable.

> *"The problem has been that there's a lot of Xanax out there, there has been, and that was shown in our study, it was coming up in deaths." – Prof Shane Drake*[117]

The disclosed risk of death is summarised in Table 11.

Table 11: Disclosure of risk of death for Xanax 2011 (an overview)

Does the CMI warning mention the risk of death of using Xanax in combination with:		
	Australia (2011)[118]	USA (2016)[119]
Alcohol	No	**Yes**
Opioids	No	**Yes**
Other Medications	No	**Yes**

Chapter 3 shows how these medications are the leading cause of prescription medication deaths in Australia.

4.3 BREACHES OF THE THERAPEUTIC GOODS ACT

The content of the CMI documents is not regulated by the TGA, yet the *Therapeutic Goods Regulations 1990* requires the CMI to be consistent with the PI. This means the side effect risks in the PI must also be explained in the CMI. The following tables identify examples of when the CMI is not consistent with the PI, and as such is a breach of the Act. **We have identified 46 examples across the ten CMIs available in January 2020**. This is not an exhaustive list, these are examples to highlight the systemic inconsistencies that exist.

Most PIs have been sourced from www.tga.gov.au/product-information-0

114 S Darke, M Torok, J Duflou, 'Circumstances and toxicology of sudden or unnatural deaths involving alprazolam', *Drug and Alcohol Dependence* 138, 2014, pp61–66.
115 National Drug & Alcohol Research Centre, UNSW, *Xanax overdose and related deaths – a podcast*, transcript.
116 National Drug & Alcohol Research Centre, UNSW, *Alprazolam related deaths soar since 2009*, News, 24 June 2014.
117 National Drug & Alcohol Research Centre, UNSW, transcript.
118 Pfizer, Xanax Consumer Medicine Information, July 2011.
119 Pfizer Medication Guide, XANAX, December 2016.

4.3.1 OxyContin – Mundipharma (Australia)

Issue	CMI (2019)	PI (2019)[120]
Is the risk of death in relation to alcohol disclosed?	No	Yes
Is the risk of death in relation to benzodiazepines disclosed?	No	Yes
Is the risk of death in relation to antidepressants or antipsychotic medications disclosed?	No	Yes

4.3.2 Targin – Mundipharma (Australia)

Issue	CMI (2019)	PI (2019)[121]
Is the risk of death in relation to alcohol disclosed?	No	Yes
Is the risk of death in relation to benzodiazepines disclosed?	No	Yes
Is the risk of death in relation to antidepressants or antipsychotic medications disclosed?	No	Yes

4.3.3 Endone – Aspen (Australia)

Issue	CMI (2015)	PI (2015)[122]
Is the risk of death from taking as prescribed disclosed?	No	Yes
Is the risk of death in relation to alcohol disclosed?	No	Yes
Is the risk of death in relation to benzodiazepines disclosed?	No	Yes
Is the risk of death in relation to antidepressant medications disclosed?	No	Yes

4.3.4 Valium – Roche (Australia)

Issue	CMI (2018)	PI (2020)[123]
Is the risk of death in relation to alcohol disclosed?	No	Yes
Is the risk of death in relation to opioids disclosed?	No	Yes
Is the risk of death in relation to other depression medication disclosed?	No	Yes
Is the risk of death in relation to pregnancy disclosed?	No	Yes
Is the risk of withdrawal syndrome disclosed?	No	Yes
Is the risk of death in relation to overdose disclosed?	No	Yes
Is the risk of suicide disclosed?	No	Yes

120 Mundipharma, OxyContin (Oxycodone Hydrochloride) Modified Release Tablets, Australian Product Information, 17 December 2019.
121 Mundipharma, Australian Product Information – Targin Modified Release Tablets, December 2019.
122 Aspen Product Information Endone, June 2015.
123 Roche Australian Product Information, Valium, January 2020.

4.3.5 Durogesic – Janssen (Australia)

Issue	CMI (2018)	PI (2019)[124]
Is the risk of addiction when taken as prescribed disclosed?	No	**Yes**
Is the risk of death in relation to benzodiazepines disclosed?	No	**Yes**
Is the risk of death in relation to addiction disclosed?	No	**Yes**
Is the risk of death from taking as prescribed disclosed?	No	**Yes**
Is the risk of death in relation to alcohol disclosed?	No	**Yes**
Is the risk of death in relation to overdose disclosed?	No	**Yes**
Is the risk of death due to an overdose when starting or changing a dose disclosed?	No	**Yes**
Is the risk of death in relation to abuse disclosed?	No	**Yes**
Is the risk of death in relation to pregnancy disclosed?	No	**Yes**
Is the risk of death in relation to patch contact with kids/ adults disclosed?	No	**Yes**

4.3.6 Dexamfetamine (Dexamphetamine) – Aspen (Australia)

Issue	CMI (2019)[125]	PI (2019)[126]
Is the risk of dependence when taking as prescribed disclosed?	No "Like all CNS stimulants, it may become habit-forming and can be abused by some people. Using this medicine strictly as your doctor prescribed will ensure that abuse or drug dependence should not be a problem."	**Yes** **"Tolerance and dependence of the amfetamine type develop on repeated administration of dexamfetamine."**
Is the risk of death from using medication at usual doses disclosed?	No	**Yes**
Is the risk of death from overdose disclosed?	No	**Yes**
Dexamfetamine is a shedule 8 medication due to the risk of addiction	No	**Yes**

124 Janssen Australian Product Information, Durogesic, December 2019.
125 Aspen Pharmacare, Aspen Dexamfetamine Consumer Medicine Information, December 2019.
126 Aspen Pharmacare Australian Product Information, Aspen Dexamfetamine, December 2019.

4.3.7 Efexor XR – Pfizer (Australia)

Issue	CMI (2019)[127]	PI (2019)[128]
Is the risk of life-threatening Serotonin Syndrome disclosed?	No	**Yes**
Is the risk of death from overdose disclosed?	No	**Yes**

4.3.8 Fluoxetine (Prozac) – Eli Lilly

Issue	CMI (2019)[129]	PI (2020)[130]
Is the risk of life-threatening Serotonin Syndrome disclosed?	No	**Yes**
Is the risk of death from overdose disclosed?	No	**Yes**

4.3.9 Lithicarb – Aspen (Australia)

Issue	CMI (2018)[131]	PI (2018)[132]
Is the risk of coma and death from Lithium toxicity disclosed?	No	**Yes**
Is the risk of Lithium toxicity at prescribed levels disclosed?	No "[Lithium toxicity] can happen if you are taking too much lithium"	**Yes** **"Lithium toxicity is closely related to serum lithium concentrations and can occur at doses close to therapeutic concentrations."**
Is the narrow risk between prescribed and toxic dosages disclosed?	No	**Yes** **"A major management problem also, is that there are relatively narrow distances between the therapeutic and toxic dosages and blood levels."**
Is the risk of death from overdose disclosed?	No	**Yes**

127 Pfizer, Efexor-XR Consumer Medicine Information, August 2019.
128 Pfizer Australian Product Information, Efexor-XR, September 2019.
129 Eli Lilly, Prozac Consumer Medicine Information, December 2019.
130 Eli Lilly Australian Product Information, Prozac, February 2020.
131 Aspen Pharmacare, Lithicarb Consumer Medicine Information, October 2018.
132 Aspen Pharmacare Australia Product Information, Lithicarb, August 2018.

4.3.10 Xanax (discontinued 1991–2013)

Issue	CMI (2011)[133]	PI (2011)[134]
Is the risk of death in relation to alcohol disclosed?	No	Yes
Is the risk of death in relation to opioids disclosed?	No	Yes
Is the risk of harm in relation to pregnancy disclosed?	No	Yes
Is the risk of withdrawal syndrome disclosed?	No	Yes
Is the risk of death in relation to overdose disclosed?	No	Yes
Is the risk of suicide disclosed?	No	Yes
Risk of physical and psychological dependence developing after one week, even at prescribed doses?	No	Yes

4.4 DETAILED CMI AND MG ANALYSIS

The following section examines in greater detail the consumer warnings provided for OxyContin, Endone, Valium and Durogesic. These medications have been selected due to the lethal risks associated with each. The detailed analysis has been undertaken to expose both the systemic nature of the warning failures and the areas in which consumers have been exposed to deadly side effects.

As part of our analysis:

- we compare, where possible, the same drugs made by the same companies in the US and Australia
- we compare CMIs and PIs from different time periods
- we obtained medical assessments from Dr Allen and Dr Calabrese on the documents.

133 Pfizer, Xanax Consumer Medicine Information, July 2011.
134 Pfizer Product Information, Xanax, July 2011.

4.4.1 OxyContin

We compared consumer warnings and the product information, publicly released by:

- Purdue (USA) MG Version: 10/2019
- Mundipharma (Australia) CMI Version: 12/2019
- Mundipharma (Australia) CMI Version: 01/2000[135]
- Mundipharma (Australia) PI Version: 12/2019
- Mundipharma (Australia) PI Version: 12/1999[136]

General Warning Side Effects
USA MG (2019) "A long-acting (extended-release) opioid pain medicine that can put you at risk for overdose and death. Even if you take your dose correctly as prescribed you are at risk for opioid addiction, abuse, and misuse that can lead to death." (page 1)
Australia CMI (2019) "All medicines may have some unwanted side effects. Sometimes they are serious but most of the time they are not. As for other medicines of this type, that is opioid analgesics, many side effects tend to reduce over time, with the exception of constipation. This means that the longer you take this medicine, the less it may cause problems for you. Your doctor has weighed the risks of this medicine against the benefits they expect it will have for you. Do not be alarmed by this list of possible side effects. Not everybody experiences them." (page 4)

135 Mundipharma, OxyContin Consumer Medicine Information, January 2000.
136 Mundipharma Product Information OxyContin, December 1999.

- The Australian CMI does not include the USA statement that taking the medication "correctly as prescribed" still exposes a person to the risk of "addiction, abuse and misuse that can lead to death". The USA document comprehensively warns the person of possible iatrogenic addiction and risk of death.
- Statements like "do not be alarmed" reduces the impact of the side effect warning and reduces the seriousness of the medications side effects in the mind of the consumer.
- It is scientifically incorrect that risks reduce over time. The risks actually increase for many side effects, like addiction. This statement may reduce, in a patient's mind, the importance of managing all the risks of this medication at all times, not just at the start of taking it. This statement is a significant failure to protect consumers against a life-threatening risk, in fact, it potentially increases the risk of it.

> That would be the opposite of what we teach. And the points that me and my colleagues emphasise when we're talking with other healthcare practitioners is if one is going to use an opioid analgesic medication to address a severe pain situation, then the lowest dose for the shortest period of time should be used. The reason that you want to limit the exposure to this medication is because of the increasing risk for side effects such as addiction, drug interaction, overdose. Those risks increase the longer someone is exposed to those medications.

– Dr Craig Allen

Note: The USA MG states, "Use the lowest dose possible for the shortest time needed." (page 1)

Alcohol Warning
USA MG (2019) "Taking OXYCODONE HCl EXTENDED-RELEASE TABLETS with other opioid medicines, benzodiazepines, alcohol, or other central nervous system depressants (including street drugs) can cause severe drowsiness, decreased awareness, breathing problems, coma, and death." (page 1) "Drink alcohol, or use prescription or over-the-counter medicines that contain alcohol. Using products containing alcohol during treatment with OXYCODONE HCl EXTENDED-RELEASE TABLETS may cause you to overdose and die." (page 1)
Australia CMI (2019) "Do not drink alcohol while you are taking OxyContin tablets. Drinking alcohol whilst taking OxyContin tablets may make you feel more sleepy and increase the risk of serious side effects, such as shallow breathing with the risk of stopping breathing and loss of consciousness." (page 3)
Australia CMI (2000) "These medicines or alcohol may increase the side effects of OxyContin. Your doctor or pharmacist can tell you what to do if you are taking any of these medicines." (page 2) "Do not take alcohol while being treated with OxyContin"; "If you drink alcohol the drowsiness may be worse." (page 3)
Australia Product Information (2019) "CNS depressants include, but are not limited to: sedatives (including benzodiazepines) antipsychotics, antidepressants, anxiolytics, hypnotics, general anaesthetics, phenothiazines, other tranquillisers, alcohol, other opioids, gabapentinoids such as pregabalin, benzodiazepines and neuroleptic drugs, etc.) Concurrent use of oxycodone with sedative medicine such as benzodiazepines or related drugs increases the risk of profound sedation, respiratory depression, hypotension, death or coma because of additive CNS depressant effect." (page 9)

- In the CMI (2019), alcohol is mentioned 9 times but not once is the risk of death associated with it. The risk of death was also not mentioned in the CMI (2000), it was included in the PI (1999).
- A comprehensive warning is included in the Australian PI for doctors, but many of the risks including coma or death are not included in the CMI for consumers. Given the content in the CMI is not consistent with the content in the PI, this is a breach of the *Therapeutic Goods Act 1989*.

> Alcohol increases the risk of overdose and overdose death. With any type of opioid analgesic you're taking, certainly something like OxyContin, alcohol should be avoided. And before someone has started on a medication such as that, part of the screening to determine what the person's risks are for developing addiction or overdose would include identifying whether or not they have a substance use disorder or alcohol use disorder and absolutely warning them about taking in substances that can be sedating. And alcohol is one of them as well as benzodiazepines and other Z-drugs or sleep medications.

– Dr Craig Allen

Benzodiazepine Warning
USA MG (2019) "Taking OXYCODONE HCl EXTENDED-RELEASE TABLETS with other opioid medicines, benzodiazepines, alcohol, or other central nervous system depressants (including street drugs) can cause severe drowsiness, decreased awareness, breathing problems, coma, and death." (page 1)
Australia CMI (2019) and CMI (2000) No benzodiazepine warning included.
Australia Product Information (2019) "Concurrent use of oxycodone and sedative medicines such as benzodiazepines or related drugs may result in sedation, respiratory depression, coma and death." (page 5)

- No comparable warning exists in the CMIs.
- In fact 'Benzodiazepine' is not mentioned once in the CMI (2019) or the earlier CMI (2000).
- A comprehensive warning is included in the Australian PI for doctors, but nothing is included in the CMI for consumers. Given the content in the CMI is not consistent with the content in the PI, this is a breach of the *Therapeutic Goods Act 1989*.

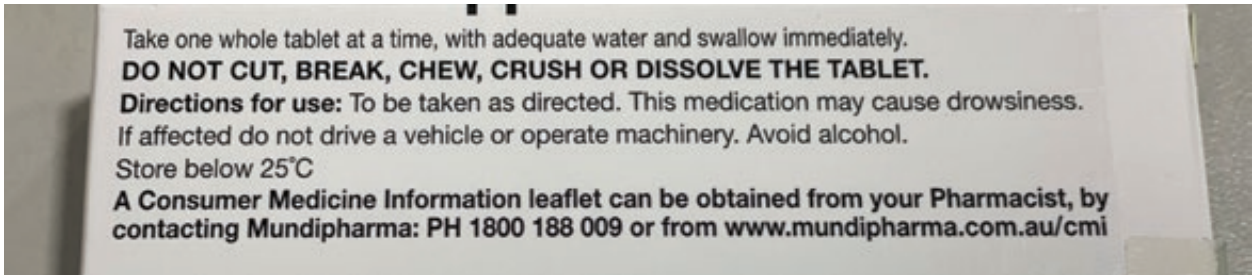
> Benzodiazepines are contraindicated if someone is on an opioid analgesic. Oxycodone is an opioid analgesic. So benzodiazepines should be avoided. There may be specific situations where someone [inaudible] a provider after assessing potential risks and educating their patient, may decide that using a benzo with an opioid is the most appropriate approach, however, that situation would then need to be closely monitored because there is an enhanced risk of suppression of the respiratory drive system and people are at risk of dying if they are on both these medications at the same time, not to mention the impact on cognitive functioning and balance risk for falls, etc.
>
> *– Dr Craig Allen*

Other Medications and Supplements Warning
USA MG (2019) "taking prescription or over-the-counter medicines, vitamins, or herbal supplements. Taking OXYCODONE HCl EXTENDED RELEASE TABLETS with certain other medicines can cause serious side effects that could lead to death." (page 1)
Australia CMI (2019) and CMI (2000) A broad and lengthy warning on page 2 indicates that a number of medicines and supplements can interact with OxyContin. This list mentions "mental health" and "anxiety" medications. It warns of possible increase in side effects. However, it does not mention any specific health risks of these interactions, nor the risk of death." (page 2)
Australia Product Information (2019) "CNS depressants include, but are not limited to: sedatives (including benzodiazepines) antipsychotics, antidepressants, anxiolytics, hypnotics, general anaesthetics, phenothiazines, other tranquillisers, alcohol, other opioids, gabapentinoids such as pregabalin, benzodiazepines and neuroleptic drugs, etc.) Concurrent use of oxycodone with sedative medicine such as benzodiazepines or related drugs increases the risk of profound sedation, respiratory depression, hypotension, death or coma because of additive CNS depressant effect." (page 9)

- No warning of the risk of death in the Australian CMIs.
- The Australian warning would not escalate the life-threatening risk to the person reading the CMI. The CMI does not explicitly mention the medication types that are the greatest risk. Comorbid mental illness and pain conditions are commonly treated with opioids and antidepressants or antipsychotics. The life-threatening polydrug risks including death are not explained to the consumer.
- A comprehensive warning is included in the Australian PI for doctors, but many of the risks including coma or death are not included in the CMI for consumers. Given the content in the CMI is not consistent with the content in the PI, this is a breach of the *Therapeutic Goods Act 1989*.

> Treating patients with psychiatric disorders and chronic pain is particularly difficult, not just because of the combined impact on the patient, but because of the dangers of the concurrent CNS medications. I don't prescribe opioids and if possible I work with new patients to deprescribe them especially if they are taking psychiatric drugs, the risk of respiratory depression and death is too great.

– Dr Lori Calabrese



Addiction Warning
USA MG (2019) "A long-acting (extended-release) opioid pain medicine that can put you at risk for overdose and death. Even if you take your dose correctly as prescribed you are at risk for opioid addiction, abuse, and misuse that can lead to death." (page 1)
Australia CMI (2019) "There is potential for abuse of oxycodone and the development of addiction to oxycodone. It is important that you discuss this issue with your doctor." (page 4)
Australia CMI (2000) "Opioid analgesics such as OxyContin have been used to treat pain for many years. In most cases addiction does not occur. However, over time your body becomes used to taking OxyContin, so if you suddenly stop taking OxyContin, you may experience some symptoms of withdrawal. It is important to discuss this issue with you doctor." (page 1 and page 4)

- The CMI (2019) does not contain the USA warning of the risk of addiction even if taken correctly as prescribed. The person is referred to their doctor to discuss the risk of addiction, however the role of the CMI is to document the risks and how to avoid them.
- The CMI (2000) does not contain the same warnings as in the USA or the CMI (2019).
- The (CMI) 2000 contains a statement that has no scientific basis: that the risk of addiction is low. This statement significantly reduces the possibility of addiction from a consumer's risk assessment before choosing to start taking it. The exact statement was included twice in the CMI. This statement was part of the original 1996 OxyContin USA consumer warning. It was removed in 2001 after Purdue agreed it was not accurate.[137] This statement was a significant part of the cause for the over prescription of the medication, as doctors believed it to be a safer alternative. This statement is also a core reason for legal action against Purdue in the USA (see Chapter 8).

> OxyContin is an opioid. All opioids factor the reward pathway and can lead to addiction. Therefore, short-term use, if use is indicated, is preferential and an assessment of a patient for their risk factors for addiction prior to prescribing this medication. People who are younger are at greater risk. People who have certain psychiatric disorders or histories of trauma are at greater risk of developing addiction. But anyone, if exposed to an opioid analgesic for a long enough period of time, high enough doses, they will become addicted to this. There are significant risks for becoming addicted to this medication. They will become tolerant to the medication, they'll become physically dependent, they will suffer from withdrawal symptoms, anyone will. The risk of becoming addicted is greater with the risk factors and the longer someone is on that medication.
>
> *– Dr Craig Allen*

137 Purdue, 'New hope for millions of Americans suffering from persistent pain', OxyContin press release, USA, 31 May 1996.

Overdose Warning
USA MG (2019) "Get emergency help right away if you take too much OXYCODONE HCl EXTENDED-RELEASE TABLETS (overdose). When you first start taking OXYCODONE HCl EXTENDED-RELEASE TABLETS, when your dose is changed, or if you take too much (overdose), serious or life-threatening breathing problems that can lead to death may occur." (page 1)
Australia CMI (2019) "If someone takes an overdose they may experience difficulties in breathing, become drowsy and tired, lack muscle tone, have cold or clammy skin, have constricted pupils, have very low blood pressure or slow heart rate and may even become unconscious or die." (page 3)
Australia CMI (2000) "If someone takes too many tablets, they will probably become drowsy, tired, confused, have a very low blood pressure, experience difficulties in breathing and possibly become unconscious." (page 3)
Australia Product Information (1999) "Symptoms: Acute overdosage with oxycodone can be manifested by respiratory depression, somnolence progressing to stupor or coma, skeletal muscle flaccidity, cold and clammy skin, constricted pupils, bradycardia, hypotension, and death." (page 8)

- The USA MG warns that an overdose can also occur when simply starting or changing a dose. This does not appear in the Australian CMIs.
- The risk of death is mentioned as the final possibility in a list of side effects in the CMI (2019). The only time the risk of death is mentioned (in the entire CMI) is in relation to taking an overdose.
- In the original CMI when OxyContin was released in 2000, risk of death as a result of an overdose is not mentioned. The risk of a respiratory depression, coma and death was actually included in the PI in 1999, making it inconsistent with the CMI. Given the content in the CMI is not consistent with the content in the PI, this is a breach of the *Therapeutic Goods Act 1989.*
- The CMI (2019) does not mention using the PBS Opioid Rescue Nasal Spray – Nyxoid, made by Mundipharma.

> The experience in the US with opioids is that an overdose can occur for many reasons and not simply because of ingesting a large dose. It can occur the first time somebody takes the medication, or when a new dose is prescribed. So the CMI 2019, it could be a lot better but the 2000 CMI is a disgrace.

– Dr Lori Calabrese

Abuse Warning
USA MG (2019) "Swallow OXYCODONE HCl EXTENDED-RELEASE TABLETS whole. Do not cut, break, chew, crush, dissolve, snort, or inject OXYCODONE HCl EXTENDED-RELEASE TABLETS because this may cause you to overdose and die." (page 1)
Australia CMI (2019) "OxyContin tablets are only designed to work properly if swallowed whole. The tablets may release all their contents at once if broken, cut, chewed, crushed or dissolved which can be dangerous and cause serious problems, such as an overdose, which may be fatal." (page 3)
Australia CMI (2000) "Do not chew, crush or dissolve tablets. OxyContin tablets were designed to work properly only if swallowed whole. They may release all their contents at once if broken, chewed or crushed, resulting in a risk of overdose." (page 2)
Australia Product Information (1999) "OxyContin tablets are to be swallowed whole, and are not to be broken, chewed or crushed. Taking broken, chewed or crushed OxyContin tablets could lead to the rapid release and absorption of a potentially toxic dose of oxycodone." (page 7)

- There are similar warnings in the CMI (2019) to the USA MG, however it uses "fatal" instead of "die".
- No warning was included of the risk of death in the CMI (2000). By 2000 Purdue was aware of an emerging crisis in the USA relating to fatal overdoses of OxyContin. The risk of a toxic dose occurring was actually included in the PI in 1999, making it inconsistent with the CMI. Given the content in the CMI is not consistent with the content in the PI, this is a breach of the *Therapeutic Goods Act 1989*.
- Before OxyContin was launched in 1996, Purdue was aware that if the tablets were chewed accidentally, it released up to 68% of the opioid immediately into the person's system. This was resulting in overdoses; many fatal. In 2001 Purdue updated its warnings to state, "Patients should be advised that OxyContin Tablets were designed to work properly only if swallowed whole. OxyContin Tablets will release all their contents at once if broken, chewed, or crushed, resulting in a risk of fatal overdose."

> The issue with the original OxyContin tablet, that could contain more oxycodone than a dozen instant-release pills, was that to release most of that oxycodone into your system, all you had to do was accidently chew not swallow. I could spend all day explaining just how deadly that is, and if they call that abuse then it needed a warning to go with the abuse risk.

– Dr Lori Calabrese

> Many patients became addicted to OxyContin without being warned of this risk. Addiction is an illness and it drives people to needing more of the drug to fulfill the psychological and physical cravings. If a person became addicted, each OxyContin pill provided a large source of oxycodone to fuel the addiction by crushing it. Only they also told people it had a low risk of abuse, when it was the opposite. It was the perfect formulae to start a national drug crisis, and it did. And when Purdue was investigated, they blamed the people who had become addicts as being the criminals to blame.

– Dr Lori Calabrese

Missed Dose Warning

USA MG (2019)

"If you miss a dose, take your next dose at your usual time." (page 1)

Australia CMI (2019)

"If you forget to take your tablets, contact your doctor or pharmacist for advice. Do not take a double dose to make up for the dose you have missed. This will increase the chance of you getting unwanted side effects." (page 3)

– The risk of taking a double dose is the risk of an overdose or death – this is not mentioned in the Australian CMI.

> Unwanted side effects, like respiratory depression, coma, circulatory collapse, hypotension, death, I guess you can call them unwanted, this is unbelievable, who regulates these leaflets in Australia?

– Dr Craig Allen

Sharing Opioids

USA MG (2019)

"Never give anyone else your OXYCODONE HCl EXTENDED-RELEASE TABLETS. They could die from taking it. Selling or giving away OXYCODONE HCl EXTENDED-RELEASE TABLETS is against the law." (page 1)

Australia CMI (2019) and CMI (2000)

"Do not give your medicine to anyone else, even if they have the same condition as you." (page 4) and (page 3)

– No risk of death warning is included in the CMI (2019) or in the CMI (2000). Yet, the TGA's *Return your opioid* campaign warns about the risk of sharing opioids with other people, including death.[138]

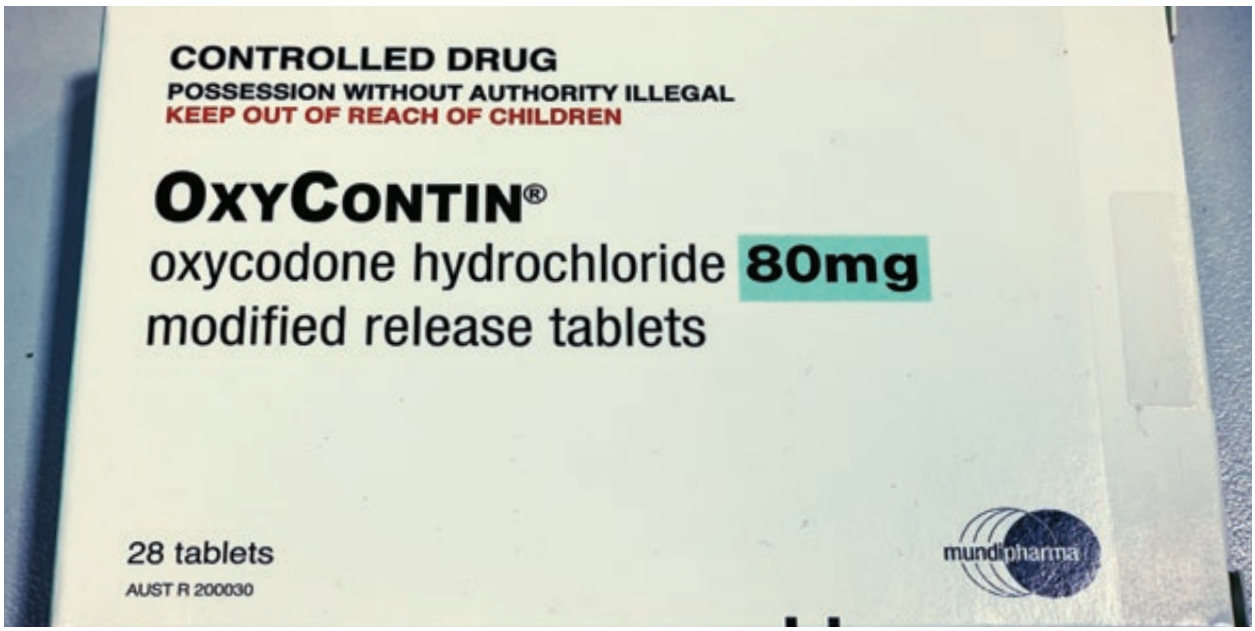
138 Australian Government Department of Health Therapeutic Goods Administration, accessed on 3 April 2020, see https://www.tga.gov.au/publication/return-your-unused-opioids-resource-kit

Recommended Use
USA MG (2019) "A strong prescription pain medicine that contains an opioid (narcotic) that is used to manage pain severe enough to require daily around-the-clock, long-term treatment with an opioid, when other pain treatments such as non-opioid pain medicines or immediate-release opioid medicines do not treat your pain well enough or you cannot tolerate them." (page 1)
Australia CMI (2019) and CMI (2000) "OxyContin tablets are used to relieve moderate to severe chronic pain when other forms of treatment have not been effective." (page 1)

- In the USA MG OxyContin is only recommended for severe pain.
- In the Australian CMI OxyContin is made available for moderate to severe pain. In Australia since its launch, OxyContin has been made available to patients with moderate pain, exposing them to side effects (including addiction and death) they would not be exposed to with other medications more appropriate for moderate pain.

> OxyContin is one of the tools that is available, however, first line treatment for non-surgical pain, certainly there are a number of less potentially dangerous options. To name a few, depending on what the injury is from, there's non-medication approaches to that injury. When considering medications, there are anti-inflammatories and other medications for pain, so acetaminophen, ibuprofen. Those are the types of medications that have been shown to be as and sometimes more effective, even for surgical pain.

– Dr Craig Allen



Pregnancy Warnings

USA MG (2019)

- "pregnant or planning to become pregnant. Prolonged use of OXYCODONE HCl EXTENDED-RELEASE TABLETS during pregnancy can cause withdrawal symptoms in your newborn baby that could be life-threatening if not recognized and treated."
- "breastfeeding. Not recommended during treatment with OXYCODONE HCl EXTENDED-RELEASE TABLETS. It may harm your baby." (page 1)

Australia CMI (2019)

"Do not take this medicine if you are pregnant or intend to become pregnant whilst taking this medicine.

Like most medicines of this kind, OxyContin tablets are not recommended to be taken during pregnancy. Your doctor will discuss the risks of taking it if you are pregnant." (page 1/2)

"This medicine is not recommended to be taken during labour. Oxycodone given to the mother during labour may cause breathing problems and signs of withdrawal in the newborn. Tell your doctor if you are breastfeeding or planning to breastfeed. Oxycodone can pass into the breastmilk and can affect the baby." (page 2)

Australia CMI (2000)

"Before you start to take it you must tell your doctor if:

- You are pregnant or plan to become pregnant.
- Your doctor will discuss the possible risks and benefits of taking OxyContin during pregnancy.
- You are breastfeeding or plan to breastfeed.
- Your doctor will discuss the risks and benefits of taking OxyContin when breastfeeding." (page 2)

- The MG (2019) contains a serious warning in relation to this area, including the actual risks to the baby. The CMI (2019) does not including the words "life threatening".
- The CMI (2000) contains no directive to "not take this medicine".
- The CMI (2000) does not specify the actual risks that taking this medicine will expose the unborn or newborn child to or that they are life-threatening.
- The CMI (2000) refers the person to their doctor for more information on the risks. The purpose of the CMI is to inform the person of the risks. This enables them to make a decision to take the medication or not. Pregnancies are not always planned, the risks should have been included to provide all the information to the consumer irrespective of if they are or planned to become pregnant.
- The CMI (2000) does not provide any comparable level of warning to the CMI (2019) nor would this warning adequately warn of life-threatening risks in this area.

> So concerns that come up with someone who is on OxyContin and has a baby, first at delivery, there's the concerns about neonatal abstinence syndrome because the medication is passed through the placental barrier. The foetus would then develop withdrawal symptoms once they were born called neonatal abstinence syndrome. Likewise, when a mother is breastfeeding, the opioid analgesic medication can be passed through the breast milk, exposing the infant to this drug, which has the potential to impact developing brains in ways that can have life-long consequences. There is quite a bit of literature about opioids and babies born to mothers who are addicted to opioids or are in other ways using opioids. And some of the controversy is around just exactly what type of neuropsychiatric and neurocognitive impairment these babies may grow up to have. Oftentimes, the thought is around learning difficulties and attentional problems and so forth. But there's no conjecture of whether or not it actually happens.

– Dr Craig Allen

In summary for the OxyContin analysis:

OxyContin Mundipharma	Australia (12/2019)	Australia (01/2000)
	Death mentioned: 2 times vs 8 times USA (2019)	Death mentioned: 0 times vs 8 times USA (2019)
Made available to people with moderate pain	Yes	Yes
Misleading statements	The risk of side effects reduces over time	The risk of addiction is low
Risk of death in relation to alcohol	Not included*	Not included
Risk of death in relation to benzodiazepines	Not included*	Not included
Risk of death in relation to other medications/ supplements	Not included*	Not included
Risk of overdose when starting or changing a dose	Not included	Not included
Risk of addiction when taken as prescribed	Not included	Not included
Risk of death from sharing opioids	Not included	Not included
Risk of death in relation to pregnancy	Not included	Not included
Advise of Nyxoid in case of overdose	Not included	n/a

OxyContin Mundipharma	Australia (12/2019)	Australia (01/2000)
	Death mentioned: 2 times vs 8 times USA (2019)	Death mentioned: 0 times vs 8 times USA (2019)
Risk of death from overdose	Included – the only time the risk of death is mentioned is overdose or abuse	Not included*
Risk of death from abuse	Included – the only time the risk of death is mentioned is overdose or abuse	Not included*

* Examples of inconsistencies between the CMI and the PI, which are breaches of the *Therapeutic Goods Act 1989*

> All of those potential risks have been known for many years, and it's **unconscionable** to not include that type of information when considering prescribing this medication, let alone introducing this type of medication to any human population.

– Dr Craig Allen

Interviewer Question:	*And am I right in saying that lack of information has been a cornerstone of why Purdue has received the attention that it has for the overdose crisis?*
Dr Allen Answer:	*Right. When Purdue launched OxyContin in the USA, they withheld warnings around the risk of death from misuse, by crushing the tablets, and they downplayed the risk of addiction. Those are the reasons that Purdue has been convicted in court, both back in 2007 and now again.*

4.4.2 Endone

We compared consumer warnings and the product information, publicly released by:

- Aspen (Aust) CMI Version: 07/2015
- Purdue (USA) MG Version: 10/2019 (for OxyContin)
- Aspen (Aust) PI Version: 06/2015

Endone does not have a direct comparison product in the USA. In Australia it is used as an alternative to OxyContin. Hence, we have compared Endone Australia versus OxyContin USA.

General Warning Side Effects
USA MG (2019) – OxyContin "A long-acting (extended-release) opioid pain medicine that can put you at risk for overdose and death. Even if you take your dose correctly as prescribed you are at risk for opioid addiction, abuse, and misuse that can lead to death." (page 1)
Australia CMI (2015) – Endone "All medicines have risks and benefits. Your doctor has weighed up the risks of you taking ENDONE against the benefits they expect it will have for you." (page 1) "ENDONE belongs to a group of medicines called narcotic analgesics. Narcotic analgesics act to relieve pain." (page 1)
Australia Product Information (2015) – Endone "Therapeutic doses of oxycodone may decrease respiratory drive and increase airways resistance in patients with acute asthma, chronic obstructive airways disease or those with substantially decreased pulmonary reserve or respiratory depression." (page 2) "Death may occur from respiratory failure." (page 5)

- The CMI does not mention or explain that it is an opioid medication once. It is described as a "narcotic analgesics" on (page 1). Consumers would not understand the connection. The PI mentions "opioid" 12 times.
- The CMI does not include the USA statement that taking the medication "correctly as prescribed" still exposes a person to the risk of "addiction, abuse and misuse that can lead to death". The USA document comprehensively warns the person of the possible iatrogenic addiction and risk of death.
- A comprehensive warning is included in the PI for doctors on the risks at therapeutic doses, but nothing is included in the CMI for consumers. Given the content in the CMI is not consistent with the content in the PI, this is a breach of the *Therapeutic Goods Act 1989*.

Note: The USA MG states, "Use the lowest dose possible for the shortest time needed." (page 1)

Alcohol Warning

USA MG (2019) – OxyContin

"Taking OXYCODONE HCl EXTENDED-RELEASE TABLETS with other opioid medicines, benzodiazepines, alcohol, or other central nervous system depressants (including street drugs) can cause severe drowsiness, decreased awareness, breathing problems, coma, and death." (page 1)

"**While taking OXYCODONE HCl EXTENDED-RELEASE TABLETS** DO NOT**:** Drink alcohol, or use prescription or over-the-counter medicines that contain alcohol. Using products containing alcohol during treatment with OXYCODONE HCl EXTENDED-RELEASE TABLETS may cause you to overdose and die." (page 1)

Australia CMI (2015) – Endone

"Things to be careful of: Be careful when drinking alcohol while you are taking ENDONE. The combination could make you more dizzy, sleepy or light-headed than usual. Your doctor may suggest you avoid alcohol while you are taking ENDONE." (page 3)

"These medicines and alcohol may be affected by ENDONE or they may affect how well it works. You may need to take different amounts of these medicines, or you may need to take different medicines." (page 2)

Australia Product Information (2015) – Endone

[Possible side effects of combining Endone and alcohol] "Respiratory depression, hypotension and profound sedation or coma may result." (page 2)

"Death may occur from respiratory failure." (page 5)

- The CMI does not mention the risk of severe drowsiness, decreased awareness, breathing problems, coma, and death as a risk of consuming alcohol with Endone.
- The CMI states that your doctor may recommend that you avoid alcohol whilst taking Endone, whilst the USA MG states, "do not drink alcohol".
- The PI states the risk of profound sedation and coma, that is not mentioned in the CMI. Given the content in the CMI is not consistent with the content in the PI, this is a breach of the *Therapeutic Goods Act 1989*.

Benzodiazepine Warning

USA MG (2019) – OxyContin

"Taking OXYCODONE HCl EXTENDED-RELEASE TABLETS with other opioid medicines, benzodiazepines, alcohol, or other central nervous system depressants (including street drugs) can cause severe drowsiness, decreased awareness, breathing problems, coma, and death." (page 1)

Australia CMI (2015) – Endone

Benzodiazepines are not mentioned in the CMI.

Australia Product Information (2015) – Endone

[Possible side effects of combining Endone and other CNS depressants] "Respiratory depression, hypotension and profound sedation or coma may result." (page 2)

"Death may occur from respiratory failure." (page 5)

- No comparable warning exists in the CMI.
- Benzodiazepine is not mentioned once in the CMI.
- The PI states the risk of profound sedation, coma and death, that is not mentioned in the CMI. Given the content in the CMI is not consistent with the content in the PI, this is a breach of the *Therapeutic Goods Act 1989*.

Other Medications and Supplements Warning

USA MG (2019) – OxyContin

"taking prescription or over-the-counter medicines, vitamins, or herbal supplements. Taking OXYCODONE HCl EXTENDEDRELEASE TABLETS with certain other medicines can cause serious side effects that could lead to death." (page 1)

Australia CMI (2015) – Endone

"These medicines and alcohol may be affected by ENDONE or they may affect how well it works. You may need to take different amounts of these medicines, or you may need to take different medicines." (page 2)

Australia Product Information (2015) – Endone

[Possible side effects of combining Endone and other medications like antidepressants] "Respiratory depression, hypotension and profound sedation or coma may result." (page 2)

"Death may occur from respiratory failure." (page 5)

- The CMI does not warn that side effects may arise or of the risk of death. A broad and lengthy warning on page 2 indicates that a number of medicines and supplements can interact with Endone. This list mentions "mental health" and "anxiety" medications. However, it does not mention any specific medication types, the material health risks of these interactions, or the risk of death. (page 2)
- The Australian warning would not escalate the life-threatening risk to the person reading the CMI. The CMI does not explicitly mention the medication types that have the greatest risk. Prescriptions for both opioids and antidepressants are common for comorbid pain/mental illness.
- The PI states the risk of profound sedation, coma and death, that is not mentioned in the CMI. Given the content in the CMI is not consistent with the content in the PI, this is a breach of the *Therapeutic Goods Act 1989*.

Overdose Warning

USA MG (2019) – OxyContin

"Get emergency help right away if you take too much OXYCODONE HCl EXTENDED-RELEASE TABLETS (overdose). When you first start taking OXYCODONE HCl EXTENDED-RELEASE TABLETS, when your dose is changed, or if you take too much (overdose), serious or life-threatening breathing problems that can lead to death may occur." (page 1)

Australia CMI (2015) – Endone

"Symptoms of overdose include feeling sleepy and/or difficulty in breathing which could lead to unconsciousness and loss of muscle control. Your heart may stop and death may occur." (page 2)

- The USA MG warns that an overdose can also occur when simply starting or changing a dose. This does not appear in the Australian CMI.
- In the CMI the risk of death is mentioned as the final possibility in a list of side effects. The only time the risk of death is mentioned (in the entire CMI) is in relation to taking an overdose.
- The CMI does not mention using the PBS Opioid Rescue Nasal Spray – Nyxoid.

Abuse Warning

USA MG (2019) – OxyContin

"Swallow OXYCODONE HCl EXTENDED-RELEASE TABLETS whole. Do not cut, break, chew, crush, dissolve, snort, or inject OXYCODONE HCl EXTENDED-RELEASE TABLETS because this may cause you to overdose and die." (page 1)

Australia CMI (2015) – Endone

"If abused it may become less able to reduce pain." (page 1)

- The CMI has no comparable warning around abuse. Endone is a schedule 8 drug due to its abuse risk.
- There is no warning of the risk of death in the CMI, only that it may become less effective.

Addiction Warning

USA MG (2019) – OxyContin

"A long-acting (extended-release) opioid pain medicine that can put you at risk for overdose and death. Even if you take your dose correctly as prescribed you are at risk for opioid addiction, abuse, and misuse that can lead to death." (page 1)

Australia CMI (2015) – Endone

"ENDONE can be addictive. If used for a long time ENDONE may become habit forming causing mental and physical dependence. If abused it may become less able to reduce pain. (page 1)

- The CMI does not contain the USA warning of the risk of addiction even if taken correctly as prescribed.
- The CMI does not contain a warning of the risk of death. The CMI does not explain the length of time that would expose a person to addiction. A "long time" does not indicate weeks, months or years.

Missed Dose Warning

USA MG (2019) – OxyContin

"If you miss a dose, take your next dose at your usual time." (page 1)

Australia CMI (2015) – Endone

"Do not take a double dose to make up for the dose that you missed. (page 2)

– The risk of taking a double dose is the risk of an overdose or death – this is not mentioned in the CMI.

Sharing Opioids

USA MG (2019) – OxyContin

"Never give anyone else your OXYCODONE HCl EXTENDED-RELEASE TABLETS. They could die from taking it. Selling or giving away OXYCODONE HCl EXTENDED-RELEASE TABLETS is against the law." (page 1)

Australia CMI (2015) – Endone

"Do not give ENDONE to anyone else, even if their symptoms seem similar to yours. It may not be safe for another person to take this medicine." (page 2)

– The risk of death is not included in the CMI. The TGA *Return your opioid* campaign warns about the risk of sharing opioids with other people, including death.[139] However, the risk isn't mentioned in the CMI.

Recommended Use

USA MG (2019) – OxyContin

"A strong prescription pain medicine that contains an opioid (narcotic) that is used to manage pain severe enough to require daily around-the-clock, long-term treatment with an opioid, when other pain treatments such as non-opioid pain medicines or immediate-release opioid medicines do not treat your pain well enough or you cannot tolerate them." (page 1)

Australia CMI (2015) – Endone

There is no information on the recommended use.

– In the USA MG OxyContin is only recommended for severe pain.
– In the CMI there is no comparable explanation of when Endone is appropriate. Stating the recommended use is a requirement for a CMI.

139 Australian Government Department of Health Therapeutic Goods Administration, accessed on 3 April 2020, see https://www.tga.gov.au/publication/return-your-unused-opioids-resource-kit

Pregnancy Warnings

USA MG (2019) – OxyContin

- "pregnant or planning to become pregnant. Prolonged use of OXYCODONE HCl EXTENDED-RELEASE TABLETS during pregnancy can cause withdrawal symptoms in your newborn baby that could be life-threatening if not recognized and treated."
- "breastfeeding. Not recommended during treatment with OXYCODONE HCl EXTENDED-RELEASE TABLETS. It may harm your baby." (page 1)

Australia CMI (2015) – Endone

"Do not take ENDONE during pregnancy or during breastfeeding as it may cause difficulty in breathing in an unborn or newborn child. Women who are pregnant, planning to become pregnant or who are breastfeeding should discuss this with their doctor. (page 1)

- The CMI does not warn against the risk of "withdrawal symptoms" nor does it include the "life-threatening" risk statement.
- The CMI refers the person to their doctor for more information on the risks. The purpose of the CMI is to inform the person of the risks. This enables them to make a decision to take the medication or not. Pregnancies are not always planned, so the risks should have been included to provide all the information to the consumer irrespective of if they are planning to become pregnant.

Tolerance Warning

USA MG (2019) – OxyContin

No information on tolerance.

Australia CMI (2015) – Endone

"High doses of ENDONE can cause unconsciousness, heart failure, low blood pressure or an inability to breath properly." (page 3).

- The CMI fails to warn of the risk of overdose and death with high doses.

Serious Side Effects are Rare

USA MG (2019) – OxyContin

No comparable warning.

Australia CMI (2015) – Endone

"These are serious side effects and may need urgent medical attention. **Serious side effects are rare**." (page 3).

- The use of the word "rare" in describing serious side effects does not give the consumer the appropriate level of danger of using an opioid, as compared to government warnings detailed in Chapter 1. The word rare or describing serious side effects as being unlikely does not exist in the USA MG.

In summary for the Endone analysis:

Endone Aspen Pharma	Australia Current (07/2015) Death mentioned: 1 time vs 8 times USA (2019)
Explanation of when use is recommended	No
Misleading statements	Describes Endone as a 'narcotic analgesic' and not as an 'opioid', which it does in the PI. The likelihood of serious side effects is described as being 'rare'.
Risk of death in relation to alcohol	Not included*
Risk of death in relation to benzodiazepines	Not included*
Risk of death in relation to other medications/ supplements	Not included*
Risk of overdose when starting or changing a dose	Not included
Risk of addiction when taken as prescribed	Not included
Risk of death when taken as prescribed	Not included*
Risk of death from sharing opioids	Not included
Risk of death in relation to pregnancy	Not included
Advise of Nyxoid in case of overdose	Not included
Risk of death from overdose	**Included – the only time the risk of death is mentioned is in relation to overdose**
Risk of death from abuse	Not included

* Examples of inconsistencies between the CMI and the PI, which are breaches of the *Therapeutic Goods Act 1989*. The **CMI has not been updated since 2015**, despite numerous TGA and Department of Health warnings (outlined in Chapter 1) being published about the use and risks of opioids since that time.

> All of those potential risks have been known for many years, and it's **unconscionable** to not include that type of information when considering prescribing this medication, let alone introducing this type of medication to any human population.

– Dr Craig Allen

4.4.3 Valium

We compared consumer warnings and the product information, publicly released by:

- Roche (USA) MG Version: 12/2016
- Roche (Aust) CMI Version: 03/2018
- Roche (Aust) CMI Version: 02/2000[140]
- Roche (Aust) PI Version: 01/2020

Alcohol Warning
USA MG (2016) "What is the most important information I should know about VALIUM? VALIUM is a benzodiazepine medicine. Taking benzodiazepines with opioid medicines, alcohol, or other central nervous system depressants (including street drugs) can cause severe drowsiness, breathing problems (respiratory depression), coma and death. VALIUM can make you sleepy or dizzy, and can slow your thinking and motor skills." (page 1)
Australia CMI (2018) and CMI (2000) "if you drink alcohol; Alcohol may increase the effects of Valium." (page 2) "Things to be careful of; Be careful if you are elderly, unwell, drinking alcohol or taking other medicines. Some people may experience side effects such as drowsiness, confusion, dizziness and unsteadiness which may increase the risk of a fall. Your doctor may suggest that you avoid alcohol or reduce the amount of alcohol you drink while you are taking Valium." (page 3)
Australia Product Information (2020) "Benzodiazepines increase the effects of other central nervous system depressants, including alcohol. When combined with other CNS depressants, the effects of overdosage are likely to be severe and may prove fatal." (page 13) [Combined use of alcohol and benzodiazepine medication] "Such concomitant use has the potential to increase the clinical effects of Valium, possibly including severe sedation that could result in coma or death" (page 3)

- The CMIs do not include the risk of "breathing problems (respiratory depression), coma and death". In fact, "respiratory depression, coma and death" are not mentioned once in the CMI.
- The CMIs do not state that a consumer should avoid or stop taking alcohol, just that "a doctor may suggest you avoid or reduce the amount of alcohol". The USA MG states, "You should not drink alcohol while taking VALIUM."
- The PI warns of the risk of overdose, coma and death if alcohol is used, but not the CMI for consumers. Given the content in the CMI is not consistent with the content in the PI, this is a breach of the *Therapeutic Goods Act 1989*.

> I could list a myriad of well-known, popular culture figures who have had comas or suffered death from using alcohol and benzodiazepines. Both in the state of Connecticut and across the United States, the risk is significant and well-known to the medical community and I think fairly well-known in the lay population.

– Dr Craig Allen

140 Roche, Valium Consumer Medicine Information, February 2000.

Opioid Warning

USA MG (2016)

"What is the most important information I should know about VALIUM? VALIUM is a benzodiazepine medicine. Taking benzodiazepines with opioid medicines, alcohol, or other central nervous system depressants (including street drugs) can cause severe drowsiness, breathing problems (respiratory depression), coma and death. VALIUM can make you sleepy or dizzy, and can slow your thinking and motor skills." (page 1)

Australia CMI (2018) and CMI (2000)

Opioids are not mentioned once in the CMIs

Australia Product Information (2020)

"However, due to the additive CNS depressant effect, the concomitant use of diazepam and opioids should be avoided (see Pharmacodynamic Drug- Drug Interaction (DDI) below).

If a decision is made to prescribe Valium concomitantly with opioids, prescribe the lowest effective dose and minimum duration of concomitant use. Follow patients closely for signs and symptoms of respiratory depression and sedation (see section 4.4. Special warnings and precautions for use and section 4.9 Overdose).

Advise both patients and caregivers about the risks of respiratory depression and sedation when Valium is used with opioids.

Advise patients not to drive or operate heavy machinery until the effects of concomitant use of the opioid have been determined (see section 4.7 Effects on Ability to Drive and Use Machines)." (page 9)

"Benzodiazepines increase the effects of other central nervous system depressants, including alcohol. When combined with other CNS depressants, the effects of overdosage are likely to be severe and may prove fatal." (page 13)

[Combined use of opioid and benzodiazepine medication] "Such concomitant use has the potential to increase the clinical effects of Valium, possibly including severe sedation that could result in coma or death" (page 3)

- The CMIs do not mention the risk of taking this medication with "opioid medicines". Opioid medicines are not mentioned once.
- Hence consumers in Australia have received no warning on the risk of "breathing problems (respiratory depression), coma and death" as is provided in the USA MG.
- The PI contains multiple warnings in relation to using a benzodiazepine with opioids. It states that the combined use should be avoided. It advises to prescribe the lowest dose for the shortest period of time if used together. It warns of the risk of overdose, respiratory depression, sedation, coma and death.
- The PI specifically states to advise patients of the risks of respiratory depression and sedation when these medications are combined. It also states to advise patients of the risk of driving whilst taking these 2 medications.
- Depsite this the multiple life-threatening warnings in the PI, including respiratory depression, have never been included in the CMIs since 2000. Given the content in the CMI is not consistent with the content in the PI, this involves multiple breaches of the *Therapeutic Goods Act 1989*.

> When you read the lead warning statements for opioids and benzodiazepines in our medical guides, they're all warnings about death because these drugs are deadly especially when taken together or with alcohol. These warnings are about real risks to real people. They are warnings that patients need to know if they're going to take an opioid or benzodiazepine because these can result in that slow march of use, tolerance, dependence, overdose, and death, even when the drug is taken as prescribed. I can't believe these Australian warnings.

– Dr Lori Calabrese

Addiction and Abuse Warnings
USA MG (2016) VALIUM is a federal controlled substance (C-IV) because it can be abused or lead to dependence." (page 1) "Abuse and dependence. Taking VALIUM can cause physical and psychological dependence. Physical and psychological dependence is not the same as drug addiction. Your healthcare provider can tell you more about the differences between physical and psychological dependence and drug addiction." (page 2)
Australia CMI (2018) and CMI (2000) Addiction is not mentioned as a risk of taking this medication. Abuse is not mentioned as a risk of taking this medication.

- The USA MG does not contain any mention of the risk of addiction to the medication.
- The CMIs do not contain any mention of the risk of addiction to the medication. The absence of a warning around addiction completely eliminates one of the most significant risks of taking this medication. Valium is a Schedule 4 drug because of the risk of addiction, but that risk is not mentioned at all.
- The CMI does not mention "abuse" once nor the risks of "abuse". Valium is a Schedule 4 drug because of the risk of abuse but that risk is not mentioned at all.

> Benzodiazepines really aren't supported for use longer than two to four weeks. There's not a lot of data showing efficacy after that point in time. And there's a significant amount of data again for developing an addiction to benzodiazepines as well as increasing risk for drug interaction and death.

– Dr Craig Allen

> Benzodiazepines are highly addictive, and that risk starts the first time it's taken, and as I said it's a march towards tolerance, dependence and addiction. The Australian warnings talk about dependence but that's not addiction; addiction is a real risk that people need to understand before they start taking it. Like with opioids, addiction can lead to abuse and the risk of death from benzodiazepine abuse is a global health issue.

–Dr Lori Calabrese

Overdose Warning
USA MG (2016) "If you take too much VALIUM, call your healthcare provider or go to the nearest hospital emergency room" (page 1)
Australia CMI (2018) and CMI (2000) "If you have taken too much Valium, you may feel drowsy, tired, confused, dizzy, have difficulty breathing, feel weak or become unconscious." (page 2)
Australia Product Information (2020) "Overdose of benzodiazepines is usually manifested by degrees of central nervous system depression ranging from drowsiness to coma. In mild cases, symptoms include drowsiness, dysarthria, nystagmus, mental confusion and lethargy. In more serious cases, symptoms may include ataxia, areflexia, hypotonia, hypotension, apnoea, cardiorespiratory depression, coma and very rarely death. Coma may be more protracted and cyclical, particularly in elderly patients." (page 13)

– The CMIs do not include many of the life-threatening risks included in the PI like cardiorespiratory depression, coma and death. Given the content in the CMI is not consistent with the content in the PI, this is a breach of the *Therapeutic Goods Act 1989.*

> Honestly, I don't know what to say, this is quite frightening what consumers are being given in Australia. So I like the product information except the I am not comfortable describing the risk of death as rare, you need to put the real risks in the consumer leaflet.

– Dr Lori Calabrese

Other Medications for Depression

USA MG (2016)

"What is the most important information I should know about VALIUM? VALIUM is a benzodiazepine medicine. Taking benzodiazepines with opioid medicines, alcohol, or other central nervous system depressants (including street drugs) can cause severe drowsiness, breathing problems (respiratory depression), coma and death. VALIUM can make you sleepy or dizzy, and can slow your thinking and motor skills." (page 1)

Australia CMI (2018) and CMI (2000)

"Some medicines may interfere with Valium. These medicines include: • medicines for depression" (page 2). "These medicines may be affected by Valium or may affect how well Valium works. Your doctor or pharmacist can tell you what to do if you are taking any of these medicines." (page 2)

"Things to be careful of; Be careful if you are elderly, unwell, drinking alcohol or taking other medicines. Some people may experience side effects such as drowsiness, confusion, dizziness and unsteadiness which may increase the risk of a fall." (page 3)

Australia Product Information (2020)

"**4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE**

Concomitant use of alcohol/CNS depressants

Patients should be advised that their tolerance for alcohol and other CNS depressants (including anxiolytics, sedatives, antidepressants including tricyclic anti-depressants and non-selective MAO inhibitors, sedative antihistamines, opioids and anaesthetics) will be diminished and that these medications should either be eliminated or given in reduced dosage in the presence of Valium. Such concomitant use has the potential to increase the clinical effects of Valium, possibly including severe sedation that could result in coma or death, clinically relevant respiratory and/or cardiovascular depression" (page 3)

- The CMIs do not warn of the life-threatening risks of using medication for depression with Valium. Suffering from both depression and anxiety is common, with antidepressants and benzodiazepines the most common polydrug treatment prescribed.
- The CMIs would not escalate the life-threatening risk to the person. Unlike the PI, CMIs do not explicitly mention the medication classes that have the greatest risk.
- The PI states the risk of combining both medications to include severe sedation, coma, death, respiratory and cardiovascular depression. It also states that patients should be advised of these risks but these risks are not mentioned in the CMI. Given the content in the CMI is not consistent with the content in the PI, this is a breach of the *Therapeutic Goods Act 1989*.

> This is the same story, mixing CNS depressants exposes a person to multiple risks that can cause death, warning a person that the medicines may not work well or that they might fall down is completely inconsistent with the real risks.

– Dr Lori Calabrese

Pregnancy Warnings
USA MG (2016) "are pregnant or plan to become pregnant. VALIUM may harm your unborn baby. You and your healthcare provider should decide if you should take VALIUM while you are pregnant. are breastfeeding or plan to breastfeed. VALIUM passes into your breast milk and may harm your baby. Talk to your healthcare provider about the best way to feed your baby if you take VALIUM. Do not breastfeed while taking VALIUM." (page 1)
Australia CMI (2018) and CMI (2000) "1) if you are pregnant or plan to become pregnant; It is not known whether Valium is harmful to an unborn baby when taken by a pregnant woman. If there is a need to take Valium when you are pregnant your doctor will discuss the risks and benefits to you and the unborn baby. 2) if you are breastfeeding or plan to breastfeed Valium may pass into the breast milk and cause drowsiness and/or feeding difficulties in the baby. Valium is not recommended for use while breastfeeding." (page 1)
Australia Product Information (2020) "**The safety of Valium for use in human pregnancy has not been established**. Diazepam and its metabolites readily cross the placenta. An increased risk of congenital malformation associated with the use of benzodiazepines during the first trimester of pregnancy has been suggested. Benzodiazepines should be avoided during pregnancy unless there is no safer alternative. Benzodiazepines cross the placenta and may cause hypotension, hypotonia, reduced respiratory function and hypothermia in the newborn infant. Continuous treatment during pregnancy and administration of high doses in connection with delivery should be avoided. Withdrawal symptoms in newborn infants have been reported with this class of drugs." (page 11)

- The USA MG does not suggest the risks are unknown. The CMIs state it is "not known" if Valium is harmful to an unborn baby. The PI states that the safety for use in human pregnancy has not been established. The PI also details a number risks associated and also states that the use of benzodiazepines should be avoided. This is clearly another situation in which the information in the CMIs is inconsistent with the PI. Given the content in the CMI is not consistent with the content in the PI, this is a breach of the *Therapeutic Goods Act 1989.*
- The USA MG directs the person not to breastfeed whilst taking Valium, however the Australian CMIs only recommend against it.

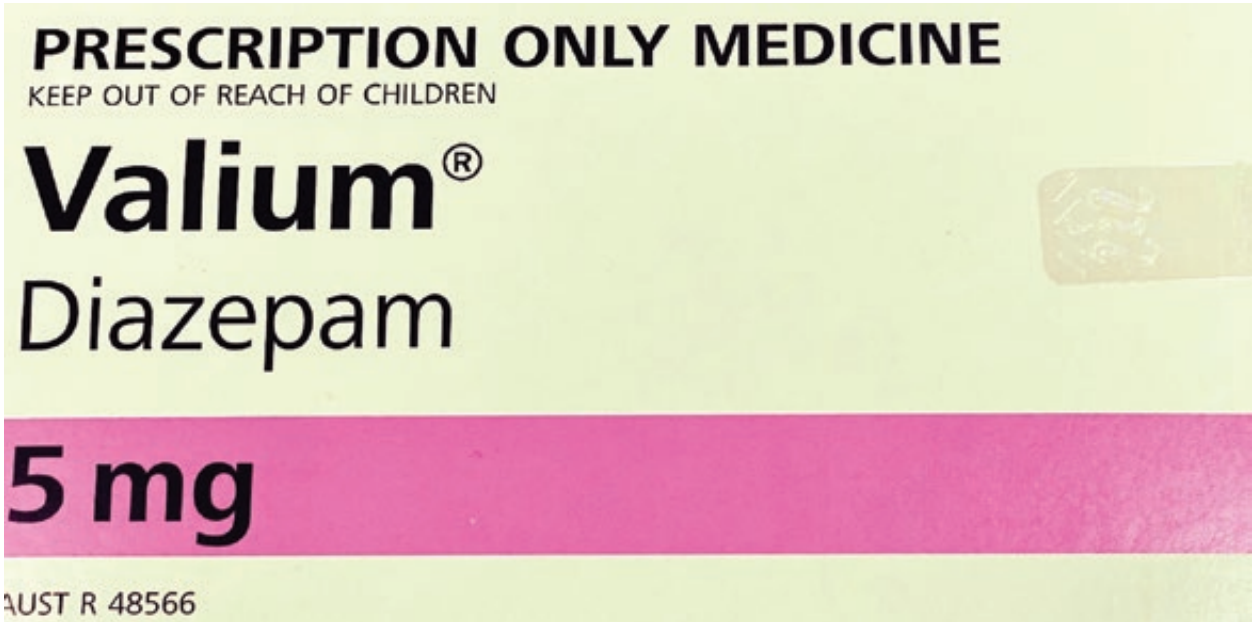
> There are known risks for benzodiazepines in exposure to developing foetus including congenital malformations and other developmental abnormalities. There is the risk that the baby will have respiratory issues, there are risks with using benzodiazepines during labor and delivery and a very real risk of experiencing withdrawal symptoms. These risks are well known and to state otherwise is preposterous and the drug will pass into the breast milk, that isn't in any doubt.
>
> *– Dr Craig Allen*

Suicide Warning
USA MG (2016) "Like other antiepileptic drugs, VALIUM may cause suicidal thoughts or actions in a very small number of people, about 1 in 500. (page 2)
Australia CMI (2018) and CMI (2000) The risk of suicidal thoughts is not mentioned in the CMIs.
Australia Product Information (2020) "Benzodiazepines should not be used alone to treat depression or anxiety associated with depression as suicide may occur in such patients." (page 3) "Benzodiazepines may increase depression in some patients and may contribute to deterioration in severely disturbed schizophrenics with confusion and withdrawal. Suicidal tendencies may be present or uncovered and protective measures may be required." (page 5)

- The CMIs contain no warning around this medication causing suicidal thoughts. This is medication prescribed predominatly to people with mental health conditions. Not providing a warning on the increased risk of suicide is a serious issue.
- Yet the PI warns of the risk of suicide. Given the content in the CMI is not consistent with the content in the PI, this is a breach of the *Therapeutic Goods Act 1989.*

> A significant increase in risk of suicide ideation and completed suicide certainly for people who have an benzodiazepine use disorder. But using medications like opioids and any other addictive drug is highly correlated with increased suicide ideation, depression, and completed suicides.

– Dr Craig Allen



Withdrawal Syndrome

USA MG (2016)

"Withdrawal symptoms. You may have withdrawal symptoms if you stop taking VALIUM suddenly. Withdrawal symptoms can be serious and include seizures. Mild withdrawal symptoms include a depressed mood and trouble sleeping. Talk to your healthcare provider about slowly stopping VALIUM to avoid withdrawal symptoms." (page 2)

Australia CMI (2018) and CMI (2000)

Withdrawal Syndrome is not mentioned in the CMIs.

"Do not stop taking Valium or lower the dose without first checking with your doctor. Stopping this medicine suddenly may cause some unwanted effects. Your doctor will explain how you should slowly reduce your dose of Valium before you can stop taking it completely." (page 3)

Australia Product Information (2020)

"After as little as one week of therapy, withdrawal symptoms can appear following the cessation of recommended doses" (page 3)

"Following the prolonged use of Valium at therapeutic doses, withdrawal from the medication should be gradual. An individualised withdrawal timetable needs to be planned for each patient in whom dependence is known or suspected. Periods from 4 weeks to 4 months have been suggested." (page 3)

"Withdrawal symptoms, similar in character to those noted with barbiturates and alcohol, have occurred once physical dependence to benzodiazepines has developed or following abrupt discontinuation of benzodiazepines. They may consist of headache, diarrhoea, muscle pain, insomnia, extreme anxiety, tension, restlessness, confusion and irritability. In severe cases, the following symptoms may occur: dysphoria, palpitations, panic attacks, vertigo, myoclonus, akinesia, hypersensitivity to light, sound and touch, abnormal body sensations (e.g. feeling of motion, metallic taste), depersonalisation, derealisation, delusional beliefs, hyperreflexia and loss of short term memory, to a major syndrome which may include convulsions, tremor, abdominal and muscle cramps, confusional state, delirium, hallucinations, hyperthermia, psychosis, vomiting and sweating." (page 4)

- The health risks whilst ceasing benzodiazepines are well established in government and medical warnings in Chapter 1.
- The CMIs contain no explanation of withdrawal syndrome. The CMIs do not warn of the actual risks associated with suddenly or slowly ceasing to use Valium. The CMIs also do not warn that the time to withdraw can be between 4 weeks to 4 months.
- Yet the PI details these risks. Given the content in the CMI is not consistent with the content in the PI, this is a breach of the *Therapeutic Goods Act 1989*.

> Withdrawing can take months, years and sometimes patients can never stop taking benzodiazepines. Any drug that creates dependence and addiction in a person will also create physical and psychological withdrawal effects. These are mentioned in the product information, that is what occurs, it can require hospitalisation, time off work, and can leave lifelong health side effects. Before anyone starts taking a benzodiazepine they must be made aware of these risks, these are not risk-free drugs and the risk can be a life sentence.

– Dr Lori Calabrese

Serious Side Effects and Rare Warnings
USA MG (2016)
n/a
Australia CMI (2018)
"These are serious side effects. You may need urgent medical attention. **Serious side effects are rare**. (page 3)

– The use of the word "rare" in describing serious side effects does not give the consumer the appropriate level of danger of using a benzodiazepine, as compared to government warnings detailed in Chapter 1. The word rare or describing serious side effects as being unlikely does not exist in the USA MG.

> These are not the most serious side effects. Dependence, addiction, death, those are serious risks for benzodiazepines. I would also not feel comfortable describing the serious side effects of any benzodiazepine as rare to any patient in this context.

– Dr Craig Allen

In summary for the Valium analysis:

Roche Valium	Australia (03/2018) Death mentioned: 0 times vs 1 time USA (11/2016)
Misleading statements	The likelihood of serious side effects is described as being 'rare'
Risk of death in relation to alcohol	Not included*
Risk of death in relation to opioids	Not included*
Risk of death in relation to other depression medications	Not included*
Risk of addiction	Not included
Risk of death in relation to pregnancy	Not included*
Risk of death from overdose	Not included*
Risk of suicide	Not included*
Risk of withdrawal syndrome	Not included*
Risk of abuse	Not included
Risk of death	Not mentioned once in the entire CMI

*Examples of inconsistencies between the CMI and the PI, which are breaches of the *Therapeutic Goods Act 1989*. The Australian CMI from 2000 is the same as the current version.

Interviewer question:	*The beginning part of the medication warnings in Australia have a similar sentence. This is the sentence for Valium: "Valium helps most people with anxiety, but it may have unwanted side effects in a few. All medicines can have side effects, sometimes they are serious, most of the time, they are not. You may need treatment if you get some of the side effects." For a document that's provided to provide assessment of the risks, to start by downplaying the risks before you've even explained them.*
Dr Allen answer:	*That's woefully inadequate. That's not informative. That would not be considered part of a document that would lead to informed consent for taking that medication.*
Interviewer question:	*So, to summarise the Australian warnings for Valium, there's no mention of the risk of death, there's no mention of the risk of taking it with an opioid, there is no rule about stopping drinking [alcohol]. There is no warning around addiction, and there is a very limited warning around pregnancy. That doesn't meet the guide for informed consent?*
Dr Allen answer:	*No. That's woefully inadequate.*

4.4.4. Duragesic (USA) and Durogesic (Australia) – Fentanyl

We compared consumer warnings and the product information, publicly released by:

- Johnson & Johnson (USA) MG Version: 10/2019[141]
- Janssen (Australia) CMI Version: 08/2018
- Janssen (Australia) CMI Version: 12/1999[142]
- Janssen (Australia) PI Version: 12/2019

Durogesic is patch that is applied to the skin every three days (72 hours). The patch releases a continuous amount of the fentanyl medication that is absorbed through the skin. After three days it is removed and disposed, and a new patch is applied.

General Warning Side Effects
USA MG (2019) "A long-acting (extended-release) opioid pain medicine that can put you at risk for overdose and death. Even if you take your dose correctly as prescribed you are at risk for opioid addiction, abuse, and misuse that can lead to death. (page 1)
Australia CMI (2018) and CMI (1999) "All medicines can have side effects. Sometimes they are serious, most of the time they are not. You may need medical treatment if you get some side effects. Do not be alarmed by this list of possible side effects. You may not experience any of them. Ask your doctor or pharmacist to answer any questions you may have." (page 4) and (page 5)
Australia Product Information (2019) "Serious, life-threatening or fatal respiratory depression can occur with the use of opioids even when used as recommended." (page 9) "The risk of respiratory depression is greater with the use of high doses of opioids, especially high potency and modified release formulations, and in opioid naïve patients." (page 9)

141 Johnson & Johnson, Medicine Guide, DURAGESIC, October 2019.
142 Janssen, Durogesic Consumer Medicine Information, December 1999.

- The CMIs do not include the USA risk statement as it relates to taking the medication "correctly as prescribed" and the risks of overdose, death, addiction, abuse and misuse. The USA MG comprehensively warns the person of possible iatrogenic addiction and risk of death. No such warning exists in the CMIs.
- Statements like "do not be alarmed" in the Australian CMI reduces the impact of the side effect warning and reduces the seriousness of the medication's side effects in the mind of the consumer.
- The PI includes a warning for fatal respiratory depression even when used as prescribed, but this is not in the CMIs for consumers. Given the content in the CMI is not consistent with the content in the PI, this is a breach of the *Therapeutic Goods Act 1989*.

> That's an important risk for people be aware of, potential for developing an addiction, potential for drug interactions and overdose and death, even at prescribed levels.

– Dr Craig Allen

Alcohol Warning
USA MG (2019) "Drink alcohol or use prescription or over-the-counter medicines that contain alcohol. Using products containing alcohol during treatment with DURAGESIC® may cause you to overdose and die." (page 1)
Australia CMI (2018) and CMI (1999) "Effect of alcohol; Avoid alcohol when using DUROGESIC since their combined effect may cause drowsiness." (page 2) and (page 2)
Australia Product Information (2019) "Concomitant use of opioids and benzodiazepines or other CNS depressants, including alcohol, may result in sedation, respiratory depression, coma and death." (page 11) "Patients and their caregivers should also be informed of the potential harms of consuming alcohol while taking DUROGESIC." (page 11)

- In both CMIs the statement that the combined effect "may" cause drowsiness does not adequately reflect the significant risk that it is highly likely to cause drowsiness.
- In the CMIs the section titled "Effect of alcohol" does not mention the risk of sedation, respiratory depression, coma and death, which are all included in the PI. The PI also specifically notes that consumers should be informed of these risks. Given the content in the CMI is not consistent with the content in the PI, this is a breach of the *Therapeutic Goods Act 1989*.

Benzodiazepine Warning
USA MG (2019) "Taking DURAGESIC® with other opioid medicines, benzodiazepines, alcohol, or other central nervous system depressants (including street drugs) may cause severe drowsiness, decreased awaareness, breathing difficulties, with slow or shallow breathing, coma, and death." (page 1)
Australia CMI (2018) and CMI (1999) No benzodiazepine warning included in the CMIs.
Australia Product Information (2019) "Concomitant use of opioids and benzodiazepines or other CNS depressants, including alcohol, may result in sedation, respiratory depression, coma and death." (page 11)

- No comparable warning exists in the CMIs.
- Benzodiazepine is not mentioned once in the Australian CMIs. It is mentioned seven times in the PI.
- The PI includes several warnings for benzodiazepines, and the risk of sedation, respiratory depression, coma and death. Given the content in the CMI is not consistent with the content in the PI, this is a breach of the *Therapeutic Goods Act 1989*.

> Taking an opioid with a benzodiazepine creates a significant risk of overdose death. Alcohol is the same issue, these are important warnings because the last 20 years have shown the deaths that can occur. The importance of these warning cannot be understated.

– Dr Craig Allen

Other Medications and Supplements Warning
USA MG (2019) "are taking prescription or over-the-counter medicines, vitamins, or herbal supplements. Taking DURAGESIC® with certain other medicines can cause serious side effects that could lead to death." (page 1)
Australia CMI (2018) "DUROGESIC may increase the sedative effect of these drugs or slow down your ability to react, breathing difficulties with slow or shallow breathing, coma and death." (page 2)
Australia CMI (1999) "Durogesic can increase the effect of drugs that are sedating or slow down your ability to react. A change in dose may be required if Durogesic is used with these medicines." (page 2)

- The CMI (2018) has a broadly worded and lengthy warning on page 2, that fills half of the page. It indicates that a number of medicines and supplements can interact with Durogesic. This list mentions "mental health" and "anxiety" medications.
- In the CMI (1999) there is no warning included about "breathing difficulties with slow or shallow breathing, coma and death."

Overdose Warning
USA MG (2019) "Get emergency help right away if you use too much DURAGESIC® (overdose). When you first start taking DURAGESIC®, when your dose is changed, or if you take too much (overdose), serious or life-threatening breathing problems that can lead to death may occur. (page 1)
Australia CMI (2018) and CMI (1999) "If you receive too much (overdose) The most important sign of overdose is difficulty in breathing. If a person using DUROGESIC has abnormally slow or weak breathing, remove the patch. Keep the person awake by talking to them or gently shaking them every now and then." (page 3) and (page 4)
Australia Product Information (2019) "DUROGESIC poses risks of hazardous and harmful use which can lead to overdose and death." (page 1) "The manifestations of fentanyl overdosage are an extension of its pharmacological actions, the most serious effect being respiratory depression." (page 20) "Serious, life-threatening or fatal respiratory depression may occur with the use of DUROGESIC. Be aware of situations which increase the risk of respiratory depression, modify dosing in patients at risk and monitor patients closely, especially on initiation or following a dose increase" (page 1)

- The USA MG warns of the risk of death and that an overdose can also occur when simply starting or changing a dose. This does not appear in the CMIs.
- The overdose warning in the PI includes the risk of respiratory depression or death, including when starting or changing a dose, which is not included in the CMIs. Given the content in the CMI is not consistent with the content in the PI, this is a breach of the *Therapeutic Goods Act 1989*.
- The Australian CMI (2019) does not mention using the PBS Opioid Rescue Nasal Spray – Nyxoid.

> Ring the emergency services and then you can administer naloxone and then you might be starting CPR. Most importantly, you would administer naloxone, an opioid overdose reversal medication. Also you are increasing the risk that they may suffer brain injury or death while you're rocking them gently, no that's not the approach to someone who's had an overdose.

– Dr Craig Allen

Abuse Warning
USA MG (2019) "A long-acting (extended-release) opioid pain medicine that can put you at risk for overdose and death. Even if you take your dose correctly as prescribed you are at risk for opioid addiction, abuse, and misuse that can lead to death." (page 1) "Do not cut, break, chew, crush, dissolve, snort, or inject DURAGESIC because this may cause you to overdose and die." (page 1)
Australia CMI (2018) and CMI (1999) The risk of abuse to the consumer is not mentioned in the CMI.
Australia Product Information (2019) "DUROGESIC contains the opioid fentanyl and is a potential drug of abuse, misuse and addiction. Fentanyl can be abused in a manner similar to other opioid agonists. Abuse or intentional misuse of DUROGESIC may result in overdose and/or death." (page 9) "Instructions to patient: - abuse of oral or transdermal forms of opioids by parenteral administration can result in serious adverse events, which may be fatal." (page 6)

- Durogesic is a Schedule 8 drug due to the risk of it being abused, yet the risks of abuse including death, or warnings around abuse, are not mentioned in the CMIs.
- The PI includes multiple warnings for abuse, and the risk of overdose and/or death which are not in the CMIs. The PI also mentions these warnings need to be given to the patient. Given the content in the CMI is not consistent with the content in the PI, this is a breach of the *Therapeutic Goods Act 1989*.

> Here in the US fentanyl is now the leading cause of overdose deaths and the most abused drug. Legal and illegal forms are the focus of law enforcement activities and in addiction centres. New patients need to be made aware of the risk of addiction and the risk of abuse upfront, because we know that addiciton can lead to abuse. They need to understand the risks of the path they are taking.

– Dr Craig Allen

Addiction Warning

USA MG (2019)

"A long-acting (extended-release) opioid pain medicine that can put you at risk for overdose and death. Even if you take your dose correctly as prescribed you are at risk for opioid addiction, abuse, and misuse that can lead to death." (page 1)

Australia CMI (2018) and CMI (1999)

"Medicines like DUROGESIC can lead to addiction. This is unlikely when DUROGESIC is used correctly." (page 4) and (page 5)

Australia Product Information (2019)

"DUROGESIC contains the opioid fentanyl and is a potential drug of abuse, misuse and addiction. Fentanyl can be abused in a manner similar to other opioid agonists. Abuse or intentional misuse of DUROGESIC may result in overdose and/or death. Addiction can occur in patients appropriately prescribed DUROGESIC at recommended doses. The risk of addiction is increased in patients with a personal or family history of substance abuse (including alcohol and prescription and illicit drugs) or mental illness. The risk also increases the longer the drug is used and with higher doses." (page 9)

- The CMIs do not include the USA risk statement that opioid addiction can occur "even if you take your dose correctly as prescribed". The USA document comprehensively warns the person of possible iatrogenic addiction and risk of death.
- Both CMIs contain a statement that has no scientific basis, that the risk of addiction "... is unlikely when DUROGESIC is used correctly". Based on this statement a consumer may assess the possibility of addiction as low. However as stated in the PI, the risk of addiction increases the longer the drug is used, the higher the dose (which is prescribed) and if the person has a mental illness.
- The PI also includes a warning for addiction and death at prescribed doses, all of this information directly contradicts the information contained in the CMIs for consumers. Given the content in the CMI is not consistent with the content in the PI, this is a breach of the *Therapeutic Goods Act 1989*.
- Note: page 1 USA MG states, "Use the lowest dose possible for the shortest time needed."

> There is a risk of developing addiction. Even when used as directed, there are a number of risk factors for developing addiction. And when those are present, the likelihood is even greater and it has nothing to do with taking the medication as prescribed if you have those risk factors. Family history of addiction. If either one of your parents had any type of addiction, if you're female, have an anxiety disorder, depressive disorder, history of trauma, other chronic diseases, if you're under the age of 21. All of those increase your risk for developing an addiction to that medication.

– Dr Craig Allen

Sharing Opioids

USA MG (2019)

"Never give anyone else your DURAGESIC®. They could die from taking it. Selling or giving away DURAGESIC® is against the law." (page 1)

Australia CMI (2018) and CMI (1999)

"Do not give the patches to anyone else, even if their symptoms seem similar to yours." (page 3) and (page 5)

– There is no comparable death warning included in the Australian CMI. The TGA *Return your opioid* campaign warns about the risk of sharing opioids with other people, including death.[143] However, the risk of death isn't mentioned in the CMI.

Patch Warning

USA MG (2019)

"If the patch accidentally sticks to a family member while in close contact, take the patch off, wash the area with water, and get emergency help right away because an accidental exposure to DURAGESIC® can lead to death or other serious medical problems. (page 1)

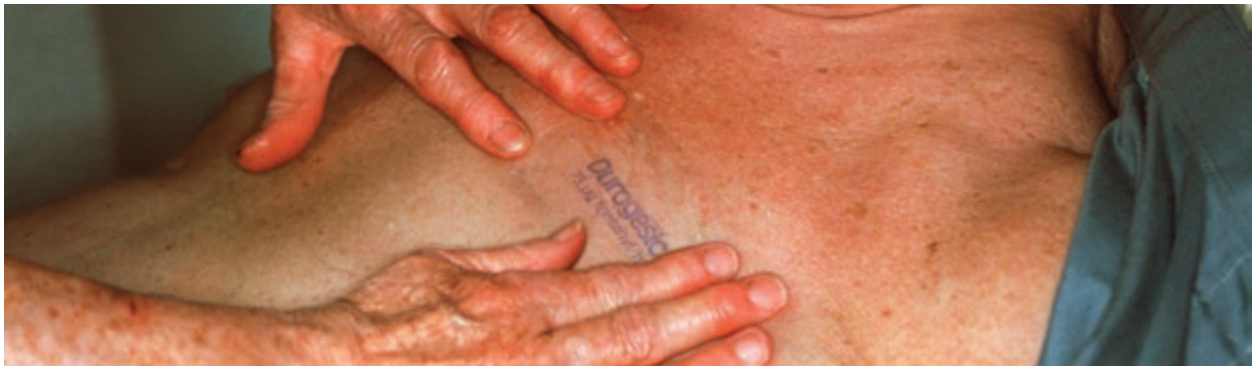
Australia CMI (2018) and CMI (1999)

"Things to be careful of; If the patch accidentally adheres to another person (for example a family member sharing the same bed), remove the patch and contact your doctor. Do this even if there are no signs of discomfort or drowsiness." (page 3) and (page 4)

Australia Product Information (2019)

"Accidental ingestion or exposure of DUROGESIC, especially by children, can result in a fatal overdose of DUROGESIC. Accidental transfer of a fentanyl patch to the skin of non-patch wearer (particularly a child), while sharing a bed or being in close physical contact with a patch wearer, may result in an opioid overdose for the non-patch wearer." (page 10)

– Fentanyl is a powerful pain killer that is applied as a patch to the skin. The risk of it coming into contact with a partner is significant and the risk of death to that person is also significant. Failing to warn of that risk in the CMIs places unaware individuals at fatal risk.
– The PI includes a warning for overdose and death, but this is not in the CMI for consumers. Given the content in the CMI is not consistent with the content in the PI, this is a breach of the *Therapeutic Goods Act 1989*.



143 See https://www.tga.gov.au/publication/return-your-unused-opioids-resource-kit

> The risk of coming into contact with a partner wearing a patch is significant to someone who is opioid naive who has not developed a tolerance, who isn't used to taking this medication, and particularly fentanyl, which is quite potent, quite strong, and used when someone is no longer getting benefit from a lower strength opioid, then that could be an immediate risk to their life.

– Dr Craig Allen

Pregnancy Warnings
USA MG (2019) "are pregnant or planning to become pregnant. Prolonged use of DURAGESIC® during pregnancy can cause withdrawal symptoms in your newborn baby that could be life-threatening if not recognized and treated. are breastfeeding. Not recommended during treatment with DURAGESIC. It may harm your baby." (page 1)
Australia CMI (2018) and CMI (1999) "You must tell your doctor if you; •are pregnant or planning to become pregnant •are breastfeeding or wish to breastfeed" (page 1) and (page 3)
Australia Product Information (2019) "The safe use of fentanyl in pregnant women has not been established with respect to possible adverse effects on foetal development." (page 16) "Use of DUROGESIC during childbirth is not recommended because fentanyl passes through the placenta and may cause respiratory depression in the newborn child, and because it should not be used in the management of acute or postoperative pain" (page 16) "Fentanyl is excreted into human milk and may cause sedation/respiratory depression in a breastfed infant." (page 16)

- The CMIs do not contain any risk warnings, nor do they specify the actual risks that taking this medicine will expose the unborn or newborn child to or that they are life-threatening.
- The PI includes life-threatening warnings but these are not in the CMI for consumers. Given the content in the CMI is not consistent with the content in the PI, this is a breach of the *Therapeutic Goods Act 1989*.

> I find it deeply disturbing that the risks to a foetus are not made very clear to patients. You can't predict all pregnancies and literature exists around the risks of exposure to fentanyl in the early stages of a pregnancy. You cannot expect female patients to understand and remember the importance of this if they are not informed, by the time the pregancy is confirmed the foetus has already been exposed.

– Dr Craig Allen

Heat Warning

USA MG (2019)

"While using DURAGESIC® DO NOT: • Take hot baths or sunbathe, use hot tubs, saunas, heating pads, electric blankets, heated waterbeds, or tanning lamps, or engage in exercise that increases your body temperature. These can cause an overdose that can lead to death." (page 1)

Australia CMI (2018)

"Things you must not do DO NOT; expose the patch to direct heat from electric blankets, heat pads, heated water beds, heat or tanning lamps, intensive sunbathing, hot water bottles, long hot baths, saunas or hot spa baths while you are using DUROGESIC. Direct exposure to such heat may cause an increase in the amount of fentanyl absorbed by the skin, resulting in possible overdose and death." (page 3)

Australia CMI (1999)

"- Avoid direct exposure of the patch to heat from electric blankets, heat pads, heated water beds, heat lamps, intensive sunbathing, hot water bottles, saunas or hot spa baths while you are using Durogesic. Direct exposure to such heat may cause an increase in the amount of fentanyl absorbed by the skin." (page 4)

– The CMI (1999) does not mention the risk of overdose and death.

Tolerance Warning

USA MG (2019)

"Call your healthcare provider if the dose you are using does not control your pain." (page 1)

Australia CMI (2018) and CMI (1999)

"Tolerance as with all opioid analgesics, DUROGESIC may lead to tolerance with continued use. Your doctor may, therefore, prescribe a higher dose of DUROGESIC after some time to continue to give you pain relief." (page 2) and (page 3)

Australia CMI (2018)

"If your pain continues, see your doctor who may prescribe additional medicines to help control the pain or change the dose of DUROGESIC. Your doctor may advise you initially to change the patch every two days (48 hours) instead of every three days (72 hours) to achieve adequate pain relief." (page 3)

"Your doctor may prescribe additional pain relievers to control occasional outbreaks of pain" (page 3)

– In the CMIs patients should never be directed to the option that a higher dose or more frequent patch change, would assist to provide pain relief. This gives the suffering patient the idea that it is acceptable to increase the dose if the pain is not controlled by the current dose.
– In the CMI (2018) patients should never be directed to the option that additional pain relievers are a possible strategy to assist with pain. This gives the suffering patient the idea that it is acceptable to add new medication if the pain is not controlled by the current medication.

Interviewer question:	*For a document that's designed to warn people of the risks, this essentially puts in the mind of someone who's suffering that a larger dose will give them increased relief.*
Dr Allen answer:	*Yeah. And that has been shown to be, in many ways, a fool's errand, and, actually, compounding the problem. And when one assesses – and it's really essential to assess for quality of life, improvement in pain, improvement in someone's mobility, and decreased pain if you're going to continue them on these types of medications or increase these doses. And sometimes what we see is that the longer someone is exposed to an opioid analgesic, it actually decreases their pain threshold and they are more sensitive to pain on the medication than off the medication.*

In summary for the Durogesic analysis:

Janssen Durogesic	Australia (08/2018)	Australia (12/1999)
	Death mentioned: 3 times vs 11 times USA (2019)	Death mentioned: 0 times vs 11 times USA (2019)
Deceptive statement	"Medicines like DUROGESIC can lead to addiction. This is unlikely when DUROGESIC is used correctly"	"Medicines like DUROGESIC can lead to addiction. This is unlikely when DUROGESIC is used correctly"
Misleading statement	".. change the patch **every two days (48 hours) instead of every three days (72 hours)** to achieve adequate pain relief."	n/a
Risk of death when taken as prescribed	Not included*	Not included
Risk of death in relation to addiction	Not included*	Not included
Risk of addiction when taken as prescribed	Not included*	Not included
Risk of death in relation to alcohol	Not included*	Not included
Risk of death in relation to benzodiazepines	Not included*	Not included
Risk of death from overdose	Not included*	Not included
Risk of overdose when starting or changing a dose	Not included*	Not included
Risk of death from sharing opioids	Not included	Not included

Janssen Durogesic	Australia (08/2018)	Australia (12/1999)
	Death mentioned: 3 times vs 11 times USA (2019)	Death mentioned: 0 times vs 11 times USA (2019)
Risk of death in relation to pregnancy	Not included*	Not included
Risk of death in relation to patch contact with adults/kids	Not included*	Not included
Advise of Nyxoid in case of overdose	Not included	n/a
Risk of death from abuse	Not included*	Not included
Risk of death from heat exposure	**Yes**	Not included
Risk of death in relation to other medications/ supplements	**Yes**	Not included

* Examples of inconsistencies between the CMI and the PI, which are breaches of the *Therapeutic Goods Act 1989*

The Durogesic CMI was updated early in 2020. Read about the changes in Chapter 7.

Summary comments

> These Australian documents are woefully inadequate, they do not give a person the multiple life-threatening risks of these medications. This doesn't provide them with an understanding of the risks to give **informed consent**

– Dr Craig Allen

> Apart from the fact that I haven't seen a single leaflet that contains the necessary information on the real risks, I am still in shock over this statement: 'All medicines can have side effects'. That's true. 'Sometimes they're serious, most of the time, they are not'. Are you kidding? That's so misleading for drugs with this level of dangerous side effects. I hope people get given some other warning information because what I have seen doesn't meet any standard for someone to give informed consent.

– Dr Lori Calabrese

> These are all very dangerous drugs, reading these Australian warnings, I am very disturbed that patients haven't been warned up front, they haven't been warned adequately, and they haven't been warned enough.

– Dr Lori Calabrese

4.5 IMPLICATIONS OF THESE FINDINGS

It is a legal requirement for patients to be made aware of all **material risks** of a medication before they start taking it. This includes when an outcome is severe, even if its incidence is rare.

The CMI analysis shows that for over 20 years, numerous medications in Australia have been dispensed to patients suffering from mental illness and pain, without warning them of the life-threatening nature of many side effects (material risks). In some cases, information is misleading and would result in material risk.

The analysis has also shown numerous examples of inconsistencies between the CMI and PI, many in relation to the risk of death. Not only does this highlight the risk consumers have been exposed to, these examples are also breaches of the *Therapeutic Goods Act 1989*. Not only have the pharmaceutical companies deliberately withheld material risks to Australian consumers in comparison to US consumers, they have also withheld material risks disclosed to Australian medical professionals.

Sadly, it has resulted in deaths and will continue to do so until these risks are clear and accurate.

The absence of warnings and the inclusion of misleading statements is a deliberate decision made by the pharmaceutical manufacturers. Given the lax regulatory framework overseen by the TGA, this has been allowed to happen for far too long. Even our trusted doctors and pharmacists have access to the details of significant risk in PI documents, yet the CMIs continue to be misleading and inaccurate.

The CMI exists to guide and warn consumers about how to use a medication, the risks and side effects. Consumers **must be made aware of the more significant side effects and life-threatening risks** – even if they are rare.

In addition, the CMIs are virtually devoid of any information about polydrug interactions, even for medication interactions that are known to cause fatal overdose risks like opioids and benzodiazepines. And severe alcohol interactions are rarely explicitly explained.

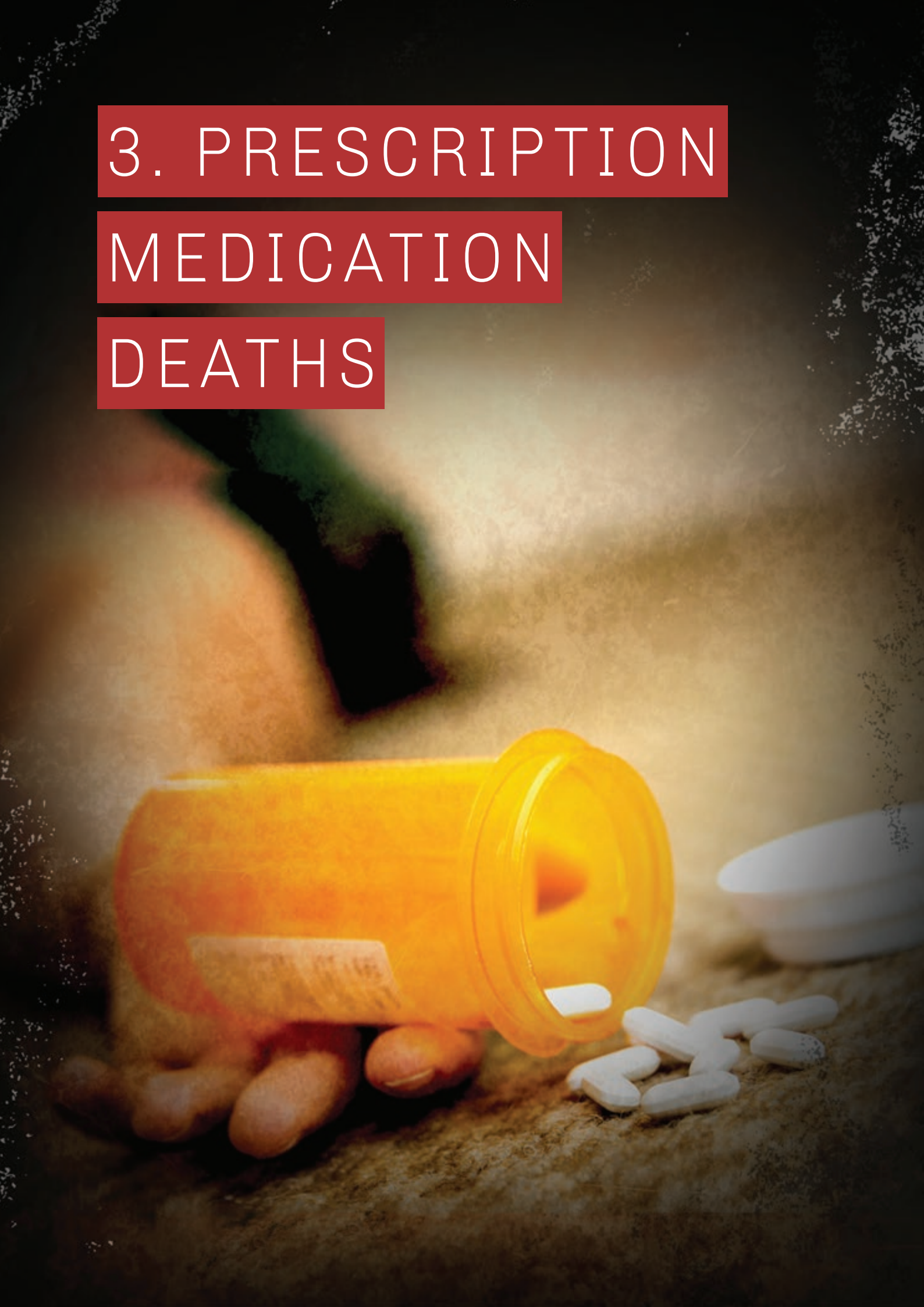
If material risks are not fully identified, then our most vulnerable people cannot take the necessary steps to protect their health. Consumers rely on the CMI to make a decision about the risks and benefits of taking the medication – which is legally referred to as *informed consent*. How can anyone make a risk assessment about risks they have not been informed about?

Read about the implications of these findings for informed consent in Chapter 5.

Warning

Do not stop taking a prescribed medication without discussing it with your doctor. Information can also be obtained by calling the NPS Medicines Line on 1300 633 424 or the Adverse Medicines Events Line on 1300 134 237 for advice. If you need support for any medical concern, including mental health matters, please contact your doctor. Lifeline also provides a 24 hour support service on 13 11 14 or www.lifeline.org.au

3. PRESCRIPTION MEDICATION DEATHS



1. INTRODUCTION

This chapter connects the CMI and PI side effects of prescription medication to adverse drug events, including deaths and hospital admissions.

For more than 20 years, the very drugs prescribed to people with mental illness and chronic pain (such as opioids, benzodiazepines, antidepressants and antipsychotics) have been causing more harm than good.

Figure 14: More than 20 years of prescription drug deaths

Drug overdose deaths are a bigger killer than car accidents. Death rates associated with prescription drug use have also been increasing over time.

Overdose deaths are most commonly associated with PBS medications, not illegal street drugs. These deaths are not healthy people abusing prescription medication for recreational purposes. They are people with chronic illnesses who are taking these drugs as prescribed by their doctors.

Deaths more commonly occur from taking combinations of drugs, because of how these drugs interact, not simply from taking too much of one drug. Yet patients take these medications as part of a polydrug prescription plan from their doctors.

Alcohol is also a significant contributor to polydrug deaths.

These are also the most commonly identified reason for hospital admissions, putting strain on our emergency health systems.

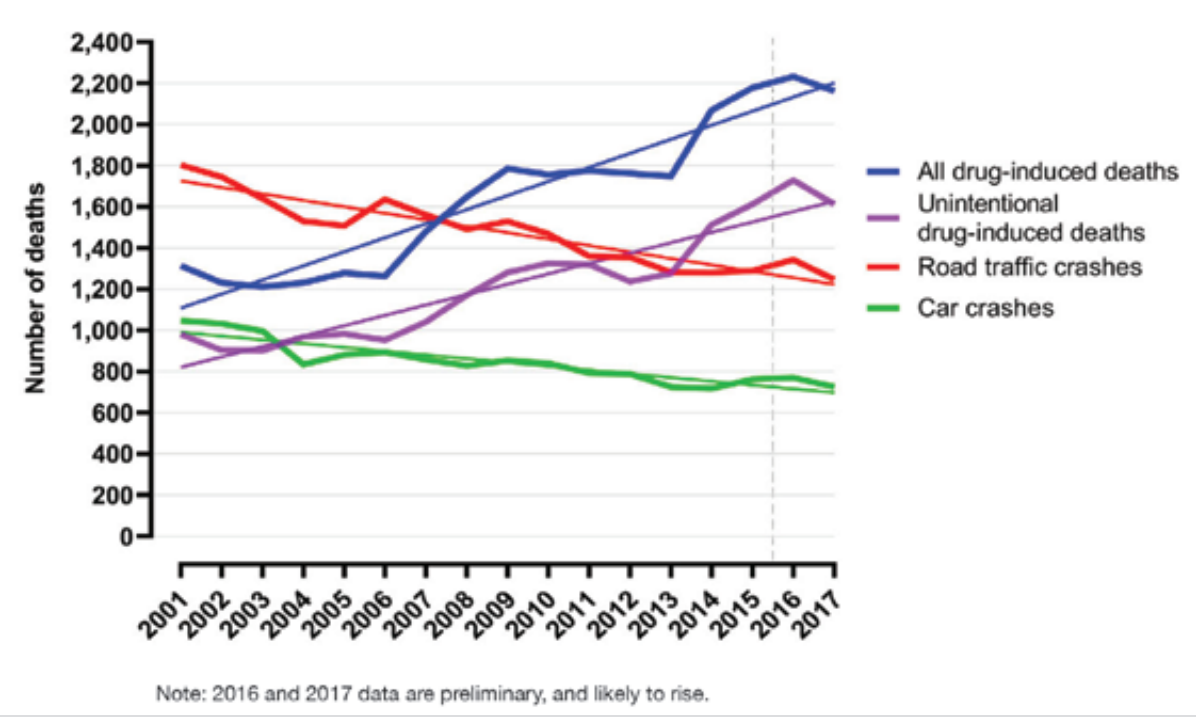
Read more about the alarming rates of suicide deaths due to prescription medications in Chapter 11.

2. AUSTRALIA'S DRUG DEATH TREND

Deaths from drug overdose has been an increasing public health issue in Australia over the last 20 years. Most noticeably, the number of Australians who die from unintentional drug overdose each year continues its long-term rise. The scale of the crisis is more apparent than ever. For example, in 2017, 1,612 people died from unintentional drug-induced overdoses in Australia, compared to 1,246 people who died on our roads.[144]

Figure 15 from the Penington Institute shows that based on the current trends from 2001 to 2017, both drug-induced deaths and unintentional drug-induced deaths have increased on average by 3.4% per year in Australia. In contrast, the road toll over the same period has decreased on average by 2.2% per year.[145]

Figure 15: Number of drug-induced deaths in Australia, compared to other causes of death (Source: Penington Institute)



144 Penington Institute, Australia's Annual Overdose Report 2019, Melbourne, 2019, pp9, 12. The Penington Institute is a not-for-profit organisation that works to identify and respond to specific substance use problems and their causes. The institute produces an annual overdose report, focusing on unintentional deaths. For further information, see http://www.penington.org.au/

145 ibid, pp9, 12, 23.

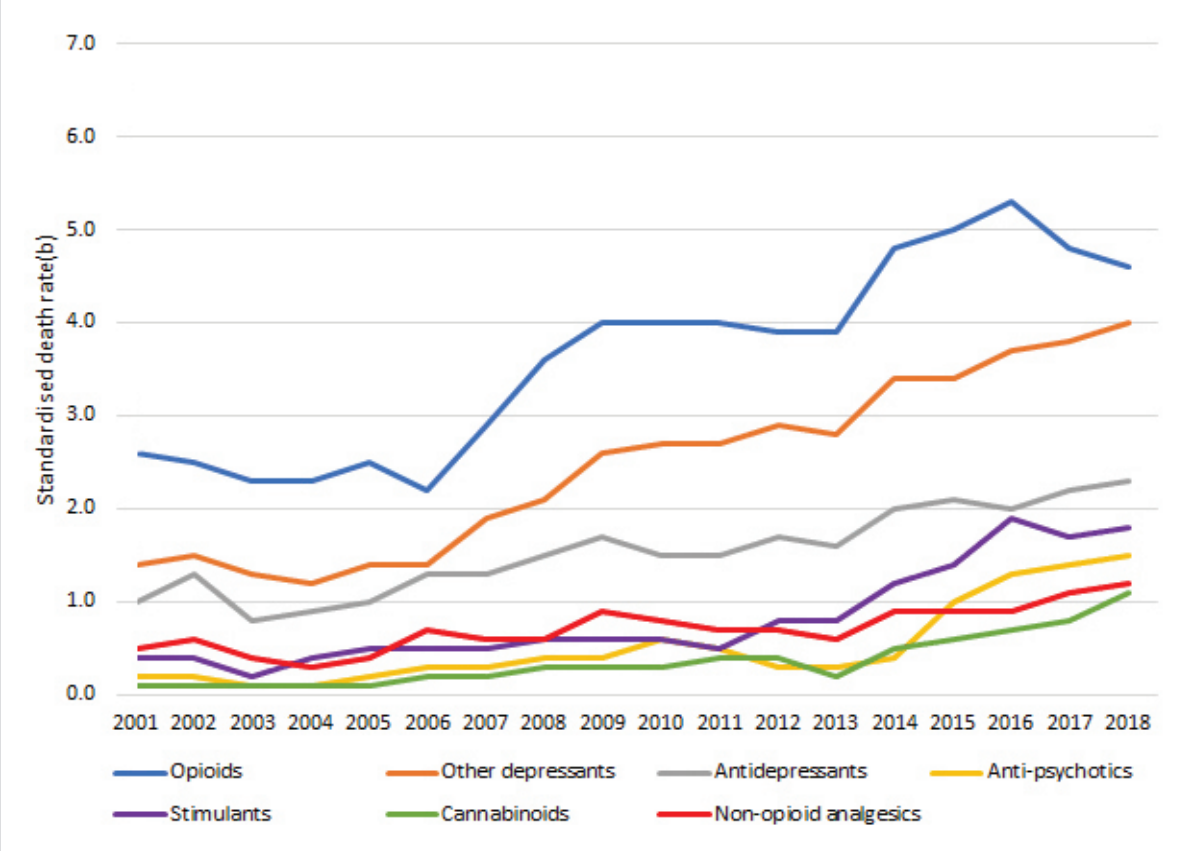
3. CLASSES OF DRUGS INVOLVED

It is a common misunderstanding in the community that overdose deaths result from taking illegal street drugs. Yet official statistics reveal a very different story. The most common class of drug identified in toxicology reports in drug-induced deaths are opioids. **Opioids (including prescription use)** have been the leading class of drug deaths for the last 20 years. **Depressants,** which include **benzodiazepines**, have consistently been the second most common class of drug, with **antidepressants** the third most common present in drug-induced deaths.[146]

These medications are regularly used for mental illness and pain conditions, and they are supported by the PBS. **They are prescribed to the most vulnerable people in our society**.

Figure 16 from the ABS shows the increasing trend in prescription medication death rates over the last 20 years.

Figure 16: Age-standardised death rates, common drug classes (Source: ABS[147])



In its 2018 report on causes of death in Australia, the ABS again had a focus on drug-induced deaths, and in particular the damage being done by opioids including in combination with other drugs.[148]

146 Australian Bureau of Statistics (ABS), Causes of Death, Australia, 2018: Opioid-Induced Deaths in Australia, 3303.0, Canberra, 25 September 2019.
147 ABS, 2019.
148 ibid.

Of the 1,740 registered drug-induced deaths in 2018, opioids were present in close to two-thirds (1,123 deaths or 64.5%). ABS data showed that prescription opioids were identified in 70.7% of opioid-induced deaths. The natural and semi-synthetic opioids, including codeine, oxycodone (OxyContin, Targin, Endone) and morphine were the most common prescription opioids present, followed by synthetic opioids (Fentanyl – Durogesic).

Of the 1,123 registered opioid-induced deaths, 88.9% of these occurred in the setting of other substances. Benzodiazepines were the most common drug to appear alongside opioids, with 708 deaths (63.1%) having both drugs present. Approximately one-quarter of opioid-induced deaths also recorded an anti-depressant or anti-psychotic drug.

Of the 1,123 opioid-induced deaths, 458 people (or 40.7%) had a mental health condition including schizophrenia, mood disorders and anxiety.[149]

These statistics provide multiple links to the points raised in Chapter 1: that the people with severe mental illness are exposed to, and in growing numbers suffering from, fatal side effects from the medication that is prescribed to treat them.

4. POLYDRUG DEATHS

Another common misunderstanding is that drug overdose deaths are a result of taking too much of just one drug. Yet research using publicly available data shows that polydrug deaths are the most common reason for deaths.

In 2017, the ABS made prescription medication deaths a focus of its annual 'Causes of Death' report for Australia. In its media release, the ABS opened with the fact that Australia had recorded the highest number of drug-induced deaths in 2016 since the late 1990s. The ABS's Director of Health and Vital Statistics, James Eynstone-Hinkins, said drug deaths were most commonly associated with benzodiazepines and oxycodone, noting that, "These are both prescription drugs which are used to manage anxiety and pain respectively".[150]

> In 2016, an individual dying from a drug induced death in Australia was most likely to be a middle aged male, living outside of a capital city who is misusing prescription drugs such as benzodiazepines or oxycodone in a polypharmacy (the use of multiple drugs) setting.[151]

– Australian Bureau of Statistics

149 ibid, p1.

150 Australian Bureau of Statistics (ABS), 'Drug Induced deaths at Highest Rates Since Late 90s', media release, Canberra, 27 September 2017.

151 Australian Bureau of Statistics (ABS), Causes of Death, Australia, 2016: Drug-induced Deaths in Australia: A Changing Story, 3303.0, Canberra, 16 May 2018.

The ABS's 2016 report on causes of death in Australia focusing on drug-induced deaths reflect the same conclusions about polydrug use:

> *Over half (59.0%) of all acute drug deaths had two or more substances identified on the toxicology report at death.*[152]

The presence of these classes of prescription drugs, and their polydrug combinations, in Australian deaths is not a recent trend. Both government and not-for-profit analysis has shown that overdose deaths involving these medications have been increasing over the last 20 years.

Apart from the ABS data already cited, the AIHW shows that between 2008 and 2017, the number of deaths where benzodiazepines or other opioids such as oxycodone were present rose by 105% and 42%, respectively.

The most common substance present was a benzodiazepine (46%) followed by other opioids such as oxycodone, morphine and codeine (30%).[153] Data from the ABS in 2016 indicated that in over 96% of drug-induced deaths where benzodiazepines were present, they were taken in conjunction with other drugs including alcohol.[154]

The Penington report zeroes in on the significance of multiple drug interaction (polydrug use) in unintentional drug-induced deaths, noting that:

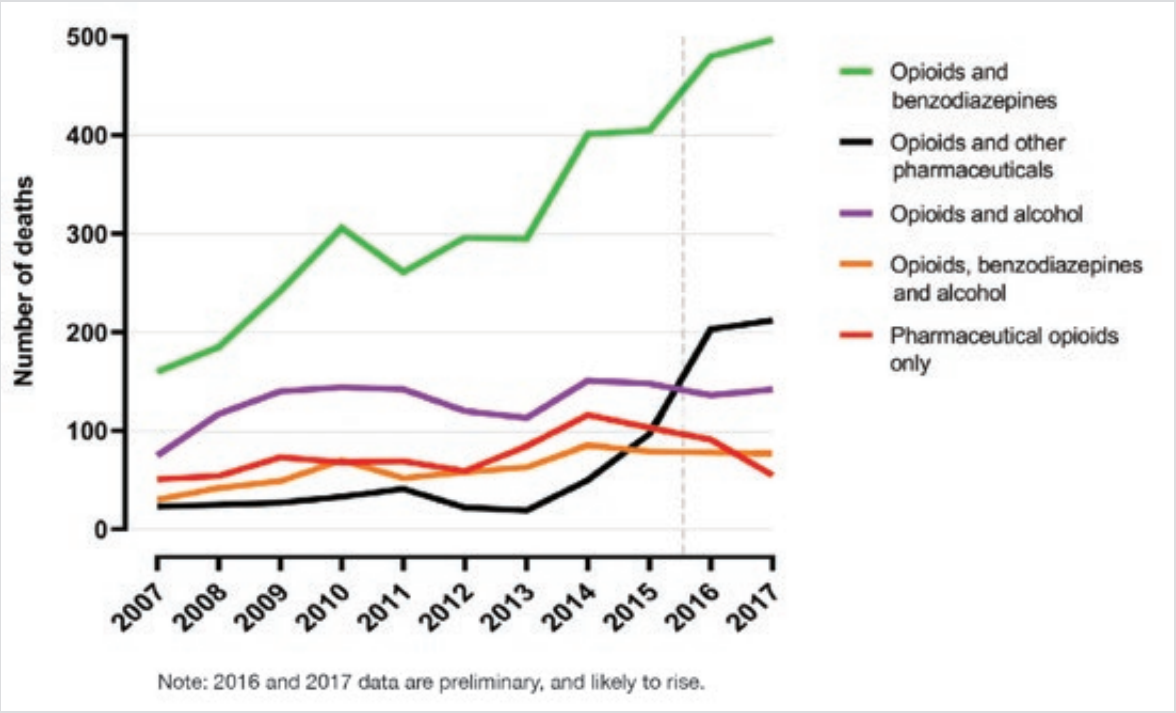
> *While a single drug may be identified in an unintentional drug-induced death, it is rare for a death to be attributable to toxicity from a single drug; deaths involving multiple drugs are the norm rather than the exception.*[155]

Polydrug deaths have been increasing over the last 20 years. The actual drug class and combinations are shown in Figure 17. The clearly identified facts are that both the drugs used and polydrug combinations are **prescription medications in the majority of deaths**. These are most commonly mental illness and pain medications, provided by the PBS.

The increasing rate of deaths using combinations of opioids with benzodiazepines, opioids with other pharmaceuticals, and opioids with alcohol shows a serious problem for Australia.

152 ibid.
153 AIHW, 2020.
154 ABS, 2017.
155 Penington Institute, 2019, p9.

Figure 17: Unintentional drug-induced deaths involving opioids by sole drug and polydrug use (Source: Penington Institute)



The most common combination of drugs is opioids with benzodiazepines, and this category of polydrug use is significantly increasing, having more than trebled from 160 deaths in 2007 to 497 in 2017. Until 2014, the combination of opioids with other pharmaceuticals (including anti-convulsants, anti-psychotics, sedatives and hypnotics, and anaesthetics, but excluding opioid analgesics and benzodiazepines) was the least common combination of drugs identified in unintentional drug-induced deaths involving opioids. Since 2014, however, the number of deaths involving these drugs has increased almost ten-fold, with opioids with 'other pharmaceuticals' now accounting for the second-highest number of unintentional drug-induced deaths involving opioids (212 deaths in 2017).

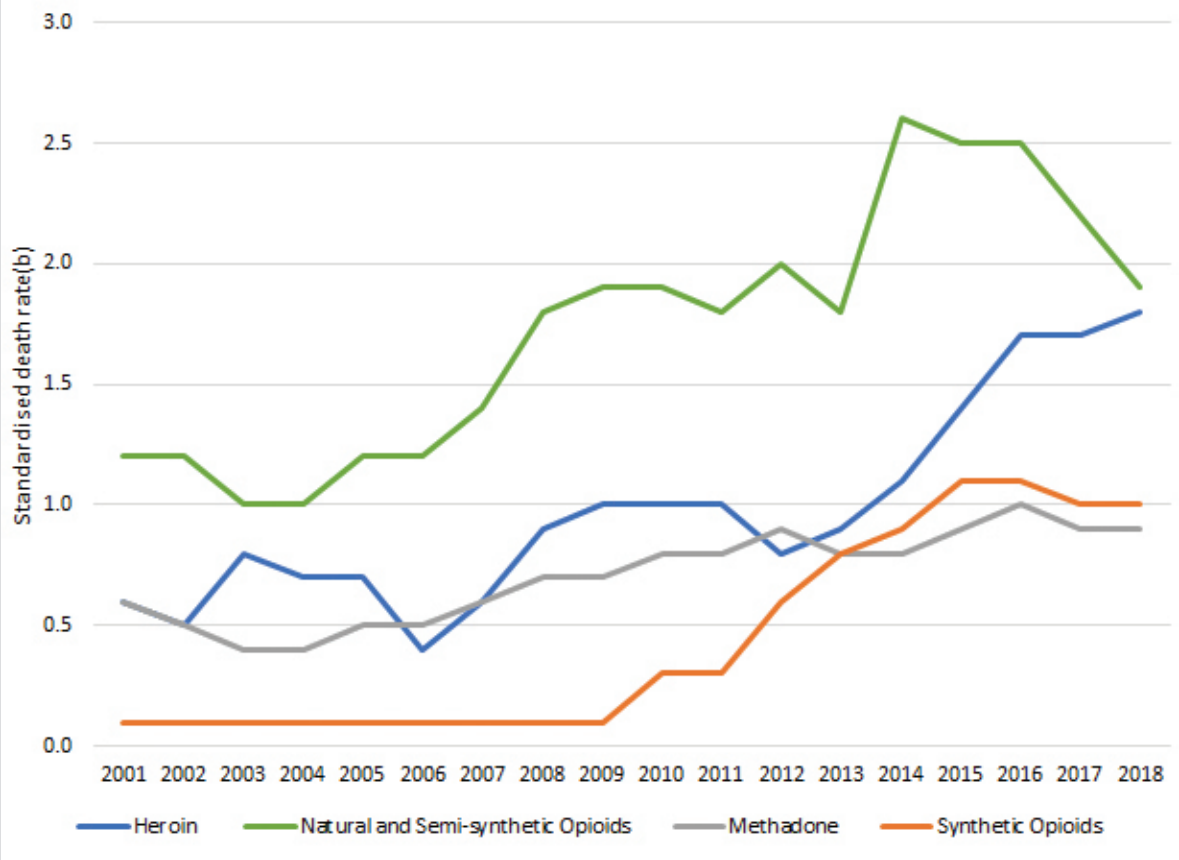
The number of unintentional drug-induced deaths that involve four or more substances has almost trebled, from 163 in 2013 to 445 in 2017.[156]

156 Penington Institute, 2019, p51, 12.

4.1 THE HEROIN CORRELATION

After a period of stability in the mid-2000s the rate of opioid-induced deaths involving heroin increased over the last five years.

Figure 18: A correlation between opioid and heroin use and death rates (Source: ABS)[157]



Community perception is that heroin overdose reflect its illegal use by drug addicts. However, **there is a high correlation between the increase in heroin-related deaths and prescription opioid deaths**. In 2018, the ABS recorded 438 heroin-induced deaths, the highest number of heroin-induced deaths since the year 2000, with the increase being significant over the last 5 years.[158]

Why is this significant in this context? Evidence from the USA and Australia shows that individuals who are addicted to prescription opioids are 40 times more likely to become addicted to heroin.[159]

In one study, about 80% of current heroin users reported that they began with prescription opioids. Therefore, the public health effects of prescription opioids and heroin are intertwined.[160]

Read about the link between heroin overdose deaths and government tightening access to opioid prescription medications in 2014 in Chapter 8.

157 ABS, 2019.
158 ibid, p1.
159 CNN Editorial Research, Opioid Crisis Fast Facts, CNN Health, 27 February 2020.
160 National Academies of Sciences, Engineering, and Medicine, 'Pain Management and the Opioid Epidemic: Balancing Societal and Individual Benefits and Risks of Prescription Opioid Use', Washington, 13 July 2017.

4.2 ANTI-PSYCHOTICS

There is little community awareness of the involvement of anti-psychotic drugs in overdose deaths. Lithium, for example, is a medication that is used to treat bipolar disorder, and it is also used off-label to treat patients with suicidal ideation. Yet an overdose on Lithium can be fatal.

According to the Penington Institute:

> *This group includes drugs such as quetiapine, olanzapine, risperidone, paliperidone, amisulpride, and lithium; though quetiapine is most commonly identified in coronial data. There were 192 unintentional drug-induced deaths involving anti-psychotics in 2017, representing 11.9% of all unintentional drug-induced deaths. Rates of unintentional drug-induced deaths involving anti-psychotics have increased markedly since 2013.*[161]

5. ADVERSE DRUG EVENTS

The TGA defines adverse drug events as:

> *unintended and sometimes harmful occurrences associated with the use of a medicine, vaccine or medical device (collectively known as therapeutic goods). Adverse events include side effects to medicines and vaccines, and problems or incidents involving medical devices.*[162]

Adverse drug events is most commonly measured by hospital separations.

According to the AIHW, a hospital separation is a completed episode of admitted hospital care ending with discharge, death, transfer, or a portion of a hospital stay.[163]

Whilst total drug overdose deaths are over 2000 a year, the number of people who experience an adverse drug event is staggering in size. The sheer volume of hospital separations indicate a broader problem with medication use in the community.

In the *Pharmaceutical Society of Australia (PSA) Medicine Safety: Take Care* report, it details the extent of harms in Australia as a result of medicine use. The report reveals that 250,000 Australians are hospitalised each year, with another 400,000 presenting to emergency departments, as a result of medication errors, inappropriate use, misadventure and interactions.[164]

Furthermore 1.2 million Australians have experienced an adverse medication event in the last 6 months.[165]

161 Penington Institute, 2019, p63.
162 Australian Government Department of Health Therapeutic Goods Administration, published on 30 October 2019, see https://www.tga.gov.au/reporting-adverse-events
163 AIHW, 2019.
164 Pharmaceutical Society of Australia Ltd, Medicine Safety: Take Care, 2019, p4.
165 ibid, p18.

5.1 HOSPITALISATIONS

The AIHW's National Hospital Morbidity Database (NHMD) showed that in 2016–17 of all separations with a drug-related principal diagnosis:

- 59% of drug-related hospital separations were due to sedatives. Benzodiazepines comprise the largest group of drugs in this class and examples include diazepam, alprazolam and temazepam.
- In 87% of separations involving sedatives, alcohol was also involved.
- 13% were for opioids, with heroin, opium, morphine and methadone accounting for half of this group (6.6% of all drug-related separations).[166]

A new report from the AIHW paints a grim picture of rapidly increasing opioid overdoses.

In its report the institute says the rate of hospitalisation where opioid poisoning was recorded as the main reason for admission rose by 25% in the decade to 2016.

> *"Every day in Australia, there are nearly 150 hospitalisations and 14 presentations to emergency departments involving opioid harm, and three people [a day] die from … opioid use," AIHW spokeswoman Dr Lynelle Moon says.*
>
> *"In the case of both deaths and hospitalisations, pharmaceuticals opioids were more likely to be responsible than illegal [heroin, opium] opioids."*[167]

Of greater concern is the number of Australians who become long-term users each year. Monash University claim 50,000 new people become long-term users of dispensed pain killers each year, putting them at risk of addiction.[168]

6. WEAK VERSUS STRONG OPIOIDS

A 2015 study published in the *Medical Journal of Australia* focused on accidental and intentional codeine overdose deaths in Australia between 2001–2013. This study analysed deaths due to 'weak' codeine opioids like **Panadeine Forte**. The study showed that mental health problems were common in those involved in intentional deaths, and the combination of chronic pain and mental health problems were common in accidental death. The study showed that **benzodiazepines were also present in 56.1% of deaths**, highlighting the dangerous polydrug combination. The study noted:

> *"An increased focus on screening for depression and suicide risk is important when prescribing codeine in primary care encounters, which represent an important opportunity for interventions that reduce the risk of suicide."*[169]

166 AIHW, 2018, Opioid Harm in Australia.

167 Australian Institute of Health and Welfare (AIHW), 'Report sheds new light on opioid harm in Australia and draws global comparisons', media release, 9 November 2018.

168 S Molloy, 'Deadlier than heroin: The crippling drug crisis Australia is ignoring', News.com.au, 5 April 2019.

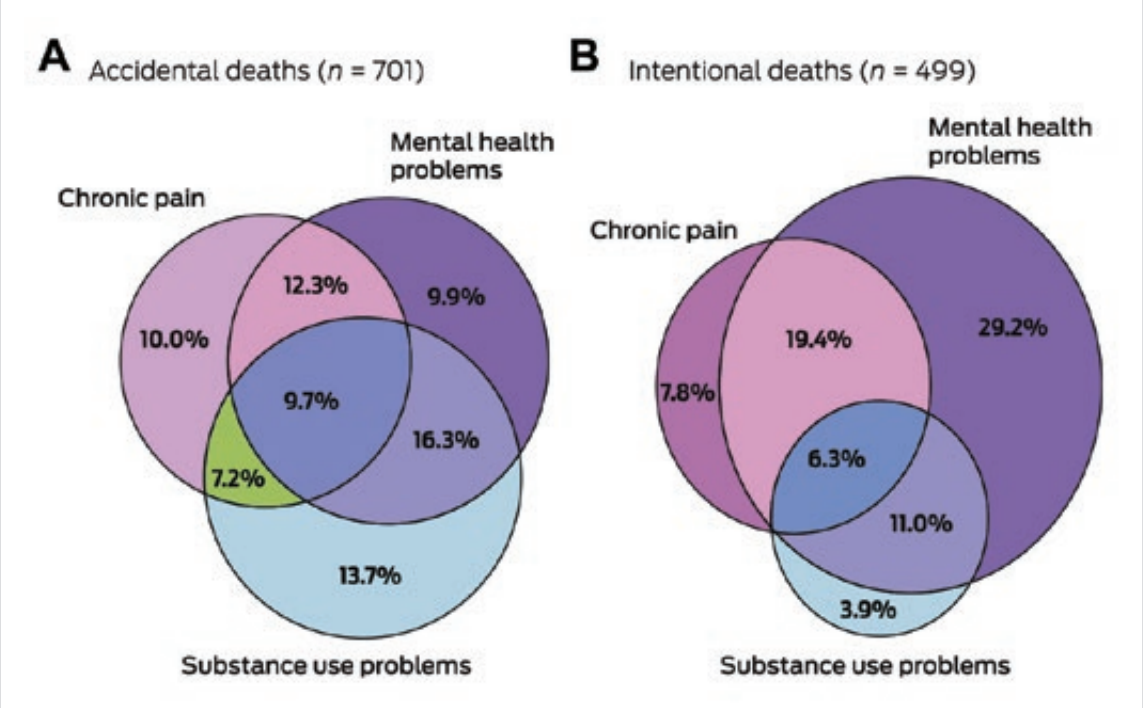
169 A Roxburgh, M Crim, W Hall, et.al., 'Trends and characteristics of accidental and intentional codeine overdose deaths in Australia', Medical Journal of Australia, vol 203, issue 7, 5 October 2015.

The study also called for better patient education on:

> *"the increased risk of fatal overdose if they combine codeine with benzodiazepines and other pharmaceutical opioids."*[170]

A clear finding of the study was the impact the prescription of these medications was having on vulnerable people with comorbid mental health and pain conditions.

Figure 19: Recorded comorbid conditions associated with codeine-related deaths (Source: Roxburgh, et al, 2015)



The TGA provides a very clear warning on its website in relation to codeine products.

> *"The use of low-dose codeine-containing medicines is associated with high health risks. Codeine is an opioid drug closely related to morphine and, like morphine, is also derived from opium poppies. Codeine, like morphine and other opioids, can cause opioid tolerance, dependence, toxicity and in higher doses, death.*
>
> *Regular use of medicines containing codeine, for example for chronic pain, has led to some consumers becoming addicted to codeine without realising it. The risks associated with codeine use are too high without oversight from a doctor."*[171]

AMA President Dr Michael Gannon is quoted as stating:

> *"Too many people are found with codeine in their body at post mortem examinations. This is a harmful drug. It's hurting people, it's killing people."*[172]

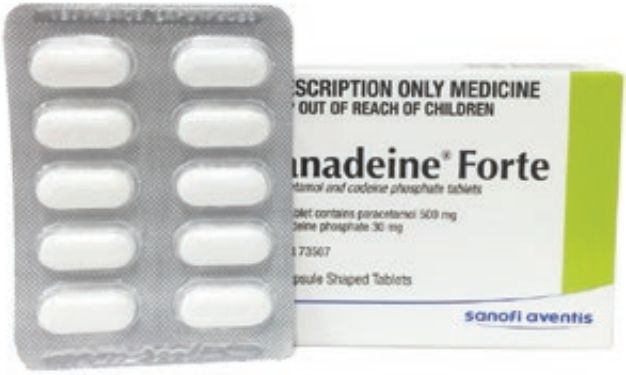
170 ibid.

171 Australian Government Department of Health Therapeutic Goods Administration (TGA), published on 10 April 2018, see https://www.tga.gov.au/codeine-info-hub

172 Australian Medical Association, Expert quotes regarding codeine, published on 12 October 2017, see https://ama.com.au/ausmed/expert-quotes-regarding-codeine

6.1 PANADEINE FORTE CMI AND PI ANALYSIS

An example of a weak opioid is Panadeine Forte. It was launched in March 2000 and is a Schedule 4 drug. The Sanofi-Aventis Panadeine Forte CMI is dated 06/2017 (for this report, we downloaded this CMI from the TGA website on 9 May 2020). The same process of analysing the CMI and PI was undertaken, as was done with other medications in Chapter 2.



Panadeine Forte is a medication that has been available for 20 years. It is regularly prescribed to young people and has been associated with a long history of adverse events including deaths.

The CMI does not contain a single mention of the risk of death, addiction, dependence, tolerance, withdrawal or abuse. It contains no mention of the side effects of using this medication with alcohol or benzodiazepines. In total, we identified 14 areas as breaches of the *Therapeutic Goods Act 1989*.

Of all the medications analysed in this report, this CMI is the most inconsistent with the PI, it has the least number of life-threatening warnings, and it is the medication most prescribed to adults and children.

Sanofi-Aventis Panadeine Forte	Australia CMI 06/2017[173]	Australia PI 04/2020[174]
	Death mentioned: Zero times	Death mentioned: 9 times
Addiction Warning **Dependence Warning**	Addiction is not mentioned once in the CMI* Dependence is not mentioned once in the CMI*	"Prolonged use of high doses of codeine may produce dependence and or addiction."
Benzodiazepine Warning	"- Benzodiazepines (medicines used as sedatives or to treat anxiety)" "These medicines may be affected by Panadeine Forte or may affect how well Panadeine Forte works."*	"Concomitant use of opioids, including codeine, with benzodiazepines may result in sedation, respiratory depression, coma and death."
Alcohol Warning	"Do not drink alcohol. Drinking alcohol increases thelikelihood of becoming drowsy."*	"Concomitant use of opioids, including codeine, with alcohol may result in sedation, respiratory depression, coma and death. Concomitant use with alcohol is not recommended."

173 Sanofi-Aventis Panadeine Forte Tablets, Consumer Medicine Information, June 2017.
174 Sanofi-Aventis, Australian Product Information – Panadeine Forte, April 2020.

Sanofi-Aventis Panadeine Forte	Australia CMI 06/2017[173]	Australia PI 04/2020[174]
	Death mentioned: Zero times	Death mentioned: 9 times
Overdose Warning	"If you take too many tablets you may feel nauseous, light headed, dizzy or drowsy."*	"Toxic symptoms include vomiting, abdominal pain, hypotension, sweating, central stimulation with exhilaration and convulsions in children, drowsiness, respiratory depression, cyanosis and coma." "Severe intoxication can lead to apnoea, circulatory collapse, cardiac arrest and death."
Abuse Warning	Abuse is not mentioned once in the CMI*	"There have been reports of drug abuse with codeine, including cases in children and adolescents."
CYP2D6 Warning	"Do not take this medicine if you have or have had any of the following medical conditions:" "-Ultra-rapid metaboliser of CYP2D6"*	"However, if the patient is an extensive or ultra-rapid metaboliser there is an increased risk of developing side effects of opioid toxicity even at commonly prescribed doses." "Deaths have been reported in children with rapid metabolism."
High Dose Warning **Withdrawal Warning** **Tolerance Warning**	"Panadeine Forte may be habit forming if taken in high doses for extended periods of time."* Withdrawal is not mentioned in the CMI* Tolerance is not mentioned in the CMI* (Note: the CMI does not define "habit forming")	"Prolonged use of high doses of codeine may produce dependence and or addiction. Tolerance may also result following repeated administration. Codeine has a primary potential for dependence. Tolerance, psychological and physical dependence develop with prolonged use of high doses with withdrawal symptoms after sudden discontinuation of the drug."
Pregnancy Warning	"This medicine contains codeine, which may produce withdrawal effects in the newborn baby."	"Codeine may cause respiratory depression and withdrawal syndrome in neonates born to mothers who use codeine during the third trimester of pregnancy."

Sanofi-Aventis Panadeine Forte	Australia CMI 06/2017[173]	Australia PI 04/2020[174]
	Death mentioned: Zero times	Death mentioned: 9 times
Breastfeeding Warning	"Do not use Panadeine Forte if you are breastfeeding or planning to breastfeed. The medicine passes into breast milk and may affect the baby."*	"Analgesic doses excreted in breast milk are generally low. However, infants of breast feeding mothers taking codeine may have an increased risk of morphine overdose if the mother is an ultra-rapid metaboliser of codeine."
Opioid Medication	Does not mention it is an opioid once.*	Details that this is an opioid drug.
Schedule 4 drug	Not mentioned*	Mentioned*

* Examples of inconsistencies between the CMI and the PI, which are breaches of the *Therapeutic Goods Act 1989*

This report also examined other codeine medications in the same class as Panadeine Forte including:

- Nurofen Plus
- Tramadol
- Paracetamol and Codeine Pain Tablets.

Each medication analysed was comparable to the Panadeine Forte analysis. The systemic issues relating to placing consumers in danger of life-threatening risks goes further than longer-term medications initially analysed in Chapter 2. It is clearly evident that these same inconsistencies in warnings exist for medication that is prescribed on a short-term basis; often to consumers with moderate issues.

Our analysis also identified these issues with Amcal, Terry White and Chemist Own brands – highlighting a situation in which the **manufacturer** and the **pharmacist** are the same organisation.

7. AUSTRALIA'S GROUND ZERO MOMENT FOR THE OPIOID CRISIS

In 2018, the National Drug and Alcohol Research Centre (NDARC) commenced a study on the adverse events associated with opioid use in Australia. The study was named POPPY II:

> *"This will be the largest postmarketing surveillance study of prescribed opioids undertaken in Australia, linking exposure and outcomes and examining risk factors for adverse outcomes of prescribed opioids."*[175]

The paper's opening statement is of profound importance in understanding how the Australian opioid crisis began.

> *"Australia has seen dramatic shifts in the rate of opioid prescribing in the last two decades, including changes in the types of opioids prescribed. Almost 15 million opioid prescriptions were dispensed in Australia in 2015 and prescribing increased 15-fold between 1992 and 2012. Originally registered to manage cancer and acute pain, since 1999, opioids have been approved to treat an increasing number of chronic non-cancer pain (CNCP) conditions, despite a lack of evidence of long-term effectiveness. There has also been a shift in the type of opioids prescribed. In 1990, 90% of opioid dispensings were for so-called weak opioids and 96% were short-acting opioids. By 2011, 40% of dispensings were for strong opioid and 50% for long-acting opioids. In parallel to escalating use, there is increasing extramedical opioid use, injection, opioid-related hospitalisation, opioid dependence and overdose."*
>
> *Oxycodone has received considerable attention due to associated harms. Its prescription has played a significant part in the US opioid epidemic. Australian evidence suggests patients at higher risk of adverse opioid outcomes may have a higher likelihood of being prescribed oxycodone; oxycodone is by far the most commonly misused prescription opioid. This is concerning given oxycodone utilisation increased 12-fold in Australia since 2000, now accounting for 34% of all pharmaceutical opioid use."* [176]

As outlined in Chapter 1, opioids can be grouped in several different ways. 'Strong' and 'weak' opioids are defined based on how much is needed to produce the desired pain-relieving effect, often in comparison with morphine. 'Strong' opioids like OxyContin are more potent, so a smaller amount is required to relieve pain compared with a 'weak' opioid.

As shown in Figure 20, oxycodone (e.g. OxyContin) is 1.5 times stronger than morphine, whilst Codeine (e.g. Panadeine Forte) is only a fraction of the strength at 0.13 of morphine. Strong opioids expose the person to a greater risk of side effects like addiction and abuse, hence drugs like OxyContin have been Schedule 8 drugs since their launch.

175 N Gisev, S-A Pearson, T Dobbins, et.al., 'Combating escalating harms associated with pharmaceutical opioid use in Australia: the POPPY II study protocol', *BMJ Open* 2018, 8:e025840, 26 September 2018.

176 ibid.

Figure 20: Opioid Dose Equivalence (Source: Faculty of Pain Medicine)

Opioid Dose Equivalence

Calculation of oral Morphine Equivalent Daily Dose (oMEDD)

oMEDD (mg) = Current Opioid Dose x Conversion factor

CURRENT OPIOID	CONVERSION FACTOR		PROPIETARY NAMES
ORAL (SWALLOWED) PREPARATIONS *Note: Modified release formulations are marked MR*			
Morphine	mg/day	1	Anamorph, Kapanol (MR), MS Contin (MR), MS Mono (MR), Ordine, Sevredol
Oxycodone	mg/day	1.5	Endone, OxyContin (MR), OxyNorm, Targin (MR)
Hydromorphone	mg/day	5	Dilaudid, Jurnista (MR)
Codeine	mg/day	0.13	Aspalgin, Codalgin, Panadeine, Panadeine Forte, Mersyndol, Nurofen Plus, others
Dextropropoxyphene	mg/day	0.1	Di-Gesic, Doloxene
Tramadol	mg/day	0.2	Durotram-XR (MR) , Tramal, Tramadol SR (MR), Zydol, Zydol SR (MR), others
Tapentadol	mg/day	0.3	Palexia-SR (MR), Palexia-IR

Weak opioids like Codeine are usually provided in short-acting versions. Products like Panadeine Forte provide around 4–6 hours of relief (according to the CMI 06/2017). OxyContin is a long-acting version that provides around 12 hours of relief. In order to deliver the longer period of pain relief, the long-acting versions contain a larger amount of oxycodone in each tablet. OxyContin is available in 10mg, 15mg, 20mg, 30mg, 40mg, and 80mg doses. Depending on the dosing, one OxyContin tablet could contain as much oxycodone as 10 short-acting tablets. The larger dose also comes with additional risks. The Purdue OxyContin Full Prescribing Information dated 10/2019[177] contains a frightening warning on long-acting OxyContin:

WARNINGS AND PRECAUTIONS

Addiction, Abuse, and Misuse

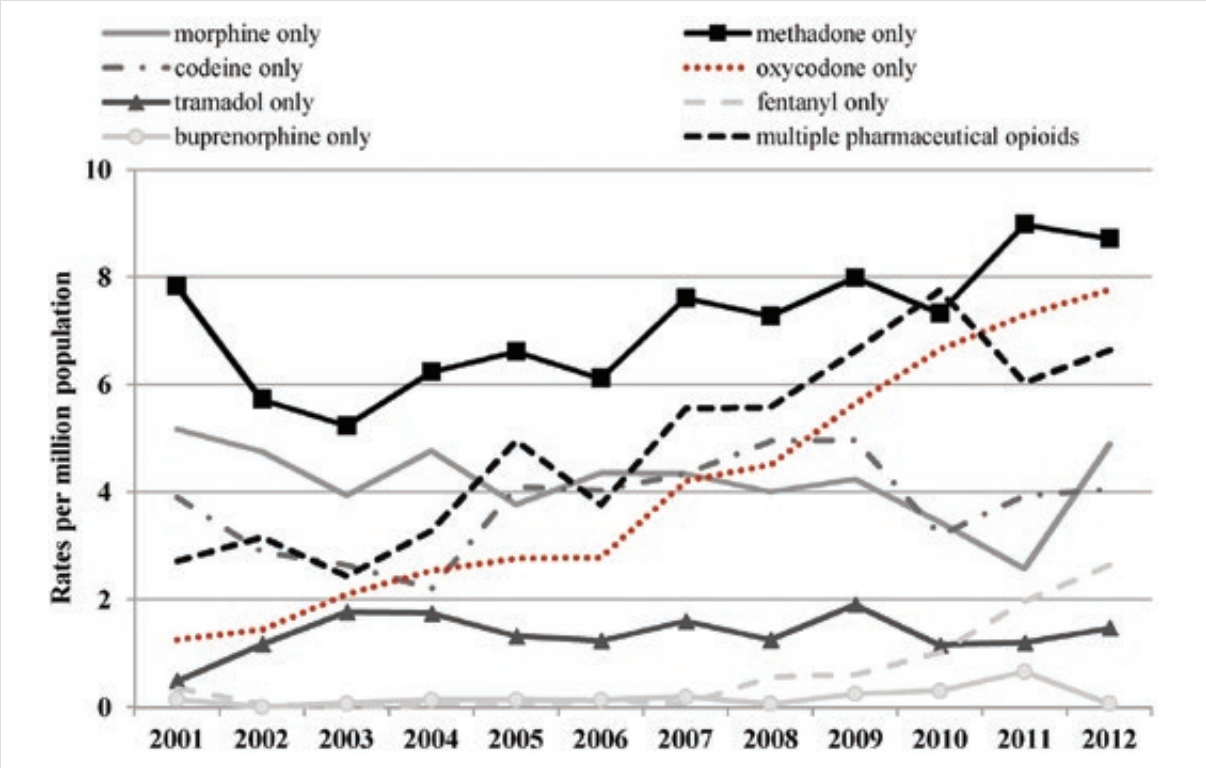
- OxyContin contains oxycodone, a Schedule II controlled substance. OxyContin exposes users to the risks of opioid addiction, abuse, and misuse. Because extended-release products such as OxyContin deliver the opioid over an extended period of time, there is a greater risk for overdose and death due to the larger amount of oxycodone present.

177 Purdue Pharma, OxyContin Full Prescribing Information, October 2019.

This statement was not included in the original Australia OxyContin CMI in 2000 or the version from December 2019. The outcome is that a stronger opioid, in a large dose per tablet, with increased life-threatening risks, was made available when OxyContin was launched in 2000. Purdue–Mundipharma knew there was a significant risk of death if the tablet was crushed, but chose to not include the risk of death warning in the CMI in 2000 at all.

Prior to 1999, the majority of opioids prescribed were weak and short-acting. Strong opioids were generally limited in use to chronic cancer pain. However, in 1999 the PBS approved the use of strong opioids for more pain conditions including moderate to severe pain, as evidenced by the OxyContin CMI (2000). The result was a shift in prescription activity from weak/short-acting opioids to strong/long-acting opioids. Deaths due to OxyContin increased with this shift in prescription rates, as clearly shown in a 2017 study into 'Trends in heroin and pharmaceutical opioid overdose deaths in Australia' (see Figure 21).[178]

Figure 21: Trends in rates of pharmaceutical opioid deaths (Source: Roxburgh, et al, 2017[179])



By allowing a greater scope for doctors to prescribe a strong opioid like OxyContin for moderate pain, the Australian Government exposed more people to life-threatening risks. By failing to ensure the CMI was accurate, it meant that all users had very little warning information to provide informed consent.

Based on the information that already existed on deaths resulting from weak codeine opioid use, allowing strong/long-acting opioids to be used without appropriate consumer warnings was the 'ground zero' moment in the Australian opioid crisis.

178 A Roxburgh, W D Hall, T Dobbins, et.al., 'Trends in heroin and pharmaceutical opioid overdose deaths in Australia', *Drug and Alcohol Dependence*, 0376-8716, 14 August 2017.

179 ibid, p 294.

7.1 OPIOIDS AND MENTAL ILLNESS

The POPPY II study is investigating Australian evidence that patients at higher risk of adverse opioid outcomes may have a higher likelihood of being prescribed oxycodone. The comorbidity of mental illness and chronic pain is well established. A review of the Purdue OxyContin Full Prescribing Information dated 10/2019 contains another horrifying warning on OxyContin:

> *"Assess each patient's risk for opioid addiction, abuse, or misuse prior to prescribing OXYCONTIN, and monitor all patients receiving OXYCONTIN for the development of these behaviors and conditions. Risks are increased in patients with a personal or family history of substance abuse (including drug or alcohol abuse or addiction) or mental illness (e.g., major depression). The potential for these risks should not, however, prevent the proper management of pain in any given patient. Patients at increased risk may be prescribed opioids such as OXYCONTIN, but use in such patients necessitates intensive counseling about the risks and proper use of OXYCONTIN along with intensive monitoring for signs of addiction, abuse, and misuse."*[180]

The Australian OxyContin PI 12/2019 includes this statement:

> *"An initial comprehensive assessment should be conducted using a biopsychosocial approach to identify a cause for the pain and the appropriateness of opioid therapy - and to identify psychosocial factors that may exacerbate pain or magnify overall distress (e.g. depression, anxiety, post-traumatic stress disorder, borderline personality disorder, marked family stressors, history of sexual abuse). In the absence of a clear indication for a strong opioid analgesic, drug-seeking behaviour must be suspected and resisted, particularly in individuals with a history of, or propensity for, drug abuse. Factors that may put the patient at increased risk of opioid abuse/addiction include a personal/family history of substance, prescription medication and alcohol abuse, and major psychosocial issues (e.g. psychological/ psychiatric disorder)."*[181]

Neither statement nor any reference to the greater risk of addiction for people with mental illnesses was included in the original Australia Oxycontin CMI in 2000 or the version from December 2019. The inaccurate and misleading OxyContin addiction warnings were detailed in Chapter 2.

However, the failure to provide a specific warning for those at a higher risk – the mental illness sufferers – is nothing short of criminal. When you look at the way OxyContin was introduced to and prescribed in Australia, and the lack of response from the mental health sector, it is impossible to see how vulnerable people stood any chance of avoiding these tragic outcomes. Considering these issues are also evident in other CMI opioid consumer warnings like Targin, the full impact of these deadly failures are yet to be truly understood.

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180 Purdue Pharma, OxyContin Full Prescribing Information, October 2019.

181 Mundipharma, OxyContin (Oxycodone Hydrochloride) Modified Release Tablets, Australian Product Information, 17 December 2019.

Warning

Do not stop taking a prescribed medication without discussing it with your doctor. Information can also be obtained by calling the NPS Medicines Line on 1300 633 424 or the Adverse Medicines Events Line on 1300 134 237 for advice. If you need support for any medical concern, including mental health matters, please contact your doctor. Lifeline also provides a 24 hour support service on 13 11 14 or www.lifeline.org.au

4. PHARMACY SUPPORT

1. INTRODUCTION

This chapter identifies the role of pharmacists in prescription medication safety.

The medication prescribed by doctors is dispensed by pharmacists and they play an important safety role in warning people about the risks and side effects – particularly those more vulnerable in our society. Their ethical and legal responsibilities are indoctrinated in professional codes and health legislation.

Pharmacists are heavily remunerated by the PBS for the safety role they play in medication dispensing.

They are responsible for dispensing the CMI documentation, so have failed to identify and address the information gaps between CMIs and PIs (as outlined in Chapter 2).

They are also responsible for medication management (polydrug dispensing) and for providing verbal advice to vulnerable consumers.

In this chapter, we highlight the failure of pharmacists to undertake their basic safety role through a sample research project involving visits to pharmacists by people with lived experience of polydrug use.

2. PHARMACEUTICAL SOCIETY OF AUSTRALIA (PSA) – CODE OF ETHICS

2.1 THE PSA

> The Pharmaceutical Society of Australia (PSA) is the only Australian Government-recognised peak national professional pharmacy organisation representing all of Australia's 31,000 pharmacists working in all sectors and across all locations.[182]

PSA National President, Dr Chris Freeman is a vocal advocate for the role of pharmacists in medication safety, saying:

> *"Pharmacists are the stewards of medicine safety. Their primary responsibility at all times is to ensure medicines are used safely and effectively."*[183]

182 Pharmaceutical Society of Australia website, accessed on 3 April 2020, see https://www.psa.org.au/about/about-psa/
183 Pharmaceutical Society of Australia website, accessed on 3 April 2020, see https://www.psa.org.au/election_asks/

2.1.1 Code of ethics

The PSA's Code of Ethics for pharmacists, *"articulates the values of the pharmacy profession and expected standards of ethical behaviour of pharmacists towards individuals, the community and society. The Code underpins the professional practice of all pharmacists in Australia."*[184]

The role of pharmacists in assisting patients to make informed choices is explicitly stated:

> *"Participation by patients in healthcare decisions is a core principle of the Australian Charter of Healthcare Rights. Patients have the right to be informed about the choices available in health care and to be involved in making decisions based on these choices."*[185]

The code further explains the responsibilities of the pharmacist including:

> *"explains the options available, including the risks and benefits, by providing information that is impartial, relevant, up-to-date and independent of any personal commercial considerations to help patients make informed decisions."*[186]

In the PSA's *Dispensing Practice Guidelines*:

> *"Pharmacists also have a professional obligation to provide all necessary and up-to-date information to enable patients to make informed decisions about their medicines. CMI leaflets should be regarded as a valuable tool for assisting the counselling process, not as an alternative to counselling."*
>
> *"Patient counselling is described as "an important part of the process of dispensing medicines. Counselling is a two-way communication process between the pharmacist and the patient, and can occur at any point in the dispensing process."*[187]

The guidelines also indicate when more detailed counselling may be required, including:

- the patient is new to the pharmacy
- the medicine is new for the patient or there is a change in strength from a previous prescription
- there are special administration instructions for the medicine
- the prescription is for a child, an older person, or a person at risk of medication misadventure (e.g. polypharmacy)
- there are special patient needs (e.g. visual, auditory or cognitive impairment; cultural and linguistic diversity)
- the medicine has a narrow therapeutic index or requires therapeutic monitoring
- the medicine is a controlled drug.[188]

The guidelines contain a detailed explanation for 'Counselling with Consumer Medicines' on pages 33 and 34.

184 Pharmaceutical Society of Australia, *Code of Ethics*, 2017, see https://www.psa.org.au/membership/ethics/
185 ibid, p 12.
186 ibid.
187 Pharmaceutical Society of Australia, *Dispensing Practice Guidelines*, June 2019, p 33,23.
188 ibid, p 24.

It states that *"Information contained in CMI leaflets is brand specific and must be consistent with the approved Product Information (PI)."*In the section titled 'Providing CMI Leaflets' the guidelines state that, *"Patients should have the opportunity to access the current version of the CMI leaflet each time a product is dispensed."*

It also provides instances of when a CMI would be important. It includes the same circumstances as listed for patient counselling, with the addition of:

- after each supply of medicine – regular reinforcement of information may be required (e.g. if the medication is cytotoxic or teratogenic, or has major contraindications for its use)
- at regular intervals for medicines used for long-term therapy (e.g. every 6 months, or on dispensing the last repeat of a prescription with five repeats)
- when the pharmacist has received advice that a sponsor has made significant changes to the CMI.

The code provides a very clear map of the responsibilities of pharmacists in providing medication safety information to consumers, including the role of the CMI. Notably, product information (PI) documents are also a resource available to pharmacists.

3. HOW THE PHARMACY INDUSTRY WORKS WITH GOVERNMENT AND REGULATORS

The Pharmacy Guild of Australia (the Guild) is a national body representing community pharmacies. A core function is to liaise and negotiate with governments, manufacturers, wholesalers and other organisations in the health care delivery system.

3.1 THE 6CPA

The Sixth Community Pharmacy Agreement (6CPA) between the Australian Government and the Guild provides approximately $18.9 billion to over 5000 community pharmacies for:

- dispensing PBS medicines
- providing pharmacy programs and services
- the Community Service Obligation arrangements with pharmaceutical wholesalers.

The 6CPA commenced on 1 July 2015 and expires on 30 June 2020.[189]

189 6th Community Pharmacy Agreement, accessed on 3 April 2020, see http://6cpa.com.au/about-6cpa/

Since 1990, the remuneration that pharmacists receive for dispensing PBS medicines and the regulations regarding the location of pharmacies has been governed by a series of agreements. Over time, these agreements have increased in scope and now also provide for professional pharmacy programs and services.

The 6CPA includes three key funding elements, namely:

1. community pharmacy remuneration, which includes dispensing fees
2. the Community Services Obligation – which ensures that all Australians have timely access to the PBS medicines they require regardless of the cost of the medicine or where they live
3. community pharmacy programmes – with a primary focus on assisting patients better manage their medications thereby reducing medication misadventure and delivering primary healthcare services through community pharmacy.

This agreement is one of the most important elements of the Australian health care system. It is due for renewal this year.

3.2 PHARMACY REMUNERATION

Pharmacists are remunerated through a number of means for dispensing a PBS medication:

1. Mark up price charged for the medication (PBS and patient funded).
2. Administration, handling and storage costs (PBS funded).
3. Pharmacists specialised skills in dispensing the medicines (PBS funded):
   a. Dispensing Fee
   b. Dangerous Drug Fee
   c. Wastage
   d. Container Fee.
4. Other (PBS funded):
   a. Premium Fee Dispensing Incentive
   b. Electronic Prescription Fee[190]

190 Australian Government Services Australia, accessed on 3 April 2020, see https://www.servicesaustralia.gov.au/organisations/health-professionals/services/medicare/pbs-pharmacists/about

Table 12 shows the remuneration for community pharmacies and friendly societies for PBS subsidised prescriptions.

Table 12: Remuneration for community pharmacists for PBS subsidised prescriptions, 2018–19 (Source: PBS)[191]

	Expenditure for PBS and RPBS Prescriptions	2018–19
Price to Pharmacists		
	Ex-Manufacturer Price	$6,836,700,876
	Wholesale Mark-up	$388,993,638
	Sub total	***$7,225,694,514***
Administration, Handling and Storage Costs		
	AHI fee*	$968,836,715
	Sub total	***$968,836,715***
	*Administration, Handling and Infrastructure fee, formerly known as Pharmacy Mark-up	
Pharmacist's Specialised Skills in Dispensing the Medicines		
	Dispensing Fee	$1,510,327,061
	Dangerous Drug Fee	$25,467,071
	Wastage	$4,553,415
	Container Fee	$681,930
	Sub total	***$1,541,029,477***
Other		
	Premium Free Dispensing Incentive	$150,062,235
	Electronic Prescription Fee	$12,141,758
	Sub total	**$162,203,992**
	Total	**$9,897,764,698**

Summary of Medicines, Wholesalers, and Pharmacy Costs	
Medicines cost	$6,836,700,876
Wholesale cost	$388,993,638
Pharmacy cost	$2,672,070,184
Total	**$9,897,764,698**

The total amount paid to pharmacists is $3,061,063,882. It comprises the wholesale mark-up cost of $388,993,637 and the fees that are paid by the PBS (Pharmacy Cost) $2,672,070,184. Some 87% of the PBS revenue paid is for fees for simply being a pharmacist; revenue from selling drugs is only 13%.

191 Australian Government Pharmaceutical Benefits Scheme (PBS), updated 13 December 2019, see http://www.pbs.gov.au/info/statistics/expenditure-prescriptions/pbs-expenditure-and-prescriptions-report

Pharmacists are generally privately owned retail businesses. Most retail businesses generate profit from the mark-up on the wholesale cost of the goods they buy. In the cases of PBS drugs, the taxpayer (via the PBS) is meeting the majority of the cost. In addition to the revenue made on the sale, pharmacists are also paid a number of other fees including for the provision of medication safety services. These fees are also funded by the PBS.

How many times does a pharmacist get paid for doing the one job?

3.2.1 Dangerous drug fee

The dangerous drug fee is $3.11.

The dangerous drug fee is paid for supplying a Schedule 8 medicine and is in addition to the administrative fee and dispensing fee. This fee is designed to cover extra costs related to:

– handling fees charged by wholesalers for dangerous medicines
– supplying and recording duties related to dangerous medicines.

Terry Barnes is a public policy consultant, and his former career in government included senior ministerial advisory roles in federal and Victorian governments. We contacted Terry Barnes in April 2020 and he confirmed his position on the PBS has not changed since this article in 2012 in which he commented:

> *Howard overlooked that most of these venerated professionals are also members of the country's most-feared interest group, the* ***Pharmacy Guild of Australia****. For decades, the guild has reduced stout-hearted politicians to quivering jelly as it zealously pursues the best commercial and professional interests of the proprietors of Australia's 5000 or so local pharmacies who themselves comprise a fraction of all pharmacists.*
>
> *Moreover, the guild negotiates exclusive funding agreements with the federal government, dictating what is paid to distribute and dispense medicines.*
>
> *The dispensing fee regime under the PBS is exceedingly generous by normal commercial standards. While most retailers apply a simple mark-up to cover their costs, including labour, under the PBS pharmacies receive not only a mark-up but professional dispensing fees and a host of other payments, with the revenue per dispensing blurred by complex cost and volume formulas.*
>
> *Ordinary retail businesses charge consumers for the cost of a good, distribution and handling, and a modest provision for a retail profit. Medicines are potentially dangerous when not handled by trained professionals, but they are still goods sold over a counter.*
>
> *PBS payments to pharmacists should be structured in the same way as any other retail business: the price of the medicine itself, adequate provision for wholesale, and dispensing and operating costs, and a profit margin.*
>
> *By sweeping away double dipping on dispensing fees and a host of miscellaneous fees for doing what essentially are routine tasks in running a pharmacy (such as required paperwork), government, pharmacists and taxpayers will all know where they stand. Perhaps, for mischievous synergy with manufacturers, pharmacists' standard PBS mark-up should be 12.5 per cent. If pharmacists want to charge above that they should be free to do so, but at a direct cost to the patient rather than the taxpayer.*[192]

192 T Barnes, 'It's time to bust open the pharmacists' closed shop', *The Australian*, 25 January 2012.

The Pharmacy Guild of Australia

3.2.2 Pharmacy Guild administration fee

The PBS paid the Guild $7,649,772 for administration fees in 2017–18. The PBS records clearly show it was paid for "Pharmacy Guild administration fees", as noted in Table 13.

Table 13: CPA Professional Pharmacy Programmes Expenditure, 2017–18 (Source: PBS)[193]

Under the Sixth CPA there were a range of professional programmes and services delivered by community pharmacy and pharmacists to support the primary health care needs of consumers. The following table details the funds spent on these programmes under CPA in 2017–18 by relevant categories.

Program Type	Actual Expenditure
Rural Pharmacy Maintenance Allowance	$14,099,312
Rural Pharmacy Workforce Program	$4,615,944
Medication Management services	$71,482,115
Medication Adherence services	$78,554,099
Aboriginal & Torres Strait Islander programs	$5,618,708
Pharmacy Guild administration fees	$7,649,772
Programs Total	**$182,019,950**

Notes:
1. For the Programs administration arrangements for 2017–18 (administered by the Pharmacy Guild), the total funding provided to the Pharmacy Guild was $182,019,950 (accrual figure). Of this, $7,649,772 was provided to the Pharmacy Guild for the purpose of Pharmacy Guild administration fees. This means the Pharmacy Guild administration fees was 4.2% of the total funds.

In 2018–19, the name of the fee was modified to remove the word "Guild", it is now called "Pharmacy program administration fees". It is still paid to the Guild. The PBS paid the Guild $7,910,697 for administration fees in 2018–19, as shown in Table 14 (refer to notes for explanation of final figure).

193 Australian Government Department of Health, The Pharmaceutical Benefits Scheme (PBS), Expenditure and Prescriptions twelve months to 30 June 2018, page updated 11 January 2018, see http://www.pbs.gov.au/info/statistics/expenditure-prescriptions/expenditure-prescriptions-twelve-months-to-30-june-2018

Table 14: CPA Professional Pharmacy Programs Expenditure, 2018–19 (Source: PBS)[194]

Under the Sixth CPA there were a range of professional programs and services delivered by community pharmacy and pharmacists to support the primary health care needs of consumers. The following table details the funds spent on these programs under CPA in 2018–19 by relevant categories.

Program Type	Actual Expenditure
Rural Pharmacy Maintenance Allowance	$17,958,390
Rural Pharmacy Workforce Program	$3,388,438
Medication Management services	$99,778,803
Medication Adherence services	$92,009,430
Aboriginal & Torres Strait Islander programs	$5,105,963
Pharmacy Program administration fees	$13,619,586
Programs Total	**$231,860,610**

Notes:
1. For the Programs administration arrangements for 2018–19, the total funding provided to the Pharmacy Programs Administrator was $231,860,610 (accrual figure). Of this, $7,910,697 was provided to the Pharmacy Guild and $5,708,889 to Australian Healthcare Associates for the purpose of Pharmacy Program administration fees. This means the Pharmacy Program administration fees was 5.87% of the total funds.

3.3 COMMUNITY PHARMACY SERVICE CHARTER

The PSA code of ethics is also supplemented with the Community Pharmacy Service Charter. The charter covers a number of key areas to ensure you are provided with safe and effective healthcare. This charter also covers some of the services that pharmacists are paid fees by the PBS for. See Figure 22 for the complete Charter.

In particular, the Charter states:

> *We will provide medicines and pharmacy related services and products to address your healthcare needs. We will provide* ***safe and effective medicines*** *and high quality pharmacy related services, with professional care, skill and competence.*
>
> *Our pharmacy will make sure you have access to the right medicine, as well as a number of other pharmacy services.*
>
> *"We will answer questions about medicines, as well as give useful information about health conditions. Our opening hours and the range of services provided will be clearly displayed and you will receive service from qualified pharmacists and trained staff."*
>
> *"Our pharmacy ensures that our staff are qualified and trained, and comply with professional standards, guidelines and codes of conduct. You will be supplied with the right medicine at the right dose. Pharmacy services you receive will be provided with professional care, skill and competence.*
>
> ***Our pharmacy will answer any questions about the services provided, including treatment options and costs.***

194 PBS, 2019.

We can discuss different brands of medicine that may be available and entitlements under the Pharmaceutical Benefits Scheme (PBS). We can also discuss the PBS Safety Net and other services that may help. With your permission we will also communicate with other members of your healthcare team such as your GP.

Our pharmacy would like to work with you to make decisions about your medicines and pharmacy services so that the care we provide works for you. With your permission we will work with your family and/or carers, and other members of your healthcare team (such as your GP), to make sure that the care we give you suits your needs. This recognises that you have the right to be included in decisions and choices about your health care.

Figure 22: The Community Pharmacy Service Charter (Source: health.gov.au)

It's everyone's right

Everyone has certain rights regarding their healthcare. Your pharmacist and your community pharmacy are part of your healthcare team. The Community Pharmacy Service Charter, based on the Australian Charter of Healthcare Rights, ensures that you know what level of service to expect from your local community pharmacy.

Customer Service Statement

A Customer Service Statement will be clearly visible at all times and, as far as practical, at the entry point of this pharmacy. It will outline:

- the pharmacy name
- opening hours and alternative/after hours services
- how you can contact us by phone, fax, email or internet
- what pharmacy services we provide.

If you would like to make a comment about our pharmacy, you can approach any of the staff who will refer you to the appropriate person.

If you would like to make a comment in writing, our contact details will be clearly displayed.

If you want more information about this Charter ask us here at this pharmacy or visit: www.health.gov.au/pharmacy

Australian Government Department of Health and Ageing

The Pharmacy Guild of Australia

This Project is funded by the Australian Government Department of Health and Ageing as part of the Fifth Community Pharmacy Agreement.

The Community Pharmacy Service Charter – what does it mean for you?

What can I expect from a community pharmacy?	
My rights	**This pharmacy's commitment to you**
Access I have a right to health care.	We will provide medicines and pharmacy related services and products to address your healthcare needs.
Safety I have a right to receive safe and high quality care.	We will provide safe and effective medicines and high quality pharmacy related services, with professional care, skill and competence.
Respect I have a right to be shown respect, dignity and consideration.	We will respect you and your culture, beliefs, values and personal characteristics and those of your carers and advocates when delivering services.
Communication I have a right to be informed about services, treatment, options and costs in a clear and open way.	We will provide you open, timely and appropriate communication about your health, medicines and related services in a way you can understand.
Participation I have a right to be included in decisions and choices about my care.	We will include you in making decisions and choices about your health, medicines and related services and products.
Privacy I have a right to privacy and confidentiality of my personal information.	Unless you otherwise consent, we will maintain your personal privacy and assure proper handling of your personal health and other information. We will provide a private area to discuss your needs.
Comment I have a right to comment on my care and to have my concerns addressed.	We will promptly address your comments or concerns about medicines or other services offered.

The Community Pharmacy Service Charter – what does it mean for you?

The Community Pharmacy Service Charter covers a number of key areas to ensure you are provided with safe and effective healthcare. These are:

Access

Our pharmacy will make sure you have access to the right medicine, as well as a number of other pharmacy services.

We will answer questions about medicines, as well as give useful information about health conditions. Our opening hours and the range of services provided will be clearly displayed and you will receive service from qualified pharmacists and trained staff.

Safety

Our pharmacy ensures that our staff are qualified and trained, and comply with professional standards, guidelines and codes of conduct.

You will be supplied with the right medicine at the right dose. Pharmacy services you receive will be provided with professional care, skill and competence.

Respect

Our staff will respect different cultures, beliefs and values and you have the right to be shown respect, dignity and consideration.

We will provide the same quality of service to you, your carer, or anyone else involved in your healthcare.

Communication

Our pharmacy will answer any questions about the services provided, including treatment options and costs.

We can discuss different brands of medicine that may be available and entitlements under the Pharmaceutical Benefits Scheme (PBS). We can also discuss the PBS Safety Net and other services that may help. With your permission we will also communicate with other members of your healthcare team such as your GP.

Participation

Our pharmacy would like to work with you to make decisions about your medicines and pharmacy services so that the care we provide works for you.

With your permission we will work with your family and/or carers, and other members of your healthcare team (such as your GP), to make sure that the care we give you suits your needs. This recognises that you have the right to be included in decisions and choices about your health care.

Privacy

Our pharmacy recognises that your privacy is extremely important.

You have the right to have your personal information kept private and confidential and we follow all professional codes of conduct, standards and guidelines, as well as privacy laws. You also have the right to discuss your health with any of our staff in a private area.

Comment

Our pharmacy welcomes your comments, both positive and negative, on the care you receive in this pharmacy. It helps us to improve our service and give you better care.

You can give comments in a number of ways. When necessary, we can also forward complaints to outside organisations to be dealt with, or you can contact the Australian Health Practitioner Regulation Agency (**www.ahpra.gov.au**) or your state or territory health complaints commission directly.

3.4 ROLE OF THE PHARMACIST

According to the Guild's website:

> *A Consumer Medicine Information (CMI) leaflet is a reader-friendly document that provides information about prescription medicines. Provided free of charge to pharmacy customers, CMIs are written in plain English by the pharmaceutical company that makes the medicine. They answer common questions about the medicine, including what it is for; how to use it properly; things to consider before taking it; and any known side effects. A CMI **can** be provided when someone is starting a new medicine for the first time, **or whenever a customer asks for it.***
>
> *While CMIs are a valuable resource, reading one does not take the place of counselling by a health professional. It is still important to talk to your doctor or pharmacist about your health and medicines.*
>
> *With the rise of the internet, people can find a vast range of information at home, but there is a need for caution when dealing with issues relating to health. The best way to guarantee you are getting reliable information about your medicines is to **ask your pharmacist for a CMI**. Meanwhile, one website that can be relied upon for authentic and trustworthy information on medicines is www.medicines.org.au. At this website, you can find CMIs for most of the prescription medicines available in Australia.*[195]

3.4.1 Money for nothing?

The PBS provides a fee payment of over $3 billion a year to pharmacists. These fees include payments for PBS medications administration and handling, dispensing, and a fee for handling dangerous drugs (including Schedule 8 medications like OxyContin, Endone, Targin and Alprazolam).

Pharmacists are the experts for prescription medication in Australia. Their training, experience and resources enable them to provide advice on all aspects of the medication, including side effects and polydrug interactions. They have committed in their Charter to upholding the highest level of safety for consumers and it is part of their code of ethics.

Yet Chapter 1 detailed the fatal side effects of many medications, and Chapter 2 identified multiple examples of current CMI documents failing to disclose side effects and providing incorrect information. Chapter 2 also identifies the information contained in the PI documents, that pharmacists have access to. Chapter 3 links the deaths that these side effects have caused.

How has the nation's pharmacy network failed to identify and urgently address these issues for over 20 years?

The Guild and pharmacists should not be allowed to pass blame to the TGA and pharmaceutical companies. Whilst both of those organisations have failed consumers, the final point of consumer protection is the pharmacist, and they are paid $3 billion a year to meet that responsibility.

Their job is to dispense PBS medication safely to vulnerable Australians, on the evidence in this report, they have failed on a gigantic scale and it has cost thousands of lives.

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195 The Pharmacy Guild of Australia, updated on 12 March 2020, see https://www.guild.org.au/resources/health-services/pharmacy-issues/consumer-medicines-information

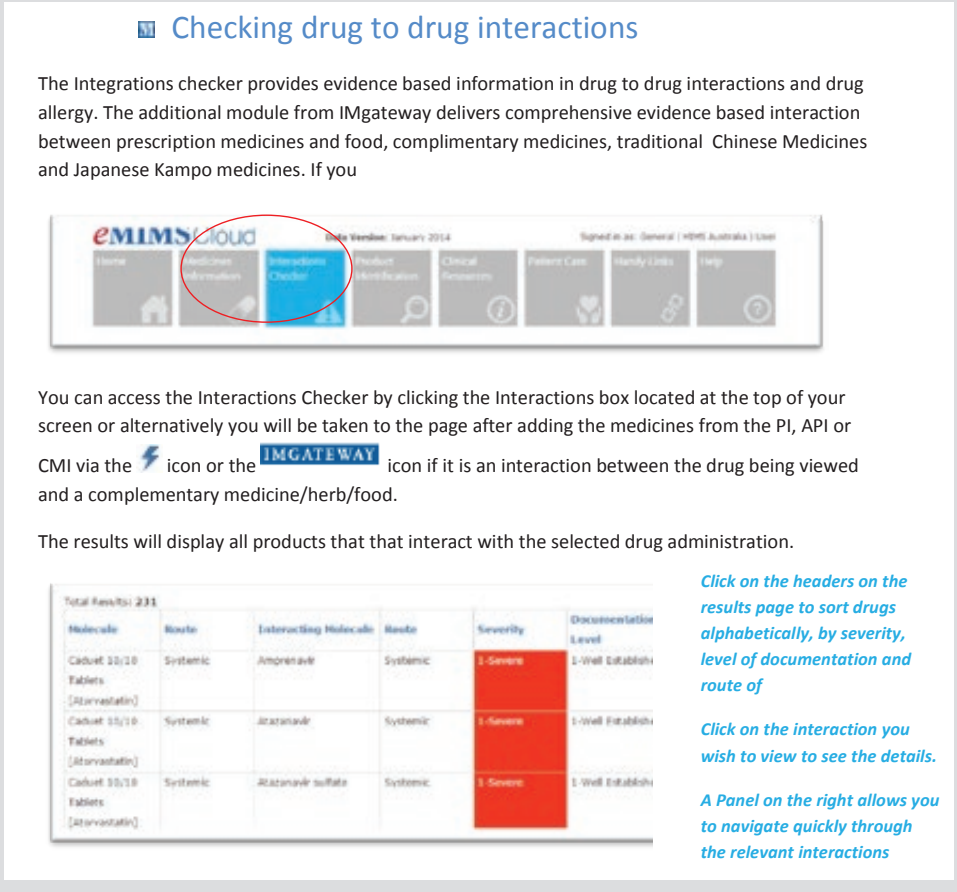
Australian pharmacists also have access to software that can produce polydrug interaction warnings. The MIMS system enables the pharmacist to produce a customised warning document, based on the medication a consumer has been prescribed – see Figure 23.[196] The MIMS platform also enables the pharmacist to view medication warnings from other countries including the USA. All of the information on the FDA medication guides in this report is already accessible to pharmacists on the MIMS platform.
The electronic 'eMIMS' is said to be:

> *the trusted resource you know and love and remains your complete guide to Product Information, Consumer Medicine Information, Product Images, Drug Interactions and PBS restrictions and pricing for all registered medicines in Australia.*[197]

Despite its availability, it is rarely used and the information seldom is passed to consumers. Considering the scale of polydrug deaths and adverse events over the last 20 years, failing to utilise this system has also resulted in unnecessary deaths.

> *The Drug Interactions module warns healthcare providers if drugs being used by a patient or prescribed to a patient may interact with each other. An interaction record in the Drug Interactions module contains a description of the interaction, what could be expected if there is an interaction, severity of the interaction, strength of the supporting evidence and precautions needed. This helps the healthcare professional and, eventually, the patient to avoid treatment failures, adverse effects and toxicities that could be life threatening.*[198]

Figure 23: Pharmacists can check drug interactions on MIMS



196 MIMS Australia, accessed on 3 April 2020, see https://www.mims.com.au/index.php/decision-support/drug-interactions
197 MIMS Australia, accessed on 3 April 2020, see https://www.mims.com.au/index.php/products/emims
198 MIMS Australia, accessed on 3 April 2020, see https://www.mims.com.au/index.php/products/product-overview

3.4.2 Providing a hardcopy CMI

CMIs provide critically important information to people about the medication they are prescribed. The CMIs themselves state the importance of keeping the document handy in case of emergencies. Government health departments stress the importance of receiving a CMI, reading it and following all warnings. However, it is **not mandatory to provide a CMI to a patient with any initial or repeat prescription**. The TGA only requires these be 'available', meaning it can be provided but not that it must be provided.

In practice pharmacists and doctors can print the CMI from the TGA website however they are not readily accessible in hard copy form and are printed on request. There exists no recording of whether a CMI was given to a person or what version of the CMI was given. Many pharmacists simply refer the consumer to the TGA website, as this meets their obligations to provide a CMI. Not everyone has access to the internet and smart devices, and the PBS does not provide free Wi-Fi. Each CMI contains the advice on page 1: "Keep this leaflet with the medicine. You may need to read it again", however it is hard to keep something that you have never been given. This is another unmitigated failure to protect vulnerable consumers from adverse medication side effects – a role they are paid to do.

According to the TGA website, for medicines that do have a CMI:

> *the sponsor is required to make it available to consumers either in the pack or in another manner that will enable the information to be given to the person to whom the medicine is administered or otherwise dispensed.*[199]

The TGA requires written information to assist patients in the use of prescription medicines to be "available to be provided when these medicines are supplied".

> *"In practice, a CMI may not be offered for repeat prescriptions but it should be available on request from a pharmacist," a TGA spokesman said.*[200]

It is a critical failure that the TGA allows a process to exist that paper hardcopy CMIs are not mandatory to be given for every medication. It is not even mandatory to provide a CMI for medications deemed "dangerous" by the TGA, including Schedule 4 or 8 drugs. This includes opioids, benzodiazepines, and stimulants. These are medications with significant side effects including the risk of overdose, addiction and death.

The access to these drugs is restricted because they are dangerous. They can only be obtained with a prescription. Seriously penalties are in place for illegal use because of the risks associated with these medications. Yet the TGA does not believe it is important to ensure that the safety information in the CMI is provided with **every prescription in hard copy form** to ensure it is received.

Despite this, the PSA and the Guild still have the ability to require their pharmacists to provide a hard copy CMI with each prescription. They have the ability to provide best practice medication safety to vulnerable consumers. They chose to not deliver this. Vulnerable consumers pay a high price for this choice.

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199 Australian Government Department of Health Therapeutic Goods Administration (TGA), updated on 3 January 2019, see https://www.tga.gov.au/consumer-medicines-information-cmi

200 D McCauley, 'Greg Hunt warns pharmacists and doctors on medicine information', *The Sydney Morning Herald*, 1 January 2019.

The Sydney Morning Herald

POLITICS FEDERAL HEALTHCARE

This was published 1 year ago

Greg Hunt warns pharmacists and doctors on medicine information

By Dana McCauley
January 1, 2019 – 5.15pm

Federal Health Minister Greg Hunt will write to pharmacists and doctors to remind them of their responsibilities, after consumer advocates raised concerns that patients were not being given vital information about medicine interactions and side effects.

The Consumers Health Forum of Australia called on Mr Hunt to step in after receiving complaints that patients were not always being given consumer medicine information documents (CMIs), which pharmaceutical companies are required by law to make available.

In a 2019 article published by *The Sydney Morning Herald*:

> *Pharmacy Guild of Australia spokesman Greg Turnbull said the organisation supported "maximum patient empowerment and health literacy" but that making the issuing of a CMI mandatory "for every one of the 300 million-plus PBS scripts per year might not be the best solution".*[201]

It is difficult to understand how consumers can reach a position of 'maximum patient empowerment and health literacy', without the information to read.

> *"One size does not fit all," Mr Turnbull said.*
>
> *"Pharmacists exercise their professional judgement and clinical discretion in determining the best way to inform patients of what they need to know, always in the patients' best interest."*[202]

Again, it is difficult to understand how providing safety information for dangerous medication to vulnerable consumers could ever be optional and left to 'clinical discretion'. How does a pharmacist assess the cognitive ability of a consumer they have never met?

The code of ethics clearly documents the process for determining when a hard copy CMI is provided and when it is not required. Instead of making it easy for consumers to get the CMI, the Guild suggests using 'CMI Request Cards' in the pharmacy; a document that most consumers are expecting to receive automatically.

201 ibid.
202 ibid.

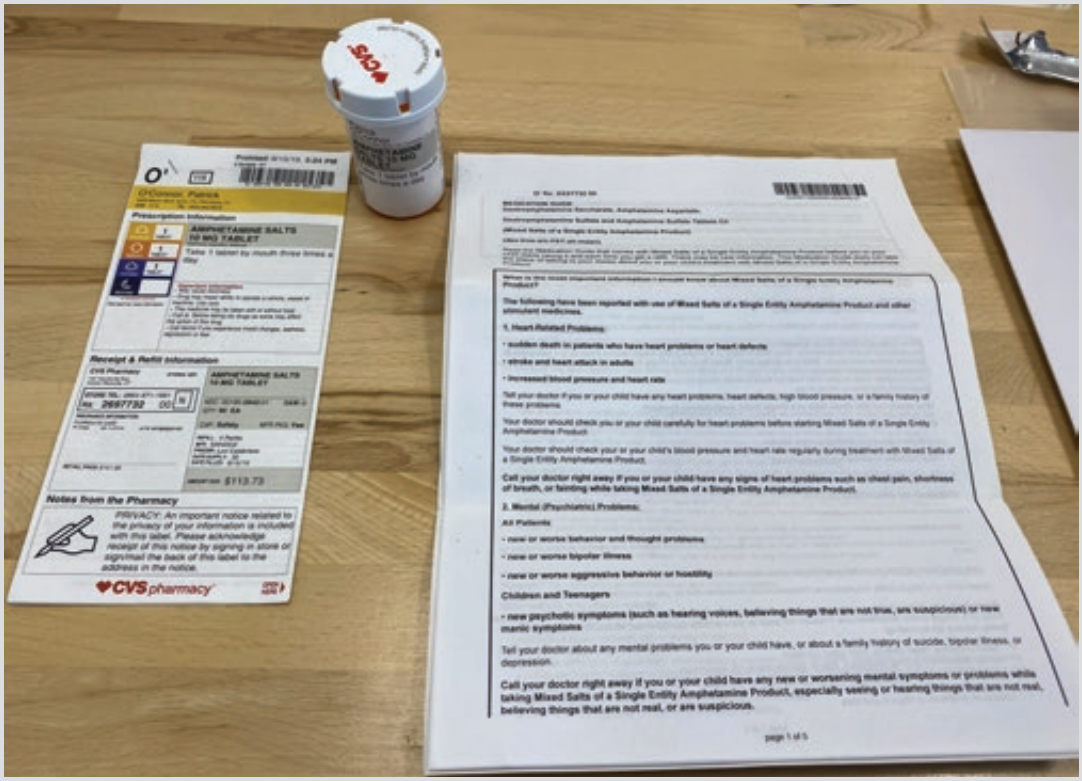
In comparison in the USA, the FDA requires that Medication Guides (MGs) be issued with certain prescribed drugs and biological products when the Agency determines that:

- certain information is necessary to prevent serious adverse effects
- patient decision-making should be informed by information about a known serious side effect with a product, or
- patient adherence to directions for the use of a product are essential to its effectiveness.[203]

Over 240 products that contain a medicine individually, or in combination, have MGs available for them. **This includes all opioids, benzodiazepines, antidepressants and antipsychotics.** In the USA, MGs are developed by the manufacturer, approved by the FDA, and required to be **given to consumers each time the medication is dispensed**.

This is a significant point of difference between the USA and Australia in relation to how warning documents are provided for opioids, benzodiazepines, antidepressants and antipsychotics. The MG is attached to the prescription medication package as per Figure 24. The MGs are barcoded, so can be recorded against the person's digital patient record. This enables verification that the MG was given to the person, including which version. If modifications are made to the MG in the future, the pharmacist can alert the patient to the new warnings.

Figure 24: MG warning documents used in USA



203 U.S. Food & Drug Administration (FDA), published on 3 January 2020, see https://www.fda.gov/drugs/drug-safety-and-availability/medication-guides

The USA regulates the content of the warning documents to ensure the highest level of patient safety information is maintained. In Australia it is left to the discretion of the pharmaceutical companies. The USA requires these documents to be given with **every prescription** for opioids, benzodiazepines, antidepressants and antipsychotics. In Australia it is at the discretion of the pharmacist.

3.4.3 Medication management

The PBS also provides a payment of $99 million to the Guild for medication management services. The medication management programs focus on reducing medicine induced deterioration and adverse reactions. In light of the consumer warning issues and the failure to provide CMI documentation, the risk that this program is not meeting its goals is significant.

3.4.4 Real time prescription monitoring

In Chapter 6, we examine the implementation of the national prescription monitoring system. The aim of the system is to assist to reduce prescription medication adverse events. The target group of medication is Schedule 8 drugs.

Despite the cause of prescription medication deaths covering many medications outside Schedule 8 drugs, the Guild has resisted widening the medication included, citing:

> *"...there are significant logistical challenges with that idea."*[204]

Nationally the system has experienced multiple delays. In the ACT, the government has made it optional for pharmacists to be part of the 'DORA' system and less than 1 in 5 pharmacists have signed up. When challenged to take up a coroner's recommendation to include Schedule 4 and 3 drugs, as noted in a *Canberra Times* article, the answer was:

> *"The government response, presented by Health Minister Rachel Stephen-Smith, said to apply this to all schedule 3 medications would be a considerable regulatory burden.*[205]

In a seemingly unrushed view, Simon Blacker, president of the ACT Branch of the Pharmacy Guild, said:

> *"...that DORA had to date had a "reasonable" uptake in the Territory, and that he hoped that as time goes on, the system becomes more widely accepted by pharmacists."*[206]

3.5 A HUMAN LIFE VERSUS THE COST OF A PIECE OF PAPER

Based on the plethora of issues raised in this chapter, covering multiple areas of medication safety, it is difficult to see how pharmacists are actively working to meet the commitments made under 6CPA and the code of ethics. Three things are certain:

1. They receive the PBS remuneration for the provision of these services.
2. They have not delivered on the services.
3. Lives have been lost from taking prescription medication.

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204 M Haggan, 'Don't add S3S to RTM, says ACT Guild', *AJP*, 17 February 2020.

205 D White and L Bladen, 'Medications to be added to ACT prescription monitoring systems following Chief Coroner recommendations', *The Canberra Times*, 12 February 2020.

206 ibid.

In 2019 whilst researching for this report in the USA, a number of pharmacists were interviewed on the process of dispensing medication and the consumers warnings that are given.

One pharmacist working in Hartford, Connecticut was asked why he thought it was important to provide a hardcopy of the consumer warnings with every prescription, to which he replied,

> *"Because every bottle of pills for controlled medication can kill a person, so every prescription goes out with the warnings to avoid that".*

Another pharmacist made a similar comment when he said,

> *"Because the cost of a human life is worth more than the cost of piece of a paper".*

If only the PSA and the Pharmacy Guild felt that way too.

4. PHARMACY RESEARCH PROJECT

People with lived experience and advocacy consumer groups have raised issues with the standard of service that is provided by pharmacists for a number of years. The complaints have gone unheeded by government and the Pharmacy Guild. These complaints have centred on the lack of provision of CMIs and the quality of the verbal advice that has been given. In addition, the CMI comparison in Chapter 2 has identified a significant gap in dangerous warnings that are provided to patients compared to that disclosed to pharmacists in the PI documentation, and disturbingly, to people taking the same drugs in the USA.

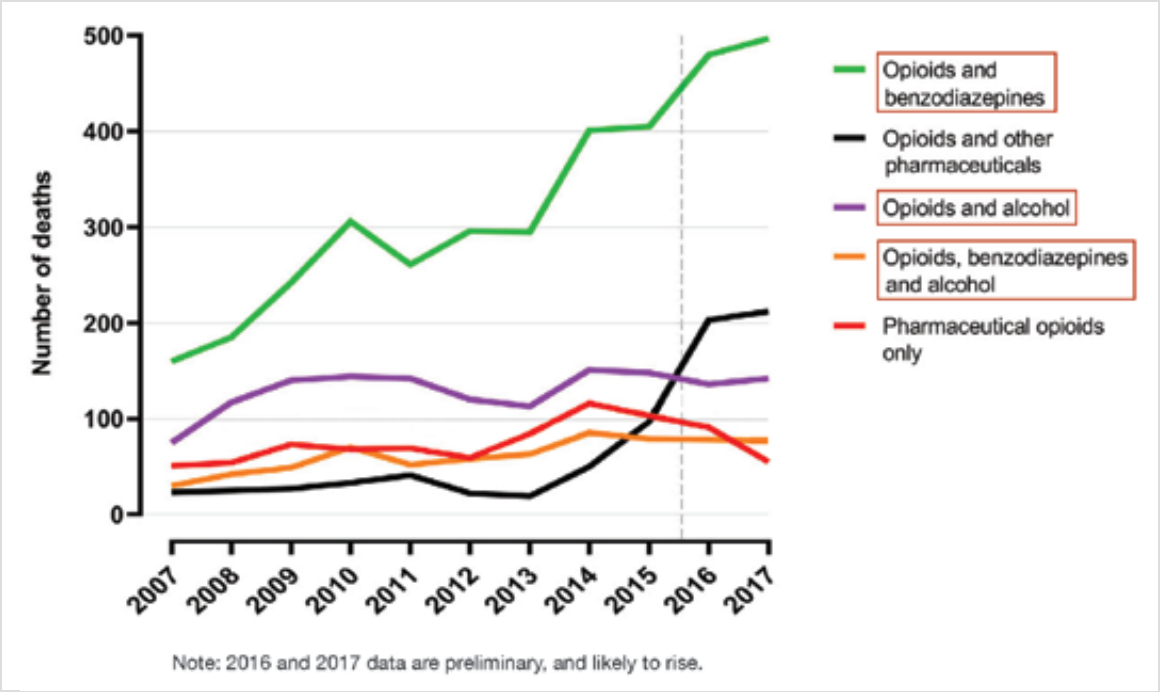
We undertook a project to visit pharmacies and record conversations with the pharmacist. All pharmacies are located in Canberra, so they fall under the jurisdiction of the ACT Health Directorate.

This project was undertaken to **document the real experiences that people with chronic illness have on a daily basis**.

The process involved asking for warning information about the side effects of prescription opioids (Endone) and benzodiazepines (Valium). The questions focused on the polydrug interactions, and what the worst side effects could be. The risk of taking alcohol was also raised given it is a lethal polydrug combination.

Remember, combining these classes of drugs is deadly and are the leading cause of drug deaths in Australia.

Figure 25: Unintentional drug-induced deaths involving opioids (Source: Penington Institute)[207]



If pharmacists are fulfilling their PBS funded obligations, their role is to make the person aware of the life-threatening risks, **despite these not being in the CMI**.

Remember, for **Valium**, the CMI does not warn of:

- the risk of death from consuming alcohol
- taking opioids (and the risk of death)
- the risk of death from taking other medications and supplements
- the risk of death from an overdose
- the risk of addiction
- the risk of withdrawal syndrome
- the risk of suicide
- the risk of death (it is not mentioned once).

And for **Endone**, the CMI does not warn of:

- the risk of death from consuming alcohol
- taking benzodiazepines (and the risk of death from taking them)
- the risk of death from taking other medications and supplements

The risk of death is only mentioned once in relation to an overdose and Endone is not described as an opioid.

Based on the publicly available information about the pharmacist's role and charter, we expected the interviewed pharmacists to respond as per Table 15.

207 Penington Institute, 2019.

Table 15: Expected pharmacist responses based on Department of Health information

	Hard copy CMI provided	Verbal: addiction warning	Verbal: advised of the risk of overdose, coma and death (Endone and/or Valium)	Verbal: advised of the risk of overdose, coma and death (Endone, Valium and alcohol)	Verbal: advised of the risk of drowsiness, sedation or respiratory failure
	Yes	Yes	Yes	Yes	Yes
Issues	– A hard copy CMI must be provided if a consumer asks for information on the risks and side effects. Especially as the sedating effects of these medications affects memory. – If the consumer is referred to a website for more information, the referral must be to TGA, Department of Health, Medicine wise or comparable authoritative website. – The Endone and Valium CMIs do not specifically contain all of the above risks of overdose, coma and death. However, pharmacists are aware of these risks and should provide verbal advice, in addition to providing the CMIs. They should also be aware that this information is not in the CMI and make consumers aware of this.				

Note: The determination of 'advised' is assessed based on the initial questions to the pharmacist of the risks and side effects. If the pharmacist advises of risks and side effects only after further probing questions, this was not counted as a 'Yes'. This is because this advice only came about in response to repeating the question or specifically asking a question on that side effect.

The findings from the research project are summarised in Table 16. Complete transcripts from each interview are available at the end of this Chapter.

4.1 SUMMARY OF 10 PHARMACY VISITS

Table 16: Summary of 10 pharmacy visits

	CMI provided	Verbal: addiction warning	Verbal: advised of the risk of overdose, coma and death (Endone and/or Valium)	Verbal: advised of the risk of overdose, coma and death (Endone, Valium and alcohol)	Verbal: advised of the risk of drowsiness, sedation or respiratory failure
Pharmacy – 10 visits	6/10	3/10	0/10	0/10	9/10
Issues	– Not one pharmacist warned of the life-threatening risks of the medications individually or when taken in combination – Not one pharmacist warned of the life-threatening risks of the medications in a combination with alcohol – Four pharmacists admitted to the life-threatening risks, after not initially providing this advice, when pressured further on the side effects – Four pharmacists did not offer a CMI at all; one handwrote some brief warnings on a notepad – Only three pharmacists mentioned the risk of addiction – Three pharmacists suggested to use Google to get information – Two pharmacists provided printed information from USA websites – All six pharmacists who gave the CMI presented it as having all the information that was needed and none identified gaps in the information – Only two pharmacists actually went through the CMI to show the information; both then admitted that the critical warning information was missing from the document – The only consistent message was the risk of drowsiness				
Pharmacist Verbal Advice Extracts	"You would have exactly what I have if you Google it up. Type in the name and read, that's exactly what I would give you."				
	"If you just type in Google, What the problem with that medicine?"				
	"So you stick Valium, Endone and alcohol together, the you've got your triple whammy there, right? You wouldn't get in the car."				
	Consumer: "I mean, shouldn't it say that death is a risk as well? [mixing Endone, Valium and alcohol]" **Pharmacist:** "No, they will not say that. So that will be there somewhere. I will show you that. Slow heart rate. That's why it says, "These are the serious side effects."				

	CMI provided	Verbal: addiction warning	Verbal: advised of the risk of overdose, coma and death (Endone and/or Valium)	Verbal: advised of the risk of overdose, coma and death (Endone, Valium and alcohol)	Verbal: advised of the risk of drowsiness, sedation or respiratory failure
Pharmacy – 10 visits	6/10	3/10	0/10	0/10	9/10

"If you'd had some Endone and some Valium and two or three beers, you'd be like, 'No, I'm home for the night', because they've all got a sedating thing. I should write it down."

"If you take it together [Endone and Valium] you will have excessive drowsiness, the medication will basically knock yourself out. But apart from that they are not really going to interact to give you any crazy side effects or anything like that."

"Same thing. It will cause drowsiness and it will slow your breathing down as well. So I definitely wouldn't combine all three of them [Endone, Valium and alcohol] together."

"Don't worry about reading the interactions because each medicine has interactions. So if you are taking two medicines, it will have some kind of interaction. But if it's severe, we always let you know. If there are some medicines you should not take, we always let you know. Very rarely, it will miss from pharmacists or doctors. But these are all the common medicines. You don't have to worry about taking it."

Consumer: "And there's information here about the side effects? [in the CMI]"

Pharmacist: "Yeah. It should list the risks and outline that it shouldn't be combined with alcohol or other sedating medicines definitely."

Consumer: "And death?"

Pharmacist: "Yes."

"You can buy it [Nyxoid] over the counter but to be honest it is really more for, to be blunt, heroin users."

Consumer: "How long does it take to get addicted? [Benzodiazepines or Opioids]"

Pharmacist: "Everyone is different."

"But there's not too much documentation and not too much information about it. Like, the information is there, but not too much, like" [explaining the CMI for Endone and Valium side effect risks]

"Yeah. Don't worry about it because you won't get any respiratory depression or nothing. But when you're drinking alcohol with Endone, just be careful because it's a class of controlled drugs."

"If you overdose, then – let me check. So the [inaudible] I mentioned is it may lead to respiratory depression, constipation problem."

"It's interesting that it doesn't say it on the packet [risk of death]. It does say in the information about the medication. Certainly the printouts, consumer medicines information, does contain information on those things."

	CMI provided	Verbal: addiction warning	Verbal: advised of the risk of overdose, coma and death (Endone and/or Valium)	Verbal: advised of the risk of overdose, coma and death (Endone, Valium and alcohol)	Verbal: advised of the risk of drowsiness, sedation or respiratory failure
Pharmacy – 10 visits	6/10	3/10	0/10	0/10	9/10

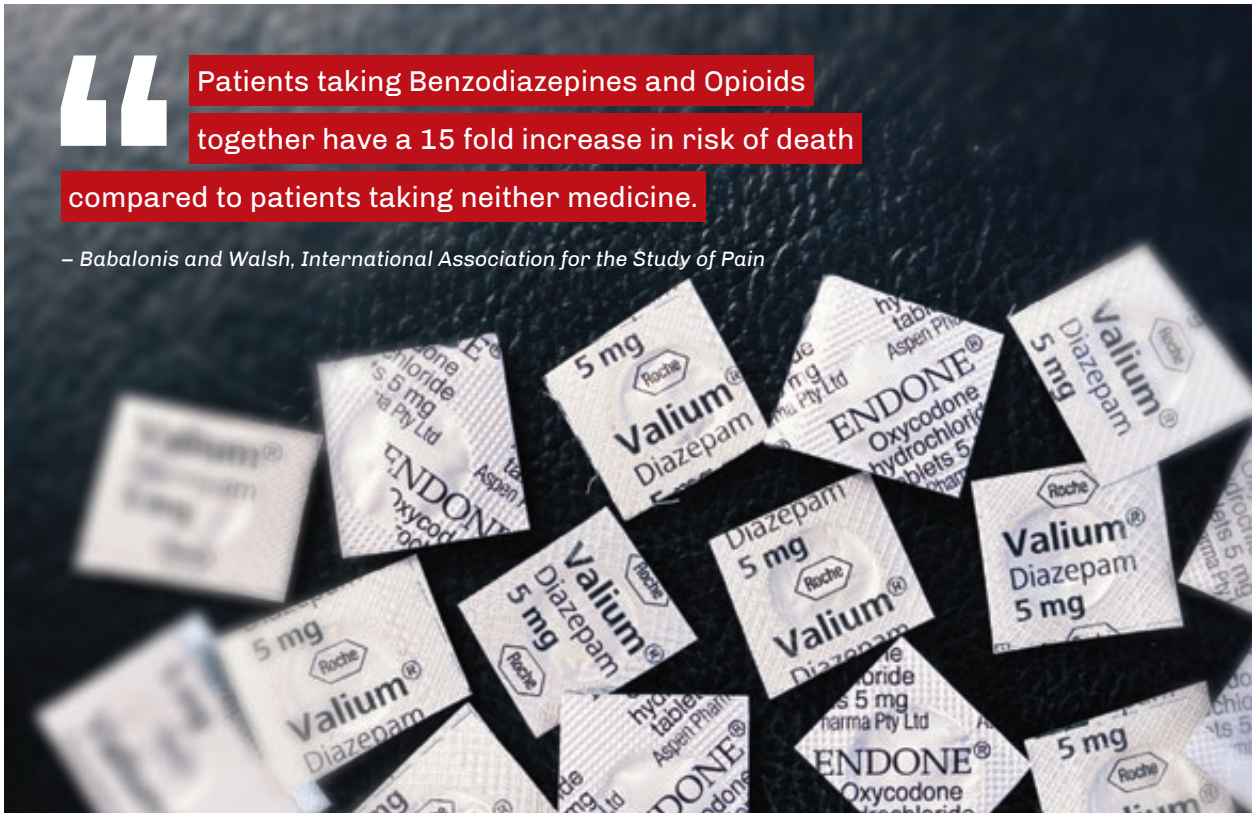
Findings from the research

All the pharmacy visits provided easy access to have a discussion with a pharmacist.

However, none of the pharmacists verbally provided the life-threatening warnings as well as the hard copy CMIs.

Every single visit failed to advise of the information (as outlined by the Department of Health) in relation to the life-threatening risks these medications expose a person to. Multiple times, information was given verbally that is factually incorrect and misleading as to the life-threatening risks.

This project confirms the position of people with lived experience, that pharmacists are failing to provide the critical information on the side effects of medication.



4.2 COMPLETE TRANSCRIPTS FROM PHARMACY VISITS

4.2.1 Pharmacy 1

	CMI provided	Verbal: addiction warning	Verbal: advised of the risk of overdose, coma and death (Endone and/or Valium)	Verbal: advised of the risk of overdose, coma and death (Endone, Valium and alcohol)	Verbal: advised of the risk of drowsiness, sedation or respiratory failure
Pharmacy 1	No	No	No	No	No
Issues	Three times advised to get the information from Google				
Advice	**Pharmacist:** "You would have exactly what I have if you Google it up. Type in the name and read, that's exactly what I would give you."				

Consumer: I want to get some information.

Pharmacist: I'll try.

Consumer: My friend just had some back surgery, English is not her first language, trying to get some information. She has been given **Endone** and **Diazepam**. I said to her that I don't know much about drugs but I hear that they are pretty dangerous.

Pharmacist: They are strong, potentially dangerous if you mix them up with alcohol and other things. **People don't make it through if they mix those things up with alcohol and other drugs**. They are very strong painkillers so just be very careful when you are using those. If you have been prescribed them then that's fine as the doctor wants you to have them just be cautious about using them. Less is best and only as needed.

Consumer: She came out of hospital and she didn't really get much so I said I would come and talk to a pharmacist so do you have any information on those drugs?

Pharmacist: You would have exactly what I have if you Google it up. Type in the name and read, that's exactly what I would give you. So they are pain killers, muscle relaxants but you need to see a doctor because I can't give you those things without a prescription.

Consumer: No we don't want the drugs, we just want some information on them.

Pharmacist: Yeah that's publicly available information, just Google up and read, that's the same thing I would print out for you. Is that going to be enough?

Consumer: Well I am just worried because you said that, "if people mix them up they don't make it through", I am bit worried.

Pharmacist: So that's an extreme case, you have come to me to ask about it so I am just giving you the worst possible case scenario. But if they are prescribed drugs and you do what's been prescribed, you should be fine. That's all I can say. Stick with what the doctor has mentioned and recommended and we reinforce when we give them to you on a prescription and you should be fine. Less is best. Err on less if you can because they are quite powerful drugs.

Consumer: She also takes Efexor.

Pharmacist: Yep again anything else you add in increases risk of problems, as you can imagine it's just a cocktail of chemicals, minimal is best.

Consumer: What is the website to go to?

Pharmacist: Just Google up the words and you will get the same thing I would print out for you, but you need to see a doctor before I can provide any more information.

Consumer: Thank you.

END OF TRANSCRIPT

4.2.2 Pharmacy 2

	CMI provided	Verbal: addiction warning	Verbal: advised of the risk of overdose, coma and death (Endone and/or Valium)	Verbal: advised of the risk of overdose, coma and death (Endone, Valium and alcohol)	Verbal: advised of the risk of drowsiness, sedation or respiratory failure
Pharmacy 2	No	Yes	No	No	Yes
Issues	Did not offer a CMI. Instead wrote some points on a note pad (see Figure 26)				
Advice	**Pharmacist:** "So you stick Valium, Endone and alcohol together, then you've got your triple whammy there, right? You wouldn't get in the car." "If you'd had some Endone and some Valium and two or three beers, you'd be like, "No, I'm home for the night," because they've all got a sedating thing. I should write it down."				

Pharmacist: Hiya.

Consumer: Hi, how you going? I wanted to get some information on some medication that I'm taking. So I take **Valium** and I've also been taking **Endone** as well. I had stem cell surgery about a month ago. So the pain is quite sharp and the surgeons recommended that I increase the dose of Endone. **And I'm just a little nervous about those two drugs and interactions between them.** So I thought I'd come and ask a pharmacist.

Pharmacist: Drowsiness really. So Valium, the main adverse effect, number one is drowsiness, same with Endone, number one. And then Endone then goes into nausea, [inaudible] addiction, same with Valium. So Valium, not so much nausea, but they both can potentially lead to an addiction. And if they have to, they slowly reduce you down. Did they want to put you on, like, a controlled release? So Endone we use for that acute pain.

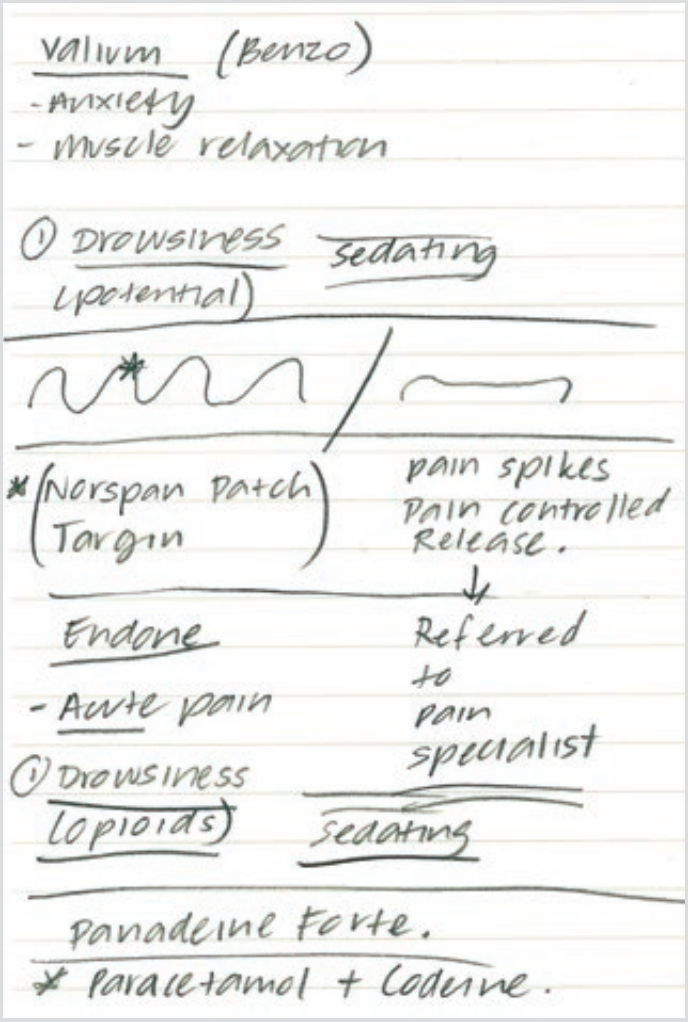
Consumer: Yeah, the sharp pain.

Pharmacist: Did they not want to give you something that's maybe --

Consumer: He spoke about moving to Panadeine Forte. But the pain has probably got worse, so he wants to keep me on the Endone and increase it from --

Pharmacist: He doesn't want to do, like, a controlled-release tablet that you have one, twice a day, and then Endone just for breakthrough pain?

Figure 26: Pharmacist hand-written notes



Consumer: No.

Pharmacist: That's what a lot of the pain specialists do.

Consumer: He's in Sydney, so I just go off the phone calls, so I don't really know about alternatives. But it's just more --

Pharmacist: That's when you come in and ask a question. You could ask him. So Valium is a benzo. So we use this for anxiety, muscle relaxation and that kind of thing.

Consumer: The Valium is for anxiety. It's separate to the operation.

Pharmacist: But the main number one adverse effect of course is **drowsiness**. And then Endone is for acute pain. And the number one adverse effect is **drowsiness**. And both of these have the potential for your body say I want more, I want more, I want more, like an addiction. After a while, they don't work like they did to start with and you need them. Does that make sense?

Consumer: So the longer I take it, I'm gonna need more to get the benefits?

Pharmacist: That's why he wanted to move you on to Panadeine Forte, we were talking about. So that's a step down.

Consumer: That's a step down from Endone?

Pharmacist: Yep. So Panadeine Forte is Paracetamol and codeine, so it's a script only these days.

Consumer: Yeah, they're all from doctors.

Pharmacist: This one you used to be able to get, well, Panadeine with Codeine. You used to be able to get that over the counter from the pharmacist. So we talked about acute pain, for instance, let's say a Norspan patch or Targin. So these kind of drugs are for pain and they're controlled-release. So it depends. If you have to be on things for a fair amount of time, I'd be talking to the doctor about those. So they control your pain. Instead of your rollercoaster of pain, they kind of make it a bit smoother.

And then what you have is only one or two of those for acute pain, like, oh, lunchtime, I need one, right? So these have the potential to be able to use less of these. We're seeing more and more of, like, the Targin used because it's controlled-release, one in the morning, one at night. It helps stop this roller coaster of pain because once you've got pain levels up

here, it takes more medication to help bring you back down. It's the pain models. So it's like say a paracetamol or Panadol Osteo. If you take it like it's directed, like, two, four times a day, instead of two I'm in acute pain now, it's not going to work as well.

So these are released in your body over that 12 hours, or Norspan is, like, 24 hours or whatever, and that keeps you from those spikes of pain. So these kind of things help with the pain spikes. But I don't know. That's how I learned it a few years ago. The model may be different now, but back when I was a kid, you'd just have a Panadol when you need it. But, now, they're using it more frequently.

Consumer: So I talk to the surgeon about those options?

Pharmacist: Yeah. You might want to be referred to a pain specialist. Surgeons are great at other stuff, you know what I mean? I had a lady come in today and she said, "I'm going to see a pain specialist." I'm like, thank God, someone who's finally going to look at your needs and send a letter back to the doctor to say, "Okay, let's do Targin once a day, Endone in the middle, one or tablets, do the Valium at night, and let's have a plan over the next three months. We'll wean down, wean down, wean down, until you eventually come down and off," because they're all opioids. They're all the family of opioids: these, these, these. Even codeine is an opioid. So they all have that addictive kind of nature. Alright?

Consumer: And so taking these two at the same time while I'm looking at these other options, I want to be clear about what the potential side effects and what's the --

Pharmacist: Drowsiness is the first thing.

Consumer: Is there anything else I should be --

Pharmacist: Apart from the usual, like I said, your nausea, constipation for these, which Targin is a good option. Valium is pretty much just drowsiness.

Consumer: And alcohol?

Pharmacist: **Again, anything that has the potential to make you feel drowsy or sedated, when you stick them together, it potentially aids that thing. So you stick Valium, Endone and alcohol together, then you've got your triple whammy there, right? You wouldn't get in the car**.

Consumer: You wouldn't get in the car?

Pharmacist: No.

Consumer: Okay.

Pharmacist: **If you'd had some Endone and some Valium and two or three beers, you'd be like, "No, I'm home for the night," because they've all got a sedating thing. I should write it down. Even alcohol is sedating. This gives you an [inaudible] and you'd be like, "Whoops."**

Consumer: Or drug tested.

Pharmacist: Yeah. I wouldn't want to be on that side of the fence if I got an alcohol reading with this and this on board. So just be aware of that. Alright? Are you good with all that?

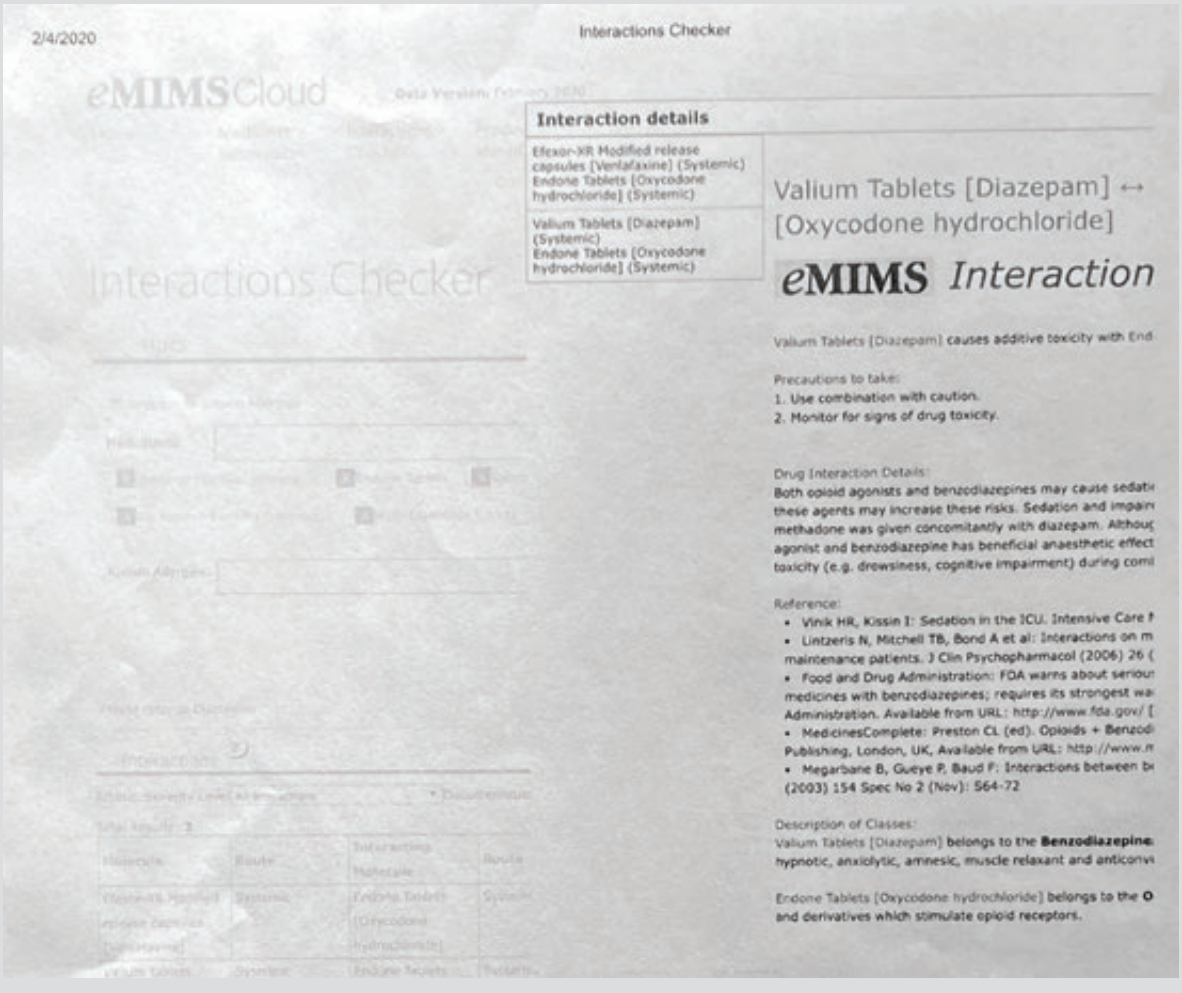
Consumer: Thank you very much.

END OF TRANSCRIPT

4.2.3 Pharmacy 3

	CMI provided	Verbal: addiction warning	Verbal: advised of the risk of overdose, coma and death (Endone and/or Valium)	Verbal: advised of the risk of overdose, coma and death (Endone, Valium and alcohol)	Verbal: advised of the risk of drowsiness, sedation or respiratory failure
Pharmacy 3	Yes	No	No	No	Yes
Issues	– Agreed that the combined effect of the drugs can be death, only after the question was directly asked – Provided an eMIMS print out that was illegible (font too small and cut off) of the risk of taking Endone and Valium (see Figure 27) – Admitted to the risk of death after reading the eMIMS printout				
Advice	**Pharmacist:** "If you take it together [Endone and Valium] you will have excessive drowsiness, the medication will basically knock yourself out. But apart from that they are not really going to interact to give you any crazy side effects or anything like that."				

Figure 27: Copy of eMIMS printout provided by pharmacist



Consumer: I am just on a couple of medications at the moment and I am just looking for some more information about side effects.

Pharmacist: Yep sure.

Consumer: I am taking **Valium** and **Endone**.

Pharmacist: That's it, ok so if you are taking those together one that you will see straight away is excessive drowsiness. That is the sensation, making your perception a little bit dull. That's one of the most common side effects. You can have serious constipation and increased GI side effects. Like you will have indigestion and constipation, you will see that.

Pharmacist: Ok what else can I give you, are you having a little bit of agitation?

Consumer: No I am just wondering what happens when you mix those two drugs together? I am just wondering about those side effects.

Pharmacist: They are not going to really interact with each other. The mechanism of action is completely differently. Valium works on the central nervous system and Endone works on your opioid receptors. They are totally different things, Valium will make you a little bit more calm and a little bit dull. It will help you with your anxiety and help you calm down. Endone just helps you to not feeling pain.

Pharmacist: If you take it together you will have excessive drowsiness, the medication will basically knock yourself out. But apart from that they are not really going to interact to give you any crazy side effects or anything like that. What you will have is excessive drowsiness, that's it. Do you want me to give you that in writing in a piece of paper?

Consumer: Oh yeah and I am wondering because I have a couple of beers every night.

Pharmacist: They are not good together, they are not good together, especially Valium. You shouldn't be really taking it with alcohol. It makes the Valium difficult to excrete from your body, the alcohol does. It blocks your receptor together with alcohol, it amplifies the side effects together with alcohol. If you want to take alcohol make sure you space it out two hours from each other otherwise it can be a little bit dangerous if you take too many.

Consumer: Because you used to get the information in the box.

Pharmacist: Yes the CMI I can get that for you, they are on a separate webpage I can just print that out for you. Both of them Valium and Endone.

Pharmacist: (hands over CMI for Endone and Valium) So that's the paper that used to go into the boxes, you have one for Endone and one for Valium.

Consumer: (Short conversation about bipolar with pharmacist – inaudible).

Consumer: Just to confirm, Endone is an opioid and Valium is a benzo. But I read a lot about mixing those two drugs can be deadly?

Pharmacist: Yes because of the drowsiness, as I said.

Consumer: So the drowsiness is what causes death? I am just confused.

Pharmacist: It can. Endone like any opioid analgesic and a strong one like Endone, it's all down to how many you take. If you take a lot, what kills you is the respiratory depression. Endone, medications like that, knocks you out. However it also gives you respiratory depression and people can die from it. Because you can't breathe. That's it.

Pharmacist: Valium is also a medication that can make you quite drowsy and low if they are mixed together. And that's why I am saying it's not good to mix them together, especially with alcohol, that's deadly.

Consumer: So it's not good to mix...

Pharmacist: ...mix any of those medications together. So, how much of the Endone? How many tablets are we talking about? Because they are just 5mg they are not going to do much if you take just one tablet. You are supposed to just take one when there is significant pain. If you are taking five at the same time and two or three Valium at the same time, I would be worried.

Consumer: I am taking Endone all the time.

Pharmacist: I understand.

Consumer: So I guess what you are saying there is a risk.

Pharmacist: There is a risk. I can have a look at the maximum dosage if you like. To give you some clear guidelines.

Consumer: We have two different answers.

Pharmacist: (returns holding a printout from eMIMS drug interaction website for Endone and Valium) This is the interaction, I was just telling you off the top of my head. The layout is funky. That is the interaction between those two and it talks about respiratory depression and severe drowsiness/sedation. So that's the point where it can be deadly.

Consumer: So this is a program that is now telling us the interaction between these two drugs. So you have that as a pharmacist.

Pharmacist: Yes I can look it up, I was just telling you that off the top of my head, but you guys need something written down.

Pharmacist: I will write down the maximum dosage a day.

END OF TRANSCRIPT

4.2.4 Pharmacy 4

	CMI provided	Verbal: addiction warning	Verbal: advised of the risk of overdose, coma and death (Endone and/or Valium)	Verbal: advised of the risk of overdose, coma and death (Endone, Valium and alcohol)	Verbal: advised of the risk of drowsiness, sedation or respiratory failure
Pharmacy 4	No	Yes	No	No	Yes
Issues	– Advised that addiction will not occur if taking as prescribed, it only occurs when taking for recreational purposes – Then advised that taking it every day can lead to tolerance, which can lead to addiction – Referred to the Australian Government Website for more information				
Advice	**Consumer:** "Right. So taking Endone and Valium and drinking, drowsiness is the risk for me?" **Pharmacist:** "Yeah, very drowsy."				

Pharmacist: How can I help you?

Consumer: Hi. I wanted to get some information about some drugs that I'm taking, some medication.

Pharmacist: Yeah.

Consumer: I'm taking **Endone and Valium**. So I just wanted to get a bit more information about what are the **risks of taking those two drugs and also the risk of taking those two drugs together**.

Pharmacist: They can be addictive, both of them. So you take them for what purpose?

Consumer: I had knee surgery, so I've got some ongoing knee pain. So that's what I take the Endone for.

Pharmacist: So [inaudible] pain, you take it, that's okay, you won't get addicted, but if you take it to feel better, then it can be addictive.

Consumer: So if I'm taking it just for the pain, then that's safe? That's not addictive?

Pharmacist: Yep.

Consumer: Okay. What about the Valium?

Pharmacist: Same.

Consumer: I won't get addicted if I just take it --

Pharmacist: For pain, yeah.

Consumer: Well, the Valium's for anxiety.

Pharmacist: Yeah, that's fine.

Consumer: So it's safe to take that for anxiety? That's not addictive?

Pharmacist: Only when needed, yeah.

Consumer: But I take it every day.

Pharmacist: If you don't take it for a day, do you miss it?

Consumer: Sorry?

Pharmacist: Say you don't take it for a day, do you miss it?

Consumer: Yeah, I definitely do. That's why I take it every day.

Pharmacist: Yeah, because you build up the tolerance. And when you don't take it, you might miss it. It means that you are, you know, maybe you -- Yeah, it's hard to say. If you take only when you need it --

Consumer: So tolerance is different to addiction?

Pharmacist: Yes. Tolerance means that your body is used to it and you need more. Whereas addiction means when you don't take it, you really crave it.

Consumer: But if I'm getting tolerance and I need more, doesn't that mean I'm at risk of getting addicted?

Pharmacist: Yes, indeed, yes.

Consumer: Okay. So is there any risk from taking them both together?

Pharmacist: Oh, yeah, very drowsy. It can cause you to be very drowsy. Then again, if your body builds up tolerance, then maybe you don't feel much. But say for me, half a tablet of Valium would kind of make me struggle to stay awake.

Consumer: What about if I, like, I have a couple of glasses of wine at night with dinner.

Pharmacist: No, don't take with wine. It makes is worse.

Consumer: Makes it worse?

Pharmacist: It makes the effect of the drugs more drowsy. You'll feel more drowsy.

Consumer: Right. So the risk is drowsiness?

Pharmacist: Drowsiness, yes.

Consumer: Is it really that bad?

Pharmacist: Yeah, it is bad. And especially if you need to drive, yeah. Your body will probably register beyond the limit if you do a breath test.

Consumer: Right. So taking Endone and Valium and drinking, drowsiness is the risk for me?

Pharmacist: Yeah, very drowsy.

Consumer: Right. So is there any other information that I should know?

Pharmacist: Well, take it as needed only. If you feel like you're anxious, maybe take a half or a quarter for the Valium.

Consumer: Okay. Is there anywhere I can go to get more information about --

Pharmacist: There's the Internet. Do you have access to Internet?

Consumer: Yeah.

Pharmacist: You can go search the Internet. Go the Australian Government website.

Consumer: Right, the Australian government website?

Pharmacist: Yeah. There is heaps of information on Valium and Endone there.

Consumer: Okay.

Pharmacist: Well, where do you get your medications from?

Consumer: I live down the South Coast.

Pharmacist: Yeah. Or talk to your pharmacist or doctors there, too. They are there to support you, or professionals over there who support you. Like, take only as you need.

Consumer: Okay. Cool, thank you.

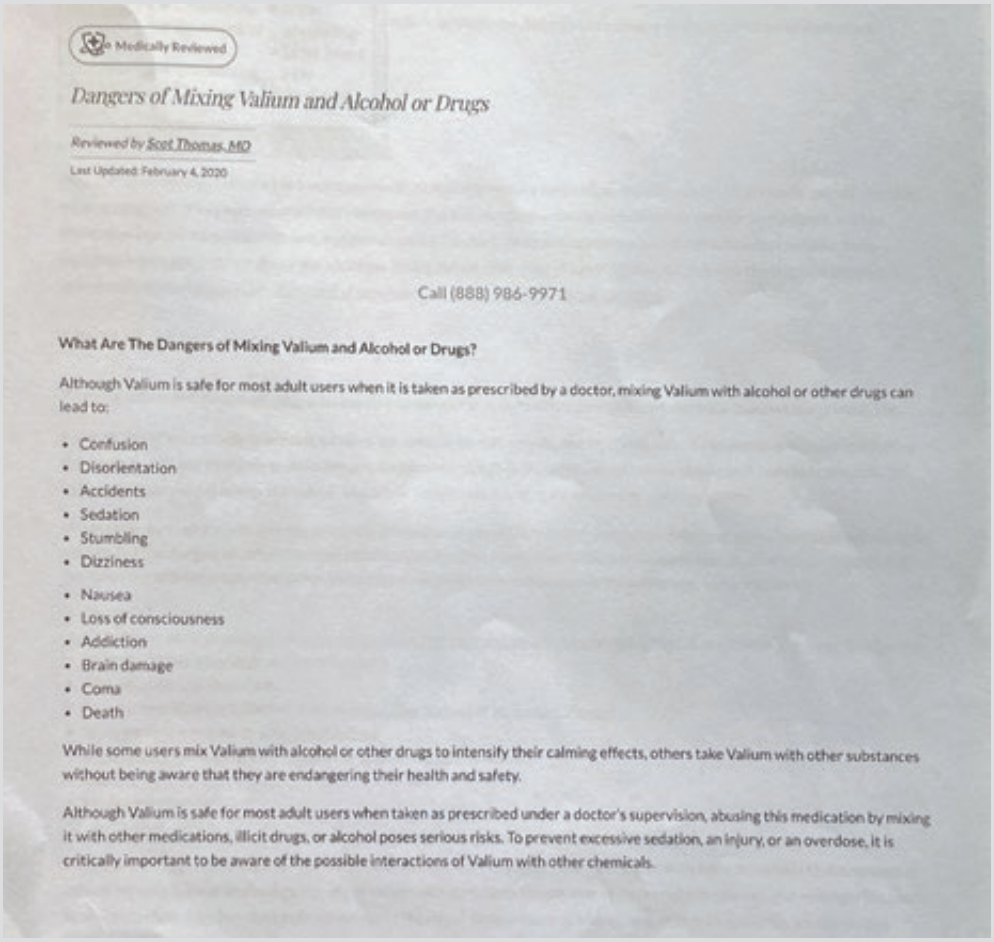
Pharmacist: You're welcome.

END OF TRANSCRIPT

4.2.5 Pharmacy 5

	CMI provided	Verbal: addiction warning	Verbal: advised of the risk of overdose, coma and death (Endone and/or Valium)	Verbal: advised of the risk of overdose, coma and death (Endone, Valium and alcohol)	Verbal: advised of the risk of drowsiness, sedation or respiratory failure
Pharmacy 5	Yes	No	No	No	Yes
Issues	– Provided a warning document from the American Addiction Centres (see Figure 28) on combining the medications as the pharmacist said they could not find an Australian option on Google – After printing the USA document, pointed out that the document warns of the risk of death – When then asked if the CMI lists the risks including combining the medication, taking with alcohol and the risk of death, replied that it did				
Advice	**Pharmacist:** "Same thing. It will cause drowsiness and it will slow your breathing down as well. So I definitely wouldn't combine all three of them [Endone, Valium and alcohol] together."				

Figure 28: Warning document from American Addiction Centre provided by pharmacist



Medically Reviewed

Dangers of Mixing Valium and Alcohol or Drugs

Reviewed by Scot Thomas, MD

Last Updated: February 4, 2020

Call (888) 986-9971

What Are The Dangers of Mixing Valium and Alcohol or Drugs?

Although Valium is safe for most adult users when it is taken as prescribed by a doctor, mixing Valium with alcohol or other drugs can lead to:

- Confusion
- Disorientation
- Accidents
- Sedation
- Stumbling
- Dizziness
- Nausea
- Loss of consciousness
- Addiction
- Brain damage
- Coma
- Death

While some users mix Valium with alcohol or other drugs to intensify their calming effects, others take Valium with other substances without being aware that they are endangering their health and safety.

Although Valium is safe for most adult users when taken as prescribed under a doctor's supervision, abusing this medication by mixing it with other medications, illicit drugs, or alcohol poses serious risks. To prevent excessive sedation, an injury, or an overdose, it is critically important to be aware of the possible interactions of Valium with other chemicals.

Consumer: Hi. I wanted to get some information about two medications that I'm taking. I'm taking **Endone** and **Valium**. I just wanted to get more information about I guess the **risks of taking those drugs**, but also **taking those drugs at the same time**. I'm taking Endone because I had knee surgery last year and the pain is still quite sharp. But I take Valium for anxiety. I'm taking them every day.

Pharmacist: Do you have to use the Endone frequently throughout the day?

Consumer: Just morning and night. So it tends to just be morning to the mid-afternoon.

Pharmacist: Because they both have a sedative effect, it's not normally recommended to take them at the same time.

Consumer: Right. When you say at the same time, do you mean like --

Pharmacist: Within a few hours.

Consumer: Oh, within a few hours? Okay.

Pharmacist: Yeah. Have you by chance done that and found that it's --

Consumer: Well, I have been taking them for a while and I had a look online at a few news articles about it and I'm a bit sort of worried about the worst possible risks and side effects. They kind of say go and talk to a pharmacist. So I don't live in Canberra, but I'm passing through, so I thought I'd drop in.

Pharmacist: Yeah. They both have, as you know, a sedative effect and they both have a respiratory depressing effect, so they're not recommended to be taken at the same time. Having said that, some who have built up a tolerance to it, are known to take them at the same time and not have any side effects, but it's not recommended. So I would try and not double over where possible.

Consumer: Okay.

Pharmacist: You can't time your panic attacks though, that's the trouble.

Consumer: Yes, true. But it tends to be in the morning when I wake up with PTSD. I suffer from nightmares. So I wake up in a heightened state of anxiety, which is why I take the Valium, but then the Endone is for the pain. It sort of tends to be at the same time.

Pharmacist: Yeah. It's a really tricky situation because most of the pain relievers that are as strong as Endone or in that same category, will cause that sedation, so you're constantly going to have this trouble. Is the long-term plan to wean you off the Endone?

Consumer: Well, I'm supposed to go back in January, but because of the fires, I haven't been able to go back to Sydney. His suggestion was to just stay on the Endone until I can get up to see him. Yeah, but, I mean, the pain should get better at some point.

Pharmacist: Yeah. I would say when you get up in the morning, have Valium, and then just try and hold off having the Endone for as long as possible, at least two, three, four hours ideally. The longer you space it out, the less likely you are to have that doubling up effect and that's why it's potentially risky.

Consumer: So the risk of them combining is the drowsiness?

Pharmacist: Excessive drowsiness and also slowing down your breathing and potentially falling asleep and – I mean, what dose of Valium are you on?

Consumer: Five milligrams.

Pharmacist: Just one?

Consumer: Well, one normally, but sometimes it could be two in the evening.

Pharmacist: And one Endone?

Consumer: Yeah, in the morning and evening.

Pharmacist: **I mean, by your size, I'd say you probably would be okay if you had them within that timeframe. The risk is that you will slow your breathing down [inaudible] that you will pass out. That's the concern with them.**

Consumer: Pass out as in I'm unconscious?

Pharmacist: Yeah, which we don't want. But looking at your build, I think five milligrams of Endone and three milligrams of Valium is not likely to cause that effect in you. But having said that, don't try and take them within three to four hours of each other if you can avoid it.

Consumer: And sometimes I'll have a **few glasses of wine with dinner**. Is that a risk?

Pharmacist: Yes.

Consumer: What's --

Pharmacist: **Same thing. It will cause drowsiness and it will slow your breathing down as well. So I definitely wouldn't combine all three of them together**.

Consumer: Because of the drowsiness?

Pharmacist: Yes, and the breathing. So if you've had the Valium with the last few hours, I wouldn't drink. And if you've had a drink, I wouldn't take the Endone, again, within four, five hours of that either, just until it's in a low enough level in your system that you won't potentially get that double-up effect.

Consumer: Is there anywhere I can get more information about all of that?

Pharmacist: Of course. I can print out the individual information on all of them if you'd like.

Consumer: Yeah, that would be great.

Pharmacist: I'll see if I can find a brochure on potentially that subject of doubling up and what the [inaudible] are.

Consumer: That would be great. Thank you.

Pharmacist: **That's the one on Endone and that's the one on Valium. This is a website I'm not familiar with, but it is good in that it lists potentially what can happen when you're combing those, the most serious one being death. So that's why we say don't take them at the same time, space them out as much as you can**.

Consumer: Okay.

Pharmacist: I think ultimately the plan would be to try and switch to something that's not sedating like what Endone is. So maybe an anti-inflammatory, something like Nurofen or a stronger version of Nurofen.

Consumer: So American Addiction Centers?

Pharmacist: Yeah. It's only that I typed in combining and this actually lists it quite well, so potential side effects.

Consumer: **You'd think that they'd give the pharmacist an Australian website**.

Pharmacist: **Yeah. I chose Australian settings, but there wasn't one to hand that concisely I could find in that time that lists these side effects as this one does**.

Consumer: Okay. Well, thank you very much for that. The death warning is kind of sobering. But I'll read up more about this and look into it.

Pharmacist: Sometimes, those stories that we hear of the Hollywood celebrities, you often find when they've passed away that it's that combination. It's a benzo, alcohol, and some sort of opioid. So it can be quite serious.

Consumer: And there's information here about the side effects? [in the CMI]

Pharmacist: Yeah. It should list the risks and outline that it shouldn't be combined with alcohol or other sedating medicines definitely.

Consumer: And death?

Pharmacist: Yes.

Consumer: Okay, great. Thanks for all that information.

Pharmacist: No worries.

Consumer: Thanks. Bye.

END OF TRANSCRIPT

4.2.6 Pharmacy 6

	CMI provided	Verbal: addiction warning	Verbal: advised of the risk of overdose, coma and death (Endone and/or Valium)	Verbal: advised of the risk of overdose, coma and death (Endone, Valium and alcohol)	Verbal: advised of the risk of drowsiness, sedation or respiratory failure
Pharmacy 6	Yes	No	No	No	Yes
Issues	– When asked, the pharmacist advised that the CMI does not contain information about combining prescription medications "because everyone is different" – Did not provide a website to research more information when asked – Did not provide any information on the time that it takes for addiction to become a risk when asked				
Advice	**Pharmacist:** "...So with both of them [Endone and Valium], causing drowsiness, muscle relation and stuff like that ... yeah."				

Consumer: I was hoping you can give me some more information about the side effects of these medications that I am taking at the moment.

Pharmacist: Yeah sure.

Consumer: I am taking **Endone and Valium**, so I wanted to get some more information about the side effects.

Pharmacist: Is there anything in particular that you want to know about either of them or do you want me to print out some information.

Consumer: Yes that would be great, anything about the side effects would be great.

Pharmacist: (returns with the CMI for Endone and Valium).

Consumer: So in terms of both of these, does it tell you anything about what happens in terms of when you are taking Endone, mixed with Valium?

Pharmacist: No but you can kinda assume that if they have similar side effects that there will be an additive or even synergistic effect. So with both of them, causing drowsiness, muscle relation and stuff like that ... yeah.

Consumer: So what do you think the biggest risk of that might be?

Pharmacist: Are you taking any other medication at the moment?

Consumer: I am taking Efexor as well.

Pharmacist: See the Efexor has kind off opposite effects to these guys, because it is a serotonin receptor uptake inhibitor, often it is more of a stimulant, where these guys are sedating.

Consumer: It doesn't say anything in here about mixing them?

Pharmacist: So no not generally, so all the information they provide generally talks about the medication as a stand-alone. Because everyone is different and obviously everyone is on different regiments of medication. So there is an understanding that your doctor has an overview of all the medication that you are taking and if there are any interactions.

Pharmacist: My only concern with the combination of these two would be the over-sedation, apart from that also it depends on the dosing.

Consumer: I usually take Endone 5mg morning and night, and the Valium its more as a prn as I need it, I am really worried about mixing them together. I do have a couple of beers each night, how is that going to affect this?

Pharmacist: Common sense would say that if you are affected by the drowsiness not to drive or do anything like that require a bit of focus and to be alert whilst you are taking this. I would just avoid it totally, even if it is in moderation? But these are generalised answers as everyone is different. Some people find that Endone or any of the opiates affect them more so than others and others need a significantly higher dose. I realise the document is not very specific.

Consumer: Is Endone an opiate?

Pharmacist: Yes it is oxycodone.

Consumer: I was reading online something about a drug that they have put out now that reverses it if you have an overdose, can we get that?

Pharmacist: You can buy it over the counter but to be honest it is really more for, to be blunt, heroin users. Especially with overdosing and things like that it can reverse the effects. You are on a relatively low dose of the drug.

Consumer: It's hard to keep track sometimes because when I am in and out of hospital, they change different medications, I am just worried because I just can't find any information on when taking them together what happens?

Pharmacist: How long have you been on them together?

Consumer: About three months.

Pharmacist: In that time have you noticed anything out of the ordinary? When you are taking them together?

Consumer: I get really itchy.

Pharmacist: A lot of people do have a mild allergy, is that recently?

Consumer: It's started since I started taking multiple medication and it's hard to know what side effect, it's all a little bit confusing.

Pharmacist: I understand that you after a bit of peace of mind and it's also hard when they change all your meds at once in hospital if you don't get that time to trial each medication to see what affect each has on you.

Consumer: Is there a website that we can go to, to look at more information on?

Pharmacist: As I said it really depends on what you are after, what you are trying to find, because there is so much information out there and trying to filter out what's relevant A) and also there is a whole host of info out there you can go as technical as you need...

Consumer: My concerns are I have seen in the media a lot of stories about people accidentally overdosing on like pain medication and I am worried that, that could happen.

Pharmacist: The other thing you need to consider is the need for pain medication, obviously with a lot of medications there is the potential for dependence and addiction. So you need to understand that is just something that can happen with a number of medications, but you also need to understand that you are better off controlling the pain, like getting on top of pain, where some people will use sub-therapeutic doses of pain meds and they just suffer and their quality of life is crap. So you are better off...

Consumer: How long does it take to get addicted?

Pharmacist: Everyone is different.

Consumer: Thank you.

END OF TRANSCRIPT

4.2.7 Pharmacy 7

	CMI provided	Verbal: addiction warning	Verbal: advised of the risk of overdose, coma and death (Endone and/or Valium)	Verbal: advised of the risk of overdose, coma and death (Endone, Valium and alcohol)	Verbal: advised of the risk of drowsiness, sedation or respiratory failure
Pharmacy 7	Yes	No	No	No	Yes
Issues	– Advised that Endone is not a strong pain medication – it's a starting medication – When showing the CMI to highlight the risks, then admitted that it does not provide much information on the combined effects of the medications, but that the pharmacist will inform people what they need to know – Gave conflicting advice on numerous occasions, for example Endone: "It's not a very harmful drug or a dangerous drug" and then "It is a dangerous, you know, it is a controlled drug because of the side effects." – Suggested to type into Google, "What's the problem with that medicine?" for more information – Advised on the risk of death after reviewing online information but then advised; "It's not like, oh, I will get respiratory depression and I will die. You don't have to worry about it, but just be careful. That's why they're saying just be careful when you're drinking alcohol and Endone. Okay? It's not that they want to make you worry about it. They just want you to be careful about it, okay? Do you have any concerns?"				
Advice	**Consumer:** "I mean, shouldn't it say that death is a risk as well?" **Pharmacist:** "No, they will not say that. So that will be there somewhere. I will show you that. Slow heart rate. That's why it says, "These are the serious side effects." "Yours [Endone and Valium] is not a very highly sedative agent. But if someone is on highly sedative agents and they're taking too much of the tablets, drinking alcohol, all those things, it can not only cause sedation, it can cause respiratory problems as well." "Don't worry about reading the interactions because each medicine has interactions. So if you are taking two medicines, it will have some kind of interaction. But if it's severe, we always let you know. If there are some medicines you should not take, we always let you know. Very rarely, it will miss from pharmacists or doctors. But these are all the common medicines. You don't have to worry about taking it." "That's why they're saying just be careful when you're drinking alcohol and Endone. Okay? It's not that they want to make you worry about it. They just want you to be careful about it, okay? Do you have any concerns?" "If you type just in Google, "What the problem with that medicine?" Or I can give you that. That's fine."				

(Edited to key points)

Consumer: Hi, how are you?

Pharmacist: Good, thanks.

Consumer: Cool. I want to talk to a pharmacist. I want to get some information on some medication that I'm taking. I've been taking **Endone** and **Valium**.

Pharmacist: Yeah, so I'll print that for you as well and I will check the interactions. So you are on Efexor, Endone, and Valium?

Consumer: Right.

Pharmacist: Yeah. Common side effect is drowsiness. The other one is some people get a bit dizzy. So even if you take at night-time, the next day also, the drowsiness can continue on the next day. So that's why it's always recommended, if you're feeling dizzy or any tiredness, do not drive. Do not drive or operate any machinery, okay? You are not allowed to drink alcohol at the same time with that because it can make you more drowsy. Because that's how the medicine works actually because it's like an opioid, like, in some ways, that's how it works, it can make you drowsy. It has an effect on the brain. That's how it reduces the pain. **But it's not like a really strong medicine or nothing like that. Compared to other pain medicines, it's the starting. Like, if someone is after having an operation, they start with the Endone**.

Other side effects are dry mouth, constipation, because they're not drinking enough water, changes in the vision, that's all really [inaudible], urinary retention like frequency or urgency, that's not really common, but you see dry mouth, all those symptoms. Are you getting any of the side effects like that?

Consumer: A few of those, but those don't particularly bother me.

Pharmacist: Okay, it's just the drowsiness?

Consumer: This drowsiness, yeah.

Pharmacist: So you're taking only two, one in the morning and evening? Do you take any between sometimes?

Consumer: Sometimes, yes. Sometimes I'll take it at lunchtime.

Pharmacist: Lunchtime, yeah. Yeah, that's the normal side effect. The problem is, because you're on Valium as well, it can make you drowsy as well, right? It will help people to sleep. It's almost like [inaudible], it's almost similar. Like, that one will help with the anxiety and all those symptoms, but this one [inaudible] receptor to help reduce the pain. But both have effects on the brain, so it can make you drowsy the next day also.

So that's why Valium is always recommended at night-time usually. Yeah. If it's for anxiety and you are taking this day tablets, you can avoid taking it, but the doctor has to give you something else for the anxiety, okay? There's so many medicines for the anxiety these days, different class of medicine. They can give you that and you can take those in the morning. It won't give you any drowsiness. Yeah. So Valium is usually night time because I don't think because of the Endone you can take too much, maybe because of this Valium, because that's one of the medicines which is given to help with the sleep as well. So that's both of those together are making it worse. So was that information not given to you?

Consumer: No. There was very little information given when I left the hospital. The just gave me the Endone and I've been on the Valium for a long time. So, you know, when I go into the pharmacy, they don't talk about the side effects.

Pharmacist: Yeah. So usually if you had the Valium before, they usually don't counsel you, but if it's the first time, they usually explain about the side effects [inaudible]. So other than that, the common side effects are dizziness, light-headedness, confusion, drowsiness, changes in your blood pressure, but that's not really common, constipation. Some people get stomach problems like vomiting when they start, but that's not really common.

Consumer: Okay. So the worst side effect of these two drugs is drowsiness?

Pharmacist: Hm, yeah. Do you experience any other side effects like constipation or anything like that?

Consumer: Not really, but I've read – when I was listening to the radio about the side effects of some of these drugs and that some of these drugs, people could **die**. So that's why I thought it could be good to come and talk and understand am I at risk with my medication?

Pharmacist: So what did you hear? Is this about the medication or is it because of the side effects of it? So, like, what they're saying is these are like opioid drugs, strong pain medicines. It can make you drowsy, it can make you dizzy. Those times, people should not drive, okay? If they drive, more chances of accidents. That's all they say, "Don't drive if you are taking it."

So the risk with an opioid is having a car accident by driving?

Pharmacist: Yes. If they are getting drowsiness, they should not drive. So if you look at the outside of the tablet, there's a note saying, "It can make you drowsy. If you're effected, do not drive or operate machinery." Yeah. That's a really important warning for that.

Okay. So I just need to be wary with Endone and Valium that the worst side effect is drowsiness and that I shouldn't drive a car?

Pharmacist: Yes, that's very important. The interaction, I will check the interaction because that's why I wanted to ask you what's the other medicines because I can put everything into a software and it will show you. It will show what interactions it is causing.

Consumer: Okay, that will be good.

Pharmacist: Yes. So those are the only five medicines you take other than this thing?

Consumer: They're the only medicines.

Pharmacist: Yes. I'll get that for you. So I will print that for you. Okay. **That's some information about Endone; they say how it works. It's probably not all the information, but only what you need to know. And the interaction advice, there's only two interactions. One is a minor. The other one is considered severe. But there's not too much documentation and not too much information about it. Like, the information is there, but not too much, like, [inaudible]**.

So one is the use of the Endone with your Efexor. So it can increase the effect of – have you heard of serotonin syndrome? So the chances are they can increase the risk, which is reported in a post-operative patient. The patient had major depression disorders, including some of the medication like the Endone is included in that, but there's not too much evidence. But, yeah, that can happen. Not really common I don't think that you'd run into that. The other one is Valium and Endone. I told you Valium and Endone because it has sedative properties that can make you drowsy. So that's why I let you know. The other reason is that if someone is on serious sedative agents and someone is drinking alcohol – **yours is not a very highly sedative agent. But if someone is on highly sedative agents and they're taking too much of the tablets, drinking alcohol, all those things, it can not only cause sedation, it can cause respiratory problems as well**.

So that's what happens when we go to sleep. We'd be going to sleep, the brain actually getting depressed during that time, so that's called [inaudible] depression. So [inaudible] depression happens when we go to sleep. So that's how the medicine works. But if it's in [inaudible] or [inaudible] mode, it's fine. If it's in severe mode, that's causing toxicity. But I don't think you have to worry too much about it. Do you have a trip planned or something like that? Do you ride a bike?

Consumer: No.

Pharmacist: What type of vehicle is it? Is it just a car you drive?

Consumer: No. **My concerns were just that this is a cocktail of medication and I just wanted to understand better the risks and the side effects and what's the worst thing that could happen, so that I'm aware and I can take action**.

Pharmacist: Yeah. So yours is not a very high dose or anything. It's a normal dose. I've seen many people on high dose. And that's [inaudible] if someone can't tolerate the pain. How is your pain now?

Consumer: Well, it does vary. So sometimes the surgeon does increase my dosage, which is why I wanted to understand.

Pharmacist: So increase the dose, is it just the Endone dose increase?

Consumer: Just the Endone.

Pharmacist: **It's not a very harmful drug or a dangerous drug. It is a controlled drug, but it can use, like, a [inaudible]**.

Consumer: Okay. **So Endone is not a dangerous drug?**

Pharmacist: **It is a dangerous, you know, it is a controlled drug because of the side effects**. You can get the prescription medicines like Panadeine Forte. Those ones are mild, so this one is compared to that.

Consumer: So why did they say it's dangerous? What's dangerous about it?

Pharmacist: Because of the side effects.

Consumer: The drowsiness?

Pharmacist: Yeah. Because if someone is taking Panadeine Forte for pain and if someone is taking say codone, so that's the name of the medicine, oxycodone, for pain. So both have different side effects. Like, the level of side effects is similar in an Endone patient compared to the Panadeine Forte. Because the Panadeine Forte contain Codeine, Endone contains oxycodone, that is stronger compared to that. But for post-operative patients, they can't [inaudible] Panadeine Forte because the pain is more, so they have to give Endone to manage the pain. And it's not like you have to worry about taking it if you are taking it just once or twice a day. That's no problem.

Consumer: So the Endone and the Valium, sorry, what did that --

Pharmacist: So Endone and the other one cause sedation, so there's more risk. Yeah, sedation, drowsiness, so just be careful. It says, "Use combination with caution and monitor for any toxicity."

Consumer: Okay. So is that something that I can have, that sheet?

Pharmacist: This one? Yeah, that's fine. Or I can write that, yeah. If you type it, you can get that.

Consumer: Sorry, when you say, "If I type it," --

Pharmacist: **If you type just in Google, "What the problem with that medicine?" Or I can give you that. That's fine.**

Consumer: Can I have a look at that? So this is the Valium one? Okay.

Pharmacist: It's usually for our reference because that's the one sheet for the consumers. But, yeah, that's fine. It gives all the information. [presents an eMIMS printout cut off]

So if you have any concerns, just talk to your doctor, so you can change to a different one. [Inaudible] can't tolerate. **Don't worry about reading the interactions because each medicine has interactions. So if you are taking two medicines, it will have some kind of interaction. But if it's severe, we always let you know. If there are some medicines you should not take, we always let you know. Very rarely, it will miss from pharmacists or doctors. But these are all the common medicines. You don't have to worry about taking it**. But the Valium, which I said, you know, the morning time, if you're taking it and you're a bit dizzy or something like that, talk to your doctor about it. They can change.

Consumer: And you said about alcohol, like, I shouldn't drink.

Pharmacist: Yeah, not at the same time with the Valium – and even with the Endone at the same time.

Consumer: And that's because?

Pharmacist: That's because, like I said, how the medicines work, it has effects on the brain. So alcohol also has an effect on the brain, so that can make you more drowsy.

Consumer: Right. So the risks of combining alcohol, Valium and Endone is drowsiness?

Pharmacist: **Drowsiness. That's the initial stage. So if it's causing too much drowsiness, it can cause respiratory depression** [inaudible]. Yeah. So, like, same like the overdose for medicines. If someone is taking all of this controlled drug overdose, it can lead to death. They usually won't give that much amounts. They just give them the normal amounts of it. But that's one of the risks.

Consumer: So the risk is death with alcohol if I combine alcohol with those drugs?

Pharmacist: **Yeah**. Like, if you're getting too much alcohol and medicines at the same time. I am not saying it will happen, but that's one of the things which you should be careful. So it's given here actually. "Do not use Endone if you currently have or have had any of the alcoholism." Yeah. So [inaudible]. Yeah, so that's not recommended at the same time with that. But you can have at the other time, but do not take at the same time. And some of the other medicines also. So all these medicines have action on the brain. So that's why they say, "Some medicines interfere with the Endone." So that's why they don't keep, you know, all those medicines together.

Consumer: So alcoholism is different to taking alcohol. So does it say in there about alcohol or taking it?

Pharmacist: **I think there is. "Drinking alcohol while you're taking Endone. The combination can make you more dizzy, sleepy, lightheaded, than usual. Avoid alcohol while you're taking Endone." And also: "Be careful while you're driving or operating machinery." Most commonly, these are the side effects: drowsiness, sleepiness, dizziness, all of those. It can affect alertness, yeah**.

Consumer: I mean, shouldn't it say that death is a risk as well?

Pharmacist: No, they will not say that. So that will be there somewhere. I will show you that. Slow heart rate. That's why it says, "These are the serious side effects."

Consumer: Right.

Pharmacist: So the respiratory depression means that, in simple language, it's, like, slowing the heart rate.

Consumer: I understand that. I have depression, I have anxiety, so I worry about these things. And what stands out in this document, and you didn't write this document, **but if slowing my heart rate and death is a risk –**

Pharmacist: No, no, no. It won't cause any of those. But that's what I'm saying, like, if you're drinking, that's why they say just be careful with the Endone. So that's what happens if you're getting too much drowsiness, and if the alcohol is also affecting your body, it can decrease the heart rate. So if you worry anything about it, just see your doctor straight away. That's why they're saying you have to see a doctor if you get any of these symptoms.

Consumer: Okay.

Pharmacist: Don't worry about it. I know you're taking medicines for anxiety. This is a common medicine given for [inaudible] pain.

Consumer: My anxiety and depression isn't what I'm worried about mixing. What I'm worried about is the not really knowing because these documents don't make it very clear. Like, you've explained it to me, but that document doesn't say if you drink alcohol or too much, you could die.

Pharmacist: No, no, it's not like that. So, like, that's what I said. If you're getting too much of the medicine in your body and alcohol also, then only it happens, not with the normal dose.

Consumer: True. But shouldn't this document say that?

Pharmacist: Uh, it's there actually. So if we look into the --

Consumer: Google?

Pharmacist: Yeah. It could be side effects of – these are called controlled drugs.

Consumer: So I Google the side effects of controlled drugs?

Pharmacist: So shallow breathing is one of them. So it will not say. That's why it's considered a controlled. See, if you look into this, so that's one of the **NIH government** --

Consumer: That's the **US government**.

Pharmacist: Yeah. So constipation, rash, nausea, respiratory depression. So it's a higher, you know, toxic effects. Usually, in the common one, this one won't tell you all those ones. It's not like, oh, I will get respiratory depression and I will die. You don't have to worry about it, but just be careful. **That's why they're saying just be careful when you're drinking alcohol and Endone. Okay? It's not that they want to make you worry about it. They just want you to be careful about it, okay? Do you have any concerns?**

Consumer: No, that's fine. I'll look in Google and I'll do some research.

Pharmacist: **Yeah. Don't worry about it because you won't get any respiratory depression or nothing. But when you're drinking alcohol with Endone, just be careful because it's a class of controlled drugs**. You can search online or locate loads of information. So some of the websites are Victoria Health. They have a website about the medicines and all. So that's a good one.

Consumer: So I go to the Victoria Health medicine website?

Pharmacist: Yeah. So when you type about any medicine, it will come. I think it's Better Health or something like that. But, yeah, you can get a load of information. But that's the common one. This one is actually the Australian TGA. They have it maybe for people who are taking it.

END OF TRANSCRIPT

4.2.8 Pharmacy 8

	CMI provided	Verbal: addiction warning	Verbal: advised of the risk of overdose, coma and death (Endone and/or Valium)	Verbal: advised of the risk of overdose, coma and death (Endone, Valium and alcohol)	Verbal: advised of the risk of drowsiness, sedation or respiratory failure
Pharmacy 8	Yes	No	No	No	Yes
Issues	Advised that the effects of an overdose of these medications is respiratory depression and constipation				
Advice	**Pharmacist:** "If you overdose, then – let me check. So the [inaudible] I mentioned is it may lead to respiratory depression, constipation problem." "It is not recommended to drink alcohol if you're using the Endone and also Diazepine. The effect for the respiratory problem will increase with the alcohol, both of the medications."				

Consumer: I wanted to get some information. I've been taking **Endone and Valium** for a while and I wanted to get some information about the side effects of those drugs, and, also, I wanted to understand better **the risks of taking those two drugs together**.

Pharmacist: The main thing is if you have some asthma problem, it may cause respiratory depression and it may get more difficult to breathe, and both medications may make you drowsy. You may feel quite sleepy if you use them together. For the diazepine, if you take it regularly, you will need a higher dose for it to work. This is the Endone. Something else like constipation is also possible if you use it regularly. And this is for the diazepines. You can see on here. [gives the CMIs for Endone and Valium]

Consumer: So they're really not that dangerous based on those side effects?

Pharmacist: **If you overdose, then – let me check. So the [inaudible] I mentioned is it may lead to respiratory depression, constipation problem**. And if you use the two together, it may affect your concentration. Also, it's not suitable for [inaudible], so they need to be alert. If you're driving or operating machinery, then it may not be so good for you to do that.

Consumer: Okay. So the biggest risk of taking these two things together is drowsiness and just --

Pharmacist: And also respiratory depression, difficulty breathing.

Consumer: Difficulty breathing? What about, like, **I have a few drinks each night, alcohol. Is that a problem?**

Pharmacist: Again, it may increase the effect of the drowsiness. It is not recommended to drink alcohol if you're using the Endone and also diazepine. The effect for the respiratory problem will increase with the alcohol, both of the medications. First thing is if you use these medications for short-term or long-term. If it's for short-term, I think it's better to finish the medication and then you just return to your normal life, so doing the alcohol. Otherwise, I would not recommend it to you.

Consumer: Okay. So the risk of taking alcohol with Endone and Valium –

Pharmacist: It just increases one more level again for these side effects that I mentioned.

Consumer: And the side effect is the respiratory depression?

Pharmacist: And also sedation.

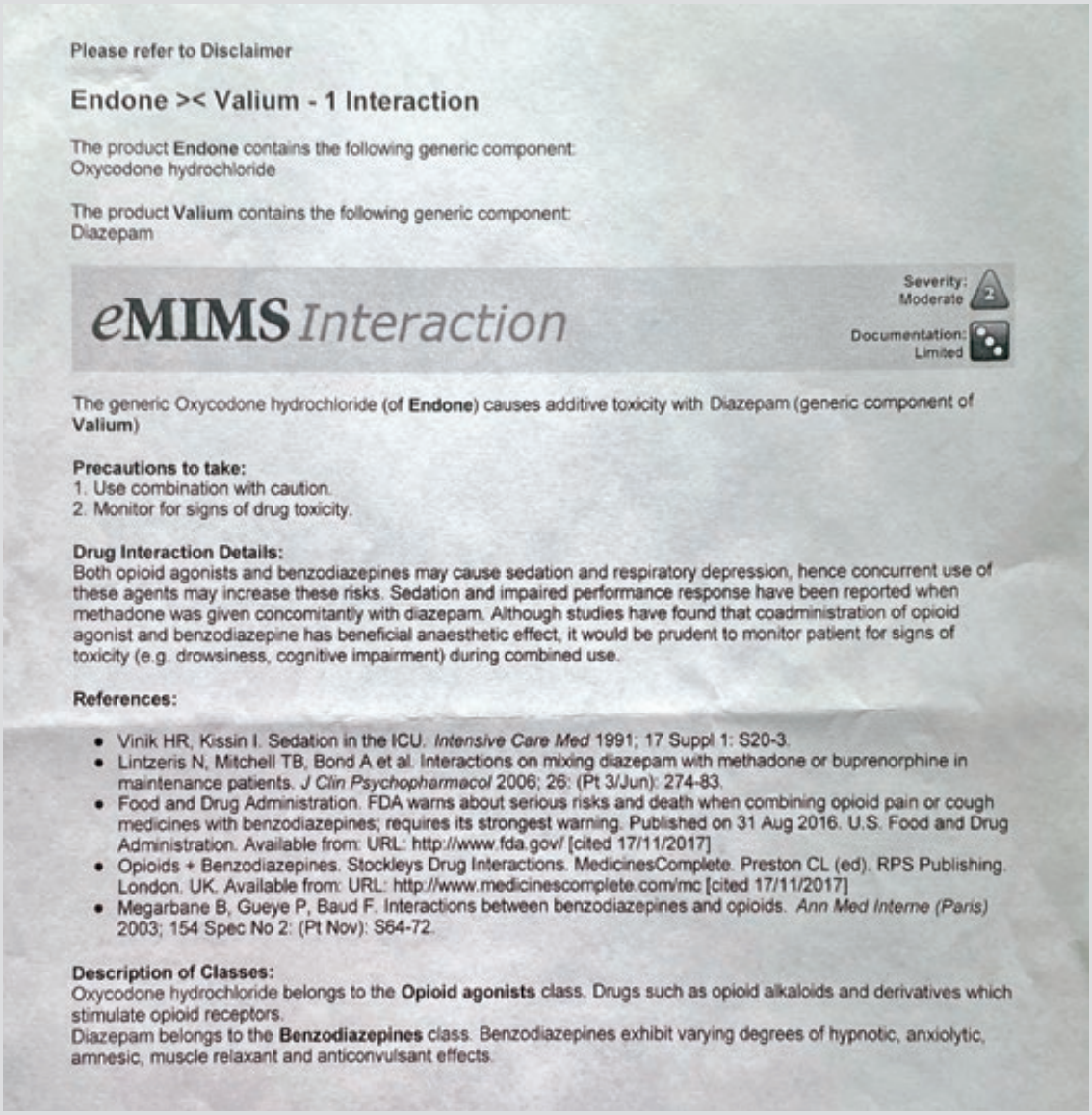
Consumer: And sedation. Okay, cool. Thanks for that. Okay.

END OF TRANSCRIPT

4.2.9 Pharmacy 9

	CMI provided	Verbal: addiction warning	Verbal: advised of the risk of overdose, coma and death (Endone and/or Valium)	Verbal: advised of the risk of overdose, coma and death (Endone, Valium and alcohol)	Verbal: advised of the risk of drowsiness, sedation or respiratory failure
Pharmacy 9	Yes	No	No	No	Yes
Issues	– Agreed that the risk of death exists, only when specifically asked – Advised that whilst the box warning does not discuss the risk of death, that the CMI does lists the risks including combining the medication, taking with alcohol and the risk of death – Advised that tolerance leads to higher doses and increased side effect risk – Provided an eMIMS drug interaction printout but did not discuss the contents (see Figure 29)				
Advice	**Pharmacist:** "Yeah, they can interact [Endone and Valium]. Certainly they make you drowsy if you're taking both of them at the same time. "It's interesting that it doesn't say it on the packet [risk of death]. It does say in the information about the medication. Certainly the printouts, consumer medicines information, does contain information on those things.				

Figure 29: eMIMS printout provided by pharmacist



Please refer to Disclaimer

Endone >< Valium - 1 Interaction

The product **Endone** contains the following generic component:
Oxycodone hydrochloride

The product **Valium** contains the following generic component:
Diazepam

eMIMS *Interaction*

Severity: Moderate 2

Documentation: Limited

The generic Oxycodone hydrochloride (of **Endone**) causes additive toxicity with Diazepam (generic component of **Valium**)

Precautions to take:
1. Use combination with caution.
2. Monitor for signs of drug toxicity.

Drug Interaction Details:
Both opioid agonists and benzodiazepines may cause sedation and respiratory depression, hence concurrent use of these agents may increase these risks. Sedation and impaired performance response have been reported when methadone was given concomitantly with diazepam. Although studies have found that coadministration of opioid agonist and benzodiazepine has beneficial anaesthetic effect, it would be prudent to monitor patient for signs of toxicity (e.g. drowsiness, cognitive impairment) during combined use.

References:

- Vinik HR, Kissin I. Sedation in the ICU. *Intensive Care Med* 1991; 17 Suppl 1: S20-3.
- Lintzeris N, Mitchell TB, Bond A et al. Interactions on mixing diazepam with methadone or buprenorphine in maintenance patients. *J Clin Psychopharmacol* 2006; 26: (Pt 3/Jun): 274-83.
- Food and Drug Administration. FDA warns about serious risks and death when combining opioid pain or cough medicines with benzodiazepines; requires its strongest warning. Published on 31 Aug 2016. U.S. Food and Drug Administration. Available from: URL: http://www.fda.gov/ [cited 17/11/2017]
- Opioids + Benzodiazepines. Stockleys Drug Interactions. MedicinesComplete. Preston CL (ed). RPS Publishing. London. UK. Available from: URL: http://www.medicinescomplete.com/mc [cited 17/11/2017]
- Megarbane B, Gueye P, Baud F. Interactions between benzodiazepines and opioids. *Ann Med Interne (Paris)* 2003; 154 Spec No 2: (Pt Nov): S64-72.

Description of Classes:
Oxycodone hydrochloride belongs to the **Opioid agonists** class. Drugs such as opioid alkaloids and derivatives which stimulate opioid receptors.
Diazepam belongs to the **Benzodiazepines** class. Benzodiazepines exhibit varying degrees of hypnotic, anxiolytic, amnesic, muscle relaxant and anticonvulsant effects.

Consumer: So I'm visiting from the coast and I take some prescription medication. I was listening to an interview on the radio and I thought I'd better come in and get some information about the risks of taking these drugs. I take **Endone** and I take **Valium**. I take Endone for pain – I had knee surgery last year and it's still pretty sharp – and Valium for anxiety. After hearing the radio story, I wanted to understand more what are the worst risks and side effects of these drugs, and also the risks and side effects of how they interact together.

Pharmacist: Yeah, they can interact. Certainly they make you **drowsy** if you're taking both of them at the same time. How long have you been on them for?

Consumer: I've been on the Endone for probably three months, and the Valium for probably two years.

Pharmacist: Okay, no worries. And what doses are you on?

Consumer: Five milligram tablets of Endone and Valium. I think it's 5 milligram.

Pharmacist: And twice a day or daily?

Consumer: Twice a day.

Pharmacist: Okay. And is it the same doctor that's prescribed both of them for you?

Consumer: Yes.

Pharmacist: Okay. So is the doctor aware that you've been on them for a while?

Consumer: Sorry, that's not true. The Endone is from my surgeon, and the Valium is from my psychiatrist.

Pharmacist: So they're from different prescribers, not your GP specifically?

Consumer: True.

Pharmacist: So is your GP aware that you're on both of them together?

Consumer: Yes.

Pharmacist: Fantastic. And what's your GP's advice to you about that as well?

Consumer: I spoke to him yesterday and it was that short, 15-minute meeting, and he suggested that I talk to a pharmacist to get some more detail about --

Pharmacist: Really? That's a very unusual thing to say because normally a doctor would be more than happy to help you.

Consumer: Well, he did say if it was a longer consult, he could explain it in more detail. But he did say that I could get information from the Internet and from a pharmacist.

Pharmacist: Look, what I can do, I can print you out an information sheet about the interaction between the two of them, so you could have a read of that. Certainly, if you've been on it for a while, I wouldn't advise stopping it cold turkey, simply because that can cause more problems. If your body is adjusted to taking it, you can get sort of rebound symptoms or withdrawal symptoms from that. So I would hold off on stopping it altogether until you talk to your doctor and work out a plan of how you're going to do it. Particularly with the Valium if you've been on it a long time, I would definitely have a chat with your doctor and planning to wean off that slowly. What symptoms are you most concerned about?

Consumer: It's not so much that I'm experiencing any symptoms. They seem to be doing what they're supposed to be doing by just sort of keeping the edge off the pain and the anxiety. **It's more that I'm worried about the long-term side effects and the interactions of these drugs**.

Pharmacist: And what did you hear on the radio per chance? I'm just interested.

Consumer: They were talking about celebrity suicide deaths and celebrity overdoses and they said that it's common that opioids are involved in those. And I understand that Endone is an opioid so that sort of flagged my attention as an uneducated patient.

Pharmacist: You don't sound uneducated. You sound quite knowledgeable.

Consumer: Well, it's not an area that I know a lot about. **And when I looked at the box of both medication, they just spoke about drowsiness, and, to me, death is a significantly bigger side effect than drowsiness. So it raised a red flag. If death is a side effect and addiction is a side effect, why doesn't it say it?**

Pharmacist: It's interesting that it doesn't say it on the packet. It does say in the information about the medication. Certainly the printouts, consumer medicines information, does contain information on those things.

Consumer: Is that what you --

Pharmacist: I can print those out, absolutely. And I can also print you out an information sheet about the interaction between the two.

Consumer: That would be great.

Pharmacist: I'm more than happy to do that. As I said, if you've been on it a long time, I would definitely not recommend stopping it cold turkey and doing it in planned fashion in consultation with your doctor. It's certainly not something that you want to withdraw from immediately.

Consumer: I'm kind of okay with taking the drugs. Where my anxiety has been spiked is that, hang on, I'm grabbing the boxes and reading the information. I'm thinking this doesn't match up to what I understand.

Pharmacist: And what you've heard on the radio.

The risks. And there was a little bit about here in Australia with opioid deaths. And I'm like, hang on, there seems to be this information gap between is it just drug abusers who are the ones dying? Because if they're prescription drugs –

Pharmacist: It's definitely not that straightforward a situation, I guess is the best way to put it. Often times it's a combination of factors. It will be people that have been taking it and are using increasingly larger doses to get the same sort of effect, because sometimes when you're on these medications, the same dose won't have the same effect if you take it for a long period of time. So people will tend to creep up on their doses and that's one of the reasons why your doctor needs to monitor it. Often the addition of illicit substances and also alcohol can increase the risk of experiencing side effects as well. So certainly I would be advising caution with using or taking any alcohol when you're on both of those medications together. And a lot of the deaths and the serious side effects are generally because people have had a lot, like an increased dose, or an adverse reaction to a combination, plus the addition of say alcohol to the mix, which most people don't think twice about these days.

Consumer: I've never thought about it.

Pharmacist: Yeah. So alcohol is a depressant as well. Similarly to opioids, they can depress your respirator system. So you can have difficulty breathing and things like that if you have alcohol at the same time. And that is on the little label one that you have. I think it says, "Avoid alcohol." But certainly I can print the information out for you. I'm more than happy. And if you have any other questions, please don't hesitate to come in.

Consumer: Lovely, yeah.

Pharmacist: I mean, obviously, you're not here for a long time by the sound of it.

Consumer: No, but it's something that's been on my mind. I know you don't make the labels, but, to me, drowsiness and death, like there's a big gap between. It just seems like the amount of warnings don't really match up to --

Pharmacist: Look, I think a lot of it comes down to advice as well. So when you go onto these medications, it's really important that the pharmacist has a chat with you about what you're [inaudible] as well and provides that advice readily to you about those risks. So that potentially is a gap that exists, but that should be happening when those medications are prescribed, so that you do have that adequate understanding of what you're taking. Did your pharmacist when you were --

Consumer: Well, I was in a hospital when I got the Endone for the surgery an –

Pharmacist: Your psychiatrist would have obviously had a conversation with you about the medications you're on I'm guessing?

Consumer: Yeah, but not stressed to this extent.

Pharmacist: It is I guess becoming a little bit more publicised I guess is the best way of putting it. And the significance and the extent of the issue perhaps hadn't been realised previously and health professionals are generally becoming more aware of it. Anyway, I'll print that information for you. Is there anything else I can help you with today? You don't need anything today at all?

Consumer: No. I feel like I want to get less drugs, not more.

Pharmacist: Do you know what? That's not a bad attitude to have. Certainly, if you can reduce as much as possible and only use them as needed, which you sound like a quite responsible --

Consumer: Yeah. I'm certainly not an irresponsible user, but I have lots of friends and my brother, he takes a lot of pain meds because he's had a lot of surgery. And I'm like, well, when you get the box, you get the same warning whether you're taking a little or a lot. So if I'm not getting the warnings, he's not getting the warnings.

Pharmacist: Potentially, yeah. I mean, it's just hard to know the individual circumstance. I can only provide advice on your situation and the medications that you're on.

Consumer: Cool.

Pharmacist: I'll go and grab those for you.

Consumer: Thank you very much.

Pharmacist: That's okay, no worries. There you are, sir.

Consumer: Great. Have a good weekend.

Pharmacist: You, too.

Consumer: Bye.

END OF TRANSCRIPT

4.2.10 Pharmacy 10

	CMI provided	Verbal: addiction warning	Verbal: advised of the risk of overdose, coma and death (Endone and/or Valium)	Verbal: advised of the risk of overdose, coma and death (Endone, Valium and alcohol)	Verbal: advised of the risk of drowsiness, sedation or respiratory failure
Pharmacy 10	No	Yes	No	No	Yes
Issues	Failed to provide any warning on the life-threatening risks				
Advice	**Pharmacist:** "Yes because Endone can cause drowsiness and Valium can cause drowsiness and if you use them both at the same time on the same day you can become more drowsy. And also these two medications especially Valium is not recommended to use with alcohol."				

Consumer: The reason for coming is to just understand better the risks and the side effects, are they dangerous?

Pharmacist: Yes as I said they are only recommended for short term use, for long term use they can be abused, you can be dependent on them, can cause drug addiction problems.

Consumer: Sorry?

Pharmacist: Drug addiction, because you are dependent on them.

Consumer: Ok but as far as short-term use if the doctors say its ok to use, is there any serious side effects apart from this addiction.

Pharmacist: Drowsiness.

Consumer: Drowsiness

Pharmacist: Yes because Endone can cause drowsiness and Valium can cause drowsiness and if you use them both at the same time on the same day you can become more drowsy. And also these two medications especially Valium is not recommended to use with alcohol.

Because I have couple of beers each night before bed.

Pharmacist: With the medication.

Consumer: Just like normal I haven't changed that.

Pharmacist: That can increase the risk of the side effects of Valium because you can lower the threshold.

Consumer: What does that mean?

Pharmacist: [inaudible].

Consumer: If it's dangerous what can it do to me?

Pharmacist: It can cause respiratory problems.

END OF TRANSCRIPT

Disclaimer

Names, locations and any other identifier(s) of pharmacists and/or other persons used in recordings reproduced in the Report will not be disclosed to any person, and the identity of any pharmacist or other person used in recordings reproduced in the Report will remain anonymous.

Warning

Do not stop taking a prescribed medication without discussing it with your doctor. Information can also be obtained by calling the NPS Medicines Line on 1300 633 424 or the Adverse Medicines Events Line on 1300 134 237 for advice. If you need support for any medical concern, including mental health matters, please contact your doctor. Lifeline also provides a 24 hour support service on 13 11 14 or www.lifeline.org.au

5. INFORMED CONSENT

1. INTRODUCTION

People with mental illness and pain conditions are especially vulnerable people. Their ability to process, remember and understand information is commonly diminished. This is due to the effects of their illnesses and the impact of the medication they are taking.

Informed Consent is the legal right of consumers to agree to medical treatment.

It can only be given after being informed of all the benefits and risks of a medical treatment. So, if an adverse event happened, they had been made suitably aware it was a risk and willingly took that risk. The CMI is the document that provides consumers with detailed information on these risks.

The CMI failures (Chapter 2) and pharmacy visit research (Chapter 4) highlight the significant warning gaps that exist around multiple medications, and the adverse drug event data in Chapter 3 highlights the alarming impact on human lives: death.

These gaps exist for individual drugs but most importantly, the gaps are bigger for polydrug treatments.

This chapter presents the argument that if **consumers have not had all the risks** of these medications disclosed to them, then they did not receive all the information to imply 'informed consent'.

In essence, they didn't know what they didn't know, so they couldn't take the appropriate safety measures.

As such any adverse drug event that happened, and corresponding consequences, should be deemed as medical negligence.

GPs form the frontline of mental health diagnosis and treatment, including medication. The process in which this occurs also raises further questions about the validity of medication informed consent.

At a government level, the failure to ensure all people, let alone our most vulnerable people, are protected is a breach of the Universal Declaration of Human Rights. Government has failed to:

- fully identify the needs of vulnerable people through information communication
- ensure CMIs are accurate
- ensure pharmacists and other health care professionals fulfill their obligations to protect vulnerable people.

2. INFORMED CONSENT TO MEDICAL TREATMENT

In light of the facts, it is important to identify the legal importance of the CMI documents.

The Australian Commission on Safety and Quality in Health Care is part of the Australian Government's health portfolio. As such, it is accountable to the Australian Parliament and the Minister for Health, Greg Hunt. The Commission defines patient safety as **prevention of error and adverse effects associated with health care**, while the aim of the Commission is to **ensure people are kept safe when they receive health care**.[208]

The Commission has developed the Australian Charter of Healthcare Rights, which details the rights of patients who use the Australian health system. The second edition of the Charter was released in 2019 (see Figure 30).

Figure 30: Australian Charter of Healthcare Rights (Source: Australian Commission on Safety and Quality in Health Care)

208 Australian Commission on Safety and Quality in Health Care, Australian Government, accessed on 3 April 2020, see https://www.safetyandquality.gov.au/about-us

The Charter states that people have the **right to clear information about my condition, the possible benefits and risks of different tests and treatments, so I can give my informed consent**.[209]

The importance of people being provided with this information to enable them to give informed consent is also detailed in the Medication Safety Standard, also produced by the Australian Commission on Safety and Quality in Health Care.

> The Medication Safety Standard aims to ensure that clinicians safely prescribe, dispense and administer appropriate medicines, and monitor medicine use. It also aims to ensure that consumers are informed about medicines, and understand their own medicine needs and risks.
>
> *– Medicine Safety Standard*[210]

The healthdirect website (a government website), states:

> *Informed consent in healthcare means you will be given understandable and clear information about your choices so you can make the right decisions about your health and healthcare.*
>
> *Consent is your agreement for a healthcare professional to provide you with treatment and care, including any tests, medicines, treatments or procedures you agree to.*
>
> *Before you give your consent, make sure:*
>
> – your doctor or healthcare professional has explained each of the options available to you that any risks, and the likelihood of those risks, are explained
> – you understand the benefits
> – you understand the purpose of the action you are consenting to[211]

Similarly, according to the ACT Government Health website:

> *Consent is your agreement for a doctor or healthcare professional to provide you with treatment, including any medical or surgical management, care, therapy, test or procedure. Informed Consent in healthcare means we give you clear and easy to understand information to help you make the right decision for your healthcare.*
>
> *Key points to remember about Informed Consent are:*
>
> – your doctor or healthcare professional must discuss your treatment options with you—please ask questions if you don't understand something
> – it's your decision to undergo a treatment or procedure
> – your doctor or healthcare professional must have your consent or refusal for each episode of treatment
> – your doctor or healthcare professional must make a formal record of the agreed decision

209 Australian Commission on Safety and Quality in Health Care, Australian Government, accessed on 3 April 2020, see https://www.safetyandquality.gov.au/publications-and-resources/resource-library/australian-charter-healthcare-rights-second-edition-a4-accessible

210 Australian Commission on Safety and Quality in Health Care, Australian Government, accessed on 3 April 2020, see https://www.safetyandquality.gov.au/standards/nsqhs-standards/medication-safety-standard

211 Healthdirect, Australian Government, accessed on 3 April 2020, see https://www.healthdirect.gov.au/informed-consent

> *It's important to remember that different procedures involve different risks, and complications can be different for each treatment. Please ensure you are fully aware of the possible risks to help you make an informed decision about having the treatment.*[212]

2.1 THE CMI AND INFORMED CONSENT

The core function of the CMI is to provide information on the risks of a medication to consumers and this information is used in their decision to give informed consent. The CMI is presented as the reliable source of truth for consumers; it is the document that the health care system and government direct consumers to for medication information.

The CMIs documented in this report clearly identify significant amounts of information relating to 'possible risks' that have **not** been provided to consumers for individual prescriptions. The report has also identified that there is almost no information provided to consumers around the 'possible risks' of polydrug prescriptions. Many of the CMIs contain (in current versions or have contained in previous versions) information that is inaccurate or misleading on the risks of the medication.

There is a significant difference between 'how to take the medicine' instructions and warnings of the 'potential side effects' of taking a medication. Advising to not consume alcohol whilst taking the medication, is a how to take instruction. Advising that the consumption of alcohol with the medication can result in respiratory depression, coma or death, is an explanation of potential side effects. The CMI analysis shows that the focus is on how to use instructions and whilst this is important, it does not provide the information on the potential risks to enable a person to give informed consent.

The CMIs do not deliver the information in a format that is 'clear and easy to understand'. The CMIs also do not accurately explain the 'likelihood of those risks' that are explained. In each of the CMIs reviewed in Chapter 2, the most commonly used description of the likelihood of a risk is 'may'. For example, Mundipharma in the Oxycontin CMI 2019 uses the word 'may' 46 times including this sentence on page 1:

> *"As with all strong painkillers, your body may become used to you taking OxyContin tablets. Taking it may result in physical dependence. Physical dependence means that you may experience withdrawal".*

The word 'may' is typically used to express the possibility of an event – it provides no information on the **likelihood** of it actually happening.

In addition, each CMI contains the following statement:

> *"All medicines may have some unwanted side effects. Sometimes they are serious but most of the time they are not."*

The vague content of these CMIs makes it impossible for vulnerable people to understand the **likelihood** of these risks occurring.

Informed consent is not a one-time event. Each time the treatment is changed, it also changes the risk to the person, and those risks have to be explained and informed consent given. This includes when doses of medication are changed or new medication added.

---

212 ACT Government Health Directorate, accessed on 3 April 2020, see https://www.health.act.gov.au/about-our-health-system/consumer-involvement/informed-consent

The CMI provides information on the risks of a medication to a consumer. This information is relied upon in the process of giving informing consent. Yet there is no legal requirement for health care professionals, including pharmacists, to give a paper CMI to consumers even:

- when they first start a prescription
- on repeat prescriptions
- when new information on the risks of the medication are added to the CMI.

The Therapeutic Goods Administration requires written information to assist patients in the use of prescription medicines to be 'available to be provided when these medicines are supplied'. Yet, a TGA spokesman noted:

> *"In practice, a **CMI may not be offered for repeat prescriptions** but it should be available on request from a pharmacist," a TGA spokesman said.*[213]

Why is it the responsibility of the vulnerable and suffering patients to ask for information?

Based on the law:

> *'Informed consent' refers to consent to medical treatment and the requirement to warn of **material risk** prior to treatment. As part of their duty of care, health professionals must provide such information as is necessary for the patient to give consent to treatment, including information on all material risks of the proposed treatment. Failure to do so may lead to civil liability for an adverse outcome, even if the treatment itself was not negligent.*[214]

The CMIs documented identify the lack of information for many material risks of prescription medication, including the risk of death. The *prescribing* of these medications is not negligent. However, if the non-disclosed adverse outcomes occur, this is grounds for civil liability.

2.2 WHAT IS MATERIAL RISK?

The RACGP states that a risk is material if:

- *a 'reasonable' person (in the same position) if warned of the risk is likely to attach significance to it, or*
- *if the medical practitioner is or should reasonably be aware that the particular patient, if warned of the risk, would be likely to attach significance to it.*

*Therefore, **a known risk should always be disclosed to the patient when**:*

- *an adverse outcome is common, even if the detriment is minimal*
- ***an outcome is severe, even if its incidence is rare**.*[215]

Given this, it is paramount that medical practitioners proposing medical treatments or procedures, inform their patients of the 'material risks' associated with the suggested treatment/procedure so they are able to make an informed decision about their healthcare.

213 D McCauley, 2019.

214 Australian Government Australian Law Reform Commission, Informed consent to medical treatment, updated 20 May 2014, see https://www.alrc.gov.au/publication/equality-capacity-and-disability-in-commonwealth-laws-dp-81/10-review-of-state-and-territory-legislation/informed-consent-to-medical-treatment/

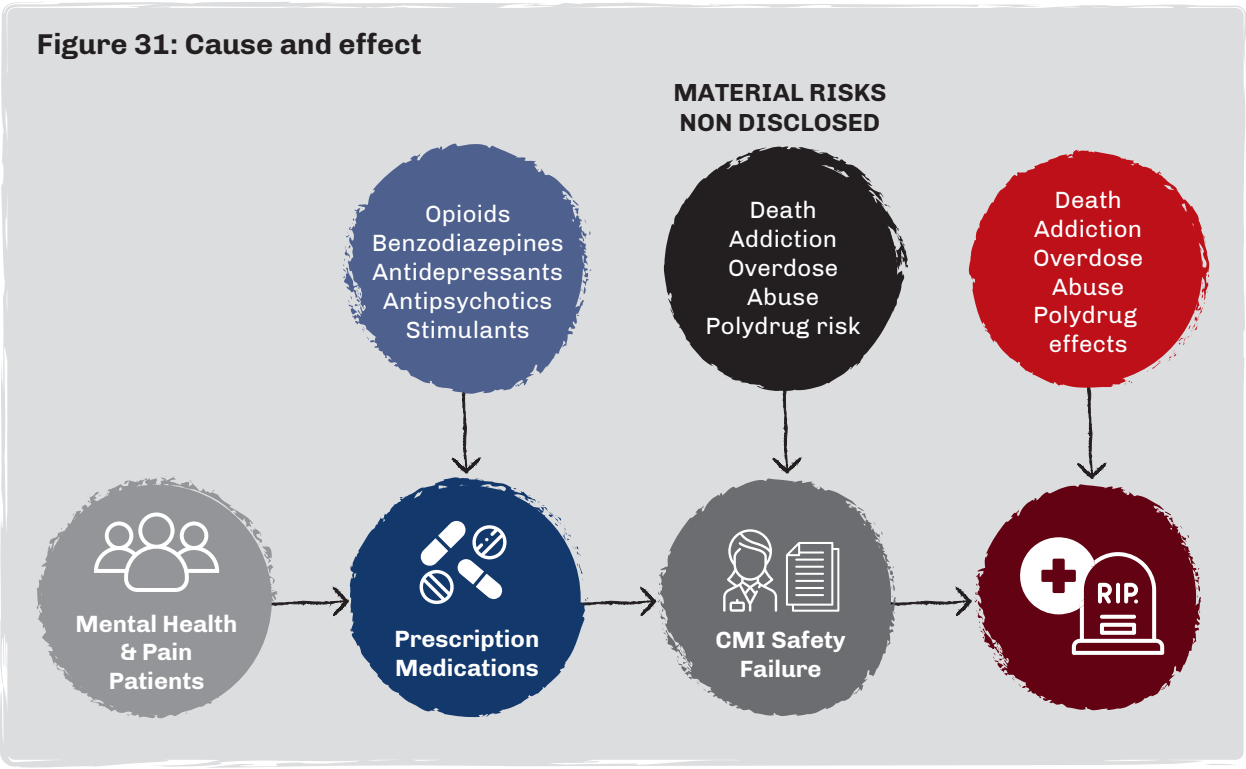
215 RACGP, Informed consent information sheet, no date.

Subsequently, a general practitioner (GP) should only undertake a medical procedure or provide treatment to a patient who has given their consent. Failure to obtain a patient's consent may increase the risk of medico-legal action.[216]

2.2.1 Risks that are material, deadly and not so rare

The people who suffer from adverse drug events are commonly people with mental health and pain conditions. The CMI for the medication prescribed to them fails to warn against a number of life-threatening risks. The exact risks not disclosed are also the most common adverse drug events that occur in Australia. The cause and effect cannot be any clearer (see Figure 31).

Figure 31: Cause and effect



The following section provides examples of when the CMI has not provided the material risk warnings for the most **commonly recorded adverse drug events** identified in Chapter 3.

2.3 MATERIAL RISKS TO POLYDRUG COMBINATIONS

OxyContin made by Mundipharma, and Valium made by Roche, demonstrate a situation where the polydrug combination of CMIs have failed to warn the patient of 'an outcome is severe, even if it is rare' and hence a material risk. Remember, the polydrug combination of opioids and benzodiazepines are the leading cause of drug overdose deaths (see Chapter 3). A person who has been prescribed these two medications, and has received the CMI for each medication, would not be made aware of multiple life-threatening risks of this polydrug prescription.

Neither CMI document identifies the risk of a fatal medication interaction between the two drugs. This is however clearly identified in the PI to medical professionals.

216 RACGP, Informed.

Benzodiazepine Warning – Oxycontin Mundipharma (Aust) Version: 12/2019	Opioid Warning – Valium Roche (Aust) Version: 03/2018
Australia CMI (2019)	**Australia CMI (2018)**
Benzodiazepines not mentioned in the CMI	Opioids are not mentioned in the CMI
Australia Product Information (2019)	**Australia Product Information (2020)**
"Concurrent use of oxycodone and sedative medicines such as benzodiazepines or related drugs may result in sedation, respiratory depression, coma and death." (page 5) "Concurrent use of oxycodone with sedative medicine such as benzodiazepines or related drugs [antidepressants, antipsychotics] increases the risk of profound sedation, respiratory depression, hypotension, death or coma because of additive CNS depressant effect." (page 9)	"Benzodiazepines increase the effects of other central nervous system depressants, including alcohol. When combined with other CNS depressants, the effects of overdosage are likely to be severe and may prove fatal." (page 13) [Combined use of opioid and benzodiazepine medication] "Such concomitant use has the potential to increase the clinical effects of Valium, possibly including severe sedation that could result in coma or death" (page 3)
Material Risks Not Disclosed	
If a person is prescribed Oxycontin and Valium, neither CMI warns of the risk of profound sedation, respiratory depression, hypotension, death or coma when these two medication are taken together.	

Daniel Bogart died from opioid drug use. His story was revisited in an article in April 2019:

Sydney man Daniel Bogart was on a ski trip with friends in 2016 when he went to sleep on Christmas Eve and never woke up. The 40-year-old took the medication he had been prescribed by his GP — oxycodone for the pain experience from pancreatitis and Valium for an anxiety condition.

Despite taking the recommended dose, the combination of the two proved lethal, his mother Sally Wilkinson told The Daily Telegraph last year.

"He had sub-therapeutic levels in his blood — lower than the recommended dose, but there is a massive risk of a multiplier effect when the drugs work together," Ms Wilkinson told the newspaper.

"People don't realise the massive risk of dying if you combine these drugs. We still have 'white coat syndrome' where we do not like to ask questions of doctors because we are conditioned to think what they are telling us is correct."[217]

217 S Molloy, 2019.

2.4 MATERIAL RISKS TO INDIVIDUAL MEDICATIONS

Valium (made by Roche) is a CMI example that demonstrates a situation of when a CMI has failed to warn the patient of 'an outcome is severe, even if it is rare' and hence a material risk. The risk not disclosed is suffering from breathing problems, respiratory depression, coma and death if a person consumes alcohol with Valium.

> *"In over 96% of drug deaths where benzodiazepines were present in 2016, they were taken in conjunction with other drugs including alcohol."*[218]

Alcohol Warning – Valium Roche (Aust) Version: 03/2018
Australia CMI (2018) "Things to be careful of; Be careful if you are elderly, unwell, drinking alcohol or taking other medicines. Some people may experience side effects such as drowsiness, confusion, dizziness and unsteadiness which may increase the risk of a fall. Your doctor may suggest that you avoid alcohol or reduce the amount of alcohol you drink while you are taking Valium." (page 3)
Australia *Product Information* (2020) **"**Benzodiazepines increase the effects of other central nervous system depressants, including alcohol. When combined with other CNS depressants, the effects of overdosage are likely to be severe and may prove fatal." (page 13) [Combined use of opioid and benzodiazepine medication] "Such concomitant use has the potential to increase the clinical effects of Valium, possibly including severe sedation that could result in coma or death" (page 3)
Material Risks Not Disclosed If a person is prescribed Valium and consumes alcohol, the CMI does not warn of the risk of breathing problems, respiratory depression, coma and death.

2.5 GPS AND INFORMED CONSENT

Complaints raised by people with lived experience around the medication warnings provided by doctors and the process they obtain informed consent is routinely dismissed. Chapter 1 discussed the diagnosis of mental illnesses by GPs. These appointments commonly include the patient assessment, diagnosis, treatment recommendations and informed consent – all in one session.

2.5.1 How are doctors gaining informed consent for medication?

Medicare Benefits Schedule

Diagnosis and treatment of mental illness requires a doctor to complete a mental health plan. This provides a comprehensive document of the patient circumstances, the diagnosis and treatments. It is covered by the Medicare Benefits Schedule (MBS) and is allocated a 20–40 minute consultation.

218 ABS, 2016.

According to the MBS, in that time the following occurs:

Assessment

*An assessment of a patient **must** include:*

- recording the patient's agreement for the GP Mental Health Treatment Plan service;
- taking relevant history (biological, psychological, social) including the presenting complaint;
- conducting a mental state examination;
- assessing associated risk and any co-morbidity;
- making a diagnosis and/or formulation; and
- administering an outcome measurement tool, except where it is considered clinically inappropriate.

Preparation of a GP Mental Health Treatment Plan

*In addition to assessment of the patient, preparation of a GP Mental Health Treatment Plan **must** include:*

discussing the assessment with the patient, including the mental health formulation and diagnosis or provisional diagnosis;

identifying and discussing referral and treatment options with the patient, including appropriate support services;

agreeing goals with the patient – what should be achieved by the treatment – and any actions the patient will take;

provision of psycho-education;

a plan for crisis intervention and/or for relapse prevention, if appropriate at this stage;

making arrangements for required referrals, treatment, appropriate support services, review and follow-up; and

documenting this (results of assessment, patient needs, goals and actions, referrals and required treatment/services, and review date) in the patient's GP Mental Health Treatment Plan.

Treatment Options

*"Treatment options can include referral to a psychiatrist; referral to a clinical psychologist for psychological therapies, or to an appropriately trained GP or allied mental health professional for provision of focussed psychological strategy services; **pharmacological treatments**; and coordination with community support and rehabilitation agencies, mental health services and other health professionals."*[219]

219 Australian Government Department of Health, *Medicare Benefits Schedule – Item 2715*, accessed on 3 April 2020, see http://www9.health.gov.au/mbs/fullDisplay.cfm?type=item&qt=ItemID&q=2715

2.5.2 How can doctors gain informed consent in 40 minutes?

If the process outlined by the MBS is followed, it would be challenging to complete it within 40 minutes. Considering the requirements of informed consent, if medication is prescribed in this appointment then this process would also need to also include:

- assessing the patient's current over-the-counter and prescription medications
- assessing the polydrug interactions of the existing medications
- selecting a medication class, type and dose for treatment
- assessing the polydrug interactions of the new medication prescribed with existing medication
- explaining how to take the medication
- explaining the benefits of the medication
- explaining the material risks including any polydrug risks
- explaining alternative options including the option of not taking it
- enabling the patient enough time to understand and ask questions
- documenting that the patient has provided informed consent.

The medication discussion alone could take over an hour. It is virtually impossible for the process from diagnosis to informed consent to be done in an appointment that lasts 20–40 minutes. **More concerning is that the RACGP is admitting that the process isn't being followed, with Dr Harry Nespolon, president of the RACGP commenting:**

> *"At the moment, there's really only one [Medicare] item number for mental health issues, which is a 20-minute consultation," he said. "In other words, you can sort out all mental health issues in 20 minutes — which we all know is not true."*
>
> *Dr Nespolon said many GPs were being forced to cram patients with complex needs into short appointments.*
>
> *"We know that people with mental health issues tend to have many more physical problems ... so the GP is there dealing with all the patient's issues, not just their mental health issue," he said.*[220]

In addition to following this process, all of the information discussed has to be documented:

> *"Once satisfied that the patient has a good understanding of the proposed treatment and the material risks and benefits involved, GPs need to record how the patient's consent was obtained, including any written information provided, specific issues raised by the patient, an overview of the options considered and general and specific risks relating to the patient."*[221]

An example of a specific risk relating to a patient with comorbid mental illness and pain conditions, is the risk of addiction. Having a mental illness increases the risk of addiction to opioid medications, a class of drug that is already highly addictive. This risk is not contained in the CMIs, and the position of people with lived experience is that it isn't typically discussed in doctor consultations either. If it was, it would be documented, because that is the law.

220 O Willis, 'Mental health still the number one reason people visit their GP, report finds', *ABCNews*, 19 September 2019.

221 Royal Australian College of General Practitioners (RACGP), *Information sheet: Informed patient decisions*, East Melbourne, Victoria, September 2019.

The outcome is that a person who is suffering with mental illness, is asked to undergo an extensive medical assessment in a condensed timeframe, and then understand not only the diagnosis, treatment, and the risks of the treatment, but to then give an informed consent to proceed. That is assuming all steps are followed. If information is provided to the patient on the medication prescribed to review later, it is the CMI or a document using information from the CMI. The onus isn't on people with disabilities to prove that informed consent hasn't been given in these appointments; the law requires doctors to prove how it could have been.

2.5.3 GP guidelines and patient information

In May 2012 the Coroner's finding from the inquest into the death of David Trengrove delivered a horrific verdict on the RACGP prescribing guidelines for benzodiazepines:

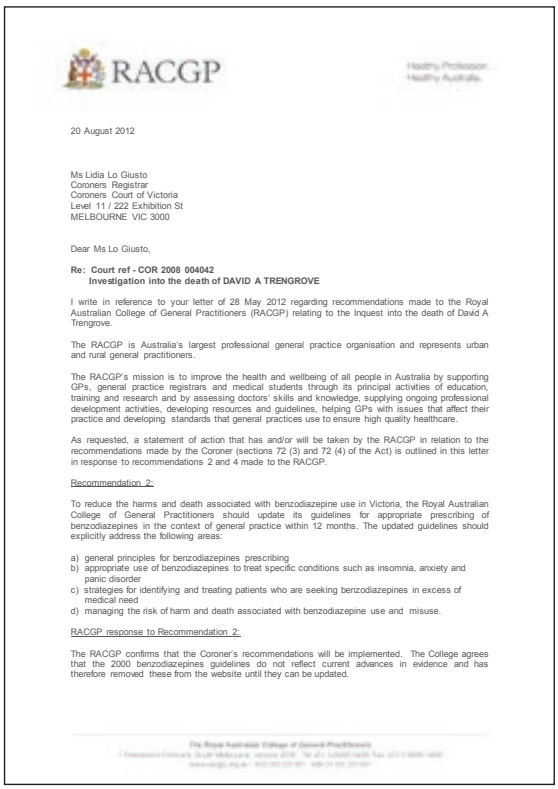
> *"I understand that the Royal Australian College of General Practitioners (RACGP) is the appropriate body to lead the development of prescribing guidelines for general practitioners. However, the RACGP's current guidelines for benzodiazepine prescribing appear to have four major shortcomings. First, they were published in 2000 and so do not reflect the significant advances in evidence that have occurred in the intervening 12 years. Second, they address prescribing principles in general terms but offer little if any guidance on appropriate use of benzodiazepines to treat specific conditions such as insomnia, anxiety and panic disorder. Third, they do not offer any substantive guidance on strategies for general practitioners to identify and treat patients who are seeking benzodiazepines in excess of medical need. Fourth, they do not discuss the risk of death associated with benzodiazepines, particularly when taken in combination with other central nervous system depressants such as opioid analgesics."*[222]

The Coroner recommended that:

> *"In light of the identification of erroneous prescribing practices of benzodiazepines by general practitioners, the RACGP should update its guidelines. (See below Recommendation 2)."*[223]

In response, the RACGP fully agreed with the ruling, noting:

> *"RACGP response to Recommendation 2:*
>
> *The RACGP confirms that the Coroner's recommendations will be implemented. The College agrees that the 2000 benzodiazepines guidelines do not reflect current advances in evidence and has therefore removed these from the website until they can be updated."*[224]



RACGP

20 August 2012

Ms Lidia Lo Giusto
Coroners Registrar
Coroners Court of Victoria
Level 11 / 222 Exhibition St
MELBOURNE VIC 3000

Dear Ms Lo Giusto,

Re: Court ref - COR 2008 004042
Investigation into the death of DAVID A TRENGROVE

I write in reference to your letter of 28 May 2012 regarding recommendations made to the Royal Australian College of General Practitioners (RACGP) relating to the Inquest into the death of David A Trengrove.

The RACGP is Australia's largest professional general practice organisation and represents urban and rural general practitioners.

The RACGP's mission is to improve the health and wellbeing of all people in Australia by supporting GPs, general practice registrars and medical students through its principal activities of education, training and research and by assessing doctors' skills and knowledge, supplying ongoing professional development activities, developing resources and guidelines, helping GPs with issues that affect their practice and developing standards that general practices use to ensure high quality healthcare.

As requested, a statement of action that has and/or will be taken by the RACGP in relation to the recommendations made by the Coroner (sections 72 (3) and 72 (4) of the Act) is outlined in this letter in response to recommendations 2 and 4 made to the RACGP.

Recommendation 2:

To reduce the harms and death associated with benzodiazepine use in Victoria, the Royal Australian College of General Practitioners should update its guidelines for appropriate prescribing of benzodiazepines in the context of general practice within 12 months. The updated guidelines should explicitly address the following areas:

a) general principles for benzodiazepines prescribing
b) appropriate use of benzodiazepines to treat specific conditions such as insomnia, anxiety and panic disorder
c) strategies for identifying and treating patients who are seeking benzodiazepines in excess of medical need
d) managing the risk of harm and death associated with benzodiazepine use and misuse.

RACGP response to Recommendation 2:

The RACGP confirms that the Coroner's recommendations will be implemented. The College agrees that the 2000 benzodiazepines guidelines do not reflect current advances in evidence and has therefore removed these from the website until they can be updated.

222 Coroners Court of Victoria, Melbourne, Finding into death with inquest, 4042/08, 18 May 2012, p 11.
223 ibid.
224 C Jackson, President, RACGP, letter to Coroner's Court of Victoria, 20 August 2012.

The recommendations by the Coroner were not "advances in evidence". Information on these deadly risks were available in the original Valium PI dated August 1994 and other benzodiazepines PIs from even earlier in the 1990s. In 2003, a report from the National Drug and Alcohol Research Centre stated:

> *"The presence of one or more drugs (such as benzodiazepines, cocaine, alcohol, anti-depressants) in addition to opioids is a consistent feature of accidental opioid deaths worldwide."*[225]

The RACGP released a new guideline in 2015 titled, *Prescribing drugs of dependence in general practice, Part B – Benzodiazepines*. It stated that since 2002, approximately 7 million prescriptions for benzodiazepines had been dispensed in Australia each year.[226] According to the Penington Institute overdose report, for the period 2001–2012, benzodiazepines were involved in 4,159 accidental deaths.[227]

Considering the absence of disclosure of the risk of death in the RACGP guidelines used during this time, as well as the CMIs, it is not hard to see how 4,159 lives were lost. It is hard to see how anyone during that time could have given valid informed consent.

2.6 THE WARNINGS WE DIDN'T RECEIVE, THE CONSENT WE NEVER GAVE

The CMI provides information on the risks of a medication to a consumer. This information is relied upon in the process of giving informing consent. Death, overdose, addiction and abuse are the risks commonly not disclosed in the CMI analysis. These risks are severe and the occurrence of these is also far from rare. Informed consent can only be given if the person has been made aware of all the material risks of the treatment. In relation to prescription medication, these risks are documented in the CMI written by the manufacturer of the medication. This report has detailed multiple medications and numerous examples of material risks that have not been disclosed, including polydrug material risks.

The CMIs do not provide the information in a way that is clear and easy to understand and the likelihood of the risks are almost impossible to assess. Despite the importance of the CMI, there is no requirement for consumers to be provided with a hard copy CMI when they are first prescribed a medication. What is even worse is that when new risks are added to the CMI, there is no requirement to provide a hard copy CMI to the people already taking the medication when they get a repeat prescription.

Informed consent is a legal right for all people. It is not a box ticking exercise nor is it a one-time event. If a patient hasn't been informed of the risks before they give consent, their consent isn't informed and as such consent has not been given. If new risks of a medication become known, then the patient has the legal right to be made aware of these risks and then informed consent has to be given again.

Based on these facts, patients have never legally been given informed consent since the introduction of these medications over 20 years ago.

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225 B Barker and L Degenhardt, *Accidental drug-induced deaths in Australia 1997–2001*, NDARC Technical Report No. 163, National Drug and Alcohol Research Centre, University of New South Wales, Sydney, 2003, p 8.

226 The Royal Australian College of General Practitioners (RACGP), *Prescribing drugs of dependence in general practice, Part B – Benzodiazepines*, Melbourne, 2015, p ix.

227 Penington Institute, 2019.

The adverse events from these medications is well documented. Patients who have suffered from adverse events or death have suffered without ever being given the opportunity to reject the medical advice to take the medication, or to take action to reduce the likelihood of the side effects.

These issues still exist today. Urgent action is required, compensation and justice is due.

2.6.1 Off-label prescriptions

There are a number of vitally important points about off-label prescriptions that relate to informed consent.

First, using a medication off-label means a person is being prescribed a drug for a medical condition that the drug was not designed or tested for.

Second, the PBS will provide no financial support for the cost, because they haven't approved its use for that condition.

Third, the CMI will not contain any information on the risks for off-label use to the person. This means that even if a person received a CMI, it will not meet the requirements for informed consent.

Off-label use is justified by psychiatrists when traditional medications have not worked for that person. Using medications off-label has a higher degree of risk, but it is deemed appropriate in order to attempt to improve the person's mental health. In another breach of our human rights, these risks are not included in the CMI.

In short, we are prescribed a drug that has never been tested or approved for the condition we suffer from; we do not receive any information in the CMI of the increased risks of doing this, and we have to pay 100% of the cost.

The TGA advises that in situations where a medicine is used 'off-label' prescribers should discuss the risks and benefits of the proposed treatment with the patient and/or their carers so that they are capable of providing informed consent. The RANZCP advises that in the case of off-label prescribing, informed consent needs to be obtained and documented. The RANZCP also state that off-label informed consent involves psychiatrists ensuring that patients understand the purpose, nature, benefits, side-effects, risks and potential out-of-pocket costs of the medication as well as the implications of not having that medication and information about alternative treatments. Consistent with the prescription of all medications, psychiatrists should ensure that they have appropriate indemnity insurance either as an individual or under their organisation's policy prior to prescribing any off-label medication. Despite these warnings to psychiatrists, no CMI provides information on the risks for off-label use to the consumer and that means that no patient could have given valid informed consent.

The RANZCP also advises that psychiatrists need to be aware of the risk of serotonin syndrome when combining two different antidepressants. Combining two antidepressants like mirtazapine and venlafaxine, is commonly used to treat patients who have severe depression. However most CMIs for antidepressants do not explain the life-threatening risks of serotonin syndrome when taken individually and they certainly provide no warning of the added risk when combinations of medications are prescribed. Again, consent can only be given when a patient has been informed. The failure to ensure this has occurred is a systemic issue across all medication classes and prescribing practices.

3. UN CONVENTION ON THE RIGHTS OF PERSONS WITH DISABILITIES

3.1 A LIFE AND DEATH ISSUE

The Mental Health Commission's 2012 National Report Card on mental health and suicide prevention told a sobering tale:

> *It is a life and death issue.*
>
> *It is a national disgrace [reduced life expectancy] and it should be a major public health concern. Mental health must be a national priority. Government funded programs must measure how they support people to achieve better physical health and longer lives – to close the gaps in life expectancy and quality of health for people living with a mental illness. The Commission sees this as an injustice that runs contrary to the United Nations Principles for the Protection of Persons with Mental Illness and the Improvement of Mental Health Care and the Convention on the Rights of Persons with Disabilities which was signed by Australia in 2008, in which Article 25 states: "Parties recognize that persons with disabilities have the right to the enjoyment of the highest attainable standard of health without discrimination on the basis of disability..."*[228]

3.2 UN HUMAN RIGHTS

The Attorney-General's Department provides guidance on our right to health, in keeping with the UN Committee on Economic Social and Cultural Rights, which states that health is a fundamental human right.

In summary, the website states:

> ***The right to health is the right to the enjoyment of the highest attainable standard of physical and mental health.*** *The UN Committee on Economic Social and Cultural Rights has stated that health is a fundamental human right indispensable for the exercise of other human rights. Every human being is entitled to the enjoyment of the highest attainable standard of health conducive to living a life in dignity.*
>
> *You will need to consider the right to health if you are working on legislation,* ***a policy or a program that****:*
>
> – ***relates to access to information on the health and well-being of families, including information and advice on family planning***
> – ***relates to training for health personnel***
> – ***relates to access to health facilities, goods, including essential medications and services, especially for vulnerable or marginalised groups***
> – *relates to health services for particular groups, including Indigenous Australians, women and children*

228 Australian Government National Mental Health Commission, 2012, p28.

- *relates to the provision of aged care services, including in nursing homes*
- ***provides services for people with disability***.[229]

The guidance is also offered for the rights of people with disability.

In summary, the website states:

> *The **Convention on the Rights of Persons with Disabilities (CRPD) recognises the barriers that people with a disability may face in realising their rights**. The rights under all human rights treaties apply to everyone, including people with disability. However, the CRPD applies human rights specifically to the context of people with disability.*
>
> *Australia is a party to seven core international human rights treaties. The rights of people with disability are contained in the Convention on the Rights of Persons with Disabilities (CRPD).*
>
> *You will need to consider the particular rights accorded to people with disability when you are working on legislation, **a policy or a program that** relates to access to:*
>
> - ***information, communications and other services, including electronic services like the Internet and emergency services***
> - *public services such as education and healthcare, public institutions such as the justice system and courts and other public activities such as voting and advocacy*
> - ***relates to capacity to make decisions or legal rights and recognition before the law***.
>
> *Persons with disabilities include those who have long-term physical, mental, intellectual or sensory impairments which in interaction with various barriers may hinder their full and effective participation in society on an equal basis with others.*
>
> *The Disability Discrimination Act 1992 defines 'disability' as:*
>
> - ***total or partial loss of the person's bodily or mental functions; or***
> - ***a disorder or malfunction that results in the person learning differently from a person without the disorder or malfunction;** or*
> - ***a disorder, illness or disease that affects a person's thought processes, perception of reality, emotions or judgment or that results in disturbed behaviour;***
>
> ***The CRPD requires countries to ensure and promote the full realisation of all human rights and fundamental freedoms for all persons with disability without discrimination of any kind on the basis of their disability**. In particular, countries are required to:*
>
> - ***take into account the protection and promotion of the human rights of persons with disability in all policies and programs***.[230]

229 Australian Government Attorney-General's Department, Right to health, accessed on 3 April 2020, see https://www.ag.gov.au/RightsAndProtections/HumanRights/Human-rights-scrutiny/PublicSectorGuidanceSheets/Pages/Righttohealth.aspx

230 Australian Government Attorney-General's Department, Rights of people with disability, accessed on 3 April 2020, see https://www.ag.gov.au/RightsAndProtections/HumanRights/Human-rights-scrutiny/PublicSectorGuidanceSheets/Pages/Rightsofpeoplewithdisability.aspx

3.2.1 National Disability Strategy

These United Nations conventions require the Australian Government to ensure the highest standard of healthcare for persons with disabilities. Australia has committed to meeting these standards. This commitment includes the safety of medication prescribed as part of any treatment program. It also includes ensuring that persons with a disability have the legal rights to make an informed decision, by being provided with information to make that decision.

Article 33 of the CRPD requires countries to establish and designate a framework to promote, protect and monitor implementation of the CRPD.[231] **The National Disability Strategy is the mechanism to ensure that the principles underpinning the Convention are incorporated into policies and programs affecting people with disability, their families and carers.**

3.3 COGNITIVE IMPAIRMENT FROM DISABILITY

People with severe disability face extra challenges around being able to easily understand information and risks due to their illnesses.

According to the Australia Pain Management Association:

> *Chronic pain is very common in Australia and people living with pain are more prone to psychological distress such as anxiety and depression than those in the general community.* ***Long term pain puts a lot of stress on the brain and cognitive issues such as low mood, difficulty with memory or concentration are familiar, no matter what the underlying pain condition is.***[232]

Even Terry White Chemist's website says that "chronic pain leads to reduced gray matter in the brain, **which can impair cognitive abilities (ability to process thoughts), memory** and lead to emotional problems."[233]

A mental illness is considered a disability. It is a "health problem that significantly affects how a person feels, thinks, behaves, and interacts with other people."[234]

It also significantly interferes with an individual's **cognitive, emotional or social abilities**.[235]

A scoping report conducted by the Mental Health Coordinating Council and the University of Sydney looked at the cognitive functioning of people with mental health conditions:

> *The literature reviewed suggests that cognitive deficits are core features of mental health conditions such as schizophrenia and affective disorders, including bipolar and depression.* ***Cognitive impairments may include problems with attention, memory recall, planning, organising, reasoning and problem solving. These cognitive skills are essential for many functional tasks including work, study, social interactions, community participation and independent living.***

231 Australian Treaty Series, Convention on the Rights of Persons with Disabilities, 2008.

232 Australian Pain Management Association, Psychological effects of chronic pain, accessed on 3 April 2020, see https://www.painmanagement.org.au/2014-09-11-13-35-53/2014-09-11-13-36-47/178-psychological-effects-of-pain.html

233 Terry White Chemmart, accessed on 3 April 2020, see https://www.terrywhitechemmart.com.au/pain-and-thoughts/

234 Australian Government Department of Health, updated in May 2007, see https://www1.health.gov.au/internet/publications/publishing.nsf/Content/mental-pubs-w-whatmen-toc~mental-pubs-w-whatmen-what

235 Everymind, accessed on 3 April 2020, see https://everymind.org.au/mental-health/understanding-mental-health/what-is-mental-illness

*Cognitive dysfunction has previously been considered a secondary symptom of some diagnosed mental illnesses, **however current evidence indicates that it is a primary symptom or core feature of schizophrenia and affective disorders** (Green, 2006; Medalia & Reyheim, 2002; O'Carroll, 2000; Trivedi, 2006; Mohamed, et al., 1999). Affective disorders are also called mood disorders. The main types of affective disorders are depression, bipolar disorder, and anxiety disorder.*[236]

3.4 COGNITIVE IMPAIRMENT FROM MEDICATION

Other than potential cognitive impairment from a disability, people with severe disability may also face challenges around being able to easily understand information and risks due to the **side effects of the medication/s** they are prescribed.

The side effects of medication prescribed to persons with chronic pain and mental illness is documented earlier in this report. Remember, benzodiazepines and opioids are associated with confusion, impaired thinking, memory loss, and drowsiness.

Many mental health medications, like antipsychotics, are also associated with sedation.[237]

> Workers providing services to mental health consumers may overlook the significant functional impacts of impaired cognition, by failing to understand the impact of both the illness itself and the treatment prescribed, for example medication and ECT.[238]

3.5 COMMUNICATING THE RISKS AND BENEFITS OF MEDICATION TO PATIENTS

In 2016, the TGA provided advice to health professionals about the importance of communicating the risks and benefits to patients of antidepressants. While the PI and CMI for the medications should contain adequate warnings, the TGA warned that many patients report being **unaware** of the potential side effects.

Its Medicines Safety Update went on to state that:

Several studies have shown that patients with mental illness and their carers feel that they have not received enough information about their medicines. One survey found that just over half of the inpatients and one third of community-based patients reported that they did not receive any medicines information.[239]

Medication is given to people to undertake their own self-care on a daily basis in their own home. The medication or combinations of medication are not taken in the presence of medication practitioner. People with chronic illnesses are more likely to have a diminished cognitive ability. This can be due not only to the conditions, but as a side effect of the medication they undertake. The complexities of the side effects and polydrug side

236 Mental Health Coordinating Council Inc. (MHCC), Cognitive functioning: supporting people with mental health conditions, 2015, p.13, 5.

237 Victorian Government Better Health Channel, accessed on 3 April 2020, see https://www.betterhealth.vic.gov.au/health/conditionsandtreatments/antipsychotic-medications

238 MHCC, 2015, p1.

239 Australian Government Department of Health Therapeutic Goods Administration (TGA), Medicines Safety Update, Vol. 7(5), October–December 2016.

effects are significant for these patients. The process of communicating the information **completely fails to provide the critical warnings** in a manner that accommodates the mental state of patients.

These people are amongst the most vulnerable people in our society. They are suffering and have a significant reduction in their ability to absorb, process and remember information. This group of vulnerable people include the mentally ill, young people, the elderly, Indigenous Australians in rural communities, and people with low levels of literacy. By any assessment, the current warning process has systemic issues that has failed to protect their right to good health.

The length of the current CMI documents is often used as an example of how comprehensive the consumer warnings are. However, telling a person about a risk and telling a person how to avoid that risk are two completely separate things. The CMIs examined in this report fail on both fronts.

The suggestion that it is the responsibility of these individuals to manage the risks, including polydrug risks, of their medication highlights the flaws in the protection of these people. If the Department of Health deems these treatments appropriate despite the adverse risks, then it is their responsibility to adequately protect people from these risks.

They are also the most vulnerable people to the risk of suicide and self-harm.

3.5.1 WHO polydrug report

According to the WHO's *Medication Safety in Polypharmacy* report:

> *"Recognizing the scale of the global problem with unsafe medication practices and medication errors, in 2017 the WHO took action and launched its third Global Patient Safety Challenge: Medication Without Harm in March 2017. The goal of the program was "reducing severe, avoidable medication related harm by 50% over the next five years, globally."*[240]

The WHO asked governments:

"to prioritize three areas for strong commitment, early action and effective management to protect patients from harm while maximizing the benefit from medication, namely:

- *medication safety in high-risk situations*
- *medication safety in polypharmacy*
- *medication safety in transitions of care."*[241]

240 World Health Organization, *Medication Safety in Polypharmacy Technical Report*, WHO/UHC/SDS/2019.11, Geneva, 2019, p 5.
241 ibid, p 6.

The report stated:

> *"Polypharmacy may have harmful implications for patients such as an increased risk of medication errors, drug–drug interactions, suboptimal patient adherence and reduced quality of life."*[242]
>
> *"Countries should therefore prioritize raising awareness of the problems associated with inappropriate polypharmacy and the need to address this issue."*[243]
>
> *"information on risks and benefits is made accessible and comprehensible for the public, in order to include patients in the decision-making process."*[244]

Chapter 12 shows that the recommendations in the report have not be incorporated into any areas of the national mental health plan.

3.6 AUSTRALIA'S MULTIPLE HUMAN RIGHTS FAILURES

Australia is in breach of its UN commitments to human rights due to our:

- failure to ensure the CMI contains all the material risks of each medication
- failure to ensure a process to warn patients of the material risks of polydrug interactions
- failure to provide the information in a clear, concise and understandable format
- failure to ensure the CMI is provided to patients **every time** they fill a prescription
- failure to warn patients when material risks become known for medication already being prescribed
- failure to ensure the diagnosis of mental health conditions is being audited for diagnostic errors
- failure to ensure the process of selecting medications meets consumer safety standards
- failure to ensure the process of informed consent meets the legal standards
- failure to respect the complaints of people with disabilities and take action on the issues raised.

As a member nation of the United Nations, Australia has committed to upholding the 'right to health' and the CRDP. These conventions require the Australian Government to ensure that medical treatment for persons with disabilities recognises the medical conditions they have and provides them with the highest possible care.

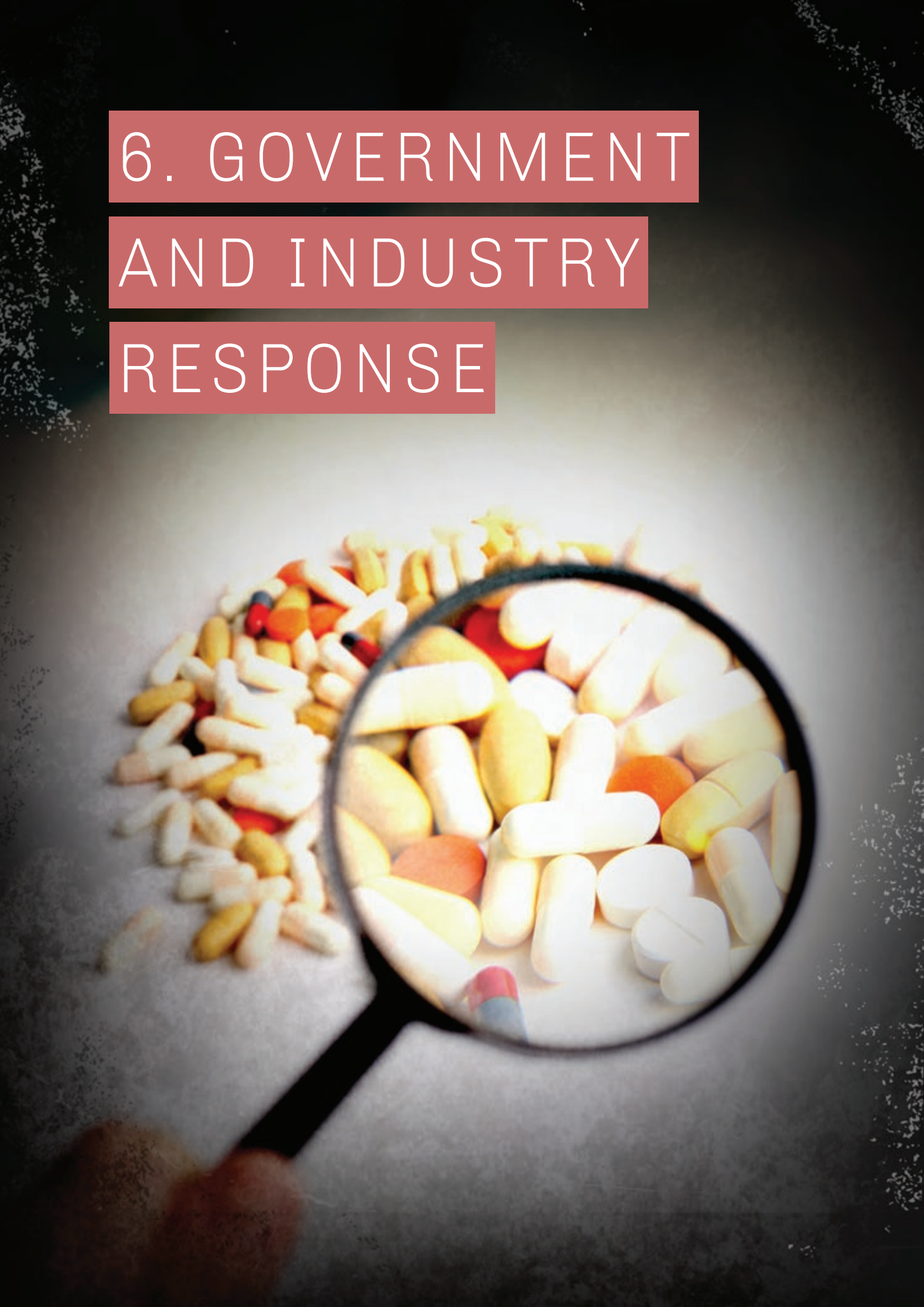
The human impact of the systemic failure to uphold these rights, is measured in thousands of lives. Despite the losses, the suffering and the grief, those who are tasked with upholding these rights are also the people responsible for the tragedy.

242 ibid, p 15.
243 ibid, p 10.
244 ibid, p 17.

Warning

Do not stop taking a prescribed medication without discussing it with your doctor. Information can also be obtained by calling the NPS Medicines Line on 1300 633 424 or the Adverse Medicines Events Line on 1300 134 237 for advice. If you need support for any medical concern, including mental health matters, please contact your doctor. Lifeline also provides a 24 hour support service on 13 11 14 or www.lifeline.org.au

6. GOVERNMENT AND INDUSTRY RESPONSE



1. INTRODUCTION

This chapter seeks to highlight that the majority of the government's response to adverse drug events centres on 'victim blaming' rather than addressing the root cause of the problems.

The chapter will highlight some of the government strategies to address the adverse drug events, including campaigns and programs to keep patients and prescribers informed.

The TGA led a number of campaigns which expose the systemic issues that exist – and that have allowed the CMI safety gaps to occur. The TGA uncovered inconsistencies between the PI and CMI yet did not take legal action, nor investigate how broad this issue is or how it came to happen in the first place. The TGA's actions on CMI disclosure are woeful and fail to urgently address the issues.

The TGA *Return your Opioid* campaign is completely inappropriate in tone and relevance, yet interestingly, some of the messages contradict information available within the CMIs.

The introduction of a Real Time Prescription Monitoring (RTPM) system again focuses on the concept of victim blaming, using 'doctor shopping' as the primary reason for such a system. Unfortunately, RTPM does not address polydrug interactions nor warn people about these risks.

The government response to the range of issues is disjointed, focused on the victims rather than the system, and lacking urgency given the severity of the problems.

2. GOVERNMENT RESPONSE

2.1 GOVERNMENT POLICY AND POSITION = VICTIM BLAMING

The adverse effects of prescription medication can occur for many reasons, including:

1. medication side effects
2. polydrug interactions
3. consumer medication warning failures
4. doctor's prescription practices
5. individual metabolic enzyme profile
6. deliberate overdose
7. accidental overdose
8. addiction
9. illegal recreational use.

The government response to overdose prescription deaths is disproportionately weighted to causes they describe as the **abuse** and **misuse** of medications. Failures of the health care system receive little attention and even less accountability. **A number of the factors that cause adverse drug events occur through no fault of the consumer**. For example, if a vulnerable person is not warned of the side effects of a medication or multiple medications, how can they be blamed if side effects like addiction or fatal overdose death occurs?

Australia now has the eighth-highest per-capita opioid consumption in the world.[245]

2.1.1 What was learnt from the US Opioid Crisis?

Purdue Pharma is a pharmaceutical company based in Connecticut USA. The company is privately owned and controlled by the Sackler Family. Purdue owns the patent rights to a number of prescription drugs including Oxycontin and Targin. In Australia, Purdue operates under the brand Mundipharma. Purdue is considered the architects of the US Opioid Crisis, based on the fact that they deliberately withheld the risk of addiction, abuse and death of Oxycontin from doctors and patients (see Chapter 8).

When the USA Opioid Crisis started in the late 1990s, Purdue was successful in introducing a response to the overdose deaths that **blamed the very people who had fallen victim to the side effects of the medication**. Instead of acknowledging the deliberate deceptive warning labels, they painted those people who suffered from addiction and overdose, as being drug abusers. It was a deliberate strategy to focus the attention of government on the actions of vulnerable people, instead of investigating the root cause of the deaths, the medication itself, the warnings and the process that led to it being prescribed to people, and the process that lead to addiction.

The Australian Government's response to adverse prescription medication events has a clear similarity to Purdue's misinformation campaign. The AIHW statistics shown in Chapter 2, clearly direct the adverse events as being attributed to **abuse** and **misuse**.

Minister for Health, Greg Hunt regularly uses this language when describing the cause of the problem. Instead of acknowledging the failings of the system, its focuses on the failings of the victims. While Australia's health system is described as "one of the best in the world, providing safe and affordable health care for all Australians"[246] the language does tend to focus on the misuse and abuse:

> *"Real time reporting will assist doctors and pharmacists to identify patients who are at risk of harm due to dependency, misuse or abuse of controlled medicines, and patients who are diverting these medicines."*[247]

Similarly, in a 2019 ABC article:

> *In a statement, a spokesperson for Federal Health Minister Greg Hunt said opioid addiction and misuse is a national challenge that the minister is dedicated to addressing.*[248]

245 F Tomazin, 2020.
246 Australian Government Department of Health, accessed on 3 Apriil 2020, see https://www.health.gov.au/about-us/the-australian-health-system
247 G Hunt (Minister for Health), National approach to prescription drug misuse, media release, Canberra, 28 July 2017.
248 O Willis, Accidental drug overdose deaths up almost 40 per cent in a decade, report finds, ABC, 27 August 2019.

And in *The Age*:

> *Health Minister Greg Hunt said the Morrison government was "deeply committed to directly addressing the needless loss of life from the misuse of prescription medicines such as opioids."*[249]

2.2 WARNING DOCTORS

The ABC reported in 2018 that the Australian Government had warned doctors about addictive painkillers such as codeine:

> *The Federal Government says it has written to 4,800 doctors to let them know they could be prescribing too many doses of addictive painkillers, as it seeks to avoid an opioid crisis like that seen currently in the United States.*
>
> *Health Minister Greg Hunt said the letter was intended to let the top 20 per cent of prescribers know where they sit, in the hope they will moderate or regulate their own actions. Federal Health Minister Greg Hunt says that the move to make over-the-counter codeine products prescription-only could save up to 100 lives a year. RMIT ABC Fact Check investigates.*
>
> *Low-dose codeine was previously available over the counter in pharmacies.* ***"We don't want to end up in the place that the United States is in where opioids are a national crisis,"*** *Mr Hunt said. Although Mr Hunt insists that Australia has the best doctors in the world,* ***it is clear the Government now sees some doctors as contributing to the problem.***
>
> *It has confirmed that one country doctor prescribed over 68,000 doses of opioids in less than a year, and another doctor in a city wrote prescriptions for over 56,000 doses over 12 months. It's everyday Aussies, not 'doctor shoppers', at the heart of the opioid crisis, experts say. Given that until February low-dose codeine was available without a prescription, those doses are likely to have been for stronger opioids.*[250]

Another article reflects a similar issue:

> *Court records show many people are currently falling through the cracks. One Victorian man was given 58 prescriptions for 1500 OxyContin tablets and a further 29 scripts for diazepam, a dangerous benzodiazepine used for anxiety, in the months before his death from an overdose. In another case, a 33-year-old security guard ended up overdosing after being prescribed oxycodone 22 times in 15 months, which he'd crush and inject for a quicker hit, along with pethidine, morphine, codeine and tramadol.*[251]

The seriousness of doctors overprescribing dangerous medication cannot be understated. In the USA, providing medication in excess of therapeutic levels is regarded as operating as a drug dealer. As such, should our doctors be charged as drug dealers?

> **"You can rest assured, when medical professionals behave like drug dealers, the Department of Justice is going to treat them like drug dealers.**
>
> *– Assistant Attorney General Brian Benczkowski, DOJ Criminal Division*[252]

249 F Tomazin, 2020.
250 M Lloyd, 'Restricting access to opioids could drive pain sufferers to buy harder drugs on the black market, experts warn', ABCNews, 26 June 2018.
251 F Tomazin, 2020.
252 C Johnson, Nearly 60 Doctors, Other Medical Workers Charged In Federal Opioid Sting, NPR, 17 April 2019.

Writing to doctors does not appear to be an appropriate response to this issue. It must be asked why further investigation was not undertaken to look at consumer health impacts for each GP that was over-prescribing these medications.

Minister Greg Hunt responds to a problem of over-supply of prescription medication, yet he does not once mention the possibility that deaths may have occurred from over-prescribing. Not only does the government have access to a report on how many prescription GPs are giving out, they also have access to the ABS data for drug overdose deaths and hospital admissions for adverse drug impacts. This ABS data could have been compared with the 4,800 doctor prescription activity to identify adverse patient impact.

Put simply, sending a letter was PR exercise alone. GPs were not – and are not – held accountable to protect our most vulnerable people.

2.3 WARNING PHARMACISTS

As shown in a *Sydney Morning Herald* article in January 2019, Minister Hunt wrote to pharmacists to remind them of their responsibilities – of which they should already be completely aware. Here are some excerpts from the article:

Federal Health Minister Greg Hunt will write to pharmacists and doctors to remind them of their responsibilities, after consumer advocates raised concerns that patients were not being given vital information about medicine interactions and side effects.

The Consumers Health Forum of Australia called on Mr Hunt to step in after receiving complaints that patients were not always being given consumer medicine information documents (CMIs), which pharmaceutical companies are required by law to make available.

In the past CMIs were provided as a leaflet inside prescription medicine boxes but most products now direct patients to read the information online, leaving it to doctors or pharmacists to print off the documents for patients starting new medications.

But consumer advocates say this makes the information inaccessible to many, particularly if busy GPs and pharmacists fail to provide the documents – which experts say are far too difficult to read and understand.

Leanne Wells, chief executive of the CHFA, said that CMIs should "ideally" be placed inside prescription medicine packets and that directing patients to a website was "not of any use to those consumers, particularly older patients who may not use the internet".

"It should be standard practice for pharmacies to give printed CMIs when dispensing prescription medicine," Ms Wells said.

"Both doctors and pharmacists should ensure patients receive simple, clear and accurate advice, preferably on paper."

The CHFA has previously called for warning labels to be mandated on the package of asthma medicine Singulair, after dozens of families reported side effects including suicidal thoughts in children who had taken the drug.

Sydney University pharmacy professor Parisa Aslani, who specialises in medicine use optimisation, said patients must be given information they could understand, whether inside the box, printed out or online.

"My biggest push is can we make this document user friendly and understandable, that people want to access," Professor Aslani said, citing Australian Bureau of Statistics data showing that 60 per cent of Australians had poor to low health literacy.

"There's no point trying to force health professionals to give out the current document – it's not going to be understood."

She said many CMIs, which could run into seven pages, were too long and complicated, making patients unlikely to read them even if they were provided in paper form.

Communication Research Institute chief executive David Sless agreed, saying the documents did not "invite reading". Professor Sless, who worked on the design of CMIs in the 1990s, said Australia had once led the world in medicine communications but had "gone to the back of the class", with the documents "designed for something that is basically one up from a typewriter". "It's a bit of a national disgrace," he said.

Australian Medical Association president Tony Bartone said CMIs were "too dense, too confusing, too non-user-friendly". "It's hard to find the information you're looking for, unless you read the whole lot," Dr Bartone said. "The information should be available, but it's got to be in a much more manageable and concise framework."

He said high-tech solutions should be explored, such as a barcode on packets that could be scanned using a mobile phone app.

Pharmacy Guild of Australia spokesman Greg Turnbull said the organisation supported "maximum patient empowerment and health literacy" but that making the issuing of a CMI mandatory "for every one of the 300 million-plus PBS scripts per year might not be the best solution".

"One size does not fit all," Mr Turnbull said.

"Pharmacists exercise their professional judgement and clinical discretion in determining the best way to inform patients of what they need to know, always in the patients' best interest."

A spokeswoman for Mr Hunt said written information to help patients taking prescription medicines "should be readily available when the medication is bought from the chemist". "This is a TGA requirement," the spokeswoman said.

"The minister encourages patients to talk to their health care professional about their prescription medication.

"[He] will also be writing to the Pharmacy Guild and the AMA to reaffirm existing responsibilities."

Wentworth MP Kerryn Phelps, who is a Sydney GP, said patients should ask their doctor for information about any new medications, as well as revisiting the CMI for any medications they are already taking to check for drug interactions.

Again, how is a letter to pharmacists appropriate in addressing serious consumer concerns?

2.4 PHARMACY TRIAL PROGRAM

The Australian Government is investing $50 million to support a Pharmacy Trial Program, which seeks to "improve clinical outcomes for patients and utilise the full scope of a pharmacist's role in delivering primary health care services. These include **medication management programs** and patient support services focusing on pain management, diabetes, mental health and **reducing medicine induced deterioration and adverse reactions**."[253]

This report has raised serious questions about the conduct of pharmacies to provide safe advice to consumers. The trial program should not be allowed to go ahead until a review of their current performance is undertaken.

2.5 TGA'S OPIOID CONSULTATION PROGRAM

In 2018, the TGA commenced a consultation process to prepare a new range of regulatory responses to the growing issues surrounding opioid drugs. A consultation paper (see Figure 32) was released to encourage discussion about regulatory options for opioid use and misuse.

Figure 32: TGA's 2018 consultation paper cover

253 Australian Government Department of Health Therapeutic Goods Administration, *Improved medicines information for consumers*, media release, 26 July 2019.

Here are some excerpts from the consultation paper:

"This paper will examine the issues around prescription opioid use and misuse in Australia and explore options for a regulatory response to any issues identified"

Can some of the problems with opioids potentially be addressed – at least in part – through regulatory measures?

There seem to be six, interrelated main outcomes and/or drivers of opioid overuse:

- *overdose resulting in morbidity or mortality*
- *tolerance, requiring higher doses of product being required to achieve analgesia, but with accompanying increases in adverse effects (including potential addiction)*
- *addiction, including following tolerance and through use at prescribed rather than excessive levels*
- *deliberate abuse, encompassing use of high doses of immediate release opioids and manipulation of 'abuse deterrent' dose forms*
- *overuse or inappropriate use*
- *diversion of legally-prescribed product to others for abuse purposes.*[254]

The consultation paper shows:

1. The TGA was aware of the issues around the lack of life-threatening warnings in CMIs. Instead of urgent action to warn consumers, the TGA embarked on a lengthy consultation process.
2. The TGA identified the issue of risks are being disclosed in the PI (that doctors use) that are not disclosed in the CMI (for consumers).
3. The TGA identified the availability issues surrounding the CMI (i.e. it is not mandatory).

All of these areas relate to information that has a life-threatening impact on consumers.

2.5.1 Options considered

The TGA identified the issue of addiction and tolerance at prescribed doses (not misuse/abuse). The paper gives a range of options, with option 5 being of particular importance as it relates to the warnings provided in the CMI (see Figure 33).

"An analysis of the TGA's role and powers under the Therapeutic Goods Act 1989 and Regulations indicates that the TGA ***could*** *implement particular measures that relate to the indications for opioid products (that is the approved circumstances in which the medicine can be prescribed), the pack sizes available, and* ***ensuring comprehensive information*** ***in the Product Information (PI) and Consumer Medicines Information (CMI) regarding the risk of dependence, addiction and the potential for misuse or abuse.****"*

"The consumer warnings in the CMI ***could*** *be updated to more clearly advise that opioids are not generally recommended for long-term use in chronic non-cancer pain, and acute treatment should be limited to a few days and then pain managed by non-opioid medication.* ***The CMI could also include information about the risks of overdose associated with high doses of opioids. While the TGA does not approve the CMI it should mirror the information in the PI, therefore ensuring the PI has***

254 Australian Government Department of Health Therapeutic Goods Administration, *Prescription strong (Schedule 8) opioid use and misuse in Australia – options for a regulatory response consultation paper V1.0*, January 2018, p9.

the correct information about the risks and appropriate use of opioids would ensure it was mirrored in the CMI. *Work is necessary to make sure the CMI remains consistent with the PI, as is currently required, but also* ***to make both the PI and CMI much more readily available****. The TGA has recently launched the Medsearch App which allows consumers and HCP to readily access PI and CMI information from their mobile phone to assist in easy access to this information."*

Figure 33: Review of label warnings option (Source: TGA[255])

Option 5: Review of label warnings and revision to the Consumer Medicines Information

For consideration

The option: Under this option, warnings could be placed on the packaging of opioid products identifying the risk of dependence and overdose and lack of efficacy in the long term treatment of chronic non-cancer pain, noting that the complexity of appropriate management of chronic non-cancer pain needs to be recognised. The CMI would also be reviewed to provide greater emphasis on risks of dependence, especially those associated with high doses.

Potential implementation: This may be able to be achieved through modification to the current Therapeutic Goods Order around prescription medicines (TGO 91), although changes to appendices to the Poisons Standard (Scheduling) and to conditions of registration of new strong (S8) opioids could also underpin this requirement. We would need to work with sponsors to obtain CMI changes. It would need to be determined whether S4 opioids such as tramadol would be included in this scheme.

2.5.2 TGA actions from consultation process

Following the consultation process, the TGA released information on their 'Prescription opioids hub' website outlining their upcoming changes to reduce harm:

Following the initial consultation, the TGA established the Opioid Regulatory Advisory Group (ORAG), which includes representatives from a range of health professional and consumer organisations, to provide independent, expert advice. ORAG has strongly supported the proposed options and provided advice on how best to implement them.

Several reviews and activities arose from the consultation. As a result:

- ***Smaller pack sizes will be available for immediate-release prescription opioid products.*** For example, following a minor procedure you may currently be given a packet containing a week's worth of opioids when you would usually only need to take them for two or three days. The unused opioids subsequently circulating in the community may be used in harmful or hazardous ways, either inadvertently or deliberately, or become targets for theft.

255 ibid, p17.

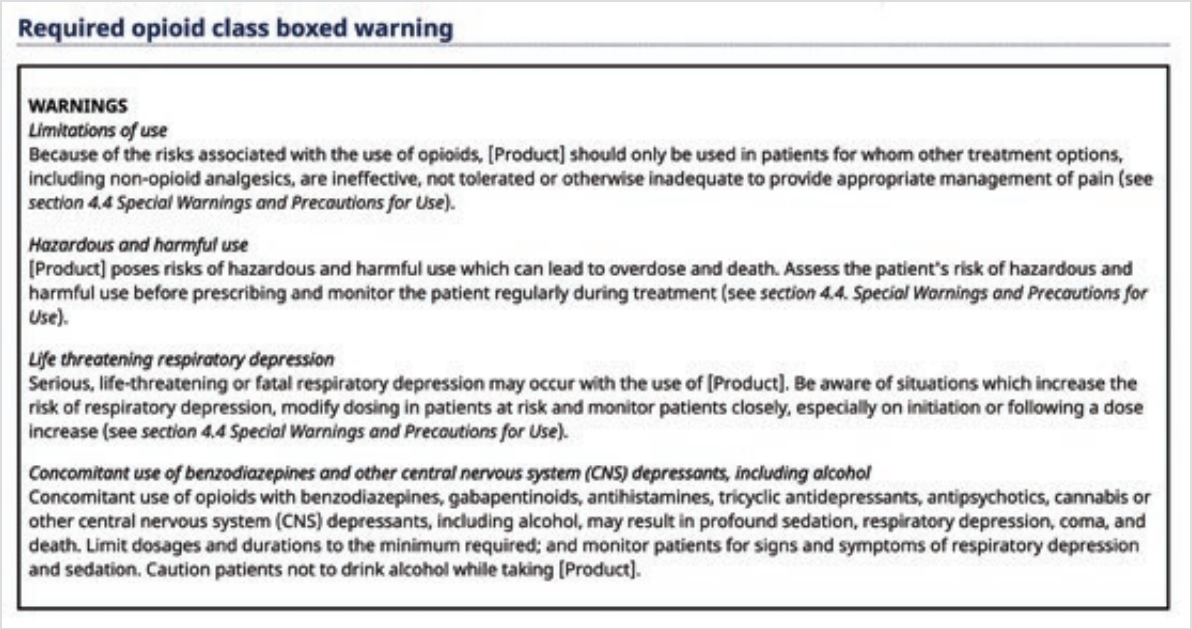
- ***We will require that sponsors include*** boxed warnings and class statements ***in*** *the Product Information (PI) documents for all prescription opioids in relation to their potential for harmful and hazardous use. These documents provide information for health professionals about medicines and their appropriate use.*
- *We will work with sponsors to ensure that safety information, including the relevant warnings, is prominently displayed in the Consumer Medicines Information (CMI) to ensure consistency of language and information across all classes of prescription opioids. These documents provide important information for consumers about medicines.*
- *The indications, which outline (the appropriate circumstances for use of a medicine), in the PI documents for immediate release (only for short-term management of severe pain) and modified release products will reinforce that opioids should only be used when other analgesics are not suitable or have proven not to be effective. In the case of modified release products, they should also only be used where the pain is opioid-responsive and the patient requires daily, continuous, long-term treatment. Modified release opioids are not indicated to treat chronic non-cancer pain (other than in exceptional circumstances), or to be used for 'as-needed' pain relief. Hydromorphone and fentanyl modified release products should also not be used in opioid naïve patients (patients who do not already use opioid medicines regularly).*
- *Fentanyl is one of the strongest opioids available in Australia. In recognition of the increased potential for harmful and hazardous use, the indication for fentanyl patches will be updated to state they should only be prescribed to treat pain in patients with cancer, patients in palliative care and those with exceptional circumstances. They should also only be used where other analgesics are not suitable or have proven not to be effective, and where the pain has been found to be opioid-responsive. The pain should be severe enough to require daily, continuous, long-term opioid treatment. The patches are not for use in patients who are opioid naïve (not already tolerant to opioids).*
- *We will be communicating the changes to both prescribers and consumers using a range of channels to ensure health professionals follow best prescribing practice and consumers are fully informed how best to use opioids.* ***We have already begun to encourage consumers to return unwanted opioids to pharmacies for destruction by distributing prescription covers with relevant messaging to every pharmacy in Australia as well as via various social media activities.***[256]

In December 2019 the TGA provided a sample of the opioid class boxed warning that will be included in the new PI documents. It includes warning that, "serious, life-threatening or fatal respiratory depression may occur". It also warns of the risk of "profound sedation, respiratory depression, coma, and death" when combining opioids with other medication like benzodiazepines, antidepressants, antipsychotics and alcohol (see Figure 34).[257]

256 Australian Government Department of Health Therapeutic Goods Administration, accessed on 19 December 2019, see https://www.tga.gov.au/alert/prescription-opioids-hub

257 Australian Government Department of Health Therapeutic Goods Administration, published on 19 December 2019, see https://www.tga.gov.au/opioids-boxed-warning-and-class-statements

Figure 34: Boxed warning statement



Required opioid class boxed warning

WARNINGS

Limitations of use

Because of the risks associated with the use of opioids, [Product] should only be used in patients for whom other treatment options, including non-opioid analgesics, are ineffective, not tolerated or otherwise inadequate to provide appropriate management of pain (see *section 4.4 Special Warnings and Precautions for Use*).

Hazardous and harmful use

[Product] poses risks of hazardous and harmful use which can lead to overdose and death. Assess the patient's risk of hazardous and harmful use before prescribing and monitor the patient regularly during treatment (see *section 4.4. Special Warnings and Precautions for Use*).

Life threatening respiratory depression

Serious, life-threatening or fatal respiratory depression may occur with the use of [Product]. Be aware of situations which increase the risk of respiratory depression, modify dosing in patients at risk and monitor patients closely, especially on initiation or following a dose increase (see *section 4.4 Special Warnings and Precautions for Use*).

Concomitant use of benzodiazepines and other central nervous system (CNS) depressants, including alcohol

Concomitant use of opioids with benzodiazepines, gabapentinoids, antihistamines, tricyclic antidepressants, antipsychotics, cannabis or other central nervous system (CNS) depressants, including alcohol, may result in profound sedation, respiratory depression, coma, and death. Limit dosages and durations to the minimum required; and monitor patients for signs and symptoms of respiratory depression and sedation. Caution patients not to drink alcohol while taking [Product].

Other warnings the TGA has highlighted in opioid PIs include:

> *"[Product] contains the opioid [active ingredient] and is a potential drug of abuse, misuse and addiction. Addiction can occur in patients appropriately prescribed [Product] at recommended doses."*
>
> *"The development of tolerance and physical dependence and risks of adverse effects, including hazardous and harmful use, increase with the length of time a patient takes an opioid."*
>
> *"Serious, life-threatening or fatal respiratory depression can occur with the use of opioids even when used as recommended. It can occur at any time during the use of [Product] but the risk is greatest during initiation of therapy or following an increase in dose."*

This majority of this information was already contained in the previous PI documents. The new PI highlights existing risks, rather than identifying new ones. However, this report has identified numerous CMIs in which these risks have not been included. Unfortunately, the TGA website did not release what new information would be included in the 'improved' CMIs. Consumers will have to wait to see if these warnings will be made available to them.

The TGA has deemed these various actions as "improvements to information for prescribers and patients [to] encourage best-practice prescribing and help consumers to be better informed about the potential risks and how to mitigate them".

Will the actions help consumers to be better informed about the **potential risks and how to manage them?**

The acknowledgement by the TGA on undisclosed risks supports the argument in Chapter 5 that patients have not been given the opportunity to give informed consent.

The USA made changes to restricting the use of opioids and Fentanyl over 10 years ago. Patients in Australia have been prescribed these drugs in circumstances where the TGA now deems the drug's use inappropriate. What measures are being taken to identify who those patients are and if they have suffered from adverse drug reactions? What action is being taken to identify people who have been adversely impacted by all the adverse drug events that were not previously included in warning documents?

The urgency of the actions is also far from ideal given these prescription medications are taking lives **now** (see Figure 35).

Figure 35: Q&A from the TGA website (Source: TGA)


When will these changes come into effect?

It is anticipated that the first of the smaller pack sizes will be registered from January 2020. The fentanyl indication changes came into effect in the first half of 2020. Due to the large number of opioid products on the Australian market the other changes will be phased in.

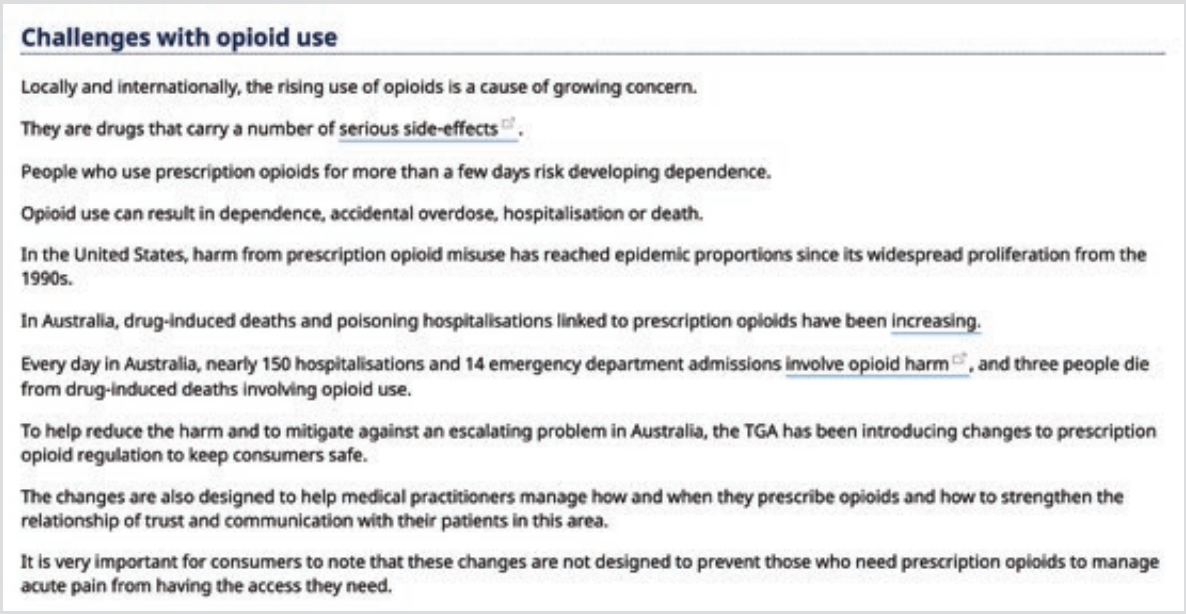
In a July 2019 media release[258], the Australian Government committed to:

- *introducing an **improved format** for CMIs that doctors and pharmacists give to patients to inform them about the safe and effective use of prescription medicines and certain over-the-counter medicines*
  - this statement fails to mention it is not mandatory to give the CMI and this issue has not been addressed
- *… in response to concerns raised by doctors, pharmacists and consumer health advocates regarding the complexity and readability of such documents.*
  - This statement fails to mention the absence of life-threatening risks that the TGA has identified as being a reason for the changes. It also does not make consumers aware of the risks that are now being disclosed, a critical FYI for people currently taking the medication.
- *The new template for the documents is shorter, better laid-out and features a one-page summary that succinctly provides people with the most critical information relating to the safe and effective use of their medicines. The format was user-tested and received excellent feedback from participants. The overwhelming majority of people preferred the new format, finding it easier to use and understand.*
- *The new template also received unanimous support from doctor, pharmacist, industry and consumer representatives, who were consulted as part of this project.*
- *Given there are several thousand CMIs, there will be a transition period as the various medicine companies progressively revise their materials. The Government will update relevant regulations later this year to clarify and standardise the CMI requirements and will continue consulting with medicine companies regarding implementation details.* ***It is important to acknowledge that useability of CMI will continue to heavily rely on the quality of the content produced by the medicine companies who are responsible for these products.***

258 Australian Government Department of Health Therapeutic Goods Administration, *Improved medicines information for consumers*, media release, 26 July 2019.

- The TGA has failed to prioritise the urgency around updating the CMIs for Schedule 4 and 8 drugs. These are warnings that are around life-threatening risks, yet the delivery has no urgency. The TGA also fails to address the reliance on pharmaceutical companies being the sole organisation responsible for disclosures of drug risks in the CMI.
- Any information that is now being recognised as a significant risk needs to also be assessed in relation to past overdose mortality and morbidity. The TGA cannot be allowed to simply update warnings without recognising that these drugs have been prescribed for over 20 years and have had a significant impact on poor health and deaths.
- Will a program be implemented to contact ALL existing users of these medications to inform them of the risks that are now in the CMIs? The TGA's own website states that "**people who use prescription opioids for more than a few days risk developing dependence**" and clearly expose the risks (see Figure 36).[259]

Figure 36: Challenges with opioid use from the TGA website



Challenges with opioid use

Locally and internationally, the rising use of opioids is a cause of growing concern.

They are drugs that carry a number of serious side-effects.

People who use prescription opioids for more than a few days risk developing dependence.

Opioid use can result in dependence, accidental overdose, hospitalisation or death.

In the United States, harm from prescription opioid misuse has reached epidemic proportions since its widespread proliferation from the 1990s.

In Australia, drug-induced deaths and poisoning hospitalisations linked to prescription opioids have been increasing.

Every day in Australia, nearly 150 hospitalisations and 14 emergency department admissions involve opioid harm, and three people die from drug-induced deaths involving opioid use.

To help reduce the harm and to mitigate against an escalating problem in Australia, the TGA has been introducing changes to prescription opioid regulation to keep consumers safe.

The changes are also designed to help medical practitioners manage how and when they prescribe opioids and how to strengthen the relationship of trust and communication with their patients in this area.

It is very important for consumers to note that these changes are not designed to prevent those who need prescription opioids to manage acute pain from having the access they need.

2.6 TGA'S RETURN YOUR UNUSED OPIOIDS CAMPAIGN

Another TGA campaign kicked off in July 2019 to encourage people to return unused prescription opioids to the local pharmacy. As stated in the media release:

> *Nearly 150 people are hospitalised in Australia every day as a result of the adverse effects of opioid pain medicines. In a concerted effort to reduce this—and opioid-related dependence, illnesses and cases of misuse—the* ***Therapeutic Goods Administration (TGA) is urging Australians to return unused prescription pain relief medicines to their local pharmacy.***

259 Australian Government Department of Health Therapeutic Goods Administration, published on 18 November 2019, see https://www.tga.gov.au/community-qa/prescription-opioids-information-consumers

Australians who are prescribed painkillers and don't use them all are advised not to keep them 'just in case' or for use down the track. ***Keeping unused prescription pain medication in the home is dangerous for children and pets if accidently consumed, and can be a target for theft and misuse. Unused pain relief medication, like all medicines, can be returned to a local pharmacy for safe disposal free of charge.***

The TGA is rolling out a social media campaign and working directly with pharmacies to promote this service. This is an important aspect of work being taken by the TGA to reduce the potential adverse impacts of opioids on the health of Australians.[260]

The TGA program delivers the information via number of methods, including a resource kit and a cartoon series on Facebook (see Figure 37 and Figure 38).

Figure 37: The TGA's Facebook page promotion (Source: TGA Facebook page, August 2019)

260 Australian Government Department of Health Therapeutic Goods Administration, *Return unused prescription opioids to your local pharmacy*, media release, 11 July 2019.

As noted in Figure 34, the TGA states that opioids are addictive. Yet many CMIs stored on the TGA website have misleading statements about the risk of opioid addiction, and downplay the risks. The TGA also states that opioids can have serious interactions with other medicines. However, it doesn't tell people what medicines these are. It also doesn't require drug interaction warnings to be present in the CMIs it stores on the same website.

Figure 38: Extracts from the TGA's 'return your opioids' campaign (Source: TGA Facebook page, August 2019)

In Figure 38, the TGA's cartoon illustrates the image of a youth removing an opioid from a medicine cabinet.

First, the opioid CMIs **do not contain any warnings on the fatal risk to kids**.

Second, putting this cartoon on Facebook enables the information to be easily accessible by young people (such as teenagers) who may be seeking to do this exact thing.

Third, this cartoon-styling of the video series significantly reduces the likelihood of people taking the message seriously. Using a cartoon reduces the chance that people will understand the gravity of the risks involved. Similarly, some of the messaging (as shown in Figure 39) is completely insensitive, inappropriate and irrelevant.

If the government buys back guns that kill people, it should buy back the opioids too. Again, the action is left up to the consumer, who may not be fully aware of the risks.

Figure 39: The TGA's Facebook page promotion (Source: TGA Facebook page, August 2019)

> If you are communicating to adults using cartoon images and simple little cutesy figures that fall over, it doesn't speak to the level of risk. It simplifies it and it trivializes it. I think those are all important messages. They're all important messages for these kinds of medicines. But presenting them in this way, I don't think is a very effective way to present them to adults. I don't know a lot of adults who watch cartoons on a daily basis. I don't know a lot of adults that would respond with the appropriate kind of attention to something that just seems like cute little figures walking by. Drug overdoses and dying aren't to be made fun of. They're not things that you want to just show in a cute way. That cartoon image is a cartoon image of somebody taking a medicine from somebody sitting next to them and then, plop, falling over, like, in a cartoon. It doesn't instill any sort of fear of the drug risks. It loses the message. It dilutes the message. It trivializes the seriousness of it. And it makes death seem like something funny. It's not what we want for people.

– Dr Lori Calabrese

2.6.1 A comparison to the USA Government's opioid return campaign

In comparison, the Centers for Disease Control and Prevention (CDC) in the USA use real stories to deliver hard-hitting opioid awareness campaign messages. In one of their real stories, Ann Marie (see Figure 40) explains the real cost of opioid addiction, reflecting the gravity of the message. Here is the transcript:

On-screen text: Prescription opioids can be addictive and dangerous.

Ann Marie: My son, Christopher Perrotto, was 20 years old when he was prescribed opioids.

Audio description: Ann Marie shows a locket with a photo of her son.

Ann Marie: It took him five days to get addicted. I'm not supposed to be the one to go get his suit and tie and pick which sneakers that I'm going to bury him in.

Audio description: Ann Marie shows a framed photo of her son Christopher.

On-screen text: It only takes a little to lose a lot.[261]

Figure 40: An extract from the CDC's opioid awareness campaign (Source: CDC.gov)

261 Centers for Disease Control and Prevention, accessed on 3 April 2020, see https://www.cdc.gov/rxawareness/stories/annmarie.html

2.7 REAL TIME PRESCRIPTION MONITORING

According to the AIHW, the policies aimed at **reducing the supply** of pharmaceutical drugs for non-medical use in Australia, include:

- *agreement to develop a national real-time prescription monitoring system*
- *the up-scheduling of codeine so that it is available as a prescription-only medication.*[262]

A national real time prescription monitoring (RTPM) system is said to:

- provide information to prescribers and pharmacists about a patient's use of controlled medicines when they are considering prescribing or supplying these medicines
- help reduce misuse and make sure that patients who genuinely need these medicines can still get them
- identify patients who are at risk of harm due to dependence or misuse of controlled medicines
- identify patients who may be diverting these medicines
- limit 'doctor shopping' — when people go to several doctors for prescriptions of a controlled medicine
- provide state and territory regulators with data to detect prescribers who are not complying with regulations
- produce real-time alerts and information for health professionals and state and territory regulators.[263]

2.7.1 The reality of doctor shopping

The system provides a flag when people fill a prescription. This system is largely focused on stopping supply for patients who are attempting to abuse medication. The practice it seeks to stop is called 'doctor shopping', which is obtaining multiple prescriptions for dangerous medications from different doctors. The theory is that by implementing a system that flags any unusual levels of prescriptions for Schedule 8 or 4 drugs, the pharmacist or doctor can intervene to stop the person accessing the medication.

Yet doctor shopping – even according to some GPs – is not the problem. Findings from the Victorian Coroners Court show that in seven out of 10 pharmaceutical drug overdose deaths, the deceased had only been to see one GP.

As noted in an ABC article in 2017:

> *Health and pain management experts, outspoken GPs, addictions counsellors and grieving family members have told The Law Report the doctor-shopping narrative has served to disguise what lies at the heart of the issue: a medical system that structurally supports problematic prescribing practices.*
>
> *"We often think of people going from doctor to doctor, and they're often [the cases] that get a lot of prominence," Matthew Frei, clinical director at the Turning Point Alcohol and Drug Centre, said.*
>
> *"But I'm sorry to say, it's individual doctor prescribing that's the issue. In most of the deaths, doctor shoppers are not the issue."*[264]

262 AIHW, 2020.

263 Australian Government Department of Health, published on 24 December 2019, see https://www.health.gov.au/initiatives-and-programs/national-real-time-prescription-monitoring-rtpm

264 J Story Carter, *Opioid prescription crisis: Everyday Aussies, not 'doctor shoppers', at heart of crisis, experts say*, ABCNews, 21 November 2017.

A 2017 report into Victorian overdose deaths made some stunning findings:

> *"Importantly, in most cases (74%) the drugs are prescribed by a single prescriber rather than multiple prescribers."*
>
> *"One of the most striking findings of this study relates to the source of drugs involved in overdose deaths. While there is a perception that pharmaceutical drug harm is fuelled by drug diversion and doctor shopping, the evidence indicates that in the majority of cases, the drugs involved in overdose deaths are prescribed by a single prescriber."*[265]

The theory of doctor shopping has been put forward by government as part of their 'victim blaming' strategy – with abuse and misuse promoted as the core reason for prescription medication deaths. RTPM is the proposed strategy to reduce supply and thus reduce prescription medication overdose deaths.

While doctor shopping and medication abuse is certainly an issue that needs to be addressed, is it as significant an issue as the other factors raised in this report?

2.7.2 Reducing accidental deaths

Despite the RTPM being focused on reducing **overdose and accidental death** from controlled medications like oxycodone and fentanyl, the system has **no functionality** to warn against side effects from polydrug interactions of these medications when used with other prescribed or over-the-counter medications. The system has been designed for abuse and misuse issues.

RTPM can have no impact on polydrug deaths as this is not part of the warnings of the system.

2.7.3 Delays on roll-out

In announcing the implementation of RTPM in 2017, Health Minister Hunt was forced to explain the delay in realising a national system:

> *The Morrison government has given the states until the end of the year to connect to a national monitoring system for powerful painkilling drugs to reduce the death rate from overdoses and avoid a US-style opioid crisis.*
>
> *Declaring he is "passionate" about reducing opioid-related harm, Health Minister Greg Hunt has sought to fast-track plans that would give GPs and pharmacists immediate information about a patient's use of addictive medication, such as Oxycontin or Endone, and other high-risk "schedule 8" drugs.*
>
> *Much of the delay has come down to each jurisdiction having fragmented software systems to track how pharmaceuticals are monitored. NSW, which has the highest rates of opioid-related deaths, does not even have the ability to monitor prescriptions in "real time" within its own state, nor does Western Australia. Victoria has its own tracking system, known as Safescript, and with Queensland is working to integrate its software into the Commonwealth's data framework. The ACT has already done so.*[266]

Why is a system that is supposed to be critical to saving lives be held up in implementation?

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265 J Dwyer, R Ogeil, L Bugeja, C Heilbronn, B Lloyd, Victorian overdose deaths: The role of pharmaceutical drugs and drug combinations, Turning Point, Victoria, February 2017, pp.14, 57.

266 F Tomazin, *Opioid crisis: Australian states told to act now or suffer a public health emergency*, *The Age*, 6 February 2020.

There are also discrepancies between the states:

> *One emerging issue is that Victoria's SafeScript system monitors both Schedule 8 controlled drugs, such as oxycodone and fentanyl, as well as prescription-only Schedule 4 drugs, which includes most benzodiazepines.*
>
> *By contrast, the proposed national system will only include Schedule 8 drugs. Tasmania's existing opt-in real-time prescription monitoring system, DORA (Drugs and Poisons Information System Online Remote Access), also only includes Schedule 8 drugs.*
>
> *That situation, Ms Mohamed said, is a major problem given many preventable deaths have occurred through mixing Schedule 8 with Schedule 4 drugs, such as combining oxycodone with benzodiazepines.*[267]

How can the Australian RTPM have significant gaps in Schedule 4 medication?

In contrast, the USA RTPM is called PMP Aware. All Schedule II to Schedule IV are included. This is the equivalent of all Schedule 4 and 8 medications in Australia including oxycodone (OxyContin), fentanyl, Dexedrine, Adderall, Xanax, Valium, Ativan, and Tramadol:

2.7.4 The ACT's system

A woman's accidental overdose and Coroner's enquiry resulted in a recommendation that all Schedule 3 and 4 drugs be included in the ACT's 'DORA' prescription monitoring system. As reported in *The Canberra Times*:

Ms Lauren Johnstone

> *ACT Chief Coroner Lorraine Walker recently determined Ms Johnstone's death was an accidental overdose as a result of taking her prescribed medication as instructed, and aggravated by over-the-counter medication her doctors were not aware of.*
>
> *She was discharged after one night and prescribed **endone** for pain.*
>
> *On her request, she was also prescribed her regular medications: imovane, valdoxan, tramadol and **valium**.*
>
> *[The doctor's] only warning to Ms Johnstone about the drugs was the risk of increased drowsiness as a result of combining the medications with endone.*[268]

The ACT's original DORA system covers Schedule 8 medications but not all Schedule 4 or other prescription medications. As a result of Ms Johnstone's death, the coroner recommended the ACT Health Minister declare tramadol, sleeping pill doxylamine and diazepam to be monitored drugs. She also suggested widening the scope of monitored medicines to include all Schedule 3 and 4 drugs, or, alternatively certain prescription and over-the-counter medications that may have significant sedating effects when taken in combination with opioids or benzodiazepines.

In response, the ACT Government has rejected the recommendation to widen the scope of monitored medicines to include all Schedule 3 (pharmacist only) and 4 (prescription only) drugs. Instead they will undertake a **consultation process in 2020** to determine

267 D Hendrie, *Why has a national real-time prescription monitoring system been delayed?*, NewsGP, 14 February 2019.
268 D White, *Accidental overdose leads to calls for changes to ACT's prescription monitoring system*, The Canberra Times, 15 July 2019.

which Schedule 4 medicines should be declared monitored medicines. The changes will be mandated when the ACT adopts a national real-time prescription monitoring system. This is due by June 2021.

The ABC reported that the **ACT Government also did not back the recommendation to mandate the use of DORA:** software that allows doctors and pharmacists to check patients' drug use. Instead, the use of DORA in Canberra has remained **voluntary**, with about **one in five prescribers and one in three pharmacists using it**.[269]

> The use of DORA by health professionals is not mandatory. However, all eligible prescribers and pharmacists are **urged** to use DORA as a new part of their clinical practice, with the aim of minimising potential harms.
>
> *– ACT Health*[270]

How can such a system be optional for pharmacists? Why is RTPM for dangerous Schedule 8 drugs optional for pharmacists who get paid a fee by the PBS to manage such dangerous drugs? It seems the system is important enough to implement but not important enough to mandate its use.

The national RTPM system is still a long way from being implemented and its fails to cover all prescription medications that can cause overdose deaths. As shown in the ACT, it lacks the commitment of the pharmacy network to implement it.

RTPM does nothing to warn Australians of the risk of becoming addicted so it won't stop people becoming addicted to prescription medication – it simply seeks to limit supply to those who already are addicted.

2.8 OPIOID RESCUE SPRAY

Naloxone hydrochloride is a drug that can temporarily reverse an opioid overdose. It works by blocking opioid drugs, such as heroin and oxycodone, from attaching to opioid receptors in the brain. Naloxone has a fast onset of action and a short half-life. When administered in the presence of an opioid, it displaces the opioid at the receptor and reverses its effects – importantly respiratory depression, which can be fatal.[271]

In 2016, naloxone injection 400 microgram/mL became available as a Schedule 3 medicine, available over-the-counter (OTC) and on prescription. It is approved for intramuscular, intravenous and subcutaneous use in Australia, and has been used by ambulance and paramedical staff to treat overdose for over 40 years. A nasal spray version is now available on the PBS.

269 T Maddocks, *Accidental overdose victim's daughter calls for mandatory scheme to stop dangerous drug sales*, ABCNews, 13 February 2020.

270 ACT Health, accessed on 3 April 2020, see https://www.health.act.gov.au/health-professionals/pharmaceutical-services/real-time-prescription-monitoring

271 M Jauncey, S Nielsen, 'Community use of naloxone for opioid overdose', *Australian Prescriber*, Issue 4 August, DOI: 10.18773/austprescr.2017.043, 1 August 2017.

According to a Public Summary Document from a March 2019 PBAC Meeting, Naloxone is the only approved antidote to opioid overdoses. It is demonstrated to be effective and safe to use with very low abuse potential and has an established history of use.[272]

2.8.1 USA version: Narcan

NARCAN® (naloxone HCl) Nasal Spray is the "first and only FDA-approved nasal form of naloxone for the emergency treatment of a known or suspected opioid overdose. It is a nasal formulation of Naloxone hydrochloride which is administered as a nasal spray. NARCAN® Nasal Spray counteracts the life-threatening effects of an opioid overdose. Since most accidental overdoses occur in a home setting, it was developed for first responders, as well as family, friends, and caregivers—with no medical training required."[273]

The website states that:

> *an opioid overdose happens when the body has been overloaded with either a medication or an illicit drug. Because they affect the part of the brain that controls breathing, if opioid levels in your blood are too high, your breathing can slow down to dangerous levels, which could even cause death.*
>
> *Examples of opioids are morphine, codeine, oxycodone, oxycodone + acetaminophen, and hydrocodone + acetaminophen.*
>
> *If there are prescription opioids in your home, NARCAN® Nasal Spray should be there, too.*[274]

2.8.2 Australian version: Nyxoid

Purdue–Mundipharma who manufacture OxyContin and Targin, have developed a version of Narcan called Nyxoid. It was approved by the TGA in 2018. The Health Minister Greg Hunt announced that Nyxoid® (naloxone 1.8mg) nasal spray has been registered in Australia as an antidote to opioid overdose. I November 2019 Greg Hunt announced it would be placed on the PBS.

According to the Nyxoid CMI dated September 2018:

> *Naloxone belongs to a group of medicines that cause temporary reversal of the effects of opioids such as methadone or heroin.*[275]

The CMI for Nyxoid does not mention oxycodone, OxyContin or Targin once. Oxycontin and Targin are opioid medications made by Purdue–Mundipharma, that can cause an opioid overdose.

The Purdue–Mundipharma Oxycontin and Targin CMIs do not mention using Nyxoid as an emergency treatment option if a person has an overdose.

Yet the Nyxoid CMI mentions 'opioid overdose' six times.

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272 Australian Government Department of Health, The Pharmaceutical Benefits Scheme (PBS), Public Summary Document (PSD) March 2019 PBAC Meeting, March 2019.

273 Narcan, accessed on 3 April 2020, see https://www.narcan.com/

274 ibid.

275 Mundipharma, Nyxoid Consumer Medicine Information, September 2018.

Essentially, the CMI for the opioids are almost silent on the risk of overdose, but the rescue spray discusses the very real risks of overdose and therefore the need for Nyxoid.

Interestingly the Nyxoid PI dated September 2018 states:

- No clinical trials have been conducted with Nyxoid. Efficacy has been inferred based on pharmacokinetic studies.
- No interaction studies with other medications have been performed with Nyxoid.
- A list of rare but serious side effects that are not mentioned in the CMI, including anaphylactic shock, seizures, and cardiac arrest.[276]

Nasal formulations of Naloxone hydrochloride having proven to be a very effective way to reduce deaths from overdoses. Making a version of this product widely available is a good strategy to assist to reduce overdose deaths. **However, how is Mundipharma allowed to profit from selling a medication that exists due to the life-threatening side effects of its opioid medications?**

3. PRESCRIPTION MEDICATION GOVERNMENT ACTION MISSES THE MARK

Action has been taken to try and stop the needless loss of life from overdose deaths.

However, the Australian Government goes to great lengths to enforce this narrative of 'misuse and abuse' and 'victim blaming' in government policy. It provides a neat cause and effect link that all prescription medication deaths are caused by abuse and misuse, without any serious examination of other alternative reasons for these adverse events.

A national RTPM and requiring a prescription for codeine medication are presented as responses to abuse and misuse. These are their frontline strategies to reduce overdose deaths. Yet these strategies rarely place any responsibility for overdose deaths on the health care system.

Even when the Health Minister states that his strategies are 'strong steps', the results of this chapter tell a different story.

> *"I can't speak for the past," says Greg Hunt, who became the federal Health Minister in 2017. "I can speak for my watch and my time where this has been one of my absolute priorities, which is why we've taken such strong steps. ... My focus has been to make sure that we don't have an American-style crisis."*[277]

276 Mundipharma, Nyxoid Nasal Spray Product Information, August 2018.
277 Associated Press, Australia faces opioid crisis as companies push drugs abroad, *Los Angeles Times*, 9 May 2019.

How can sending warning letters to doctors who overprescribe medication and to pharmacists who fail to provide medication safety warnings, constitute 'strong steps'. Warning letters are a hollow attempt to stop overdose deaths.

The government's strategies do not cover a number of actions that are occurring in the USA in response to their crisis:

- legal action against doctors and pharmacists who overprescribe
- legal action against pharmaceutical companies for failure to warn patients (see Chapter 8)
- compensation for the victims (see Chapter 8)
- enhanced medication safety for consumers
- engaging with pharmaceutical companies to improve the safety of the existing medication
- trialling new treatments that have a higher level of safety.

The TGA Opioid review exposed systemic issues in all areas of medication regulation. Dangerously incomplete and misleading CMI documents are not being addressed fast enough, and uncertainty exists about how comprehensive the changes will be. The root cause of the CMI issues is that the content is left solely to the discretion of the pharmaceutical companies. This issue hasn't been resolved. More importantly consumers still have to request hard copies of CMI documents, even for dangerous Schedule 4 and 8 medications.

The TGA has stated that they have identified instances where dangerous warnings have not been included in the CMIs regarding the risk of dependence, addiction and the potential for misuse or abuse. They have also identified that warnings exist in the PI that have not been replicated in the CMI. Instead of treating this matter with the seriousness it deserves, referring it for legal investigation for breaches of safety standards, the TGA response is that, **"We will work with sponsors to ensure that safety information, including the relevant warnings is updated"**.[278]

This report has identified other issues that have not been acknowledged nor addressed. The lack of consumer warnings in other non-opioid medications is widespread. In-pharmacy advice failures – as shown in Chapter 4 – requires a considered and forceful response. Why has there not been more investigation into how vulnerable people became addicted in the first place? By failing to really listen, document and address the complaints of people with lived experience, the core problems have continually been overlooked and ignored. This report is a belated but significant move to change that.

While Greg Hunt may not view Australia's opioid problem as a crisis, many people do not share that view:

> It's time to call this what it is: Australia's very own overdose crisis. And make no mistake; it's a crisis that is getting worse.

– John Ryan, Chief Executive Officer of drug policy organisation, Penington Institute[279]

278 Australian Government Therapeutic Goods Administration, published 4 February 2020, see https://www.tga.gov.au/alert/prescription-opioids-hub

279 E Lewin, Australia's overdose crisis is 'getting worse', newsGP, 27 August 2019.

A few facts that seem to be lost in the Australian Government's responses:

- We have **the same American pharmaceutical companies** that created the USA crisis.
- The same drugs that killed 400,000 Americans in the USA Opioid Crisis are also **PBS medications** that these same companies distribute in Australia.
- The same American pharmaceutical companies are distributing the same **dangerously incomplete and misleading consumer warnings** that contributed to the USA Opioid Crisis.
- These medications are now the **leading cause of drug overdose deaths** in Australia.

There is no question that an American-style crisis exists. It was brought to Australia by the same architects of the USA crisis.

Read Chapter 8 to see how the American drug companies responsible for the US Opioid Crisis are distributing the same medications here in Australia.

Warning

Do not stop taking a prescribed medication without discussing it with your doctor. Information can also be obtained by calling the NPS Medicines Line on 1300 633 424 or the Adverse Medicines Events Line on 1300 134 237 for advice. If you need support for any medical concern, including mental health matters, please contact your doctor. Lifeline also provides a 24 hour support service on 13 11 14 or www.lifeline.org.au

7. TGA OPIOID RESPONSE

1. INTRODUCTION

In Chapter 6, we detailed some of the responses of the TGA to the opioid consultation process that commenced in 2018. Among the list of actions was a commitment to modify the existing CMI and PI documents to better reflect the risks of these medications.

They also committed to making these consumer warnings more accessible to consumers:

> *"We will work with sponsors to ensure that safety information, including the relevant warnings, is prominently displayed in the Consumer Medicines Information (CMI) to ensure consistency of language and information across all classes of prescription opioids. These documents provide important information for consumers about medicines."*[280]

In October 2019 the TGA posted a blog titled, *Not so much TMI as CMI: empowering consumers with clear, accessible information about their medicines*. It suggested,

> *"And in the world of medicine, credible, factual and reliable information carries even more weight – sometimes, a matter of life and death. Better informed health consumers get better health outcomes for themselves and their families."*

The blog finished with the statement:

> *"New improved CMIs are coming – simpler, clearer, more accessible. We need more people to know more about CMIs – because the more you know, the more empowered you are to manage your medicines to reduce risks and maximise their benefits."*[281]

The blog contained no information about the content that is being updated in terms of actual risks to consumers.

2. CMI UPDATES

The TGA identified that Fentanyl would be the first CMI updated in 2020 for consumers, with other opioids like Endone, Targin and OxyContin to follow.

In February of 2020, Janssen updated its CMI for Durogesic. As at 10 April 2020, the TGA website or social media channels contained no information for users of Fentanyl advising that a new CMI had been made available. Janssen had yet to provide an update on its website, social media or news network.

280 Australian Government Department of Health Therapeutic Goods Administration (TGA), updated on 4 February 2020, see https://www.tga.gov.au/alert/prescription-opioids-hub

281 Australian Government Department of Health Therapeutic Goods Administration (TGA), *Not so much TMI as CMI: empowering consumers with clear, accessible information about their medicines*, blog, 3 October 2019.

2.1 DUROGESIC CMI UPDATE IN FEBRUARY 2020

We have conducted an analysis of the CMI Janssen updated and released in February 2020 (see extract at Figure 41).

Importantly the CMI has been modified to reflect the risk of death in over 10 key areas. The risk of addiction has been changed from being unlikely if taken as prescribed to being a risk even if you take it as prescribed.

This is an enormous admission of the true risk of addiction and the misinformation that the previous CMIs contained. The new 'shorter' CMI has gone from five pages to seven pages.

Benzodiazepines are mentioned in the CMI for first time since its release in 1999. The risk of death in combination with benzodiazepines is mentioned on three separate occasions.

However, the TGA's current focus in only opioid medications, so the current CMIs for benzodiazepines have not been updated to reflect this polydrug risk.

Durogesic is patch that is applied to the skin every three days (72 hours). The patch releases a continuous amount of the fentanyl medication, that is absorbed through the skin. This statement on page 3 has been deleted, indicating it was deemed inappropriate advice for consumers:

> *If your pain continues, see your doctor who may prescribe additional medicines to help control the pain or change the dose of DUROGESIC. Your doctor may advise you initially to change the patch every two days (48 hours) instead of every three days (72 hours) to achieve adequate pain relief.*

The opioid rescue spray, Nyxoid is still not mentioned, despite the need to reduce opioid deaths being the driving reason for the changes. The CMI has a new box on the first page that highlights the key risks of Durogesic (see Figure 41). Yet the document has no notification on the first page that it is a **new updated document** with new warnings included, nor is the date listed.

Despite the significant changes to the CMI, neither the TGA, The Pharmacy Guild nor the Pharmaceutical Society of Australia (PSA) have implemented a mandatory issuing of the CMI for all repeat prescriptions or new prescriptions.

The CMI includes the statements to "Keep this leaflet with your medicine. You may need to read it again" (on page 1) and "When seeking medical attention, take this leaflet and remaining medicine with you to show the doctor. Also tell them about any other medicines or alcohol which have been taken" (on page 4), yet consumers still will have no automatic receipt of the document to keep.

In practice, there is not a single change to the existing process that would see an existing or new patient be given the new CMI nor made aware of what is new in the document.

Figure 41: Updated Durogesic CMI, 2020

DUROGESIC®

Transdermal System

Fentanyl

Consumer Medicine Information

WARNING

Limitations of use
DUROGESIC should only be used when your doctor decides that other treatment options are not able to effectively manage your pain or you cannot tolerate them.

Hazardous and harmful use
DUROGESIC poses risks of abuse, misuse and addiction which can lead to overdose and death. Your doctor will monitor you regularly during treatment

Life threatening respiratory depression
DUROGESIC can cause life-threatening or fatal breathing difficulties (slow, shallow, unusual or no breathing) even when used as recommended. These problems can occur at any time during use but the risk is higher when first starting DUROGESIC and after a dose increase, if you are older, or have an existing problem with your lungs. Your doctor will monitor you and change the dose as appropriate.

Concomitant use of benzodiazepines and other central nervous system (CNS) depressants, including alcohol
Using DUROGESIC with other medicines that can make you feel drowsy such as sleeping tablets (e.g. benzodiazepines), other pain relievers, antihistamines, antidepressants, antipsychotics, gabapentinoids (e.g. gabapentin and pregabalin), cannabis and alcohol may result in severe drowsiness, decreased awareness, breathing problems, coma and death. Your doctor will minimise the dose and duration of use; and monitor you for signs and symptoms of breathing difficulties and sedation. You must not drink alcohol while using DUROGESIC.

What is in this leaflet

This leaflet answers some common questions about DUROGESIC patches. It does not contain all the available information. It does not take the place of talking to your doctor or pharmacist.

All medicines have risks and benefits. Your doctor has weighed the risks of you using DUROGESIC against the benefits this medicine is expected to have for you.

If you have any concerns about using DUROGESIC, ask your doctor or pharmacist.

Keep this leaflet with your medicine. You may need to read it again.

What DUROGESIC is used for

DUROGESIC is used for the long-term management of pain that is severe enough to require daily around-the-clock pain relievers, when other treatment options are not able to effectively manage your pain or you cannot tolerate them. DUROGESIC is only used in people who have previously been using other opioid-based pain relief. DUROGESIC is not used to treat pain that you only have once in a while.

DUROGESIC patches contain a medicine called fentanyl. This strong pain reliever belongs to a group of medicines known as opioid analgesics. Fentanyl relieves pain by blocking the nerves that recognise pain messages from the body.

Each patch is applied onto the skin every three days (72 hours). The patch releases a continuous amount of fentanyl that is absorbed through the skin in contact with the patch.

Ask your doctor if you have any questions about why this medicine has been prescribed for you.

Before you use DUROGESIC

Warning

Opioids can be abused and misused, and you are at risk for opioid addiction, even if you take

2.2 A COMPARISON BETWEEN OLD AND NEW CMIS FOR DUROGESIC (AUST) – FENTANYL

We compared consumer warnings publicly released by:

- Janssen (Australia) Version: 12/1999
- Janssen (Australia) Version: 08/2018
- Janssen (Australia) Version: 02/2020[282]

The breadth of the additional risks added in the February 2020 CMI in comparison to the earlier versions of the CMI highlight just how dangerously misled consumers have been for over 20 years.

The comparison shown in Table 17 is a horrific demonstration of how consumers have not been able to give informed consent as they simply have not been made aware of the material risks, and they have been provided with deliberately misleading information.

A further question needs to be answered by the TGA, based on the significant void of information in earlier CMIs: do they actually meet the legal definition of a CMI? When assessing the breaches of the *Therapeutic Goods Act 1989* for inconsistencies between the CMI and PI, it is impossible to consider these earlier consumer warnings to be complete of all material risks. It is expected that these same warnings will soon be included in the CMIs for all opioids including OxyContin, Targin and Endone.

This situation has only been changed after the TGA became aware of the situation, however for thousands of people, these changes come too late.

Table 17: Disclosure of risks – a comparison between the old and new Durogesic CMIs

Issue	CMI 1999	CMI 2018	CMI 2020
Risk of death from using Durogesic disclosed?	No	3 times	15 times
Risk of addiction disclosed?	"Medicines like DUROGESIC can lead to addiction. This is unlikely when DUROGESIC is used correctly"	"Medicines like DUROGESIC can lead to addiction. This is unlikely when DUROGESIC is used correctly"	"**Before you use DUROGESIC.** Warning; Opioids can be abused and misused, and you are at risk for opioid addiction, **even if you take your dose as prescribed**. Opioid addiction, abuse and misuse can lead to overdose and death."
Risk of addiction when taken as prescribed disclosed?	No	No*	**Yes**

282 Janssen, Durogesic Consumer Medicine Information, February 2020.

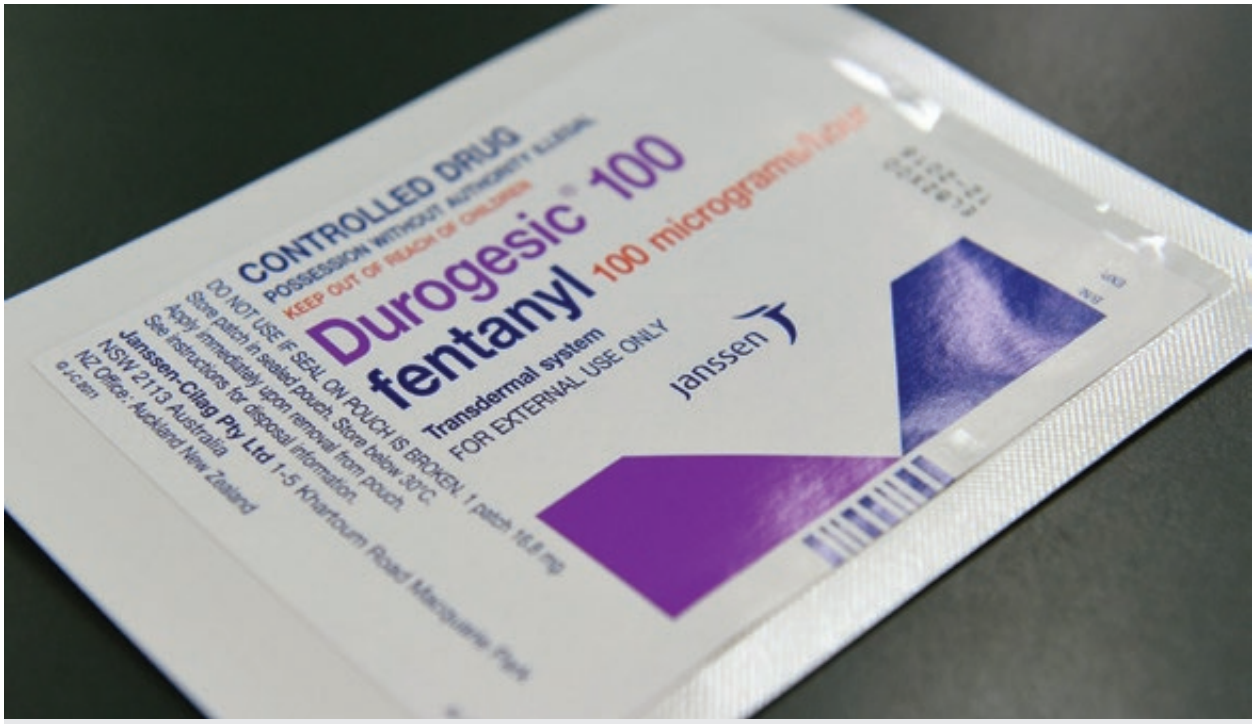
Issue	CMI 1999	CMI 2018	CMI 2020
Misleading statement ".. change the patch **every** two days **(48 hours) instead of every** three days **(72 hours)** to achieve adequate pain relief."	**Not included**	Included	**Not included**
Risk of death in relation to **addiction** disclosed?	No	No*	**Yes**
Risk of death from **taking as prescribed** disclosed?	No	No*	**Yes**
Risk of death in relation to **alcohol** disclosed?	No	No*	**Yes**
Risk of death in relation to **benzodiazepines** disclosed?	No	No*	**Yes**
Risk of death in relation to **overdose** disclosed?	No	No*	**Yes "even if you take as prescribed"**
Risk of death in relation to **abuse** disclosed?	No	No*	**Yes "even if you take as prescribed"**
Risk of death in relation to **pregnancy** disclosed?	No	No*	**Yes**
Risk of death in relation to **sharing opioids** disclosed?	No	No	**Yes**
Risk of death in relation to **patch contact with kids/adults** disclosed?	No	No*	**Yes**
Risk of death in relation to **starting or changing a dose** disclosed?	No	No*	**Yes "even if you take as prescribed"**
Risk of death from **heat exposure** disclosed?	No	**Yes**	**Yes**
Risk of death in relation to other **medications/ supplements** disclosed?	No	**Yes**	**Yes**
Advised of Nyxoid in case of overdose?	N/A	No	**No**

* Examples of inconsistencies between the CMI and the PI, which are breaches of the *Therapeutic Goods Act 1989.*

A detailed comparison of the CMIs and PI are provided later in this chapter.

2.3 ABOUT FENTANYL

According to Dr Craig Allen via interview:



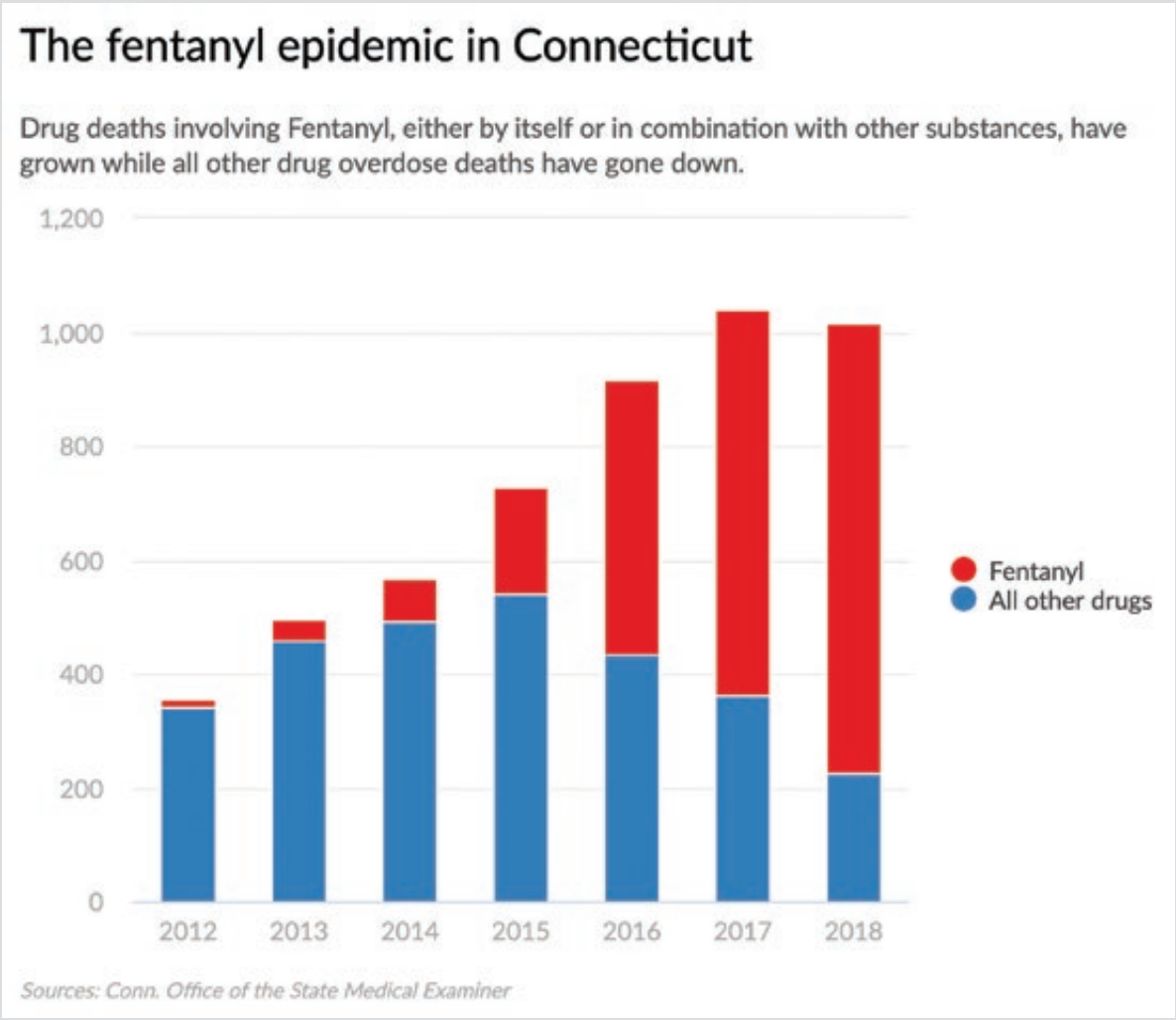
"Fentanyl is a substance that has the potential to cause death in amounts as little as 2mgs, it's 50x more potent than heroin and 100x more than morphine. When prescribing fentanyl the important risks for people to be aware of, are the potential for developing an addiction, potential for drug interactions and potential for overdose and death. I am happy to see the new CMI does a much better job at providing this information. However, the changes that have been made, are about risks that have been known since fentanyl was first released in the 1990s. ***There is nothing new from a medical standpoint, these warnings have been posted in the United States for decades, it's concerning that this may be new information for Australians. The warnings could go a lot further, but this is the minimum level of information required for a person to give informed consent.*** *The lack of patient education regarding potential harms and regarding the availability of naloxone, the overdose reversal medication, shows a significant gap in understanding and appreciations for overdose risks."*

"Safe disposal is also critical as even after being worn by the patient for three days a patch can retain more than 50 per cent of the fentanyl."

"Here in Connecticut, fentanyl is the leading cause of overdose deaths, it has surpassed heroin and accounts for over 85% of opioid overdose deaths. The escalation has been staggering, we are a state in the nation's hardest-hit region. For people who do become addicted to fentanyl, it may happen faster and be more challenging to treat. Highly potent addictive substances rapidly entering the brain lead to dramatic releases of dopamine that can remodel the neuro-pathways driving motivation and reward. Your brain is telling you that this substance is worth pursuing at all costs. To illustrate the power of an addiction sometimes I use the metaphor of a moth, infatuated with the light, flying to its death in a flame. Once fentanyl addiction has taken hold, the path to recovery gets a lot harder."

Reports show that fentanyl is killing people at an alarming rate in Connecticut (see Figure 42).

Figure 42: The fentanyl epidemic in Connecticut (Source: The CT Mirror)[283]



And sadly, the lethal nature of fentanyl to children is not a recent development:

> *"As far back as 2006 the NSW Therapeutic Advisory Group (TAG) alerted health services to a number of safety warnings following reports of deaths and adverse reactions in patients overseas using fentanyl skin patches. An elderly patient died following application of a heat pack over a patch, a child died after applying one of his mother's patches on himself and several children escaping near death applying patches to themselves."*[284]

Similar information has also been noted by medicinewise[285] and *The Australian Journal of Pharmacy*.[286]

283 J Carlesso and J Kara, 'Best of 2019: Blacks dying from fentanyl at same rate as whites for first time', *The CT Mirror*, 27 December 2019.
284 NSW Department of Health, 'Fentanyl: an emerging public health concern', Your Room, 4 July 2019.
285 NPS MedicineWise, 'Accidental fentanyl exposure in children can be fatal', News, 9 February 2015.
286 M Haggan, 'Kids at risk of fentanyl exposure: NPS', AJP, 3 March 2015.

2.4 PHARMACY RESEARCH ABOUT NEW DUROGESIC CMI

The pharmacy CMI research project in Chapter 4 documented the issues that people with lived experience and advocacy consumer groups have raised about the standard of service that is provided by pharmacists. The visits showed that there is a lack of commitment by pharmacists to ensuring medication safety standards are being met.

Following the release of the new CMI for Durogesic in February 2020, we undertook a further project to visit five pharmacies and record conversations with the pharmacist. All pharmacists visited were different to those earlier interviewed for Chapter 4. All pharmacies are located in Canberra.

The process involved asking for information about the new warning information that had been released. The aim was to obtain the new CMI and to understand what are the new warnings included in the CMI. We also asked about the pharmacy's process of providing a CMI when an update has been made to the content.

The expectation is that the pharmacists would provide the CMI, and verbally explain all the new changes. This service is part of the PBS fees they are paid and the charter they promise to deliver. It is also critical to inform existing users of opioid medications of the warnings that they have not previously received.

2.4.1 Summary of five pharmacy visits

Table 18: Summary of five pharmacy visits

	Was the pharmacist aware that a new Durogesic CMI was available?	Did the pharmacist provide a copy of the new Durogesic CMI?	Was the pharmacist able to explain the new side effect/risk warning information that has been added to the CMI?	Is the pharmacist planning on giving the new CMI to all repeat Durogesic prescriptions?
Pharmacy – 5 visits	0/5	3/5	0/5	0/5
Pharmacist Verbal Advice Extracts	"It is just highlighting information that was already in the leaflet they have just reformatted to put it at the top to make sure people read it."			
	"Some of this stuff isn't new, I think the box is [formatting information]."			
	"There is no new information they are just trying to highlight potential side effects or risks related to the medication to monitor its use…"			
	"So for someone who is already taking it, there is nothing new that they should be aware of?" **Pharmacist:** "No [there isn't anything new]."			
	"We do not get notified when there is a new leaflet [by the TGA]."			
	"I am on the TGA website now and I can't see anything [about a new Durogesic warning]."			
	"So the only update to the warning is to not use it illegally". **Pharmacist:** "Yes that's what it's saying."			
	"So you can just compare them [the CMI dated 2018 and the one dated 2020]."			
	"My MIMS at the moment is down, where I print information from is down."			
	"Are you planning on giving this [the new CMI] to people when they get a repeat prescription for Durogesic so they can see the new warnings?" **Pharmacist:** "Only if they ask for it."			

	Was the pharmacist aware that a new Durogesic CMI was available?	Did the pharmacist provide a copy of the new Durogesic CMI?	Was the pharmacist able to explain the new side effect/risk warning information that has been added to the CMI?	Is the pharmacist planning on giving the new CMI to all repeat Durogesic prescriptions?
Pharmacy – 5 visits	0/5	3/5	0/5	0/5
Issues	– None of the pharmacists were aware of the changes announced by the TGA in relation to the prescribing of opioids in late 2019. None were aware that new CMIs are being released for all opioids in 2020. – None of the pharmacists could explain the new warnings that have been added such as the risk with the use of benzodiazepines. None could explain the new warnings around the risk of death that have been added to the CMI. – One pharmacist did not provide a CMI, citing that the MIMS software was not working. The pharmacist did not check the TGA website. They also did not advise that information could be found on the TGA or medicine wise websites. They advised to come back later in the week. – One pharmacist printed a copy of the February 2020 CMI from the TGA website and the August 2018 CMI from MIMS, and advised the patient to read them both to identify what is new. – The MIMS software as at March 2020 contained the CMI from August 2018. – One pharmacist did not offer to provide a hard copy CMI despite being asked three times for information about the new CMI. – The only consistent message was that the new CMI is simply a reformatting of existing information and hence not important to provide to existing users.			
Findings from the research	Fentanyl is the most lethal prescription medication dispensed in Australia. The government program to target reducing adverse prescription medication deaths includes providing more warning information to consumers. It also includes making these warnings more accessible to consumers. Despite this, the TGA has failed to ensure that the pharmacists are aware of the new warnings, understand what is new and require them to provide it to new or existing users. Apart from the CMI being updated, nothing has changed to ensure consumers are better informed. This project confirms again the position of people with lived experience, that pharmacists are failing to provide the critical information on the side effects of medication.			

2.5 DETAILED ANALYSIS OF DUROGESIC (AUST) CMIS – FENTANYL

We compared consumer warnings publicly released by:

- Janssen (Australia) Version: 12/1999
- Janssen (Australia) Version: 08/2018
- Janssen (Australia) Version: 02/2020

General Warning Side Effects
Australia CMI (2018) and CMI (1999) "All medicines can have side effects. Sometimes they are serious, most of the time they are not. You may need medical treatment if you get some side effects. Do not be alarmed by this list of possible side effects. You may not experience any of them. Ask your doctor or pharmacist to answer any questions you may have." (page 4) and (page 5)
Australia CMI (2020) **"Hazardous and harmful use** DUROGESIC poses risks of abuse, misuse and addiction which can lead to overdose and death. Your doctor will monitor you regularly during treatment" (page 1) **"Life threatening respiratory depression** DUROGESIC can cause life-threatening or fatal breathing difficulties (slow, shallow, unusual or no breathing) even when used as recommended. These problems can occur at any time during use but the risk is higher when first starting DUROGESIC and after a dose increase, if you are older, or have an existing problem with your lungs. Your doctor will monitor you and change the dose as appropriate." (page 1)

- The current CMI (2020) now warns that the risks of overdose, death, addiction, abuse and misuse can occur even when using the medication "as recommended". Overdose, addiction, and abuse is mentioned in this section and other sections. The document now comprehensively warns the person of possible iatrogenic addiction and risk of death. It also warns these risks are higher when starting or changing a dose.
- The current CMI (2020) still includes statements like "do not be alarmed" (on page 5), which reduces the impact of the side effect warning and reduces the seriousness of the medications side effects in the mind of the consumer.

Alcohol Warning
Australia (2018) and (1999) "Effect of alcohol; Avoid alcohol when using DUROGESIC since their combined effect may cause drowsiness." (page 2) and (page 2)
Australia (2020) **"Concomitant use of benzodiazepines and other central nervous system (CNS) depressants, including alcohol** Using DUROGESIC with other medicines that can make you feel drowsy such as sleeping tablets (e.g. benzodiazepines), other pain relievers, antihistamines, antidepressants, antipsychotics, gabapentinoids (e.g. gabapentin and pregabalin), cannabis and alcohol may result in severe drowsiness, decreased awareness, breathing problems, coma and death. Your doctor will minimise the dose and duration of use; and monitor you for signs and symptoms of breathing difficulties and sedation. You must not drink alcohol while using DUROGESIC." (page 1) **"Effect of alcohol** You must not drink alcohol while using DUROGESIC since their combined effect may cause severe drowsiness, decreased awareness, breathing problems, coma and death." (page 3)

– The current CMI (2020) now has a new warning added to page 1, which warns of the risk of death and to not drink alcohol. The existing warning on page 3 now includes breathing problems, coma, death.

Benzodiazepine Warning
Australia CMI (2018) and CMI (1999) No benzodiazepine warning included in the CMIs.
Australia CMI (2020) **"Concomitant use of benzodiazepines and other central nervous system (CNS) depressants, including alcohol** Using DUROGESIC with other medicines that can make you feel drowsy such as sleeping tablets (e.g. benzodiazepines), other pain relievers, antihistamines, antidepressants, antipsychotics, gabapentinoids (e.g. gabapentin and pregabalin), cannabis and alcohol may result in severe drowsiness, decreased awareness, breathing problems, coma and death. Your doctor will minimise the dose and duration of use; and monitor you for signs and symptoms of breathing difficulties and sedation. You must not drink alcohol while using DUROGESIC." (page 1) "medicines that makes you sleepy, reduce anxiety such as sedatives, hypnotics, sleeping tablets, tranquillisers (benzodiazepines) Taking these medicines with DUROGESIC may make you even more drowsy, slow down your ability to react, have decrease awareness, breathing difficulties with slow or shallow breathing, coma and death. A change in dose by your doctor" (page 3)

- The CMI (2020) now includes a warning on page 1 of the risk of coma and death and on page 3 in relation to using benzodiazepines.
- In the older CMIs (2018) and (1999) benzodiazepine is not mentioned once in the documents. The current CMI (2020) now mentions it three times and each time in relation to the risk of death.

Overdose Warning
Australia CMI (2018) and CMI (1999) "If you receive too much (overdose) The most important sign of overdose is difficulty in breathing. If a person using DUROGESIC has abnormally slow or weak breathing, remove the patch. Keep the person awake by talking to them or gently shaking them every now and then." (page 3) and (page 4)
Australia CMI (2020) **"Hazardous and harmful use** DUROGESIC poses risks of abuse, misuse and addiction which can lead to overdose and death. Your doctor will monitor you regularly during treatment" (page 1) "**Before you use DUROGESIC** **Warning** Opioids can be abused and misused, and you are at risk for opioid addiction, even if you take your dose as prescribed. Opioid addiction, abuse and misuse can lead to overdose and death." (page 1 and 2)

- In the Australian CMIs (2018) and (1999) the risk of death as a result of an overdose is not mentioned. The current Australian CMI (2020) now warns of the risk of death twice in relation to overdose. It also now warns of the risk of overdose even if being taken correctly as prescribed.
- The current Australian CMI (2020) does not mention using the PBS Opioid Rescue Nasal Spray – Nyxoid.
- In the current Australian CMI (2020) the warning on page 4 still advises to "Keep the person awake by talking to them or gently shaking them every now and then."

Abuse Warning

Australia CMI (2018) and CMI (1999)

The risk of abuse to the consumer is not mentioned in the CMI.

Australia CMI (2020)

"Hazardous and harmful use

DUROGESIC poses risks of abuse, misuse and addiction which can lead to overdose and death. Your doctor will monitor you regularly during treatment" (page 1)

"Before you use DUROGESIC

Warning

Opioids can be abused and misused, and you are at risk for opioid addiction, even if you take your dose as prescribed. Opioid addiction, abuse and misuse can lead to overdose and death." (page 1 and 2)

"Do not cut, break, chew, crush, dissolve, snort or inject DUROGESIC. This can result in serious side effects and death." (page 5)

- In the CMIs (2018) and (1999) Durogesic is a Schedule 8 drug due to the risk of it being abused, yet the risks of abuse including death, or warnings around abuse are not mentioned.
- In the current CMI (2020) the CMI now includes three new warnings of the risk of death in relation to abuse. It also now warns of the risk of abuse even if being taken correctly as prescribed.

Addiction Warning

Australia CMI (2018) and CMI (1999)

"Medicines like DUROGESIC can lead to addiction. This is unlikely when DUROGESIC is used correctly." (page 4) and (page 5)

Australia CMI (2020)

"Hazardous and harmful use

DUROGESIC poses risks of abuse, misuse and addiction which can lead to overdose and death. Your doctor will monitor you regularly during treatment" (page 1)

"Before you use DUROGESIC

Warning

Opioids can be abused and misused, and you are at risk for opioid addiction, even if you take your dose as prescribed. Opioid addiction, abuse and misuse can lead to overdose and death." (page 1 and 2)

- The CMIs (2018) and (1999) contain a statement that has no scientific basis: that the risk of addiction "...is unlikely when DUROGESIC is used correctly". This statement significantly reduces the possibility of addiction from a consumer's risk assessment.
- The current CMI (2020) now includes two new warnings of the risk of death in relation to addiction. It also warns of the risk of addiction and death even if being taken correctly as prescribed. The statement that addiction "...is unlikely when DUROGESIC is used correctly" has been deleted.

Sharing Opioids

Australia CMI (2018) and CMI (1999)

"Do not give the patches to anyone else, even if their symptoms seem similar to yours." (page 3) and (page 5)

Australia CMI (2020)

"Do not give the patches to anyone else, even if their symptoms seem similar to yours as they could die from taking it." (page 5)

- The TGA's *Return your opioids* campaign warns about the risk of sharing opioids with other people, including death. However, the risk of death isn't mentioned in the earlier CMIs.
- The current CMI (2020) now includes this death warning.

Patch Warning

Australia CMI (2018) and CMI (1999)

"Things to be careful of; If the patch accidentally adheres to another person (for example a family member sharing the same bed), remove the patch and contact your doctor. Do this even if there are no signs of discomfort or drowsiness." (page 3) and (page 4)

Australia CMI (2020)

"Keep used and unused patches where children cannot reach them. A patch may be tempting to a child. Accidental exposure or ingestion of used or unused DUROGESIC patches, particularly in children, may result in breathing difficulties, with slow or shallow breathing, that could lead to death. Improper use including DUROGESIC patches sticking to another person can be life-threatening." (page 2)

"Keep used patches out of sight and reach of children – even used patches contain some medicine which may harm children and may even be fatal." (page 4)

- The CMI (2018) and (1999) do not warn of the risk. Fentanyl is a powerful pain killer that is applied as a patch to the skin. The risk of it coming into contact with a partner is significant and the risk of death to that person is also significant. Failing to warn of that risk places unaware individuals at fatal risk.
- The current CMI (2020) now includes this death warning three times.

Pregnancy Warnings

Australia CMI (2018) and CMI (1999)
"You must tell your doctor if you; •are pregnant or planning to become pregnant •are breast feeding or wish to breastfeed" (page 1) and (page 3)

Australia CMI (2020)
"If you are pregnant or plan to become pregnant, you should inform your doctor, who will decide whether you may use DUROGESIC. DUROGESIC should not be used during childbirth as the medicine can slow the breathing of the newborn child. Prolonged use of DUROGESIC during pregnancy can cause withdrawal symptoms in your newborn baby that could be life-threatening if not recognised and treated. If you are breast feeding, you should not use DUROGESIC since it may be present in your milk. See your doctor." (page 5)

– The CMIs (2018) and (1999) do not contain any risk warnings, nor do they specify the actual risks that taking this medicine will expose the unborn or newborn child to, or that they are life-threatening.
– The current CMI (2020) now includes the life-threatening risks to babies.

Tolerance Warning

Australia CMI (2018) and CMI (1999)

"Tolerance as with all opioid analgesics, DUROGESIC may lead to tolerance with continued use. Your doctor may, therefore, prescribe a higher dose of DUROGESIC after some time to continue to give you pain relief." (page 2) and (page 3)

Australia CMI (2018)

"If your pain continues, see your doctor who may prescribe additional medicines to help control the pain or change the dose of DUROGESIC. Your doctor may advise you initially to change the patch every two days (48 hours) instead of every three days (72 hours) to achieve adequate pain relief." (page 3)

"Your doctor may prescribe additional pain relievers to control occasional outbreaks of pain" (page 3)

Australia CMI (2020)

"As with all opioid analgesics, DUROGESIC may lead to tolerance with continued use. Tolerance means that the effect of the medicine may decrease and more is needed to produce the same effect. Therefore, it is possible your doctor will prescribe a higher dose of DUROGESIC after some time to produce the same result." (page 2)

"Your doctor may prescribe additional pain relievers to control occasional outbreaks of pain" (page 3)

– As included in the CMI (2018) and (1999), patients should never be directed to the option that a higher dose would assist to provide pain relief. This gives the suffering patient the idea that it is acceptable to increase the dose if the pain is not controlled by the current dose.
– Only the statement that the doctor may advise to change the patch every two days instead of three has been deleted in the current CMI (2020).

2.6 THE PHARMACY GUILD'S RESPONSE TO THE TGA

Option 5 of the TGA Opioid Response included the addition of the warnings shown in this Durogesic analysis. In March 2018, the Pharmacy Guild provided a response to the TGA. The Guild's response commenced by restating the TGA option:

> ***"The option:** Under this option, warnings could be placed on the packaging of opioid products identifying the risk of dependence and overdose and lack of efficacy in the long term treatment of chronic non-cancer pain, noting that the complexity of appropriate management of chronic non-cancer pain needs to be recognised. The CMI would also be reviewed to provide greater emphasis on risks of dependence, especially those associated with high doses."*[287]

These life-threatening warnings should have already been included in the CMI in 1999, explained by the pharmacist when commencing the medication, and reiterated regularly. The Pharmacy Guild then provides their position on the inclusion of these additional warnings:

> *"Whilst the Guild does not disagree with this suggestion we believe that this measure may have the potential to send mixed messages to the consumer and could cause unnecessary alarm or distress e.g. if a patient is stabilised on a particular therapy that they believe is working they may be alarmed to read a new warning label on their medicine."*[288]

This horrifying position by the Pharmacy Guild to option 5 is diametrically opposed to the Guild's responsibilities – in at least 10 ways:

1. It doesn't support the Guild's stated position of 'maximum patient empowerment and health literacy'.
2. It is completely in breach of the *Australian Charter of Healthcare Rights*, in which people receive all information of the risks of medications. It is not a negotiable position.
3. It ignores the obvious situation that in addition to being informed of these risks, the consumer then has to provide informed consent to continue to take the medication.
4. It ignores the fact that new patients would be better informed of the risks with these changes.
5. It is in breach of the PSA Code of Ethics and the Pharmacy Guild Charter to not provide a CMI when updates are made.
6. Providing up-to-date medication safety warnings is what they are remunerated for through the PBS, plus they are paid an additional fee for dangerous drugs like Durogesic.

287 The Pharmacy Guild of Australia, *Therapeutic Goods Administration: Prescription strong (Schedule 8) opioid use and misuse in Australia – options for a regulatory response*, 2 March 2018.
288 ibid, p 13.

7. If pharmacists had provided this information to consumers verbally when dispensing prescriptions, then there would be no reason for them to be alarmed.
8. Being alarmed is important if the warnings could save their lives.
9. The absence of these warnings is resulting in adverse events including deaths.
10. It displays a lack of urgency to take steps to ensure this information is provided to consumers.

Two years after this response on this issue, the Pharmacy Guild has not taken any steps to inform people taking opioids that these warnings are not in the CMIs. And it has not ensured pharmacists are delivering the new CMIs in 2020.

The Pharmacy Guild does suggest that consumers would be better informed through:

> *"...implementation of a Pain MedsChecks program where consumers can have a one on one discussion about their pain medicines with their local community pharmacist."*[289]

This is a program that would involve additional PBS remuneration being paid to the pharmacist, for doing a job that they have already been paid to do – that is, explaining the opioid medication risks.

The 6th Community Pharmacy Agreement (6CPA) between the Australian Government and the Pharmacy Guild must be the last. It expires in June 2020. It is time to end the overly generous remuneration paid to an organisation that is not only failing to deliver on the agreed services, but the failure is costing lives.

In January 2018, the TGA released the original consultation paper that clearly outlined the lack of critical warnings in the CMIs. That is, they made it clear that the current CMI is dangerously incomplete of life-threatening risks. The TGA received responses from organisations including the AMA, PSA, Medicines Australia, Mundipharma, NPS MedicineWise, and the RANZCP. Fully aware that each day thousands of opioids were being dispensed and that they all have a responsibility to ensure medication safety and informed consent, they all chose to immediately not warn consumers. Even now the Pharmacy Guild and the PSA are not distributing these updated CMIs.

At least they made submissions to the consultation process; the NMHC as well as other mental health and suicide prevention bodies, didn't even bother.

2.7 ENDONE CMI UPDATE IN APRIL 2020

Shortly before the completion of this report, the TGA released a new version of the Aspen Pharma Endone CMI, dated April 2020. The CMI contains a new warning box, similar to the updated Durogesic CMI. The Endone CMI now contains eight new warnings relating to the risk of death. The CMI now contains warnings of the risk of death relating to taking benzodiazepines and/or alcohol. It also now contains a warning of the risk of addiction even when taking Endone as prescribed. As with Durogesic, the additional information added to the CMI highlights how poorly informed consumers have been since Endone was released in 2009.

289 ibid.

Aspen Pharma	Endone (2015)	Endone (2020)
Issues	Death mentioned: 1 time	Death mentioned: 9 times
Explanation of when use is recommended	No	**This medicine is used for the short term management of severe pain.**
Misleading statements	Describes Endone as a 'narcotic analgesic' and not as an 'opioid', which it does in the PI. The likelihood of serious side effects is described as being 'rare'.	**Still describes it as 'narcotic analgesic' but does mention it is an opioid in other sections.** **No longer mentions the word 'rare'.**
Risk of death in relation to alcohol	Not included*	**Yes**
Risk of death in relation to benzodiazepines	Not included*	**Yes**
Risk of death in relation to other medications/ supplements	Not included*	**Yes**
Risk of overdose when starting or changing a dose	Not included	**Yes**
Risk of addiction when taken as prescribed	Not included	**Yes**
Risk of death when taken as prescribed	Not included*	**Yes**
Risk of death from sharing opioids	Not included	**Not included**
Risk of death in relation to pregnancy	Not included	**Not included**
Advise of Nyxoid in case of overdose	Not included	**Not included**
Risk of death from overdose	Included – the only time the risk of death is mentioned is in relation to overdose	**Yes**
Risk of death from abuse	Not included	**Yes**

*Examples of inconsistencies between the CMI and the PI, which are breaches of the *Therapeutic Goods Act 1989*.

Warning

Do not stop taking a prescribed medication without discussing it with your doctor. Information can also be obtained by calling the NPS Medicines Line on 1300 633 424 or the Adverse Medicines Events Line on 1300 134 237 for advice. If you need support for any medical concern, including mental health matters, please contact your doctor. Lifeline also provides a 24 hour support service on 13 11 14 or www.lifeline.org.au

8. US AND AUSTRALIA OPIOID EPIDEMICS

1. INTRODUCTION

American pharmaceutical company, Purdue Pharma, filed for bankruptcy due to its role in creating and enabling the US Opioid Crisis. The organisation is negotiating a settlement with US states and victims to the value of USD $12 billion.

The US Government and court rulings attribute Purdue's deliberate strategy to deceive doctors and consumers from the true risk and benefits of its opioid medication OxyContin, as a key driver of the crisis.

Purdue was found to have lied that the drug had a low risk of addiction and abuse, when in fact it had a high risk for both.[290]

Sadly, unaware consumers suffered from adverse drug events and death.

Other drug companies, such as Johnson & Johnson (who make Duragesic) followed Purdue's strategy and are only now being held accountable in court rulings.

This chapter reveals how these companies have employed **the same strategies in Australia** through local subsidiaries Mundipharma and Janssen, yet they have never been investigated nor held accountable.

In fact, Mundipharma now sells an opioid rescue medication to treat overdoses, funded by the PBS (as introduced in Chapter 6).

2. PURDUE AND OXYCONTIN – A SUMMARY

Our interviews with Dr Craig Allen and Dr Lori Calabrese gave us this summary:

Why are opioids deadly?

- Opioids work by blocking your brain's sensation of pain, however they also affect the pleasure centre of your brain, causing a sense of euphoria.
- It is normally a drug reserved for patients with chronic pain like cancer, or severe pain conditions when other analgesics have failed.
- One of reasons for limiting the use is that it is not a risk-free drug, in fact the risks include addiction and death.
- The body very quickly begins to develop a tolerance for the opioid medication, and hence the same dose of medication offers less pain relief.
- This can lead to increased doses or more frequent use and in doing so the patient is exposed to becoming addicted to the medication.

290 M Mariani, 'How the American opiate epidemic was started by one pharmaceutical company', *The Week*, 4 March 2015.

– Hence, we recommend the smallest dose for the shortest period of time as the risks increase the longer someone is taking the medication and the higher the dose.

What is OxyContin?

– Opioids were generally a fast release formulation in the 1990s, providing around four hours of pain relief.
– Released in 1995, OxyContin was a new formulation that has a slow release (controlled-release) action, meaning it releases the medication over 12 hours.
– When the controlled-release tablet is swallowed whole, some oxycodone is released immediately and the rest is released into the body slowly due to a protective coating.
– Depending on the dose prescribed, just one OxyContin tablet could contain more oxycodone than 12 instant-release pills.

How did Purdue and OxyContin start a deadly epidemic in the US?

– Worried that doctors would not prescribe OxyContin due to fears of patient safety, Purdue deliberately lied about three key areas:

1. They stated the risk of addiction was “low”, “rare” and “less than 1%”.
2. They stated that the drug had a low risk of abuse due to the slow release formulation.
3. They stated that it worked for 12 hours.

The truth

In reality opioids are known to cause addiction even when taken as prescribed and there was no evidence to support Purdue’s low addiction claims. The pill could easily be crushed by chewing, which Purdue knew would release as much as 68% of the oxycodone immediately into the person’s system. The risk of abuse was not low, it was actually very high. Purdue also knew from multiple studies that pain relief was not lasting 12 hours; many patients showed only 8 hours of relief.

> In a nutshell, here is what Purdue did. They targeted vulnerable people who were suffering from moderate pain, and exposed them to a drug that is highly addictive and potentially deadly at any dosage, and didn’t tell them the truth of the risks. In fact they told them it was safe. They told people the pain relief would last 12 hours and it didn’t for many patients, sometimes barely 8 hours. This created a need for more frequent use or higher dosing, exposing the person to an even greater risk of addiction and death. If a person became addicted, each OxyContin pill provided a large source of oxycodone to fuel the addiction by crushing it. Only they also told people it had a low risk of abuse, when it was the opposite. It was the perfect formulae to start a national drug crisis, and it did. And when Purdue was investigated they blamed the people who had become addicts as being the criminals to blame.

– Dr Lori Calabrese

3. WHO IS BEHIND PURDUE AND ITS SUBSIDIARY, MUNDIPHARMA

Purdue Pharma is pharmaceutical company based in Connecticut, USA. The company is privately owned and controlled by the Sackler Family. Forbes has estimated the Sackler family's total worth at USD$13 billion. Purdue owns the patent rights to a number of prescription drugs including OxyContin and Targin. They also manufacture those drugs.

Outside of the USA and Canada, Purdue operates under the brand *Mundipharma*, including in Australia. Mundipharma is also owned by the Sackler family. In Australia, Mundipharma sell OxyContin and Targin (which are PBS drugs).

According to an article in *The Age*:

> *"Eleven members of the Sackler family sat on the inaugural board of Mundipharma Australia from 1998 – as Purdue was ramping up sales of OxyContin on the other side of the globe – until 2012."*[291]

4. THE US OPIOID CRISIS

The wave of addiction fuelled by opioids over the past 20 years has taken more than 400,000 lives across the USA. More than 200,000 people have died from prescription opioid overdoses since 1999. Another 200,000 have died from overdoses attributed to heroin and fentanyl, many of these deaths occurred after originally becoming addicted to prescription opioids from their doctor for medical conditions.

4.1 HOW DID PURDUE CAUSE THE OPIOID CRISIS?

4.1.1 Misleading material risks

In order to gain market share with its new drug, OxyContin, Purdue developed a coordinated plan to target the USA (chronic non-cancer) pain market from its launch in 1995. Purdue claimed OxyContin:

- was a long acting/slow release drug that worked over 10–12 hours; the existing competitor opioids where fast release drugs like Percocet or Vicodin, which lasted four hours
- was less likely to be abused than fast release drug versions (like Percocet or Vicodin)

291 F Tomazin, 2020.

– the risk of addiction was less than 1% and significantly less than its competitors
– with its low risk of abuse and addiction, was made possible by its patented time-release formula, which release the opioid medication slowly over 12 hours
– was a 'safe' opioid that could be used for even moderate pain conditions, instead of limiting its use to chronic pain – and so marketed it to doctors this way.

They aggressively promoted these claims through an array of promotional materials including literature, brochures, videotapes, TV advertisements and web content.

They built a detailed database of doctors who already prescribed opioids and recruited a sales team to promote OxyContin to these doctors using the marketing material.

Doctors relying on Purdue's marketing material prescribed OxyContin to patients.[292]

4.1.2 Misbranding

The cornerstone marketing message was based on the medication's low level of risk of addiction and abuse – particularly compared to its competitors. However, this claim was **not actually true**, and Purdue knew, long before they launched OxyContin, that there was not a scientific basis upon which to make this claim.

As noted in a 2019 paper about the promotion of OxyContin:

> *"A consistent feature in the promotion and marketing of OxyContin [from its launch in 1995] was a systematic effort to minimize the risk of addiction in the use of opioids for the treatment of chronic non–cancer-related pain. One of the most critical issues regarding the use of opioids in the treatment of chronic non–cancer-related pain is the potential of iatrogenic addiction. The lifetime prevalence of addictive disorders has been estimated at 3% to 16% of the general population. However, we lack any large, methodically rigorous prospective study addressing the issue of iatrogenic addiction during long-term opioid use for chronic nonmalignant pain."*[293]

In 2007, in United States of America v. The Purdue Frederick Company, Inc., Purdue and its top executives pleaded guilty to charges that it misled doctors and patients about the addictive properties of OxyContin and misbranded the product as "abuse resistant". US Court notes state:

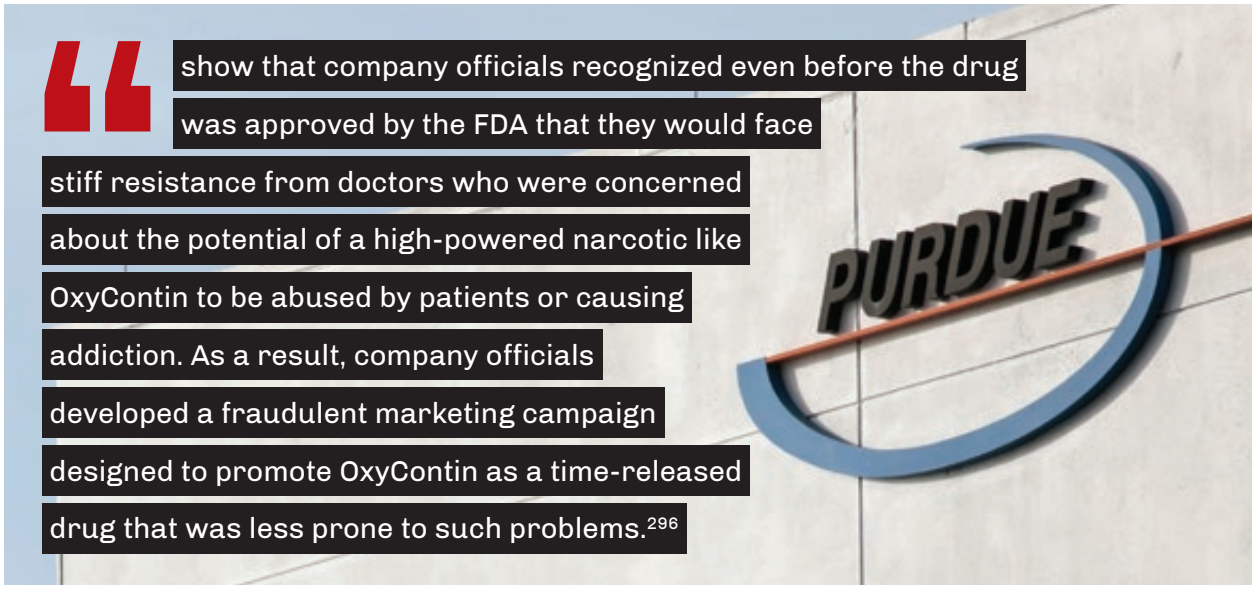
> *"[b]eginning on or about December 12, 1995, and continuing until on or about June 30, 2001, certain PURDUE supervisors and employees, with the intent to defraud or mislead, marketed and promoted OxyContin as less addictive, less subject to abuse and diversion, and less likely to cause tolerance and withdrawal than other pain medications..."*[294]

Purdue Pharma paid USD$600 million in fines; among the largest settlements in US history for a pharmaceutical company. Also, three executives of Purdue Pharma, including its president and its top lawyer, pleaded guilty as individuals to misbranding, a criminal violation. They agreed to pay a total of US$34.5 million in fines.[295]

292 B Meier, 'Origins of an Epidemic: Purdue Pharma Knew Its Opioids Were Widely Abused', *The New York Times*, 29 May 2018.
293 A Van Zee, *The Promotion and Marketing of OxyContin: Commercial Triumph, Public Health Tragedy*, American Journal of Public Health, 2009 February; 99(2): 221–227, doi: 10.2105/AJPH.2007.131714, 2009.
294 J P Jones, United States of America v. The Purdue Frederick Company, Inc. et.al., Case No. 1:07CR00029, Opinion and Order.
295 B Meier, 'In Guilty Plea, OxyContin Maker to Pay $600 Million', *The New York Times*, 10 May 2007.

Purdue made a number of claims in the marketing and promotion of OxyContin that positioned it as a relatively safe choice for patients. This court case exposed that not only where these claims false, but that Purdue knew they were and deliberately promoted these dangerous messages.

Internal Purdue Pharma documents:



> show that company officials recognized even before the drug was approved by the FDA that they would face stiff resistance from doctors who were concerned about the potential of a high-powered narcotic like OxyContin to be abused by patients or causing addiction. As a result, company officials developed a fraudulent marketing campaign designed to promote OxyContin as a time-released drug that was less prone to such problems.[296]

Court documents showed that Purdue's own testing in 1995 had demonstrated that 68% of the oxycodone could be extracted from an OxyContin tablet when crushed. This can occur by accidently chewing the medication instead of swallowing it.

Given OxyContin is pure oxycodone, with a large amount in each tablet due to its time-release design, this makes chewing it deadly. The larger dose is required as it is released over 12 hours, not four hours like its competitors. When this larger dose is released immediately, like when crushed by chewing, the person has a high risk of addiction, overdose and possibly death. In effect, OxyContin was not safer than the existing competitors' slow release medications – it was actually a higher risk medication for addiction, abuse and overdose deaths.

The impact of the fraudulent marketing campaign provided the catalyst for the US Opioid Crisis. By promoting OxyContin as a safer alternative to the four-hour release medications, using an aggressive marketing strategy, it immediately became a widely prescribed medication. Doctors began prescribing it to patients because they thought it was safer, when in fact **it was significantly more dangerous than the existing medications**.

Between 1995 and 2001, OxyContin brought in $2.8 billion in revenue for Purdue Pharma. At one point, the drug accounted for 90% of the company's sales.

The direct outcome of the deliberate misbranding was that patients received a drug without being made aware of the true risks of the medication. By not disclosing fully the risks, patients did not get the opportunity to give informed consent to taking the medication. The resulting epidemic of opioid addiction and overdose is attributed to patients not being warned.

The marketing campaign put this high-risk medication in the hands of millions of vulnerable people, however it was the underlying lack of consumer warning that caused the adverse events.

296 ibid.

> Nearly six years and longer ago, some employees made, or told other employees to make, certain statements about OxyContin to some health care professionals that were inconsistent with the F.D.A. approved prescribing information for OxyContin and the express warnings it contained about risks associated with the medicine. The statements also violated written company policies requiring adherence to the prescribing information. "We accept responsibility for those past misstatements and regret that they were made," the statement said.

– Purdue Pharma[297]

The time period covered by the guilty pleas runs from **late-1995, when the FDA approved OxyContin for sale, to mid-2001**, when Purdue Pharma, faced with both public criticism and regulatory scrutiny, dropped its initial marketing claims for the drug.

4.1.3 Medication information changes

The FDA forced Purdue to change the consumer warning material in 2001, to accurately reflect the side effects and risks of the medication.

> *When OxyContin entered the market in 1996, the FDA approved its original label, which stated that iatrogenic addiction was "very rare" if opioids were legitimately used in the management of pain.*
>
> *In July 2001, to reflect the available scientific evidence, the label was modified to state that data was not available for establishing the true incidence of addiction in chronic-pain patients. The 2001 labelling also deleted the original statement that the delayed absorption of OxyContin was believed to reduce the abuse liability of the drug.*[298]

4.1.4 Reformulated OxyContin in 2010

Recognising that OxyContin had a high risk of abuse – and in response to the 2007 settlement – in 2010 Purdue gained approval for a new form of OxyContin that was "abuse resistant" in that it could not be "crushed". The original formulation was so flawed and unsafe that they had to make a new version of OxyContin to stop the abuse risks that they originally completely understated.

The FDA noted in 2010:

> *"Because of its controlled-release properties, each OxyContin tablet contains a large quantity of oxycodone, which allows patients to take their drug less often. However, people intent on abusing the previous formulation have been able to release high levels of oxycodone all at once, which can result in a fatal overdose and contributes to high rates of OxyContin abuse.*
>
> *The reformulated OxyContin is intended to prevent the opioid medication from being cut, broken, chewed, crushed or dissolved to release more medication. The new formulation may be an improvement that may result in less risk of overdose due to tampering, and will likely result in less abuse by snorting or injection; but it still can be abused or misused by simply ingesting larger doses than are recommended."*[299]

297 E Chasan, 'Purdue Frederick pleads guilty in OxyContin case', *Reuters*, 11 May 2007.
298 A Van Zee, 2009.
299 U.S. Food & Drug Administration (FDA), 'FDA Approves New Formulation for OxyContin', news release, 4 April 2010.

5. OXYCONTIN IN AUSTRALIA

OxyContin was released in Australia by Purdue–Mundipharma in 2000. They marketed the medication to be used for **moderate to severe persistent pain** in the CMI in 2000 and that statement is still included in the 2019 CMI and PI (note, the FDA restricts the use of OxyContin to **chronic pain**).

An examination of the information they made available to doctors and consumers at this time in Australia exposes a number of issues that are identical to the USA release. The two central issues for Purdue–Mundipharma was that it deliberately understated the risk of **addiction** and the potential for **abuse**. Table 19 shows a comparison of the warnings from Purdue OxyContin 1996 and Mundipharma OxyContin CMI in 2000.

Table 19: Comparison of warnings between Purdue OxyContin (1996) and Mundipharma OxyContin (2000)

Purdue OxyContin (1996)[300]	Mundipharma OxyContin Australia (2000)[301]
Recommended Use	**Recommended Use**
"For the management of moderate to severe pain where use of an opioid analgesic is appropriate for more than a few days."	"OxyContin tablets are used to relieve moderate to severe persistent pain when other forms of treatment have not been effective."
Addiction	**Addiction**
"Iatrogenic "addiction" to opioids legitimately used in the management of pain is very rare."	"Opioid analgesics such as OxyContin have been used to treat pain for many years. In most cases addiction does not occur."
Abuse	**Abuse**
"Delayed absorption, as provided by OxyContin tablets, is believed to reduce the abuse liability of a drug." "OxyContin tablets were designed to work properly only if swallowed whole. They may release all their contents at once if broken, chewed or crushed, resulting in a risk of overdose."	"OxyContin tablets were designed to work properly only if swallowed whole. They may release all their contents at once if broken, chewed or crushed, resulting in a risk of overdose."

300 Purdue press release, 1996.
301 Mundipharma Oxycontin CMI Jan 2000.

Purdue OxyContin 1996	Mundipharma OxyContin Australia 2000
Overdose	**Overdose**
"Acute overdosage with oxycodone can be manifested by respiratory depression, somnolence progressing to stupor or coma, skeletal muscle flaccidity, cold and clammy skin, constricted pupils, bradycardia, hypotension, and death."	"If someone takes too many tablets, they will probably become drowsy, tired, confused, have a very low blood pressure, experience difficulties in breathing and possibly become unconscious."
Alcohol	**Alcohol**
"Do not combine OxyContin with alcohol or other central nervous system depressants (sleep aids, tranquilizers) except by the orders of the prescribing physician, because additive effects may occur"	"You may feel drowsy when you begin to take OxyContin tablets. If you drink alcohol the drowsiness may be worse."
Pregnancy	**Pregnancy**
"OxyContin is not recommended for use in women during and immediately prior to labor and delivery because oral opioids may cause respiratory depression in the newborn."	"Before you start to take it you must tell your doctor if: You are pregnant or plan to become pregnant. Your doctor will discuss the possible risks and benefits of taking OxyContin during pregnancy. You are breastfeeding or plan to breastfeed. Your doctor will discuss the risks and benefits of taking OxyContin when breastfeeding."

> When I compare the original warnings, at least Purdue warned that an overdose could cause death. In many ways the Australian warnings are worse than what Purdue did in 1995.

– Dr Lori Calabrese

> When Purdue launched OxyContin in the USA, they withheld warnings around the risk of death from misuse, for example by crushing the tablets, and they downplayed the risk of addiction. Those are the reasons that Purdue has been convicted in court...

– Dr Craig Allen

5.1 UNDERSTATING THE RISK OF ADDICTION

The OxyContin CMI (2000) contains the consumer information that was provided around the material risk of addiction to OxyContin. As with the USA, the CMI included a deliberately misleading statement that the risk of addiction is low.

Addiction Warning – OxyContin Mundipharma (Australia) Version: 2000

Australia CMI (2000)

"Opioid analgesics such as OxyContin have been used to treat pain for many years. In most cases addiction does not occur. However, over time your body becomes used to taking OxyContin, so if you suddenly stop taking OxyContin, you may experience some symptoms of withdrawal. It is important to discuss this issue with you doctor." (page 1)

This statement is included twice in the CMI.

Remember, based on the findings in the USA, in 2000, Purdue–Mundipharma was aware of addiction issues, however they still presented the risk of addiction to Australian consumers in this dangerously misleading way. As in the USA, they lied.

The actual levels of addiction to OxyContin in the USA and Australia since that time highlights just how widespread the risk and impact of opioid addiction from OxyContin is. If doctors and consumers relied on this statement when assessing the risks of the medication then they did so not accurately understanding the high risk of addiction. Consumers that subsequently suffered from addiction of OxyContin did not have the true nature of the material risk disclosed to them.

In comparison, the current 2019 FDA warning for OxyContin highlights the true material risks of this medication. Australian consumers were under-warned in 2000.

Addiction Warning – OxyContin Purdue (USA) Version: 2019

USA MG (2019)

"A long-acting (extended-release) opioid pain medicine that can put you at risk for overdose and death. Even if you take your dose correctly as prescribed you are at risk for opioid addiction, abuse, and misuse that can lead to death." (page 1)

The FDA forced Purdue to change the warning in 2001.[302] The new label modified the statement that the risk of addiction was rare. In July 2001, to reflect the available scientific evidence, the label was modified to state that data was not available for establishing the true incidence of addiction in chronic-pain patients. However, Purdue–Mundipharma **did not make any changes to the Australian CMI** as evidenced by the 2003 CMI. This ensured that Australian consumers still received dangerously misleading information that Purdue–Mundipharma had already deleted from its USA material.

The 2010 CMI shows that Purdue–Mundipharma finally removed this reference to the low risk of addiction. It now stated, "There is potential for abuse of oxycodone and the development of addiction to oxycodone". However, it now included a new and equally misleading statement that side effects reduce over time and this statement still exists in the CMI (2019). An almost identical statement was included in the US consumer warnings in 1996: "Common opioidrelated side effects (except constipation) diminished over time,

302 D Eligman, G B Collins, J Falender, N Shembo, C Keegan, S Tohan, 'The marketing of OxyContin: A cautionary tale', *Indian Journal of Medical Ethics*, DOI 10.20529/IJME.2019.043, 2019.

even as daily doses increased."[303] The FDA made Purdue remove it in 2001.[304] Nine years later they introduced it to the Australian CMI (2010), fully aware it was scientifically wrong and dangerously misleading to consumers. Medical research, as explained in Chapter 1 and Chapter 2, strongly states that the side effects increase, not decrease, overtime, especially in relation to addiction.

General Warning Side Effects – OxyContin Mundipharma (Australia) Version: 11/2010
Australia CMI (2010) "All medicines may have some unwanted side effects. Sometimes they are serious but most of the time they are not. As for other medicines of this type, that is opioid analgesics, many side effects tend to reduce over time, with the exception of constipation. This means that the longer you take this medicine, the less it may cause problems for you. Your doctor has weighed the risks of this medicine against the benefits they expect it will have for you. Do not be alarmed by this list of possible side effects. Not everybody experiences them." (page 4)

The USA 2019 addiction warning in the earlier table, was also included the 2010 MG. These extracts highlight the measures that Purdue–Mundipharma have undertaken to deliberately mislead Australian consumers on the risk of addiction since the launch of OxyContin in 2000. This strategy directly mirrors the USA operations; the only difference being that the USA material now reflects the true risks, whilst the Australian CMI still puts lives at risk.

5.2 UNDERSTATING THE ABUSE POTENTIAL

The term "abuse" in relation to taking medication relates to deliberate action to misuse the drug. However, it also encompasses **accidental misuse**.

For OxyContin, the abuse warning is for "broken, chewed or crushed" actions. These actions can release all of the opioid medication causing a fatal overdose. Considering the medication is taken orally by vulnerable people, the potential for the medication to be accidently "chewed or crushed" is real, especially for new users of the medication. Note that not all prescription medications are swallowed. Some mental health medications like Lamotrigine are recommended to be chewed.[305]

Suffering addiction or a fatal overdose is a high price to pay for chewing, not swallowing, a prescription medication. Prescribing this medication to vulnerable people is questionable, however not making this material risk well understood is criminal.

> By crushing the original formulation, the entire opioid contents could be metabolised, causing drug addiction.

– Dr Craig Allen

303 Purdue press release, 1996.
304 Purdue, OxyContin Package Insert, April 2001.
305 Lamictal consumer medicine information, accessed on 3 April 2020, see https://www.nps.org.au/medicine-finder/lamictal-chewable-tablets

Purdue was aware of the risk of death if OxyContin tablets are crushed (chewed) in the 1990s, and the Australian OxyContin CMI in 2000 does warn of the risk of overdose if this occurs.

Abuse Warning – OxyContin Mundipharma (Australia) Version: 01/2000
Australia CMI (2000) "How to take it Swallow OxyContin tablets whole with a full glass of water or other fluid. Do not chew, crush or dissolve tablets. OxyContin tablets were designed to work properly only if swallowed whole. They may release all their contents at once if broken, chewed or crushed, resulting in a risk of overdose." (page 1)

However, the same CMI, when explaining the side effects of an overdose, does not include the risk of coma or death that Purdue knew was a likely outcome of an overdose. The risk of death from an overdose was included in the 1996 USA consumer warnings.

Considering the number of deaths from overdoses that had occurred in the USA by 2000, Purdue had full knowledge of the fatal overdose impact, yet they chose to not include it in the Australian CMI. In fact, in the 2000 CMI, the risk of death from taking OxyContin, due to any side effect, is not mentioned once.

Overdose Warning – OxyContin Mundipharma (Australia) Version: 01/2000
Australia CMI (2000) "If you take too much (overdose) If someone takes too many tablets, they will probably become drowsy, tired, confused, have a very low blood pressure, experience difficulties in breathing and possibly become unconscious." (page 3)

In the Product Information for Australian doctors that Mundipharma released in 1999, the fatal risks associated with abuse and overdose were clearly identified. These inconsistencies are breaches of the *Therapeutic Goods Act 1989*. **Considering that not placing these warnings in the CMI was deliberate, and thousands of lives have been lost since this time, the significance of this information is the single most important aspect of this analysis.**

Abuse Warning – OxyContin Mundipharma (Australia) Product Information Version: 12/1999
Australia Production Information (1999) "OxyContin tablets are to be swallowed whole, and are not to be broken, chewed or crushed. Taking broken, chewed or crushed OxyContin tablets could lead to the rapid release and absorption of a potentially toxic dose of oxycodone." (page 7)

Overdose Warning – OxyContin Mundipharma (Australia) Product Information Version: 12/1999
Australia Production Information (1999) "Symptoms: Acute overdosage with oxycodone can be manifested by respiratory depression, somnolence progressing to stupor or coma, skeletal muscle flaccidity, cold and clammy skin, constricted pupils, bradycardia, hypotension, and death." (page 8)

In comparison, the current 2019 FDA warnings for OxyContin highlight the true material risks of this medication, and how under-warned Australians consumers were in 2000. Remember, Purdue was aware of these risks in the 1990s.

Abuse Warning – OxyContin Purdue (USA) Version: 2019
USA MG (2019)
"A long-acting (extended-release) opioid pain medicine that can put you at risk for overdose and death. Even if you take your dose correctly as prescribed you are at risk for opioid addiction, abuse, and misuse that can lead to death." (page 1)

Overdose Warning – OxyContin Purdue (USA) Version: 2019
USA MG (2019)
"Swallow OXYCODONE HCl EXTENDED-RELEASE TABLETS whole. Do not cut, break, chew, crush, dissolve, snort, or inject OXYCODONE HCl EXTENDED-RELEASE TABLETS because this may cause you to overdose and die. (page 1)

The OxyContin warning in Chapter 3 shows a further warning consumers in the US are now given.[306]

WARNINGS AND PRECAUTIONS

Addiction, Abuse, and Misuse

- OxyContin contains oxycodone, a Schedule II controlled substance. OxyContin exposes users to the risks of opioid addiction, abuse, and misuse. Because extended-release products such as OxyContin deliver the opioid over an extended period of time, there is a greater risk for overdose and death due to the larger amount of oxycodone present.

By 2003, the number of overdose deaths from OxyContin was a national emergency in the USA. The FDA made Purdue update the consumer warnings in 2001 to reflect the risk of abuse: "OxyContin has been reported as being abused by crushing, chewing, snorting, or injecting the dissolved product. These practices will result in the uncontrolled delivery of the opioid and pose a significant risk to the abuser that could result in overdose and death".[307] However, Purdue–Mundipharma did not make any changes to the Australian CMI as evidenced by the 2003 CMI. This ensured that Australian consumers still received a dangerously misleading CMI without the full material risks. In fact, at this point the CMI still did not mention the risk of death at all in the CMI.

306 Purdue Pharma, OxyContin Full Prescribing Information, October 2019.

307 United States General Accounting Office, Report to Congressional Requesters, *OxyContin Abuse and Diversion and Efforts to Address the Problem*, December 2003.

5.3 NEW FORMULATION FOR OXYCONTIN IN 2014

In 2010, Purdue–Mundipharma released the new abuse resistant version of OxyContin in the USA. The 2010 CMI shows that Purdue–Mundipharma finally included a reference to the risk of death if the medication is abused. Despite updating the CMI, Purdue did not release the safer version of OxyContin in Australia for another four years (in 2014). The Australian Government allowed Purdue–Mundipharma to replace the old formulation with the new on the PBS in April 2014, without investigating the adverse events that necessitated the new formulation.

Side Effects – Oxycontin Mundipharma (Australia) Version: 11/2010
Australia CMI (2010)
"OXYCONTIN tablets are only designed to work properly if swallowed whole. The tablets may release all their contents at once if broken, chewed, crushed or dissolved which can be dangerous and cause serious problems, such as an overdose or even death. (page 2)

5.4 A HISTORY OF MISLEADING INFORMATION

These are not the only examples of Purdue–Mundipharma not fully disclosing material risks of OxyContin from 2000 as highlighted at the start of this chapter. The CMI comparison in Chapter 2 identifies a number of other instances when the material risks of death has not been included in the CMI, and are still not included in the CMI 2019, such as:

- no warning of the risk of death from consuming alcohol
- no warning around taking benzodiazepines at the same time (and the risk of death)
- no warning of the risk of death from taking other medications and supplements
- does not warn about the risk of overdose when starting or changing a dose
- does not warn about the risk of addiction even when being taken as directed
- no warning on the life-threatening risks to unborn or newborn babies.

All of these warnings are included in the current USA MG 2019. Even more horrifying is that all of these warnings were included in the USA MG 2010.

These extracts highlight that, exactly as in the USA, Purdue–Mundipharma in Australia has implemented the same marketing strategy to deliberately not disclose the true material risks associated with Oxycontin, including the risks of addiction and abuse. The difference being that the current USA material now accurately discloses these risks, however the Australian 2019 version still doesn't.

The legal action against Purdue in the USA based on the non-disclosure of material risks is discussed in Chapter 9.

6. DOCTOR TRAINING AND EDUCATION

The marketing of OxyContin to doctors in the US played a significant part in promoting its widespread use. The lack of correct disclosure of the material risks in the marketing materials is also part of the reason for the USA Opioid Crisis. Purdue were found to have lied to doctors, who believed the lie, and then prescribed the medication. As a result people suffered from addiction and death.

The following evidence demonstrates that Purdue–Mundipharma undertook the same marketing strategy to convince doctors to prescribe OxyContin in Australia.

6.1 BREACHES OF THE CODE OF CONDUCT

The Australian Pharmaceutical Manufacturers' Association (APMA) Code of Conduct provides guidelines for the ethical marketing and promotion of prescription pharmaceutical products in Australia. It complements the legal requirements of the Therapeutic Goods Regulations and the Therapeutic Goods Administration. The Code provides guidelines for promotional tools such as advertising, product starter packs (samples), mailings, gifts, trade displays, travel, sponsorship, entertainment, and the behaviour and training of medical representatives. It also covers relationships with health professionals, and most recently, information on the internet.[308]

In 2000, Mundipharma was fined by the APMA for distributing marketing materials that "overstated the attributes of oxycontin" (see Figure 43). As OxyContin was a new PBS medication at this time, this initial promotional information formed the platform of training for doctors. As such, this information was the basis for their decision to prescribe to OxyContin to patients, how they assessed the risk/benefits of the medication for each patient, and the advice they gave to patients on how to take it. This material is the same as the material that they admitted was deliberately misleading in the 2007 'misbranding' settlement in the USA.

308 'APMA Code of Conduct', Australian Prescriber, 2001;24:42-3, 1 February 2001.

Figure 43: Extract of recorded APMA breaches (Source: Australian Prescriber[309])

Table 1

Breaches of the Code of Conduct July 1999 – June 2000

Company	*Breaches*	*Drug – brand name*	*Drug – generic name*	*Sanction imposed by Code of Conduct Committee*
Alcon	1	Betoptic S	betaxolol	Corrective letter to be sent to specialists
Boehringer Ingelheim	1	Persantin	dipyridamole	$5000 fine; withdrawal of promotional material
Bristol-Myers Squibb	4	Pravachol	pravastatin	$12500 fine for repeat of previous breach; withdrawal of material
		Serzone	nefazodone	$5000 fine
		Iscover	clopidogrel	Withdrawal of promotional material
Eli Lilly	1	Evista	raloxifene	Withdrawal of promotional material
Galderma	1	Loceryl	amorolfine	Withdrawal of promotional material
Glaxo Wellcome	2	Relenza	zanamivir	Withdrawal of advertising
		Pritor	telmisartan	Warning against future breach of Code; review of internal procedure
Merck Sharp & Dohme	4	Zocor	simvastatin	None
		Fosamax	alendronate	$5000 fine; withdrawal of advertising. Further $10000 fine for repeat of previous breach
		Vioxx	rofecoxib	$10 000 fine
Mundipharma	1	Oxycontin	oxycodone	Material not to be used again
Novartis	1	Lamisil	terbinafine	Withdrawal of material
Novo Nordisk	2	Kliogest	norethisterone/ oestradiol	$5000 fine; material not to be used again
		Kliovance	norethisterone/ oestradiol	Cessation of activity; corrective letter to be sent to prescribers
Pfizer	2	Zoloft	sertraline	$10 000 fine; withdrawal of material. Further $25 000 fine (including $10 000 fine for repeat breach); withdrawal of material
Pfizer/Searle	1	Celebrex	celecoxib	$10 000 fine; withdrawal of promotional material
Pharmacia & Upjohn	2	Fragmin	dalteparin	Withdrawal of promotional material
		Caverject	alprostadil	Action to ensure use of correct font size in advertisements
Rhone-Poulenc Rorer	1	Clexane	enoxaparin	$15 000 fine; withdrawal of promotional material
Roche	1	Rocaltrol	calcitriol	$7500 fine; withdrawal of advertising
Sanofi-Synthelabo	1	Plavix	clopidogrel	Withdrawal of material
Searle	1	Lomotil	atropine/ diphenoxylate	Withdrawal of material; corrective advertisement placed
Wyeth	1	Premarin and Premia	conjugated oestrogens	Withdrawal of material

Oxycontin

Statements in the promotional material overstated the attributes of oxycontin and promised more than the product could reasonably be expected to deliver. One statement was probably misleading because it implied that oxycontin is first-line therapy (contrary to the approved indications). Statements used in an unqualified manner may have encouraged excess usage of oxycontin and were therefore inappropriate and misleading.[310]

309 ibid.
310 ibid.

They were also found in breach in 2003 (see Figure 44).

Figure 44: Extract of recorded APMA breaches (Source: Australian Prescriber)[311]

Table 1

Breaches of the Code of Conduct July 2002 – June 2003

Company	Complaint		Sanction imposed by Code of Conduct Committee
	Drug – brand name	Drug – generic name	
Mundipharma	Oxycontin	oxycodone	Withdrawal of promotional material

Australian Pharmaceutical Manufacturers Association (APMA) is now known as Medicines Australia. As recently as 2019, Mundipharma is still undertaking misleading activity, as highlighted in an ABC News article on 23 December 2019:

> *Mundipharma has been fined $302,400 by the Therapeutic Goods Administration for a series of ads it distributed to doctors and other health professionals.*
>
> *The regulator issued the company with 24 infringement notices over claims relating to nine types of its oxycodone-based drug Targin.*
>
> *The TGA agreed with concerns that the company was falsely advertising, finding that its marketing to GPs was "misleading, imbalanced and otherwise inaccurate".*[312]

Another article in 2019 questioned whether Mundipharma's promotional materials were giving bad advice:

> *Dr Holliday said the company had widely distributed a misleading brochure to Australian GPs advocating Mundipharma's new-generation strong opioid, Targin. Two claims in the brochure combined to falsely suggest strong opioids — like oxycodone — were better for chronic pain than weak ones — like codeine.*
>
> *When Dr Holliday complained to the industry body Medicines Australia, he was told they could not take action because Mundipharma was not a member. The company chose to opt-out of the complaints process under Australia's system of self-regulation, and Dr Holliday said he was concerned this system was not sufficient to crack down on misleading marketing.*
>
> *In a statement, a spokesman for the Therapeutic Goods Administration (TGA) defended the self-regulatory system for the industry, saying it allowed the regulator to focus on* ***consumer protection****.*
>
> *"The TGA expects prescription medicine sponsors to engage constructively with the self-regulatory system, irrespective of whether they are members of the industry body concerned," he said.*
>
> *In a statement, Mundipharma said it declined to have its complaint dealt with by Medicines Australia because it felt the brochure was "balanced accurate and correct" and said only one in five pharmaceutical companies in Australia were members of the industry body.*

311 'Medicines Australia Code of Conduct: breaches', Australian Prescriber, 2004;27:176, 1 February 2004.

312 A Branley, 'Pharmaceutical giant Mundipharma hit with hefty fine over misleading opioid drug information', *ABCNews*, 23 December 2019.

A TGA spokesman said it had written to Mundipharma following the complaint, but Australia's false advertising laws for therapeutic goods explicitly excluded marketing direct to doctors. A TGA spokesman said physicians had the "critical analytical skills" to interpret scientific information and "question claims in promotional materials that may be perceived to mislead a consumer".

*"**Mundipharma has always prioritised the safety and wellbeing of patients**," a spokesman said in a statement.*[313]

7. BANKRUPTCY

The 2007 settlement provided the catalyst for more litigation against Purdue across the US. As the US opioid epidemic grew, claiming lives and burdening the health system, so too did the litigation against Purdue. Individuals, health care networks, states and counties brought forward literally thousands of claims for compensation. Governments sought the funds for future costs to treat those suffering from addiction and to save lives from further overdoses.

The case against Purdue in 2007 was sealed, meaning the evidence was unable to be accessed by the public. Over time as the evidence from this and other investigations was made available, following legal action to gain access, the wave of public anger against Purdue became a tsunami.

The Washington Post is credited as being one of the lead media organisations that brought many of these sealed documents to the public's attention.[314] In July 2019 it published a previously unreleased Drug Enforcement Administration database that tracks the path of every pain pill sold in the US. The database is a virtual road map to the epidemic. The exhibits, which include internal drug company emails and memos, regulatory records and other documents, reveal the business practices that gave rise to the opioid crisis.[315]

In 2019, approximately 2,600 plaintiffs in the USA commenced a 'multi-district litigation' case in Federal Court in Cleveland Ohio against Purdue. This includes every state in the USA as well as many counties, cities and tribes. The plaintiffs accused Purdue of deceptively marketing its blockbuster opioid pain pill OxyContin. The lawsuit includes the Drug Enforcement Administration database.

Even though it is reported that the "company sold a fraction of the opioid prescriptions in the United States but nonetheless is most closely identified with the epidemic because of its pioneering role in the sale of narcotic pain pills."[316]

313 A Branley, 'Pharma giant using loophole to falsely promote opioid pain relief product across Australia', *ABCNews*, 10 July 2019.

314 'Follow The Post's investigation of the epidemic', *The Washington Post*, 24 January 2020.

315 S Higham, S Horwitz, S Rich, '76 billion opioid pills: Newly released federal data unmasks the epidemic', *The Washington Post*, 17 July 2019.

316 C Rowland, 'Purdue Pharma, drugmaker accused of fueling the opioid epidemic, files for bankruptcy', *The Washington Post*, 16 September 2019.

Other drug manufacturers "emulated Purdue's false marketing strategy" and sold billions of dollars of prescription opioids "as safe and efficacious for long term use, knowing full well that they were not," Wisconsin's Oneida County alleges in its November 2017 federal court suit.

Purdue argued that the FDA approved all of their products as "safe and effective." They also argued that it was doctors who prescribed medications and managed patients, not Purdue. In addition, Purdue argued that pharmacists distribute the medication to most patients, not Purdue.

Even so, Purdue Pharma filed for bankruptcy in September 2019 as part of a broad opioid settlement proposal with 24 states but that is opposed by 24 states and the District of Columbia. Oklahoma and Kentucky separately have already settled with Purdue Pharma.

7.1 PURDUE'S SETTLEMENT PROPOSAL

> The settlement, which does not include any admission of wrongdoing, would reorganize Purdue during the bankruptcy into a trust that would continue to produce OxyContin, as well as overdose "rescue" drugs that would be distributed at no cost to communities across the country.[317]

The Sackler family issued a statement in September 2019 calling the settlement and bankruptcy a "historic step" to address a "tragic public health situation."

> *"It is our hope the bankruptcy reorganization process that is now underway will end our ownership of Purdue and ensure its assets are dedicated for the public benefit," the family said.*[318]

In the settlement, they offer to turn over assets they claim are worth USD $10 billion to $12 billion.

The proposed settlement includes:

- No admission of any wrongdoing.[319]
- The Sackler's agree to relinquish control of Purdue. Steve Miller, chairman of the company's board, estimated Purdue's assets at about USD $3.5 billion, including its manufacturing plants. It would continue to produce OxyContin, which is still under patent. Any profits from the sale of Purdue's drugs such as OxyContin would go to the cities, counties and states if they agree to the settlement. Much of the benefit to the public would be funded by the continued sales of the powerful narcotic OxyContin.[320]

317 ibid.
318 ibid.
319 ibid.
320 R Merle, L Berstein, 'Purdue Pharma's bankruptcy plan includes special protection for the Sackler family fortune', *The Washington Post*, 19 September 2019.

– The company would be reorganised into a "public benefit trust" whose primary mission would be to produce addiction treatment and anti-overdose drugs. The overdose "rescue" drugs would be distributed at no cost to communities across the country. The value of the anti-addiction and anti-overdose medication supplies is USD $4.5 billion. This is based on the assumption that the FDA will approve a trio of "rescue drugs" that Purdue has in the works. Those include a generic form of Suboxone, used to treat opioid addiction; an inexpensive version of naloxone opioid rescue nasal spray, the drug that first responders and others carry to reverse overdoses; and the drug nalmefene, which Purdue is developing to reverse overdoses from illegal street fentanyl.[321]

– The proposed minimum contribution from the Sackler family is USD $3 billion in cash. The Sackler family has announced it will be selling the family-owned international drug company called **Mundipharma** to generate these funds. The USD $3 billion in cash is to be paid over seven years.

> The Sackler's are now offering to pay USD $3 billion over seven years, plus an additional USD $1.5 billion, but with significant contingencies. The second payment would depend on the eventual sale of Mundipharma, netting at least USD $4.5 billion, after taxes, which is not a certainty. The family is aiming to have that sale finance their entire payout.[322]

8. PURDUE–MUNDIPHARMA AUSTRALIA

The central issue with the Australian operation is that Purdue–Mundipharma withheld critical information on the side effects of its medication.

The resulting bankruptcy is directly attributed to the human loss and suffering caused by this deliberate action over the past two decades. We have demonstrated that this same strategy has been occurring on an ongoing basis in Australia since the launch of OxyContin in 2000.

8.1 COMPARING ACTION IN THE US AND AUSTRALIA IN 2020

Following years of legal action for Purdue in the US, here is a summary of the situation for those in Australia who have been taking OxyContin (and other opioids such as Targin) for 20 years:

– Purdue has filed for bankruptcy following federal legal action for deliberately **misleading** critical addiction and overdose warnings and as a result, causing the US Opioid Crisis.

321 ibid.

322 M Goldstein, D Hakim, J Hoffman, 'Sacklers vs. States: Settlement Talks Stumble Over Foreign Business', *The New York Times*, 30 August 2019.

- Purdue is negotiating a multi-billion dollar payout to deliver compensation and treatment to those affected. This includes providing the opioid overdose rescue medication for free.
- The Australian Government has commenced no legal action against Mundipharma (Purdue's subsidiary).
- Mundipharma still profits from selling the opioids OxyContin and Targin in Australia, funded by the PBS.
- Mundipharma now profits from selling the Opioid rescue spray Nyxoid in Australia, funded by the PBS.
- Purdue's current consumer warnings (in the US) accurately reflect the material risks of their opioids
- Mundipharma has deliberately provided misleading critical addiction and overdose warnings in Australian CMIs since 2000, and still does today.
- Mundipharma has been deliberately providing misleading information to doctors since 2000 (and has been found to breach the pharmaceutical code of conduct).
- The Sackler family is now selling the global Mundipharma network to fund the USD $3-4.5 billion in cash they are offering in the opioid bankruptcy settlement. Australians buying opioids and opioid rescue medication from Mundipharma through the PBS enhances the sale value of Mundipharma and revenue to Purdue.
- The Sackler's are offering no settlement for Australians affected by OxyContin or Targin. Nor are they offering Nyxoid for free to Australians suffering from opioid addiction.
- The sale of Mundipharma could prevent future legal action being taken against the Sackler family.
- Purdue Pharma said the proposed bankruptcy settlement has been engineered "for the benefit of the American public." The settlement agreement, however, will provide no benefit for people in Australia.

8.2 NYXOID – AUSTRALIA

As shown in Chapter 6, Purdue–Mundipharma developed a version of Naloxone hydrochloride, called Nyxoid. It was approved by the TGA in 2018. The Federal Health Minister Greg Hunt MP announced that Nyxoid® (naloxone 1.8mg) nasal spray had been registered in Australia as an antidote to opioid overdose and it was placed on the PBS.

Mundipharma committed to finding an access model to make the product available to those who need it.

Interestingly, Mundipharma also paid for The Penington Institute to undertake a study on naloxone. According to a Denver Post article, the Australian Government used the study:

> *"...as a blueprint for a 10 million Australian dollar ($6.8 million) pilot program to distribute naloxone, including Nyxoid. And in October, Australian Health Minister Greg Hunt announced that Australia's government would subsidise Nyxoid prescriptions, meaning it costs Australians as little as AU$6.50 ($4.50) per pack, versus around AU$50 without the subsidy.*

In a strong endorsement for Purdue–Mundipharma, Minister Greg Hunt has defended using PBS funds to buy an opioid rescue medication from the same organisation that created the US opioid epidemic.

> *Asked in an interview whether the government had any concerns about following the recommendations of a Mundipharma-funded report that stood to benefit the company financially, Hunt replied: "All of the advice is that this is a product that will save lives and protect lives and our approach is to be* ***fearless of the source of the product****."*[323]

The article went on to say:

> *"You're in the business of selling medicine that causes addiction and overdoses, and now you're in the business of selling medicine that treats addiction and overdoses?" asked Dr. Andrew Kolodny, an outspoken critic of Purdue who has testified against the company in court. "That's pretty clever, isn't it?"*
>
> *"The way that they've pushed their opioids initially and now coming up with the expensive kind of antidote -- it's something that just strikes me as deeply, deeply cynical," said Ross Bell, executive director of the New Zealand Drug Foundation and a long time advocate of greater naloxone availability. "You've got families devastated by this, and a company who sees dollar signs flashing."*[324]

Mundipharma does not associate the need for Nyxoid with their own prescription opioids. Instead, they link the need for Nyxoid to illegal opioids.

9. OKLAHOMA OPIOID SETTLEMENTS

It is reported that "Oklahoma experienced more than 6,100 prescription opioid-related deaths from 2000–2017."[325]

In 2017 Oklahoma's attorney general, Mike Hunter commenced legal action against a number of opioid manufacturers. He targeted **Purdue** for its drug OxyContin and **Johnson & Johnson** for its drug Durogesic. The basis of the court cases was their marketing campaigns for painkillers. The companies successfully had Judge Thad Balkman to break up the case and hold multiple trials rather than have all defendants face jurors at the same time.

9.1 PURDUE

In 2016, there were 444 opioid-related overdose deaths in Oklahoma, which ranked it 28th in the US for such deaths, according to data analysed by the Centers for Disease Control and Prevention.[326]

In March 2019, Purdue Pharma LP reached a USD $US270 million settlement just before the trial started. Among the terms of the settlement:

– Purdue will pay USD $103 million to establish the National Center for Addiction Studies and Treatment at Oklahoma State University.

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323 C Galofaro and K Gelineau, 'Purdue Pharma's foreign affiliate now selling overdose cure', *The Denver Post*, 15 December 2019.
324 ibid.
325 R Ellis, 'Verdict to be announced Monday in state's lawsuit against opioid manufacturers', *Tulsa World*, 22 August 2019.
326 J Feeley, 'Purdue Pharma Reaches Deal to Settle Oklahoma Opioid Case', Bloomberg, 26 March 2019.

– Purdue will donate USD $20 million worth of medicine to the Center and contribute USD $72 million for counties and cities and the cost of the litigation.
– The Sackler's, whose total fortune has been estimated at USD $13 billion, have pledged USD $75 million to the Center over five years even though they weren't named as defendants.

"The agreement reached today will provide assistance to individuals nationwide who desperately need these services -- rather than squandering resources on protracted litigation," the family said in an emailed statement.

"This agreement is only the first step in our ultimate goal of ending this nightmarish epidemic," Oklahoma Attorney General Mike Hunter said in a press release. The state is pressing ahead to "hold other defendants in this case accountable for their role in creating the worst public health crisis our state and nation has ever seen."[327]

According to *The Guardian*:

Oklahoma's attorney general, Mike Hunter, called the settlement a "monumental victory" and "a new day in battle against opioid epidemic".[328]

The opioid rescue nasal spray is part of the settlement discussions. It will be provided free to the state to assist reduce overdose deaths.

10. JOHNSON & JOHNSON

Johnson & Johnson has also been subject to litigation for their role in the US Opioid Crisis. As with Purdue, in 2017 Oklahoma's attorney general, Mike Hunter commenced legal action against Johnson & Johnson for its marketing of the fentanyl opioid Duragesic.

The trial against Johnson & Johnson commenced in May 2019. As reported at that time:

Oklahoma's attorney general, Mike Hunter, told the civil trial, that Johnson & Johnson through its opioid medication Duragesic, played a leading role in "the worst manmade health crisis in the history of the country and the state". Calling the trial a "day of reckoning" for the company, Hunter accused the company of "destroying lives and families". "How did it happen?" Hunter asked. "Greed."

Brad Beckworth, another lawyer for the state, told the judge "It is a manmade crisis. The evidence will show this is a drug company made crisis," he said.[329]

After the ruling:

An Oklahoma judge has ordered Johnson & Johnson to pay USD $572m for its role in driving Oklahoma's opioid epidemic.

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327 ibid.

328 C McGreal, 'Purdue Pharma agrees to settle OxyContin opioid case with Oklahoma', *The Guardian*, 27 March 2019.

329 C McGreal, 'Johnson & Johnson boosted opioid sales via 'cynical brainwashing', court hears', *The Guardian*, 29 May 2019.

*"The Defendants, acting in concert with others, embarked on a major campaign in which they used branded and unbranded marketing to disseminate the messages that pain was under-treated and 'there was **a low risk of abuse and a low danger' of prescribing opioids**".*

*This is the core of the judge's finding. By "branded" he means efforts by Johnson & Johnson's sales reps to sell its own drugs [Duragesic], often by persuading doctors to prescribe them with claims that they carried **little risk of addiction** and were effective for long term treatment of chronic pain.*

The judge said this contributed to an oversupply of opioids because of increased prescribing, which caused addiction and deaths.

"False, misleading, and dangerous marketing campaigns have caused exponentially increasing rates of addiction, overdose deaths."

The judge found that Johnson & Johnson took distorted or discredited claims of a very low addiction rate from opioid painkillers and presented them to doctors as proof of the drugs' safety.

"In 2001, Defendants were advised by Defendants' own hired scientific advisory board that many of the primary marketing messages Defendants used to promote opioids in general, and Duragesic [the company's high-strength drug] specifically, were misleading and should not be disseminated."

Balkman ordered the company to pay USD $572m in compensation initially with additional payments to be negotiated to cover treatment, overdose prevention [Naloxone Nasal Spray] and other costs of abating the epidemic in Oklahoma in the coming years.

*The court found that Johnson & Johnson was repeatedly warned that its sales materials for its high-strength drug Duragesic were misleading at best. The warnings came not only from its own advisory board but the Food and Drug Administration (FDA). The company adapted some of the materials but maintained the central thrust of its sales pitch: that its opioids were effective, safe and **could be widely prescribed without significant risk of addiction.***[330]

Oklahoma's attorney general, Mike Hunter, was also reported as saying:

"...the ruling confirmed his claim that "Johnson & Johnson maliciously and diabolically created the opioid epidemic in our state", contributing to 6,000 deaths in Oklahoma alone since 2000.

"Today is a major victory for the state of Oklahoma, the nation and everyone who has lost a loved one because of an opioid overdose," he said. "Our evidence convincingly showed that this company did not just lie and mislead, they colluded with other companies en route to the deadliest man-made epidemic our nation has ever seen."[331]

The same article noted, "In one company memo presented in evidence at the trial, a rep said she dismissed a doctor's fears that patients might become addicted by telling him that those who didn't die probably wouldn't get hooked."

330 C McGreal, 'Johnson & Johnson opioid ruling explained – the key points', *The Guardian*, 27 August 2019.

331 C McGreal, 'Johnson & Johnson to pay $572m for fueling Oklahoma opioid crisis, judge rules', *The Guardian*, 27 August 2019.

10.1 DUROGESIC IN AUSTRALIA

Johnson & Johnson did the exact same thing in Australia.

In Australia Johnson & Johnson operate as Janssen.

In Australia, Durogesic is the opioid sold by Johnson & Johnson/Janssen. The CMI comparisons in Chapter 2 examined the CMIs for Durogesic in 1999, 2018, with a further review of the 2020 CMI in Chapter 7. This comparison showed that just as in the USA, the material risks for addiction and abuse have not been accurately disclosed since the product was launched.

The CMI has contained a medically incorrect and misleading warning on addiction since 1999. The CMI contains a statement that has no scientific basis – that the risk of addiction "...is unlikely when DUROGESIC is used correctly". This statement significantly reduces the possibility of addiction from a consumer's risk assessment. This is also a breach of the *Therapeutic Goods Act 1989* as this warning is inconsistent with the PI. The CMI (2020) now includes two new warnings of the risk of death in relation to addiction. It also warns of the risk of addiction and death even if being taken correctly as prescribed.

Addiction Warning
Australia CMI (2018) and CMI (1999) "Medicines like DUROGESIC can lead to addiction. This is unlikely when DUROGESIC is used correctly." (page 4)
Australia Product Information (2019) "Addiction can occur in patients appropriately prescribed DUROGESIC at recommended doses. The risk of addiction is increased in patients with a personal or family history of substance abuse (including alcohol and prescription and illicit drugs) or mental illness. The risk also increases the longer the drug is used and with higher doses." (page 9)
Australia CMI (2020) **"Hazardous and harmful use** DUROGESIC poses risks of abuse, misuse and addiction which can lead to overdose and death. Your doctor will monitor you regularly during treatment" (page 1) **"Before you use DUROGESIC** **Warning** Opioids can be abused and misused, and you are at risk for opioid addiction, even if you take your dose as prescribed. Opioid addiction, abuse and misuse can lead to overdose and death." (page 1 and 2)

In relation to the disclosed risks of abuse, the lack of information is even more staggering.

The CMIs from 1999–2019 have never contained a warning around the abuse risk to the consumer of Durogesic. Durogesic is a Schedule 8 drug due to the risk of it being abused, yet the risks of abuse including death, or warnings around abuse are not mentioned. Yet the Australian PI includes a warning for abuse, and the risk of death, for doctors. This is breach of the *Therapeutic Goods Act 1989* as this warning is inconsistent with the PI. The CMI now includes three new warnings of the risk of death in relation to abuse. It also warns of the risk of abuse even if being taken correctly as prescribed.

Abuse Warning
Australia CMI (1999) and CMI (2018) The risk of abuse to the consumer is not mentioned in the CMI.
Australia Product Information (2019) "Abuse or intentional misuse of DUROGESIC may result in overdose and/or death." (page 9)
Australia CMI (2020) **"Hazardous and harmful use** DUROGESIC poses risks of abuse, misuse and addiction which can lead to overdose and death. Your doctor will monitor you regularly during treatment" (page 1) **"Before you use DUROGESIC** **Warning** Opioids can be abused and misused, and you are at risk for opioid addiction, even if you take your dose as prescribed. Opioid addiction, abuse and misuse can lead to overdose and death." (page 1 and 2) "Do not cut, break, chew, crush, dissolve, snort or inject DUROGESIC. This can result in serious side effects and death." (page 5)

Refer to the detailed Durogesic CMI comparison in Chapter 7, which shows the warnings given in the 1999, 2018 and 2020 versions.

These extracts show that as in the USA, Janssen has deliberately misled Australian consumers on the material risks of Durogesic, including addiction and abuse for over 20 years. As shown in Chapter 1 and Chapter 2, Durogesic in 100 times more powerful than morphine and is responsible for an increasing number of deaths in Australia. The risks of this medication in relation to addiction and death is not only very real, but the occurrence of these outcomes in Australia is now at crisis levels.

This strategy directly mirrors the USA operations and the accountability for these actions in now being felt by Johnson & Johnson in the USA, but not in Australia.

10.2 COMPARING ACTION IN OKLAHOMA AND AUSTRALIA IN 2020

Remember, Oklahoma experienced more than **6,100** prescription opioid-related deaths from 2000–2017. That's for a population of around 3.9 million people.

Here is a summary of the situation:

- In the 1990s, Purdue and Johnson & Johnson deceived doctors and patients about the risk of addiction and abuse, causing the USA Opioid Crisis.
- Governments recognise "people are the victims of the drug company" and take legal action.
- Oklahoma's attorney general, Mike Hunter, called the Purdue settlement a "monumental victory" and "a new day in battle against opioid epidemic".
- Purdue settled for USD $270m.

- Purdue gives opioid rescue spray as part of settlement.
- Oklahoma's attorney general, Mike Hunter, told the civil trial, that Johnson & Johnson played a leading role in "the worst manmade health crisis in the history of the country and the state". Calling the trial a "day of reckoning" for the company, Hunter accused the company of "destroying lives and families".
- Johnson & Johnson found guilty and fined USD $572m.
- Johnson & Johnson to provide opioid rescue spray as part of settlement.

In comparison, **Australia experienced 13,269 opioid deaths from 2000–2017**.[332] Here is a summary of the situation:

- Janssen take $580 million from the PBS each year and Purdue–Mundipharma $280 million.
- Purdue and Johnson & Johnson/Janssen deceived doctors and patients about the risk of addiction and abuse, causing the Australian Opioid Crisis.
- The government response is to "blame the victims" for "abuse and misuse" of prescription medication.
- No government court cases are undertaken against any drug company.
- Purdue–Mundipharma and Johnson & Johnson/Janssen opioids remain on the PBS.
- Purdue–Mundipharma and Johnson & Johnson/Janssen have deliberately included misleading critical addiction, abuse and overdose warnings in Australian CMIs since 1999, and still does today.
- Greg Hunt rewards Purdue–Mundipharma with Nyxoid on the PBS.
- The Sackler family are offering no settlement for Australians affected by OxyContin or Targin. Nor are they offering Nyxoid for free to Australians suffering from opioid addiction.
- The sale of Mundipharma could prevent future legal action being taken against the Sackler family.
- Minister for Health, Greg Hunt has said, "we are in a better position than the USA" and "We will avoid an American style opioid crisis."

The commonalities between the USA deaths and Australia are irrefutable. The drug manufacturers deliberately mislead doctors and the public about the risks of these drugs. The lawsuits in the USA demonstrate the resulting addiction and deaths that result from this action are **criminal** and legal action has been successful.

It is now time for Australia to take the same steps.

332 Penington Institute, 2019, p 92.

11. SUMMARY TIMELINE

USA – PURDUE

AUSTRALIA – MUNDIPHARMA

1995

Oxycontin FDA Approved (1)

1996

1996–2000

Sales grew from $48 million in 1996 to almost $1.1 billion in 2000 (1)

1999

Issues around not lasting 12 hours, addiction and abuse reported (4)

Reports of large numbers of OxyContin overdose deaths begin to emerge (2)

OxyContin TGA approved

2000

Purdue announces investigation into abuse issues (4)

OxyContin released

FDA and DEA commence investigation of Purdue (4)

Fined by APMA for OxyContin marketing material

2001

FDA changes the OxyContin label to remove the statements that the risk of addiction and abuse was low (3)

2002

OxyContin overdose deaths reported

2003

300 active lawsuits accusing Purdue of lying about effectiveness, addiction and abuse (4)

CMI update

FDA issued a warning to OxyContin's manufacturer, Purdue Pharma, for misleading advertisements. Among many other details, the warning specified that the ads left out and minimised the serious safety risks associated with OxyContin and promoted it for uses beyond those which had been proven safe and effective. Specifically, the letter pointed out that the advertisements failed to clearly present information from the product label's Boxed Warning regarding the potentially fatal risks and the danger of abuse. (3)

2007

Fined by APMA for OxyContin marketing material

USA vs Purdue, Purdue plead guilty to criminal charges of misbranding OxyContin by claiming that it was less addictive and less subject to abuse and diversion than other opioids, and will pay USD $634 million in fines

2010

CMI update

2014

New 'tamper resistant version" released

Purdue releases new 'tamper resistant version" (3)

2019

CMI update

Nyxoid added to the PBS

Purdue settle lawsuit with the state of Oklahoma for USD $270 million

Fined by the TGA for false advertising of opioid Targin

Multi District Litigation commences in Ohio against Purdue

Purdue file for bankruptcy

US General Accounting Office – report to congress on OxyContin abuse (4)

1. A Van Zee, *The Promotion and Marketing of OxyContin: Commercial Triumph, Public Health Tragedy*, American Journal of Public Health, 2009 February; 99(2): 221–227, doi: 10.2105/AJPH.2007.131714, 2009.
2. M R Jones, O Viswanath, J Peck, et. al., *A Brief History of the Opioid Epidemic and Strategies for Pain Medicine*, Pain and Therapy, 2018 June; v7(1): 13–21, doi: 10.1007/s40122-018-0097-6, 2018.
3. U.S. Food & Drug Administration (FDA), published on 20 December 2019, see https://www.fda.gov/drugs/information-drug-class/timeline-selected-fda-activities-and-significant-events-addressing-opioid-misuse-and-abuse
4. United States General Accounting Office, Report to Congressional Requesters, *OxyContin Abuse and Diversion and Efforts to Address the Problem*, December 2003.

12. GOVERNMENT POLICY ON NYXOID

Purdue and Johnson & Johnson have been found guilty of facilitating the opioid addiction of millions of people through its failure to disclose the material risks of its opioid medication. As part of the legal action against both companies in the USA, they are now providing a Nyxoid equivalent for free to assist to help protect those addicted to opioids.

However, in Australia Nyxoid is sold for profit, supported by the PBS.

Why has the Australian Government not demanded it is offered for free as in the USA? Why are Australian taxpayers forced to buy a rescue drug to save people from the side effects of a therapeutic medication made by the same company? If it didn't have these side effects, people would not need the medication.

Warning

Do not stop taking a prescribed medication without discussing it with your doctor. Information can also be obtained by calling the NPS Medicines Line on 1300 633 424 or the Adverse Medicines Events Line on 1300 134 237 for advice. If you need support for any medical concern, including mental health matters, please contact your doctor. Lifeline also provides a 24 hour support service on 13 11 14 or www.lifeline.org.au

9. CLASS ACTION

1. INTRODUCTION

Based on the response by the US government and legal action against pharmaceutical companies, a clear roadmap of accountability has taken place. It is clear that the deceptive information provided to consumers has caused deaths and resulted in adverse side effects like addiction for an unimaginable number of victims.

This report has documented a level of deceptive conduct and lack of consumer warnings in Australia that is arguably far worse than what occurred in the US.

The cost to human life is well detailed and as is the legal right to safe healthcare that has not been met for over 20 years. Given informed consent has not been given, those affected (and their families) are entitled to compensation and justice.

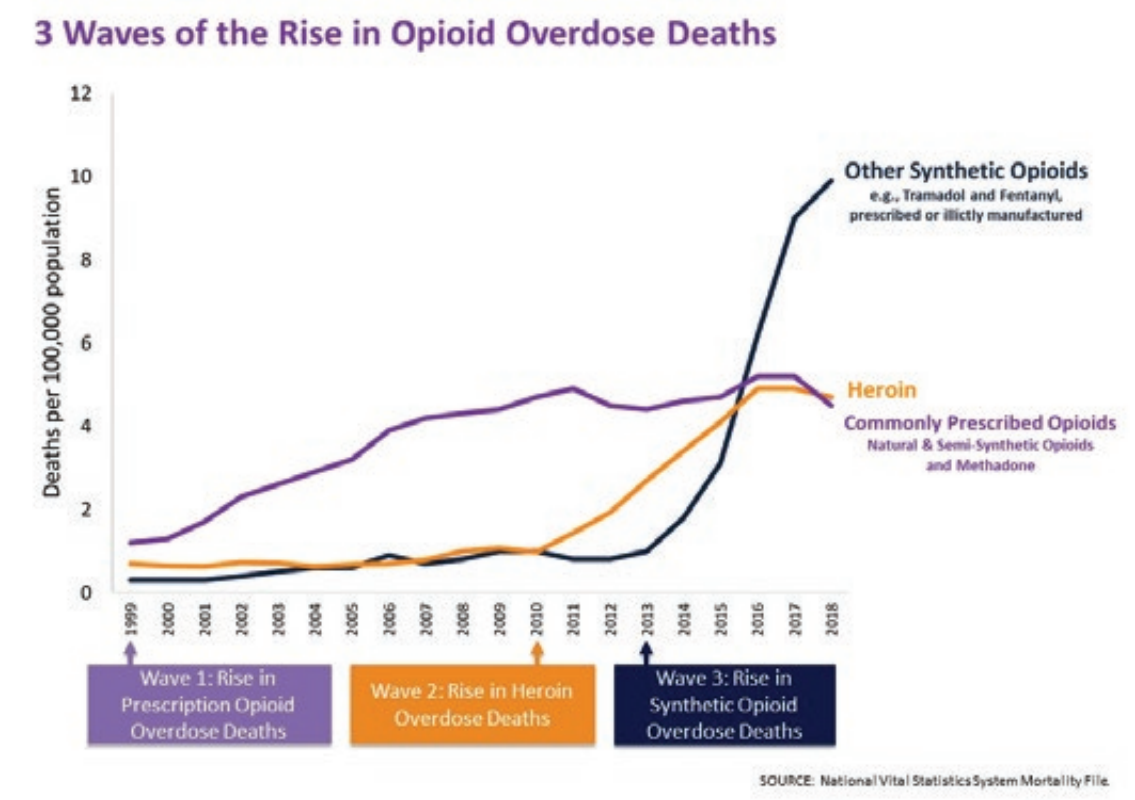
For those who were unknowingly exposed to addictive prescription medication, and then went onto a path of addiction to illegal drugs like heroin, are also due compensation.

Whilst the pharmaceutical companies are the architects of this national tragedy, accountability extends to all areas of the healthcare system.

2. THE THREE WAVES OF OPIOID DEATHS IN THE USA

In the US, the rise of opioid overdose deaths occurred in three waves, as shown in Figure 45. The CDC shows that the first wave occurred in the 1990s following the release of high strength opioids like OxyContin.

Figure 45: The three US waves of opioid overdose deaths (Source: CDC[333])



As shown in *The Washington Post*:

> *Wave 2 began in 2010 when Purdue released its new abuse resistant form of oxycontin and governments implemented restrictions to prescription opioid supply. People who had become addicted to prescription Oxycodone, now were forced to find an alternative opioid so they turned to illegal Heroin. This group including many people who had become addicted through pain medication for legitimate medical conditions. US studies with opioid-treatment seeking individuals found evidence of displacement to other opioids –both pharmaceutical-opioids and heroin. The result was a rapid increase in heroin overdose deaths. The heroin death rate never*

333 Centers for Disease Control and Prevention (CDC), accessed on 3 April 2020, see https://www.cdc.gov/drugoverdose/epidemic/index.html

surpassed that of prescription pills, but it served as a transition into the illegal market for many of those already addicted to opioids. There, they would find an even deadlier drug awaiting them.[334]

In 2012, the New England Journal of Medicine published a study that found "76 percent of those seeking help for heroin addiction began by abusing pharmaceutical narcotics, primarily OxyContin".[335]

> In one study, about 80 percent of current heroin users reported that they began with prescription opioids (Muhuri et al., 2013). Therefore, the public health effects of prescription opioids and heroin are intertwined (Kolodny et al., 2015).

– National Academies Press[336]

In response to the 2007 settlement with the FDA in which Purdue pleaded guilty to not disclosing the abuse, addiction and overdose risks of OxyContin, it released a new formulation in 2010. The FDA approved the modified version on the basis that the new form of OxyContin was "abuse resistant" in that it could not be "crushed". By crushing the original formulation, the entire opioid contents could be metabolised, causing drug addiction.[337]

The new formulation of OxyContin was not the only strategy implemented in the USA to combat the opioid crisis. The government undertook a number of strategies to:

- reduce the use of opioids by doctors
- raise awareness of the risks of the medication
- to encourage people to hand back the used drugs.

State authorities also began arresting doctors who had been overprescribing opioid medication.

According to an article in December 2019:

And at the center of the burgeoning epidemic, states cracked down on "pill mills," where doctors rapidly dispensed painkillers, often for cash. At one ring of 40 Florida clinics broken up in 2011, doctors saw up to 100 patients a day and made $1 million a year. That same year, "Operation Pill Nation" saw the arrests of 60 doctors across the Sunshine State.[338]

Wave 3 occurred around 2013, with synthetic opioids, such as fentanyl, considered the source of overdose deaths.

In a *The Washington Post* article:

Fentanyl has been used in the United States for decades, most of that time as a legally prescribed medicine. The drug, an opioid 100 times more powerful than heroin, had been given primarily to patients in excruciating pain. Starting in 2013, it began to flow into the country illegally in unprecedented quantities, the vast majority of it coming from China. It found its way into the hands of drug users primarily by being cut with heroin.[339]

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334 S Rich, M Kornfield, B R Mayes, A Williams, 'How the opioid epidemic evolved', *The Washington Post*, 23 December 2019.
335 MetroNews, 'Outside experts and gubernatorial campaigns disagree on Cole's drug plan', *MetroNews*, 22 August 2016.
336 National Academies of Sciences, Engineering, and Medicine; Health and Medicine Division, *Pain Management and the Opioid Epidemic: Balancing Societal and Individual Benefits and Risks of Prescription Opioid Use*, National Academies Press, Washington US, 13 July 2013.
337 U.S. Food & Drug Administration (FDA), 2010.
338 D Vergano, 'This Was The Decade Drug Overdoses Killed Nearly Half A Million Americans', BuzzFeed, 6 December 2019.
339 S Rich, et.al., 2019.

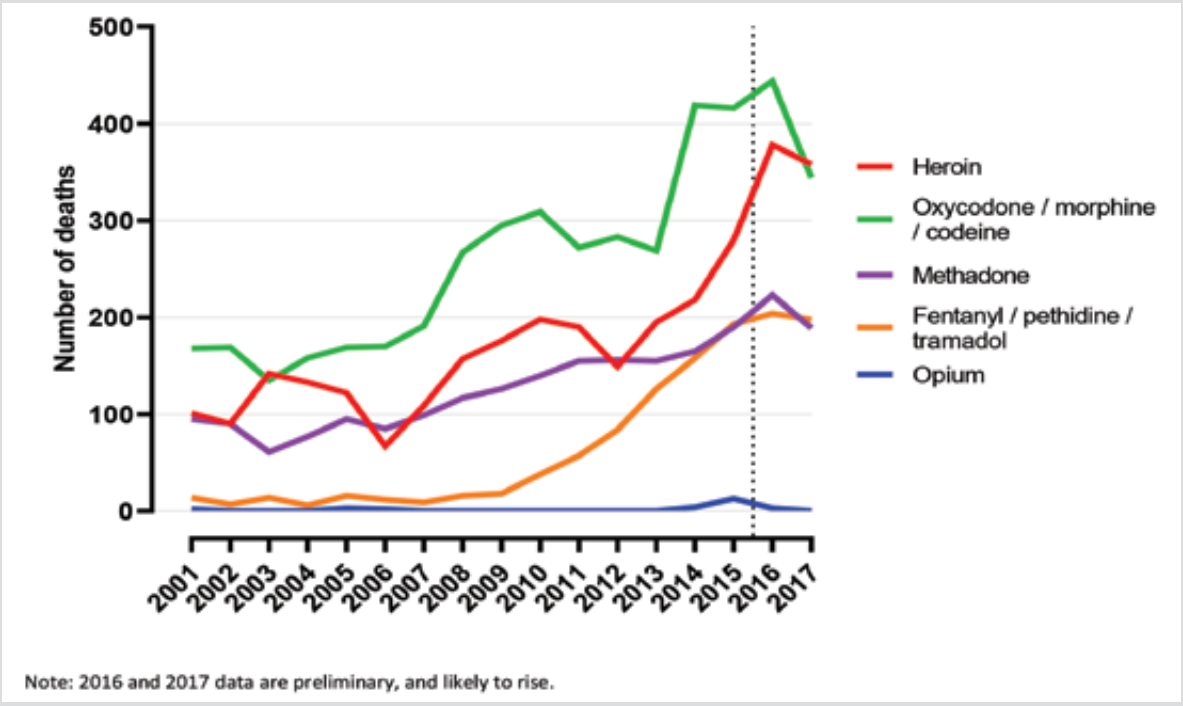
3. AUSTRALIA'S WAVES OF OPIOID DEATHS

As introduced in Chapter 3, Australia is experiencing a similar trajectory of opioid-related deaths.

3.1 WAVE 1: OXYCONTIN

The increase in opioid overdose deaths since the release OxyContin in 2000 is well documented by the AIHW and the Penington Institute in its Annual Overdose Report 2019 (see Figure 46).

Figure 46: Unintentional drug-induced deaths by opioid type (Source: Penington Institute[340])



The number of unintentional drug-induced deaths involving opioids has nearly **trebled in the last 12 years**, increasing from 338 in 2006 to 904 in 2017.

Over the same period:

- deaths involving heroin increased by 434% (from 67 to 358 in 2017)
- deaths involving oxycodone / morphine / codeine increased by 102% (from 170 to 344 in 2017)

340 Penington Institute, 2019.

– deaths involving fentanyl / pethidine / tramadol increased by over 1,000% (from 12 to 198 in 2017)
– deaths involving methadone increased by 122% (from 85 to 189 in 2017).

3.2 WAVE 2: HEROIN

In April 2014, a tamper resistant, difficult to crush formulation of OxyContin was introduced in Australia. This was "in response to growing concerns about its contribution to an increase in opioid use and related harms".[341]

It took Purdue an additional four years to bring this version to Australia after it was released it in the USA in 2010.

As per the trend in the USA, the new formulation pushed a number of OxyContin users to heroin.

According to a paper about trends in heroin and pharmaceutical-opioid related harms:

> *Heroin-related deaths in Australia were relatively stable between 2001 and 2012. Our findings indicate that heroin-related harm began to rise around mid-2014. This study showed a plateauing of overdoses attributed to pharmaceutical-opioids alongside increased heroin-related ambulance and ED attendances.*[342]

This study found a change in pharmaceutical-opioid related harm around the middle of 2014. Reformulated 'tamper-resistant' oxycodone was introduced in the US in 2010, then in Australia in April 2014.

In comparison to the US where multiple opioid policies were introduced during the time of reformulation, the reformulation was the main change in Australia, and therefore a location where impacts may be more 'cleanly' observed; especially as original formulations of oxycodone were withdrawn overnight without advance notification to prevent stockpiling.

A medically supervised injecting centre in NSW found that during the time of reformulation, visits to inject oxycodone fell, while visits for heroin, morphine and fentanyl increased. Due to this partial displacement, the overall number of opioid-overdoses managed by the centre remained stable.

The reduction in pharmaceutical-related harms in Victoria may have been offset by partial substitution with heroin.

An article in *The Age* in August 2019 noted:

> *A new study by the centre finds there was a 25 per cent increase in heroin overdoses in Victoria from 2014 to 2018.*
>
> *The [Victorian Department of Health and Human Services] says on its website that Australian sales of OxyContin 80mg tablets decreased by 28 per cent in the five months following the introduction of reformulated OxyContin on April 1, 2014.*
>
> *This was backed up by a report last year by the Penington Institute which found there was a 50 per cent increase in heroin-related deaths in Victoria from 2014-2015.*

341 National Drug & Alcohol Research Centre, *The Lancet Psychiatry: Tamper-resistant oxycodone tablets have no impact on overall opioid use or harm*, media release, 11 January 2018.

342 T Lam, L Kuhn, J Hayman, M Middleton, et.al, Recent trends in heroin and pharmaceutical opioid-related harms in Victoria, Australia up to 2018, doi.org/10.1111/add.14784, *Addiction*, 29 August 2019.

"This paper appears to be the first to analyse and report a clear emerging trend starting around mid-2014 of increasing heroin-related harm and a flattening or decreasing of harms relating to pharmaceutical opioids," the study says.[343]

3.3 WAVE 3: FENTANYL

A CSIRO blog noted that Fentanyl has become the leading cause of drug overdose deaths in the United States. Similarly here in Australia, "there has been an alarming increase in the number of accidental fentanyl-related deaths in recent years. Deaths from fentanyl increased 1800 per cent in 15 years in Australia. The drug was listed in Australia's Annual Overdose Report as a major factor driving a rapid increase of accidental opioid-related deaths since 2011. This surge in use was confirmed by a 2018 national wastewater drug monitoring program."[344]

Australia's experts are reporting that our third wave is taking a similar course to the US:

Penington Institute chief executive John Ryan warned that this rise was reminiscent of the North American opioid epidemic around 2012, when some patients who were shifted off prescription drugs turned to illicit drugs such as heroin and ice and to abusing painkiller fentanyl.

"Reducing access to prescription drugs without addressing the underlying causes simply changes the type of drugs that are abused – with fatal consequences," Mr Ryan said. "Australia shouldn't follow America's failed approach."[345]

Similarly:

The rapid increase in the use of synthetic opioids, especially fentanyl, has been identified in the Australian Criminal Intelligence Commission's 2018 and 2019 wastewater monitoring reports, research by the Australian National University and the most recent Pennington Institute report on overdose deaths. The ABC has confirmed how easy it is to purchase fentanyl and its precursors online.[346]

343 J Topsfield, 'Heroin overdose spike linked to painkiller changes', *The Age*, 30 August 2019.
344 A Green, Detecting the 'drop dead' drug–fentanyl, blog, CSIROscope, 1 April 2019.
345 J Topsfield, 'Australia's drug overdose crisis: unintended deaths head for record high', *The Sydney Morning Herald*, 26 August 2019.
346 V White, 'The opioid problem in Australia: connecting the dots', *The Strategist*, 19 September 2019.

4. ADDICTION CAN START FROM THE FIRST PRESCRIPTION

The trend described in the USA and Australia as waves is in reality demonstrating the flow on effects of prescription opioid addiction.

The similarity in the trends is due to the similarity in the underlying causes. When people become addicted to prescription medication, like OxyContin, they become addicted to opioid drugs. When supply is restricted, people turn to heroin and fentanyl.

Hence the root cause of the addiction remains the reason for the deaths, irrespective of it being OxyContin, heroin, fentanyl or other drugs.

Responsibility for these deaths remain with those who enable the addiction to develop at the time of the original prescription. This has been argued successfully in multiple court cases in the USA against Purdue, Johnson & Johnson and others.

As argued by Kate Allman in a LSJ Online article, Australia is next in line for an opioid class action:

"If a person develops a crippling addiction from a drug prescribed for common pain problems, and they've relied on representations that said it was not addictive, then they can claim damages for misleading and deceptive conduct," says Ben Slade, Managing Principal of Maurice Blackburn in Sydney and head of the firm's NSW class actions department. "They may also be able to claim for personal injury under Australian Consumer Law, depending on the extent of the addiction and the harm caused."

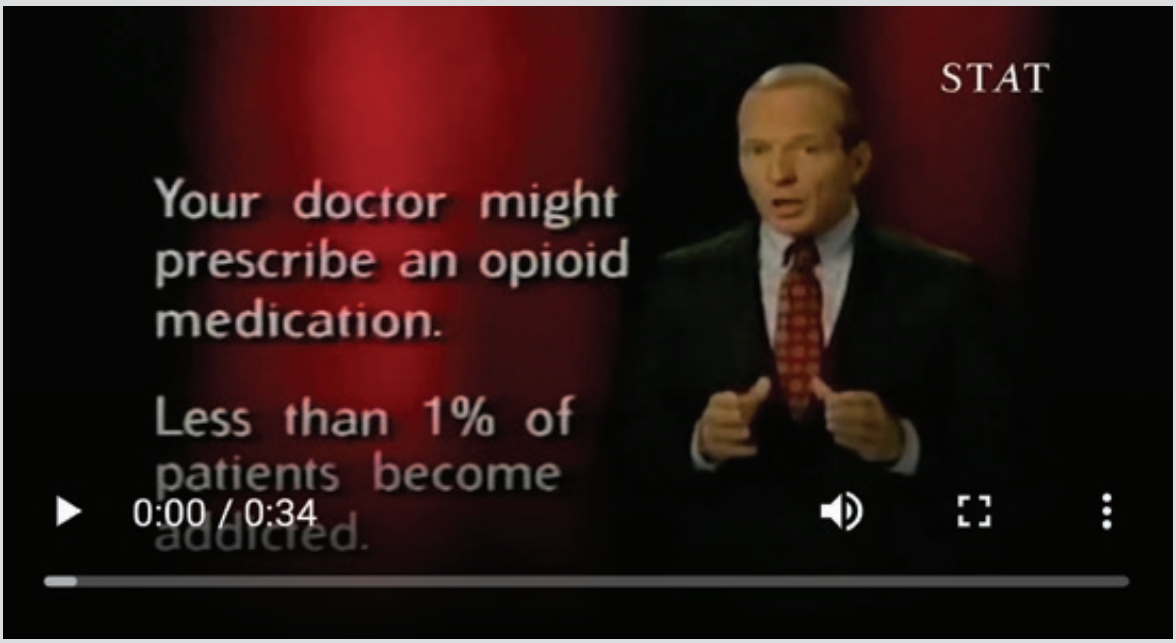
"If the evidence is that the impact of drugs is as severe as the Americans allege – people becoming chronically addicted and unable to keep working, losing their jobs and income – it could well be that a class action is in the wind for Australia," says Slade.

"To put it another way, 1.9 million Australian adults initiate opioid use, and 3 million use opioids each year." Samanta Lalic, a clinical pharmacist and PhD candidate at Monash University says dependant users are often first exposed to prescription painkillers for chronic conditions like back pain. They need stronger doses as the pain persists and they grow accustomed to the medication. If they hit obstacles sourcing legal prescriptions, they might turn to illegal opioids. Heroin is a common progression. "People assume that the stereotype of a drug user or 'addict' is the depraved, criminal, homeless junkie or druggie," says Lalic. "But what we have actually seen is that it can be anyone who initiates opioid use and becomes dependant. The reality is more mainstream, suburban, white-collar and regional."

"If a drug company fails to warn you about addiction risks of taking drugs, and you become addicted, and that addiction is so crippling that it's regarded as imposing an injury on you of greater than 15 per cent of total bodily injury, you can claim," says Slade. "If you then lose your employment, you will have an economic loss associated with that. Serious crippling addictions will do that."

The USA Opioid Crisis involved aggressive marketing tactics to doctors and community marketing practices, including national television advertising (see Figure 47). Thankfully, pharmaceutical television advertising is banned in Australia. Even so, the misleading statements about risk – on which people rely – still exist in pharmaceutical practices.

Figure 47: Still from a misleading TV advertisement run in the US by Purdue in 1999



As shown in the Oklahoma ruling against Johnson & Johnson:

> *An Oklahoma judge has ordered Johnson & Johnson to pay USD $572m for its role in driving Oklahoma's opioid epidemic.*
>
> *"The Defendants, acting in concert with others, embarked on a major campaign in which they used branded and unbranded marketing to disseminate the messages that pain was under-treated and 'there was a low risk of abuse and a low danger' of prescribing opioids".*
>
> *This is the core of the judge's finding. By "branded" he means efforts by Johnson & Johnson's sales reps to sell its own drugs [Duragesic], often by persuading doctors to prescribe them with claims that they carried little risk of addiction and were effective for long term treatment of chronic pain.*
>
> *The judge said this contributed to an oversupply of opioids because of increased prescribing, which caused addiction and deaths.*
>
> *"False, misleading, and dangerous marketing campaigns have caused exponentially increasing rates of addiction, overdose deaths."*[347]

The false, misleading and dangerous practices in Australia are exactly the same.

347 C McGreal, 'Johnson & Johnson opioid ruling explained – the key points', 2019.

5. WHO IS ACCOUNTABLE?

It is easy to examine the CMI documentation and breaches of the Therapeutic Goods Act, and lay the blame solely with the pharmaceutical companies.

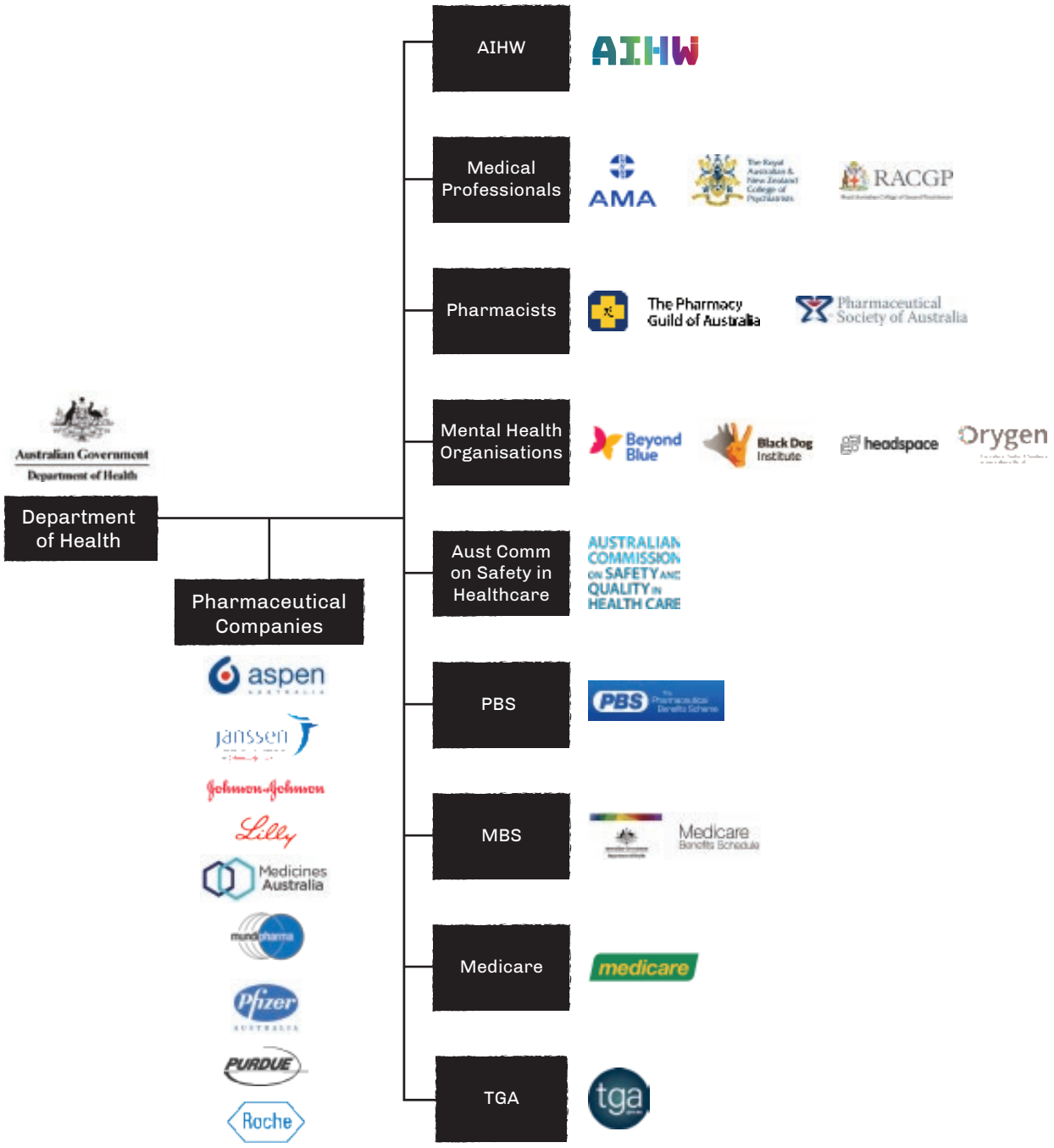
However horrific their actions are, they are only one part of the health care system.

As shown in Chapter 4, pharmacists have failed in their duty to ensure safe medication and polydrug medication prescribing – demonstrating what people with lived experience have reported for years.

A point widely recognised in the US is that neither the pharmaceutical companies nor pharmacists are physicians and they do not prescribe medication. The role of prescribing medication and monitoring side effects is primarily the role of doctors. It seems incomprehensible that polydrug deaths can occur on the scale seen in Australia, without any focus on the role of physicians in this tragedy. They are responsible for obtaining informed consent, so they are responsible for providing the patient with all the risks and benefits of a medication.

Invalid informed consent means no consent and a complete legal liability for any ensuing adverse events.

The Australian Government, through the Department of Health, has overseen these healthcare system failures. The TGA has failed in its duty in multiple areas, however it is a regulatory body implementing government policy. The lax nature of consumer medication safety laws sits with the Australian Government. Mental health organisations like Orygen/ Headspace, Black Dog Institute and Beyond Blue receive tens of millions of dollars each year from the Department of Health, and have direct access to government, yet have remained silent on these issues for decades.



The government has not only failed to protect vulnerable people, they have blamed them for the problem. The saddest part? No matter which entity or entities become the focus of future class actions, the fact remains that many of those people the government chose to blame are **no longer here to see justice served**.

Warning

Do not stop taking a prescribed medication without discussing it with your doctor. Information can also be obtained by calling the NPS Medicines Line on 1300 633 424 or the Adverse Medicines Events Line on 1300 134 237 for advice. If you need support for any medical concern, including mental health matters, please contact your doctor. Lifeline also provides a 24 hour support service on 13 11 14 or www.lifeline.org.au

10. CONFLICTS OF INTEREST

1. INTRODUCTION

A number of the organisations mentioned in this report have significant, and long-term, lobbying power with government.

The underlying door-opener for these organisations is arguably the political donations that they make.

The Pharmacy Guild of Australia, as well as many pharmaceutical companies, have invested heavily in political donations over the years, gaining them access and input to government policy.

The pharmaceutical companies are also heavily investing directly into mental health organisations, many who represent people with lived experience.

In light of the issues raised in this report, how have these donations influenced – directly or indirectly – the trend in prescription medication deaths in Australia?

2. POLITICAL DONATIONS

As outlined in Chapter 4, The Pharmacy Guild receives $7.9 million a year from the PBS for administration fees. Yet the Guild also donates nearly $800,000 back to political parties, based on AEC data shown in an ABC article (see extract at Figure 48).[348] Effectively these political donations are funded by the PBS.

Figure 48: Political donations made by The Pharmacy Guild of Australia (Source: ABCNews)

Donor name	Donation made to	Amount ($)
The Pharmacy Guild of Australia	Australian Labor Party	590,811
The Pharmacy Guild of Australia	Liberal/National Party of Australia	182,980
	Total	773,791

348 A Bogle and J Snape, 'Coalition's $165 million war chest that helped Scott Morrison win election revealed', *ABCNews*, 3 February 2020.

They also made donations to One Nation:

> *Lobby group the Pharmacy Guild of Australia, which represents pharmacy owners, has defended making a $15,000 donation to Pauline Hanson's One Nation. Payments of $7,500 were made to the political party by the guild's Queensland branch in June and July. In March, the branch made a $1,450 donation to Katter's Australian party. While the guild has also made donations to Labor, the Liberals and the Nationals, no donations have been made to the Queensland Greens.*[349]

George Tambassis (left) – National president, Pharmacy Guild of Australia with Community pharmacy owner Greg Hunt (right) – Minister for Health.

Another lobby group, Medicines Australia, is actively involved in engaging with government. They state their role is to represent "the discovery-driven pharmaceutical industry in Australia. Our member companies invent, manufacture and supply innovative medicines and vaccines to the Australian community".[350]

In the same AEC data, Medicines Australia were shown to make political donations totalling $153,432 (see Figure 49).

A full list of members of Medicines Australia is listed on their website, and includes Eli Lilly Australia Pty Ltd, GlaxoSmithKline Australia Pty Ltd, Janssen Pty Ltd, Novartis Pharmaceuticals, Pfizer Australia Pty Ltd and Roche Products Pty Limited.[351]

Members of Medicines Australia and the Medicines Australia secretariat remain in close contact with Members of Parliament and government departments to monitor activities and promote policy options to ensure the continuation of a viable medicines industry.

Figure 49: Political donations made by Medicines Australia (Source: ABCNews)

Donor name	Donation made to	Amount ($)
Medicines Australia Limited	Australian Labor Party (ALP)	71,827
Medicines Australia Limited	Liberal Party of Australia	67,250
Medicines Australia Limited	National Party of Australia	14,355
	Total	153,432

Beyond lobby groups, there is a widespread number of direct contributions from pharmaceutical companies to many major political parties, as shown in Figure 50.

349 M Davey, 'Pharmacy Guild of Australia defends making $15,000 donation to One Nation', *The Guardian*, 6 April 2019.
350 Medicines Australia, accessed on 3 April 2020, see https://medicinesaustralia.com.au/about-us/our-role/
351 Medicines Australia, accessed on 3 April 2020, see https://medicinesaustralia.com.au/about-us/our-members/

Figure 50: Political donations made by pharmaceutical companies (Source: ABCNews)

Donor name	Donation made to	Amount ($)
Pfizer Australia	Australian Labor Party (ALP)	24,560
Pfizer Australia	Liberal/National Party of Australia	27,480
	Total	52,040

Donor name	Donation made to	Amount ($)
Johnson & Johnson Pty Ltd	Australian Labor Party (ALP)	49,080
Johnson & Johnson Pty Ltd	Liberal/National Party of Australia	64,580
	Total	113,660

Donor name	Donation made to	Amount ($)
Roche Products Pty Ltd	Australian Labor Party (ALP)	53,500
Roche Products Pty Ltd	Liberal/National Party of Australia	17,000
	Total	70,500

2.1 INFLUENCING ADVICE

The Guardian reported on the influence of the pharmaceutical industry on Australia's political parties in 2018:

The pharmaceutical industry is engaging vast numbers of lobbyists and donating millions to both political parties, creating a level of influence that a former health department secretary has linked to Australia's high medicine prices.

A Guardian Australia analysis of donations and lobbyist records has revealed the true extent of the industry's influence.

About 72 separate pharmaceutical businesses engage paid lobbyists to influence government decisions and policy. They are represented by 29 separate lobbying firms, many of which have former ministerial or political advisers as staff.

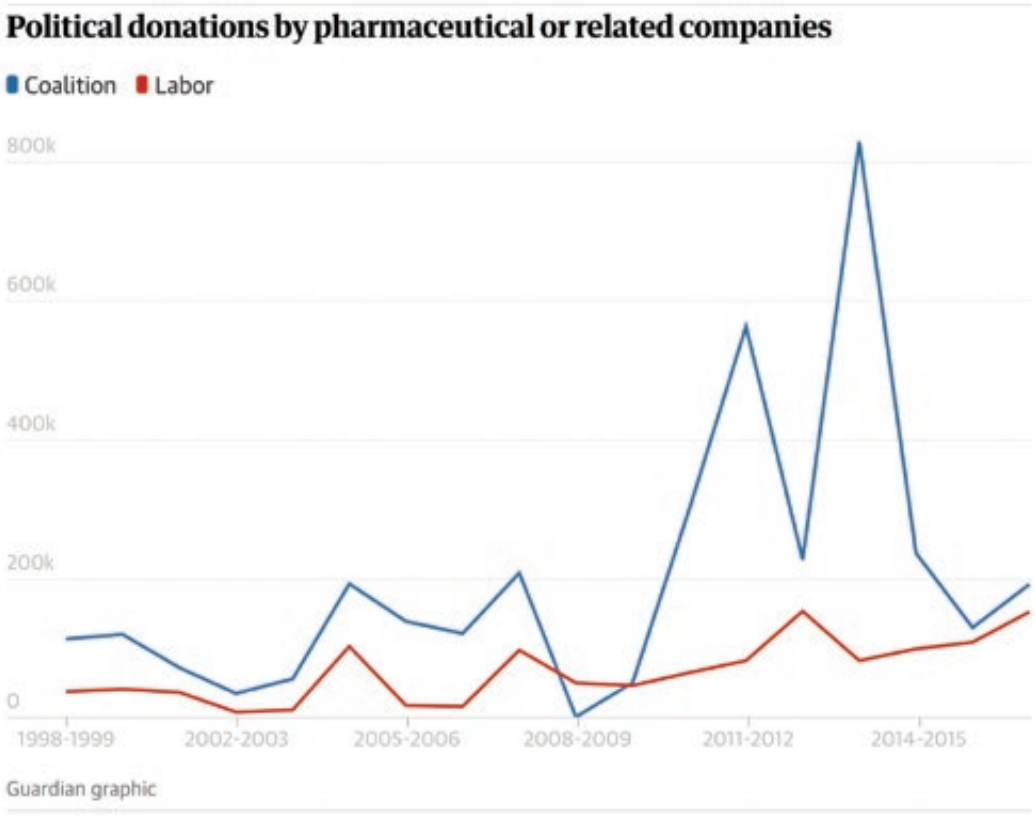
A separate analysis of donations data shows that between 1998-99 and 2016-17, companies that research and manufacture drugs, or distribute and sell drugs at the retail level, such as chemist and pharmacy companies, donated $4.7m to the Liberal, National and Labor parties.

Twenty-two of the 72 companies that engage lobbyists have also made political donations in the past 19 years. Donations peaked in the 2013-14 financial year, which coincided with the 2013 federal election.

Big pharmaceuticals have a significant financial stake in the way government behaves, particularly in decisions or policy affecting medicine pricing or approval processes for new drugs.

A former federal health department secretary, Stephen Duckett, now a leading health researcher at the Grattan Institute, said the pharmaceutical industry was "extremely powerful" and exerted significant influence on government.

A spokesman for the health minister, Greg Hunt, completely rejected any suggestion that the pharmaceutical lobby had influence over the listing of medicines on the pharmaceutical benefits scheme, a process which he said was completely separate from government.



"We have some of the world's best medical experts running the independent Pharmaceutical Benefits Advisory Committee (PBAC) and they make decisions in the interests of Australian patients and only Australian patients," he said.

"PBAC recommends all listings of medicines on the PBS. The committee is independent of government by law and in practice."

"By law the federal government cannot list a new medicine without a positive recommendation from PBAC."[352]

352 C Knaus and N Evershed, 'Pharmaceutical industry donates millions to both Australian political parties', *The Guardian*, 25 September 2018.

A decision by the PBAC is not binding for the government. The selection of medication is directed by the PBAC but the final decision is made by government, who is the organisation accepting the political donations. They can choose to ignore recommendations or delay a decision.

The Liberal Government has gone to great lengths to claim good management of the PBS and its additions of new drugs:

> *"Since 2013, the Morrison Government has made more than 2,200 new or amended medicines listings on the PBS. This represents an average of around 30 listings per month – or one each day – at an overall cost of around $10.6 billion."*[353]

2.2 INFLUENCING POLICY

While political donations may not influence the PBAC, the final decision on policy is made by politicians that have accepted millions in pharmaceutical industry donations. The argument that political donations do not influence decisions by government will always be subject to ridicule whilst political parties continue to accept political donations.

Pharmaceutical companies have also lobbied heavily against industry regulation that inhibits their market powers.

Medicines Australia is the peak national body representing the pharmaceutical industry. They are also responsible for Medicines Australia's Code of Conduct, which sets the standards for the ethical marketing and promotion of prescription pharmaceutical products in Australia. It supposedly complements the legislation requirements of the Therapeutic Goods Regulations and the *Therapeutic Goods Act 1989*. Not all pharmaceutical companies are members of Medicines Australia, like Mundipharma, so the code doesn't apply to them.

The Code of Conduct states:

> *"As the custodians of our medicines we conduct ourselves ethically, appropriately communicating relevant information to those relying on our medicines, including patients, their carers and families, healthcare professionals and the broader community."*
>
> *"Information relevant to prescribing, in particular product and safety information, are clearly communicated in all promotional materials. Promotional materials are designed by Companies to not only create awareness of Therapeutic Goods Administration (TGA) approved medicines, but to support proper assessment of their risks and benefits."*[354]

353 G Hunt (Minister for Health), PBS listings to save melanoma and multiple sclerosis patients up to $128,900 a year, media release, 28 October 2019.

354 Medicines Australia, *Code of Conduct Edition 19*, 30 March 2020.

The Code contains very specific rules on including medication side effects in the PI documents. In relation to CMIs, the Code only requires that the CMIs be made available:

13. Interactions with the General Public

Consume Medicine Information, risk management materials and Product Information are credible, non-promotional sources of information about a Company's products. A Company may make these documents available to members of the general public, providing they appear in their entire form and are not amended, abridged or displayed in a promotional manner.[355]'

Why are pharmaceutical companies allowed to regulate pharmaceutical companies?

Medicines Australia and the government have resisted calls to make the Code of Conduct legally enforceable, overseen by a government regulator, with criminal penalties. Seems like political donations help the industry with more than just PBS medications.

This report has identified numerous systemic issues that pharmaceutical companies are responsible for creating. These issues have directly resulted in the deaths of thousands of Australians. The failure of government to adequately protect vulnerable Australians, has now been exposed. In light of the significant political donations that have been accepted, the question has to be asked: what influence have these companies had in creating the current prescription health crisis?

2.3 INFLUENCING THE MENTAL HEALTH ORGANISATIONS

Pharmaceutical companies have almost no limit to the organisations they are seeking to influence. The money they distribute extends into many organisations within the mental health care system.

The RANZCP accepts advertising and sponsorship funding from the pharmaceutical industry.[356] This can only be described as the greatest conflict of interest imaginable. Their 2017 Annual Report lists Janssen, Lundbeck, Pfizer, Merck Sharp and Dohme, Servier, Otsuka and Teva Pharma as financial supporters.

Major drug companies are now principal sponsors of many mental health advocacy groups, as reported in *The Age*:

> *"The so-called "Pharma Collaboration", unreported in the Australian media, linked the Mental Health Council of Australia directly to global pharmaceutical giants Pfizer, Eli Lilly, Glaxo SmithKline, Bristol Myers Squibb, Lundbeck, Wyeth and Astra Zeneca."*[357]

Mental Health Australia (formerly the Mental Health Council of Australia) is regarded as "the peak, national non-government organisation representing and promoting the interests of the Australian mental health sector and committed to achieving better mental health for all Australians."[358]

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355 ibid.

356 The Royal Australian & New Zealand College of Psychiatrists (RANZCP), RANCZP engagement with the pharmaceutical industry, June 2016.

357 R Baker, 'Mental health takes industry pills', *The Age*, 8 August 2006.

358 Mental Health Australia, accessed on 3 April 2020, see https://mhaustralia.org/about-us

However, they have a long and financially rewarding partnership with the pharmaceutical industry:

> *"Mental Health Australia (formerly the Mental Health Council of Australia) has a formal collaboration with a group of pharmaceutical companies. Known as the Mental Health Australia Pharma Collaboration, partner companies agree on an annual workplan of specific activities along with a broad range of core benefits for all parties that are outlined in the Working Together Guide."*[359]

Similarly, SANE Australia, a national mental health charity, also accepts pharmaceutical funding, namely from Janssen.[360] [361]

This report has demonstrated that when it comes to achieving better mental health outcomes for Australians, the pharmaceutical industry has failed to deliver on even the most basic consumer warnings. Partnering with Mental Health Australia or other mental health organisations is unacceptable and must cease.

359 Medicines Australia, *Working Together Guide*, accessed on 3 April 2020, see https://medicinesaustralia.com.au/community/working-together-guide/case-studies/mental-health-australia-using-the-guide-in-public-discussion-about-collaborative-relationships/

360 SANE Australia, *Pharmaceutical policy*, accessed on 3 April 2020, see https://www.sane.org/about-sane/policy-on-engagement-with-pharmaceutical-companies

361 SANE Australia, *Janssen Australia*, accessed on 3 April 2020, see https://www.sane.org/about-sane/supporting-partners/2070-janssen-australia

Warning

Do not stop taking a prescribed medication without discussing it with your doctor. Information can also be obtained by calling the NPS Medicines Line on 1300 633 424 or the Adverse Medicines Events Line on 1300 134 237 for advice. If you need support for any medical concern, including mental health matters, please contact your doctor. Lifeline also provides a 24 hour support service on 13 11 14 or www.lifeline.org.au

11. SUICIDE BY PBS

1. INTRODUCTION

> The facts on suicide in Australia are stark. Just over 3000 people are lost to suicide each year in Australia, an average of more than 8 people per day. It is the leading cause of premature death in Australia's young adults, accounting for around one-third of deaths among people aged 15–24. For every death by suicide, as many as thirty people attempt suicide and are hospitalised due to intentional self-harm. **And there has been no significant and sustained reduction in the death rate from suicide over the past decade, despite ongoing efforts to make suicide prevention more effective.**

– Productivity Commission Draft Report Overview & Recommendations – Mental Health, October 2019

As described in this report, prescription medication can have life-shortening and life-threatening side effects. Yet many prescription medications also are life-taking.

The same medications prescribed to vulnerable people with mental health and pain conditions are also toxic enough to be used as a means of suicide death.

The statistics from the last 20 years show that the medication prescribed to treat mental illness and pain conditions are also **the same medications used in suicide attempts and deaths.**

These medications are as **lethal as firearms** and the World Health Organization (WHO) advises on the risks of these medications to vulnerable people.

So why are these medications legally prescribed and PBS-funded, with almost no consumer warnings to help patients and their families protect against the use of these drugs in suicides?

There is growing use of these medications in the treatment of young people, with an aligned exponential increase in self harm in Australia.

Strangely, global recognition of the risks of medications and programs to reduce these deaths are largely ignored in Australia. Despite all the evidence, Australia still refuses to acknowledge and address the issue, urgently adopt safer medicine treatments, or even to warn consumers.

2. SUICIDE AND PRESCRIPTION MEDICATION

Fact: the most common drug classes used in suicide deaths and attempted suicides are **PBS medications** and in the majority of those instances, the medication used was legally prescribed to the person. As outlined in this chapter, commonly these medications are:

Benzodiazepines

Antidepressants

Opioid Analgesics

Antipsychotics

A consistent fact in multiple reports on drug overdose for both completed and attempted suicide is:

> *"The same broad categories of medications identified in earlier studies were found to contribute to the majority of overdoses in this study, namely **benzodiazepines, antidepressants, analgesics and antipsychotics**."*[362]

And contrary to the government commentary that these medications are predominantly obtained illegally:

> *"Patient interviews revealed three main reasons for the original acquisition of the medications used in overdose: treatment purposes (77%); recreational use (16%); and overdose (7%). **The most common source of medications (68%) used in overdose was prescription by the patient's usual doctor**."*
>
> *and*
>
> *"Consistent with the finding that most participants acquired their medication for legitimate therapeutic purposes, the majority of participants obtained their medication via a prescription issued by their usual GP or psychiatrist (68%).*[363]

2.1 CAUSES OF SUICIDE DEATHS

The ABS provides annual suicide data in its Causes of Death reports. In 2018 it reported that mood disorders, including depression, were the most commonly mentioned co-morbidity across all 3,046 suicide deaths (mood disorders were present in 43.9% of these deaths). While pharmaceutical opioids were the most common opioid present in suicidal overdose, with 80% having had a natural or semi-synthetic opioid present.[364]

362 P Buykx, W Loxley, P Dietze, A Ritter, Medications used in overdose and how they are acquired – an investigation of cases attending an inner Melbourne emergency department, *Australian and New Zealand Journal of Public Health*, vol.34, issue 4, Victoria, Australia, 3 August 2010.

363 ibid.

364 Australian Bureau of Statistics, 2019.

The 2016 report identified that "benzodiazepines were the most common substance present in drug induced deaths in 2016."[365]

This is not a new trend. From 1997 to 2011, the most common types of poisoning agent reported for suicide deaths were **benzodiazepines** and **antidepressants**.[366]

Horrifyingly, in some instances, the very medication prescribed to treat the risk of suicide is used as a method of poisoning in suicide.

As noted in a paper on suicide prevention and intervention about the seemingly contradictory nature of one type of medication:

> *"Lithium can significantly reduce the incidence of suicide attempts and completed suicide in patients with major mood disorders, compared to those not treated with lithium.*
>
> *Lithium, valproate, carbamazepine and lamotrigine are dangerous in overdose and lethal quantities may be available on a single prescription."*[367]

Many antidepressants also have a risk of increasing suicidal thinking, as noted by the TGA in their Medicines Safety Update:

> *"The TGA has published articles reminding health professionals of the risk of suicidality and/or other psychiatric adverse events associated with antidepressants (October-December 2016), isotretinoin (August 2016), varenicline (February 2016 and August 2010), anticonvulsant pregabalin (December 2014), atomoxetine (October 2013) and montelukast (April 2013) in previous issues of Medicines Safety Update."*[368]

2.2 ATTEMPTED SUICIDES

It is estimated that for every life lost to suicide, as many as 30 other people attempt suicide.

The most common method of suicide attempt is intentional overdose with medicines. Medications prescribed for mental health symptoms and/or painkillers are the most likely to be used in cases of medication overdose.[369]

An AIHW report also shows that prescription medication is the most commonly used method in suicide attempts. In 2010–11 there were 20,499 hospitalisations in Australia due to intentional over-dose with medicines. One in three people admitted to hospital for intentional overdose had taken benzodiazepines or paracetamol, one in four had taken an antidepressant and one in six had taken an opioid medicine."[370]

A 2017 report on Victorian overdose deaths concluded that of all Victorian overdose deaths involving pharmaceutical drugs:

- 73% of the deceased in the study cohort had a diagnosed mental illness and for most of these deceased, the duration of mental illness was at least 10 years
- 28% of the deaths were classified as intentional self-harm overdose deaths, and a further 18% where intent was unable to be determined

365 Australian Bureau of Statistics, 2018.
366 Australian Institute of Health and Welfare (AIHW), *Suicide and hospitalised self-harm in Australia: trends and analysis*, cat no. INJCAT 169, Canberra, Australia, 3 December 2014, pp.8,35.
367 J Anderson, P B Mitchell, H Brodaty, Suicidality: prevention, detection and intervention, *Australian Prescriber*, doi 10.187773, 3 October 2017.
368 Australian Government Department of Health Therapeutic Goods Administration, *Medicines Safety Update*, Volume 9, Number 2, June 2018.
369 P Buykx, et.al.,2010.
370 AIHW, 2014.

– benzodiazepines are the most commonly detected drug group, contributing in an average of 51% of overdose deaths annually
– the next most frequent pharmaceutical drug groups are opioid analgesics (48% of overdose deaths each year), antidepressants (34% annually) and antipsychotics (19% annually).

It also stated that "in most Victorian overdose deaths involving pharmaceutical drugs, the drugs are prescribed to the deceased rather than diverted or accessed OTC."[371]

Tellingly only **two of the top 20 drugs contributing to overdose deaths are illegal** (see Table 20). The inclusion of alcohol highlights the dangers of its use and the significance of the lack of consumer warnings in the CMIs.

Table 20: The 20 most frequent contributing drugs in overdose deaths, Victoria 2009–2015 (Source: J Dwyer et.al.)

Individual drug	Drug group	n	% Single drug	% Multiple drug
Diazepam	Benzodiazepine	995	0.1	99.9
Heroin	Illegal	948	28.9	71.1
Alcohol	Alcohol	641	21.1	78.9
Codeine	Opioid	481	1.7	98.3
Methadone	Opioid	456	9.9	90.1
Oxycodone	Opioid	337	9.8	90.2
Alprazolam	Benzodiazepine	314	0.6	99.4
Methamphetamine	Illegal	278	14.4	85.6
Quetiapine	Antipsychotic	278	2.9	97.1
Paracetamol	Non-opioid analgesic	236	15.7	84.3
Mirtazapine	Antidepressant	202	1.0	99.0
Temazepam	Benzodiazepine	200	5.0	95.0
Amitriptyline	Antidepressant	198	9.6	90.4
Oxazepam	Benzodiazepine	192	1.0	99.0
Citalopram	Antidepressant	160	2.5	97.5
Tramadol	Opioid	143	2.1	97.9
Olanzapine	Antipsychotic	142	1.4	98.6
Clonazepam	Benzodiazepine	125	1.6	98.4
Nitrazepam	Benzodiazepine	124	4.8	95.2
Venlafaxine	Antidepressant	117	6.8	93.2

A 2019 Belgium study concluded that

> *"Intentional drug overdose is the most common method of self-harm. As psychiatric disorders are very common in self-harm patients, the medication used to treat these disorders can become the means for the self-harm act."*
>
> *"...the availability of medication via prescriptions plays an important role in the choice of the medication ingested during the self-harm act."*[372]

371 J Dwyer, et.al., 2017.
372 N Vancayseele, I Rotsaert, G Portzky, K van Heeringen, Medication used in intentional drug overdose in Flanders 2008-2013, *PLoS ONE*, 14(5): e0216317, 2 May 2019.

3. YOUTH SUICIDES IN AUSTRALIA

A more distressing trend was reported in a study released in February 2019 about trends in self-poisoning and psychotropic drug use in people aged 5–19 years.[373] A University of Sydney news article reported:

> *"The study found there were more than **33,500** self-poisonings in young people from 2006 – 2016, with a **98** per cent increase over this time."*
>
> *"The most common medicines involved were over-the-counter pain medicines like paracetamol and ibuprofen, as well as antidepressants and antipsychotics."*
>
> *The study also investigated trends in medicine dispensing in the pharmaceutical benefits scheme (PBS) database.*
>
> *"We also looked at use of psychotropic medications in children and adolescents, and saw large increases, particularly with antidepressants," said Dr Cairns.*
>
> *"We found there is substantial overlap between the most dispensed psychotropics and medicines most commonly used in self-poisoning episodes, which could mean that young people are overdosing on psychotropic medicine prescribed for them."*
>
> *"Self-harm is a key risk factor for eventual suicide, so these alarming findings could unfortunately herald increasing Australian suicide rates."*
>
> *"People who self-poison have substantially higher risk of completed suicide, especially in the year immediately following their self-poisoning."*
>
> *"The study results signal a generation that is increasingly engaging in self-harm and is increasingly prescribed medications used to treat symptoms of mental disorders," said senior author Professor of Clinical Pharmacology Nicholas Buckley from the University of Sydney's Medical School, Charles Perkins Centre and the NSW Poisons Information Centre."*[374]

Tragically the results of this report have been ignored across all sections of the government and health care network. Our kids are under threat; they are crying out for help, yet nothing is being done.

An even more concerning fact is that a number of medications identified in the report, like venlafaxine (efexor) and temazepam, are not approved for use in children, so how did they get them?

These facts validate the views presented in this report that mental illness, comorbid conditions, addiction and prescription medication are extremely common amongst the most vulnerable people in Australia.

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373 R Cairns, E A Karanges, A Wong, et. al., Trends in self-poisoning and psychotropic drug use in people aged 5–19 years: a population-based retrospective cohort study in Australia, BMJ Open 2019;9:e026001, doi: 10.1136/bmjopen-2018-026001, 20 February 2019.

374 K Print, *Steep rise in self-poisoning in children and adolescents*, The University of Sydney, News article, 21 February 2019.

The use of prescription medication in suicides is reported annually in the ABS Cause of Death report, while the life-ending risks of many prescription medications including opioids, benzodiazepines, antidepressants and antipsychotics is well documented. Yet very little government policy acknowledges a very simple and clear fact: **vulnerable people are being prescribed the very medication that they are using to end their own lives. The PBS is funding the means of death.**

To have any impact on reducing the tragic loss of life from suicide, each of these factors has to be addressed under a coordinated plan of action. For that to happen, government needs to acknowledge that the very medication being prescribed to treat vulnerable people is also a lethal means of suicide.

4. SUICIDE PREVENTION STRATEGIES

Reducing access to *means of death* is a critically important suicide prevention strategy for the WHO. This includes medications that can cause fatal overdoses.

> *"Restricting access to the means for suicide works. An effective strategy for preventing suicides and suicide attempts is to restrict access to the most common means, including pesticides, firearms and certain medications."*[375]

> *"In most European countries, self-poisoning with medication is the second or third most common method of suicide and suicide attempts. Restricting access to and availability of medications that are commonly used in suicide has been shown to be an effective preventive measure."*[376]

The WHO is leading a global initiative to ensure that all countries have a national suicide prevention strategy in place. A key focus is to reduce access to lethal means like medications.

As stated in their publication to encourage national health programs:

> *A systematic way of developing a national response to suicide is to create a national suicide prevention strategy. A national strategy indicates a government's clear commitment to dealing with the issue of suicide. Typical national strategies comprise a range of prevention strategies such as surveillance, means restriction, media guidelines, stigma reduction and raising of public awareness as well as training for health workers, educators, police and other gatekeepers. They also usually include crisis intervention services and postvention."*[377]

375 World Health Organization (WHO), *Preventing Suicide: A global imperative*, 2014, p13.
376 ibid, p34.
377 World Health Organization (WHO), *Preventing suicide: A global imperative*, Luxembourg, 2014, p 8.

In a more recent program released by the WHO, they recommend nations include a specific objective of 'reducing suicides using medications' in suicide prevention strategies and measure the results.

Reduce access to the means of suicide:

Develop interventions to reduce access to means of suicide.

Specific objectives:

Reduce the number of suicides as a result of overdose of medications.[378]

The WHO makes a very important point in the 2014 *Preventing suicide: A global imperative* report: the greater the accessibility to lethal means, the greater the risk of suicide.

*Access to the means of suicide is a **major risk factor for suicide.** Direct access or proximity to **means** (including pesticides, firearms, heights, railway tracks, poisons, medications, sources of carbon monoxide such as car exhausts or charcoal, and other hypoxic and poisonous gases) **increases the risk of suicide**.*[379]

That means that having lethal prescription medications in the possession of a person actually increases the risk of suicide.

4.1 SUICIDE PREVENTION IN THE USA – REDUCING THE MEANS

The US Government-funded Suicide Prevention Resources Center (SPRC) website provides advice to families to assist them to reduce access to the means of suicide (see Figure 51).

Figure 51: Website page for Suicide Prevention Resource Center

378 World Health Organization (WHO), *National suicide prevention strategies: progress, examples and indicators*, Geneva, 2018, p 21.

379 WHO, 2014, p 32.

"Reducing access to lethal means of self-harm for a person at risk of suicide is an important part of a comprehensive approach to suicide prevention. Firearms are the most lethal among suicide methods. Also of concern are medications that are lethal at high doses."[380]

To highlight the lethality of both firearms and medications, the website features a picture of each, side by side (shown in Figure 51).

"Families, organizations, health care providers, and policymakers can take many actions to reduce access to lethal means of self-harm. Some of these are general household health and safety precautions that should be used regardless of suicide risk. Examples include limiting access to medications and storing firearms safely when not in use.

Other actions may be more appropriate when a person is at risk for suicide. If someone in the home is feeling suicidal, has recently attempted suicide, or is experiencing a crisis, it is safest to remove lethal means from the household entirely until the situation improves. For example:

Store firearms with law enforcement (if allowed), or lock up firearms and put the key in a safe deposit box or give the key to a friend until the crisis has passed.

Ask a family member to store medications safely and dispense safe quantities as necessary."[381]

4.1.1 The 'how' of suicide

The Harvard T.H. Chan School of Public Health is a world leader in suicide prevention research and programs.

The *Means Matters* program focuses not just on why people attempt suicide but 'how' and the strategies to stop access to lethal means. The work forms part of the US Suicide Prevention Resource Center.

Their research concludes that:

"When it comes to suicide, the most lethal method of attempt (and death) is firearms, and the most common method of attempt (but not death) is medications. So let's start there."[382]

Their research provides statistics about how people commonly attempt and complete suicide in the USA:

More use a firearm (52%) than every other method combined. Suffocation (mostly hanging) accounts for 23%, poisoning/overdose for 18%, jumps 2%, cuts 2%, and other 4%.

Most nonfatal self-harm treated in the emergency department results from poisoning/overdose (64%), followed by cutting (19%). Less than 1% of nonfatal attempts are with a gun."[383]

380 Suicide Prevention Resource Center, accessed on 3 April 2020, see https://www.sprc.org/comprehensive-approach/reduce-means

381 ibid.

382 Harvard T.H. Chan School of Public Health, accessed on 3 April 2020, see https://www.hsph.harvard.edu/means-matter/recommendations/clinicians/

383 Harvard T.H. Chan School of Public Health, accessed on 3 April 2020, see https://www.hsph.harvard.edu/means-matter/basic-suicide-facts/how/

4.1.2 The 'when' and 'where' of suicide

Many suicides are not planned and occur very soon after someone makes the decision to end their own life.

> *"A study of people who nearly died in a suicide attempt asked: "How much time passed between the time you decided to complete suicide and when you actually attempted suicide?" 24% said less than five minutes and another 47% said an hour or less."*[384]

Even more worrying is the location of suicides:

> *"About three-quarters of suicide incidents occur at home. Most (85%) die at the scene and never make it to the hospital."*[385]

4.1.3 Reducing access to medications

The gravity of the problem is well stated by the SPRC:

> *"Reducing access to lethal means in the home, such as firearms and medication, can determine whether a person at risk for suicide lives or dies."*[386]

As part of their work to provide new strategies to reduce suicide deaths, the SPRC developed a program that trains emergency department providers to counsel families of youths at high risk for suicide to restrict access to lethal medications.[387]

On their website, under '**Medications**', they suggest to:

- *Safely dispose of unused, expired, and unwanted medications.*
- *Lock abuse-prone medications like opioids (prescription pain pills), anxiety pills, muscle relaxants, amphetamines, sedatives, and barbiturates.*
- *Keep small quantities of those medications the family needs on hand. Lock the rest. The goal is to limit medicines on hand to a quantity that even if taken together would not cause serious harm.*
- *A pharmacist can advise on specific medications and quantities. For example, if the patient is at risk for overdose but must take a regular prescription, they may be safer with weekly or monthly refills.*[388]

They also provide information to families and carers:

> *"Medications – Don't keep lethal doses at home. Your doctor, pharmacist, or the poison control center (1-800-222-1222) may be able to help you determine safe quantities for the medicines you need to keep on hand. Click here for information on how to dispose of excess medications safely. Be particularly aware of keeping prescription painkillers (such as oxycodone and methadone) under lock and key both because of their lethality and their potential for abuse."*[389]

384 Harvard T.H. Chan School of Public Health, accessed on 3 April 2020, see https://www.hsph.harvard.edu/means-matter/basic-suicide-facts/when/

385 Harvard T.H. Chan School of Public Health, accessed on 3 April 2020, see https://www.hsph.harvard.edu/means-matter/basic-suicide-facts/where/

386 Suicide Prevention Resource Center, accessed on 3 April 2020, see https://www.sprc.org/resources-programs/calm-counseling-access-lethal-means

387 Harvard T.H. Chan School of Public Health, accessed on 3 April 2020, see https://www.hsph.harvard.edu/means-matter/lethal-means-counseling/

388 Harvard T.H. Chan School of Public Health, accessed on 3 April 2020, see https://www.hsph.harvard.edu/means-matter/recommendations/clinicians/

389 Harvard T.H. Chan School of Public Health, accessed on 3 April 2020, see https://www.hsph.harvard.edu/means-matter/recommendations/families/

4.2 AUSTRALIA'S STRATEGIES

The Australian Commission on Safety and Quality in Health Care released a report in 2017 titled *Medication safety in mental health,* which detailed many of the issues presented in this chapter. The report noted:

> *"Similarly, pharmacists can educate consumers, their families and carers to recognise and understand medication safety as a suicide prevention activity. Removal of expired or unused medication from the home, for example, acts as a protective factor for people with thoughts of self-harm, actual self-harm, suicidal ideation or for those who have attempted suicide."*[390]

Tragically neither pharmacists nor anyone else in healthcare has implemented any program that delivers on these recommendations.

4.3 AUSTRALIAN MENTAL HEALTH ORGANISATIONS

Orygen is a not-for-profit organisation with a mission to reduce the impact of mental ill-health on young people, their families and society. They provide support through the Headspace network of clinics around Australia. Headspace centres act as a one-stop shop for young people who need help with mental health.[391]

The **lethality** of medication is not regularly discussed by Orygen on their website, except in this training document for mental health professionals:

> *"Ensure that the environment is made safe for a young people who has clear suicidal intent and a plan. Discuss the availability of potentially lethal means (such as paracetamol, other medications, sharp objects or rope), and ask the young person to remove these items from their environment."*[392] *(page 4)*

Similarly, Beyond Blue briefly identifies the issue in their suicide prevention resources:

> *"Risk factors – sometimes called vulnerability factors, these factors increase the likelihood of suicidal behaviour.*
>
> *Risk factors include:*
>
> *– Access to harmful means, such as medication or weapons"*[393]

These mental health organisations place their emphasis on stigma reduction, early intervention and seeking treatment. The risks of prescription medication are virtually hidden.

4.3.1 An independent role?

Headspace clinics are able to **prescribe medication to young people**, primarily being Selective Serotonin Reuptake Inhibitor (SSRI) antidepressants like fluoxetine (more commonly known as Prozac), and they endorse its use in publications:

> *"In Australia, guidelines published in 2011 by beyondblue and the National Health and Medical Research Council indicate that fluoxetine should only be considered for young people with moderate to severe depression (not mild depression)..."*[394]

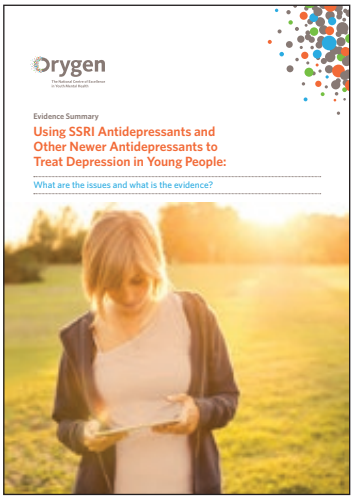
390 L Roughead, N Procter, K Westaway, J Sluggett, C Alderman, June 2017, p 59.
391 Orygen, accessed on 3 April 2020, see https://orygen.org.au/
392 Orygen, *Managing ongoing suicidality in young people diagnosed with Major Depressive Disorder (MDD)*, 2017.
393 Beyond Blue, accessed on 3 April 2020, see https://www.beyondblue.org.au/the-facts/suicide-prevention/feeling-suicidal/suicidal-warning-signs
394 Orygen, *Using SSRI Antidepressants and Other Newer Antidepressants to Treat Depression in Young People: What are the issues and what is the evidence?*, 2015.

More disturbingly this resource and others produced by Orygen/Headspace states:

> *"**No deaths have been reported that are attributable to SSRI prescription**."*[395]

This statement completely ignores the plethora of information on the life-shortening, life-threatening and life-ending deaths caused by SSRIs. A simple review of the Prozac PI (2020) states:

> *"During a 13-year period, there were 34 fatal reports of overdose where fluoxetine was the only reported ingestant."*



On the management of suicide risk, the PI states:

> *"Prescriptions for PROZAC should be written for the smallest quantity of medicine consistent with good patient management, in order to reduce the risk of overdose."*

The PI also warns:

> *"Development of serotonin syndrome may occur."*

However, the Prozac CMI (2019) provides no warning of the risk of death from an overdose, no mention of serotonin syndrome and no warning to limit access to the medication supplies to prevent suicide attempts from an overdose. Yet again, a CMI is inconsistent with the PI, and informed consent could not have been legally given based on this information.

Read Chapter 5 to find out more about informed consent.

Headspace argue in support of their use of fluoxetine (Prozac):

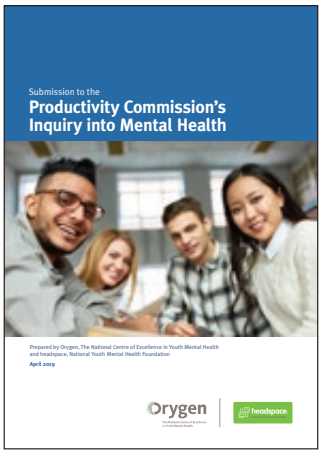
> *"There is evidence that fluoxetine is modestly effective for reducing symptoms of depression in young people. Balanced against these findings are the even greater risks of not treating depression, be it pharmacological or psychological."*[396]

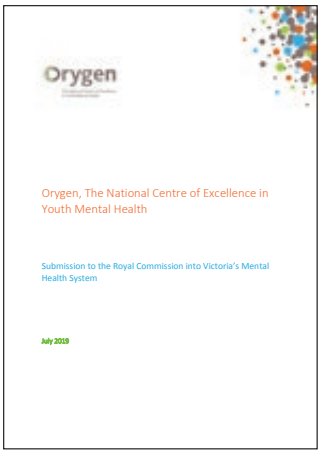
This might be true, but based on the CMI and online Headspace resources, it appears unlikely that the young person was informed of the fatal risks of fluoxetine when making this decision. The 2019 study on the trends in self-poisoning and psychotropic drug use in people aged 5–19 years, showed that fluoxetine was the third most common substance ingested in child and adolescent self-poisoning.

In February 2019 Professor Patrick McGorry was quoted in an article about the 2019 study referenced earlier in this chapter. Professor McGorry is the executive director of the youth mental health research institute, Orygen, and he is also a founding director of Headspace. The article contained no comment from Professor McGorry on the results of the study, only that he believed there was inadequate funding for Headspace: "That's part of the reason why we are seeing increases in self harm and suicidal behaviour."[397]

395 ibid.
396 ibid.
397 M Davey, ''Struggling to cope': child suicide rates may rise as intentional self-poisoning rates double', *The Guardian*, 21 February 2019.

Despite the horrifying trends in youth self-poisoning, the submissions to the Productivity Commission and Victorian Royal Commission by Orygen and Headspace make no mention of this national medication crisis; even in the sections of the reports on reducing self-harm and suicide-related behaviours in young people.





Olanzapine and Clopine (clozapine) are another two medications in which the CMI contains no warning on the risk of death from an overdose.[398] [399] The PIs for both medications state that overdoses can be fatal.[400] [401]

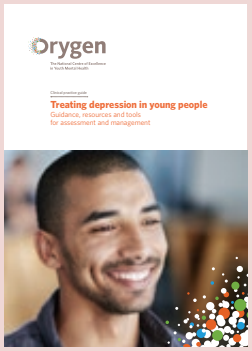
Orygen and Headspace produce numerous resources for health service providers on the research evidence and best practices for the care of young people with mental health and substance abuse problems. Two of Orygen's documents propose medications where our report has identified life-threatening risks are not disclosed in the CMIs. These are:

Australian Clinical Guidelines for Early Psychosis: A Brief Summary for Practitioners[402]

- Fluoxetine
- Olanzapine
- Clozapine
- Benzodiazepines
- Antidepressants
- Lithium

Treating depression in young people: Guidance, resources and tools for assessment and management[403]

- Fluoxetine
- Antidepressants (SSRI)



"Prescribing clinicians should consider the toxicity of overdose and/or limit the amount prescribed if the person is assessed to be at-risk of suicide."

In addition to Fluoxetine, other medications in these guidelines like olanzapine, clozapine, benzodiazepines and risperidone are also evident in the trends in self-poisoning and psychotropic drug use in people aged 5–19 years. Based on these facts it demands urgent investigation as to the use of medication in Headspace clinics, the warning information provided to young people and their families, and the process of obtaining informed consent. What impact have the clinical guidelines produced by Orygen/Headspace had in influencing other doctors to prescribe these medications to youths?

398 Apotex, APO-Olanzopine Film Coated Tablets, Olazapine Consumer Medicine Information, March 2020.
399 Pfizer, Clopine Consumer Medicine Information, January 2020.
400 Apotex, APO-Olanzopine Film Coated Tablets, Olazapine Australian Product Information, March 2020.
401 Pfizer, Australian Product Information – Clopine (Clozapine), January 2020.
402 Orygen, Early Psychosis Guidelines Writing Group, *Australian Clinical Guidelines for Early Psychosis: A Brief Summary for Practitioners*, Melbourne, 2010.
403 Orygen, *Treating depression in young people: Guidance, resources and tools for assessment and management*, 2017.

4.3.2 A strategic responsibility?

Beyond Blue, The Black Dog Institute and Orygen all made submissions to the Productivity Commission Inquiry into mental health and the Royal Commission into Victoria's Mental Health System that do not mention prescription medication issues **once**. Why are all mental health organisations not doing more with the taxpayer funding they are provided to ensure that consumers and their families are made aware of the measures they can put in place to **try and reduce these tragic deaths** from prescription medication? Any organisation that encourages Australians to get help for mental health issues has an obligation to ensure that the help they get is safe.

Considering the rising numbers of young people overdosing on mental health medication as reported in February 2019, this also demands urgent investigation.

The need to reduce accessibility to medication can be found on the government's healthdirect website:

> *"While waiting for the person to receive treatment, remove any possible means of suicide from their immediate environment, such as medicines, knives or other sharp objects, and household chemicals, such as bleach."*[404]

The issue is also being acknowledged in the suicide deaths of Australian Defence Force veterans, as reported in *The Canberra Times* in November 2019:

> *"Australia's defence veterans are taking their own lives at higher rates and being prescribed more antidepressants and opioids than the general population."*[405]

However, a review of the CMIs on the TGA website for benzodiazepines, opioid analgesics, antidepressants and antipsychotics has a very consistent outcome: **none** contain any explicit warnings to inform consumers of this risk nor provide measures to help them to reduce these risks.

Despite the plethora of information that exists, the lethal means of medication is rarely discussed in Australia. In fact, as outlined in Chapter 12, reducing prescription medication deaths is almost universally ignored in Australia's mental health and suicide prevention strategies.

5. A DEADLY REALITY

Firearms are the most lethal means of death available.

Statistics on firearm deaths in Australia show that restricting access has had a significant impact in reducing suicide deaths by firearms.[406]

The National Firearms Agreement was introduced in 1996 following the Port Arthur tragedy. The legislation that followed in various state and federal laws prohibit a person who has a diagnosed mental illness from legally possessing and using a firearm.

404 Australian Government, healthdirect, accessed on 3 April 2020, see https://www.healthdirect.gov.au/warning-signs-of-suicide

405 F O'Mallon, K Bermingham, 'More vets than civilians take own lives', *The Canberra Times*, 29 November 2019.

406 Parliament of Australia, *After Port Arthur - Issues of Gun Control in Australia*, Current Issues Brief 16 1995-96.

In 1994, 420 lives were lost to suicide by firearms. In 2018 it was 169.[407]

Mental health and pain medications with serious life-threatening risks are prescribed to vulnerable people as a method of treatment. Many of these medications are toxic enough to be classified as a lethal means of death, just like firearms. Many people are prescribed multiple medication types, providing access to even more lethal polydrug combinations like opioids and benzodiazepines.

In Australia these medications are prescribed to adults and children who already suffer from health conditions that increase the risk of suicide. In some cases, the condition itself is suicidal ideation, and the medication prescribed to treat it is lethal even at prescribed doses.

These medications are stored in homes. People can easily access lethal quantities; sometimes just one prescription is enough. By making it easily accessible we also increase the risk of someone completing a suicide, exactly as if they had been given a loaded gun to keep unsecured in the house.

The consumer warnings for these medications provide no information to help individuals and their families to protect against this deadly risk. The lack of information fails to provide them with the ability to give informed consent to expose themselves to this risk. The warnings provided by health professionals stop well short of what is required to stop these tragic deaths.

Is there a greater failing of any society, or a greater breach of our human rights, than when a health care system deliberately provides vulnerable people with a deadly means of ending their suffering, funded by taxpayers?

> Doctors classify my PBS medication as a treatment for my mental illness. Suicide prevention experts regard it as lethal means of death. The difference is just how many pills I take. Suicide prevention experts recommend keeping prescription medication in a gun safe with firearms. I don't have that problem in Australia because I can't buy a gun.

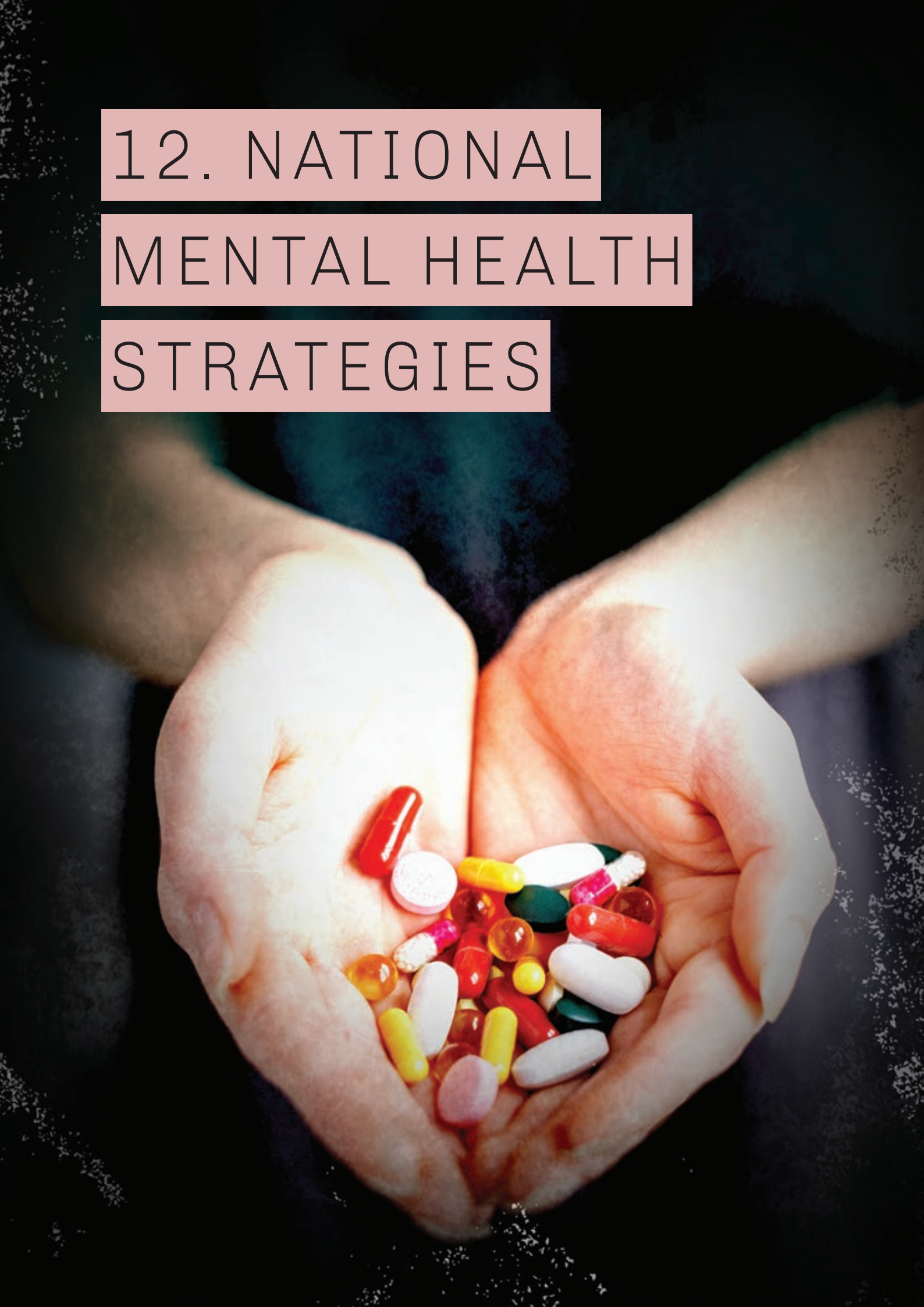
– Patrick O'Connor, author

407 ABS, 2018.

Warning

Do not stop taking a prescribed medication without discussing it with your doctor. Information can also be obtained by calling the NPS Medicines Line on 1300 633 424 or the Adverse Medicines Events Line on 1300 134 237 for advice. If you need support for any medical concern, including mental health matters, please contact your doctor. Lifeline also provides a 24 hour support service on 13 11 14 or www.lifeline.org.au

12. NATIONAL MENTAL HEALTH STRATEGIES



1. INTRODUCTION

For decades people with lived experience have voiced the urgent need for government and the health care network to urgently act to address the deadly problems with prescription medication – all raised in this report.

Our world is filled with the three risks of prescription medication:

1. Life-shortening – poor physical health
2. Life-threatening – overdose deaths
3. Life-taking – suicide deaths.

Vulnerable people have been calling out for help to resolve problems created and ignored by those whose role is to protect and help us. Meanwhile the ABS continues to count the deaths.

In the US, the NIMH has been a world leader in detailing the cause of the issues, implementing prevention measures and also working to find new treatments that are safer and more effective.

In Australia, various commissions and mental health not-for-profit organisations have universally ignored these issues and almost no strategies exist to address the problems.

Tragically they have also ignored all of the work conducted by the NIMH in the US where new treatments are saving lives; just not here in Australia.

2. THE *FIFTH NATIONAL MENTAL HEALTH AND SUICIDE PREVENTION PLAN*

The Australian Government's *Fifth National Mental Health and Suicide Prevention Plan* was endorsed in August 2017. The plan sits within the National Mental Health Policy, which is said to provide:

> *"a strategic framework to guide coordinated government efforts in mental health reform and service delivery. Its vision, aims and policy directions provide a context for the development of national, state and territory mental health plans."*[408]

According to the Plan, the eight priority areas are:

1. achieving integrated regional planning and service delivery
2. effective suicide prevention
3. coordinating treatment and supports for people with severe and complex mental illness
4. improving Aboriginal and Torres Strait Islander mental health and suicide prevention
5. improving the physical health of people living with mental illness and reducing early mortality
6. reducing stigma and discrimination
7. making safety and quality central to mental health service delivery
8. ensuring that the enablers of effective system performance and system improvement are in place.[409]

If there is one organisation and one document that should not only capture a deep understanding of all the content in this report, it is **this national Plan**. However, the Plan does not recognise three distinct concerns (as raised in this report), detailed in Table 21.

408 Australian Government National Mental Health Commission, *Fifth National Mental Health and Suicide Prevention Plan*, August 2017, p1.
409 ibid, p4.

Table 21: Addressing prescription medication risks in the government's plan

Prescription Medication Risk	Reference/s	NMHC Plan Priority Area	Actions
Life-shortening – poor physical health of people living with mental illness due to prescription medication side effects	RANZCP reports that the side effects of prescription medication are a significant reason for reduced life expectancy (see Chapter 1)	5 – Improving the physical health of people living with mental illness	**No strategies to address prescription medication causing poor physical health**
Life-threatening – accidental overdose deaths of people living with mental illness from prescription medication side effects	ABS, DOH and Penington Institute reports on the growing number of accidental overdose deaths (see Chapter 3)	5 – Reducing early mortality of people living with mental illness	**No strategies to address prescription medication causing overdose deaths**
Life-shortening – poor physical health and Life-threatening – accidental overdose deaths of people living with mental illness from prescription medication side effects	ABS, DOH and Penington Institute reports on the growing number of accidental overdose deaths (see Chapter 3)	7 – Making safety and quality central to mental health service delivery for people living with mental illness	**No strategies to address prescription medication causing poor physical health or overdose deaths**
Life-taking – suicide deaths of people living with mental illness from prescription medication overdoses	ABS, DOH reporting on the number of people who intentionally die from prescription medication overdoses. WHO strategies for reducing prescription medication suicides (see Chapter 2 and Chapter 10)	2 – Effective suicide prevention	**No strategies to address issues with prescription medication as a means of suicide deaths** **No specific objectives to measure and reduce the number of suicides as a result of overdose of medications**

An assessment of the priority areas 2, 3 and 7 in the Plan reveal that prescription medication, used in any context, is not mentioned once. None of the three priority areas acknowledge:

- the negative health impacts of prescription medication
- the lack of efficacy of prescription medication
- the information issues with medication safety or prioritise the urgent need for new medications.

Reducing deaths from prescription medication (accidental or intentional) has no measurable target in the Plan.

Considering the well-known comorbidity of mental health and chronic pain, it is staggering that the Plan does not include a reference to chronic pain once.

> Recognition of the relationship between the related conditions and inclusion of specific measures in the mental health policy would be an important first step in addressing this burden of disease

– Pain Australia 2019[410]

The NMHC appears to have taken a position to not engage in any prescription medication reform. The Plan does not mention prescription medication or even the PBS once. This was not the case in the 2012 NMHC report. At some stage a decision has been made to remove the need for safer medications.

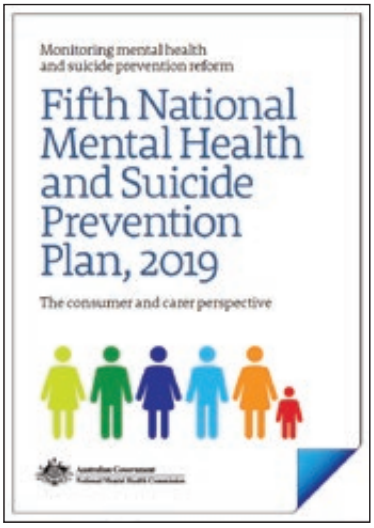
Mrs Lucinda Brogden (left) – Chair National Mental Health Commission and Ms Christine Morgan (right) – CEO of the National Mental Health Commission and National Suicide Prevention Adviser to Prime Minister Scott Morrison

The TGA consultation on opioids (as discussed in Chapter 6), gave the NMHC an opportunity to at least provide some input into safer prescription medications for people with comorbid pain and mental illness conditions. The use of opioid medication in suicide attempts and completed suicides has been documented for decades. Yet the NMHC didn't make a submission. Of the 49 submissions to that consultation process, there was not one from the largest mental health institutions including Beyond Blue, Orygen/Headspace, Black Dog Institute or any suicide prevention organisation.

410 Painaustralia, *Productivity Commission Inquiry into the role of improving mental health to support economic participation and enhancing productivity and economic growth*, April 2019.

2.1 THE CONSUMER AND CARER PERSPECTIVE

In a more recent release of the Plan for consumers and carers based on survey results, the issue remains unaddressed.



> *"This year, the NMHC undertook a consumer and carer survey for the first time to help us understand whether implementation of the Fifth Plan is affecting experiences of care. The results of the survey form the basis of this report, and I am pleased to present the Fifth National Mental Health and Suicide Prevention Plan, 2019: The consumer and carer perspective (2019 Consumer and Carer Report)."*[411]

Under Priority Area 5, which is 'Improving the physical health of people living with mental illness and reducing early mortality':

> *"Specific physical health challenges highlighted by respondents, that were related to or could be compounded by mental illness, included: access to affordable dental care, managing the side effects of certain medications (such as weight gain), and maintaining a healthy lifestyle (such as a healthy diet and adequate exercise)."*[412]

Consumers have reported the issues around significant side effects of medication for many years to the NMHC, yet it still fails to receive any focus in the Plan. From suicides to surveys, the steadfast refusal of the NMHC to step up and start saving lives from prescription medications demands the most urgent and forceful response to change the leadership of this organisation.

3. PRODUCTIVITY COMMISSION MENTAL HEALTH REPORT

In 2019 the Department of Treasury undertook a nationwide investigation to:

> *"examine the effectiveness of current programs and Initiatives across all jurisdictions to improve mental health, suicide prevention and participation, including by governments, employers and professional groups;"*[413]

411 Australian Government National Mental Health Commission, *Fifth National Mental Health and Suicide Prevention Plan, 2019 The consumer and carer perspective*, 2019, p4.

412 ibid, p17.

413 Australian Government Productivity Commission, accessed on 3 April 2020, see https://www.pc.gov.au/inquiries/current/mental-health/terms-of-reference

The Draft Report was released in October 2019 and as with the NMHC, the findings ignored the major issues raised in the submissions of people with lived experience about prescription medication. The report didn't totally ignore the issue; they recommended that medical practitioners receive training on medication side effects:

> *"DRAFT RECOMMENDATION 11.5 — IMPROVED MENTAL HEALTH TRAINING FOR DOCTORS*
>
> *Improve medical practitioners' training on medication side effects and consider specialist registration for GPs who have advanced specialist training in mental health. In the short term (in the next 2 years)"*[414]

This is staggering considering that prescribing medication is what doctors are qualified to do, and have been doing since these medications became available. The need for this training should have alerted the Productivity Commission to the need for even more urgent action.

If the Productivity Commission believes doctors haven't been adequately informing patients, then why not also recommend an urgent program to inform these patients of the risks they were not made aware of?

The section of the report on suicide prevention is even more disturbing. The priority recommendation is:

> *"Australian, State and Territory Governments should offer effective aftercare to anyone who presents to a hospital, GP or other government service following a suicide attempt."*[415]

The lead suicide prevention action is to assist people who survive a suicide attempt. Shouldn't averting the original suicide be a greater focus? For those already receiving treatment for mental health conditions, what assistance is going to be provided that is different from the mental health treatment offered pre-suicide attempt?

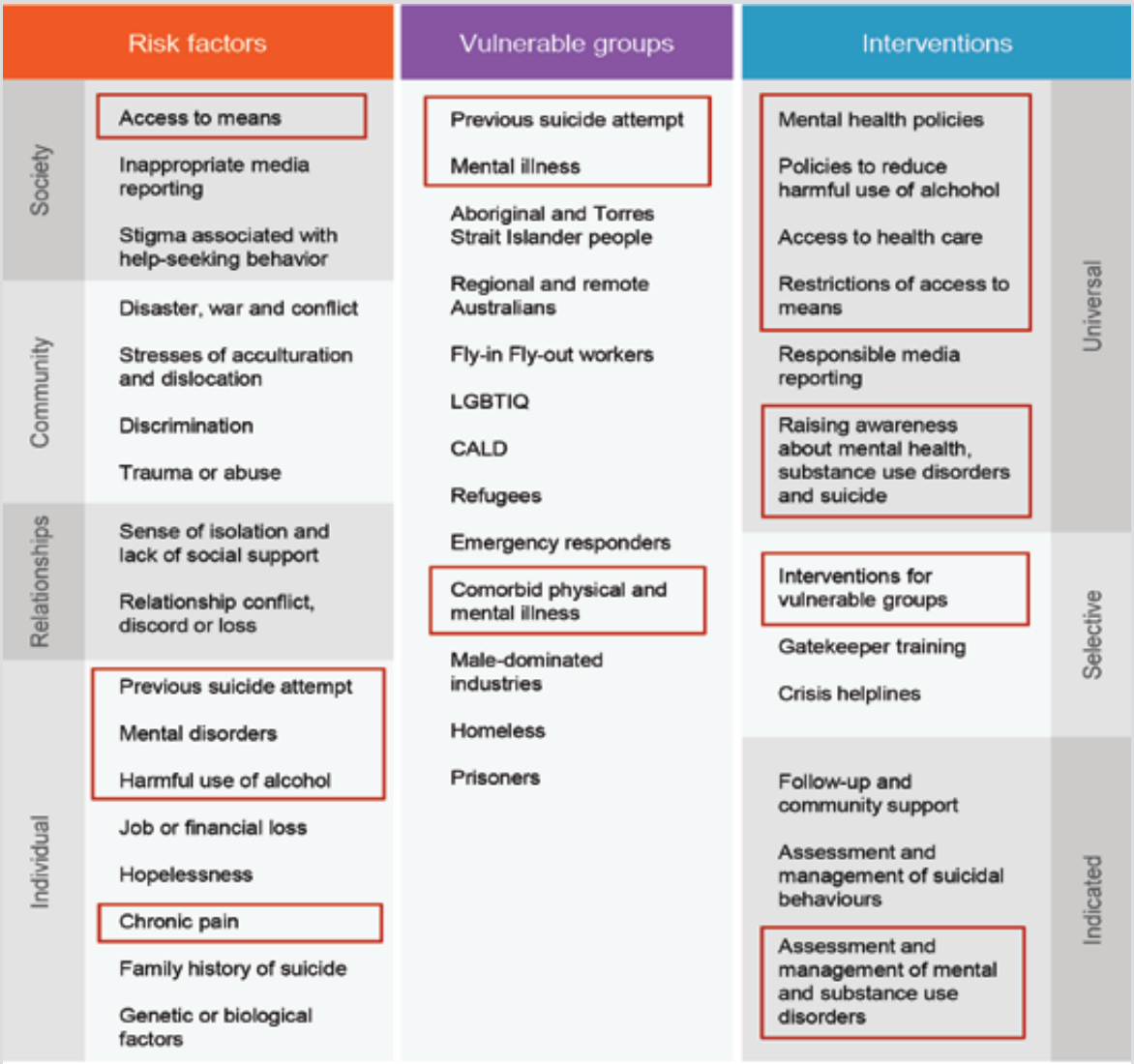
Tellingly, the draft report recommends no action on prescription medication overdosing, which is the means of attempted suicide for the majority of people. For most, these medications are also what they resume taking when they are discharged from hospital.

The Productivity Commission's draft report includes a table (shown at Figure 52). We have boxed in red the factors that relate to prescription medication issues contained in our report.

> *"Given the many risk factors for suicide there are many types of suicide prevention activities. They generally fall into three categories (figure 21.7)."*[416]

414 Australian Government Productivity Commission, *Mental Health Draft Report*, October 2019.
415 ibid.
416 ibid, vol 2, p853.

Figure 52: Key suicide risk factors, vulnerable groups and interventions (Source: Mental Health draft report)



Source: Adapted from WHO (2014a).

The draft report then summarises Australia's performance in these suicide prevention activities, stating:

> *"Australia has been reasonably successful at progressing interventions in some of these areas. For example, means-restriction is clearly an effective approach, and has been associated with reduced suicide rates in Australia in the past.* ***However, it is difficult to take this intervention much further. It is also important to note that means-restriction does not target the underlying causes of suicide.***
>
> *However, there is room to improve Australia's efforts towards mental health services, support for people who have attempted suicide and school-based awareness programs. Many other potential interventions hold promise, but more research and evidence is needed to thoroughly determine their effectiveness."*[417]

417 ibid.

It is tragic that the Productivity Commission concludes that it is just too hard to take **suicide means reduction** any further. Based on the actions that haven't been attempted in the area of prescription medication safety (based on the USA's learnings), progress actually wouldn't be that hard.

The Productivity Commission states that means restriction does not target the underlying cause of suicide. Ineffective prescription medication has proven to be a risk factor in suicide deaths – addressing this targets both the means and the cause, something they completely fail to acknowledge.

In commenting on the draft report, Minister for Health, Greg Hunt said in an article for *The Australian*:

"Health Minister Greg Hunt said the states and Commonwealth would share responsibility for mental health and undertake a "once-in-a-decade transformation" of the system. "We should be tracking, with the consent of individuals, with support services for every single person in Australia who's been discharged from a state hospital for suicidality or suicide attempt when they're in the recovery phase..."[418]

We don't need to be tracked, we need to be treated.

Even the PSA has reacted to the draft report with amazement, stating:

> *"Unfortunately, what the draft report seems to overlook is the need for improved medicine safety practices and strategies for people with mental ill health and across mental health services."*
>
> *"We need to ensure we are using medicine as effectively as possible in the treatment of mental ill-health. For this reason, PSA does not think it is possible to look at mental health care without considering the safe and quality use of medicines," A/Prof Freeman said.*[419]

The Productivity Commission's draft report on mental health is described as a once in a decade opportunity to address the mental health crisis in Australia. Based on the failure to take action on prescription medication issues, our shorter lifetimes won't be made longer anytime soon.

418 R Lewis, S Lunn, 'Ongoing care for suicidal patients plan', *The Australian*, 31 October 2019.

419 Pharmaceutical Society of Australia, 'Better use of medicines has a role in mental health care', media release, 4 November 2019.

4. ROYAL COMMISSION INTO VICTORIA'S MENTAL HEALTH SYSTEM

The interim report released in November 2019 from the Royal Commission into Victoria's Mental Health System contained substantial references to the issues raised in this report.

This extract typifies the messages we have been delivering:

> *While medications provide a range of benefits to people living with mental illness, people have described experiencing a number of adverse consequences as a result of medications offered to manage symptoms:*
>
> > *"Medication inevitably has dramatic side effects. Over the years, I have suffered eye sight disturbance, sedation, weight gain, increased appetite, high cholesterol, confusion, akathisia, dry mouth, dental issues, constipation, diabetes, low blood pressure, low motivation resulting in lack of exercise, incontinence, asthma complications, clashing with other medications, urinary retention, sex drive impairment, stomach reflux, cognitive impairment, Parkinsonian-type tremors, nausea and a stomach ulcer.*
> >
> > *That treatment made me feel worse, suffer damaging side-effects, and rendered me incapacitated of my full potential."*
>
> *Many consumers are advocating for more information about medication and treatment so they can inform themselves and be aware of the potential side effects.*[420]

And as a case study in the report highlighted:

> *Dave would like a better quality of care, where information about medication and treatment is provided so people are aware of the potential side effects such as weight gain, nausea, stimulated appetite, fluid retention, metabolic syndrome, shortened life span, early mortality from cardiovascular disease, diabetes and stroke:*
>
> **"Even if a person is on a treatment order, they should still be informed of the risks involved with their treatment and it is a breach of their human rights to deny this."**
>
> *Having experienced both mental and physical health problems, Dave would like to see better access and navigation options for the physical health needs of people living with chronic and acute mental health conditions.*[421]

In the report's section on 'Immediate action and ongoing work', prescription medication is not mentioned. However:

> *"The Royal Commission recommends that the Victorian Government, through the Mental Health Implementation Office, expands follow-up care and support for people after a suicide attempt."*[422]

420 Royal Commission into Victoria's Mental Health System, *Interim Report*, November 2019, p240.
421 ibid, p241.
422 ibid, p444.

It is again confusing that establishing a program to help people after a suicide attempt requires immediate action, while not addressing the prescription medication that is the most common means in a suicide attempt.

> *"The Commission received evidence that about 60 per cent of people who die by suicide have had contact with a public or private health service for mental health–related problems in the preceding 12 months. Around 50 per cent had contact with a health service in the six weeks preceding their death. Data provided to the Commission from the Victorian Coroners Court shows that around 30 per cent of people who die by suicide see their GP about a mental health problem in the six weeks preceding their death."*[423]

Similar information was contained in the Productivity Commission report. The seemingly obvious conclusion that was not mentioned in either report is that the **mental health treatments these people received were not successful in preventing their death by suicide.** The treatments were ineffective at improving their symptoms and quality of life.

Australia has the second largest use of antidepressants in the world. The medications are ineffective for two-thirds of people. How is it that 60% of people who die by suicide are receiving mental health services, yet they still died by suicide? Clearly the prescription medication wasn't helping these people.

This leads to another conclusion: the people who are at the greatest risk of suicide are people who are not responding to mental health medication, and the longer the time this extends, the greater their risk of suicide.

So why are we not looking for new medications that do work?

5. MEDICATION EFFICACY

The ineffective nature of medication was established in the STAR*D trial, a study funded by NIMH (see Chapter 1). According to a paper on new medications for depression:

> *Two out of three patients with depression do not fully recover on an antidepressant medication according to findings from STAR*D, the largest clinical trial study of treatments for major depressive disorder, funded by the National Institute of Mental Health. (One-third of patients do have a remission of their depression symptoms.)*
>
> *These results "are important because previously it was unclear just how effective (or ineffective) antidepressant medications are in patients seeking treatment in real-world settings," said James Murrough, M.D., board-certified psychiatrist and a research fellow at the Mount Sinai School of Medicine Mood and Anxiety Disorders Program.*

423 ibid, p335.

As Murrough explained, depression treatment can be thought of in thirds: "for one third of patients, symptoms remit; another third don't have as good of an outcome, experiencing residual symptoms and waxing and waning course or chronic course and are at risk for relapse whether they're on or off medication; and then a third don't get much benefit at all."

He added that around "10 to 20 percent have persistent clinically significant symptoms that aren't decreased by current treatment — these are the patients that we are the most worried about."[424]

6. NEW MEDICATIONS FOR MENTAL ILLNESS TREATMENT

NIMH is the lead US federal agency for research on mental disorders. With an annual budget of USD $2 billion, it is the largest mental health research centre in the world.

Professor Joshua A. Gordon, M.D., Ph.D. is the Director of NIMH. He oversees an extensive research portfolio of basic and clinical research that seeks to transform the understanding and treatment of mental illnesses, paving the way for prevention, recovery, and cure. The Strategic Plan for Research has focus not only on developing new treatments, but also on treatments that can cure mental illness.

"For illnesses in other areas of medicine, increased understanding of their biological bases has transformed previously dire diagnoses into manageable, if chronic, illnesses. For example, we have seen dramatic improvements in remission rates for specific types of cancer and large drops in mortality rates from cardiovascular disease. We have not seen equivalent improvements for mental illnesses, which can be no less deadly or disabling."[425]

Professor Gordon and the NIMH have been a driving force behind many new medications that are now available in the USA to treat mental illness including:

- **Ketamine** – administered via an IV drip, it is described by the NIMH as having strong, rapid antidepressant effects within hours, even for people who have not responded to previous medications. It has been effective for people with treatment-resistant depression and bipolar depression, as well as reducing suicidal thoughts. For over two decades numerous careful NIMH-sponsored studies have consistently demonstrated that ketamine rapidly reduces depressive symptoms when given intravenously. The treatment is now available in over 200 private clinics across the US as well as in hospitals including Yale School of Medicine and Mount Sinai Hospital.

424 M Tartakovsky, 'Depression: New Medications On The Horizon', *PsychCentral*, 8 October 2018.

425 National Institute of Mental Health Strategic Plan, accessed on 3 April 2020, see https://www.nimh.nih.gov/about/strategic-planning-reports/strategic-objective-3.shtml

- **Spravato** – is a nasal version of ketamine that targets treatment-resistant depression (TRD). TRD is a form of depression that doesn't get better even after the patient has tried at least two antidepressant therapies. Spravato was approved by the FDA in March 2019, having grown out of a long line of NIMH-sponsored research. It is now funded by Health Insurance in the US.
- **Brexanolone** – a revolutionary new medication that acts to rapidly reduce symptoms and restore function to those struggling with the devastating effects of postpartum depression. Brexanolone was approved by the FDA in March 2019 after an extensive period of NIMH-sponsored research.[426]

6.1 OTHER PROMISING NEW MEDICATIONS

There are a number of new medications that are at trial stage in the US and around the world. The FDA in the US assists new medication gaining approval to be used through its Breakthrough Therapy Status process. This is awarded to medications that have the potential to treat a serious condition in a substantially more effective fashion than the current forms of available treatment.

6.1.1 Psilocybin

The FDA has granted a Breakthrough Therapy designation to psilocybin in the treatment of major depressive disorder. Psilocybin is now also in clinical development for TRD in Canada and Europe and could be legal for therapy by 2021. Trials are underway around the world including at Yale University, John Hopkins, New York University, University of Southern California, Compass, and the Imperial College of London.[427]

6.1.2 MDMA

The FDA has granted a Breakthrough Therapy designation to MDMA combined with psychotherapy as treatment for PTSD. MDMA can reduce fear and resistance to explore painful memories associated with the PTSD, while a therapist supports the therapeutic process with MDMA. Trials are underway around the world including at Multidisciplinary Association for Psychedelic Studies (MAPS), Yale University, John Hopkins, and the Imperial College of London.[428]

6.2 AUSTRALIA'S EXPLORATION OF NEW MEDICATIONS

The NMHC, Productivity Commission, or the Victorian Royal Commission make no mention of these new medications that the NIMH has assisted to develop, nor of those that are being trialled around the world.

The absence of this information in the Productivity Commission's report is even more staggering given they were asked to answer a specific question in an Issues Paper released in January 2019:

> *"What overseas practices for supporting mental health and reducing suicide and comorbidities should be considered for Australia? Why? Is there formal evidence of the success of these practices, such as an independent evaluation?"*[429]

426 J Gordon, *New Hope for Treatment-Resistant Depression: Guessing Right on Ketamine*, NIMH, 13 August 2019.
427 Y Saplakoglu, 'FDA Calls Psychedelic Psilocybin a 'Breakthrough Therapy' for Severe Depression', *LiveScience*, 25 November 2019.
428 A Feduccia, 'MDMA Breakthrough Therapy Designation Results Published', Psychedelic Support, 7 May 2019.
429 Australian Government Productivity Commission, *The Social and Economic Benefits of Improving Mental Health – Issues Paper*, January 2019, p16.

Unbelievably, the work of the world's largest mental health research organisation and the medications they have produced has been completely ignored.

The Black Dog Institute commenced a trial of ketamine for TRD in 2015. The trial received $2 million in government funding, and was due to be completed in 2018.[430] This trial and earlier work completed by the Black Dog Institute was not mentioned in either of their submissions to the Productivity Commission or the Victorian Royal Commission.

Unlike the NIMH, finding new medications to treat and cure mental illness isn't a priority action identified in any of the Australian reports. The NIMH is continuously searching for new medications to treat mental illness, whilst in Australia, finding new medications isn't a priority, nor is fixing the dangers of the existing ones.

You would imagine that prescription medication would be part of any government mental health and suicide prevention plan. In the USA the interconnectivity of these issues has seen the National Institute on Drug Abuse (NIDA) and the National Institute of Mental Health (NIMH), combine to drive awareness of the issue.

According to an article posted by Professor Gordon, NIDA and NIMH recognise the interrelated factors of pain, mental illness, prescription medication and suicide. Specifically, they are working collaboratively on the links between opioid use, opioid use disorder (OUD), and suicide. The NIMH believes as many as up to 30% of opioid overdoses may be suicides.[431] In Australia the recognised AIHW statistic is 16%.[432]

In the NIMH article, Professor Gordon states:

> *"Pain is another important factor when considering the complex relationships between opioids, overdose (both suicidal and accidental), and mental illnesses. Individuals suffering from chronic pain conditions—the primary reason people are prescribed opioids—may also have comorbid depression or other mental illnesses, and they may be at increased risk of suicide simply because of their pain."*
>
> *"Our Institutes are engaged in research initiatives that address the suicide component of the opioid crisis. NIDA funds research aimed at understanding the complexities of addiction, including co-occurring mental health problems and shared environmental and genetic risk factors for addiction and mental illness. NIMH funds research aimed at understanding the causes of suicide and suicidal ideation and seeks to develop new prevention and treatment interventions specifically targeting suicide."*[433]

The importance of this position cannot be understated. THE NIMH recognises the comorbidity crisis of mental illness and chronic pain. They are actively talking about the hidden suicides in overdose figures. They acknowledge that the prescribed drugs for these people are lethal enough to facilitate a deliberate overdose to suicide. They are working on new treatments to provide safer therapies for patients. If only the NMHC had the same plan for Australians.

430 Australian Government National Health and Medical Research Council, Department of Industry, Innovation and Science, Australian Clinical Trials, *Ketamine for Adult Depression Study*, accessed on 3 April 2020.
431 J Gordon, *Suicide Deaths Are a Major Component of the Opioid Crisis that Must Be Addressed*, NIMH, 19 September 2019.
432 ABS, 2018.
433 J Gordon, 19 September 2019.

7. HOPE SAVES

Sergeant Kevin Briggs is a retired officer from the California Highway Patrol. He served for 23 years, the majority of which included patrolling the southern end of Marin County, which includes the Golden Gate Bridge. He frequently had to respond to suicide attempts when people attempted to jump from the bridge. He became known as the 'Guardian of the Golden Gate Bridge' due to his work convincing hundreds of people to not jump from the bridge in successful suicide interventions.

In 2019, I interviewed Kevin in the USA on World Suicide Prevention Day. He had just presented to a group of medical professionals about his career. I asked him: "What do you say to people in those interventions that has the most impact?"

He responded saying that he lets them speak as much as he can get them to. Then he asks questions about the problems they have discussed and solutions that didn't work. He explained that the majority of people are suffering from a mental illness and the lack of success of the medical treatments is the main reason for the suicidal despair.

A question he asks in these situations is, "Have you tried this?" and discusses mental health treatment options.

Kevin is not a medical practitioner and doesn't claim to know the impact these treatments could have on these people. He said, "I'm not trying to get them to sign up for that treatment; I'm getting them to consider that they haven't tried everything that could help them". He then said, "They climbed over the rails on the bridge because they lost all hope for a better life; I'm trying to give them that hope back, because **hope saves**".

Kevin authored a book titled, *Guardian of the Golden Gate: Protecting the Line Between Hope and Despair*.

7.1 A LIVED-EXPERIENCE SUBMISSION

In my submission to the Productivity Commission Mental Health Inquiry, I made the following points:

- Severe mental illness brings suffering; suffering brings suicide.
- To stop suicide, you have to stop the suffering.
- 74% of those lives lost to suicide suffered a mental illness.
- People with hope for the future do not end their own lives.
- People who suffer with no relief are the vulnerable people that need urgent treatments.
- We don't need hashtag campaigns and awareness, we are already aware we are suffering.
- The refusal to prioritise finding better medication is the single biggest cause of the mental health crisis.
- Cancer kills, mental illness kills. We don't 'manage' cancer, we kill it!
- We have to stop 'managing' mental illnesses and start killing them.

- To kill them we need new treatments because the ones we have now just kill the sufferers, not the illness.
- The current national mental health and suicide prevention plan doesn't give sufferers hope for the future – they have no hope for new treatments, because the national plan has said they don't think the sufferers need them.
- **When hope is gone. The fight is over**.[434]

> Trying to stop suicides without better medications is like trying to put out a house fire without water. You can try but people will keep dying because you won't try something new.

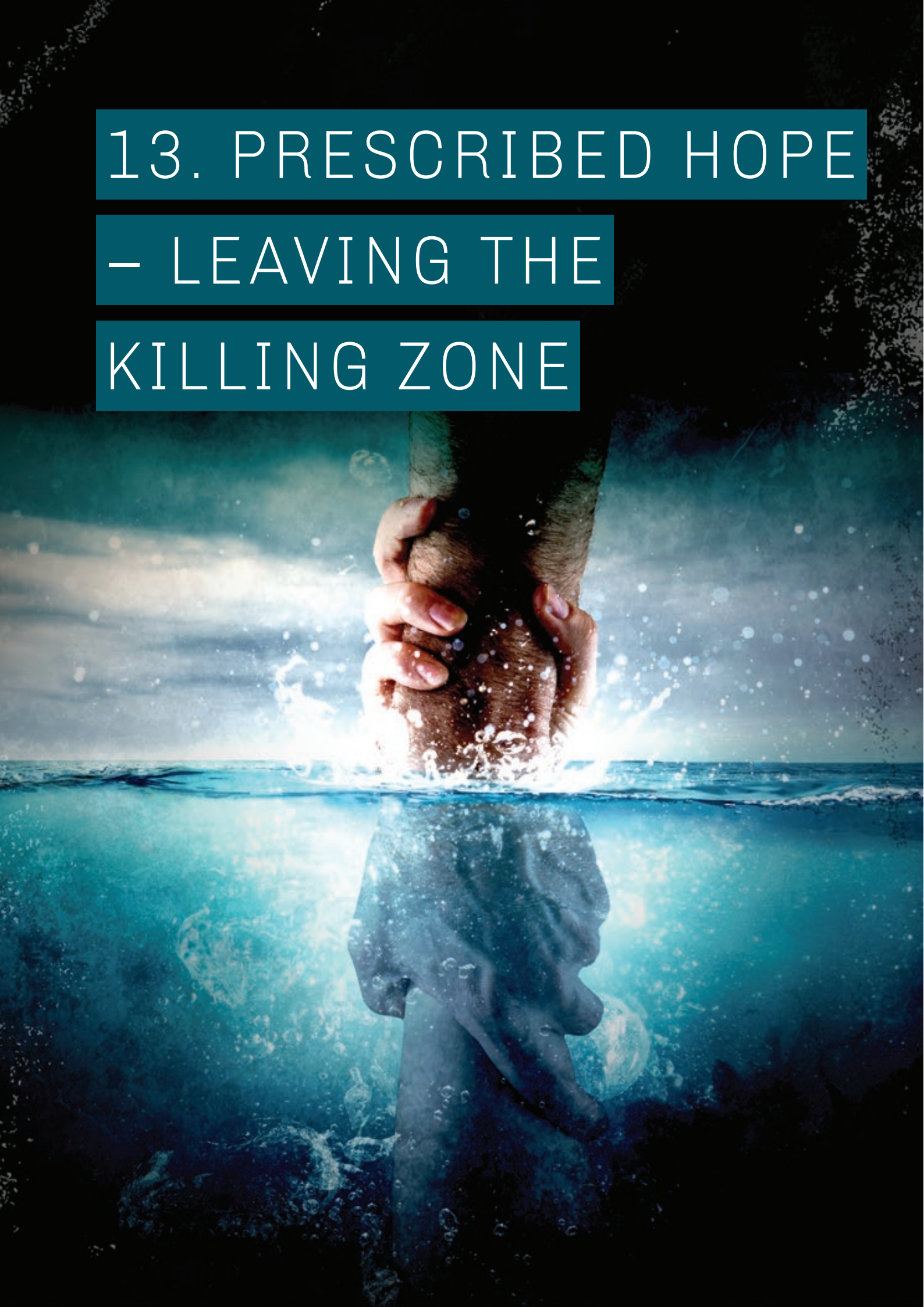
– Patrick O'Connor

434 P O'Connor, *Productivity Commission "Improving Mental Health" The Killing Zone*, April 2019

Warning

Do not stop taking a prescribed medication without discussing it with your doctor. Information can also be obtained by calling the NPS Medicines Line on 1300 633 424 or the Adverse Medicines Events Line on 1300 134 237 for advice. If you need support for any medical concern, including mental health matters, please contact your doctor. Lifeline also provides a 24 hour support service on 13 11 14 or www.lifeline.org.au

13. PRESCRIBED HOPE – LEAVING THE KILLING ZONE



1. INTRODUCTION

The concept of 'Prescribed hope' is an introduction to the treatment strategies that are proving successful in improving the lives of people with severe mental illness in other countries – as introduced in Chapter 12.

Pharmacogenomics testing and ketamine IV treatment is already in place in Australia.

We need to make these treatments more widely available immediately.

Funding both the Medicare Benefits Schedule (MBS) and PBS, as well as providing full PBS coverage for off-label prescriptions for severe mental illness patients, are actions that can be implemented now.

2. PRESCRIBED HOPE – NEW STRATEGIES

There are new strategies that are used by mental health professionals in the US.
The strategies that should be considered in Australia can be grouped into three areas:

1. **Better tools** – ways to help physicians improve the treatment decisions they make
2. **Better treatments** – new methods of improving mental health conditions
3. **Better access** – removing the barriers to people getting access to mental health support.

Some of these strategies are already available in Australia and could be used on a broader scale, including:

- pharmacogenomic testing (tool)
- medication warnings (tool)
- ketamine treatment for mental illness and suicide prevention (treatment)
- full PBS subsidies for all mental health medication (access).

3. BETTER TOOLS

Diabetes is diagnosed through blood tests. Cancer is diagnosed through biopsies and medical imaging. But mental illness is largely diagnosed through a **checklist of self-reported symptoms** from an individual who is suffering from a condition they don't understand talking to a person they often barely know.

The government's healthdirect website states:

> *"Mental illness can be diagnosed after a doctors talks to you in detail about your symptoms. There are generally no blood tests or brain scans that can confirm a mental illness, although these tests may be useful in finding out other possible causes of the symptoms.*
>
> *The first step is to visit a doctor or mental health professional. Assessment will include questions about your thoughts, mood and behaviours and it may be helpful to include a family member or carer. Questionnaires are sometimes used, although a diagnosis should not be made on the basis of a questionnaire alone.*
>
> *The symptoms of different mental illnesses are described in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), published by the American Psychiatric Association. This manual is used by doctors to decide which mental illness you have."*[435]

Mental illness is not only a difficult illness to treat, it is also as difficult to diagnose. Can you imagine trying to diagnose cancer through a questionnaire? Considering that many patients have multiple **health conditions** and, in some cases, multiple **mental health conditions**, the challenge in making a correct diagnosis is colossal.

Not surprisingly many people with lived experience have voiced these issues, suggesting that it can take years before they are correctly diagnosed.

In a blog on the Psychology Today website, it reported that in a 2009 global meta-analysis including Australia, "general practitioners can only correctly identify depression in 47.3 percent of cases—and many doctors diagnose depression in people who just don't have it".[436]

General Practitioners (GPs) are at the frontline of our healthcare system and have significant time constraints in assessing and diagnosing mental health conditions. A misdiagnosis leads to incorrect medication being prescribed. The wrong medication can increase the symptoms of a mental illness, expose the patient unnecessarily to side effects, and worse, delay the time in improving a patient's symptoms.

Medication is the lead treatment for mental health conditions in Australia and the majority of medications are prescribed by GPs. GPs are tasked with being the first point of diagnosis and treatment for mental health conditions. Interestingly, 86.3% of mental health related prescriptions are prescribed by GPs and only 7.7% by psychiatrists (see Figure 53).[437]

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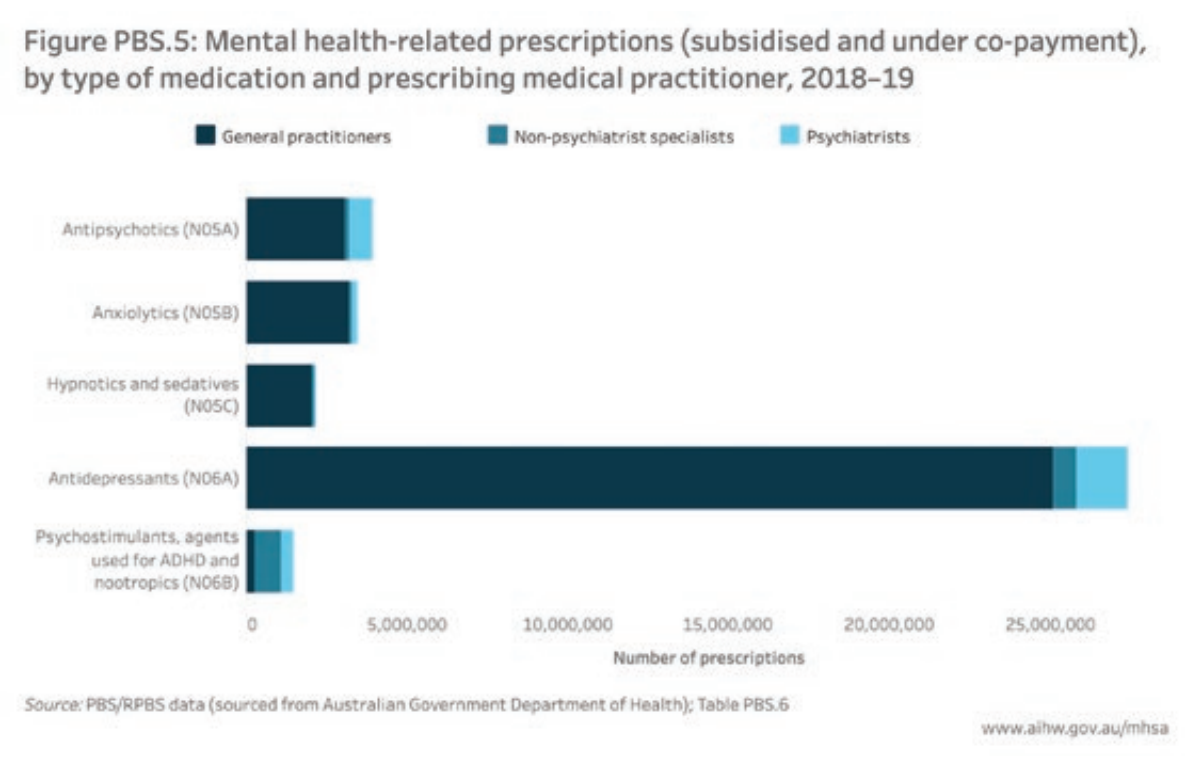
435 Australian Government healthdirect website, last reviewed November 2018, see https://www.healthdirect.gov.au/diagnosis-of-mental-illness

436 R Ryback, 2016.

437 Australian Institute of Health and Welfare (AIHW), *Mental health services in Australia*, last updated 20 January 2020.

> Of the 39.0 million mental health-related prescriptions (subsidised and under co-payment) provided in 2018–19, the majority (86.3%) were prescribed by general practitioners (GPs), with another 7.7% prescribed by psychiatrists and 4.5% by non-psychiatrist specialists.[438]

Figure 53: Mental health-related prescriptions (Source: AIHW)



Due to the side effects of these medications and the lack of adequate consumer warnings this report has detailed, the impact of this situation affects literally millions of Australians every day. Right now there are two measures that can be adopted to help improve medication selection and safety: **pharmacogenomic testing combined with medication interaction software**.

3.1 PHARMACOGENOMIC TESTING

In October 2019, the same month that the Productivity Commission released their report into mental health, the Australian Government's Minister for Health, Greg Hunt, made this statement about pharmacogenomic testing:

> *"Although psychological strategies are the first-line of treatment, antidepressants and other drugs form an important part of the care provided. But only about half of patients have a positive response from their first medication prescription, and the response diminishes with subsequent alternatives.*

438 ibid.

Current approaches of trialling different medications may result in prolonged episodes of depression, which impacts on quality of life and may increase the risk of suicide."[439]

It is encouraging to see that the core issue surrounding people with severe mental illness – the ineffective medication – is finally gaining some acknowledgement.

The ineffectiveness of medication for many people is in part due to their **biology**. Chapter 1 gave the example of how codeine is processed differently and a person experiences different outcomes due to their genes. The only way to know what genes a person has and to understand how they will likely respond to medication is through pharmacogenomic testing, which in most cases is a simple swab from a person's mouth.

THE RACGP explains pharmacogenomics:

Genetic variations play a role in our ability to metabolise and respond to drugs, both in terms of efficacy and toxicity. Pharmacogenomic testing assesses the type of response a patient may have to a particular drug. Testing before prescribing medication can provide information about the likely effectiveness or risk of side effects for the patient.

The benefits of pharmacogenomic testing arise from the ability to tailor medication to the individual: specifically, to predict the correct dose to avoid toxicity or adverse events, and to know whether a particular drug will be effective in any given patient.

The benefits of pharmacogenomics include:

- *achieving optimal drug doses quickly – the trial-and-error approach combined with repeated monitoring could be avoided*
- *minimising toxicity and adverse effects – knowledge of a patient's genetic profile could reduce the likelihood of adverse outcomes and help direct clinicians towards suitable alternatives*
- *efficacious medications – genetic variations can predict which patients are likely to respond to certain medications, allowing clinicians to personalise treatment.*

At present, there are several limitations of pharmacogenomic testing:

- *Cost – currently there is no Medicare Benefits Schedule (MBS) rebate for testing, therefore patients incur an out-of-pocket cost.*

The ultimate goal of pharmacogenomics is the ability to target or 'tailor' drug therapy to individuals. Being able to prescribe the right drug at an appropriate dose to maximise efficacy and avoid adverse effects. This goal feeds into the wider concept of personalised medicine, where an individual's genetic profile is used to make decisions about all aspects of healthcare (i.e. prevention, diagnosis, treatment).[440]

The use of pharmacogenomics is already well established in psychiatrist practices in the US. Testing service providers like Genomind are now used by many psychiatrists before any medication is prescribed.[441]

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439 G Hunt, Minister for Health, *Pharmacogenomics research funding to improve mental health care*, media release, 30 October 2019.

440 Royal Australian College of General Practitioners (RACGP), Genomics in general practice, accessed on 3 April 2020, see https://www.racgp.org.au/clinical-resources/clinical-guidelines/key-racgp-guidelines/view-all-racgp-guidelines/genomics-in-general-practice/pharmacogenomics-more-information

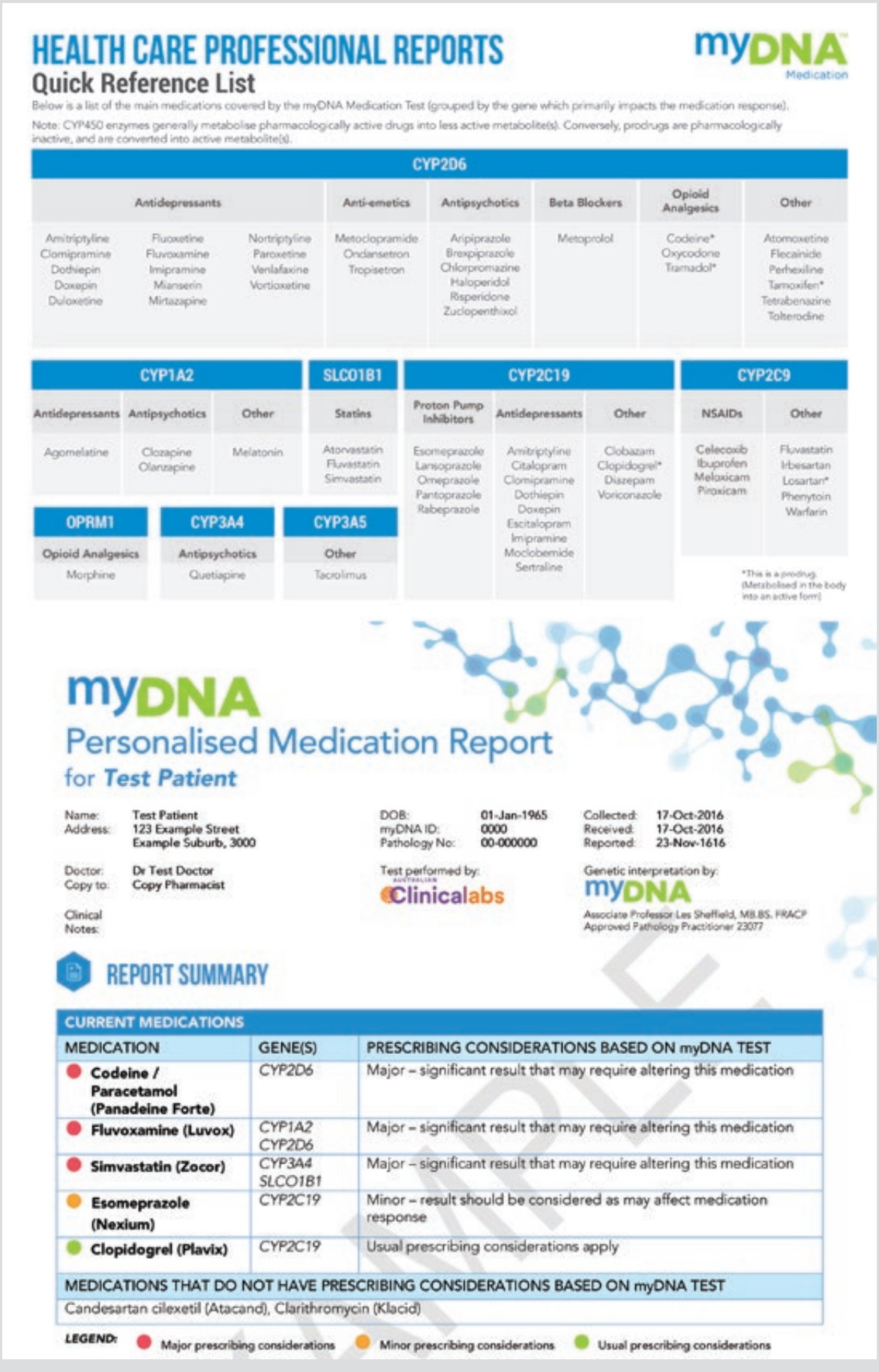
441 Genomind website, accessed on 3 April 2020, see www.genomind.com

> Medication selection is mostly a trial and error process. We assess a patient and make a best guess, using our clinical experience. Pharmacogenomics is a game changer in so many ways. Without the test I have no way of knowing my patient's genetic profile. Knowing the profile means I can make far better decisions to avoid adverse side effects, and it improves the likelihood of prescribing the medication with the best chance of improving my patient's symptoms. It provides real scientific input into the medication decision and my experience has been that it has changed lives for dozens of patients already on medication in just weeks. When a new patient comes in my door, most are already taking medication; I want to know why this isn't working before anything else. Patients understand medication selection is not black and white and they appreciate seeing the report, they appreciate more information to help them consent to the treatment. It helps give them hope that they can try something different, more tailored to them, something that they can believe in. The report makes recommendations on medication types and I don't always agree with it. I do take this into account but it is the genetic profiling in the report that is the science I want. Without the test, all a doctor is doing is guessing.
>
> *– Dr Lori Calabrese*

Pharmacogenomic testing is already available in Australia. This report does not endorse any one test or organisation. However, we have utilised the 'my DNA' functional pathology test that analyses the DNA of an individual patient and pharmacogenomics. The test costs $149 (as at April 2020) and is available in over 600 pharmacies and health companies Australia-wide. The test provides information on a person's genes and likely results from various medications.[442] Extracts from a sample report are shown at Figure 54.

442 myDNA website, accessed on 3 April 2020, see https://www.mydna.life/medication/

Figure 54: myDNA report extract



HEALTH CARE PROFESSIONAL REPORTS

myDNA Medication

Quick Reference List

Below is a list of the main medications covered by the myDNA Medication Test (grouped by the gene which primarily impacts the medication response).

Note: CYP450 enzymes generally metabolise pharmacologically active drugs into less active metabolite(s). Conversely, prodrugs are pharmacologically inactive, and are converted into active metabolite(s).

CYP2D6

Antidepressants			Anti-emetics	Antipsychotics	Beta Blockers	Opioid Analgesics	Other
Amitriptyline Clomipramine Dothiepin Doxepin Duloxetine	Fluoxetine Fluvoxamine Imipramine Mianserin Mirtazapine	Nortriptyline Paroxetine Venlafaxine Vortioxetine	Metoclopramide Ondansetron Tropisetron	Aripiprazole Brexpiprazole Chlorpromazine Haloperidol Risperidone Zuclopenthixol	Metoprolol	Codeine* Oxycodone Tramadol*	Atomoxetine Flecainide Perhexiline Tamoxifen* Tetrabenazine Tolterodine

CYP1A2

Antidepressants	Antipsychotics	Other
Agomelatine	Clozapine Olanzapine	Melatonin

SLCO1B1

Statins
Atorvastatin Fluvastatin Simvastatin

CYP2C19

Proton Pump Inhibitors	Antidepressants	Other
Esomeprazole Lansoprazole Omeprazole Pantoprazole Rabeprazole	Amitriptyline Citalopram Clomipramine Dothiepin Doxepin Escitalopram Imipramine Moclobemide Sertraline	Clobazam Clopidogrel* Diazepam Voriconazole

CYP2C9

NSAIDs	Other
Celecoxib Ibuprofen Meloxicam Piroxicam	Fluvastatin Irbesartan Losartan* Phenytoin Warfarin

*This is a prodrug. (Metabolised in the body into an active form)

OPRM1

Opioid Analgesics
Morphine

CYP3A4

Antipsychotics
Quetiapine

CYP3A5

Other
Tacrolimus

myDNA Personalised Medication Report

for ***Test Patient***

Name: Test Patient
Address: 123 Example Street, Example Suburb, 3000

Doctor: Dr Test Doctor
Copy to: Copy Pharmacist

Clinical Notes:

DOB: 01-Jan-1965
myDNA ID: 0000
Pathology No: 00-000000

Collected: 17-Oct-2016
Received: 17-Oct-2016
Reported: 23-Nov-1616

Test performed by: Australian Clinicalabs

Genetic interpretation by: myDNA
Associate Professor Les Sheffield, MB.BS. FRACP
Approved Pathology Practitioner 23077

REPORT SUMMARY

CURRENT MEDICATIONS		
MEDICATION	GENE(S)	PRESCRIBING CONSIDERATIONS BASED ON myDNA TEST
● **Codeine / Paracetamol (Panadeine Forte)**	*CYP2D6*	Major – significant result that may require altering this medication
● **Fluvoxamine (Luvox)**	*CYP1A2* *CYP2D6*	Major – significant result that may require altering this medication
● **Simvastatin (Zocor)**	*CYP3A4* *SLCO1B1*	Major – significant result that may require altering this medication
● **Esomeprazole (Nexium)**	*CYP2C19*	Minor – result should be considered as may affect medication response
● **Clopidogrel (Plavix)**	*CYP2C19*	Usual prescribing considerations apply
MEDICATIONS THAT DO NOT HAVE PRESCRIBING CONSIDERATIONS BASED ON myDNA TEST		
Candesartan cilexetil (Atacand), Clarithromycin (Klacid)		

LEGEND: ● Major prescribing considerations ● Minor prescribing considerations ● Usual prescribing considerations

The use of pharmacogenomic testing was supported by the PSA in their submission to the Productivity Commission:

> *Incorporate pharmacogenomic testing in primary care supported by medicines expertise of pharmacists for people with mental ill health to personalise medicine therapies to improve the safe and quality use of medicines.*[443]

And in October 2019, the Minister for Health announced:

> *The Morrison Government will invest $7 million for ground-breaking research into the use of pharmacogenomics to improve mental health treatment outcomes and help reduce suicide.*[444]

In the same announcement, Greg Hunt commented that:

> *It estimated that genetics is responsible for over a third of varied response to antidepressants. This investment, through the Medical Research Futures Fund, will support research that aims to improve or develop new pharmacogenomic tests that will change how medications are prescribed for patients with mental health challenges.*
>
> *Testing of these genes may help identify the best and most effective treatment for an individual patient. However, while these pharmacogenomics tests show great promise in improving the prescription given to each patient, these tests are still imperfect.*[445]

DNA testing is widely recognised as being a lifesaving tool that can assist to reduce adverse drug events and improve the quality of life for people with mental illnesses. Considering the science has been widely advanced overseas, and is already in place in clinical use in the US, why does Australia need to research it further?

Based on the myDNA testing kit, $7 million could provide 47,000 sufferers with a report that could change their life in weeks. In mental health treatment, nothing is perfect. Diagnosis is a best guess and medication doesn't work for the majority of people. Pharmacogenomic tests might be regarded as imperfect, but having the results is better than not having the results, and let's not forget that right now in Australia when it comes to medication selection, doctors simply take a best guess.

Integrating pharmacogenomic testing and the use of drug interaction software like eMIMS into GP clinics would deliver a game changing improvement in prescription medication use in Australia overnight.

3.2 MEDICATION WARNINGS

3.2.1 The role of psychiatrists

> *"The Royal Australian and New Zealand College of Psychiatrists (RANZCP) is the principal organisation representing the medical specialty of psychiatry in Australia and New Zealand and has responsibility for training, examining and awarding the qualification of Fellowship of the College to medical practitioners."*[446]

443 Pharmaceutical Society of Australia, Importance of medicine safety in mental health care cannot be ignored, media release, 23 January 2020.
444 G Hunt, 30 October 2019.
445 ibid.
446 Royal Australian and New Zealand College of Psychiatrists (RANZCP) website, accessed on 3 April 2020, see https://www.ranzcp.org/about-us/about-the-college

The RANZCP's *Your Health in Mind* website for consumers provides an explanation of the role of psychiatrists in Australia:

> *Psychiatrists are medical doctors who are experts in mental health. They specialise in diagnosing and treating people with mental illness.*
>
> *They make a diagnosis and work with you to develop a management plan for your treatment and recovery. Psychiatrists provide psychological treatment, prescribe medications and do procedures such as electroconvulsive therapy.*
>
> *Psychiatrists provide and recommend a range of treatments, including:*
>
> – *psychological treatment (also called psychotherapy or talking therapy)*
> – *medication*
> – *brain stimulation therapies, such as electroconvulsive therapy.*
>
> *They will also offer practical advice about diet, sleep and other ways you can help yourself get better. They will provide you with information about your condition, which can help you to understand your symptoms and treatments.*
>
> ***Your psychiatrist will only suggest treatments that are proven to be safe and effective.***
>
> *Your psychiatrist will explain:*
>
> – *why they recommend this treatment*
> – *how it works*
> – ***what the side-effects are***
> – ***any risks of the treatment***
> – *how much it costs.*
> – *It's up to you whether you agree to have the treatment.*
>
> *Remember*
>
> – *Psychiatrists are specialist medical doctors who are experts in mental health.*
> – *A psychiatrist's training means they understand both physical and mental health conditions.*
> – *You need a referral from your GP or another medical doctor to see a private psychiatrist.*[447]
>
> *Antidepressant medications can **sometimes** cause side effects, especially when you start a new medication. Side effects of antidepressants differ between medications and from person to person. Ask your doctor or pharmacist to explain the possible side effects of your medication. You can ask for a printed leaflet, or read about the medication at medicine wise (nps.org.au).*[448]

The NPS Medicinewise website advises that to reduce the risk of medication problems that consumers should "*read the consumer medicine information (CMI) for your medicines and keep this information handy for future reference.*"[449]

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447 Royal Australian and New Zealand College of Psychiatrists (RANZCP) Your Health in Mind website, accessed on 3 April 2020, see https://www.yourhealthinmind.org/psychiatry-explained/what-s-a-psychiatrist

448 Royal Australian and New Zealand College of Psychiatrists (RANZCP) Your Health in Mind website, accessed on 3 April 2020, see https://www.yourhealthinmind.org/treatments-medication/antidepressant-medication

449 NPS Medicinewise, Managing your medicines, accessed on 3 April 2020, see https://www.nps.org.au/consumers/managing-your-medicines#risks-of-taking-multiple-medicines

3.2.2 Getting psychiatrists to acknowledge side effects

People with lived experience have told their story of the adverse side effects of prescribed medication at every opportunity. Our challenge to change the attitude and behaviours of psychiatrists is epitomised in this interview with Victorian Mental Illness Awareness Council (VMIAC) CEO Maggie Toko in April 2019:

> *"Too many of us are disabled when we needn't be."*
>
> *Toko urged clinicians and services to cut back prescriptions of multiple antipsychotics at once, to consider lower doses, safer treatment options like therapy, and to start being honest with consumers about side effects and health risks of the treatments they prescribe."*[450]

Most importantly she said:

> *"Consumers are very clear that the biggest priority are the health problems that are caused by psychiatric treatment, the health problems we wouldn't have if we hadn't been to your services, like obesity, diabetes, cardiovascular disease, movement disorders and too much more.*
>
> *We have the right to know if a treatment will shorten our lives, even if you force us to take it. Leaving us in the dark means that too many people never get the chance to try and improve their health.*
>
> *If we are ever going to make a difference in the physical health of consumers, it starts with the prescribing practices of psychiatrists."*[451]

In Chapter 1, we discussed the RANZCP's acknowledgement of the adverse side effects of mental health medication and the shorter life expectancy they contribute to. However, the attitude of psychiatrists in Australia to this matter has long been seen as a barrier to acknowledging the required changes to the prescribing practices of psychiatrists. On 6 March 2018, RANZCP in a media release (which has since been deleted) said:

> *"Psychiatrists are highly trained medical professionals with expertise in managing both physical and mental health. The prescription of antidepressant or antipsychotic medications is something that a psychiatrist only ever does in partnership with the patient and after due consideration of the risks and benefits."*[452]

Many people with lived experience have vocally disputed that these discussions have ever taken place. Irrespective of that, the RANZCP has repeatedly stated that CMIs provide patients with information on these risks. Considering the comorbidity of mental health and pain conditions of many of their patients, this report has provided irrefutable evidence of drug and polydrug side effects that have never been disclosed.

450 M McInerney, ' Why the physical health of people with mental illness is a critical human rights issue', *Social Global*, RMIT, 7 April 2019.

451 ibid.

452 N McLaren, 'Psychiatrist Dr. Niall McLaren writes to the Royal Australian and New Zealand College of Psychiatrists (RANZCP)', *Mad In America*, 24 March 2018.

Pharmacists regard themselves as the stewards of medication safety, when in reality the role of medication safety for people with mental health conditions rests with the RANZCP. They have an ethical and legal responsibility to ensure patients are given the information they need to make an informed decision on medication treatment. They have a responsibility to uphold the human rights of people with disabilities. They have a job to save not harm.

The RACGP integrate the clinical practice guidelines that are produced by the RANZCP into their treatment of mental health patients. For example, within the clinical practice guidelines for mood disorders.[453] As such, the failure of the RANZCP to ensure that all consumer warnings like in the CMI accurately represent the risks of the medications they endorse, has directly impacted their patients and those of GPs around Australia.

3.2.3 Improved medication safety

Improved medication safety doesn't simply mean producing new CMIs that accurately warn of the risks. It also means reviewing these side effects against the benefits of the medication, including polydrug treatments. Based on that review, the question must then be asked: are these medications appropriate for human use and if so when?

The TGA has now restricted the use of medications like opioids to more severe pain conditions. After 20 years they now recognise that the risk/benefit assessment of these medications is not appropriate for moderate pain conditions. Potentially there are many mental health medications that are only appropriate for more severe mental illness conditions.

An urgent review of the efficacy and side effects of mental health medication has to be conducted. This should focus on what these medications have proven they deliver in clinical use, not what the pharmaceutical trials (many completed over 30 years ago) showed before the PBS and TGA approved their use. Based on this review, the RANZCP has to provide updated guidelines in the use of these medications. It is time to give GPs better information to assist them in medication selection and patient education.

Informed consent starts with informing the prescribers.

453 Royal Australian and New Zealand College of Psychiatrists (RANZCP), Guidelines and resources for practice, accessed on 3 April 2020, see https://www.ranzcp.org/practice-education/guidelines-and-resources-for-practice

4. BETTER TREATMENTS

4.1 THE KETAMINE MIRACLE

Ketamine has proven to have rapid-acting antidepressant and rapid-acting anti-suicidal effects. It is the treatment that works when everything else has failed. The NIMH is leading the world in ketamine research and use for mental illness.:

> *"Ketamine is the first new anti-depressant medication with a novel mechanism of action since the 1980s. Its ability to rapidly decrease suicidal thoughts is already a fundamental breakthrough," said Janine Simmons, M.D., Ph.D., chief of the NIMH Social and Affective Neuroscience Program.*[454]

Ketamine is an anaesthetic medication. According to the WHO it is possibly the most widely used anaesthetic in the world. It is a fast-acting medication and starts to work within seconds when given as an IV administration.[455] [456]

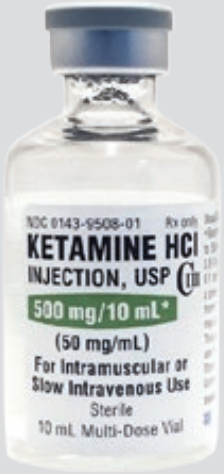
It doesn't slow down a person's breathing or heart rate, making it a very safe medication and the likelihood of an overdose is very unlikely due to the wide margin of safety (the safety margin also makes it a popular medication in veterinary procedures). It has been used for over 50 years and in 1985 the WHO put ketamine on the *List of Essential Medicines*. These are the most effective and safe medicines needed in a health system.

Ketamine is a dissociative anaesthetic, meaning it causes you to feel disconnected from your body. For mental illness sufferers it can also disconnect their illness from their body. The side effects are described as mild, like nausea, and pass very quickly.[457] [458]

Ketamine is an incredibly versatile drug. Whilst it is approved as an anaesthetic, it is used 'off-label' for many other conditions in Australia (as shown in Figure 55).

454 National Institute of Mental Health (NIMH), Ketamine Reverses Neural Changes Underlying Depression-Related Behaviors in Mice, press release, 11 April 2019.
455 National Institute of Mental Health (NIMH), *Post by Former NIMH Director Thomas Insel: Ketamine*, blog, 1 October 2014.
456 J Gordon, 13 August 2019.
457 National Institute of Mental Health (NIMH), *Side Effects Mild, Brief with Single Antidepressant Dose of Intravenous Ketamine*, press release, 18 November 2019.
458 National Institute of Mental Health (NIMH), *Highlight: Ketamine: A New (and Faster) Path to Treating Depression*, accessed on 3 April 2020, see https://www.nimh.nih.gov/about/strategic-planning-reports/highlights/highlight-ketamine-a-new-and-faster-path-to-treating-depression.shtml

Figure 55: Ketamine's off-label uses



1. Surgical Anaesthetic (including children, pregnant women)
2. Severe Burns
3. Chronic Pain (CRPS, Fibromyalgia, Cancer)
4. Dentistry
5. Paramedics (Pain, Patient sedation – Royal Flying Doctors)
6. Mental Illness

1. S A Schug, G M Palmer, D A Scott, R Halliwell, J Trinca, APM:SE Working Group of the Australian and New Zealand College of Anaesthetists and Faculty of Pain Medicine, *Acute Pain Management: Scientific Evidence* (4th edition), ANZCA & FPM, Melbourne, 2015.
2. ibid.
3. ibid.
4. ibid.
5. ACT Emergency Services Agency, ACT Ambulance Service Clinical Management Guidelines, Ketamine hydrochloride pharmacology, May 2019.
   Royal Flying Doctor Service Western Operations, Clinical Manual Part 2, Drug Infusion Guidelines, Version 8.0, August 2018.
6. The Royal Australian & New Zealand College of Psychiatrists, Clinical Memorandum, Use of ketamine for treatment-resistant depression, November 2019.

4.2 KETAMINE, MENTAL ILLNESS AND SUICIDE PREVENTION

Ketamine has been hailed as the most important advance in the treatment of depression of the past 50 years.

Findings from clinical trials since 2000 have shown that a single, slow, intravenous dose given of ketamine over about 40 minutes produces a rapid decrease in depressive symptoms felt within minutes to hours. Studies also consistently show the positive effects last from weeks to months. The benefits are increased with repeat infusions. The response rate has shown to be between 50-70%.[459]

What is even more incredible is that the patients treated are those who have failed to receive benefits from multiple courses of antidepressants. Ketamine works for those when nothing else has. Studies have also shown that a single infusion can reduce suicidal ideation.

Ketamine is now available for use in mental health treatment in the US in many different forms. A nasal spray has been patented and is funded by health insurers for use in a doctor's practice.

459 J Krystal, C Abdallah, G Sanacora, D Charney, R Duman, 'Ketamine: A Paradigm Shift for Depression Research and Treatment', *Neuron*, Vol 1010, Issue 5, 6 March 2019.

The administration using an IV is available in many private clinics and hospitals. It is also being used to treat US military veterans with depression and suicidal ideation.

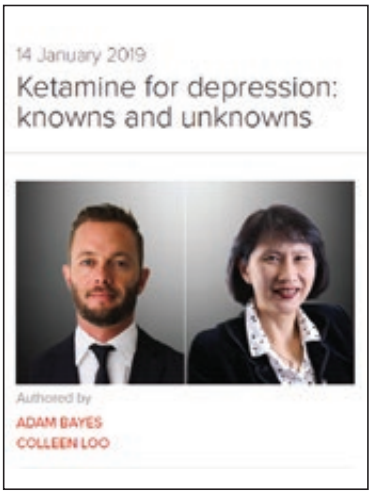
We have conducted multiple interviews with some of the USA's leading ketamine physicians including:

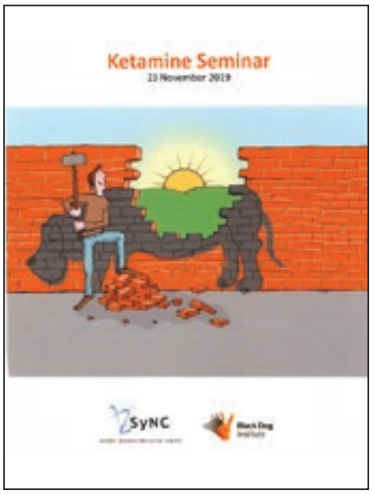
Gerard Sanacora, PhD, MD is a Professor of Psychiatry at Yale University and the Director of the Yale Depression Research Program. He is one of the world's pioneers in ketamine's use in mental illness treatment and oversees the ketamine research work at Yale. Prof Sanacora also works with the NIMH and the American Psychiatric Association.

Gerald W. Grass MD is a former Assistant Professor of Anaesthesiology and Pain at the Yale University School of Medicine and worked with the department of psychiatry in the use of ketamine. He founded and runs the Ketamine Institute that has advanced the clinical use of ketamine for depression, anxiety, PTSD and chronic pain. He is internationally regarded as a leader in ketamine therapy.

Dr. Calabrese MD is a psychiatrist who specialises in treating patients with severe mental illness and suicide risks. Her ground-breaking strategies, including the use of ketamine, has been presented at several national and international conferences, including the International Association for Suicide Research and the American Suicide Foundation International Research Summit on Suicide.

The content of these interviews will be included in a further report titled, *Prescribed Hope – Leaving The Killing Zone*. This future report will examine the progress of using ketamine in treating mental illness and suicide prevention in Australia. The report will examine the ketamine trials conducted by the Black Dog Institute, their ketamine publications and materials from a ketamine training program run by the institute in 2019.

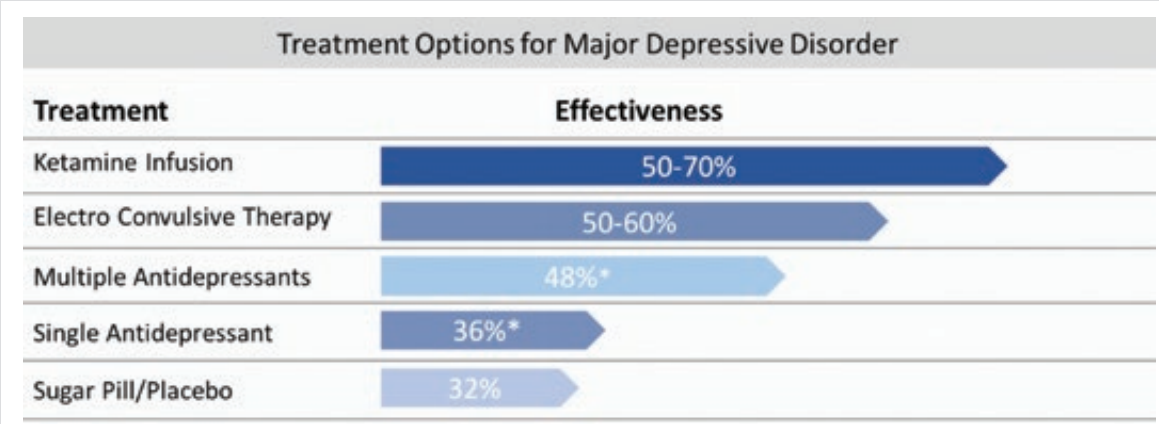




Each of these has been peer reviewed for the report and the opinions are deeply concerning. The report will also examine the ground-breaking work of Dr Stephen Hyde from Tasmania, who published a book in 2015 titled, *Ketamine for Depression*. The book was acclaimed overseas for its forward thinking in many areas of using ketamine for depression and suicidality. The report will examine the response in Australia to the book by the RANZCP and the Black Dog Institute.

In comparison to existing treatments, IV treatment using ketamine demands immediate focus (see Figure 56).

Figure 56: Treatment options for major depressive disorder (Source: Ketamine Institute[460])



Anaesthesiologists are already using ketamine IV to treat patients with pain conditions. Ketamine provides an incredible opportunity for psychiatrists and anaesthesiologists in Australia to collaborate to deliver a safe and effective treatment for those who have tried everything else – all within in a controlled medical facility.

Ketamine is not replacing any existing treatments because it's for the people who don't have any treatments left to try. For many it is the path out of The Killing Zone, if only they can get access to the treatment.

A vial of ketamine costs around $30, which can treat as many as five patients. Based on this, as little as $2 million of taxpayer funds could be used to buy enough ketamine to save generations.

Suicidal behaviour is described as a Psychiatric Emergency. Ketamine is available in nearly every hospital and ambulance in Australia. It is time to start saving lives.

460 Ketamine Institute website, accessed on 3 April 2020, see http://ketamineinstitute.com/restore-ketamine-infusion-treatment/

5. BETTER ACCESS

5.1 OFF-LABEL MEDICATION

Using already approved medications to treat conditions that they were not originally designed for is a common practice used in medicine. A recent example of that is the proposed use of existing medications, like head lice medication Ivermectin, to treat COVID-19.

Off-label prescribing is commonly used in the treatment of severe mental illness. However, in these instances given the medication isn't PBS approved for that condition, the person has to pay the full cost.

> *"Your doctor may recommend a medication that is provided 'off-label'. This is where a medication is used for a condition or for an age group (for example children) that is not listed on the product information. If this is the case, your doctor should explain why they recommend this treatment. You will have to pay the full amount for the medication, which can make it expensive."*[461]

The issue is explained in more detail by RANZCP:

> *"...the RANZCP has highlighted that in Australia, out-of-pocket costs can have a particularly negative impact on people with mental illness and can be a barrier to appropriate, timely health care. There are significant impacts on particular subgroups, including:*
>
> – *people with comorbid physical conditions requiring regular care*
> – *people who are regular users of prescription medicine for either a mental or physical condition*
> – *people on low incomes, including people who are homeless and/or unemployed*
> – *people with serious mental health conditions, such as psychosis and schizophrenia.*
>
> *A likely consequence of high out-of-pocket costs is that people avoid or delay seeking medical attention. This can lead to the development of more serious illnesses, creating a higher demand for hospital-based mental health services and other interventions, including possibly those from the community sector and law-enforcement sectors, not to mention the costs to the individual."*[462]

Cost is certainly an issue that needs greater consideration. In the Productivity Commission's draft report:

> *"An estimated 44% of Australians with mental ill-health stated that they skipped healthcare treatment because of the cost. People with depression, anxiety and other mental health illnesses were 7.7 times more likely to skip treatment than people who were not living with any health condition."*[463]

461 Royal Australian and New Zealand College of Psychiatrists (RANZCP) Your Health in Mind website, accessed on 3 April 2020, see https://www.yourhealthinmind.org/treatments-medication/medication
462 Royal Australian and New Zealand College of Psychiatrists (RANZCP), *Keeping Body and Mind Together*, 2015, p14,17.
463 Australian Government Productivity Commission, vol 2, October 2019, p1132.

For many people the ability to access the prescribed medication comes down to whether it is 'on' or 'off' label. If a psychiatrist deems a medication as the appropriate treatment for a MBS condition then the PBS should meet all the costs; why should there be any other outcome?

Why is the cost of consultation met by the health care system but not the cost of medication prescribed in the consultation?

The absurdity is epitomised in the use of Lithium Carbonate, a medication PBS approved for treatment of bipolar disorder. However, it is also prescribed 'off-label' to treat patients who are at risk of suicide due to their mental illness. The classification by the PBS is in many cases the difference between life and death.

It is highly likely that any off-label use of medication to treat COVID-19 would be fully PBS-funded.

Saving lives should never be about the cost of a prescription.

Warning

Do not stop taking a prescribed medication without discussing it with your doctor. Information can also be obtained by calling the NPS Medicines Line on 1300 633 424 or the Adverse Medicines Events Line on 1300 134 237 for advice. If you need support for any medical concern, including mental health matters, please contact your doctor. Lifeline also provides a 24 hour support service on 13 11 14 or www.lifeline.org.au

14.
RECOMMENDATIONS

1. INTRODUCTION

In 1996 Purdue Pharma was implementing a marketing campaign to bring a new and highly lethal medication into the homes of millions of vulnerable people. OxyContin immediately started a drug epidemic that is still ravaging 25 years later. It is causing the deaths of over 50,000 Americans each year and it all started with a deliberate lying strategy to the very people they had been entrusted to help.

On the other side of the world, fierce debate was taking place in Australia about a new method of consumer warnings being introduced for prescription medication. The consumer product information (CPI) leaflets, later to be renamed consumer medicine information (CMI), were being debated following the 1991 Baume report. It was deemed that the newly formed TGA, was not going to be able to evaluate these documents; apparently there were just too many. So, instead, they focused on the PIs.[464]

The industry broke out in a war to avoid being burdened with the responsibility the leaflets would create. Pharmaceutical companies argued that producing warning documents to go with medications created the risk of these warnings being out of date by the time they reached the consumer. Doctors argued of a risk that patients would refuse to take their medication after reading the side effects. Pharmacists argued that if they had to produce the leaflets in-house, that they would need to be reimbursed for the new printers they would have to buy, and all the printing costs that would be ongoing.

Eventually the framework for the shambolic system we have examined in our report was agreed. By the time OxyContin arrived on our shores in 2000, the healthcare industry was perfectly positioned to ensure that as in the US, the most vulnerable people would be prescribed lethal medication with no warnings of the deadly risks.

In discussing the CPI document in 1996, the AMA delivered a prophetic statement:

> *"...obtaining informed consent from patients suffering from impaired mental capacity, in nursing homes and hostels, or even at home, and certainly patients with psychiatric illness will bedevil the profession for years to come."*[465]

However, the most telling statement came from the Pharmacy Guild:

> *"The greatest cost will be associated with the pharmacist's time in counselling 'in concert' with a CPI document."*[466]

No, the greatest cost came about because you didn't provide that service. Twenty-five years later and that cost is still being paid every single day, by those whose only failing was asking for help.

If this report does not force the entire Australian healthcare profession to immediately transform into what it should always have been, then we will keep writing reports until it does.

464 J S Dowden, 'Consumer product information affects us all', *Australian Prescriber*, Issue 2, 1 April 1996.
465 ibid.
466 ibid.

2. NATIONAL SAFETY IN HEALTHCARE ROYAL COMMISSION

The recommendations are:

1. The contents of this report to be used as the basis of a Royal Commission into the failure of the healthcare system to ensure the safety of all Australians receiving prescription medication.
2. Human rights as they relate to the right to health, the rights of persons with disabilities and the right to safe healthcare will be the principles that the Australian healthcare system will be assessed against by the Commission.
3. Include content for legislation of a National Safety in Healthcare Act to provide civil and criminal penalties for the failure to uphold human rights in healthcare. The Act would encompass all areas of healthcare but will have particular focus on clinical diagnosis, consumer information, the provision of medications, gaining informed consent, regular review of ongoing treatments, and holistic patient collaboration between physicians.
4. The terms of reference must be broad and encompassing. It must cover all areas of healthcare and include all direct and indirect adverse consequences on human wellbeing. It must include all government (including defence) organisations, private sector, not-for-profit, charity, medical service providers, and advocacy organisations.
5. The role of not-for-profit, charity and advocacy organisations in delivering healthcare treatment, research and consumer advocacy is to be examined, with specific attention to the results of programs funding by government such as Headspace.
6. The failure to introduce new advancements in healthcare, the reasons for this and recommendations on how to prevent this occurring in the future to be examined.
7. The Commission will examine the process in which new medications and treatments are assessed by government and the monitoring of clinical results for efficacy and adverse events.
8. The 7th Community Pharmacy Agreement between the Australian Government and the Pharmacy Guild that is due to commence in June 2020, must not be formalised. The Commission should investigate alternative options for the provisions of medications to Australians.
9. The findings of completed government enquiries and investigations are to be examined as to why the submissions of people with lived experience were not reflected in the recommendations, for example, the Productivity Commission, NMHC and the Royal Commission into Victoria's Mental Health System.
10. A new national system of reporting on healthcare safety including prescription medication to be established.
11. The Commission to be asked to recommend civil and criminal action as part of the findings.
12. A compensation scheme implemented for the victims.

13. As part of the compensation scheme, access to the MBS and PBS records for victims to be fast-tracked.
14. The Commission to provide an interim report on critical actions after a period of 12 months, and every 12 months following, until the appointed commissioner believes that a final report can be prepared. Every story must be heard. Every life lost deserves to be recognised. Every failing must be identified and addressed. This can never happen again.

3. NATIONAL HEALTHCARE SAFETY REGULATOR

The recommendations are:

1. A government body, independent of the health portfolio, to be established to ensure the safe provision of healthcare services in Australia. The National Healthcare Safety Regulator (NHSR) is to have legal authority to investigate and prosecute breaches across all government, private sector, not-for-profit, charity, medical and advocacy organisation.
2. The responsibility of the NHSR will be to ensure that *all Australians have access to a healthcare system the delivers the highest level of safety and efficacy in healthcare*.

4. IMMEDIATE GOVERNMENT ACTION

4.1 SEVERE MENTAL ILLNESS – CRITICAL ACCESS PROGRAM

The recommendations are:

1. Recognising the higher morbidity and mortality of people with severe mental illness, and the prevalence of comorbidities, a fully funded government program to be established to provide additional medical treatment options.
2. All existing patients who have been on mental health medication for longer than six months without improvement in symptoms or who are taking more than one mental health medication, are immediately offered free pharmacogenomic testing. Physicians are provided with training and assistance on interpreting the testing results.
3. The program will enable people who have failed to achieve remission from their illness using existing therapies to access new or trial therapies that meet an acceptable risk/benefit assessment by a panel collective of physicians. For example, immediate access to treatments that are in FDA breakthrough status like psilocybin and MDMA. It would also include treatments that are approved off-label, like ketamine IV.

4. All patients would be required to meet a clinical classification assessment for the program. They would also acknowledge the risks of the treatment.
5. The central benchmark for the risk/benefit assessment is the understanding that the risk of not successfully treating severe mental illness is lower life expectancy and this is assessed against the risks/benefits of the new treatment.
6. The MBS to add a billing option that enables GPs of the patients in the program to treat all comorbid health issues in the one consultation.
7. The Australian Government Department of Health to form a partnership with NIMH to provide sharing of information and access to research trials.

4.2 MEDICATION

The recommendations are:

1. The Australian Government Department of Health to review the efficacy and side effects of mental health medication focusing on the global experience in efficacy and side effects in clinical use. This must include polydrug treatments. Medication that does not meet the TGA and PBS standards should have their availability reassessed. This review should occur annually based on adverse drug events and consumer complaints.
2. This information is to be provided by the RANZCP who will use it to update clinical guidelines for other users like GPs and consumers.
3. The TGA immediately takes over the responsibility for the contents and warnings in all medication guides, including the CMI and PI documents (as per the FDA operations in the USA).
4. A category of 'High Risk' pharmaceuticals must be defined and embedded into the health care industry. These are medications that in isolation or in polydrug combinations, pose a serious threat to the health of the person. This should cover all Schedule 4 and 8 drugs, as well as all mental health medications (i.e. antidepressants, antipsychotics, mood stabilisers).
5. This report forms the basis of an independent assessment of the warnings provided in Australian CMIs across all medication categories, not just 'High Risk' drugs. Particular focus is the comparison of FDA warnings and PI information.
6. Introduce a new 'High Risk' *quick guide* CMI. It should be a one page, FDA-style, warning guide.
7. High Risk medication should also come with a boxed warning placed on the packaging stating the highest risk side effects.
8. Consumer Medicine Information (CMI) documents to be urgently redesigned including:
   - rewritten with simpler language, avoiding medical or legal terms, that consumers can understand
   - clearer explanation of the likelihood of risks
   - clearer explanation of the physical side effects including the risk of life-threatening conditions
   - clearer explanation of the polydrug risks
   - boxed warnings (place on medication packages) to be reviewed, with life-threatening risks noted

  - boxed warnings specific for polydrug combinations being prescribed to a person are noted (for example, opioids and benzodiazepines each to warn the polydrug risks of taking both at the same time).

9. Providing a 'High Risk' *quick guide* CMI should be mandatory. No exceptions. A full CMI for all 'High Risk' medication must be offered with each prescription. A patient can request a text or email version but a paper version must be provided at least once annually and anytime the CMI is updated. The option to send a copy to a nominated carer should be provided.
10. Personalised MIMS polydrug risk warnings must be provided with every prescription that contains two or more 'High Risk' prescriptions in addition to the 'High Risk' CMI.
11. Barcode CMI tracking to be implemented. Every 'High Risk' CMI and MIMS to be barcoded and recorded for every prescription.
12. ALL medication *quick guide* CMIs to be provided as mandatory for the first prescription, when a new CMI is updated and at least annually for ongoing prescriptions
13. An online app is to be made available to help people find out more about drugs and drugs interactions.
14. Alcohol labelling is updated to include the risks of taking with prescription medication.
15. A Consumer Warning Program is to be implemented that monitors global changes in 'High Risk' medication side effects. The program would use the Real Time Prescription Monitoring (RTPM) database to inform any existing users of medication of any changes to side effect risks. The TGA makes it mandatory for a pharmaceutical company to provide them all details of any changes in international regulatory warnings or drug information changes.
16. A compulsory RTPM system to be implemented nationally. The RTPM is expanded to cover all 'High Risk' medications irrespective of the poison schedule.
17. RTPM is utilised at every prescription to identify if a person needs MIMS information.

4.3 CONFLICTS OF INTEREST

The recommendations are:

1. The pharmaceutical industry self-regulation through Medicine Australia must end. The Code of Conduct to be regulated under federal law, with civil and criminal penalties for breaches. The existing Code must be reviewed following a consultation process, and gain input from all areas of the healthcare system and people with lived experience. The Code should be regulated by the NSHR.
2. Political parties must ban all donations from pharmaceutical companies. This includes any indirect financial support provided through fundraising events, lobbying groups and third-party entities.
3. Organisations that receive government grants or funding are to be banned from making political donations, such as the Pharmacy Guild.
4. Any lobbying that is done by or on behalf of the pharmaceutical industry must be done in writing and be on the public record.
5. Any meetings between the pharmaceutical industry, government or government departments, should also be on the public record.
6. The pharmaceutical industry should be banned from priority access to any government buildings or parliaments.

7. Pharmaceutical companies should be banned from directly providing funding to any medical body that has direct influence in the delivery of medication to consumers, like the RANZCP, and the RACGP.
8. Pharmaceutical companies should be banned from directly providing funding to any organisation that also receives government funding, including charities, and not-for-profit organisations.
9. Pharmaceutical companies only be allowed to provide funding to external organisations via a central funding pool, which independently assesses and distributes the funds on an application basis following the stated purpose of the funding donated.
10. 20% of all PBS revenue for new medications is to be held in trust for three years following the launch of the medication. These funds are to be used for consumer claims for compensation against the pharmaceutical company for that medication and all claims assessed by an independent panel. After three years the funds are only released following an assessment of the safety of the medication.

4.4 LIVED EXPERIENCE – MENTAL HEALTH

The recommendations are:

1. A national organisation representing people with lived experience is to be established, funded by government.
2. This organisation is to be recognised as a stakeholder by government in mental health matters including new medications and treatments, government policies and industry feedback.
3. Submissions from this organisation must be acknowledged and assessed by any government inquiry. The recommendations of these inquiries must discuss the submission/s and respond to the matters raised when they are not part of the recommendations.

4.5 GOVERNMENT REPORTING

The recommendation is:

1. Implement a National Prescription Medication Reporting Standard. This will focus on the classifying and reporting of adverse events of prescription medication. This should include a consistent method for reporting on adverse drug events, attempted suicides and suicide deaths that involve prescription medication.
2. The ABS will include summary information in the annual causes of death report that is released publicly. The report will identify all deaths by prescription medication class, including if the death was accidental or suicide.
3. The ABS will include the means of suicide in the annual causes of death report. This will also include a specific category of suicide from prescription medication.
4. The ABS will develop and release a monthly National Mental Health Indicator Report, similar in design to the daily COVID-19 report from the Department of Health. The report will identify the quantitative factors that indicate the nation's mental health. This report will include:
    a. New mental health plans – MBS
    b. Mental health GP consultations – MBS
    c. Mental health prescriptions – PBS

d. Mental health referrals from GPs to specialists – MBS
e. Suicides – ABS
f. Hospitalisations for intentional self-harm – ABS

4.6 GOVERNMENT MENTAL HEALTH PROGRAMS

The recommendations are:

1. A review of the *Fifth National Mental Health and Suicide Prevention Plan* and the recommendations of the Productivity Commission into mental health to include a greater focus on:

– new strategies to reduce access to means of death
– incorporating all core areas identified by the WHO guidelines on mental health, prescription medication and suicide prevention
– including a program that focuses on research into new treatments
– reviewing all government-funded mental health and suicide prevention trials and programs.

5. COMPENSATION FOR VICTIMS

The recommendations are:

1. The Australian Government must fund and establish a body to assess the compensation claims for victims and families affected by the issues identified in this report. No time period limitations should be placed. All claims should be assessed on the basis of whether *an individual suffered from the known side effects from the 'High Risk' medication they were prescribed*.

Warning

Do not stop taking a prescribed medication without discussing it with your doctor. Information can also be obtained by calling the NPS Medicines Line on 1300 633 424 or the Adverse Medicines Events Line on 1300 134 237 for advice. If you need support for any medical concern, including mental health matters, please contact your doctor. Lifeline also provides a 24 hour support service on 13 11 14 or www.lifeline.org.au

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ABOUT THE REPORT

Prescribed Deaths – Life in the Killing Zone offers a detailed, holistic and wide-ranging assessment of the Australian mental health care sector. The report contains honest opinions and critical examinations of the end-to-end treatment experience for those living with severe mental illness. These conclusions are backed by multiple research references from reputable sources.

The research and findings provide an integration of lived experience, detailed investigations, expert opinions, and matters of public health concern.

The author of this report, Patrick O'Connor, has been an advocate for reform in mental illness support services over many years. As a person with lived experience of the issues facing millions of Australians, public interest is at the forefront of the author's intent.

All statements made in the report are presented as critical examinations of the topic. There is no malice intended and the strength of language used in the report is designed to maximise the education and awareness of critical safety failures, with the goal to warn other Australians.

By investigating government policy and legislation, the report provides a link between systemic healthcare failures and the legal implications of these failures. The author provides these assessments **as a complaint to multiple organisations** with the responsibility to uphold these legal standards.

The author has no conflicts to disclose at the time of publication. The preparation of the entire report, all travel and associated costs have been funded by the author. No government or third-party funds or donations have been received nor requested. Further to this, donations post-release will not be accepted.

The author would also like to strongly note that the report has been produced for no commercial benefit. The report will be made available electronically at no cost. Access will not be limited and will be provided on an ongoing full access commitment. Any costs to obtain the report will only be incurred if hard copy materials are requested through a publication organisation.

Any potential litigation or claims for compensation by people with lived experience against organisations assessed in this report, will have no financial interest to the author or any entity the author is associated with. **This is a lived experience report, provided for free for the primary purpose of bringing urgent attention to physical risks that Australians are exposed to every day, without warning.**

All interviewees provided their time and opinion at no cost. They neither requested nor were offered any remuneration for their services. Their personal disclosures can be obtained from their organisational websites.

All recorded interviews were undertaken whilst asking questions for the sole purpose of obtaining medication safety information. No information was requested that did not relate directly to the topics examined in this report. Any information that has not been included relates to personal information that does not meet the purpose of the report and would breach the commitment to confidentiality.

Prior to publication of this report, the author has on multiple occasions provided, or attempted to provide, the information in this report to organisations including the National Mental Health Commission (NMHC), Australian Government Department of Treasury, Australian Government Department of Health, Beyond Blue, Orygen/Headspace, and the Black Dog Institute. Feedback has been provided to individual pharmacies around Australia on multiple occasions, with no evidence of changed dispensing practices. The universal lack of any interest in understanding the information provided or offered to these organisations has necessitated the publication of this report. While the author attempted to warn numerous parties in the Australian healthcare system, he failed to obtain any engagement from these parties.

Further reports are in production and are expected to be published after a period of public feedback following release of this report. Any modifications to this report will be included in the document available on the author's website at www.prescribeddeaths.com.au