Independent expert report on the risks of intentional self-poisoning with paracetamol

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Correction

A minor amendment to this report was made on 20 September 2022 to correct the attribution for grocery and convenience stored sales data as having only been obtained from IRI.

Executive summary

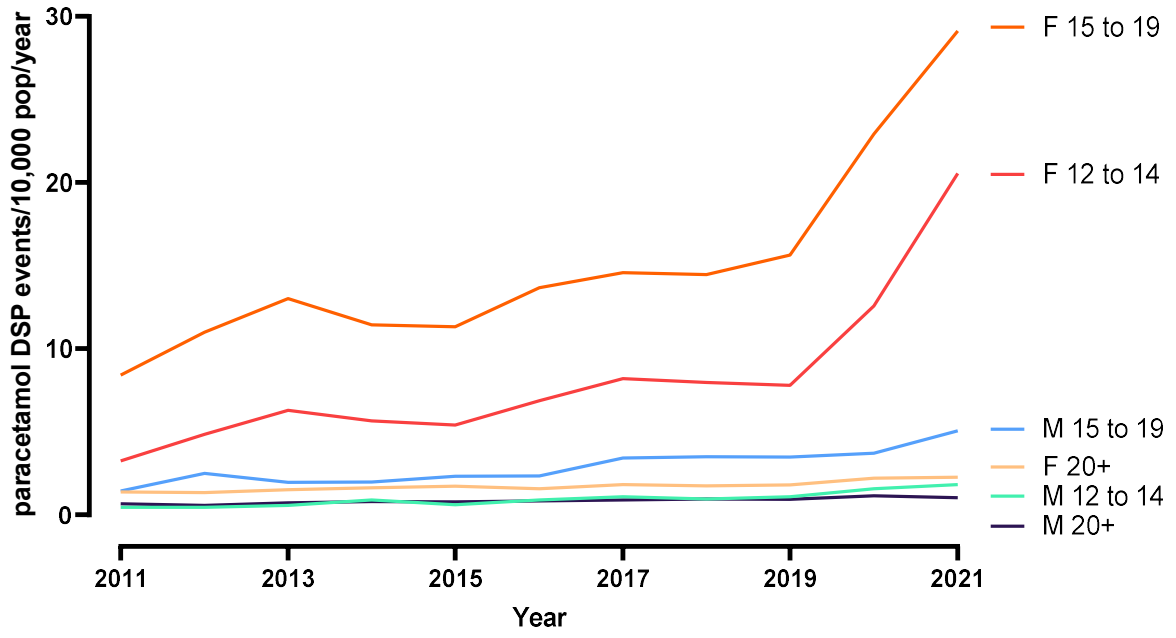
This report was commissioned by the Therapeutic Goods Administration (TGA) in response to concerns of increasing prevalence of intentional paracetamol poisoning, especially among young people, and involving paracetamol obtained via general sale in supermarkets and convenience stores. In these settings, there is not the healthcare professional oversight that is available in pharmacies. The report was commissioned to guide their considerations of whether any changes to the scheduling of paracetamol, such as access controls, may be warranted.

Specifically the report aims to:

- Provide an overview of clinical aspects of paracetamol toxicity and current treatment.
- Examine contemporary Australian data on the burden of paracetamol poisoning from a range of sources, identifying high risk groups for poisoning and toxicity.
- Review relevant literature on the burden of paracetamol poisoning internationally and how this has tracked in relation to access, including any recent regulatory changes.
- Review relevant literature on options for and effectiveness of restrictions and other strategies to reduce harms.
- Review relevant literature on the intent and underlying social/psychiatric issues experienced by those engaging in paracetamol self-poisoning to inform whether other strategies to reduce harms from intentional self-poisoning are needed.
- Critically analyse the balance of the benefits and risks of the current access to paracetamol on the Australian market in relation to intentional self-poisoning, particularly in regard to paracetamol available by general sale.
- Discuss the possible outcomes in the community of restricting general sale access or purchasing controls to paracetamol, including deliberate self-poisoning with other medicines.

Summary of the problem

The review confirmed from several sources that there were increasing rates of intentional self-poisoning with paracetamol in the last decade in Australia, with the greatest proportion of cases in adolescents and young adults, and females being significantly over-represented. This is against a backdrop of very large increases in all intentional self-poisonings in older children/adolescents (ages ~10 to 19) worldwide over the recent decade, underscoring the importance of factors independent of paracetamol access controls to the problem. As such, although paracetamol is the most commonly used medicine in overdoses in young Australians (around 50%), this proportion has not increased. Self-poisonings in adolescents may have further accelerated during the COVID-19 pandemic (only Poisons Information Centre data is available for up-to-date intentional paracetamol self-poisonings events generating calls have more than doubled since 2011, and these have tripled for those aged < 20). The figure provides a summary of the more detailed data later in the report indicating the magnitude of the increase and the key population affected.



Estimated population adjusted annual rates for intentional self-poisoning events/10,000 pop generating calls to the NSW Poisons Information Centre

NB – Based on NSW PIC receiving 50% of Australian intentional self-poisoning with paracetamol calls and that 84% of calls in the 5-to-14-year age group are in the 12-to-14-year age range. Resident age-sex population from ABS website.

The key risk factors for severe liver toxicity and death—late presentation, high doses and modified release (MR) paracetamol ingestion—remain unchanged, each occurring in around 5 to 10% of overdoses. Many proposed interventions are designed to reduce the proportion of such high-risk overdoses (rather than to completely prevent overdoses). Despite very effective treatments, there is still morbidity (acute liver injury/failure in 2 to 5% of overdoses) and deaths (0.2 to 0.5%), largely confined to such higher risk overdoses. These outcomes are extraordinarily tragic but are extremely rare: approximately 9 hospitalisations with liver injury and 2 deaths per million head of population. Moreover, they are infrequent compared to the volume of paracetamol consumed in the community each year: 3 hospitalisations with liver injury and <1 deaths per million units of paracetamol sold.

Further information was obtained from commissioned studies run by the NSW Poisons Information Centre to inform a range of options for intervention. These studies found that most paracetamol self-poisonings in all age groups are impulsive but with suicidal intent. It is common for these individuals to have repeated episodes of self-harm. Over half the time, the paracetamol taken in intentional self-poisoning was present in the home. Only around 10% reported recently purchasing paracetamol (usually on that day); 1 or 2 packs were purchased. Therefore, although about one-third of paracetamol sales in Australia are in grocery and convenience stores, and multiple packs are frequently purchased in both grocery stores and pharmacies (25% of paracetamol transactions), these purchasing trends contribute only in part to intentional self-poisoning. Similarly, the pack size most commonly ingested, and in roughly equal proportions were 20/24s and 96/100s with at least 25-30% of ingestions involving unscheduled products. This roughly matched the national sales volumes for

paracetamol products, indicating that general sales are not over-represented in the problem of intentional poisoning with paracetamol, and a change in the availability and pack size of paracetamol in this setting would have limited impact.

The systematic literature review findings on the population were largely concordant with the Australian data, in terms of demographics, intent, and ingestion. For example, it was apparent from the literature that self-harming with paracetamol tends to be impulsive. People are taking what is readily available in the home and for most people, particularly young people, this is paracetamol as they don't have access to other medications, such as prescription drugs. Additional findings from the review included that paracetamol is likely to be the first substance used for self-poisoning, particularly among young people, and that not all of those with intentional self-harm with paracetamol have a psychiatric diagnosis or mental health symptoms (and thus population (rather than individual) focused approaches are important). It was also apparent from the literature that public knowledge of the harms of paracetamol is mixed and that paracetamol packet warnings are unlikely to deter people from self-poisoning.

Our survey of the international landscape has shown that access to paracetamol products varies considerably between jurisdictions. Due to the limited availability of published data, we were unable to identify clear trends between the level and means of access controls on paracetamol, and the incidence of poisoning, morbidity and mortality, between jurisdictions. However, a number of foreign jurisdictions have tighter controls on paracetamol access, such as paracetamol not being available by general sale or smaller pack size limits for general sale compared to Australia.

Rationale for paracetamol targeted solutions in Australia

In Australia, unlimited numbers of packs of paracetamol can be purchased without a prescription at pharmacies or supermarkets, with 96 or 100 tablet packs and 20 tablet packs, respectively, being the most commonly purchased through these channels. Many countries, including the EU, UK, and New Zealand have introduced some restrictions to target the problem. For example, this includes greater restrictions on MR preparations and tighter limits on paracetamol pack sizes or packs sold. Our literature review noted that reduction in pack size has been found to reduce deaths from poisonings by about a third, although effects may be less for non-lethal outcomes. One study restricted the sale of paracetamol to people over 18 years and found a 17% reduction in self-poisoning for those under 18 years (but no change in the other age cohorts). There was little evidence across the 15 studies identified in the review that method substitution arises as a result of restrictions. Consistent with these findings, NSW PIC data showed the 2018 codeine prescription only (S4) restriction was followed by a large reduction in paracetamol combination product ingestions (and also reduced ibuprofen and codeine ingestions). In contrast, the 2010 codeine and 2020 MR paracetamol 'pharmacist only' (S3) restrictions were not effective.

Recommendations to the TGA to inform scheduling deliberations

There are four means restriction and harm minimisation interventions to consider that are supported by overseas experience with regulation:

1. **Pack size restrictions.** For example, maximum pack sizes for unscheduled products reduced from 20 to 12 or 16 tabs; S2 pack sizes reduced from 100 to 24 or 50.

2. **Pack number limits.** Most (~95%) sales of paracetamol tablets involve the purchase of 1 or 2 packs. Making this the maximum number of packs that can be purchased in one transaction would almost certainly reduce home stockpiles, and likely also reduce the number of very large overdoses, which have much higher morbidity and risk of death.
3. **MR paracetamol restrictions.** This product is designed for long-term use (e.g., for osteoarthritis), rather than for acute pain. Prescription only (S4) scheduling would be expected to reduce casual use of this more dangerous product and therefore overdoses.
4. **Age restrictions.** An 18+ age restriction on the purchasing of over-the-counter analgesics would be expected to reduce poisonings among 10-17 year-olds.

The biggest impact is likely to come from MR paracetamol being made S4, followed by smaller pack size limits and pack number limits for S2, as both would be likely to reduce the number of grams of paracetamol routinely held in homes and thus the numbers of very large overdoses taken in impulsive self-poisonings.

There are also some non-medication specific recommendations to reduce self-poisoning.

5. **Use safe reporting guidelines for any communication around the harms associated with paracetamol (or any other) overdose.** Any communication around the potential harms of paracetamol must comply with safe reporting guidelines and be rigorously evaluated prior to implementation.
6. **Maintain and expand support for aftercare services.** All intentional self-poisonings should be offered appropriate care and Australian recommendations for aftercare (follow-up care and support after self-harm) implemented.
7. **Inform safer storage of medicines and reduced stockpiling of unwanted medicines.** Generic messages around keeping medications and chemicals out of harm's way might reduce intentional poisoning risks for children and adults.

Gaps in the Australian data and the research literature were identified which, if filled in the future, could inform additional recommendations and better strategies to reduce harms from paracetamol self-poisoning. Additional information and data are needed in relation to understanding the motivations and behaviours of young Australians who have taken paracetamol (and other medicines) for deliberate self-harm or attempted suicide, trends in self-harm with paracetamol over time to identify changing risks, the long-term outcomes after non-fatal self-harm to identify changing risks, and medical and psychiatric management of paracetamol self-poisoning.

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Glossary of key terms

Aspirin: (also acetylsalicylic acid) is a common analgesic that is available over-the-counter in pharmacies and in supermarkets in Australia. It is also classified as a non-steroidal anti-inflammatory medication.

Ibuprofen: is a common analgesic that is available over-the-counter in pharmacies and in supermarkets in Australia. It is also classified as a non-steroidal anti-inflammatory medication.

Intentional self-poisoning: (also deliberate self-poisoning; intentional overdose) refers to deliberate self-exposure to a substance with potential to cause harm in the exposed quantity. This review focuses on intentional self-poisoning by ingestion of paracetamol or similar medication in a quantity exceeding the therapeutic dose. The purpose of intentional self-poisoning is most often self-harm or a suicide attempt, but it may also include intentional misuse or recreational use.

Method substitution: refers to the use of an alternate method of self-harm, or suicide following the restriction of access to another means. For example, this review focuses on whether restricting access to paracetamol or other similar medications (e.g., via up-scheduling) results in a 'switching' to alternative unrestricted medications or alternate methods of self-harm and suicide.

Over-the-counter medication: refers to a medication freely accessible at point-of-purchase without the need for a prescription from a health professional.

Over-the-counter analgesics: refers to medications belonging to the analgesic category that are available without prescription. In Australia, this category includes paracetamol, aspirin and ibuprofen.

Pack size: refers to the number of tablets or capsules sold within a single packet of a medication.

Paracetamol: (also acetaminophen) is a common analgesic that is available over-the-counter in pharmacies and in supermarkets in Australia. It is the most common over-the-counter painkiller used in Australia.

Scheduling, Up-scheduling, Down-scheduling: Scheduling is a national classification system that controls the availability of various medications (and poisons) to the general public. Up-scheduling refers to a change in classification of medication from a less strict to a more strict category, making the medication more difficult to access. For example, up-scheduling occurred in Australia in 2018 when low-strength codeine products were reclassified from Schedule 3 (Pharmacist Only Medicine) to Schedule 4 (Prescription Only Medicine). Down-scheduling refers to a change in classification of a medication from a more strict category to a less strict category, making the medication more accessible.

Self-harm: refers to intentional infliction of injury or harm to oneself to cope with, or express emotional distress and internal turmoil. Self-harm may not necessarily involve suicidal intent but can result in fatal outcomes.

Suicidal ideation: refers to thoughts of ending one's life.

Unintentional self-poisoning: (also accidental self-poisoning; unintentional overdose) refers to accidental self-exposure to a substance with potential to cause harm in the exposed quantity. This can include accidental ingestion (common in children) or unintentional ingestion of more than the recommended dosage (i.e., therapeutic misadventure) that is either acute or occurs over time.

Abbreviations

A & E – Accident and Emergency
ACT – Australian Capital Territory
ADHD – Attention deficit hyperactivity disorder
AIHW – Australian Institute of Health and Welfare
ALT – alanine transaminase (a liver enzyme & injury biomarker)
AST – aspartate aminotransferase (a liver enzyme & injury biomarker)
CYP – cytochrome P450 (liver enzymes that make toxic metabolite)
DDD – defined daily dose**,**
DSP – deliberate self-poisoning
ED – emergency department
eMR – electronic medical record
EU – European Union
HATS – Hunter Area Toxicology Service
ICD – International Classification of Diseases (coding system for hospital/death data – current Australian version is ICD-10-AM)
INR – International normalised ratio (a test of clotting function)
ICU – Intensive care unit
IQR – interquartile range
IQVIA – company providing national sales data from pharmacies
IRI – company providing data on grocery/convenience store sales
IR – immediate release
MR – modified release
NAPQI – N-acetyl-P benzoquinonamine (toxic metabolite of paracetamol)
NCIS – National Coronial Information System
NHMD – National Hospital Morbidity Database (NHMD)
NAC- acetylcysteine (also widely referred to as N-acetylcysteine)
NSAID – Nonsteroidal anti-inflammatory drug
NSW – New South Wales
OECD – Organisation for Economic Co-operation and Development
OTC – over-the-counter
PIC – Poisons Information Centre
PSS – poisons severity score
PTSD – post-traumatic stress disorder
Rx – prescription
S2 – Schedule 2 (pharmacy only)
S3 – Schedule 3 (pharmacist only)
S4 – Schedule 4 (prescription only)
SD – Standard deviation
SE – standard error,
SIS – Suicidal Intent Scale
SSRI – selective serotonin reuptake inhibitor
TGA – Therapeutic Goods Adminstration
UK – United Kingdom
USA – United States of America

1. Introduction

1.1 Background

Paracetamol is the most common drug taken in overdose in Australia. We have effective treatments (e.g., activated charcoal to reduce absorption, acetylcysteine to reduce liver damage, intensive care) and these work extremely well if people have taken moderate size overdoses of standard preparations (< 30 g) and present within 4-8 hours. However, there is still morbidity and the need for hospitalisation, and paracetamol poisoning is still the most common cause of acute liver failure in most of the Organisation for Economic Co-operation and Development (OECD) countries.

In Australia, unlimited numbers of packs of paracetamol can be purchased without a prescription at pharmacies (purchases are commonly of 96 or 100-tablet packs) or supermarkets (commonly 20-tablet packs). Many countries, including the EU, UK, and New Zealand have introduced some restrictions to target the problem. For example, this includes greater restrictions on modified release (MR) preparations and tighter limits on paracetamol pack sizes or packs sold.

In Australia, medicine access restrictions are most commonly implemented through scheduling. This is a national classification system that controls how medicines and chemicals are made available to the public. Medicines and chemicals are classified into Schedules in the Poisons Standard based on intended use and risks of harm. This determines the ease of access and aims to protect public health and safety.

This report aims are to

- Provide an overview of clinical aspects of paracetamol toxicity and current treatment.
- Examine contemporary Australian data on the burden of paracetamol poisoning from a range of sources, identifying high risk groups for poisoning and toxicity.
- Review relevant literature on the burden of paracetamol poisoning internationally and how this has tracked in relation to access, including any recent regulatory changes.
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- Critically analyse the balance of the benefits and risks of the current access to paracetamol on the Australian market in relation to intentional self-poisoning, particularly in regard to paracetamol available by general sale.
- Discuss the possible outcomes in the community of restricting general sale access or purchasing controls to paracetamol, including deliberate self-poisoning with other medicines.

1.2 Overview of clinical aspects of paracetamol toxicity

The major risk from paracetamol poisoning is acute liver toxicity. This is caused by a minor toxic metabolite of paracetamol (NAPQI) produced in the liver. This metabolite accounts for much less than 10% of paracetamol metabolism and in therapeutic doses is readily detoxified by the antioxidant glutathione. In overdose glutathione levels may be insufficient to detoxify NAPQI and it binds to a wide range of proteins in the liver causing acute liver injury.

The minimum toxic overdose is generally regarded as 10 g (or 200 mg/kg in patients under 50 kg). This is typically the minimum amount that leads to a concentration over the paracetamol nomogram line. The nomogram (Figure 1) is used to confirm that a toxic dose has been ingested and thus indicates the need for antidote treatment with acetylcysteine.(Buckley et al., 2020; Chiew et al., 2020) Acetylcysteine replenishes glutathione stores and also directly detoxifies paracetamol.

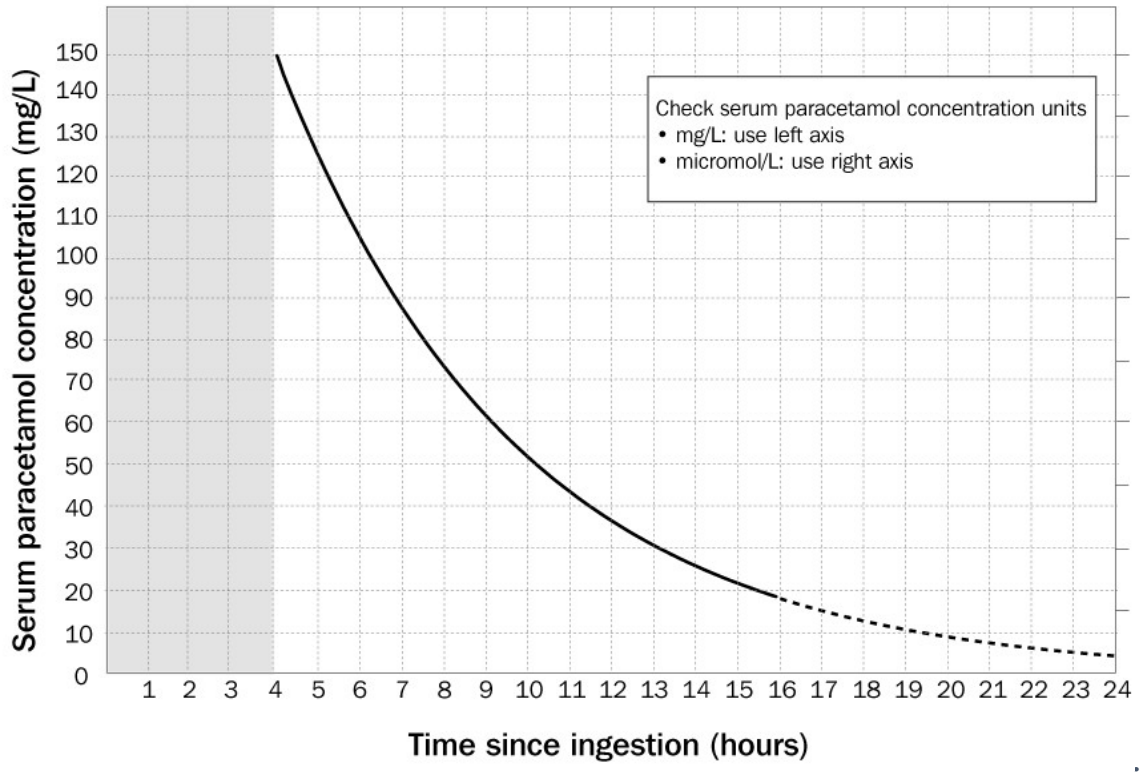

Figure 1 The paracetamol poisoning nomogram

NB. Right hand axis units are not shown, all concentrations mentioned in the report are in mg/L.

A few people who have low glutathione stores or metabolise to NAPQI in greater than usual amounts may be susceptible to toxicity with lower overdoses, but this is not a frequent problem. Generally, starting treatment with acetylcysteine within 8 hours for those over the nomogram line leads to complete protection.(Chiew & Buckley, 2021; Chiew, Gluud, Brok, & Buckley, 2018) People with much higher ingestions, manifested as higher concentrations on the nomogram, are at higher risk despite standard treatment.(Cairney et al., 2016; Chiew et al., 2017) The figure demonstrates this risk – those with mg/L concentrations double ('301-

500') or triple ('501+') the nomogram line have a risk of toxicity despite treatment within 8 hours and even if they have no evidence of liver toxicity (a normal ALT) on arrival. (Figure 2). This risk is reduced by giving higher than usual acetylcysteine doses.(Chiew et al., 2017).

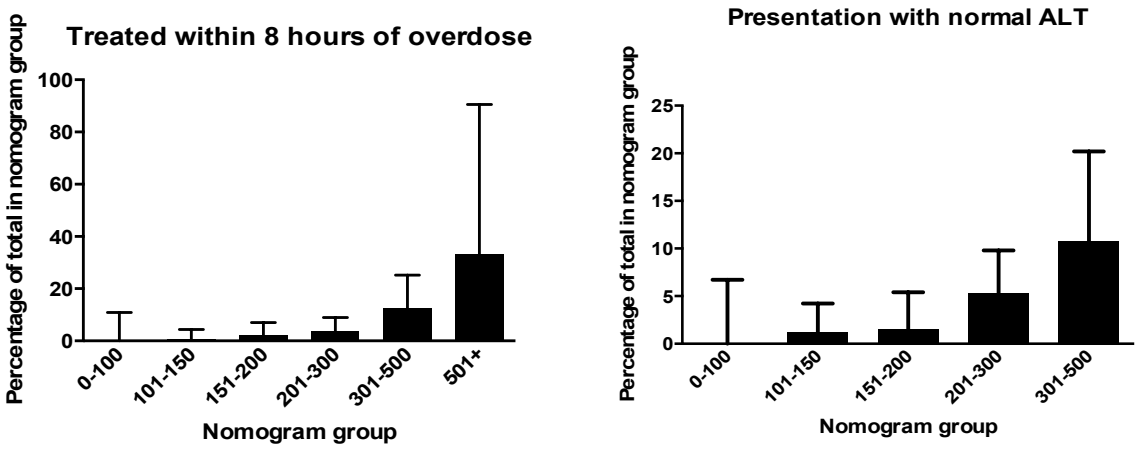

Figure 2 Rates of liver injury following paracetamol poisoning stratified by paracetamol concentrations plotted against the nomogram in mg/L.(Cairney et al., 2016)

Note the standard Australian nomogram line is a '150 line' reflecting that it starts at 150mg/L at 4 hours.

This means most people who develop liver toxicity are those who have taken very large overdoses (i.e., > 2 to 3 times the minimum toxic dose). Modified release paracetamol tablets contain larger amounts of paracetamol and also appear to lead to a higher risk of liver injury.(Chiew, Isbister, et al., 2018) The acute liver injury may be fatal, although the majority of people with severe acute liver injury recover after several days.(Chiew & Buckley, 2021) However, they may require prolonged intensive care and occasionally they receive a liver transplant.

The peak demographic group for deliberate self-poisoning generally is adolescent females (considered further below). The highest risk groups for liver toxicity after poisoning, are very large overdoses, MR paracetamol overdoses, late presenters, and those with underlying risk factors (conditions leading to malnutrition and/or induced CYP enzymes).(Chiew & Buckley, 2021)

2. Latest data on extent and nature of the problems

2.1 Data sources

We have triangulated multiple Australian sources to provide data that is as up-to-date, accurate and complete as possible (Table 1). All these sources have quite different coverage and also significant limitations in terms of currency, accuracy or completeness – and these should be considered when reading the results from each section below.

Table 1. Main original data sources used in this report and key limitations

Data source	*Coverage*	*Years*	*Limitations*
Australian Institute of Health and Welfare (AIHW)- National Hospital Morbidity Database (NHMD)	*All Australian public hospital poisoning admissions*	*2011-June 2020*	*Does not capture non-admitted presentations, out of hospital deaths. Coding of most medicines other than paracetamol is very imprecise.*
National Coronial Information System (NCIS)	*All notified deaths in Australia*	*2008-June 2020*	*Several fields of varying uncertainty implicating paracetamol. Very variable degrees of documented evidence supporting paracetamol as a cause of death.*
NSW PIC database	*All calls about exposures to paracetamol*	*2011-2021*	*Referral biases. Around 45-50% of national PIC calls. No routine follow up.*
NSW + Other PIC requested datasets	*All calls about exposures to paracetamol*	*2017-2021*	*Different databases providing data. Age recorded in broad categories. Sex data not provided.*
NSW PIC with electronic medical record (eMR) review	*Deliberate self poisoning calls*	*2022*	*Limited numbers, NSW admissions data only. Referral bias.*
NSW PIC prospective survey	*Deliberate self poisoning calls*	*2022*	*Limited numbers, NSW PIC call data only. Survey data often not able to be provided – 'unknown.'*
National sales data Pharmacies (IQVIA) Grocery/convenience stores (IRI)	*Sales of paracetamol products*	*2017-21*	*Data grouped into similar products – specific brands not identifiable.*

2.2 Hospital admissions - Australian Institute of Health and Welfare (AIHW) data

- Total Australian paracetamol poisoning hospital admissions steadily increased up until around 2017 and decreased thereafter. Deliberate self-poisoning accounted for the majority of poisoning admissions in those aged over 10 years. The increases were most marked in those aged between 10 and 24, and for females, who accounted for two-thirds of admissions.
- The younger age groups generally had better outcomes after hospitalisation, with lower rates of toxic liver injury and fatal outcomes.
- Paracetamol poisoning admissions accounted for a substantial proportion (between approximately 5 – 50%, depending on age group) of all poisoning admissions. However, this proportion is not increasing over time, indicating that this general increase in intentional adolescent poisonings is across all medicines and not just paracetamol.
- The rescheduling of codeine from Schedule 3 to Schedule 4 of the Poisons Standard in February 2018 may explain some of the recent reduction in paracetamol poisonings.
- The number of admissions due to poisoning with "other NSAIDs" was approximately 10-15% of those due to paracetamol and increased steadily up to 2017, thereafter sharply decreasing since codeine became a Schedule 4 medicine in 2018.

Data description and methods

The AIHW NHMD data are collated annually and available for a ten-year period from 2009-10 to 2019-20 (financial years). These data do not record the specific agent involved in poisonings but use the ICD-10-AM drug class coding system. The data were searched for cases with an ICD-10-AM code of T39. 1 (poisoning by 4-aminophenol derivatives). Note that the only 4-aminophenol derivative in use in Australia is paracetamol, and this is one of the few drugs that can be confidently identified using ICD codes. These T39.1 codes were recorded in the principal diagnosis field or the following nine additional diagnosis fields (in some admissions paracetamol may have been one of several agents ingested, and also not necessarily the most important one). The data on the overall cohort is presented for this diagnostic code along those with codes of K71* indicating toxic liver disease. We also examined for those poisonings that also had the code T40.2 ('other opioids') which combined with T39.1 likely indicated codeine poisoning and specifically a paracetamol/codeine combination was ingested.

The "in hospital death" flags were also extracted. It should be noted that many poisonings involve more than one agent, and it is likely that other agents ingested may have been responsible for the admission or death in many cases.

External causes codes were used to identify exposure intent with the codes commencing X6* indicating deliberate self-poisoning. Sex, age (in five-year age brackets) are used to demonstrate the demographic characteristics of the populations in the various selected groups

– with the child-adolescent categories (age < 20) highlighted in orange-red shades, and older ages in green-blue shades (see Figure 3 et al below).

For comparison purposes data was extracted on other poisonings with other T39 codes, indicating poisoning by non-opioid analgesics, antipyretics and antirheumatics (which would include other OTC analgesics such as aspirin (T39.0) and other NSAIDs (T39.3), the most common of which would be ibuprofen. These were a relatively uncommon cause of poisoning admission with only 2753 admissions and 9 deaths over the ten-year period. Most of these were T39.3 codes and we have only shown these data.

We also extracted the overall number of poisoning admissions and deliberate self-poisoning admissions by year to indicate the extent to which paracetamol poisonings are just tracking overall poisoning trends.

The AIHW does not allow the presentation of numerical results with n of < 5 and thus a more limited breakdown of age-sex categories is provided where cell sizes for some sub-groups in some years fall below this threshold. We have shown most of these data in Figures in this report, but tabulated values are provided for the AIHW data in Appendix A.

To examine the impact of the three relevant scheduling changes that occurred the data are also shown by month of poisoning. Note that month was not provided for 1% of the poisonings, specifically those with a length of stay > 30 days.

Results

It can be seen that there was an overall increase in paracetamol poisoning admissions up until around 2017 and a slight decline since, and that deliberate self-poisoning accounts for the majority of poisoning admissions in those aged over 10 (Figure 3).

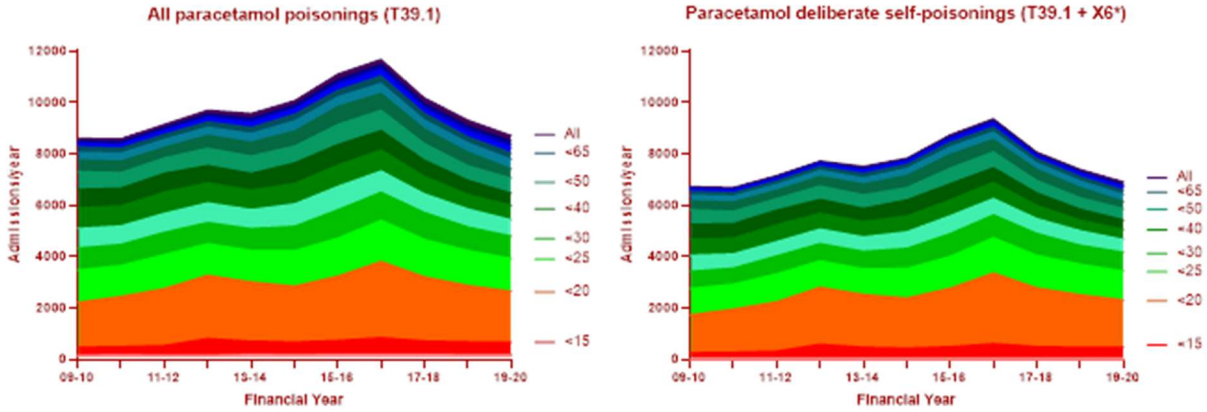

Figure 3 Paracetamol poisoning admissions and deliberate self-poisoning admissions in Australia (AIHW NHMD 2009-2020)

The increases were most marked in those aged between 10 and 24 and females accounted for over two-thirds of admissions (Figure 4).

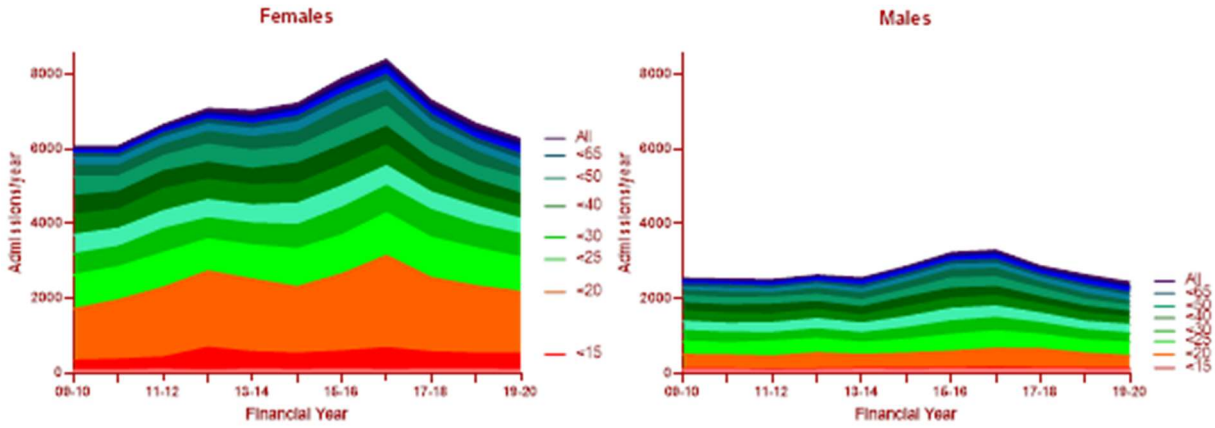

Figure 4 Paracetamol poisoning admissions in Australia – males vs females (AIHW NHMD 2009-2020)

The younger age groups generally had better outcomes after hospitalisation, with lower rates of toxic liver injury and fatal outcomes (Figure 5). Two percent (2149/106,815) of paracetamol poisoning admissions were coded as having toxic liver injury overall, but this was 0.9, 1.5, 2.6 & 3.7% for the 10-19, 20-29, 30-49 & 50+ age groups respectively. It is worth noting that fatal outcomes may reflect the effects of other agents ingested in some cases, and also would include deaths from unrelated causes during the hospital admission. Only 30% (136/461 over the 11 years) of the deaths in hospital after paracetamol poisoning also had the toxic liver injury code.

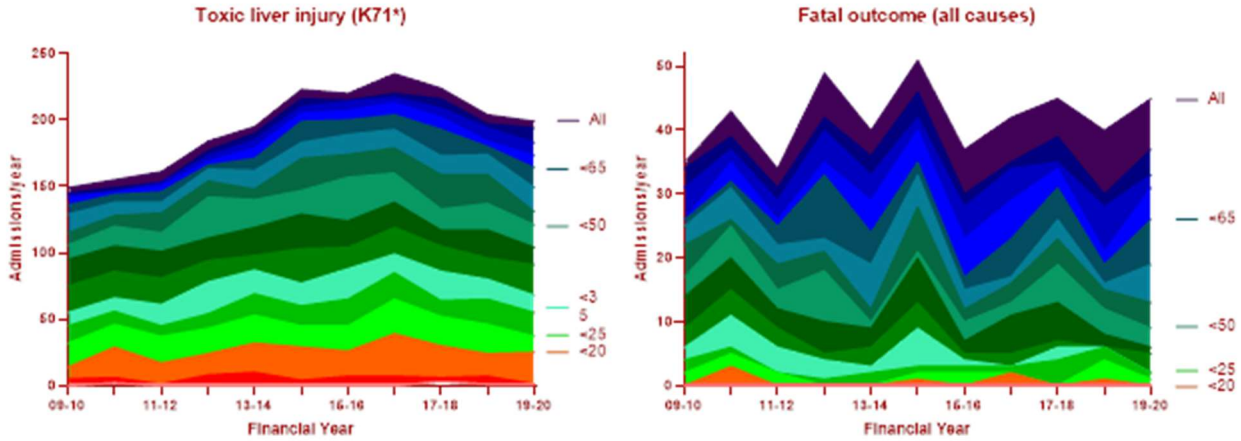

Figure 5 Harms from hospitalised paracetamol poisoning admissions in Australia (AIHW NHMD 2009-2020)

The increases and decreases over time to a large extent reflect overall trends in poisoning and deliberate poisoning admissions (Figure 6).

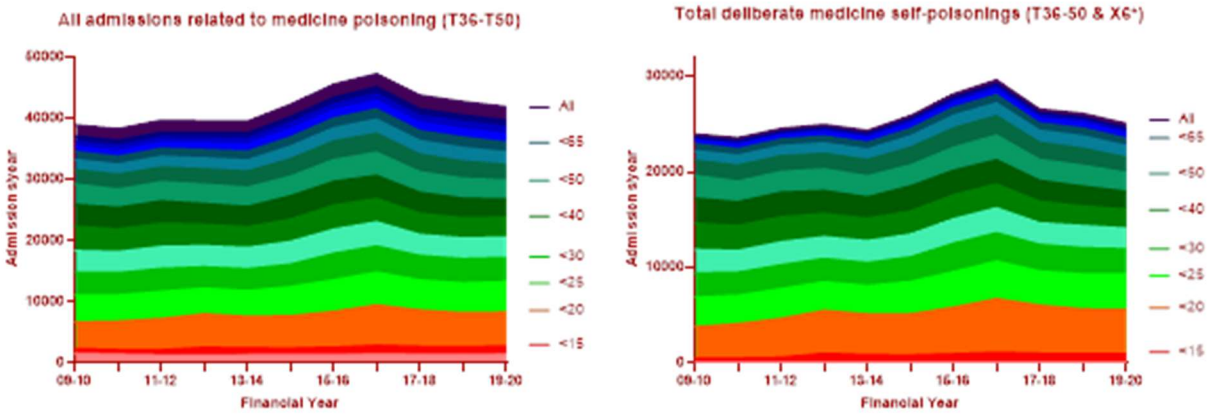

Figure 6 Changes in total and intentional medicine poisoning admissions in Australia (AIHW NHMD 2009-2020)

Paracetamol poisoning admissions accounted for a substantial proportion of all poisoning admissions, and around half of those in adolescent age groups (Figure 7). However, this proportion is not increasing over time, and may even have fallen a little in recent years, indicating that this general increase in intentional adolescent poisonings is across all medicines not just paracetamol.

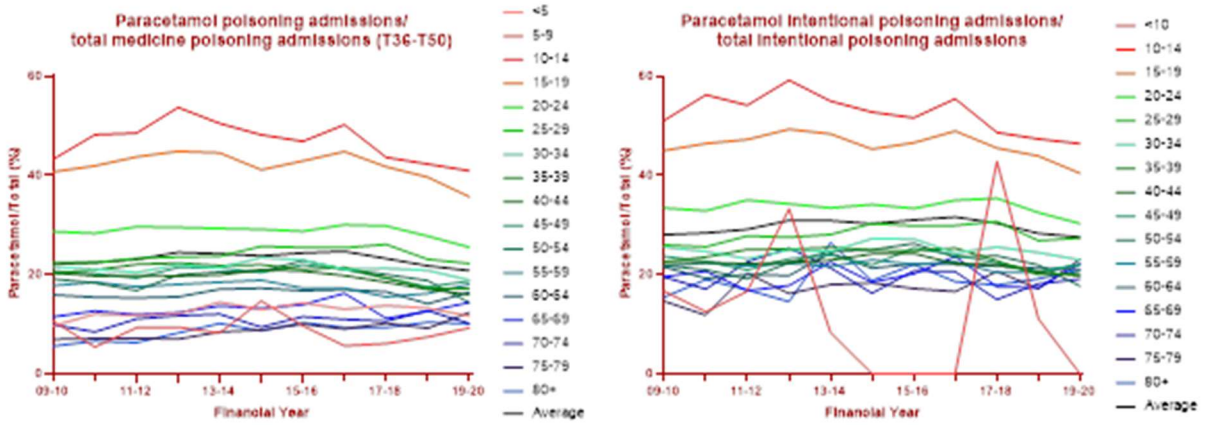

Figure 7 proportion of total and intentional medicine poisoning admissions in Australia due to paracetamol (by age group) (AIHW NHMD 2009-2020)

Effects of recent codeine scheduling changes on paracetamol poisoning admissions

The Feb 2018 (announced in Dec 2016) scheduling of all previously S3 codeine containing products (many of which contained paracetamol) to S4 may explain some of the recent reduction (Figure 8).

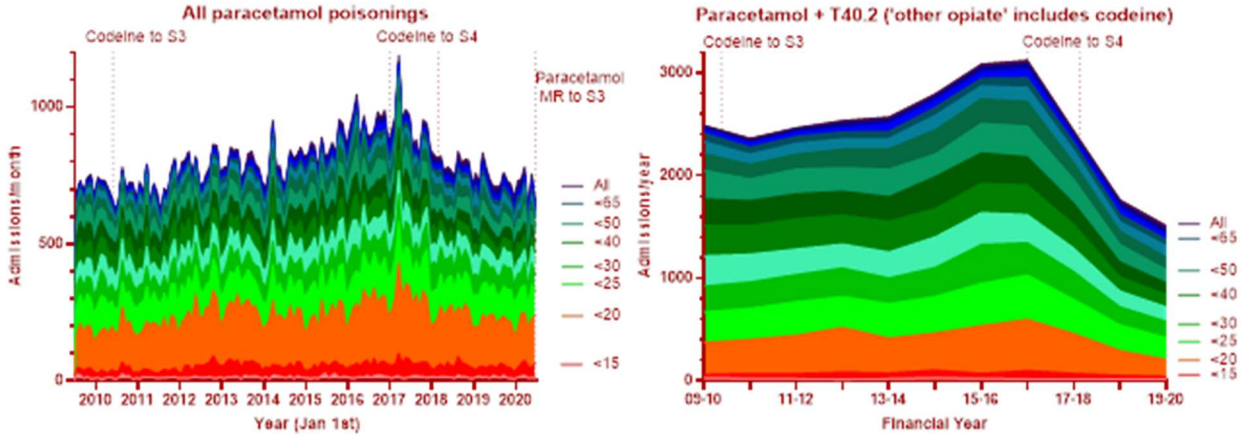

Figure 8. Total paracetamol poisonings per month, and annual totals of combinations of paracetamol and opiates in Australia (by age group) (AIHW NHMD 2009-2020).

Vertical lines indicate possibly relevant dates – codeine to S3 (May 2010), announcement (Dec 2016) and implementation (Feb 2018) of codeine to S4 (also indicating paracetamol MR to S3 June 2020) is not reflected in these data).

Comparison to (presumed) ibuprofen poisonings in AIHW PIC data

Ibuprofen has a very similar scheduling to paracetamol and is the most readily substituted OTC product for analgesia. It is also co-formulated with codeine and was potentially impacted by the 2018 codeine rescheduling. The ICD coding of ibuprofen poisonings is to a non-specific code of T39.3 ("other NSAIDs"); it is likely that ibuprofen accounts for a majority of such codes given its OTC status.

There is a similar apparent increasing trend to 2017 with 'other NSAIDs' tracking the overall trends in poisonings shown above. The total numbers are only 10-15% of those due to paracetamol. This reflects the lower toxicity in overdose of ibuprofen, and indeed it is likely many of these admissions were required because of ingestion of other substances. It is noteworthy that combinations with 'other opiates' account for a very high proportion of 'other NSAID' poisoning admissions. There is an obvious large fall coinciding with the S4 scheduling of codeine (Figure 9).

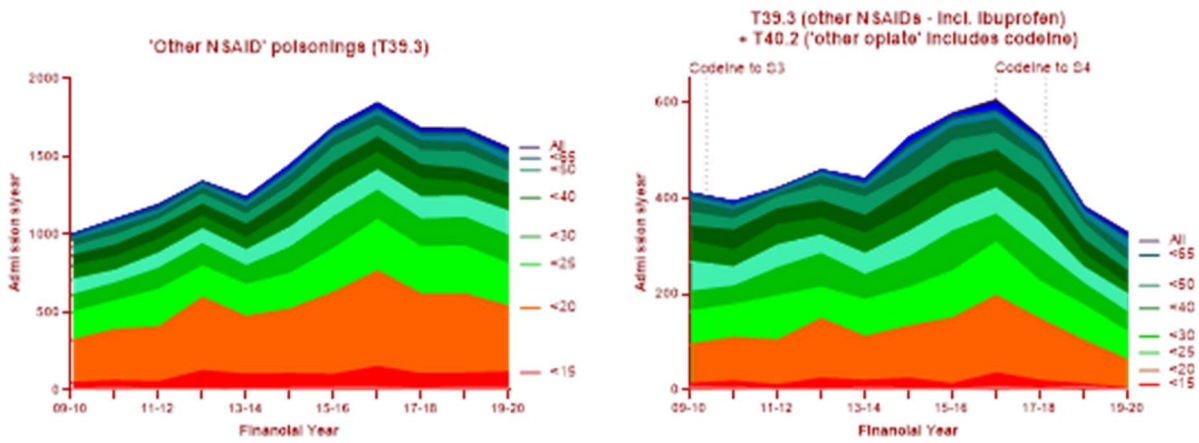

Figure 9. 'Other NSAID' poisonings in Australia (by age group) (AIHW NHMD 2009-2020) – total and those in combination with 'other opiates'.

Vertical lines indicate possibly relevant dates – codeine to S3 (May 2010), announcement (Dec 2016) and implementation (Feb 2018) of codeine to S4.

2.3 Deaths - National Coronial Information System (NCIS) data

- Paracetamol poisoning was the probable cause of approximately 40 to 50 deaths per year in Australia over the period 2007/8 – 2019/20. Approximately half were due to liver failure, with the remaining likely being cases where paracetamol was ingested in the poisoning, but other co-ingested agents contributed largely or entirely to the mode of death.
- Many of the deaths occur in hospital and it is likely there is very substantial overlap between the NCIS and AIHW datasets.
- About twice as many cases have paracetamol poisoning denoted as a cause of death by the coroner and nearly ten times as many again have paracetamol coded as a 'pharmaceutical substance causing injury".

Methods

This is an update of an analysis done in an earlier published study (Cairns et al., 2019). We searched the NCIS for cases from the period July 2007 to June 2020 and closed by June 2022 for which "paracet*" was recorded in the cause of death field (all levels) or "paracetamol" was listed as the parent drug of the pharmaceutical substance causing injury. As the coronial coding of drugs causing death is inconsistent (people often take several drugs at once, and the primary cause of death can be expressed in different ways), cases were manually reviewed. They were designated 'probable' major contributor to death if the death appeared more likely to be attributable to paracetamol than any other co-ingested agents (based on history of overdose, and elevated levels with hepatotoxicity, or massive levels that could lead to coma). The free text of electronic reports was reviewed for the paracetamol product and amount taken. We recorded whether the NCIS cases occurred in hospital and in these cases a significant overlap between deaths included above in the AIHW NHMD and NCIS is very likely.

Effects of definitions used for attributing death to paracetamol

Our primary analysis was based on cases where case review (by both NSW PIC staff and expert reviewer) indicated it was more probable than not that paracetamol was a primary cause of death based on the above definitions. We also present the same analysis including all cases where paracetamol is mentioned, where its role was likely relatively minor or insignificant (typically out-of-hospital deaths where other drugs were detected at toxic concentrations and there was no evidence of acute liver necrosis/failure typical of paracetamol). About twice as many cases have paracetamol poisoning denoted as a cause of death by the coroner (527 vs 258 determined as probable on our review) and nearly ten times as many again have paracetamol coded as a 'pharmaceutical substance causing injury'. The designation of ICD codes is not closely related to any other measure (Table 2).

Table 2. Highly variable mentions in NCIS and AIHW, indicating the importance of clear descriptions when examining data on deaths from poisoning.

Paracetamol only codes	
NCIS Paracetamol as 'pharmaceutical substance causing injury'	5296
NCIS _ T39.1 (paracetamol poisoning) all levels ICD-10	2391
NCIS Paracetamol listed in Cause of death (all levels)	527
Paracetamol poisoning 'probable' major contributor to death	258
* AIHW T39.1 and death	461
* AIHW T39.1, K71. and death	136
OTC analgesic codes	
NCIS X40 'Accidental poisoning by and exposure to nonopioid analgesics, antipyretics and antirheumatics (underlying)'	138
NCIS X60 'Intentional self-poisoning by and exposure to nonopioid analgesics, antipyretics and antirheumatics (underlying)'	121
NCIS Y10 'Poisoning by and exposure to nonopioid analgesics, antipyretics and antirheumatics, undetermined intent (underlying).'	32
Other OTC analgesics (aspirin and ibuprofen)	
NCIS Aspirin as 'pharmaceutical substance causing injury'	269
NCIS T39.0 (salicylate poisoning) all levels ICD-10	54
NCIS Aspirin listed in Cause of death (all levels)	35
NCIS Ibuprofen as 'pharmaceutical substance causing injury'	1157
NCIS Ibuprofen listed in Cause of Death (all levels)	36

* AIHW data from 2009/10 to 2019/20, whereas NCIS data from 2007/8 to 2019/2020

The changes over time in the mentions of causing injury and the relative role of the three main OTC analgesics is shown in Figure 10 – noting that the 'cause of death' rates for these drugs are roughly one tenth of these figures (and such small annual numbers cannot be shown under the terms of NCIS access).

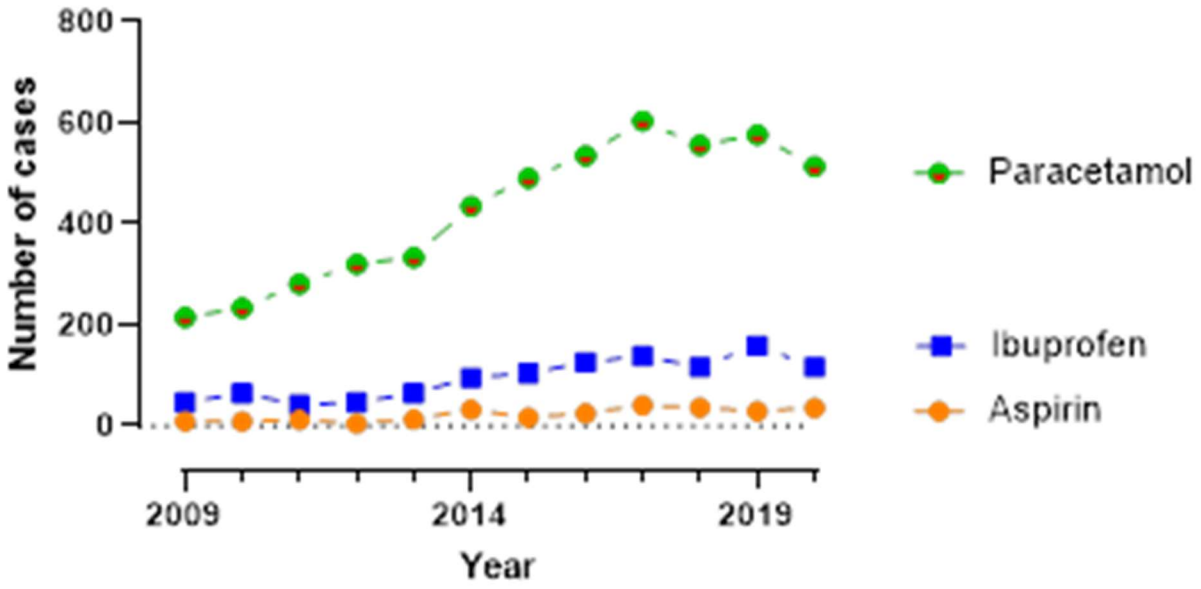

Figure 10. NCIS deaths where OTC analgesics are listed as 'pharmaceutical agents causing injury'

The annual number of deaths attributed to paracetamol poisoning is around 40 to 50 and those due to liver failure from paracetamol poisoning are around 20 and the data show no substantive change over time (Figure 11). [Note that the most recent years shown for NCIS (2019-2020) appear lower but it is likely there were some cases where the cause of death had not been finalised as this may take more than two years.] Many of these deaths occur in hospital and it is likely there is very substantial overlap in the two sets of data, but we have not attempted to reconcile the individuals in the data. The higher annual estimates of around 50 deaths, for both AIHW and NCIS, are both likely to include many cases where paracetamol was ingested in the poisoning, but other co-ingested agents contributed largely or entirely to the mode of death.

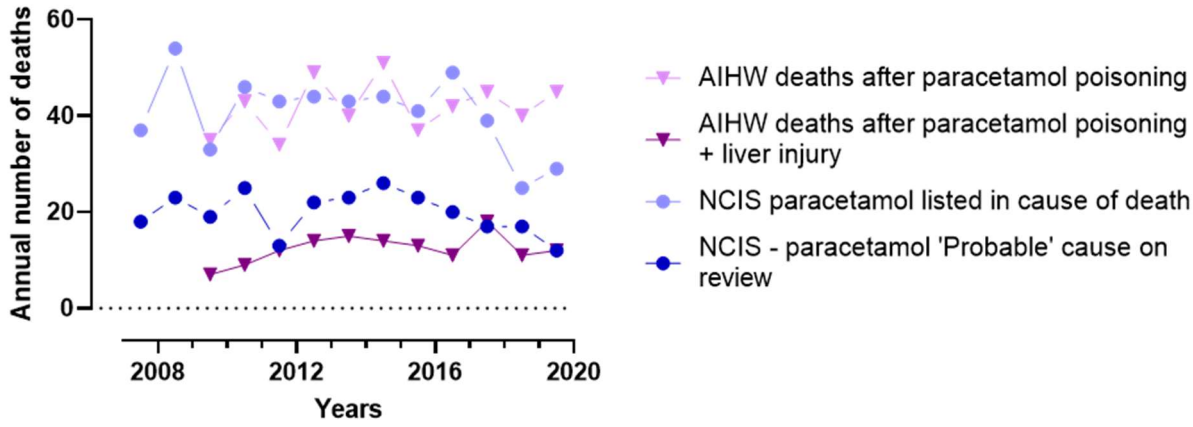

Figure 11. High and low estimates on in-hospital (AIHW) and total (NCIS) deaths

2.4 Poisoning cases - NSW PIC and total Australian PIC calls

- Paracetamol poisoning events (particularly intentional poisonings) reported to NSW PIC steadily increased from 2011 to 2021. The increase was considerably greater than changes in poisonings from all sources, medicine exposures or total analgesic exposures.
- Paracetamol poisoning events, particularly intentional poisonings, were 2 to 3-fold more common in females than males, with a notable increase in events involving adolescent females in 2019-2021.
- Intentional poisonings are now almost twice as common as non-intentional poisonings.
- Paracetamol exposure events, both intentional and non-intentional, due to products in which paracetamol was the only active ingredient were more common and increased to a greater extent than for combination products containing paracetamol along with other active ingredients, particularly in young people. Intentional exposures with combination products have been decreasing and appear to be far less likely to be ingested by young people.

This section provides several sources of information from poisoning call data from the New South Wales Poisons Information Centre (NSW PIC). NSW PIC is Australia's largest PIC, taking nearly 50% of the nation's annual poisoning calls. The NSW PIC takes most calls from NSW, ACT and TAS covering (~147/168 hours/week), but also a substantial number from other states, covering other state's PICs 50 to 60 hours/week for the national after-hours roster. NSW PIC receives calls from healthcare professionals and members of the public; most calls related to intentional self-poisoning come from healthcare staff in public hospitals.

2.4.1 Longer term NSW PIC epidemiological data 2011-2021

Methods

Exposure events involving paracetamol were extracted from the NSW PIC database, 2011-2021. Data extracted included age group, sex, whether the exposure was to single ingredient products or combination products, dose, product type. Dose and product type fields were cleaned for analysis by standardising information entered in free text fields. Product type was categorised to modified release paracetamol vs immediate release paracetamol. Dose was cleaned to grams and number of tablets. If a range was stated, the upper end of the range was used.

Poisoning events may involve multiple calls; recalls are generally noted as such and we have not double counted these but have extracted relevant further information recorded for parts of the report.

Poisoning Severity Score (PSS) is provided from 2017 onwards (when NSW PIC started to record this information, 10 August 2017).(Persson, Sjoberg, Haines, & Pronczuk, 1998). The

score is applied to the whole call where more than one substance is ingested. The relevant thresholds for minor, moderate, and severe paracetamol poisoning are shown in Table 3.

Table 3. Poison severity score thresholds most relevant to paracetamol poisoning

	Minor	Moderate	Severe
Liver	Minimal rise in serum enzymes (AST or ALT 2-5 x normal)	Rise in serum enzymes (AST or ALT 5-50 X normal) but no diagnostic biochemical (e.g., ammonia, clotting factors) or clinical evidence of liver dysfunction	Rise in serum enzymes (> 50 x normal) or biochemical (e.g., ammonia, clotting factors) or clinical evidence of liver failure
Selected Other	Vomiting	Prolonged vomiting, Renal dysfunction, (e.g., oliguria, polyuria, serum creatinine of 200-500 µmol/L)	Renal failure (e.g., anuria, serum creatinine of > 500 µmol/L)

*PSS was developed as a tool to be used when final outcome is known. NSW PIC collects a modified PSS which is based on the last available information known to NSW PIC. NSW PIC does not routinely conduct follow up calls and thus lacks complete outcome data. PSS of many cases may have gotten worse following call to PIC, which would not be captured in this data. Finally, since polypharmacy overdose cases were included, some PSS reported here would be attributable to agents other than paracetamol.

Results

Longitudinal trends in NSW PIC data (2011-21)

There has been a steady increase in paracetamol poisonings events. This has been considerably greater than changes in overall exposures, medicine exposures or total analgesic exposures. It is also apparent that the increase is for intentional paracetamol poisonings in particular (Figure 12). Note further details of all numbers underlying the NSW PIC figures are shown in Appendix B.

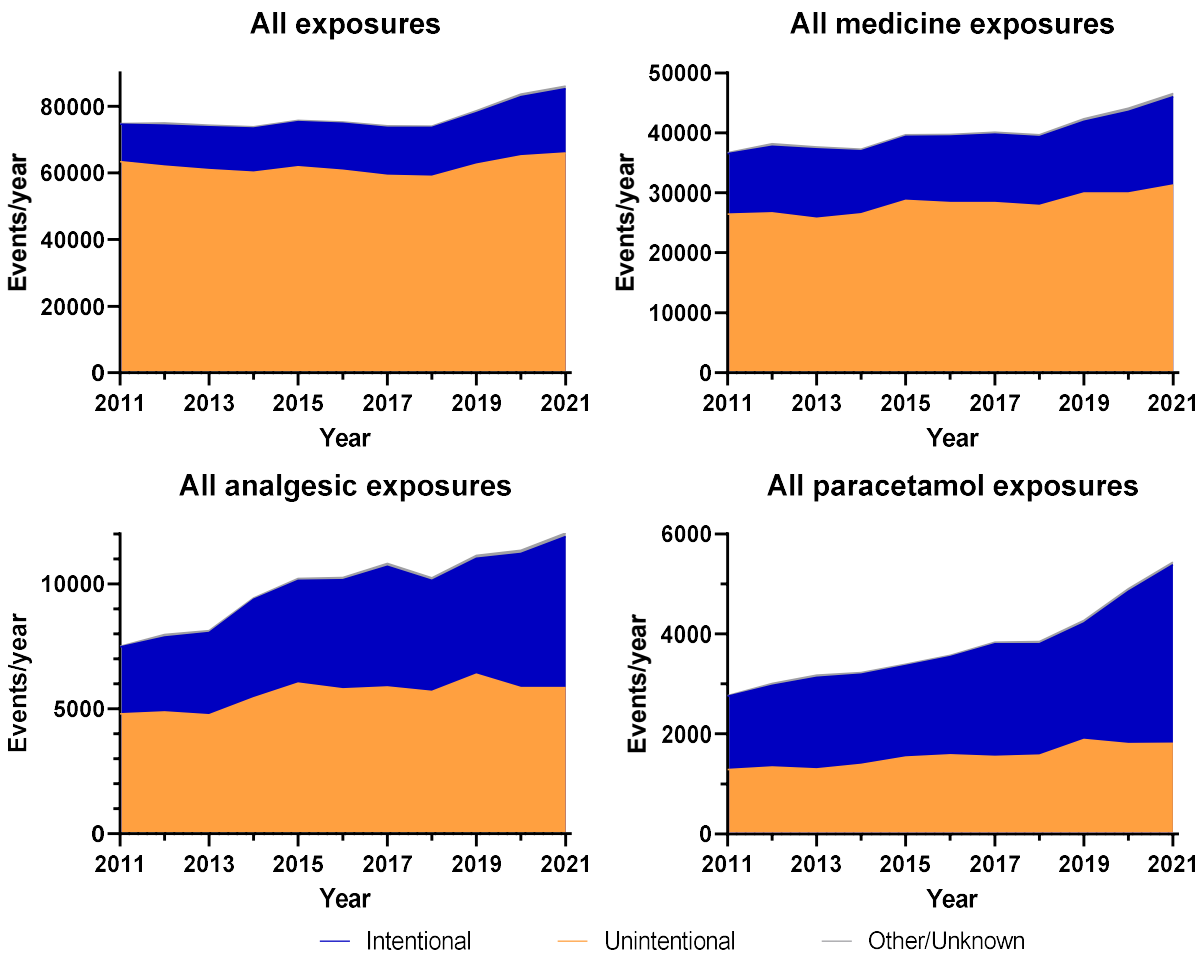

Figure 12 Changes in poisoning exposure events, overall, for paracetamol and for comparable categories. (NSW PIC 2011-2021)

This can be further seen in the following figures, with single ingredient paracetamol products being more common and also increasing to a greater extent (Figure 13). The problem is increasing particularly in young people. Age categories were generally recorded, the small numbers of unknown are shown in the total.

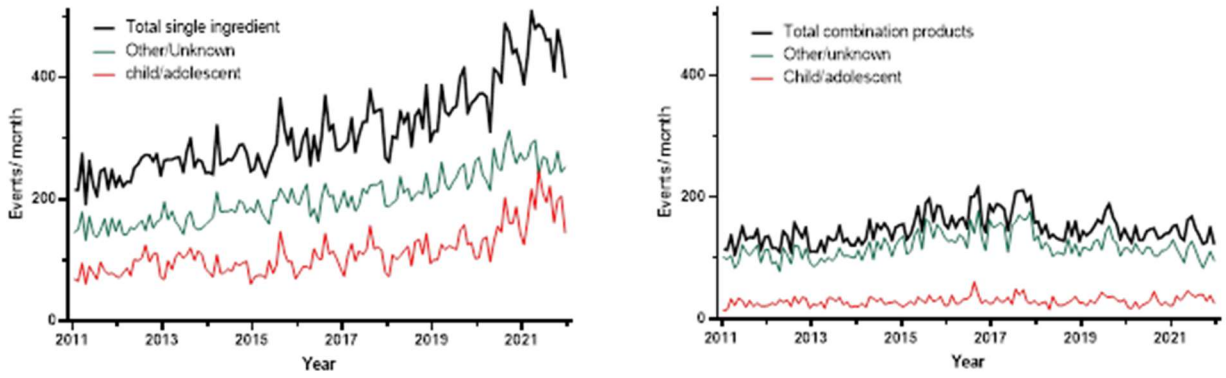

Figure 13 Single ingredient and combination product paracetamol poisoning exposure events. (NSW PIC 2011-2021)

This has been notably driven by increasing events involving adolescent females with intentional self-poisoning, and this increased considerably in the last two years (Figure 14).

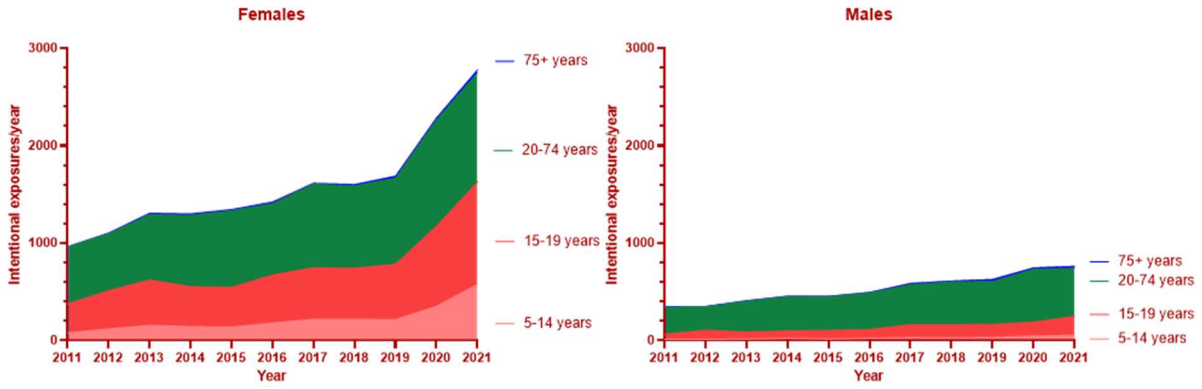

Figure 14 Intentional single ingredient paracetamol poisoning exposure events (NSW PIC 2011-2021)

Note. Sex was not recorded in 343 cases (114 child/adolescent) over the 11 years and these are not shown in this figure.

This may partly reflect increasing PIC utilisations for advice on paracetamol with new Australian guidelines being published in late 2019 (Chiew et al., 2020), but the non-intentional poisoning events show a very different (albeit still increasing) trajectory (Figure 15). The intentional poisonings are now roughly twice as common (3575 vs 1810), and females and the younger age groups are much more over-represented in intentional poisonings.

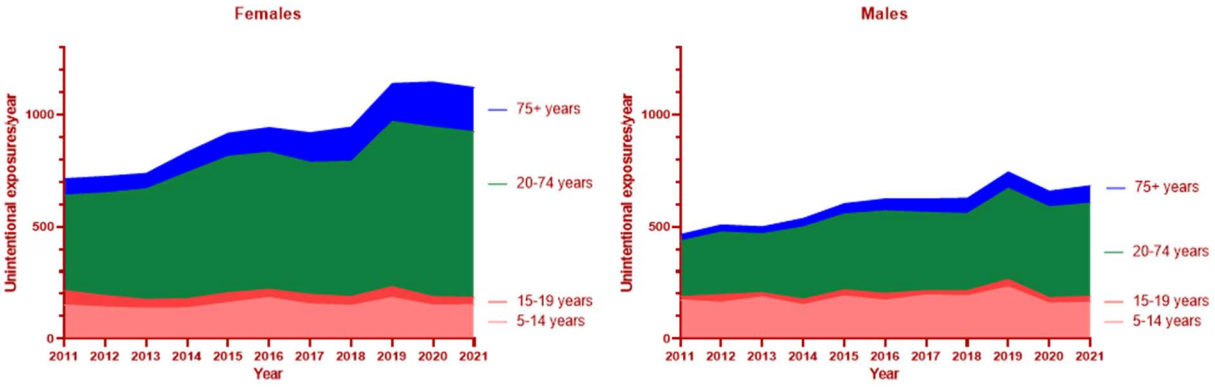

Figure 15 Non-intentional single ingredient paracetamol poisoning exposure events in those aged ≥ 5 (NSW PIC 2011-21)

Note there were also 40-50 exposures/year in other/unknown categories over the 11 years (405 in total, 105 in children and adolescents). These data are not shown in these two figures, but generally reflect calls with very limited data recorded.

The paracetamol combination products have much lower numbers and show a different trajectory (Figure 16 & 17). These appear less likely to be ingested by young people and have not shown the same increases. To some extent this may reflect the rescheduling of codeine which is present in many of these products (the impact of the rescheduling of codeine is further considered below). Note the much lower numbers on the Y axis. In 2021, paracetamol combination product exposures totalled 2038 vs 5637 for single ingredient paracetamol products. Children and adolescent intentional poisonings were around six times more likely to involve single ingredient preparations vs these combinations (1933 vs 355, in 2021).

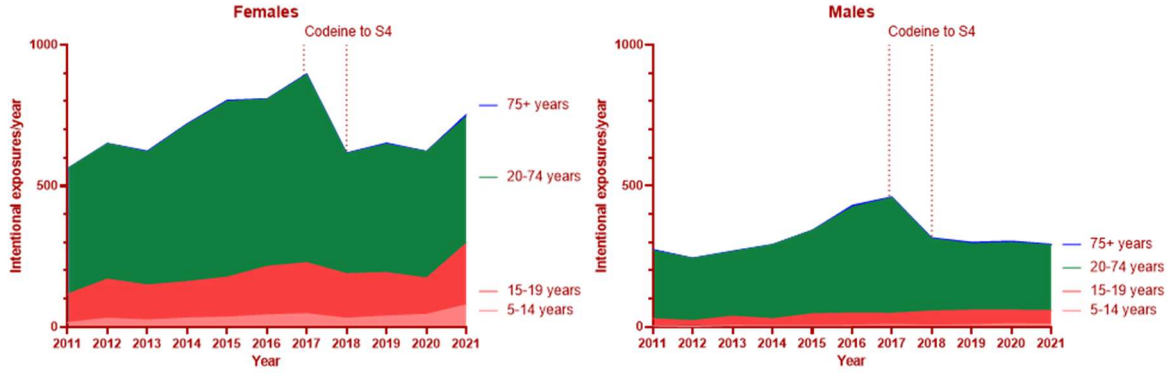

Figure 16 Intentional paracetamol combination product poisoning exposures generating calls (NSW PIC 2011-21)

*paracetamol combination products include: paracetamol/codeine, paracetamol/codeine/doxylamine, paracetamol/ibuprofen, cough and cold preparations containing paracetamol, paracetamol/tramadol, paracetamol/metoclopramide, paracetamol/caffeine, and paracetamol/dextropropoxyphene.

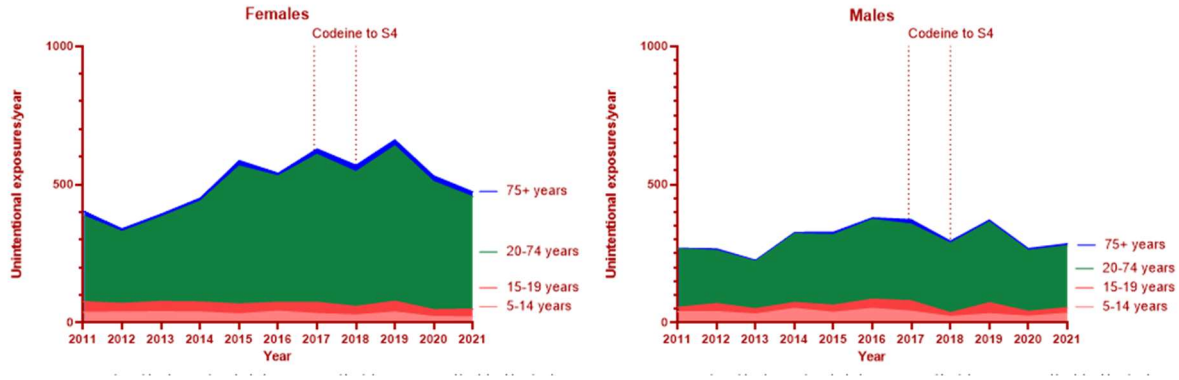

Figure 17 Non-intentional paracetamol combination product poisoning exposures generating calls (NSW PIC 2011-21)

*paracetamol combination products include: paracetamol/codeine, paracetamol/codeine/doxylamine, paracetamol/ibuprofen, cough and cold preparations containing paracetamol, paracetamol/tramadol, paracetamol/metoclopramide, paracetamol/caffeine, and paracetamol/dextropropoxyphene.

Trends in modified release (MR) paracetamol & dose ingested

The data on dose and MR paracetamol reflect the overall numbers – that is the high dose groups and MR paracetamol poisonings are increasing in line with the overall increasing numbers of calls, but the proportion of all paracetamol calls remains much the same (Figure 18, Appendix B).

In terms of the highest risk ingestions, in 2021 there were 359 calls about ingestions over 30 grams, and 362 MR paracetamol ingestions. (Note: National numbers are likely slightly more than double these numbers, and there is likely substantial overlap between MR and high dose ingestions).

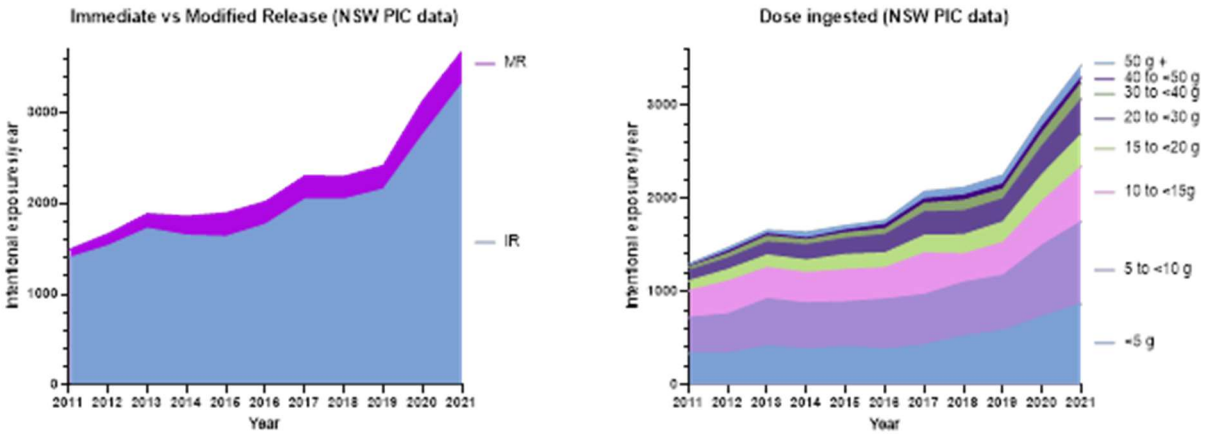

Figure 18. Annual NSW PIC calls about intentional paracetamol poisoning, showing the change in MR paracetamol and the reported dose ingested (2011-2021)

Note data from ingestions of combination products are not included in these two figures.

These high-risk large ingestions and modified release ingestions are less common in the child/adolescent age groups and increases in these categories are not being driven by these age groups (Figure 19 & 20).

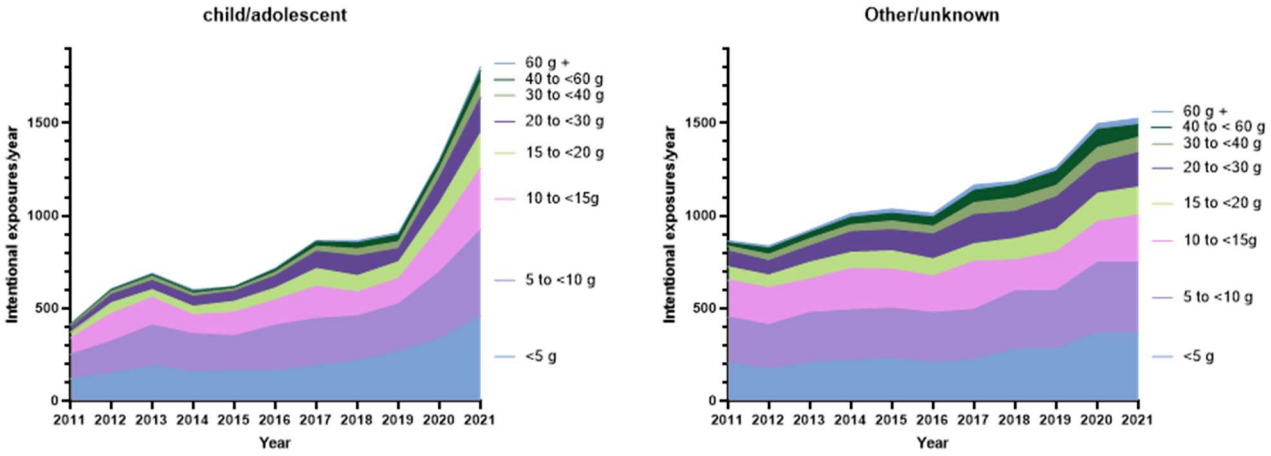

Figure 19. Change in the reported dose ingested by age group (2011-2021).

Note data from ingestions of combination products are not included in these two figures.

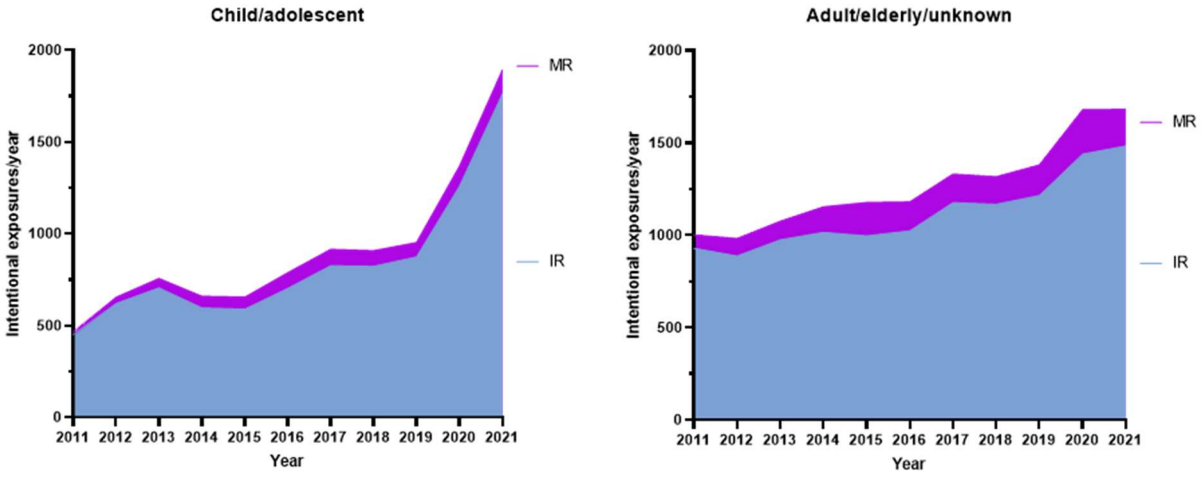

Figure 20. Change in MR vs IR preparations ingested by age group (2011-2021)

Effects of 2018 codeine scheduling changes on paracetamol combination poisoning events

The Feb 2018 (announced in December 2016) scheduling of all previously S3 codeine containing products (many of which contained paracetamol) to S4 may explain some of the changes in combination products (Figure 21). Large reductions were seen particularly for intentional poisonings in older age groups.

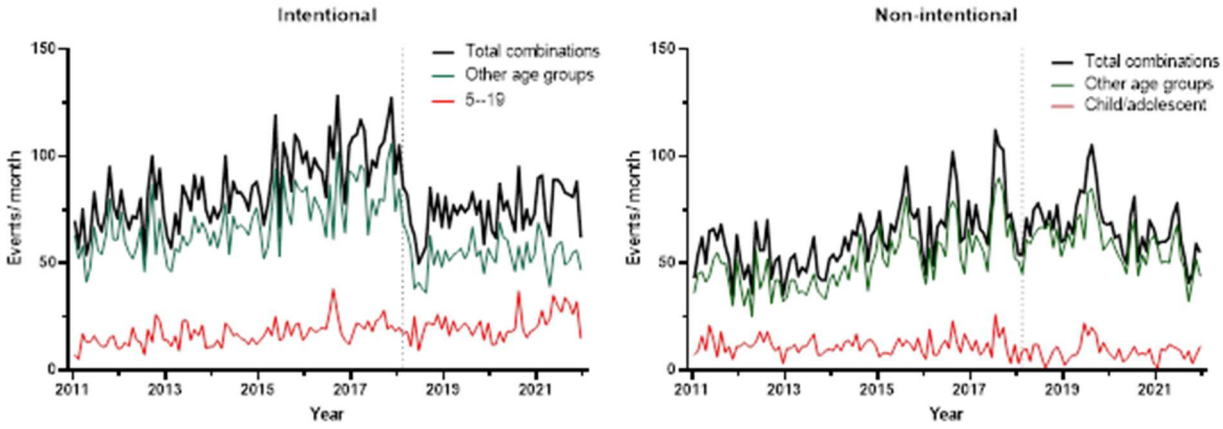

Figure 21. Combination product paracetamol poisonings per month (by intent and by age group) (NSW PIC 2011-2021).

Vertical line indicates implementation (Feb 2018) of codeine to S4.

Effects of 2020 paracetamol MR scheduling changes on paracetamol poisoning events

The June 2020 scheduling of MR paracetamol products to S3 did not have any obvious impacts on single ingredient product ingestions (Figure 22). It should be noted this change was close in timing to COVID-19 lockdowns and potential stockpiling or supply disruptions.

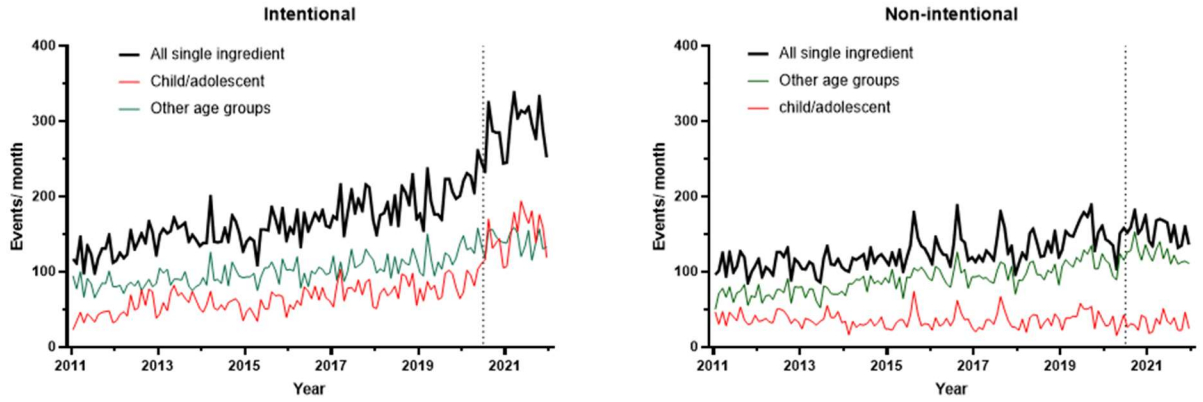

Figure 22. Monthly single ingredient paracetamol poisonings by intent and age group per month (NSW PIC 2011-2021)

Vertical line indicates the date paracetamol MR went to S3 (June 2020).

The Figure indicates that these increased following rescheduling but this was in the context of a general increase in analgesic poisoning calls in 2020-21 (which may reflect the COVID-19 pandemic and stockpiling or other factors).

There was however no significant reduction (or other change) in the proportion of all non-opioid analgesic poisonings due to paracetamol MR (6.8% pre intervention vs 6.5% post intervention, *P*= 0.23, Mann Whitney) (Figure 23).

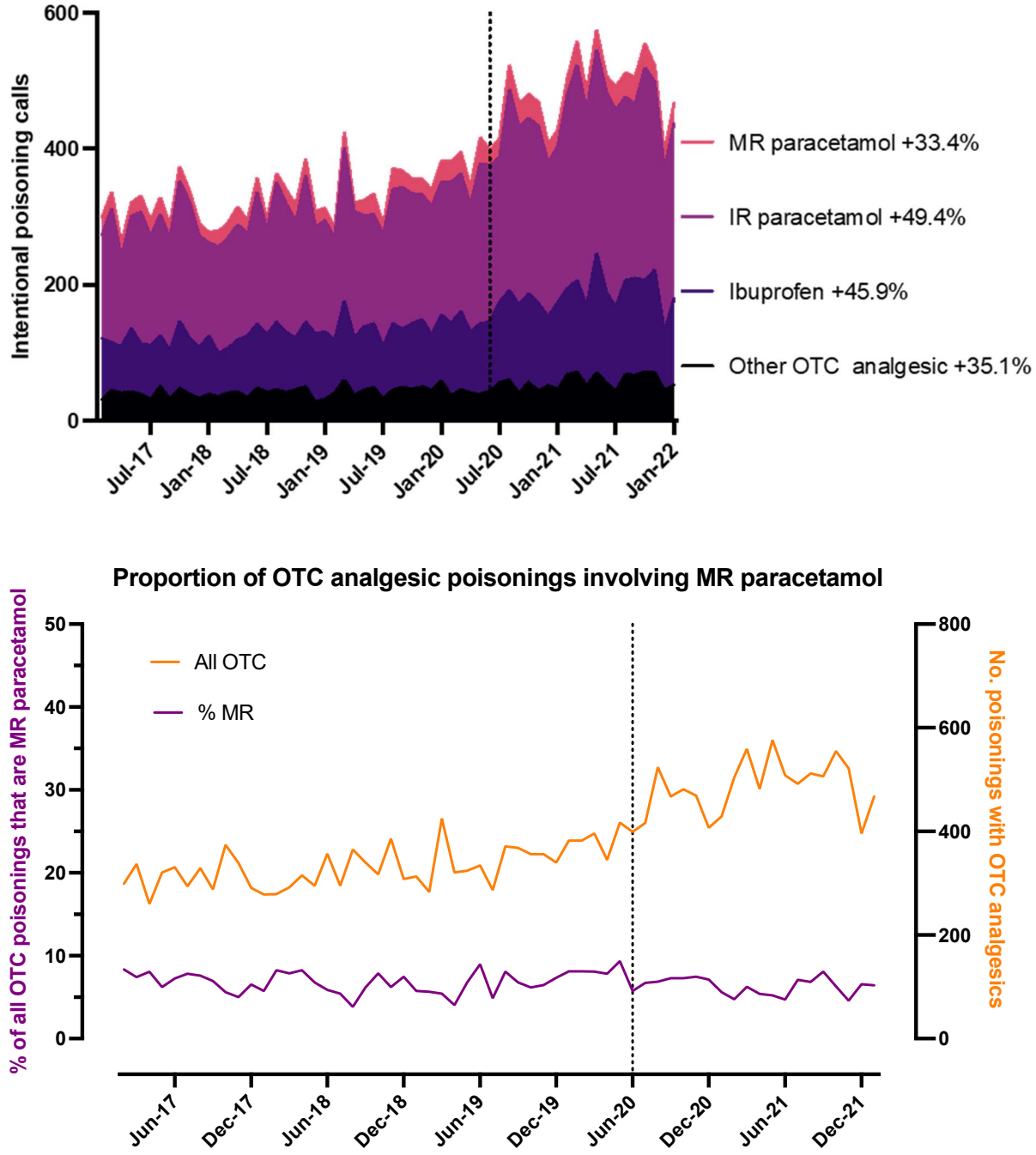

Figure 23. Monthly NSW PIC calls about OTC available analgesic poisonings per month and change in total and proportion due to MR paracetamol (2017-1/2022)

Comparison to ibuprofen poisonings in NSW PIC data

As noted above, ibuprofen has a very similar scheduling to paracetamol and is the most readily substituted OTC product for analgesia. It is also co-formulated with codeine and was potentially impacted by the 2018 codeine rescheduling.

There is a similar apparent increasing trend to 2017 with ibuprofen tracking the overall trends in poisonings shown above. The total numbers are about half of those due to paracetamol (Figure 22 & 24). This may partly reflect the lower toxicity in overdose of ibuprofen, and

advice being sought less often. There is an obvious large fall in combination ibuprofen products coinciding with the S4 scheduling of codeine.

The NSW PIC data show similar trends to AIHW data but notably indicate that the number of calls about ibuprofen is higher than just 10-15% of admissions compared to paracetamol, suggesting there are very many more NSAID poisonings than those admitted to hospital.

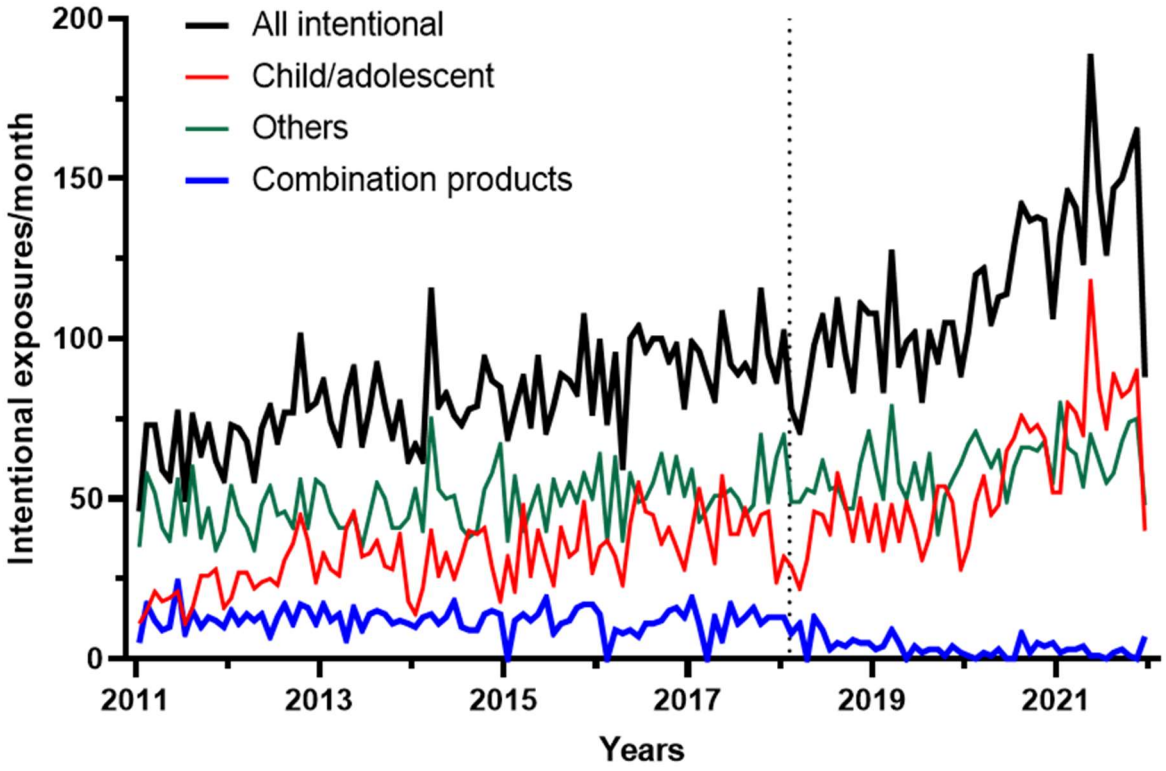

Figure 24. Intentional ibuprofen poisoning events per month (by age group), and change in total and proportion due to ibuprofen combinations after 2018 codeine S4 scheduling (NSW PIC 2011-21).

Poisons severity scores on NSW PIC calls 2017-21

The poisons severity score (PSS) was recorded in 18,530 (86%) of calls after it was introduced in late 2017. Note the PSS is scored at the time of call, may include effects of co-ingested agents, and does not involve follow up for a final determination of severity. Of all calls (these data also include recalls) around 8% and 2% had moderate and severe toxicity respectively. Combination products averaged slightly greater PSS than single ingredient poisonings. Child/adolescent poisonings were generally less severe, noting that these data still included 66 calls about severe paracetamol poisoning in these age groups (Tables 4 & 5).

Table 4. Poisons Severity Score (PSS) for single ingredient paracetamol poisonings.

PSS Score	Child/adolescent	Adult/elderly/unknown	Total
NONE (0)	2606 (34.1%)	2647 (29.9%)	5253 (31.9%)
MINOR (1)	3358 (43.9%)	3792 (42.9%)	7150 (43.4%)
MODERATE (2)	440 (5.8%)	899 (10.2%)	1339 (8.1%)
SEVERE (3)	59 (0.8%)	222 (2.5%)	281 (1.7%)
Unknown	382 (5%)	413 (4.7%)	795 (4.8%)
Left Blank	799 (10.5%)	867 (9.8%)	1666 (10.1%)
Total	7644 (100%)	8840 (100%)	16484 (100%)

Table 5. Poisons Severity Score (PSS) for combination ingredient paracetamol poisonings.

PSS Score	Child/adolescent	Adult/elderly/unknown	Total
NONE (0)	404 (28.2%)	876 (23.4%)	1280 (24.8%)
MINOR (1)	775 (54.1%)	1920 (51.4%)	2695 (52.1%)
MODERATE (2)	75 (5.2%)	358 (9.6%)	433 (8.4%)
SEVERE (3)	7 (0.5%)	92 (2.5%)	99 (1.9%)
Unknown	57 (4%)	184 (4.9%)	241 (4.7%)
Left Blank	115 (8%)	306 (8.2%)	421 (8.1%)
Total	1433 (100%)	3736 (100%)	5169 (100%)

2.4.2 Recent evidence on products and burden of disease in NSW PIC calls

- The median dose ingested of paracetamol in single ingredient paracetamol product exposures (of greater than 10 g) in 2020-21 was 17.5 g and 10.3% of calls were referred to clinical toxicologists.
- There was little variation in time to presentation by age groups, with most presenting before 8 hours (and thus having a good prognosis with acetylcysteine treatment). Only one fifth presented within 2 hours or less.
    - One patient with a very delayed presentation died; 351 had some evidence of liver injury (ALT >50), and 119 had severe liver injury (ALT >1000).
- In a February to March 2022 cohort of paracetamol exposure cases (predominately female and median age 19 years), the majority were documented as suicide attempts, and majority of the remainder as self-poisonings. Psychiatric diagnoses were commonly recorded however, the majority also indicated to be impulsive and relatively few had significant planning documents.

Methods

NSW PIC call records for 2020-2021 of single ingredient paracetamol product exposures were subject to additional manual review to obtain extra detail on product, poisoning severity

and treatment for deliberate self-poisoning of 10 g or greater (a widely accepted threshold dose for significant risk of liver injury).

The following cases were reviewed:

- Deliberate self-poisonings where people took at least 10 g of paracetamol (as a single agent and/or polypharmacy exposures)

This generally involved calls from healthcare professionals, as all such patients are referred to hospital, but we also examined such calls from members of the public. Call data was manually cleaned to extract the following information:

- Product name
- Morbidity (including peak ALT, and peak INR for cases where ALT > 1000)
- Treatment advice given (activated charcoal and NAC, including whether standard course, increased dose, or increased duration NAC was recommended).
- Number of calls about each case (as a proxy for severity or complexity of management)
- Whether a clinical toxicologist was consulted (as a proxy for severity or complexity of management).
- Time from overdose to presentation to hospital (where known, otherwise time of first call to PIC, or time of first paracetamol level is taken, whichever is earliest).

Where multiple calls were received about the one case, the case was only counted once, and additional information contained in the records of subsequent calls ("recalls") was extracted for that case, where relevant.

Note NSW PIC does not routinely follow up each case, and thus final outcome data is often lacking. This should be taken into account when interpreting these results. However, in PIC experience, hospital staff usually call back in the event of significant hepatotoxicity developing.

Results

There were 4883 calls reviewed with stated dose 10 g or more, including 3095 unique exposures; 11.6% (n=358) involved MR paracetamol. The majority were female, especially in the child/adolescent age groups (Table 6).

Table 6. Sex distribution of paracetamol intentional self-poisonings ≥ 10 g, by age group.

	5-19 years		Others	
	n (total=1578)	%	n (total=1517)	%
Female	1355	85.9%	1035	68.2%
Male	218	13.8%	468	30.9%
Unknown	5	0.3%	14	0.9%

The median age was 18 (IQR: 15 – 29 years, n=210 missing). The median dose ingested was 17.5 g (IQR: 12 – 26g, n=5 missing), and 10.3% (319/3095) of calls were referred to clinical toxicologists. Around a third of exposures generated more than one call (36%, n=1126), with 12.6% (n=391) generating 3 or more calls (indicating complexity). The majority were recorded as requiring acetylcysteine treatment, where the treatment received was known (Table 7).

Table 7. Acetylcysteine (NAC) dosing by age group.

	5-19 years		Others	
	n (total = 1578)	%	n (total = 1517)	%
Not required	115	7.3%	103	6.8%
Administered, standard regimen	682	43.2%	612	40.3%
Administered, extended regimen	94	6.0%	66	4.4%
Double dose	160	10.1%	136	9.0%
Double dose, extended regimen	42	2.7%	51	3.4%
Triple dose	4	0.3%	3	0.2%
Triple dose, extended regimen	2	0.1%	2	0.1%
Quadruple dose	1	0.1%	1	0.1%
Unknown/no follow up	478	30.3%	543	35.8%

Double, triple and quadruple dosing refers to the 100mg/kg bag over 16 hours (i.e. 2nd bag in standard 2-bag NAC regimen). This is recommended due to very elevated paracetamol levels (>2x nomogram line for double NAC, 3x nomogram line for triple NAC, etc.). Extended regimen refers to continuing the 100mg/kg bag beyond the standard 16 hours. This is recommended when the patient has persistently high paracetamol levels or rising LFTs at the end of the standard 20-hour treatment.

There was little variation in time to presentation by age group (Table 8), with most people presenting before 8 hours and thus having a good prognosis with acetylcysteine treatment. However, only a fifth of patients presented within 2 hours, and less than this were recorded as receiving charcoal (Table 9). [Although for many patients it was 'unknown' if they received charcoal, it is likely that for most of these that they were later than 2 hours and did not receive it in accordance with Australian guidelines to offer charcoal to those presenting within 2 hours of an immediate release formulation.(Chiew et al., 2020)]

Table 8. Time from exposure to presentation, paracetamol poisonings ≥ 10 g, by age group.

	5-19 years		Others	
	n (total =1578)	%	n (total=1517)	%
<2h	349	22.1%	269	17.7%
2-<4h	518	32.8%	421	27.8%
4-<8h	248	15.7%	257	16.9%
8-<24h	280	17.7%	239	15.8%
24h+	100	6.3%	179	11.8%
Unknown time	83	5.3%	152	10.0%

If time to presentation not stated, time to initial bloods, or time to call to PIC is taken (whichever is earliest)

Table 9. Charcoal administration

	5-19 years		Others	
	n (total =1578)	%	n (total =1517)	%
No	238	15.1%	255	16.8%
Yes	346	21.9%	226	14.9%
Unknown	994	63.0%	1036	68.3%

Clinical outcomes, liver injury & death.

One patient with a very delayed presentation died; 351 had some evidence of liver injury (ALT >50), and 119 had severe liver injury (ALT >1000). There were 12 cases who also had INR >3 (indicating acute liver failure). Outcome data was not obtained for all calls, these data likely underestimate hepatotoxicity and deaths.

Of the 119 cases with ALT >1000, 44 (2.8%) were in the 5-19 years age group and 75 (4.9%) in the other age group. The median age was 23 years (IQR: 16- 42). The median dose ingested was 22 g (IQR: 15 – 40). Modified release paracetamol was ingested in 16% (n=19). Only two were documented to have received charcoal. Most of these patients presented with a considerable delay (Table 10).

Table 10. Time from exposure to presentation, cases with ALT >1000

	5-19 years		Others	
	n (total=44)	%	n (total=75)	%
<2h	0	0%	0	0%
2-<4h	3	6.8%	4	5.3%
4-<8h	1	2.3%	2	2.7%
8-<24h	16	36.4%	22	29.3%
24h+	19	43.2%	36	48.0%
Unknown time	5	11.4%	11	14.7%

If time to presentation not stated, time to initial bloods, or time to call to PIC is taken (whichever is earliest)

The dose ingested was also clearly important, as demonstrated in the concentrations of those with and without liver injury recorded against the nomogram (Figure 25).

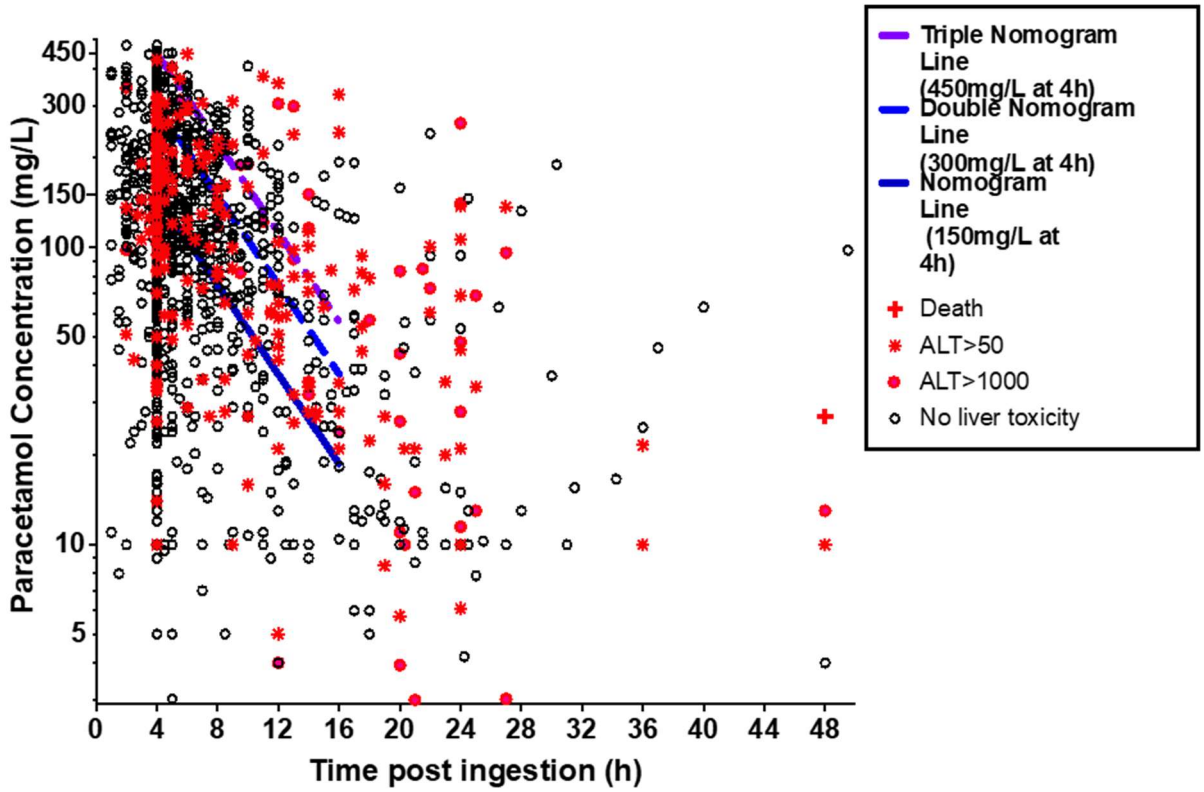

Figure 25. Peak paracetamol levels of 1513 cases where paracetamol level and known time of ingestion was documented in PIC call record.

Note: Paracetamol concentrations are plotted against paracetamol nomogram treatment lines. Levels that were reported in micromol/L were converted to mg/L by dividing by 6.614. Those with hepatotoxicity (defined as ALT >50 or >1000 for severe toxicity) are coloured red, and the one death is marked with a cross.

2.4.3 Electronic medical record (eMR) data on NSW PIC cases

Methods

As there was no follow-up the above data are likely a significant underestimate of morbidity. The PIC also collects very little data on intent or underlying reasons for self-poisoning. Therefore, between 1 February 2022 and 30 March 2022, we attempted to gain full outcome data on paracetamol self-poisoning exposures reported to NSW PIC. To do this we extracted data from electronic medical records to which NSW PIC has access (approximately 50% of NSW based cases).

The following information was collected:

1. Treatment received (N-acetylcysteine, activated charcoal)
2. Peak ALT
3. Peak INR

4. Peak paracetamol level and time of level
5. Whether the patient was transferred to a liver centre/received a transplant
6. Other treatments (e.g., dialysis)
7. Psychiatric disposition (admitted under psychiatry, scheduled under NSW Mental Health Act)
8. Psychiatric diagnoses
9. Reason for self-poisoning
10. Prior deliberate self-poisonings or suicide attempts
11. Medical length of stay

Results

Of the 171 cases reviewed, 148 were female (86%). The median age was 19 (IQR: 15-28 years, 8 missing). About half (87, 51%) had taken 10 g of paracetamol or more.

Table 11. Psychiatric diagnoses recorded in paracetamol self-poisonings

	5-19 years		Others	
	(n=88)	%	(n=83)	%
Depression	47	53%	50	60%
Anxiety	40	45%	38	46%
PTSD	14	16%	20	24%
Borderline personality disorder	7	8%	19	23%
ADHD	12	14%	8	10%
Other	9	10%	9	11%
Eating disorder	7	8%	8	10%
Bipolar disorder	3	3%	9	11%
Other mood disorder	3	3%	4	5%
Obsessive compulsive disorder	3	3%	3	4%
Other personality disorder	2	2%	4	5%
Psychosis	2	2%	2	2%
Autism	4	5%	0	0%
Schizophrenia	0	0%	3	4%

Can have >1 diagnosis recorded per patient. There were 27 patients (16%) with no documented psychiatric diagnosis.

The majority were documented as suicide attempts, and most of the rest as self-poisonings. Psychiatric diagnoses were commonly recorded (Table 11). However, the majority also indicated to be impulsive and relatively few had significant planning documented (Table 12). Over half the patients were discharged home (not admitted to a psychiatric facility) and 80% of children/adolescent intentional paracetamol poisonings were neither admitted nor scheduled (involuntarily detained under the mental health act) at any time.

Table 12. Reason for exposure, and extent of planning

		5-19 years		Others	
		n (total=88)	%	n (total=88)	%
Reason					
	Self-poisoning	33	38%	19	23%
	Suicide	47	53%	55	66%
	Other intentional	2	2%	5	6%
	Unknown	6	7%	4	4%
Planning					
	Impulsive	47	53%	50	60%
	Same day plan	8	9%	3	4%
	More advanced plan	11	13%	5	6%
	Unspecified plan	4	5%	0	0%
	Unknown	18	20%	25	30%
History of previous self-harm					
	No	8	9%	10	12%
	Yes	57	65%	43	52%
	Unknown	23	26%	30	36%
Psychiatric disposition					
	None	70	80%	45	54%
	Admitted under psychiatry	5	6%	18	22%
	Scheduled under NSW Mental Health Act	8	9%	12	14%
	Admitted and Scheduled	5	6%	7	8%
	Other*	-	-	1	1%

*one patient died before decision required (from co-ingested drugs rather than paracetamol)

Medical treatments & complications

Activated charcoal and acetylcysteine were the most common treatments. A significant minority required more than the standard 20-hour regimen of acetylcysteine.

Around 10% had some evidence of liver injury (ALT >50). Four patients had an ALT >1000 and two of these also had an INR >2, indicating severely impaired liver function. None of the patients reviewed received transplants, dialysis, or liver unit admissions.

Table 13. Medical treatments and liver damage by age group.

	5-19 years		Others	
	n (total=88)	%	n (total=88)	%
Acetylcysteine (NAC) treatment				
No	52	59%	55	66%
Yes, standard regimen	25	28%	24	29%
Yes, double dose NAC	10	11%	4	5%
Yes, triple dose NAC	1	1%	-	-
Extended (> 20h)	10	11%	4	5%
Charcoal				
No	71	81%	58	70%
Yes	14	16%	21	25%
Recommended, not received	1	1%	4	5%
Other/unknown	2	2%	-	-
Hepatotoxicity				
ALT >50	10	11%	8	10%
ALT >1000	1	1%	3	4%

Figure 26 explains the rationale for acetylcysteine (NAC) treatment. It shows the highest measured paracetamol level against the standard nomogram line. Those over the line or with evidence of any liver damage would have received NAC; those over double the nomogram line are those likely to have received double dose NAC, and extended NAC generally included those with ALT >1000 and those ingesting MR paracetamol with prolonged high levels.

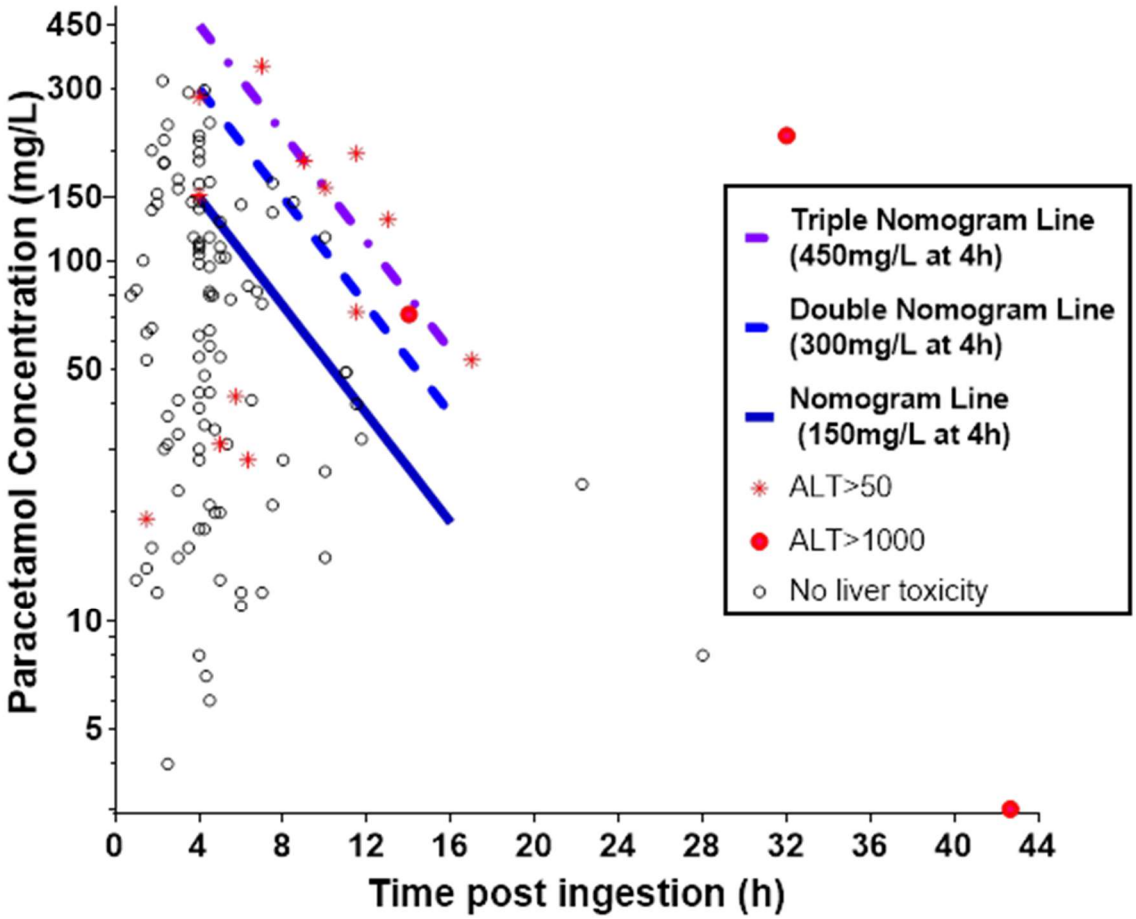

Figure 26. Peak paracetamol levels (n=121 patients with detectable paracetamol level and known time of ingestion).

Each patient is represented by a dot. Red stars indicate patients with mild hepatotoxicity (ALT >50), red dots indicate patients who developed severe hepatotoxicity. (ALT >1000). Lines represent paracetamol treatment nomogram. Note: the 4th patient who developed hepatotoxicity had an undetectable paracetamol level on presentation, >3 days post overdose.

It is worth noting that the results from the NSW PIC database review and those involving a full eMR review were very similar in terms of the proportion requiring treatment with acetylcysteine, and those with minor and severe liver injury, and thus reinforcing that estimates of morbidity based on Australian PIC data alone are reasonably accurate (relevant to international comparisons).

2.4.4 Total Australian PIC calls

- Nationally, the total number of poisoning calls and proportion of calls due to paracetamol have remained reasonably constant until an increase in 2021.
- Deliberate self-poisoning is the category of exposure increasing the most in recent years, in particular amongst children and adolescents, which is consistent with increases in the number of poisoning hospital admissions in those aged 10 years and over.
- Although NSW PIC data accounts for nearly half of all Australian PIC calls, data from all four PICs show similar trends with respect to paracetamol exposures, paracetamol deliberate self-poisonings and child/adolescent paracetamol poisonings.

Methods

The TGA requested 2017-2021 data on paracetamol exposure calls from Western Australia, Queensland and Victorian PICs, providing a template for data extraction. This included data on all calls, calls by broad age categories, intent, and separating paracetamol only exposures from those involving multiple agents. No dose, gender, or specific preparation data was provided within this template. Similar data from NSW was also extracted to create a national PIC dataset.

This was analysed to determine the proportion of total exposure calls, paracetamol poisoning, and deliberate self-poisoning PIC calls were taken by each poisons centre. Queensland data for 2017 was from two databases with two different database structures and was difficult to collate and compare for some measures.

A further analysis was done on 2018-2021 data from all PICs against population denominators (www.abs.gov.au/statistics/people/population/national-state-and-territory-population/dec-2021#data-download) to examine whether there was any substantial variation in call rates overall, for paracetamol poisonings and subsequent hospitalisations. The latter were also compared to the AIHW admission data to examine whether state of hospitalisation results in different rates of PIC consultation.

Five-year trends in combined PIC calls (2017-21)

Overall national trends in calls

The total poisoning exposure calls and the proportion of calls due to paracetamol have been reasonably constant across these years until an increase in 2021 (Table 14). The age range for all exposures (Figure 27) shows many infant exposures, but also increasing child adolescent exposures in recent years.

Table 14. Numbers of exposure calls to Australian PICs 2017-21

Year	Total exposure calls	Paracetamol exposures	%
2017	164176	16573	10.1%
2018	162855	15406	9.5%
2019	171078	16779	9.8%
2020	177236	16343	9.2%
2021	180856	18296	10.1%

Note – Recalls generally excluded but recalls to a different PIC may be counted more than once

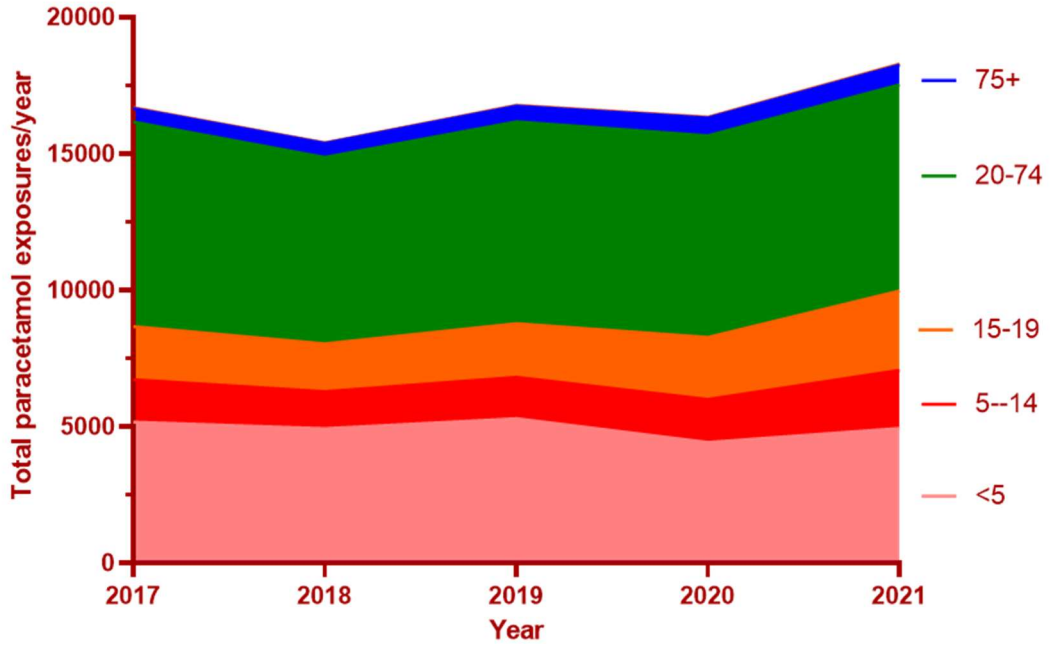

Figure 27. National PIC calls about paracetamol exposures – Trends by age 2017-21

It can be seen that deliberate self-poisoning is the category of exposure increasing most in recent years (Figure 28) and further that this in particular is being driven by increasing calls about children and adolescents (Figure 29).

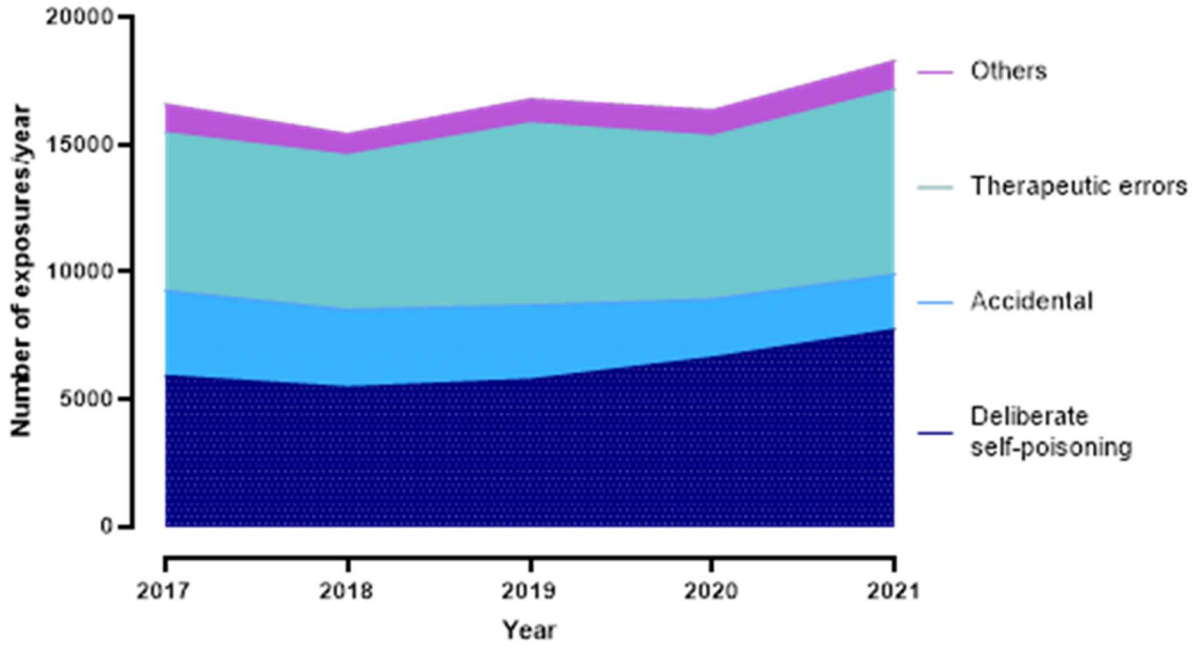

Figure 28. National PIC calls about paracetamol exposures – Trends by Intent 2017-21

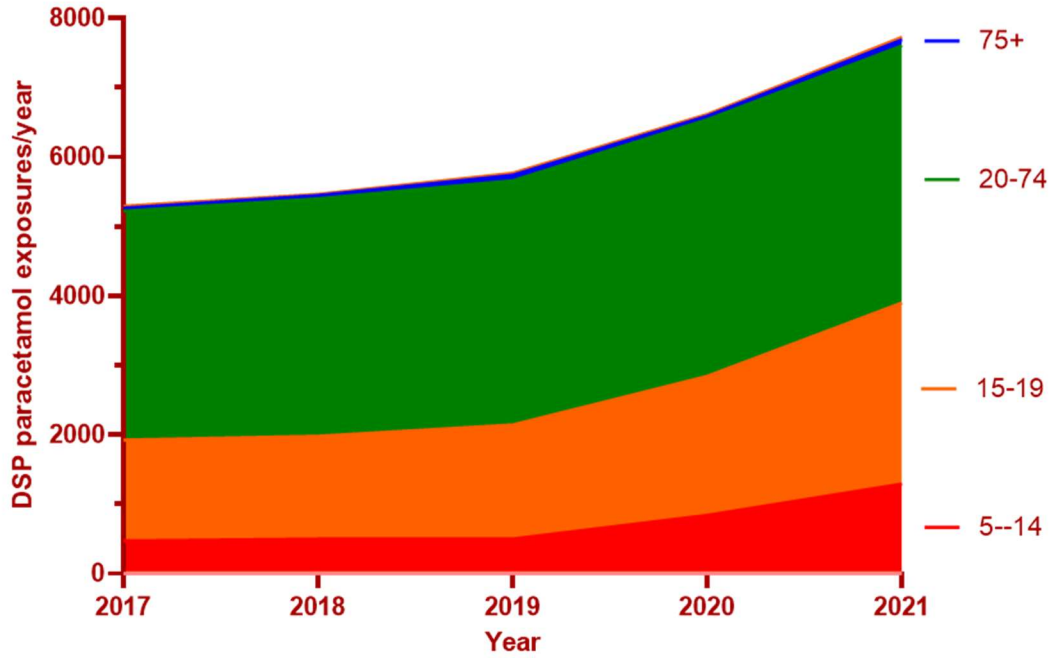

Figure 29. National PIC calls about deliberate self-poisoning with paracetamol – Trends by Age 2017-21

The products being ingested are most commonly single ingredient paracetamol products although there are a very substantial proportion that are due to combination products, which make up over a third of calls where no other agents are ingested (Table 15).

Table 15. Trends for single vs multiple agents

Age group	Year	Single ingredient products only	Paracetamol combination tablets (e.g., panadeine) + or – paracetamol	Paracetamol + other co-ingestants
0-4 years	2017	4383	1956	1149
	2018	4288	1966	1069
	2019	4574	2182	1239
	2020	3870	1751	991
	2021	4359	1932	1116
5-14 years	2017	1101	619	543
	2018	979	433	415
	2019	1126	547	458
	2020	1082	582	558
	2021	1435	669	759
15-19 years	2017	951	553	922
	2018	803	478	823
	2019	895	581	981
	2020	1152	599	1026
	2021	1466	724	1350
20-74 years	2017	2935	2290	3531
	2018	2586	2247	3291
	2019	2815	2344	3585
	2020	2943	2087	3619
	2021	3084	2077	3749
75+ years	2017	253	146	243
	2018	250	146	265
	2019	264	143	284
	2020	325	202	325
	2021	373	198	334
Total	2017	9623	5564	6388
	2018	8906	5270	5863
	2019	9674	5797	6547
	2020	9372	5221	6519
	2021	10717	5600	7308

Comparison of data from the four PICs

Four key measures are shown in the figure below indicating the NSW PIC data accounts for nearly half of all Australian PIC calls, and this carries through into subgroups such as paracetamol exposures, paracetamol deliberate self-poisonings and child/adolescent paracetamol poisonings (Figure 30).

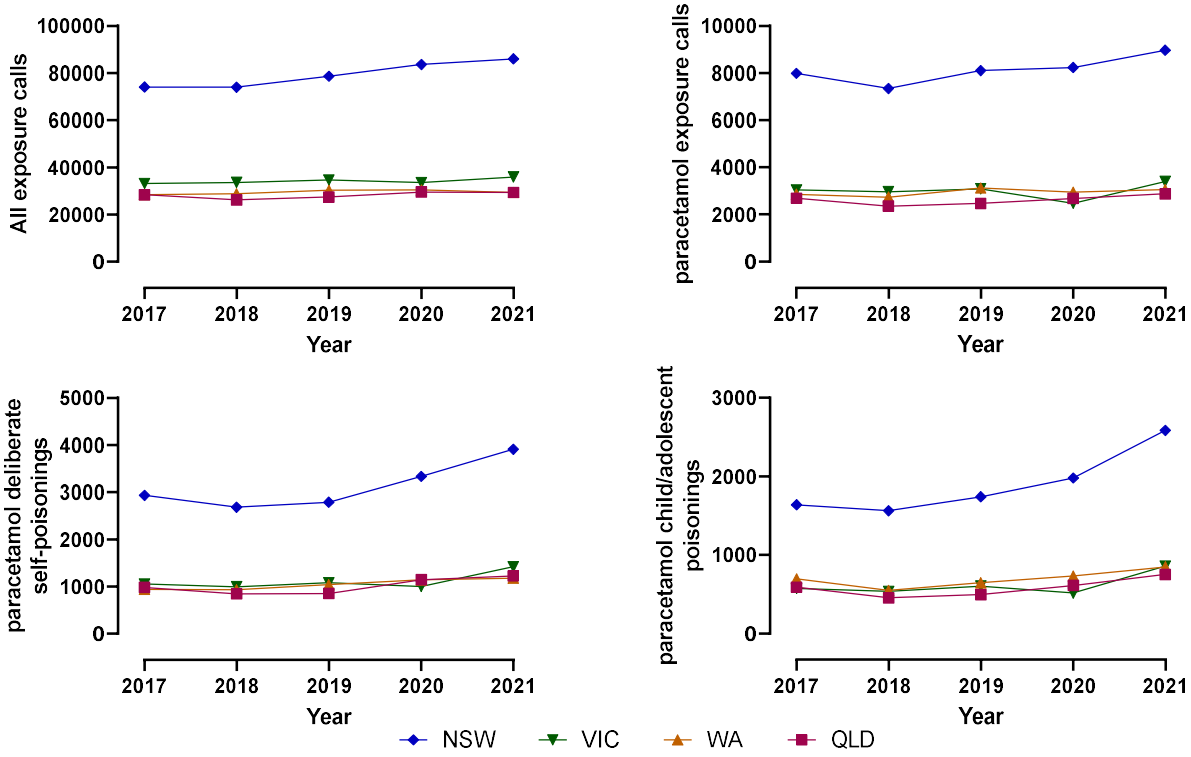

Figure 30. Comparison of numbers of patients providing relevant data from the four PICs, 2017-21

PIC calls by State of origin 2018-21

All four PICS provided further data on the state of origin of the calls (Figure 31). There were a small number of calls from international locations, and these have been excluded from the calculations of rates. These indicate higher exposures in recent years from the ACT and Tasmania, which may partly reflect higher utilisation of PIC services rather than higher poisoning rates (as neither jurisdiction has any local toxicology services) (Figure 31).

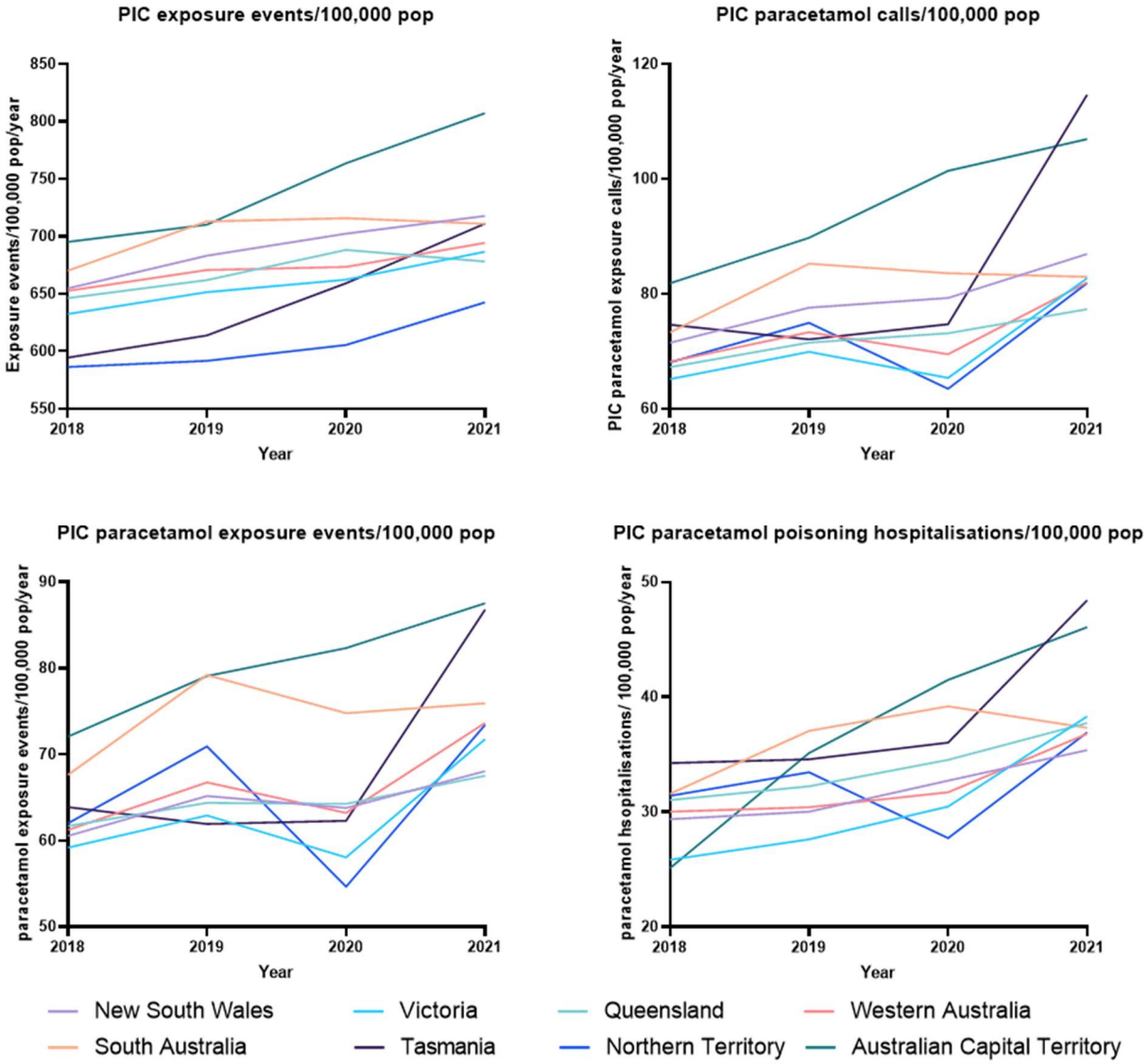

Figure 31. Comparison of rates of exposures, paracetamol related calls, events and hospitalisations (All PIC data 2018-21).

2.4.5 Prospective NSW PIC study (enhanced dose & product detail)

- Most paracetamol self-poisonings were impulsive but with suicidal intent.
- Specific purchasing for the purpose of self-poisoning was uncommon and most commonly the paracetamol ingested was already present in the home (for all age groups).
- Where information was obtained, most paracetamol self-poisonings involved the ingestion of multiple packs.
- The pack size ingested reflected the most common pack sizes purchased (20-packs and 100-packs), with scheduled and unscheduled paracetamol products used in self-poisonings in approximately equal proportions.

Methods

Between 1 February 2022 and 31 May 2022 NSW PIC collected additional data for paracetamol deliberate self-poisonings. In addition to routine history taking, the NSW PIC Specialist in Poisons Information attempted to collect the following additional data:

1. The exact product, including brand and pack size
2. Who purchased the paracetamol
3. Where was the paracetamol purchased (supermarket, pharmacy, convenience store, etc.)
4. When was the paracetamol purchased (was there planned stockpiling, was it purchased impulsively, or was it present in the home)
5. The number of packs purchased (if purchased for purposes of self-poisoning)

The initial call data and these data were further analysed to estimate:

- Doses and numbers of packs of paracetamol consumed and expected morbidity based on severity scores
- Likely class of paracetamol-containing product (unscheduled, Schedule 2 or Schedule 3, if reported or able to be determined, of the Poisons Standard February 2022)

Some assumptions were made based on brand and/or product type:

1. Modified release paracetamol, and combinations with codeine, pseudoephedrine, dextromethorphan, or sedating antihistamines were coded as purchased from pharmacy (even if the caller stated they didn't know), as these are scheduled products.
2. Where a brand was given that only comes in one pack size, this pack size was assumed, even if the caller didn't know. Examples of this are Panamax (100 tabs) and Panadol Osteo (96 MR tabs).

Results

During this period, NSW PIC received 1683 calls about deliberate self-poisonings with paracetamol. Of these, there were 1208 unique exposure events (the remainder of calls are recalls regarding the same exposure).

Questions were asked approximately one third of the time (35.5%, 429/1208 eligible cases). Questions were unable to be asked for various reasons, including time-critical calls, caller too busy to answer questions, many calls waiting in PIC queue, distressed callers (community-based calls), or the specialist forgot to ask. Even when questions were asked, often the answer was not known by the caller. It is also notable that the questions appeared to be asked more often for child and adolescent poisonings [265/622 (43%) vs 164/586 (28%)].

Results are largely reported just on the subset of calls for which questions were asked.

The median age of these cases was 16 years (IQR: 15-23 years, 28 missing), median dose in tablets was 20 (IQR: 10 to 33.5 tablets, 14 missing) and the median dose in grams was 10 (IQR: 5.6 to 17.4, 14 missing).

Table 16. Demographics of poisoning where further questions on intent and source were answered.

Sex	Child/adolescent	Adults	Grand Total
Female	234	124	358
Male	31	40	71
Grand Total	**265**	**164**	**429**

Most self-poisonings were impulsive but with suicidal intent. Specific purchase for the purpose of self-poisoning was uncommon, most commonly the paracetamol ingested was present in the home for all age groups (Table 17).

Table 17. Response to further questions on intent and source, by age group.

	Child/adolescent	Adults
Place of purchase	n=265	n=164
Pharmacy	83 (31%)	61 (37%)
Supermarket	37 (14%)	18 (11%)
Convenience store	3 (1%)	1 (1%)
Other	2 (1%)	1 (1%)
Supplied by hospital	1 (<1%)	4 (2%)
Multiple Sources	1 (<1%)	-
Unknown	138 (52%)	79 (48%)
Purchaser		

	Themselves	56 (21%)	75 (46%)
	Family member	70 (26%)	10 (6%)
	Friend	4 (2%)	-
	Other	54 (20%)	8 (5%)
	Unknown	81 (31%)	71 (43%)
Timing of purchase			
	< 24 hours	17 (6%)	17 (10%)
	Past week	2 (1%)	1 (1%)
	Over a week ago	3 (1%)	1 (1%)
	N/A, present in the home	162 (61%)	81 (49%)
	Unknown	81 (31%)	64 (39%)
Planning			
	Impulsive	121 (46%)	72 (44%)
	Same day plan	4 (2%)	2 (1%)
	Planned (longer duration or duration not specified)	54 (20%)	24 (15%)
	Unknown	86 (32%)	66 (40%)

The number of packs purchased was not known in the majority of cases, but where known it was often multiple (Table 18). Note, these data might imply multiple packs are the norm, however we believe it is far more likely to be reported to the caller if it was multiple packs purchased for the purpose of the overdose.

Table 18. Number of packs purchased, where specifically purchased for the overdose

Number of packs	5-19 years	others	Grand Total
1	12	5	17
2	13	10	23
3	3	1	4
4	2	1	3
5	1		1

NB If the cases where questions were not answered is included, it is: 1 pack (18), 2 packs (26), 3 packs (4) 4 packs (4) 5 packs (3).

Pack sizes ingested reflected the most common pack sizes purchased (Table 19 & section 12), and the scheduling also reflects the source and schedule of the most common agents (Table 20 & section 12).

Table 19. Pack size of paracetamol taken in all ingestions

Pack size	5-19 years (n=265)	%	Others (n=164)	%
9			1	1%
10	4	2%	6	4%
12	4	2%	3	2%

20	62	23%	32	20%
24	10	4%	3	2%
30	1	<1%		
40	2	1%		
48	4	2%		
50	1	<1%		
60	1	<1%	1	1%
96	14	5%	9	5%
100	41	15%	30	18%
200			1	1%
100, 10	1	<1%		
20, 24	1	<1%		
16, 100	1	<1%		
96, 10			1	1%
96, 20	2	1%		
Unknown	116	44%	77	47%

Note: Where multiple pack sizes are listed, the exposure involved multiple paracetamol products of differing pack sizes.

Table 20. Schedule of ingested products

Schedule	5-19 years (n=265)	%	Others (n=164)	%
Not scheduled	80	30%	39	24%
Not scheduled/S2	28	11%	26	16%
Not scheduled/S2/S3	2	1%		
S2	56	21%	33	20%
S2/S3	1	<1%		
S3	16	6%	12	7%
S4	6	2%	8	5%
Multiple*	11	4%	12	7%
Unknown	65	25%	235	21%

*patients ingested multiple paracetamol containing products belonging to different Schedules. Note: this information was inferred from information in the call record/survey response, cross referenced to the ARTG and SUSMP. Brand name, pack size, ingredients, and place of purchase was used to infer information when necessary.

Comparison of annual numbers of poisonings covered in datasets

A comparison of the numbers in the various datasets sheds some light on how likely this detailed retrospective and prospective PIC call data is to be representative of the typical admissions (Table 21). As can be seen the PICs record a similar number of paracetamol deliberate self-poisoning events as the AIHW admissions data (6629 vs 6918 in 2019). The majority of deliberate self-poisonings are admitted to hospital (even if not particularly unwell, they are admitted for observation and psychiatric assessment), and this suggest a high degree of overlap is likely. The AIHW data may be missing some cases of toxic liver injury,

given the rate compared to that recorded by NSW PIC is roughly half (noting the PIC are also likely to miss some cases due to a lack of routine follow-up).

Table 21. Comparison of coverage and annual numbers from different sources in 2019/20.

	NSW PIC (exposures)	All PICs (exposures)	AIHW (admissions)	NCIS (deaths)
Numbers of poisonings	83630	177236	41920	NA
Paracetamol poisonings	8240	16341	8723	29
Deliberate self-poisonings (DSP)	17780	NA	25069	NA
Paracetamol DSP	3337	6629	6918	NA
Liver injury	209	NA	199	12

NA=not available

2.5 Sales data on paracetamol-containing products

- Paracetamol containing products dominated sales of non-prescription analgesics in both pharmacies, and in grocery and convenience stores, amounting to around 40 million units and 25 million units a year, respectively, in 2021. Overall, two-thirds of all non-prescription analgesics are through pharmacies, although this varies to some extent by state.
- Larger pack sizes of 96 or 100 accounted for more than half of all paracetamol unit sales in pharmacies. Outside of pharmacies, 95% of total paracetamol product units sold were 20 packs sold in grocery stores.
- Approximately 85-90% of pharmacy visits where a paracetamol product was purchased involved the purchase of only a single unit of a paracetamol-containing product, with multi-unit purchases tending to involve smaller pack sizes. In grocery and convenience stores, most paracetamol purchasing visits involved the purchase of either 1 pack (~75%) or 2 packs (~20%) only, these 95% of visits accounting for approximately 85% of units sold.
- Around 25% of the time multiple units are purchased in a single transaction and most frequently involve multiple 20 packs being purchased.

Pharmacy sales

IQVIA data were obtained by the TGA, on absolute and relative sale volumes of paracetamol-containing medicines in Australian pharmacies, segmented wherever possible by type, scheduling status, retail supply type, year and jurisdiction.

Data provided by IQVIA about the volume of sales of units of individual products represented 100% of sales across all Australian pharmacies. This was based on point of sale data across 60.7% of pharmacy stores, which account for 90% of paracetamol sales. The remaining 10% of paracetamol sales were projected to 100% using various methods. The transaction level data provided was not projected and as such was intended to be used to

determine relative rather than absolute basket level volumns and purchasing patterns in Australia.

These show paracetamol containing products dominate the non-prescription analgesic market in pharmacies, selling around 40 million units a year in the most recent data. The S4 codeine scheduling in 2018 might account for the drop in combinations from 2018 onwards (Figure 32). Further evidence for this is seen in the drop in Schedule 3 paracetamol products at the same time (Figure 33).

It was notable that large pack sizes (96 or 100, both containing 50 or more grams of paracetamol, assuming 96s are of MR paracetamol) accounted for around half of all unit sales (Figure 34, left).

These can be converted to a proportion of grams sold by assigning 500 mg per unit for all unit pack sizes except for 1 and 96 units with a >50 g classification. The 1s are assumed to be syrups and have been arbitrarily assigned a 5000 mg dose; these 96 packs >50 g have been assigned assuming they are MR preparations of 665 mg tablets. It can be seen that these large pack sizes dominate total non-prescription sales of paracetamol in terms of total doses (Figure 34, right).

Most paracetamol-containing transactions (85-90%) involve the purchase of only one paracetamol item (Figure 35). The proportion of transactions in which multiple units of paracetamol are purchased is generally higher in those getting the smaller pack sizes, for example being only around 5% of those getting the 100-pack size (Figure 35).

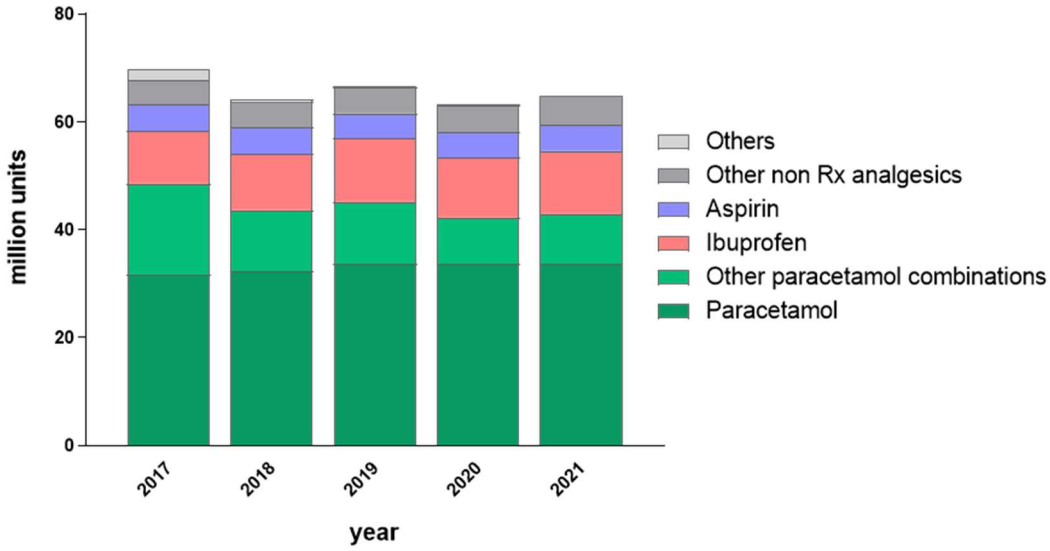

Figure 32. Unit sales of non-prescription analgesics, IQVIA 2017-2021

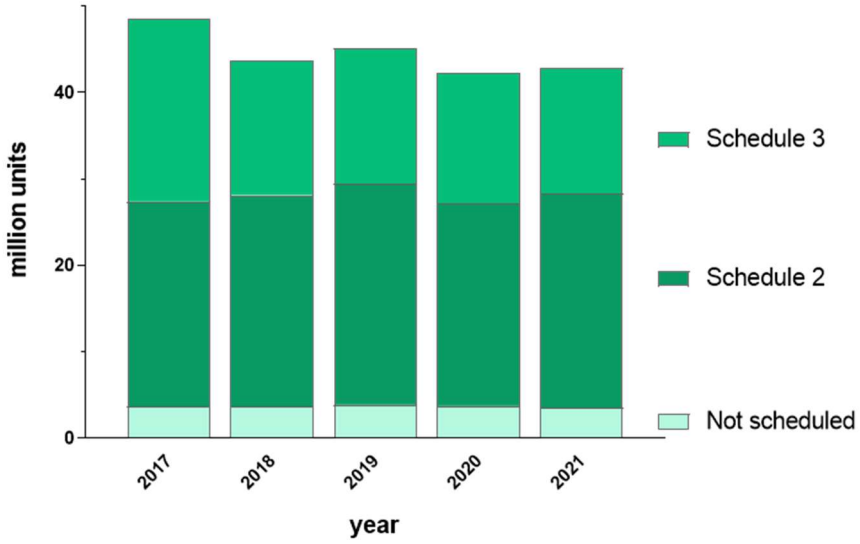

Figure 33. Pharmacy unit sales of non-prescription paracetamol by Schedule, IQVIA 2017-21

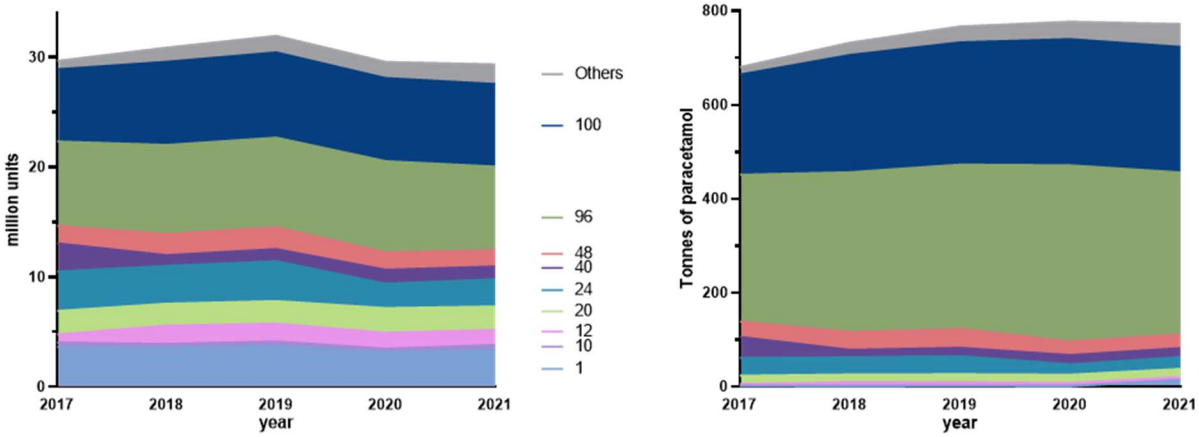

Figure 34. Pack size of pharmacy sales of non-prescription paracetamol, IQVIA 2017-21, million units and tonnes of paracetamol

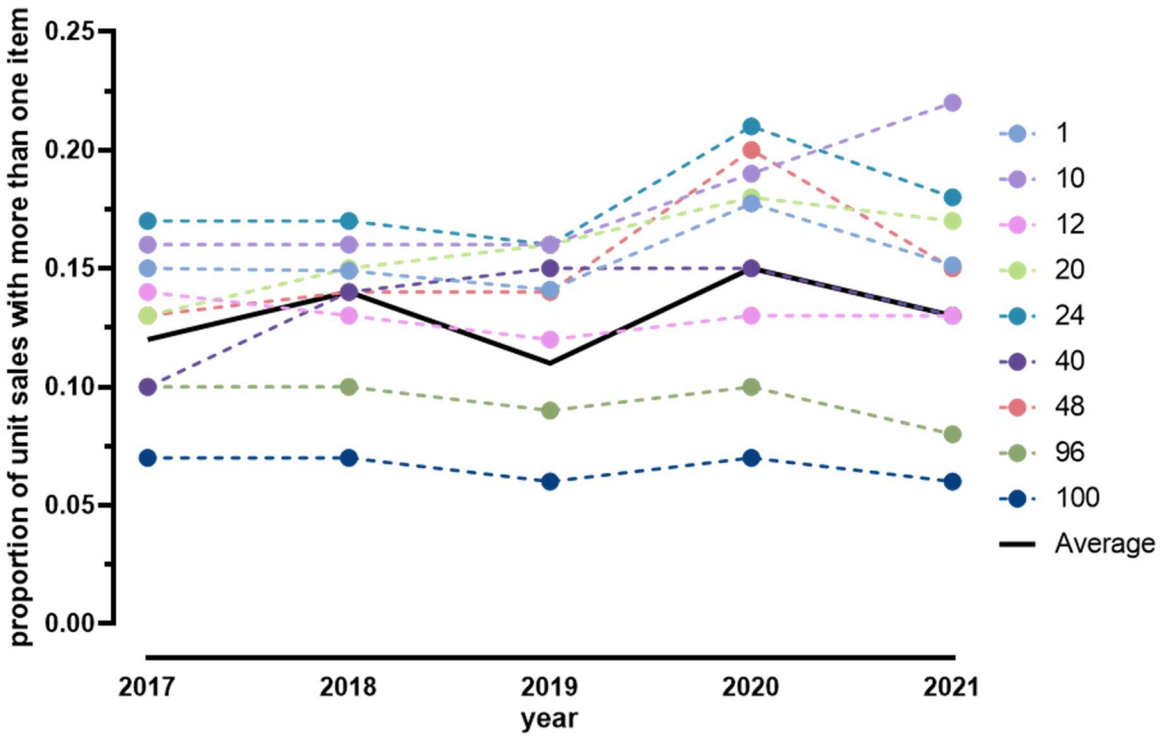

Figure 35. Proportion getting more than one paracetamol item by unit pack size, IQVIA 2017-21.

Grocery and convenience store sales

Data were obtained by the TGA from IRI on absolute and relative sale volumes for paracetamol-containing medicines in Australian grocery and convenience stores, segmented wherever possible by pack size, type, year and jurisdiction. The grocery store unit sales data provided by IRI represent approximately 85% market share and the remainder were projected to obtain a figure for 100% of Australian sales. The convenence store unit sales data are projected to 100% from data representing approximately 65% market share. The transactional (basket level) grocery store data represent 35% of all analgesic sales and are reported only as proportions of transactions rather than absolute numbers as these cannot be projected to absolute numbers due to technical and data collection limitations.The grocery data cover 2017-21 and convenience store data only 2020 & 2021.

These data show paracetamol containing products account for approximately half of non-prescription analgesic sales in grocery and convenience stores, selling around 25 million units a year in the most recent data (Figure 36). Most sales are through grocery stores (95% of total; Table 22), with 20 x 500 mg tablet packs overwhelmingly favoured (Figure 37). Most of the relevant data, and the only pre-2020 data, are for grocery sales, and so that is the focus of the figures.

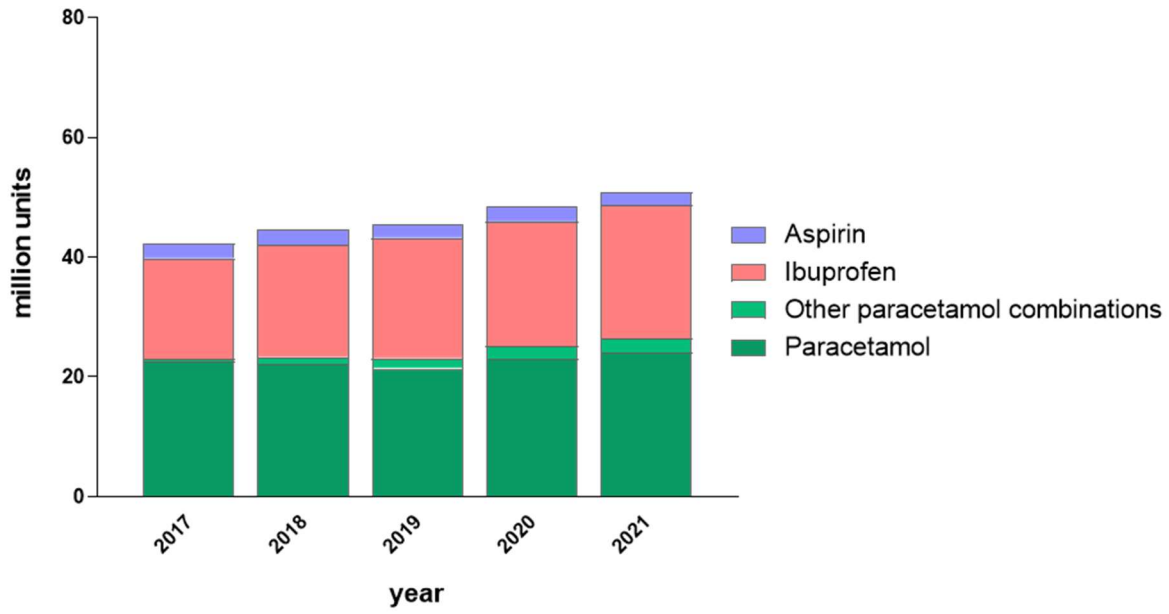

Figure 36. Unit sales of non-prescription analgesics in grocery stores, IRI2017-2021

The unit sales of non-prescription analgesics are nearly two-thirds of the unit sales through pharmacies (Table 22), but this varies to some extent by state (perhaps reflecting less access to pharmacies in areas of the least densely populated states).

Table 22. The number and proportion of paracetamol units sold through pharmacy, grocery and convenience stores in 2021 (IQVIA and IRI 2021).

	Units sold (millions) by channel			
Jurisdiction	**Pharmacy**	**Grocery**	**Convenience**	**Total**
NSW	14 (62.3%)	8.1 (36.1%)	0.4 (1.6%)	22.53
QLD	7.7 (51.4%)	6.9 (46.1%)	0.4 (2.5%)	15.01
VIC	11.2 (65.9%)	5.5 (32.5%)	0.3 (1.6%)	16.94
WA	4.4 (57.3%)	3.1 (40.7%)	0.1 (2%)	7.62
TAS	1.2 (66.2%)	0.6 (33.3%)	0 (0.5%)	1.78
ACT/NT/SA	4.4 (67.1%)	2.1 (32.2%)	0 (0.6%)	6.61
National	42.9 (60.9%)	26.4 (37.4%)	1.2 (1.7%)	70.48

Twenty tablet pack sales dominated the paracetamol unit sales through these other sources (Figure 37, left). All pack sales can be converted to a proportion of grams sold by assigning 500 mg per unit for all unit pack sizes except for the 16 unit sales which are specified as containing 250 mg. It can be seen that these many smaller pack sizes sold through grocery stores account for about 10% of total doses (tonne) sold (Figure 37, right).

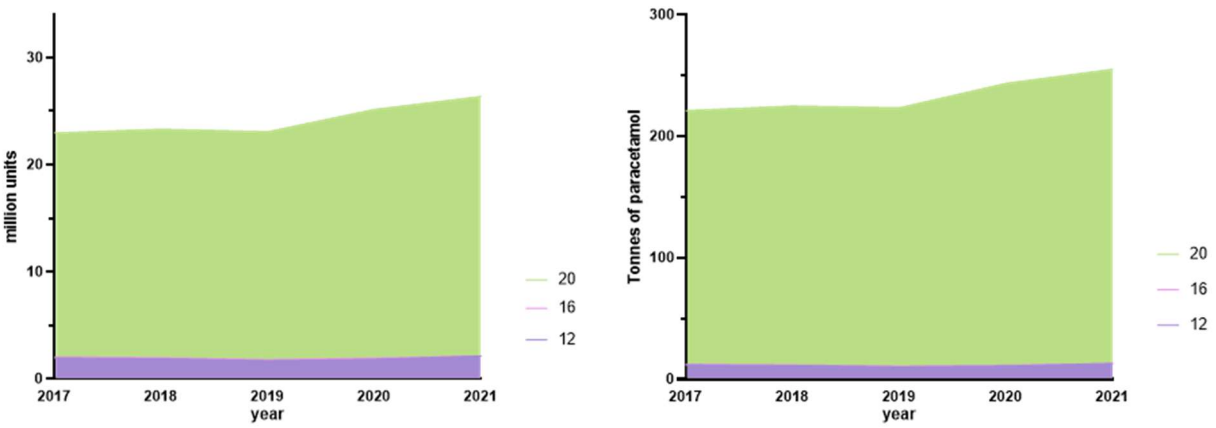

Figure 37. Grocery sales of non-prescription paracetamol andIRI 2017-21, million units and tonnes of paracetamol

Most transactions in which paracetamol is purchased in grocery stores involve the purchase of 1 (~75%) or 2 (~20%) packs only (which accounts for around 85% of pack sales by volume). Purchasing multiple units in a single transaction is common (~ 25% of the time) (based on 2021 data). However, 98% of transactions (accounting for 93% of units sold) involve three packs or less; a very small proportion of transactions (< 0.1%) involve the purchase of very large (10+) numbers of units on the one occasion (Figure 38).

20-packs are infrequently brought alongside other pack sizes (< 1% of total visits are of a 20-pack along with either a 10-pack or 12-pack). Therefore, although multiple-pack visits are common (25% of the time), these most frequently involve multiple 20 packs being purchased together without other pack sizes, consistent with 20 packs being the most popular pack size purchased (by number of units sold) (Appendix C).

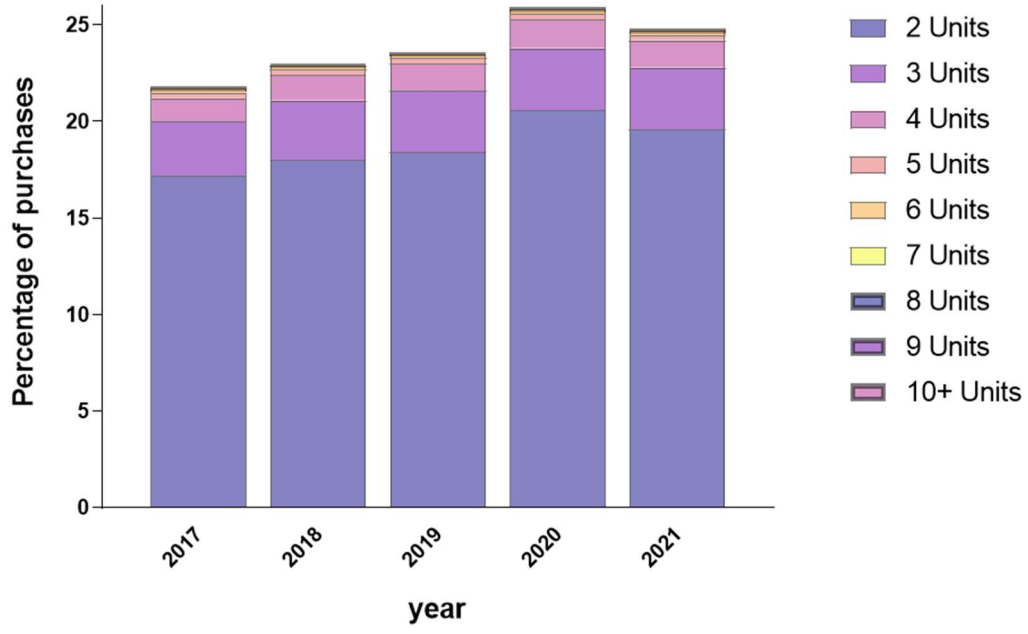

Figure 38. Grocery sales of non-prescription paracetamol and IRI 2017-21, number of packs purchased when more than one item purchased.

2.6 Comparison of data normalised to population and units sold

Introduction

The purpose of this task was to contextualise the number of poisonings, hospitalisations, and deaths per head of population or units of paracetamol sold, noting how prevalent use of paracetamol is in the Australian community. In particular, we sought to determine how incidences have trended over time as both the population and amount of paracetamol sold in the community may have varied.

Findings

Trends per head of population

- The units of paracetamol sold per million people decreased between 2017 and 2018 and this could be attributed to the rescheduling of codeine to S4. Since 2018 the units sold has continued to increase, however have not reached the same level pre-2018.
- Conversely, the units per population of other non-prescription analgesics have continued to increase between 2017 to 2021 (Table 23).
- Paracetamol poisoning hospital admissions and deliberate self-poisoning admissions per million people has decreased between 2016-17 and 2019-20, whereas hospital admissions with liver injury have been consistent between the years 2015-16 through to 2019-20 (Table 24).
- NCIS data shows two deaths per million people from paracetamol poisoning and almost one death per million people with liver injury (Table 25).
- There has been an increase in the number of deliberate paracetamol exposures reported to all PICs between 2018 to 2021 (217 to 300 respectively), which is consistent with findings indicated in Section 2.4 (Table 26).
- The data also shows that the number of intentional paracetamol poisoning exposure events has almost doubled between 2018 and 2021 for females aged between 15-19 years and also increased in females aged 20-74 years, which is consistent with findings referred to earlier in the report. Poisonings in this cohort is disproportionately increasing compared to other age groups and in males (Table 27).

Trends per unit of paracetamol sold

- Paracetamol poisoning and deliberate self-poisoning admissions are decreasing per million units sold and those with liver injury has remained constant (Table 28).
- Deliberate paracetamol self-poisonings were approximately 100 per million units of paracetamol sold in 2019-20.
- Conversely, paracetamol deliberate exposures reported to all PICs has been increasing (Table 30).

Table 23. Units of paracetamol and other non-prescription analgesics sold in Australia by head of population

Product type	Purchase location	Measure	2017	2018	2019	2020	2021
Paracetamol (single or multi active)	Pharmacy[1]	Total units	48,503,672	43,647,173	45,176,021	42,231,391	42,909,145
		Units per million people	1,958,107	1,733,393	1,770,070	1,643,603	1,665,301
	Grocery[2]	Total units	22,966,654	23,306,892	23,082,043	25,160,591	26,377,433
		Units per million people	927,170	925,604	904,392	979,225	1,023,706
	Convenience[2]	Total units	n/a	n/a	n/a	1,044,817	1,197,109
		Units per million people	n/a	n/a	n/a	40,663	46,460
	All channels	Total units	71,470,326	66,954,065	68,258,064	68,436,799	70,483,687
		Units per million people	2,885,277	2,658,997	2,674,462	2,663,492	2,735,467
Other non-prescription analgesics (including multi-actives)	Pharmacy[1]	Total units	21,150,168	20,440,461	21,420,730	20,925,859	22,006,754
		Units per million people	853,838	811,767	839,299	814,413	854,080
	Grocery[2]	Total units	19,389,160	21,298,841	22,521,151	23,258,006	24,551,912
		Units per million people	782,746	845,857	882,415	905,178	952,858
	Convenience[2]	Total units	n/a	n/a	n/a	1,240,694	1,372,570
		Units per million people	n/a	n/a	n/a	48,287	53,269
	All channels	Total units	40,539,328	41,739,302	43,941,881	45,424,559	47,931,236
		Units per million people	1,636,584	1,657,624	1,721,714	1,767,878	1,860,208

[1] Source of data = IQVIA (see section 2.5), [2] Source of data = IRI (see section 2.5). n/a = not available due to unavailability of sales data. Sales data is per calendar year. Population data was sourced through the ABS: www.abs.gov.au/statistics/people/population/national-state-and-territory-population

Table 24. AIHW admissions data by head of population

Hospital admission cause	Measure	2015-2016	2016-2017	2017-2018	2018-2019	2019-2020
All medicine poisonings	Total number	45,607	47,327	43,807	42,766	41,920
	Number per million people	1,885	1,924	1,755	1,688	1,634
Paracetamol poisonings	Total number	11,122	11,697	10,186	9,327	8,723
	Number per million people	460	476	408	368	340
Paracetamol deliberate self-poisonings	Total number	8,748	9,381	8,078	7,404	6,918
	Number per million people	362	381	324	292	270
Paracetamol poisoning with liver injury	Total number	220	235	224	204	199
	Number per million people	9	10	9	8	8
'Other NSAID' poisonings	Total number	1,694	1,847	1,682	1,680	1,555
	Number per million people	70	75	67	66	61

AIHW data provided in Appendix A and is based on financial year. Population data for each financial year was sourced through the ABS – *Population- states and territories, Quarterly population by sex, by state and territory, from June 1981 onwards.*

Table 25. NCIS data by head of population

Event	Measure	2008-2020
Paracetamol poisoning deaths	Total average yearly number	50
	Number per million people	2
Paracetamol poisoning deaths with liver injury (probable cause based on case review)	Total average yearly number	20
	Number per million people	0.78

Table 26. Poisonings in Australia from all PIC data by head of population

Exposure	Measure	2017	2018	2019	2020	2021
All	Total number	164,176	162,855	171,078	177,236	180,856
	Number per million people	6,628	6,468	6,703	6,898	7,019
Paracetamol	Total number	16,573	15,406	16,779	16,343	18,296
	Number per million people	669	612	657	636	710
Paracetamol deliberate	Total number	5,910	5,462	5,767	6,629	7,729
	Number per million people	239	217	226	258	300

Combined PIC data from Appendix D and is based on calendar year. Population data was sourced through the ABS: www.abs.gov.au/statistics/people/population/national-state-and-territory-population

Table 27. Intentional single ingredient paracetamol poisoning exposure events by gender and age reported to NSW PIC by head of population

Age	Measure	2017	2018	2019	2020	2021
5 - 14 years female	Total reported (NSW)	219	217	216	352	577
	Total projected (Aus)	476	472	470	765	1254
	Projected per million ppl	320	311	304	489	797
5 - 14 years male	Total reported (NSW)	31	28	32	47	54
	Total projected (Aus)	67	61	70	102	117
	Projected per million ppl	43	38	43	62	70
15 - 19 years female	Total reported (NSW)	528	525	568	824	1050
	Total projected (Aus)	1148	1141	1235	1791	2283
	Projected per million ppl	1,591	1,577	1,702	2,486	3,181
15 - 19 years male	Total reported (NSW)	131	134	134	142	194
	Total projected (Aus)	285	291	291	309	422
	Projected per million ppl	375	381	378	403	553
20 to 74 years female	Total reported (NSW)	859	846	884	1092	1123
	Total projected (Aus)	1867	1839	1922	2374	2441
	Projected per million ppl	220	213	219	267	275
20 to 74 years male	Total reported (NSW)	412	439	442	543	495

	Total projected (Aus)	896	954	961	1180	1076
	Projected per million ppl	107	113	112	136	124
>75 years female	Total reported (NSW)	7	14	19	17	30
	Total projected (Aus)	15	30	41	37	65
	Projected per million ppl	17	32	43	37	63
>75 years male	Total reported (NSW)	11	9	19	13	19
	Total projected (Aus)	24	20	41	28	41
	Projected per million ppl	33	26	54	35	49

Data provided in Appendix B was used to calculate the average number of all exposure calls received by all PICs between the years 2017-2021. Likewise, an average of all exposure calls received by NSW PIC was calculated (2017-2021). Taking the ratio of these, the proportion of all calls received by NSW PIC (*Total reported (NSW)*) was calculated to be 46%, based on which the factor of 1/0.46 was applied to extrapolate NSW numbers to national totals (*Total projected*). Population data for each financial year was sourced through the ABS – *Population- states and territories, Quarterly population by sex, by state and territory, from June 1981 onwards.* Note, ABS data was for financial years and NSW PIC data was calendar year. Total projected figures for Australia were then normalised per million people.

Table 28. AIHW admissions data per unit of paracetamol sold

Hospital admission cause	Measure	2015-16	2016-17	2017-18	2018-19	2019-20
Paracetamol poisoning	Total number	11,122	11,697	10,186	9,327	8,723
	Number per million units sold	n/a	164	152	137	127
Paracetamol deliberate self-poisoning	Total number	8,748	9,381	8,078	7,404	6,918
	Number per million units sold	n/a	131	121	108	101
Paracetamol poisoning with liver injury	Total number	220	235	224	204	199
	Number per million units sold	n/a	3	3	3	3
'Other NSAID' poisoning	Total number	1,694	1,847	1,682	1,680	1,555
	Number per million units sold	n/a	46	40	38	34

Note: Sales data is per calendar year and AIHW data is per financial year. For example, AIHW data for financial year 2016-17 is normalised for calendar year 2017 sales data.
n/a = not available due to unavailability of sales data.

Table 29. NCIS data per unit of paracetamol sold

Event	Measure	2008-2020
Paracetamol poisoning deaths	Total average yearly number	50
	Number per million units sold	0.73
Paracetamol poisoning deaths with liver injury (probable cause based on case review)	Total average yearly number	20
	Number per million units sold	0.29

Table 30. Combined PICs data per unit of paracetamol sold

Exposure type	Measure	2017	2018	2019	2020	2021
Paracetamol	Total number	16,573	15,406	16,779	16,343	18,296
	Number per million units sold	232	230	246	239	260
Paracetamol deliberate	Total number	5,910	5,462	5,767	6,629	7,729
	Number per million units sold	83	82	84	97	110

2.7 Summary and conclusions on Australian data on paracetamol poisoning

There are increasing rates of paracetamol poisoning in the last decade. Predominantly this increase is in intentional self-poisoning in children and adolescents, and females in particular. This increase may have further accelerated during COVID years (but only the PIC data is available in the last two years).

This is in the setting of a large increase in all self-poisonings in children/adolescents, which roughly doubled over the decade up to 2018. Paracetamol is taken in around 50% of these events and this proportion has not substantially changed in the last decade.

The majority of paracetamol self-poisonings in all age groups are impulsive but with suicidal intent. It is common for these individuals to have repeated episodes of self-harm. Depression, anxiety, PTSD, borderline personality disorder and ADHD were the top 5 psychiatric diagnoses recorded in all age groups.

Over half the time, the paracetamol taken was present in the home. Only around 10% reported recently purchasing paracetamol (usually on that day); 1 or 2 packs were purchased.

The pack size ingested most commonly and in roughly equal proportions were 20/24s and 96/100s. At least 25-30% of ingestions were of unscheduled products.

Sales of paracetamol are predominantly of these pack sizes – and are roughly equal in number of packs sold, but therefore the larger packs account for a much larger proportion of total grams sold.

The codeine prescription only (S4) restriction was followed by a large reduction in paracetamol combination product ingestions (and also reduced ibuprofen and codeine ingestions).

The MR paracetamol pharmacist only (S3) restriction was not followed by any substantial change in events.

Paracetamol poisoning may cause severe liver injury (2-5%) and death (0.2-0.5%), despite current treatments usually being effective. These severe outcomes appear to be less likely in young people overall. The risk factors of high doses, and MR paracetamol ingestion appear in much the same proportion in ingestions in recent years, indicating the average severity of paracetamol poisoning is probably not increasing greatly.

3. International comparisons of scheduling and paracetamol poisoning

Paracetamol is very commonly taken in self-poisoning in many countries. Cross-sectional international comparisons based around the current 'scheduling'[1] of paracetamol are not informative, as the countries with the largest burden of disease are generally those that have introduced the tighter restrictions. Generally, the data is not sufficiently detailed to determine if the size of the overdoses, or the proportion of poisonings resulting in liver injury and death are less in those countries with tighter restrictions.

The scheduling of paracetamol varies considerably within OECD countries, with respect to availability of IR and MR paracetamol, sales of paracetamol outside of pharmacies, and the maximum pack sizes available (Figure 39). The schedules below are approximate equivalents of Australian schedules (see Appendix E for further details).

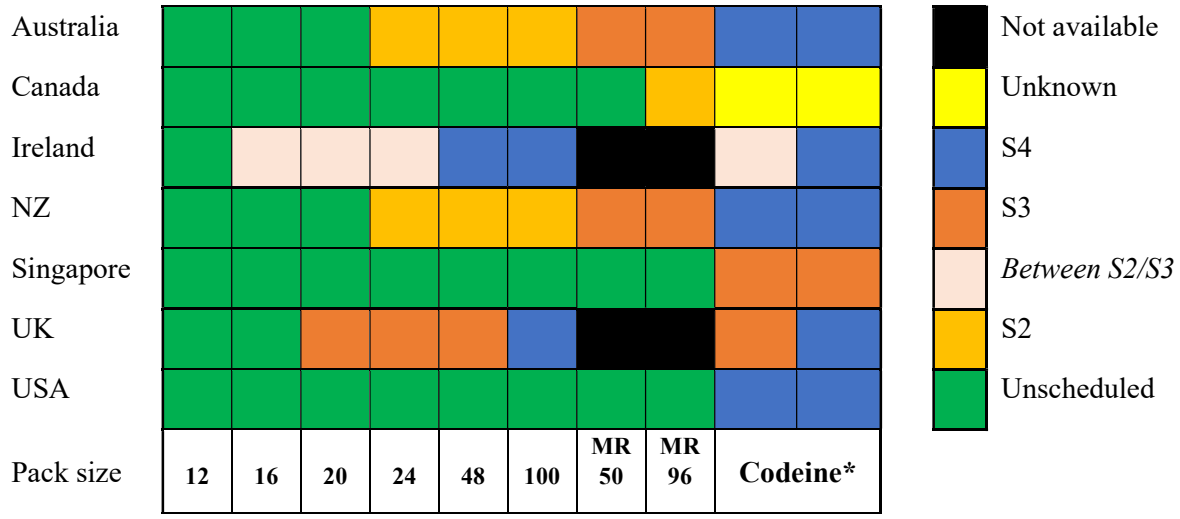

Figure 39. Scheduling status of paracetamol in selected other OECD countries

*Scheduling dependent on the strength of codeine.

Limitations

There are limitations when trying to assign equivalent Australian schedules against the scheduling categories in some overseas jurisdictions. Notably, most overseas jurisdictions do not have an equivalent Schedule 2 and Schedule 3 categorisation, moreover their 'equivalent' category sits somewhere between Schedule 2 and Schedule 3. In addition, some countries do not have pack size limits (or these could not be determined) resulting in greater difficulty in assigning equivalent status.

[1] Used in this chapter to refer to the categorisation according to the level of access control even if the mechanism is not called 'scheduling' in the foreign jurisdiction.

In terms of other OECD countries, the majority of European countries (including France, Germany and Italy) do not allow any sales outside of pharmacies (Morthorst et al., 2020). Most also have lower limits on pharmacy pack sizes (e.g. France 8 g, Germany 10 g, Italy 15 g) (Morthorst et al., 2020). MR paracetamol is also not available in most European countries now (Chiew, Isbister, et al., 2018).

Many countries are reporting similar recent rises in child/adolescent female poisonings that we are observing in Australia, and often highlighting paracetamol as the most common agent ingested (Fridriksdottir Th, Jonsdottir, Snook, Lindal, & Bjornsson, 2021; Hopkins et al., 2020; McNicholas et al., 2019; Midtervoll, Allen, Eriksen, Bakken, & Skjerdal, 2020; Tyrrell, Kendrick, Sayal, & Orton, 2018).

However, few countries have published comprehensive data to judge whether the availability impacts on the severity of poisoning. Some studies have focussed on changes in severity with the changes in packaging and are discussed in the next section under evidence for changes with packaging. In the next few paragraphs are the limited contemporary data on clinical effects from paracetamol poisoning. Identification of these involved review of the references retrieved in the systematic search outlined in the section below, with further references from the expert reviewer's knowledge of those publishing clinical data. This has been focussed on the most recent reports from any datasets, and in any case, restricted to papers published since 2011, as earlier publications may be reporting outcomes based on very different scheduling to those summarised above.

The USA

The USA appears to have few or no restrictions on pack sizes of standard paracetamol products. They have had a near doubling in OTC analgesic poisoning in child/adolescent (5 to 19 years old) between 2011 and 2018 (73% female), and half of their analgesic poisonings are in this age group (Hopkins et al., 2020).

The USA 2020 data from their Poisons Centre calls records 105,861 paracetamol exposures (Gummin et al., 2021). This was 7% of all medicine poisonings, 15% of adolescent (ages 13-19) poisonings, and 14% of intentional poisonings. There were 242 deaths from paracetamol (197 listed as first or sole agent), 87 from paracetamol combination tablets. The death rate was thus 0.2-0.3% of exposures, and 2.0 % of exposures were rated serious with the poison severity score. However, only a third of exposures were from healthcare facilities (and only a quarter were intentional) – and if the admitted group was taken as the denominator the severe ratings and deaths would be three times higher (i.e. 6% and 0.6% respectively)(Gummin et al., 2021). These are considerably higher proportions than we recorded at NSW PIC in the last 4 years, however the USA PIC routinely follow up all calls, and NSW PIC does not.

Canada

In Canada, 33% of measured levels (1187/3599) are more than double the nomogram line (Yarema et al., 2018). This is much higher than we found in our audit (22%, 339/1515). Unfortunately, overall outcomes were not reported in this study.

New Zealand

New Zealand has very similar scheduling to Australia (Freeman & Quigley, 2015). Paracetamol-containing products available through general sale are limited to 500 mg or less per tablet or capsule in packs containing not more than 10 g. In pharmacies pack sizes containing not more than 50 g can be purchased. MR preparations are only available through pharmacies (with a maximum strength of 665 mg and there are no limits on the maximum quantity that can be purchased in one transaction. They have done some interesting studies, reporting the large amounts of paracetamol (median > 30 g) stored in a typical New Zealand home (E. K. Kumpula, Norris, & Pomerleau, 2020). However, there are no recent data on the clinical outcomes of paracetamol poisoning in New Zealand.

Singapore

Singapore has far less restrictive scheduling compared to Australia for both IR and MR preparations. IR preparations can be sold in supermarkets (outside of pharmacies) and in pharmacies with no restrictions on quantities that can be purchased. Interestingly, MR preparations can also be purchased outside of pharmacies without any restrictions on the quantity permitted for sale.

Europe

The availability of paracetamol from pharmacies and general sale differs considerably between European countries (Morthorst et al., 2018). Whilst some states have implemented restrictions other have no limits on the quantities per pack or number of packs that can be purchased (predominantly in Eastern Europe and Russia). Fourteen countries have implemented pack size restrictions within pharmacies ranging from 8-30 g in the last two decades (which are lower than in Australia). Furthermore, in twelve countries paracetamol-containing analgesics are not available outside of pharmacies, with larger quantities only available with a valid prescription from a doctor.

Only seven countries allow sales of paracetamol from outside of pharmacies, with six of them having a range between 5-8 g and Russia allowing unlimited quantities for sale. Sweden now only markets effervescent tablets for sale from general sale. Indicating that apart from Russia all the remaining countries have tighter restrictions on access outside of pharmacies compared to Australia (either through smaller quantities or no access at all).

UK

The UK is an example of a country with tighter scheduling of paracetamol, which it enacted in 1998 as a response to the very considerable problems they have faced. That included, the large number of people taking paracetamol overdoses and increasing numbers of deaths and liver transplants due to paracetamol induced hepatotoxicity. From a behavioral aspect this change was introduced to address acts of self-harm that were often impulsive and involved the use of drugs already stored in the home. They now have low pack limits (16 tablets),

purchase limits (2 packs) from general sale and 32 tablet packs from pharmacies, and do not have MR paracetamol. There are recent studies that suggest the morbidity and mortality are lower than we observe in Australia. For example, a recent study comparing regimens of acetylcysteine, reported no deaths from liver disease in a large series of treated patients in Edinburgh, with severe liver injury (ALT >1000) occurring in 3.9 % (131/3340)(Pettie et al., 2019).

Changes to pack sizes has resulted in a 43% reduction in paracetamol deaths involving suicide or undetermined verdicts in England and Wales between 1998 and 2009 (Hawton et al., 2013). A 61% reduction in registration for liver transplants for paracetamol-induced hepatotoxicity was observed, however there was no reduction in actual transplantations.

Reducing pack sizes in the UK reduced median number of tablets taken in intentional overdose attempts (50 to 20 tablets for males and 20 to 16 tablets for females) (Morgan et al., 2007). There was also a reduction in the proportion of patients who took higher doses in the range of 33 to 100 tablets, which fell from 25% to 19%. Although the regulatory changes produced a decline in the severity of paracetamol poisonings, there was no decline in the frequency of cases reported to Guy's and St Thomas' Poisons Unit (London).

Denmark

In Denmark, they have an unscheduled pack limit of 10 tabs and a pharmacy pack limit of 20 tabs and no MR products. Hepatotoxicity occurred in 4% (31/767) of paracetamol poisonings treated with acetylcysteine with 2 deaths (Schmidt et al., 2018).

Ireland

Ireland has even tighter scheduling, with maximum pack size of 12-tablets for unscheduled products, that was introduced in 2001. In a recent study roughly a third of young people (ages 10 to 24) took ≤ 12 tablets and two-thirds ≤ 24 tablets (Daly et al., 2021b). These proportions are about 25% higher than for the overdoses taken in Australia where roughly half are ≤ 10 g). Clinical outcomes were not reported, but it would be assumed that the outcomes in these people were favorable.

Pack size reductions introduced in 2001 resulted in a reduction in the number of tablets taken in deliberate paracetamol overdoses, with fewer cases involving more than 24 tablets (Donohoe et al., 2006). Although Ireland has lower pack size limits compared to the UK, this does not appear to have resulted in major differences in sizes of overdoses (Hawton et al, 2011). There were significantly more pack equivalents (based on maximum non-pharmacy pack sizes) used in overdoses in Ireland compared to the UK, noting however the overall size of overdoses did not differ significantly between the two.

Iceland

Iceland has a maximum pack size of 15 g in pharmacies and no grocery sales.(Morthorst et al., 2020) A study on paracetamol poisoning admissions found similar demographics to Australia, with adolescent women with intentional self-poisoning being over-represented.

Median doses were similar to our series: 52% (211/407) of patients ingested 5–10 grams of paracetamol, 31% (126/407) ingested 11–20 grams, 11% (46/407) ingested doses larger than 20 grams. The mortality rate in intentional self-poisoning was 0.5% (2/437) (Fridriksdottir Th et al., 2021).

Comparable Australian research on paracetamol poisoning

Similar to the international research literature there have been several recent studies reporting paracetamol poisoning outcomes. One reports similar information to that presented in the earlier sections above (Cairns et al., 2019). Two focussed on two high-risk patient groups and aimed to identify better treatment strategies (Chiew et al., 2017; Chiew, Isbister, et al., 2018). These resulted in a change in local guidelines but also demonstrated frequent liver injury and a continuing need for better management options. Another Australian study reported hepatotoxicity occurring in 4.2% (21/476) of treated paracetamol poisonings, but excluded all those who presented with toxicity, without providing numbers (McNulty, Lim, Chandru, & Gunja, 2018). Again, this highlights potential benefits might come from better treatments.

A recent study from several toxicology treatment units provides the best potential comparison to the recent UK case series (Wong et al., 2020). While focussed on comparing to standard treatment approaches it does report on overall deaths (3/2211) and severe liver injury (7.8% - 172/2211). The liver injury rate is considerably higher than the 3.9% (131/3340) noted in treated patients in the UK (Pettie et al., 2019). The Australian data is in line with the higher estimates from the USA, or perhaps worse (reflecting greater use of MR products?). Even allowing for lower treatment thresholds for treatment in the UK, these data indicate that UK restrictions may be reducing the number of severe poisonings.

4. Literature review of characteristics, motivations and behaviour of individuals who intentionally overdose with paracetamol

- A review of the literature was carried out to investigate:
    1) the characteristics, motivations and behaviours of people who intentionally overdose with paracetamol and similar medications, and
    2) the effect of restricting access to paracetmaol and similar medications on method substitution to other medications or other methods of self-harm.
- Across sixty-six studies that examined characteristics, motivations or behaviours, intentional self-poisosoning tended to be more common in females compared to males, and in adolescents and young adults compared to other age groups.
- Young people who intentionally self-poiosoned with paracetmaol often did not have a history of self-harm, but approximately half of cases had a past or current psychiatric disorder.
- The majority of people who intentionally self-poisoned had suicidal intent, and did so impulsively with paracetamaol that was easily accessible in the home or purchased from retailers.
- Common overdose sizes were similar to a pack or multiples of a pack, and general population samples overestimated the quantity required for a harmful or lethal dose.
- Across fifteen studies that examined the impact of five historical instances of reduced access to one medication on method substitution, there was little evidence that restriction led to means substitution.

Background

A critical, systematic review of the literature was undertaken to identify the characteristics and behaviour of individuals who intentionally self-poison with paracetamol and similar medications. A specific focus of the review was on identifying available research on self-harm intent, ideation and planning, and the potential for method substitution in response to medication restrictions. Understanding the characteristics and behaviours associated with intentional self-poisoning is important in establishing the aetiology of the problem and to assist in identifying ways to reduce intentional self-poisoning behaviour through targeted intervention and restrictions. Restricting access to paracetamol could be helpful in reducing the number of intentional self-poisoning cases via paracetamol. However, this effort would be counterproductive if it led to the increased use of other more lethal or toxic medications, therefore examining the potential for method substitution is crucial.

Research Questions

Two key research questions have guided the present systematic review of the literature:

1. What are the demographic and clinical characteristics of people engaging in self-poisoning via paracetamol or other non-opioid analgesics available over-the-counter, such as ibuprofen and aspirin in Australia and similar countries? What are the motivations, intentions, decision-making processes and behaviours of people who overdose with paracetamol or other non-opioid analgesics? What does the general population know about the safety/toxicity of paracetamol or similar medications?

2. What is the effect of restricting access to paracetamol and other similar medications on individual self-poisoning behaviours and use of alternate means of suicide and self-harm (method substitution) in Australia and similar countries? Does increasing access to paracetamol and other medications (e.g., through down-scheduling) have an effect on means of suicide and self-harm?

The methodology used as part of the literature review is included in Appendix F.

Results

The results are described separately for Question 1 (Table 31, Table 32) and Question 2 (Table 33).

Question 1: Characteristics, motivations and behaviours of people engaging in self-poisoning via paracetamol or other non-opioid analgesics

Sixty-six of the eighty-one identified studies contained data relevant to research Question 1. For ease of interpretation, Table 31 presents the findings of studies that report on participant demographic and clinical characteristics, such as sex, age, self-harm history and psychiatric history, as well as paracetamol dose characteristics. Table 32 presents the findings of studies assessing the motivations, knowledge and behaviours of people engaging in self-poisoning via paracetamol, including access to paracetamol and planning.

The identified studies were published in a range of countries, including the UK and Ireland (*n* = 24), US (*n* = 14), Europe (*n* = 12), Canada (*n* = 8), Australia (*n* = 6) and New Zealand (*n* = 3). Some studies focused only on paracetamol self-poisoning, while others assessed trends in self-poisoning across substances including paracetamol, other analgesics or over-the-counter medications and prescription drugs.

The vast majority of studies were observational (*n* = 55), examining administrative datasets with samples ranging from 34-549,807 participants. The remaining studies were qualitative interview studies (*n* = 5), case-control studies (*n* = 3) or cross-sectional surveys (*n* =3). These remaining studies tended to have smaller samples than observational studies, ranging from 60-280 participants for qualitative interview studies and 95-582 participants for case-control and cross-sectional studies. The study populations varied across studies and included

emergency department presentations, hospitalisations, deaths, or a combination of these events. The studies also spanned a range of age groups, with some studies including participants of all ages from infants to older adults, while others focused on paediatric or adult populations.

Table 31 presents the findings of studies assessing the demographic and clinical characteristics of people engaging in self-poisoning via paracetamol or other non-opioid analgesics.

Demographic characteristics: Of the thirty-seven studies that examined sex, the vast majority found that intentional self-poisoning with paracetamol and similar medications was more common among females than males (Alander, Dowd, Bratton, & Kearns, 2000; Alaniz & Janusz, 2007; Angalakuditi, Coley, & Krenzelok, 2006; Bloch, Drachmann, & Pedersen, 2013; Budnitz, Lovegrove, & Crosby, 2011; Cairns et al., 2019; Caroll et al., 2015; Casey et al., 2020; Daly et al., 2018; Daly et al., 2021a; Fridriksdottir Th et al., 2021; Gedeborg et al., 2017; Gyamlani & Parikh, 2002; K. Hawton et al., 2007; K. Hawton, Simkin, & Deeks, 2003; K. Hawton et al., 1996; Hopkins et al., 2020; Kaur, McFaull, & Bang, 2020; Kjartansdottir, Bergmann, Arnadottir, & Bjornsson, 2012; Kominek, Pawlowska-Kamieniak, Mroczkowska-Juchkiewicz, Krawiec, & Pac-Kozuchowska, 2015; Kummer, Muller, Exadaktylos, Krahenbuhl, & Liakoni, 2021; Makin & Williams, 2000; Manthripragada, 2011; Myers, Li, & Shaheen, 2007; Nourjah, Ahmad, Karwoski, & Willy, 2006; Pezzia, Sanders, Welch, Bowling, & Lee, 2017; Piotrowska et al., 2019; Schiodt, Rochling, Casey, & Lee, 1997; Shah, Uren, Baker, & Majeed, 2002; Shekunov, Lewis, Vande Voort, Bostwick, & Romanowicz, 2021; L. G. Taylor, Xie, Meyer, & Coster, 2012). Three of these studies also found that this sex difference favouring females narrowed in older age groups (Budnitz et al., 2011; Hopkins et al., 2020) or in adult samples compared to paediatric samples (Alaniz & Janusz, 2007). However, six studies did not find a gender difference in the use of paracetamol (Beautrais, Joyce, & Mulder, 1998; Craig et al., 2011; K. Hawton, Harriss, L., 2008; Townsend, Hawton, Harriss, Bale, & Bond, 2001) or similar medications (A. E. Rhodes et al., 2008; Vancayseele, Rotsaert, Portzky, & Van Heeringen, 2019) in intentional self-poisoning. Four studies also found that the gender ratio did not differ between intentional and unintentional self-poisoning cases (Craig et al., 2011; Gyamlani & Parikh, 2002; Kjartansdottir et al., 2012; A. E. Rhodes et al., 2008).

Studies were highly varied in the age group included (see Table 31). Many studies found that the highest incidence of intentional self-poisoning with paracetamol and similar medications occurred in younger age groups, particularly adolescents and/or young adults under 25 years of age (Bloch et al., 2013; Budnitz et al., 2011; Daly et al., 2018; Daly et al., 2021a; Downes, Lovett, & Isbister, 2021; Fridriksdottir Th et al., 2021; Gedeborg et al., 2017; Graudins, 2015; Hopkins et al., 2020; Kaur et al., 2020; Kummer et al., 2021; Mikhail et al., 2018; Myers, Li, & Shaheen, 2007; Neilson & Morrison, 2012; Smith, 1995; L. G. Taylor et al., 2012; Ticehurst et al., 2002; Townsend et al., 2001). Similarly, three studies reported that the prevalence of intentional self-poisoning with paracetamol and similar medications declined with increasing age (Budnitz et al., 2011; K. Hawton et al., 2007; Smith, 1995). In contrast, one study found that the use of paracetamol alone increased with age, but this study was primarily focused on self-poisonings with co-proxamol (K. Hawton et al., 2003). Studies that

compared the prevalence of intentional and unintentional self-poisonings found that intentional poisoning was more common in older adolescents than in younger children, whose poisonings were more often unintentional (Alander et al., 2000; Myers, Li, Fong, Shaheen, & Quan, 2007; Neilson & Morrison, 2012). The ratio of intentional to unintentional self-poisoning was also greater in adolescents and young adults compared to older adults (Craig et al., 2011; Graudins, 2015; Gyamlani & Parikh, 2002; Kjartansdottir et al., 2012; Myers, Li, Fong, et al., 2007). Some studies also found that younger people tended to use paracetamol more often in comparison to other drugs (Beautrais et al., 1998; Caroll et al., 2015; K. Hawton et al., 2007; Townsend et al., 2001) or were more likely to take paracetamol or similar analgesics on their own rather than in compound forms or in combination with other drugs (Alsen et al., 1994; Casey et al., 2020).

Two studies from the US and two studies from Canada reported on ethnicity. Both US studies found that intentional self-poisoning with paracetamol was more common among white or Caucasian people compared to Hispanic or Latinx people (Pezzia et al., 2017), or other ethnicities (Schiodt et al., 1997). In contrast, one Canadian study found that self-poisoning with similar over-the-counter drugs was more common for people of non-Caucasian ethnicity (Mikhail et al., 2018). The other Canadian study found that intentional paracetamol self-poisoning was more common for non-Indigenous people compared to Indigenous people (Myers, Li, & Shaheen, 2007).

Clinical characteristics: Regarding suicidal intent, the majority of studies found that over 80% of people who had intentionally overdosed with paracetamol or similar medications had suicidal intentions (Alaniz & Janusz, 2007; Alsen et al., 1994; Angalakuditi et al., 2006; Gyamlani & Parikh, 2002; Hedeland et al., 2013; Hedeland, Teilmann, Jorgensen, Thiesen, & Andersen, 2016; Hopkins et al., 2020; Makin & Williams, 2000; Mikhail et al., 2018; Pezzia et al., 2017; Piotrowska et al., 2019; Schiodt et al., 1997). Exceptions included one study in which patients hospitalised for paracetamol self-poisoning were recruited to participate in a structured interview (K. Hawton et al., 1996), and another study in 12-19 year-olds in which 44% of cases had suicidal intent (Schmidt, 2001). One study reported that people who self-poisoned with paracetamol had significantly lower median scores on the Suicidal Intent Scale (SIS) than people who self-poisoned with salicylates, gas, or opiates and recreational drugs (Haw, Casey, Holmes, & Hawton, 2015). There were no differences in suicidal intent between those who self-poisoned with paracetamol and those self-poisoning with prescription medication, including antidepressants (Haw et al., 2015). Two additional studies measured suicidal intent using the SIS (Simkin, Hawton, Kapur, & Gunnell, 2012; Townsend et al., 2001).

Regarding self-harm history, studies of young people engaging in intentional self-poisoning with paracetamol reported lower rates of previous suicide attempts (21-32%) (Hedeland et al., 2013; Hedeland et al., 2016; Shekunov et al., 2021) compared to studies with broad age ranges (38-67%) (Caroll et al., 2015; Casey et al., 2020; Cowman & Bakheet, 2017; K. Hawton et al., 1996; Simkin et al., 2012). One study reported that 29% of patients who had been admitted to hospital for intentional paracetamol self-poisoning had previously taken a paracetamol overdose (K. Hawton et al., 1996), while another study reported that 49% of patients had had a repeated paracetamol self-poisoning event (Payne, Oliver, Bain, Elders, & Bateman, 2009). There was some evidence to suggest that paracetamol and similar analgesics

were more commonly used in the first episode of self-harm compared to in a repeat self-harm episode (Alsen et al., 1994; Townsend et al., 2001). However, two Australian studies found that patients presenting to hospital for a repeat self-poisoning episode were more likely to ingest paracetamol compared to patients who self-poisoned on a single occasion (Martin, Chapman, Rahman, & Graudins, 2012; D. M. Taylor, Cameron, & Eddey, 1998). Further, one study found that analgesics and antipyretics were more likely to be used in a first-time self-harm attempt in comparison to other drugs (Vancayseele et al., 2019). In contrast, another study found that history of self-harm did not differ for paracetamol in comparison to other drugs (Caroll et al., 2015). A study by Daly and colleagues (Daly et al., 2020) found that 11% of people who intentionally self-poisoned with an analgesic had a repeat episode, and that 15.4% of these cases switched method within 12 months of their index attempt. Finally, a study by Payne and colleagues (Payne et al., 2009) reported that compared to anticonvulsants, antidepressants, antidiabetic drugs, benzodiazepines, and opiates, paracetamol was associated with a decreased risk of re-admission for self-poisoning, but risk of readmission did not differ between paracetamol and other drug categories, such as anticoagulants, antihistamines and salicylates.

Amongst studies that assessed psychiatric history, the proportion of cases with current symptoms and past psychiatric diagnoses varied from 46% to 95% (Cowman & Bakheet, 2017; Craig et al., 2011; K. Hawton et al., 1996; Pezzia et al., 2017; Piotrowska et al., 2019; Shekunov et al., 2021; Simkin et al., 2012). Notably, studies varied in how they assessed psychiatric history. Three studies examining history of psychiatric treatment reported rates between 26-40% (Caroll et al., 2015; Casey et al., 2020; Pezzia et al., 2017; Schiodt et al., 1997), with one of these studies finding no difference in receipt of past psychiatric treatment between people who had an intentional overdose with paracetamol compared to other drugs (Caroll et al., 2015). A small number of studies investigating the presence of chronic alcohol or substance abuse reported ranges from 11-42.7% (Caroll et al., 2015; Craig et al., 2011; Gyamlani & Parikh, 2002; Kjartansdottir et al., 2012; Mikhail et al., 2018). Findings regarding how the prevalence of chronic alcohol abuse differs between people engaging in intentional and those engaging in unintentional self-poisoning were mixed (Craig et al., 2011; Gyamlani & Parikh, 2002; Kjartansdottir et al., 2012; Myers, Li, & Shaheen, 2007; Pezzia et al., 2017; Schiodt et al., 1997). Two studies reported that the use of over-the-counter drugs in overdose was associated with the absence of a substance use disorder, relative to the use of other substances (e.g., prescription drugs) (Lo, Shalansky, Leung, Hollander, & Raboud, 2003; Mikhail et al., 2018).

Dose characteristics: Across the twelve studies that reported dosage in grams or by number of tablets, the mean or median dosage reported in intentional self-poisoning ranged from approximately 9 g or 18 tablets (Casey et al., 2020) to 27.5 g or 55 tablets (Craig et al., 2011), with a number of studies reporting median doses in this range (Cairns et al., 2019; Daly et al., 2021a; Graudins, 2015; Hedeland et al., 2013; Hedeland et al., 2016; E.-K. Kumpula, Lambie, Quigley, Nada-Raja, & Norris, 2020; Pezzia et al., 2017; Piotrowska et al., 2019; Schiodt et al., 1997; Shekunov et al., 2021). Other studies reported dose in milligrams per kilogram of body weight (192-262 mg/kg) (Bailey, Lalkin, Kapur, & Koren, 2001; Kominek et al., 2015), defined daily dose (2.2) (Martin et al., 2012), or provided information about the

distribution of the sample (Makin & Williams, 2000; Simkin et al., 2012). Some studies examined whether dosage varied by other participant characteristics, but results were mixed. While three studies found that a larger dose was associated with greater suicidal intent (K. Hawton et al., 1996; Schiodt et al., 1997) or that dose was greater for intentional than accidental self-poisonings (Craig et al., 2011), two other studies found that dosage did not differ between accidental and intentional self-poisonings (Alander et al., 2000; Alaniz & Janusz, 2007) and one found that the duration of suicidality was not associated with dosage (Hedeland et al., 2016). Findings were mixed as to the association between dosage and both age (Budnitz et al., 2011; Daly et al., 2021a) and gender (Casey et al., 2020; Daly et al., 2021a; Hedeland et al., 2016). One study found that self-poisonings using modified release paracetamol tended to be larger than those with immediate release paracetamol (Cairns et al., 2019). Only a few studies examined the relationship between access to paracetamol and dosage consumed, with one reporting that 58% of people took all available tablets in their self-poisoning episode(Simkin et al., 2012) and another reporting that 26% of people ingested the equivalent of one pack or multiples of a pack of tablets (Casey et al., 2020). Finally, two studies reported that staggered rather than acute self-poisoning occurred in 11% (Craig et al., 2011) and 13% (Piotrowska et al., 2019) of cases respectively.

Of the included studies, twelve reported on substances co-ingested in intentional overdose of paracetamol or over-the-counter analgesics. The majority of these studies reported that between 25% and 68% of cases involved co-ingestion of other drugs (Budnitz et al., 2011; Craig et al., 2011; Daly et al., 2021a; K. Hawton et al., 1996; Hopkins et al., 2020; Kjartansdottir et al., 2012; Piotrowska et al., 2019; Simkin et al., 2012; Weir & Ardagh, 1998), however one Swedish study reported that 88% of people used paracetamol in combination with other drugs (Alsen et al., 1994), while another study in adolescents reported that 13% of cases co-ingested over-the-counter medication with prescription medication (Larson, Johnson, & Sheridan, 2022). One study reported an average number of medications ingested of 1.51 (Shekunov et al., 2021). Two studies found evidence to suggest that single ingredient paracetamol was more often used on its own for younger age groups (Budnitz et al., 2011; Daly et al., 2021a). Finally, one study reported that other analgesics (Alsen et al., 1994) were the most common drugs co-ingested with paracetamol.

Most studies examining co-ingestion of alcohol reported that between 23% and 54% of people ingested alcohol at the time of intentional self-poisoning with paracetamol or similar medications (Casey et al., 2020; Craig et al., 2011; Daly et al., 2021a; Gyamlani & Parikh, 2002; K. Hawton et al., 1996; John et al., 2016; Pezzia et al., 2017; Schiodt et al., 1997; Simkin et al., 2012). However, one study conducted in Switzerland found that only 13% of intentional paracetamol self-poisoning patients co-ingested alcohol (Piotrowska et al., 2019). Two of these studies also found that males were more likely than females to consume alcohol at the time of self-poisoning (Casey et al., 2020; Daly et al., 2021a). There were mixed findings as to whether the prevalence of alcohol co-ingestion was different for intentional compared to unintentional self-poisoning cases (Craig et al., 2011; Kjartansdottir et al., 2012). One study found that rates of alcohol co-ingestion did not differ depending on whether the drug used in the intentional overdose was paracetamol or another drug (Caroll et al.,

2015). Another study found that use of analgesics or antipyretics rather than other self-harm methods was associated with alcohol co-ingestion among males (Vancayseele et al., 2019).

Other characteristics: For some characteristics, there were insufficient studies to draw conclusions. Only two studies examined previous exposure to suicide (Hedeland et al., 2013; Hedeland et al., 2016). Only one study reported on each of rurality (A. Rhodes et al., 2008), living situation (Hedeland et al., 2016), parental status (Mikhail et al., 2018), marital status (Pezzia et al., 2017), physical health (Mikhail et al., 2018), discovery of suicide attempt (Hedeland et al., 2013), location of self-poisoning (Hopkins et al., 2020), duration of suicidal ideation (Hedeland et al., 2016), presence or absence of a prescription for other medications (Vancayseele et al., 2019), and whether other self-harm methods were used in conjunction with self-poisoning (Daly et al., 2021a).

Table 32 presents the findings of studies that assessed the motivations, behavioural characteristics and knowledge of people engaging in self-poisoning via paracetamol or other non-opioid analgesics and tended to include outcomes such as self-poisoning motives, planning, access, impulsiveness of the self-poisoning behaviour, and knowledge of the effects and harms of paracetamol.

Method choice: Two of the identified studies assessed the reasons people choose to self-harm with paracetamol and found that the availability and ready access of paracetamol (both in the home and to purchase) was a key driver to its use, as well as an awareness that it could be dangerous and an effective method of self-poisoning (K. Hawton et al., 1995; Simkin et al., 2012). Knowing someone else who had self-poisoned with paracetamol was also a reason why some people chose to self-poison with paracetamol, as well as identifying it as a method of self-harm on the internet or reading or seeing it in the media (Simkin et al., 2012).

Access to paracetamol: Seven studies reported on access to paracetamol, with a recent study conducted with adolescents aged 11-17 years finding that 65.8% of participants self-poisoned with an over-the-counter medication that was available in their home (Larson et al., 2022). Another study in adults found that 53.3% of participants self-poisoned with paracetamol that was already in the home, while 35% accessed paracetamol from a supermarket, 28.3% from a pharmacy, and 13.3% from a local shop (Simkin et al., 2012). Three studies further reported that 52%-58.3% of participants purchased paracetamol specifically for intentional self-poisoning (K. Hawton et al., 1995; K. Hawton et al., 1996; Simkin et al., 2012). The ready access to paracetamol in the home, particularly among young people, was supported by a study by Gilbertson and colleagues (Gilbertson, Harris, Pandey, Kelly, & Myers, 1996) who reported that 86%-94% of students in the USA and UK reported having access to paracetamol in their homes. Two other studies also found that people who use over-the-counter medications and analgesics to self-harm are less likely to possess a prescription for psychotropic medications (Corcoran, Heavey, Griffin, Perry, & Arensman, 2013; Lo et al., 2003).

Planning and impulsivity: For the vast majority of people (73.3%-80%) who self-poison with paracetamol the period of planning or contemplation of the act occurs within 24 hours and for a proportion of these people (41%-50%) the period is even shorter and reported to be less than an hour (K. Hawton et al., 1996; Simkin et al., 2012). Similar levels of planning or impulsivity have been reported in studies conducted with young people. In one study of adolescents aged 10-17 years, only 21% of intentional self-poisonings with paracetamol were planned for more than 24 hours (Hedeland et al., 2016), while in a second study with young people aged 11-15 years the rate was even lower with only 12.5% of self-poisonings planned (Hedeland et al., 2013). According to a study by Simkin and colleagues (Simkin et al., 2012), people who took impulsive overdoses (within an hour of thinking about it) were more likely (63.3%) to take tablets already available in the home.

Motivations: Six of the identified studies assessed participant motives for paracetamol self-poisoning (K. Hawton et al., 1996; Hedeland et al., 2013; Hedeland et al., 2016; Makin & Williams, 2000; Schmidt, 2001; Simkin et al., 2012), with three focused only on young people aged 19 years and under. Some of the more common motives included a desire to die, to relieve a terrible state of mind or escape an intolerable situation, to make other people understand how desperate they were feeling, and to seek help (K. Hawton et al., 1996; Hedeland et al., 2013; Hedeland et al., 2016; Simkin et al., 2012). A smaller proportion of people reported self-poisoning to influence others or make them feel sorry (K. Hawton et al., 1996; Hedeland et al., 2013; Simkin et al., 2012). The act of self-poisoning was also reported as being an impulsive response to adverse life events (Makin & Williams, 2000; Schmidt, 2001), as a result of psychiatric disorders (Makin & Williams, 2000; Schmidt, 2001), or social problems with parents, friends, or school (Hedeland et al., 2013; Hedeland et al., 2016; Schmidt, 2001). In the most recent study with young people aged 10-17 years (Hedeland et al., 2016), 46.5% reported the purpose of their overdose was to die, 28.5% wanted to obtain relief from their thoughts, and 18.5% wanted to show how badly they were feeling. The most common reasons for self-poisoning were problems with parents (66%), problems with boyfriend/girlfriend (17%), non-academic problems in school (e.g., bullying; 17%), problems with friends (14.5%), and loneliness (12%). In terms of perceived support, 62% of cases reported feeling not heard or understood when they attempted to talk to their parents or another adult about their problems up to two months before their self-poisoning episode. Compared to age and gender-matched controls, young people who self-poisoned with paracetamol tended to report less close relationships with parents, siblings and friends (Hedeland et al., 2016).

Knowledge: Four of the identified studies reported on participant knowledge of paracetamol and its associated effects and potential for physical harm or death (Bolger, O'Connor, Malone, & Fitzpatrick, 2004; Gilbertson et al., 1996; K. Hawton et al., 1995; Simkin et al., 2012). Participants reported knowing that a paracetamol overdose could cause death and that it could cause harm to the liver, although the level of knowledge differed across studies (K. Hawton et al., 1995; Simkin et al., 2012). Another common finding was that people erroneously believed that self-poisoning with paracetamol would result in the loss of consciousness (Gilbertson et al., 1996; K. Hawton et al., 1995; Simkin et al., 2012). This was reported in studies with both adults and young people. One study further reported that 54.8%

of participants indicated that they wouldn't have self-poisoned with paracetamol if they had known that they would not lose consciousness (Simkin et al., 2012). Participant knowledge of the number of tablets needed to do harm or cause death was also mixed. In a study of young people aged 14-20 years 52% estimated that 30 or more tablets would need to be taken before any adverse effects would be experienced (Bolger et al., 2004), while a second study reported that 45% of UK students and 41% of USA students overestimated the dose of paracetamol needed to kill at 100 or more tablets (Gilbertson et al., 1996).

Two studies also assessed potential deterrents of intentional self-poisoning, finding that box warnings were unlikely to deter behaviour in most people (K. Hawton et al., 1996; Simkin et al., 2012). In the first study, only 25% of participants thought a warning label would have stopped them from self-poisoning (K. Hawton et al., 1996), while in a second study 80% of participants reported that a packet warning would not have affected their self-poisoning behaviour (Simkin et al., 2012). The effect of smaller pack sizes was variable between the two studies that assessed it, with 37% of participants in one study indicating that they would have taken a smaller overdose or no overdose if packs had been smaller (12 tablets) (K. Hawton et al., 1996), while the other study reported that 89.7% of participants would still have taken an overdose (although pack size was not specified) (Simkin et al., 2012). The majority of participants (64%) in one study indicated that they wouldn't have intentionally self-poisoned if paracetamol contained an antidote to stop the harms of self-poisoning (K. Hawton et al., 1996).

Summary of the findings for Research Question 1:

Intentional self-poisoning with paracetamol tends to be more common among females compared to males, and among adolescents and young adults, rather than children or older adults. The majority of intentional self-poisoning cases have suicidal intent, with other motivations including seeking help from others and emotion regulation. Past or current psychiatric disorders are evident in at least half of cases, and include diagnoses of major depression, anxiety, adjustment disorder, and alcohol and substance use disorders. Young people who self-poisoned with paracetamol often do not have a prior history of self-harm, suggesting that paracetamol might be commonly used in a first attempt. Regarding dose characteristics, the most common overdose sizes are similar to one pack, or multiples of a pack. A proportion of people co-ingest other medications and/or alcohol, with the latter being more common among males.

The ready accessibility of paracetamol was a key contributor to its use, with people tending to access it from supplies already in the home, or to purchase it from pharmacies or supermarkets. Self-poisoning with paracetamol was most often impulsive, with periods of planning reported to be less than one hour in approximately half of cases, and less than a day in approximately three quarters of cases. Use of paracetamol for intentional self-poisoning was more common when there was reduced access to other medications, including prescription medications. In general population samples, knowledge of the effects of paracetamol overdose was often poor. The quantity of paracetamol required for a harmful or lethal dose was often overestimated and self-poisoning with paracetamol was unlikely to be deterred through packet warnings.

There was little explicit data on the role of education of the public around the dangers of paracetamol and its storage in the home. Our review did not find any studies investigating the effects of awareness programs around paracetamol safety on the rate of self-poisoning.

Question 2. The restriction of paracetamol or other medications and method substitution

Research examining the impact of restricting access to medications commonly used in self-poisoning is important to determine if it results in a reduction in use and whether other means of self-poisoning or self-harm are used in substitution. In total we identified 15 articles (see Table 33) that contained data relevant to the restriction of paracetamol or other medications and method substitution. The identified studies were published in a range of countries including the UK (n = 8), Australia (n = 4), Ireland (n = 2), and Denmark (n = 1).

These studies were observational, reporting outcomes before and after the implementation of the restriction. Medications that were restricted included paracetamol, aspirin, codeine and co-proxamol. Types of restrictions included pack size limits (n = 5; four of these also involved warnings of the danger of overdose and conversion to blister packs), withdrawal of a particular medication (n = 5), recall of a product (n = 2), change in the schedule of a

medication (*n* = 2), restriction in age for purchase *(n* = 1), and improving sales guidelines (*n* = 1). To elucidate the impact of each restriction, a narrative synthesis has been conducted discussing each restriction imposed in each country separately.

Pack size limits of paracetamol and aspirin in the UK: Legislation introduced in 1998 in the UK reduced packs containing paracetamol, aspirin or both to 32 tablets in pharmacies and 16 tablets in other retail outlets. Restrictions on pack sizes was applied to both paracetamol and aspirin due to concerns that if only paracetamol were included then there would be a risk of substitution with aspirin. In addition, warnings were placed on packs highlighting the danger of overdose, and paracetamol became almost exclusively available in blister-pack form.

Impact on paracetamol use

Three of the four studies examining the 1998 pack size restriction in the UK found evidence of a reduction in paracetamol related deaths (K. Hawton et al., 2004; O. Morgan, Griffiths, & Majeed, 2005; O. W. Morgan, Griffiths, & Majeed, 2007), and this pattern was consistent when intentional and non-intentional self-poisoning deaths were considered separately (K. Hawton et al., 2004). The effect on other outcomes was less clear, with mixed evidence of a reduction in non-fatal overdoses (K. Hawton et al., 2004; O. Morgan et al., 2005; Turvill, Burroughs, & Moore, 2000), and some evidence of a reduction in liver toxicity complications (K. Hawton et al., 2004). One study also found the number of tablets taken in a self-poisoning episode reduced following the restriction and was sustained in subsequent years (K. Hawton et al., 2004).

Impact on potential method substitution

There was mixed evidence of method substitution. All deaths from ibuprofen increased 2.2-fold and suicide/open verdict deaths increased 2.1-fold following the legislation change, suggesting some evidence of substitution. However the total number of deaths was small (less than 10 deaths in 3 years) (K. Hawton et al., 2004). There was also an increase in non-fatal overdoses using ibuprofen which was not accompanied by a change in the number of ibuprofen tablets or number of large (i.e., over 32 tablets taken) ibuprofen overdoses (K. Hawton et al., 2004). In contrast, suicides with non-drug poisoning declined after the restriction (O. W. Morgan et al., 2007). The frequency of overdose with benzodiazepine, the next most common cause of deliberate self-harm after paracetamol remained stable (Turvill et al., 2000). Mortality associated with compound paracetamol, which was not affected by the legislation, remained relatively constant throughout the study period (O. Morgan et al., 2005) or decreased when age-standardised mortality rate was assessed (O. W. Morgan et al., 2007). Similarly, there was a decrease in age-standardised mortality rates for all poisonings (excluding opioids and paracetamol) (O. Morgan et al., 2005).

Recall causing lack of supply of paracetamol in Australia: In Australia, paracetamol was recalled in 2000 from two major suppliers in two stages causing a limit on its supply. These recalls were due to extortion threats made to two pharmaceutical companies in Australia,

involving the addition of strychnine to some paracetamol-containing capsules. All paracetamol-containing products made by these companies during the respective time period were recalled, irrespective of the date of purchase (Balit, Isbister, Peat, Dawson, & Whyte, 2002). Other brands of paracetamol were still available during this period, however the recall caused an overall reduction in the supply of paracetamol and provided a unique environment to examine the impact on rates of deliberate self-harm calls and hospital admission for paracetamol poisoning.

Impact on paracetamol use

The first recall period was associated with a non-significant reduction in calls to a PIC for paracetamol intentional self-poisoning (Balit et al., 2002). The effect of the recall on hospital admission for paracetamol overdose varied (Balit et al., 2002; Kisely, Lawrence, & Preston, 2003). While one study conducted at the Hunter Area Toxicology Service (HATS; an inpatient service for a population of approximately 500,000 people) did not find a significant change in the proportion of deliberate self-harm presentations (Balit et al., 2002), a second study in Western Australia reported a decrease in admission rates for paracetamol poisoning (Kisely et al., 2003). This difference may be attributed to different locations, population and number of admissions to services or consideration of intentional admissions as compared to all admissions. It is important to note that other brands of paracetamol were available during the study period and may have contributed to these results. Mortality was not assessed in these studies.

Impact on potential method substitution

To characterise if there was method substitution during this period, the use of aspirin, ibuprofen and other non-paracetamol agents were measured concurrently. One study found that there was an increase in the number of deliberate self-harm calls to NSW PIC for ibuprofen, but not aspirin (Balit et al., 2002). Presentations to HATS significantly increased for aspirin but not for ibuprofen during the recall period (Balit et al., 2002). In contrast, hospital admissions did not increase for aspirin, ibuprofen or other non-paracetamol agents during the paracetamol recall period. As above, this may be due to differences in study parameters. On the whole, these findings suggest that there was minimal method substitution during the paracetamol recall period in 2000.

Withdrawal of co-proxamol in the UK and Ireland: Five identified studies focused on the withdrawal of a compound analgesic composed of 325 g paracetamol and 32.5 g dextropropoxyphene, licenced as the painkiller co-proxamol. Based on a review of co-proxamol's efficacy/safety profile by the Medicines and Healthcare products Regulatory Agency, it was advised by the Committee on Safety of Medicines to withdraw co-proxamol, starting January 2005 with completion by 31 December 2007. Based on this, Ireland also withdrew co-proxamol (referred to as Distalgesic) from their market in 2006.

Impact on co-proxamol use

All studies reported significant reductions in the proportion of poisoning deaths due to co-proxamol following its withdrawal (K. Hawton et al., 2009; K. Hawton et al., 2012; Sandilands & Bateman, 2008). Similarly, non-fatal self-poisoning using co-proxamol reduced after the restriction (K. Hawton et al., 2011). Reductions in hospital presentations for intentional drug overdose from co-proxamol were also observed in Ireland after withdrawal (Corcoran et al., 2010).

Impact on potential method substitution

Results consistently showed that non-fatal self-poisoning and mortality associated with other medications measured in parallel did not increase in response to co-proxamol withdrawal (K. Hawton et al., 2009; K. Hawton et al., 2012; K. Hawton et al., 2011; Sandilands & Bateman, 2008). The number of prescriptions increased for many of these medications, however it did not result in a change in mortality (K. Hawton et al., 2009; Sandilands & Bateman, 2008). In Ireland, there were increased presentations to hospital involving intentional self-poisoning for other prescription compound analgesics, however the magnitude of this rate increase was five times smaller than the magnitude of the decrease in co-proxamol-related overdose (Corcoran et al., 2010). Therefore, the withdrawal of co-proxamol resulted in increased prescription of other medications, however this did not translate to an increase in mortality.

Sales guidelines for codeine in Ireland: In Ireland in 2010, the guidelines for the sale of codeine were tightened to include specific criteria for its sale, reiterating its pre-existing classification as a Schedule 5 drug (available over-the-counter under pharmacist supervision). This increased guidance resulted in a reduction of codeine-related intentional overdoses (Birchall, Perry, Corcoran, Daly, & Griffin, 2021). There was no change identified in overdoses due to other opiates, or all medications as a whole (Birchall et al., 2021). Instead, the rate of intentional overdose with non-opioid analgesics decreased over the study period.

Age restriction and pack size limits in Denmark: In 2011 in Denmark, an age restriction was implemented for the purchase of over-the-counter non-opioid analgesics, such that they could not be purchased by people under the age of 18 years. The age restriction resulted in a 17% reduction in non-opioid analgesics poisonings in people aged 10-17 years, however no change was observed in the other age groups (Morthorst et al., 2020). The age restriction was also associated with a 10% reduction in hospital admissions for poisoning by substances other than non-opioid analgesic (Morthorst et al., 2020). This appeared to be associated with the age restriction placed on purchasing as when stratified by age, the reduction was observed in 10 to 17 year-olds, but not in other age groups.

In 2013, a second piece of legislation was introduced reducing pack sizes to 20 tablets for non-opioid analgesic medication. This resulted in a substantial reduction in hospital admissions for over-the-counter non-opioid analgesics, and for substances other than non-opioid analgesics (Morthorst et al., 2020). A reduction in suicide attempts using violent methods following the pack size restriction indicates that substitute methods of self-harm were not used.

Up-scheduling of codeine in Australia: In 2018 in Australia, low-strength codeine products were up-scheduled from Schedule 3 (pharmacist only) to Schedule 4 (prescription only). Overall, there were reductions in the number of calls related to intentional codeine poisoning, a reduction in emergency department presentation for low-strength codeine and reduced deaths related to codeine (Cairns, Schaffer, Brown, Pearson, & Buckley, 2020a; Harris, Jiang, Knoeckel, & Isoardi, 2020). This up-scheduling did not result in increased calls (Cairns et al., 2020a) or increased hospital presentations (Harris et al., 2020) for other pharmaceutical opioids and over-the-counter products (Cairns et al., 2020a), suggesting these medications were not used as a substitute.

Summary of the findings for Research Question 2:

Included studies examined the effect of changes in the availability of various medications on self-poisoning using the restricted medication, and on self-harm using other medications or means. Types of restrictions examined included pack size reductions, medication withdrawals, up-scheduling and age restrictions. Assessment was made using various outcomes (e.g., calls to poisoning helplines, hospitalisations, deaths) with all except one study reporting a decrease in the use of the restricted medication in self-poisoning. Despite the high incidence of self-poisoning using paracetamol among young people, the effect of an 18+ age purchasing restriction was only examined in one study, conducted in Denmark. This study reported a decrease in self-poisoning using over-the-counter non-opioid analgesics among people aged 10-17 years. Overall, there was little evidence of method substitution across studies.

Limitations and identified gaps in the literature

While the search terms were comprehensive, it is possible that some relevant papers were not captured in the search process. For instance, some papers examining the effect of restricting prescription drugs (relevant to research question two) may not have been identified as the search did not include the names of specific prescription drugs (as was the case for non-prescription drugs), but rather used the 'pharmaceutical preparations' major subject heading. While this did limit the search outcomes, which was required given the short timeframe for the review, it is unlikely to have affected the overall findings of the review, which was focused on the effects of paracetamol self-poisoning and related over-the-counter medications.

Some of the studies identified in the current review had small sample sizes. The results of these studies should be interpreted with this limitation in mind, with greater weight and consideration given to the larger studies. The majority of studies examining characteristics of people who self-poison identified their sample through presentations or admissions to hospital emergency departments. Given that many people who self-harm do not seek medical treatment or present to hospital, these samples may not accurately reflect the characterises of all those who self-poison with paracetamol (Arensman, 2018).

Included studies also varied in their definition of 'intentional self-poisoning', with some studies using this term to refer exclusively to instances of deliberate self-harm, while others included recreational use and intentional misuse under this label. For the first research question, studies were excluded from the current review if they did not differentiate between intentional and accidental self-poisoning, as aetiology of these can be different. However, studies addressing the second research question did not need to distinguish between intentional and accidental self-poisoning, meaning we are limited in our understanding of the effect of restrictions on *intentional* self-poisoning.

The research captured in this review spanned the past 30 years and while this is still very informative, it is possible that the effects of more recent sociocultural changes may not have been adequately captured. For instance, research on the use of online pharmacies to access paracetamol or other drugs to self-harm was not identified. Furthermore, no studies examined the effect of the COVID-19 pandemic on self-poisoning using paracetamol; nonetheless, data examined by the NSW PIC in this report does capture paracetamol self-poisoning trends since the onset of the pandemic.

Much of the research identified is based on administrative datasets, with a few generally older qualitative studies assessing participant motives and planning processes. None of these qualitative studies had been conducted in Australia. As such, there would be value in undertaking further qualitative research with people with a lived experience of self-harm with paracetamol to better understand their experiences, potential triggers for the self-harming behaviour and insights into preventative factors.

In the studies obtained, six different restrictions were identified with only three including paracetamol or other over-the-counter analgesics. This may either indicate that few restrictions have been implemented or that they have not been examined in depth. Examination of reduced pack sizes was completed in two countries (UK and Denmark) as was the withdrawal of co-proxamol (UK and Ireland), however all other restriction were only conducted in one country. Whilst most studies indicated the restrictions were effective, it does highlight the need to consider research in the design phase of the restriction to be able to monitor and ensure safety and efficacy of the approach.

In addition, we focused only on papers that reported on the effect of the restriction on the medication of interest and possible method substitution. In doing so, nine studies were excluded as they did not measure other methods that may be used in substitution to the restricted medication. Measuring other means of self-harm and suicide in parallel are important when designing a study to ensure that other more lethal or toxic means are not used. Therefore, consideration of this in future research is important to ensure any reductions observed are not due to the use of different methods.

Summary of findings from literature review

Below is a high-level summary of the findings of the literature review and associated implications for suicide prevention approaches.

Literature review findings	Implications for suicide prevention approaches
Paracetamol use in intentional self-poisoning is greater in females than males, and more common among adolescents and young adults aged under 25 compared to children or older adults.	Although suicide deaths are more frequent in men than women in Western countries, the reverse is the case with self-harm. More research is needed to understand why rates of self-harm are rising in young females at younger ages and the longer-term impact of these rising rates (e.g., in terms of future mental health outcomes, self-harm and suicide). Such research would also assist in the development of early intervention programs targeting women, children and adolescents to reduce the frequency of self-harm and hospitalisations in this cohort in Australia.
Paracetamol is likely to be the first substance used for self-poisoning at the first attempt, particularly among young people. Not all of those with intentional self-harm with paracetamol have a psychiatric diagnosis or mental health symptoms.	Attempts to reduce paracetamol use should cast a wide net. Universal preventative strategies, such as means restriction, are likely to reduce first attempts at self-harm and reduce the severity of such attempts. Many of those at risk do not have current psychiatric symptoms so remain unidentified through clinical or educational services.
The median dose used in an attempt ranges from 9 g or 18 tablets to 27.5 g or 55 tablets, and there is some evidence that users take the full package available to them when making an attempt.	Package size restriction is likely to be an effective harm minimisation strategy.
Between 25-68% of attempts involve co-ingestion of other substances (usually other analgesics) or alcohol (23-54%) although co-ingestion in young people may be less common than in older people, and co-ingestion of alcohol specifically more likely to be a feature in men.	Efforts to successfully reduce alcohol use in young people through school-based programs should be continued. Specific education around alcohol and self-poisoning should be considered through education to the public, clinicians, youth workers, schools and workplaces.
Paracetamol is readily available. Access is made through home supplies and/or by deliberate purchasing in supermarkets and pharmacies*.	Easy access to paracetamol should be restricted through relevant means, such as reducing pack size (in order to reduce paracetamol supply within the home). Specific warning labels on the medication themselves do not seem to be an effective strategy. Although there were no explicit studies, public education messages about the importance of safety with respect to medications in the home (use- by-dates, keeping medications out of harm's way; potential physical health effects of taking wrong medications) might be a useful but untested

	strategy to reduce the use of paracetamol for self-harm.
Planning is generally short term (less than 24 hours) and often less than an hour among young people. Impulsive self-poisoning often occurs using products found in the home.	More research is required to increase our understanding of the behaviours and motivations of young people engaging in intentional self-poisoning using paracetamol. Self-harm is likely to be reduced by limiting availability of paracetamol in the home, potentially through reducing pack sizes. Age restriction of 18 years for purchase in pharmacies or supermarkets, should be considered given the small but promising data from Denmark that shows reduced rates.
The motivations to take paracetamol appear similar to other forms of self-harm- people want to die, need to escape, and want to alert people to how desperate they are.	Continue current suicide prevention activities, consistent with the National Suicide Prevention Advisor's final advice https://www.mentalhealthcommission.gov.au/national-suicide-prevention-office/national-suicide-prevention-adviser-final-advice This includes better access to treatment for all age groups, systematic approaches to community support to adults and young people, education and health supports for parents and young people, access to healthcare after emergency presentation, and to evidence-based treatment.
Mental health literacy around paracetamol is potentially limited or not known. This includes knowledge about the effects, the dose, that consciousness may not be lost, that effects can be catastrophic even at doses considered "low".	Increase health literacy while maintaining control of the real potential effects of contagion. Explicit messaging around suicide risk should not be considered unless potential contagion effects are considered. Any messaging should take into account media guidelines around suicide prevention (https://mindframe.org.au/suicide/communicating-about-suicide/mindframe-guidelines) and suicide messaging guidelines for youth (https://www.orygen.org.au/chatsafe) .
Reduction in pack size has been found to reduce deaths from poisonings by about a third, although its effects may be less for non-lethal outcomes. There is very little evidence across 15 studies that method substitution arises, and thus may be of low risk.	Restrict access to paracetamol by further restricting access (e.g., reducing pack sizes), while monitoring potential increases in use by other substances. To reduce the risk of means substitution, any pack size restrictions or purchasing limits placed on paracetamol in supermarkets or pharmacies should also be considered for consistency for other over-the-counter medications, such as ibuprofen and aspirin (i.e., treating all analgesics available in the same types of stores similarly). Educate the community about the reasons for tighter restrictions to ease any potential fallout.

Table 31. Studies examining characteristics associated with intentional self-poisoning with paracetamol or other non-opioid analgesics

First author (Year) Region, Country	Study type	Medication(s) examined (comparison medications)	Population description	Sample Size	Age (years)	Proportion Intentional	Key findings for intentional self-poisoning cases
Studies examining paracetamol							
Alainz (2007) (Alaniz & Janusz, 2007) USA	Observational or cohort	Paracetamol	Patients with presumed paracetamol toxicity who presented to a large university hospital from July 1999 to June 2002	179 (128 adults; 51 paediatric)	Adults: M = 36; SD = 12.5 Paediatric M = 14.3; SD = 4.0	60.9% of adult cases, 82.4% of paediatric cases	**Sex:** A significantly greater proportion of the paediatric cases were female (78.6%) compared to the adult group (64.1%) **Suicidal intent:** 19.6% of paediatric cases and 8.3% of adult cases were classified as intentional without suicidal intent (e.g., angry gesture) **Dosage:** Did not differ based on intentionality for adult or paediatric cases **Adult cases:** more likely to be younger, not have a history of alcohol abuse, and have a history of depression **Paediatric cases:** More likely to be older, and have a history of depression
Alander (2000) (Alander et al., 2000) Kansas City & Seattle, USA	Observational or cohort	Paracetamol	Paediatric presentations to ED or inpatient unit at two hospitals in the US with a chief complaint of paracetamol ingestion from January 1, 1988, to December 31, 1997	332	Total sample: M = 7.9; SD = 6.1, range = 2 months-17; Intentional ingestion: M = 14.3; SD = 1.3; range = 11-17	43.5%	**Sex:** 78.6% female. **Age:** Tend to be older than non-intentional ingestions (median age = 14) **Dosage:** Median dose was 4-8.3mg/kg and did not vary by intentionality
Alsen (1994) (Alsen et al., 1994) Lund, Sweden	Qualitative	Paracetamol (other self-poisoning drugs)	Subsample of patients over 18 years old admitted to the ICU of Lund University Hospital after intentional self-poisoning suicide attempt from 1987 to 1990	280	Males: M = 38; range = 18-92 Females: M = 39; range = 19-87	100%	**Age:** Younger cases more likely to only use analgesics in attempt **Suicide intent:** 100% participants reported self-poisoning as a suicide attempt **Co-ingestion of substances:** 88% cases used paracetamol in combinations with another drug, most often other analgesics **Self-harm history:** Use of analgesics more common in first episode of self-harm (vs. repeaters)
Angalakuditi (2006) (Angalakuditi et al., 2006) USA	Observational or cohort	Paracetamol	Poisonings in children under 18 years reported to an American Association of Poison Control Centre from 2000 to 2003	473	Range = <18. Females: M = 6.3; SD = 5.9 Males: M = 3.5; SD = 3.9	19.0%	**Sex:** 86.57% of intentional cases 13-17 years were female **Suicidal intent:** 87.8% of intentional poisonings in cases 13-17 years suspected suicide
Bailey (2001) (Bailey et al., 2001) Toronto & Ontario, Canada	Observational or cohort	Paracetamol	Children admitted to the Hospital for Sick Children, Toronto, Ontario with a diagnosis of paracetamol overdose from January 1, 1990, to June 31, 1996	110 (106 adolescents)	Adolescents: M = 14.8; SD = 1.3; range = 10-16	100%	**Dosage:** Mean dose for adolescents was 262mg/kg (SD = 192)

First author (Year) Region, Country	Study type	Medication(s) examined (comparison medications)	Population description	Sample Size	Age (years)	Proportion Intentional	Key findings for intentional self-poisoning cases
Beautrais (1998) (Beautrais et al., 1998) Christchurch, New Zealand	Case-control	Paracetamol	Consecutive series of individuals aged under 25 years who made medically serious suicide attempts (requiring hospital admission for more than 24 hrs) from September 1, 1991, to May 31, 1994, in Christchurch	129	M = 19.4; SD = 3.0; range = 13-24	100%	**Age:** Teenagers who made serious suicide attempts by self-poisoning tended to use paracetamol (54.2%) more often, while those in the older bracket (20-24 years) more frequently used tricyclic antidepressants (54.2%) **Sex:** No significant gender differences in the types of drugs used by young people who made serious suicide
Bloch (2013) (Bloch et al., 2013) Nuuk, Greenland	Observational or cohort	Paracetamol (other self-poisoning drugs)	Patients who resided in Nuuk admitted to Dronning Ingrids Hospital for medicine-induced suicide attempt from 2008 to 2009	74 cases (43 with paracetamol)	Range = 15+	100%	**Age:** Paracetamol self-poisoning was most prevalent in the 20-24 age group (77% of suicide attempts with medication). The highest incidence was among women aged 20-24
Budnitz (2011) (Budnitz et al., 2011) USA	Observational or cohort	Paracetamol	ED visits for an overdose of a paracetamol-containing product from January 1, 2006, to December 31, 2007, identified from the National Electronic Injury Surveillance System	2,717 cases (1,857 intentional overdose)	Intentional overdose: Median = 29; range = 10-85 Therapeutic misadventure: Median = 35; range = <1-93 Unsupervised child ingestion: Median = 2; range = <1-10.	69.8%	**Sex:** 65.9% of cases were female; difference between genders narrowed with age **Age:** Population rates of self-directed violence visits highest amongst cases 15-24 years and declined with increasing age **Co-ingestion of substances:** 52.7% cases involved >1 medication, although single ingredient paracetamol involved in most cases 24 years and under **Dosage:** 39% of cases ingested 10 or fewer pills, 24% 11-20 pills,14.7% 21-30 pills, 4.8% 31-40 pills, 3.8% 41-50 pills, 8.6% ≥51 pills, 5.1% ≥ half a bottle. Number of pills did not vary by age
Cairns (2019) (Cairns et al., 2019) Australia	Observational or cohort	Paracetamol	Paracetamol overdoses identified through the New South Wales Poisons Information Centre (NSW PIC) from 2004 to 2017	22,997 intentional overdose calls	Median = 18; IQR = 16-28	100%	**Sex:** 70.4% of calls were about female cases **Dosage:** Median number of tablets taken per self-poisoning reported was 15 in 2004 (IQR = 10-24) and 20 in 2017 (IQR = 10-35). Self-poisonings with modified release paracetamol (Median = 19 tablets) were larger than with immediate release paracetamol (Median = 16 tablets)
Carroll (2015) (Caroll et al., 2015) Bristol, UK	Observational or cohort	Paracetamol (other self-poisoning drugs)	Patients 16 and older who had taken an overdose of paracetamol or another drug from May 2011to April 2012 recorded in the Bristol Self-harm Surveillance Register after presentation to the Bristol Royal Infirmary ED with self-harm	851 cases (374 with paracetamol, 477 non-paracetamol)	Paracetamol overdose sample: Median = 29; IQR = 21-43 Non-paracetamol overdose sample: Median = 33; IQR = 24-36	100%	**Sex:** 61.8% paracetamol cases were female, and this gender ratio was not significantly different to that of non-paracetamol self-poisoning cases **Age:** Cases self-poisoning with paracetamol were significantly younger than other self-poisoning cases **Self-harm history:** 67.1% of paracetamol cases had a previous self-harm episode, and the proportion with a previous self-harm episode history was not significantly different to other self-poisoning cases **Past psychiatric treatment:** 37.1% of paracetamol cases had received psychiatric treatment in the past, and the proportion with past psychiatric treatment was not significantly different to other self-poisoning cases. **Alcohol use:** 42.1% paracetamol cases reported alcohol misuse, and rate of alcohol misuse was not significantly different for other self-poisoning cases

First author (Year) Region, Country	Study type	Medication(s) examined (comparison medications)	Population description	Sample Size	Age (years)	Proportion Intentional	Key findings for intentional self-poisoning cases
Casey (2020) (Casey et al., 2020) England, UK	Observational or cohort	Pure paracetamol, excluding compounds	Data collected from Multicentre Study of Self-harm in England which included self-harm presentations to five Eds from 2004 to 2014	13,171 people (18,011 episodes)	10-19 = 37.9% 20-34 = 24.6% 35-54 = 16.6% 55+ = 20.2%	100%	**Sex:** Rates of self-poisoning were higher in females as compared to males **Age:** Cases aged 10-19 years significantly more likely to have used pure paracetamol in self-poisoning compared to other age groups **Alcohol use:** 53.7% cases also consumed alcohol (higher in males) **Self-harm history:** 59.7% had self-harmed in the past **Current psychiatric treatment:** 38.7% cases receiving current treatment **Past psychiatric treatment:** 49.4% cases received psychiatric care in past **Dosage:** Mean = 24.5 tablets, Median = 18 tablets, Maximum = 400. 24.2% of cases consumed >2 packs, and 40.2% used equivalent of up to 1 pack (16 tablets). 26.3% took an exact multiple of 16 tablets (i.e., consumed by the pack). Males took larger doses than females. Proportion of people taking more than 2 packets increased with age group
Cowman (2017) (Cowman & Bakheet, 2017) UK	Observational or cohort	Paracetamol	Sequential patients presenting to Accident and Emergency at a British hospital from March 2015 to July 2015 with a final diagnosis of paracetamol overdose	34	M = 27; range = 1-65	85%	**Self-harm history:** 38% of intentional self-poisoning patients had a history of previous overdoses **Previous psychiatric history:** 76% of intentional self-poisoning patients had a previous history of psychiatric illness, such as depression, unstable personality disorders, and anorexia nervosa
Craig (2011) (Craig et al., 2011) UK	Observational or cohort	Paracetamol	Patients admitted to the Scottish Liver Transplant Unit from November 1, 1992, to October 31, 2008, with suspected severe acute liver injury due to paracetamol overdose	938	Intentional: Median = 33; IQR = 24-43 Unintentional: Median = 40; IQR = 30-48	75.4%	**Sex:** 50.4% of intentional self-poisoning cases were female, and this gender ratio was not significantly different from unintentional cases **Age:** Intentional self-poisoning cases were younger than unintentional poisoning cases **Dosage:** Median dose was higher for intentional self-poisoning cases (27.5g, IQR = 20-45) compared to unintentional self-poisoning cases (11.0g, IQR = 5-29). **Co-ingestion substances:** 48.1% paracetamol only, 24.7% compound narcotic/paracetamol use; 27.2% mixed overdose **Alcohol use:** 42.7% co-ingested alcohol; 20.8% experienced alcohol abuse. Rate of alcohol co-ingestion and alcohol abuse were both lower for intentional compared to unintentional cases. **Staggered overdose:** Prevalence of staggered overdose was significantly lower for intentional self-poisoning (10.6%) than unintentional self-poisoning (90.8%). **Previous psychiatric history**: Prevalence of previous psychiatric history was higher for intentional self-poisoning (46.2%) than unintentional self-poisoning **Active illicit drug use:** 16.7% of intentional self-poisoning cases had active drug use, and this was not significantly different for unintentional cases
Daly (2021) (Daly et al., 2021a) Ireland	Observational or cohort	Paracetamol	Data obtained from the National Self-Harm Registry Ireland, a national surveillance system which monitors hospital-	10,985	Range = 10-24	100%	**Sex and Age:** Male to female ratio of presentations was 1:4; 40.9% cases in females aged 18-24 years (40.9%) **Dosage:** 72% paracetamol only cases involved fewer than 25 tablets (median = 20), and the median number of tablets taken was

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			presenting self-harm episodes across all acute hospitals in the Republic of Ireland. Presentations made by young people aged 10-24 years, from January 1, 2007, to December 31, 2018, were included				significantly higher among males and for persons aged 18-24 years. Median tablets taken in 10-17 year males = 20 (IQR= 19), females 10-17 years = 18 (IQR =15), males 18-24 years = 24 (IQR = 27); females 18-24 years = 23 (IQR = 22) **Co-ingestion substances:** 55.3% cases involved more than one drug type and 30.9% young people took three or more distinct drug types **Alcohol use:** 24.6% also consumed alcohol and this was higher in males **Other self-harm methods:** 91.2% cases involved no other methods
Daly (2018)* (Daly et al., 2018) Ireland	Observational or cohort	Paracetamol (other self-poisoning drugs)	Intentional drug overdoses for the period January 1, 2012, to December 31, 2014, drawn from the National Self-Harm Registry Ireland.	18,329 (5,087with paracetamol)	Median = 33; IQR = 23-45	100%	**Sex:** Paracetamol was involved significantly more often in female intentional self-poisonings (32.0% vs. 21.7%) **Age:** Paracetamol intentional self-poisoning highest among persons under 25 years (36.2%) and was present in 43.8% of intentional self-poisonings by females aged under 25 years
Downes (2021) (Downes et al., 2021) Australia	Observational or cohort	Paracetamol (other self-poisoning drugs & bites/stings)	All emergency department presentations of paediatric poisoning cases under 18 years reported to a tertiary toxicology service from January 1, 2015, to December 31, 2016	677 (150 with paracetamol)	Pre-school: Median = 2; IQR = 1–3 Primary school: Median = 9; IQR = 8-10 Adolescents: Median = 16; IQR = 14-17 Adults: not reported	66%	**Age:** Paracetamol intentional self-poisoning more common in paediatric sample compared to adult sample
Friðriksdóttir (2021) (Fridriksdottir Th et al., 2021) Iceland	Observational or cohort	Paracetamol	All patients with a measurement of serum paracetamol who had been admitted to Landspitali University Hospital in Iceland between January 1, 2010, and December 31, 2017	542	All ages	81%	**Sex:** Intentional self-poisoning occurred more often in females (85% vs. 70%) **Age:** 45% of intentional self-poisoning occurred in the age group 16-25 years
Gedeborg (2017) (Gedeborg et al., 2017) Sweden	Observational or cohort	Paracetamol	Potential cohort members were identified from hospital discharge diagnoses and cause of death in national health-care databases, as well as laboratory results on serum paracetamol. All 21 regions in Sweden were asked to provide serum paracetamol results from January 1, 2000, to December 31, 2013	12,068 poisonings	Median = 28	85%	**Sex:** 79% of intentional cases female **Age:** 41% of intentional cases aged 15-24 years (highest proportion)
Graudins (2015) (Graudins, 2015) Australia	Observational or cohort	Paracetamol	Patients with paracetamol poisoning presenting to Monash Health Eds from October 1, 2009, and September 30, 2013	867 (220 adolescents, 647 adults)	Adolescents: Median = 16; IQR = 12-17 Adults:		**Age:** Adolescents were significantly more likely to present with intentional self-poisoning and less likely to present with report of an accidental supratherapeutic ingestion of paracetamol than adults **Dosage:** No acetylcysteine treatment required: 7g (IQR = 5-10g); Acetylcysteine treatment required: 18g (IQR = 12-25g)

First author (Year) Region, Country	Study type	Medication(s) examined (comparison medications)	Population description	Sample Size	Age (years)	Proportion Intentional	Key findings for intentional self-poisoning cases
					Median = 27; IQR = 18-88		
Gyamlani (2002) (Gyamlani & Parikh, 2002) USA	Observational or cohort	Paracetamol	Patients with a discharge diagnosis of paracetamol overdose from January 1996 to April 1999 at the Nassau University Medical Center	93	Intentional: M = 27; SD = 15; range = 12-75 Accidental: M = 35; SD = 22, range = 1-88	86%	**Suicidal intent:** 100% of intentional cases had suicidal intent **Age:** Intentional cases tended to be younger than the accidental cases **Sex:** Intentional cases had a female to male ratio of 2:1, which was not significantly different from accidental cases **Alcohol use:** 45% also consumed alcohol during their overdose; 18% experienced chronic alcohol abuse (not significantly different from those with accidental overdose)
Haw (2015) (Haw et al., 2015) UK	Observational or cohort	Paracetamol (other self-poisoning drugs)	Patients who presented to John Radcliffe Hospital in Oxford following an episode of self-harm from 2004 to 2011, identified via the Oxford Monitoring System for Attempted Suicide who had undergone psychosocial assessment	2,164 single method self-poisonings (892 with paracetamol, 1,272 with another drug)	Range = 12+	100%	**Suicidal intent:** People who self-poisoned with paracetamol (pure paracetamol, co-proxamol or other paracetamol compounds) had significantly lower median scores on the Suicidal Intent Scale than people who self-poisoned with salicylates, gas, or opiates and recreational drugs. There was no significant difference in suicidal intent for self-poisoning with paracetamol compared to antidepressants, benzodiazepines and hypnotics, major tranquilisers, mood stabilisers, non-ingestible poisons, nonsteroidal analgesics, other prescribed medicines, or other drugs
Hawton (1996) (K. Hawton et al., 1996) England, UK	Qualitative	Paracetamol	Consecutive self-poisoning patients who were admitted to the John Radcliffe Hospital in Oxford from September 1992 to March 1993, having taken overdoses of paracetamol or paracetamol-containing compounds, or both	80	13-20 = 40% 21-35 = 40% 36+ = 20%		**Sex:** Self-poisoners included more females (66%) than males (34%) **Mental health symptoms:** 47% moderate to severe depressive symptoms **Self-harm history:** 48% previous self-harm; 29% previous paracetamol self-poisoning **Suicidal intent:** 60% reported low to moderate suicidal intent according to SIS. Clinical assessors thought 39% participants wanted to die, 25% had not wanted to die, and 36% did not mind either way. Cases who took more than 25 tablets had higher suicidal intent than those who took 25 or less tablets **Co-ingestion substances:** 25% took other substances in addition to paracetamol **Alcohol use:** 23% also consumed alcohol **Dosage:** The number of tablets taken were 1-25 (35 patients), 26-50 (27 patients), >50 (15 patients), unknown (3 patients)
Hawton (2003) (K. Hawton et al., 2003) England & Wales, UK	Observational or cohort	Paracetamol (other self-poisoning drugs)	Data from the Office for National Statistics on deaths in people aged 10 years and over in England and Wales from 1997 to 1999	4,162 (368 paracetamol alone deaths)	Range = 10+	100%	**Sex:** Women more likely to use paracetamol alone than men **Age:** The use of paracetamol alone increased with age

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Hawton (2007) (K. Hawton et al., 2007) England, UK	Observational or cohort	Paracetamol (other self-poisoning drugs)	Patients who presented with self-harm to Eds at general hospitals in Oxford (one hospital), Manchester (three hospitals) and Leeds (two hospitals) from March 1, 2000, to August 31, 2001	7,344 (all cases of self-harm; not specific to self-poisoning)	All ages	100%	**Sex:** More females than males used paracetamol for self-poisoning **Age:** Proportion of self-poisonings involving paracetamol decreased with increasing age
Hawton (2008) (K. Hawton, Harriss, L., 2008) UK	Observational or cohort	Paracetamol and compounds	Patients presenting to a general hospital following deliberate self-harm from January 1, 1978, to December 31, 2003	710 individuals (831 episodes)	8 = 0.1% 9 = 0.1% 10 = 1.3% 11 = 2.4% 12 = 9.3% 13 = 27.7% 14 = 59.0%	100%	**Sex:** A similar proportion of male (54.4%) and female (55.6%) patients used paracetamol (and compounds) for intentional self-harm
Hedeland (2013) (Hedeland et al., 2013) Denmark	Case-control	Paracetamol	Admissions to the Paediatric Department of Hillerød Hospital because of suicide attempts with paracetamol between January 2006 and July 2011 (identified through ICD10 diagnoses DT39, DT390, DT398 & DT398A)	107 cases (+ 59 aged- and gender-matched healthy controls)	Cases: M = 13.5; range = 11-15 Controls: M = 13.4; range = 11-15	100%	**Suicidal intent:** 100% of cases were classified as having suicidal intent **Dosage:** Mean paracetamol intake was 10.8g (SD = 7.3, range = 0.5-45) **Discovery of suicide attempt:** 42% told their parents; 30% told it to friends/boyfriend/girlfriend; 12% were discovered without the child wanting it to be discovered; 10% told other adults; 6% discovered in other ways **Self-mutilation:** 40% of children mutilated themselves repeatedly (>3x in previous 6 months) **Self-harm history:** 21% of children had 1+ previous suicide attempt **Exposure to suicide:** 23.5% of children had been exposed to suicide attempts in their surroundings
Hedeland (2016) (Hedeland et al., 2016) Denmark	Case-control	Paracetamol	Adolescents admitted to a paediatric department in Denmark after a suicide attempt with paracetamol between November 2011 and August 2014. All 17 paediatric departments in Denmark and the Medical Department of Bornholms hospital participated in the study	381 (+ 296 aged- and gender-matched healthy controls)	Cases: M = 14.8; range = 10-17 Controls: M = 14.6; range = 11-17	100%	**Suicidal intent:** 100% of cases were classified as having suicidal intent **Dosage:** Mean intake of 11.4g (range 2.5-70g). Intake not associated with gender, relationship with parents/siblings/friends; purposes or reasons for the suicide attempt, self-mutilation, the duration of suicidal ideation, previous suicide attempts, whether the suicide was planned or not, suicide deaths or suicide attempts in the adolescent's surroundings **Living situation:** 58% of parents in the study group were divorced vs. 25% of parents in the control group **Self-mutilation:** 44% of cases had mutilated themselves repeatedly (>3x in past 6 months) **Duration of suicidal ideation:** 44% with SI for at least one month; 44% with SI for more than 6 months; 37% only experienced SI for minutes/hours before suicide attempt **Exposure to suicide:** 40% of cases had been exposed to suicide attempts or suicide deaths in their surroundings **Self-harm history:** 32% had a previous suicide attempt

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John (2016) (John et al., 2016) Wales, UK	Observational or cohort	Paracetamol	Incidents of non-accidental, non-fatal poisoning across Wales, identified from electronic ambulance call centre records and paper records completed by attending ambulance crews, from December 2007 to February 2008	1,827 (484 with paracetamol)	M = 34.85	100%	**Co-ingested alcohol:** 45.3% **Suicidal ideation:** 6.2%
Kaur (2020) (Kaur et al., 2020) Canada	Observational or cohort	Paracetamol	Admissions to one of 19 paediatric and general hospital emergency departments across Canada for paracetamol-related poisonings from April 1, 2011, and February 23, 2019	3,721	Median = 14; IQR = 2-16	48.6%	**Age:** Intentional poisonings significantly higher in those aged 15-19 years **Sex**: Intentional poisonings significantly higher in females. Intentional poisonings (as compared to unintentional poisonings) predominated in both sexes from age 10 years and over
Kjartansdottir (2012) (Kjartansdottir et al., 2012) Iceland	Observational or cohort	Paracetamol	All residents within the catchment area who presented to the National University Hospital from 2004 to 2009 with overdose or liver injury and whose reported paracetamol ingestion exceeded the recommended daily dose of 4g or detection of serum paracetamol levels greater than 10mg/l	286 patients (326 visits), 182 hospitalised index visits	Hospitalised index visits: Median = 28; IQR = 19-43	91%	**Age:** Intentional cases tended to be younger than unintentional cases **Sex:** 73% of intentional cases female, with no difference when compared to unintentional cases **Alcohol consumption:** Present in 46% of intentional cases, with no difference when compared to unintentional cases **Alcohol abuse:** 30% of intentional cases had a history of alcohol abuse, and this proportion was higher in accidental cases (63%)
Kominek (2015) (Kominek et al., 2015) Poland	Observational or cohort	Paracetamol	Patients hospitalised in the Paediatric Clinic at the Children's Clinical Hospital in Lublin from 2004 to 2012 due to paracetamol poisoning	44	Intentional: M = 15; range = 12-17 Accidental: M = 3; range = 2-4 Drug overdose: M = 15; range = 14-16	68.2%	**Sex:** 93.3% of patients with intentional self-poisoning were female **Dosage:** 56-490mg/kg body weight (average = 192mg/kg body weight)
Kummer (2021) (Kummer et al., 2021) Switzerland	Observational or cohort	Paracetamol (other self-poisoning drugs)	Cases presenting at the ED of the University Hospital of Bern, Switzerland, from May 2012 to August 2016, after attempted suicide with drugs	488 (111 with paracetamol)	M = 37, SD = 16, median = 33; range = 16-93	100%	**Sex:** Females more likely to use paracetamol **Age:** Paracetamol more commonly used among patients under 30 years compared to older age groups
Kumpula (2020) (E.-K. Kumpula et al., 2020) New Zealand	Cross-sectional	Paracetamol (other self-poisoning medications)	Purposeful, non-representative sample of patients presenting to three New Zealand public hospital Eds with intentional self-poisoning. Data was collected from May 2016 to October 2017 from Dunedin Hospital, September 2016 to October 2017 in Wellington Regional Hospital, and March 2017 to September 2017 in Southland Hospital	102	Median = 21.5; IQR = 18.3-29; range = 16+	100%	**Dosage:** Median amount of paracetamol exposure was 3.3DDD (IQR =2.0-4.3; equivalent to 10g – 20 x 500mg tablets)

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Makin (2000) (Makin & Williams, 2000) London, UK	Observational or cohort	Paracetamol	Patients treated for paracetamol-induced severe hepatoxicity in the Liver Failure Unit of King's College Hospital from January 1987 to December 1993	553	<30 = 54% 30-50 = 37% >50 = 9%	93.1%	**Sex:** More cases in females **Suicidal intent:** 93.1% self-poisoned at a single time point with suicidal intent **Dosage:** 49.5% >30g paracetamol, 38.6% 15-30g paracetamol, 8% 10-15g paracetamol, 3.1% 6-10g paracetamol, 0.4% 4-6g paracetamol
Manthripragada (2011) (Manthripragada, 2011) USA	Observational or cohort	Paracetamol	Paracetamol overdose-related ED visits at approximately 500 hospitals participating in the National Hospital Discharge Survey	Average of 33,520 hospitalisations annually (2,228 cases)	M = 29.6 years, SE = 0.6 for all hospitalisations	74.2%	**Sex:** More females (70.8%) than males were hospitalised for intentional self-poisoning, however little variation by gender was observed for unintentional overdoses
Martin (2012) (Martin et al., 2012) Australia	Observational or cohort	Paracetamol	Retrospective chart review of deliberate self-poisoning presentations to Monash Health's three Eds during 2011	1,076 presentations (755 single patient presentations, 93 repeat patient presentations)	Single poisoning presentation: Median = 35; IQR = 23.7-45.0 Repeat poisoning presentation: Median = 37; IQR = 26.1-43.6	100%	**Self-harm history:** Repeat poisoning presentation patients were more likely to ingest paracetamol than single poisoning presentation patients **Dosage:** Median dosage of paracetamol ingested did not significantly differ for single poisoning presentations (2.2DDD, IQR = 1.3-4.4) compared to all repeat poisoning presentations (3.3DDD, IQR = 1.7-5.0). However, median dosage of paracetamol for single poisoning presentations was significantly lower than for people with 5 or more presentations (3.8DDD, IQR = 2.6-6.0)
Myers, Li, & Shaheen (2007) (Myers, Li, & Shaheen, 2007) Canada	Observational or cohort	Paracetamol	Calgary Health Region residents visiting an ED for paracetamol overdose from April 1, 1997, and March 31, 2002	2,699	Median = 22; range = 0-96	69%	**Sex:** More intentional self-poisoning cases in females **Age:** Highest rates in those aged 10-19 and 20-29 years **Ethnicity:** Intentional cases more common among non-Aboriginal participants **Substance abuse:** Alcohol-related diagnoses more common among intentional cases compared to unintentional cases
Myers, Li, Fong, et al. (2007) (Myers, Li, Fong, et al., 2007) Canada	Observational or cohort	Paracetamol	Calgary Health Region residents hospitalised for paracetamol overdose from 1994-95 to 2003-04	1,543 people (1,680 hospitalisations)	Median = 26, IQR = 2-85	85%	**Age:** The proportion with intentional self-poisoning cases decreased with age (45% in senior patients 65+ years vs. 86% in younger patients; all overdoses in patients under 10 years were accidental)
Neilson (2012) (Neilson & Morrison, 2012) Scotland, UK	Observational or cohort	Paracetamol (other self-poisoning drugs)	Patients under 17 years presenting to Ninewells Hospital's ED with self-poisoning from December 1, 2008, to November 30, 2009	206	0-11 = 41% 12-16 = 59%	Not reported	**Age:** 95.2% of paracetamol self-poisoning cases in the older age group (12 to <17 years) were classified as intentional vs. none of the paracetamol cases in the younger age group (0-11 years)
Nourjah (2006) (Nourjah et al., 2006) USA	Observational or cohort	Paracetamol	Patients experiencing a paracetamol-associated overdose, identified from the National Multiple Cause of Death File (1996-1998) or the Food and Drug Administration Adverse	1,375 deaths. 458 annually (National Multiple Cause of Death File); 478 cases	Not reported	National Multiple Cause of Death File: 74% FDA AERS: 41.8%	**Sex:** Intentional self-poisonings more common in females (based on National Multiple Cause of Death File data + FDA AERS data)

First author (Year) Region, Country	Study type	Medication(s) examined (comparison medications)	Population description	Sample Size	Age (years)	Proportion Intentional	Key findings for intentional self-poisoning cases
			Event Reporting System (AERS; 1998-2001)	(AERS)			
Payne (2009) (Payne et al., 2009) Scotland, UK	Observational or cohort	Paracetamol (other self-poisoning drugs)	People admitted to a hospital in Scotland with diagnosis of poisoning in addition to diagnosis of intentional self-harm from 1996 to 2002, using data from the Information Services Division of the NHS National Services Scotland. Patients with a 'true' index admission were included (no previous episodes of self-poisoning)	50,891 (all self-poisonings with any drug)	15-24 = 35% 25-34 = 26% 35-44 = 21% 45-64 = 15% >65 = 3%	100%	**Readmission for self-harm:** Paracetamol was the most common drug taken at index admission (31%), and 28% of readmissions involved paracetamol. Compared to anticonvulsants, antidepressants, antidiabetic drugs, benzodiazepines, and opiates, paracetamol was associated with a decreased risk of re-admission for self-poisoning, but risk of readmission did not differ between paracetamol and other drug categories. Paracetamol had particularly high proportion of repeated use at 49%
Pezzia (2017) (Pezzia et al., 2017) USA	Cross-sectional survey	Paracetamol	Patients hospitalised for paracetamol-related acute liver failure or injury, enrolled at one of eight different study sites from February 2007to June 2013 who consented to participate in a questionnaire	95 (44 intentional, 51 unintentional)	Total: Median = 35; IQR = 28-46 Intentional: Median = 35; IQR = 27-46 Unintentional: Median = 34; IQR = 28-46	46.3%	**Sex:** 72.7% of intentional cases were female **Suicidal intent:** 100% of intentional cases were classified as having suicidal intent **Dosage:** median = 20,000mg (IQR = 7,625-42,500) **Ethnicity:** 86.4% Caucasian, 9.1% Hispanic/Latino **Marital status:** 48.3% never married, 27.6% married, 24.1% divorced/separated, 3.4% in a relationship/not married **Previous psychiatric history:** 77.3% had a history of psychiatric disease (9.1% anxiety, 47.7% depression, 25% bipolar, 2.3% schizophrenia, 15.9% other). 41% and 55.6% had a current and past major depressive episode, respectively. 10.5% had a chronic pain disorder; 46.3% had the perception of problematic chronic pain **Psychiatric medication:** 36.4% using SSRI; 50% using psychiatric medication; 45.5% using opioids; 20.5% using benzodiazepine **Alcohol and illicit drug use:** 47.5% drank alcohol within 48h of overdose; 25% reported illicit drug use (4.5% amphetamines, 4.5% narcotics, 4.5% cocaine, 4.5% other); Intentional self-poisoning patients report more problems with alcohol and other substance use disorders compared to unintentional poisoning patients
Piotrowska (2019) (Piotrowska et al., 2019) Switzerland	Observational or cohort	Paracetamol	All patients 16 years of age or older presenting to University Hospital Bern ED from May 1, 2012, to October 31, 2018, due to paracetamol overdose	181	Total: M = 25; range = 16-85 Intentional cases: M = 23; range = 16-85	79%	**Sex:** 85% of intentional cases were female **Nationality:** 83% of intentional cases were Swiss citizens **Suicidal intent:** 94% of cases were classified as having suicidal intent, remaining 6% reported no strict suicidal intention but intention to harm themselves **Dose:** Median daily dose = 12.9g (max = 90g). 80% of cases were ingestion via a single dose, 13% had staggered intake, while 6% intake unknown **Co-ingested substances:** 50% of intentional cases co-ingested other substances including psychotropic drugs (48.6%) or other analgesics (44.4%) **Alcohol use:** 13.3% of intentional cases co-ingested alcohol **Previous psychiatric history:** 95% of intentional cases had a

First author (Year) Region, Country	Study type	Medication(s) examined (comparison medications)	Population description	Sample Size	Age (years)	Proportion Intentional	Key findings for intentional self-poisoning cases
							psychiatric history, which included 49% with borderline personality disorder, 33% depressive disorder, 11% acute psychological crisis/depressive adjustment disorder, 4% schizophrenia, 2% addiction disease, and single cases of patients with eating disorder and dementia
Rhodes, Bethell, Jaakkimainen et al. (2008) (A. Rhodes et al., 2008) Ontario, Canada	Observational or cohort	Paracetamol	Data from the National Ambulatory Care Reporting System were used to identify ED presentations to hospitals in Ontario by Ontario residents from April 1, 2001, to March 31, 2002, for medicinal self-poisoning	16,294	Range = 12-64	Not reported	**Rurality:** Deliberate self-poisonings in rural areas equally as likely as non-rural areas to involve paracetamol
Schiodt (1997) (Schiodt et al., 1997) USA	Observational or cohort	Paracetamol	All patients admitted to Parkland Memorial Hospital, Dallas County, Texas, for potential or actual paracetamol hepatotoxicity from January 1, 1992, to April 30, 1995	71	Intentional: M = 29; SD = 13; range = 14-83 Accidental: M = 34; SD = 10; range = 16-54	70%	**Sex:** 74% of intentional cases were female, and gender ratio did not differ for accidental overdoses **Suicidal intent:** 86% of intentional cases were classified as having suicidal intent, 10% angry gesture, 4% denied suicidal ideation **Dosage:** Mean for intentional cases = 24g (Median 20g, range = 3-125g), and was higher compared to people with an accidental overdose **Alcohol use:** 39% also consumed alcohol, and proportion did not differ for accidental overdoses **Alcohol abuse:** 25% chronic alcohol consumption, and proportion was lower than for accidental overdoses **Co-ingested substances**: 34% also consumed other drugs, and proportion did not differ for accidental overdoses **Illicit drug use:** 26% intravenous drug abuse, and proportion did not differ for accidental overdoses **Ethnicity:** Intentional cases were more likely to be white (vs. another race)
Schmidt (2001) (Schmidt, 2001) Denmark	Observational or cohort	Paracetamol	The charts of all patients with paracetamol poisoning admitted to Copenhagen University Hospital, Denmark, from 1994 to 2000, were reviewed	110	Range = 12-19	91%	**Suicidal intent:** 49% of intentional self-poisoning cases were classified as having suicidal intent
Shah (2002) (Shah et al., 2002) UK	Observational or cohort	Paracetamol (other self-poisoning drugs)	Suicide and undetermined deaths from drug overdose from 1993 to1999 in people over 65 identified from the Office for National Statistics database of deaths from overdose and poisoning	1,864	Range = 65+	100%	**Sex:** 63% paracetamol deaths in females **Age:** Suicide rates from paracetamol higher in 75+ years age group compared to 65-74 age group
Shekunov (2021) (Shekunov et al., 2021) USA	Observational or cohort	Paracetamol	Data collected using the Rochester Epidemiology Project (REP), an ongoing collaboration of medical facilities in Olmsted County, Minnesota, that collects	110	Total: M = 14.65; SD = 4.02 Intentional cases: M = 15.58; SD = 2.14	88%	**Sex:** 82% intentional cases were female **Dosage:** Mean number of tablets ingested = 40.72, SD = 64.65. **Co-ingestion substances:** Mean number medications ingested = 1.51, SD = 1.54

First author (Year) Region, Country	Study type	Medication(s) examined (comparison medications)	Population description	Sample Size	Age (years)	Proportion Intentional	Key findings for intentional self-poisoning cases
			data from community members. All patients in the REP database aged 0-18 who were evaluated for excessive paracetamol exposure between January 1, 2004, and December 31, 2010, were included		Unintentional cases: M = 7.77; SD = 7.22		**Self-harm history:** 23% prior suicide attempt (Mean prior attempts = 1.09, SD = 2.25) **Psychiatric history**: 6% no psychiatric/alcohol-related diagnoses, 49% one diagnosis, 44% multiple diagnoses, 24% dual diagnosis (psychiatric and substance-related). 62% major depressive disorder, 12% anxiety, 27% adjustment disorder, 18% cannabis abuse, 17% alcohol abuse, 14% alcohol dependence, 11% other substance dependent, 8% borderline personality disorder, 10% relational problem, 4% stimulant abuse, 4% opioid analgesic use, 3% dysthymic disorder, 2% bipolar disorder, 1% pain disorder, 1% eating disorder, 1% benzodiazepine abuse
Simkin (2012) (Simkin et al., 2012) England, UK	Qualitative	Paracetamol	General hospital patients at John Radcliffe Hospital, Oxford that had taken an overdose of more than 16 pure paracetamol tablets, were aged at least 16 years and had received a psychosocial assessment by a member of the clinical self-harm team in the Department of Psychological Medicine at the hospital	60	Females: M = 29.9; SD = 13.2; range = 16-65 Males: M = 33.3; SD = 14.9; range = 19-65	100%	**Self-harm history:** 40% first overdose. 53.3% previously self-poisoned with paracetamol **Suicidal intent:** 56% score high or very high on the SIS **Psychiatric history:** 72.9% reached case status for anxiety and 62.7% for depression **Alcohol use:** 38.3% consumed alcohol at the time of the self-poisoning episode **Co-ingestion substances:** 28.3% took one or more other drugs in their self-poisoning episode **Dosage:** 45% took up to 32 tablets (>1-2 packs), 33.3% 33-48 tablets (>2-3 packs), 21.7% over 48 tablets (>3 packs); range = 18-224. 58.3% took all tablets that were available
Smith (1995) (Smith, 1995) Scotland, UK	Observational or cohort	Paracetamol (other self-poisoning drugs)	Patients admitted to Tayside hospitals for self-inflicted injury or poisoning, from 1991 to 1993	3,264	All ages	100%	**Age:** Self-poisoning with paracetamol became less common with age (a third of admissions in patients under 30 years vs. 16% in patients aged 45 years+
Taylor (1998) (D. M. Taylor et al., 1998) Australia	Observational or cohort	Paracetamol (other self-poisoning drugs & other self-inflicted injury)	Patients presenting to Geelong Hospital ED from January 1, 1993, to December 31, 1994, where the attending doctor diagnosed overdose or other self-inflicted injury	441 patient presentations (335 single presenters, 46 repeaters)	All ages	100%	**Self-harm history:** Repeaters had a greater proportion of paracetamol self-poisonings and self-poisonings where paracetamol was the sole drug
Taylor (2012) (L. G. Taylor et al., 2012) USA	Observational or cohort	Paracetamol	Cases of paracetamol overdoses identified from the Military Health System Database from October 1, 2003, to September 30, 2008	1,239	All ages	64.9%	**Sex:** Intentional self-poisoning was more common in females **Age:** More common in individuals in the 15-17, 19-24 and 25-44 age groups
Ticehurst (2002) (Ticehurst et al., 2002) Australia	Observational or cohort	Paracetamol	All deliberate self-poisoning cases with an index admission to the Newcastle Mater Hospital from January 1991 to June 1998	2,667	Not reported	100%	**Age:** Ingestion of paracetamol was less common in those aged 65+ years compared to those <65 years

First author (Year) Region, Country	Study type	Medication(s) examined (comparison medications)	Population description	Sample Size	Age (years)	Proportion Intentional	Key findings for intentional self-poisoning cases
Townsend (2001) (Townsend et al., 2001) UK	Observational or cohort	Paracetamol (other self-poisoning drugs)	People presenting to the general hospital in Oxford following self-poisoning from 1985 to 1997	11,830 episodes	Range = 15+	100%	**Sex:** No significant gender differences in the use of paracetamol to self-poison **Age:** Paracetamol was significantly more common in episodes by younger self-poisoners than in older self-poisoners **Self-harm history:** First timers more often used paracetamol for self-poisoning than did repeaters **Suicide Intent**: Beck SIS score for paracetamol overdose: Mean = 10.1 (SD = 6.2), Median = 9
Weir (1998) (Weir & Ardagh, 1998) New Zealand	Observational or cohort	Paracetamol (other self-poisoning drugs)	Deliberate self-poisoning presentations to Christchurch Hospital ED from December 16, 1995, to December 15, 1996	713	Range = 10+ (70.1% <35)	100%	**Co-ingestion substances:** 58% of people who self-poisoned with paracetamol also co-ingested other substances
Studies examining OTC analgesics drug class (including paracetamol)							
Daly (2020) (Daly et al., 2020) Ireland	Observational or cohort	Analgesics (other self-poisoning drugs)	Data obtained from the National Self-Harm Registry Ireland from January 1, 2007, to December 31, 2018	16,800 index intentional drug overdose episodes (767 with analgesics)	Range = 10-24	100%	**Repeat self-harm episode:** 10.8% cases with an index analgesic intentional self-poisoning episode had a repeat episode. 15.4% of these switched method (e.g., self-cutting) within 12 months of their index attempt
Hopkins (2020) (Hopkins et al., 2020) USA	Observational or cohort	OTC analgesics, with 48% involving paracetamol alone	Single-substance and multi-substance exposures to OTC analgesics with suicidal intent among individuals 6 years of age and older from January 1, 2000, to December 31, 2018. Cases were identified from the National Poison Data System database	549,807 calls	6-19 = 49.7% 20-29 = 27.3% 30-39 = 11.1% 40 = 11.9%	100%	**Suicidal intent:** 100% of cases were classified as having suicidal intent **Sex:** 72.7% of cases female. Sex difference more pronounced among younger age groups **Age:** 49.7% of cases were among individuals aged 6-19 years **Co-ingestion substances:** 32.5% multi-substance **Location:** 96% self-poisonings occurred within the home
Larson (2022) (Larson et al., 2022) Oregon, USA	Observational or cohort	OTC medications (other prescription medications used in self-poisonings)	Patients seen by the Doernbecher Child and Adolescent Psychiatry Consultation-Liaison Service for intentional ingestion from 2015 to 2017	434 (240 OTC drug overdoses)	M = 15; range = 11-17	100%	**Co-ingestion substances:** 13% cases included a combination of both OTC and prescription medication
Lo (2003) (Lo et al., 2003) Vancouver, Canada	Observational or cohort	OTC medications (other prescription medications used in self-poisonings)	Patients who presented at St Paul's Hospital from August 1, 1997, to July 31, 1998, with a discharge diagnosis of medication overdoses. Patients were excluded if they had accidental poisoning or overdose	95 (28 OTC drug overdoses)	Overall: M = 43; SD = 13 OTC drugs: M = 35; SD = 9 Other drugs: M = 42; SD = 14	100%	**Age:** Younger patients more likely to use OTC medications for overdose as compared to older patients **Substance abuse:** Those using OTC drugs in self-poisoning less likely to have a substance abuse disorder compared to those using prescription drugs in self-poisoning

First author (Year) Region, Country	Study type	Medication(s) examined (comparison medications)	Population description	Sample Size	Age (years)	Proportion Intentional	Key findings for intentional self-poisoning cases
Mikhail (2019) (Mikhail et al., 2018) Montreal, Canada	Observational or cohort	OTC medications (other prescription medications used in self-poisoning)	All patients who presented to the ED in two university affiliated hospitals in Montreal with a suicide attempt from January 2009 to March 2010	181 (85 with OTC drugs, 96 with non-OTC drugs)	OTC drugs: M = 33.9; SD = 14.9 Non-OTC drugs: M = 42.0; SD = 16.8	100%	**Suicidal intent:** 100% of cases were classified as having suicidal intent **Ethnicity:** OTC drug overdose associated with non-Caucasian ethnicity **Family:** OTC drug overdose associated with having no children **Substance abuse:** OTC self-poisoning associated with no diagnosis of substance abuse **Physical health:** OTC self-poisoning associated with no medical comorbidities
Rhodes, Bethell, Spence et al. (2008) (A. E. Rhodes et al., 2008) Canada	Observational or cohort	Aromatic analgesics including paracetamol (other self-poisoning drugs)	Data from the National Ambulatory Care Reporting System were used to identify ED presentations to hospitals in Ontario, Canada from April 1, 2001to March 31, 2002, for self-poisoning by Ontario residents aged 12 years and older	18,383	Range =12+	50%	**Sex:** Among those aged 12-64 who self-poisoned with aromatic analgesics, males and females were equally likely to be identified deliberate
Vancayseele (2019) (Vancayseele et al., 2019) Belgium	Observational or cohort	Analgesics and antipyretics (other self-poisoning methods)	Individuals who presented with intentional self-harm to the Eds of 31 general hospitals and two university hospitals in Flanders from 2008 to 2013	9,478	M = 39; SD = 15.5	100%	**Sex:** The consumption of analgesics and antipyretics during self-harm was similar across males (16%) and females (17%) **Prescription:** No relationship between odds of using analgesics and antipyretics during a self-harm act and prescription rates of these drugs **Self-harm history:** The odds of using analgesics and antipyretics during a self-harm act increased significantly when there was no history of self-harm episodes **Alcohol use:** When males used alcohol during the self-harm act, the odds of using analgesics and antipyretics during the self-harm act increased significantly

Notes. DDD = defined daily dose**,** ED = emergency department; ICD = International Classification of Diseases, IQR = Inter-quartile range, M = Mean, OTC = over-the-counter, SD = Standard deviation, DSP = deliberate self-poisoning, SE = standard error, SIS = Suicidal Intent Scale, SSRI = selective serotonin reuptake inhibitor
*There is overlap between the dataset used by this study and the study by Daly et al. (2021).

Table 32. Studies examining motivations, planning, and knowledge of harm associated with intentional self-poisoning with paracetamol or other non-opioid analgesics

First author (Year) Region, Country	Study type	Medication(s) examined (comparison medications)	Population description	Sample Size	Age (years)	Proportion Intentional	Key Findings
Alsen (1994) (Alsen et al., 1994) Lund, Sweden	Qualitative	Paracetamol (other self-poisoning drugs)	Subsample of patients over 18 years old admitted to the ICU of Lund University Hospital after deliberate self-poisoning suicide attempt between 1987 and 1990	280	Males: M = 38; range = 18-92 Females: M = 39; range 19-87	100%	**Access:** Cases accessed analgesics via prescription (32%), OTC (39%), family and friends (27%) or other (2%)
Bolger (2004) (Bolger et al., 2004) Ireland	Qualitative	Paracetamol (other self-poisoning drugs)	Young people aged 14-20 who attended the Mater Hospital A&E Department with suicidal ideas or self-harming or self-poisoning behaviour between June 2001 and May 2002	89 young people attended the A&E, 31 agreed to an interview	A&E group: 14-16 = 28%; 17-20 = 72% Interview group: 14-16 = 32%; 17-20 = 68%	61% of A&E group had used deliberate self-poisoning (but study included other methods, and suicidal ideation without self-harm)	**Knowledge:** Most interviewees (55%) thought paracetamol was not a dangerous drug. 52% estimated that 30 or more paracetamol tablets would need to be taken before any adverse effects would be experienced
Corcoran (2013) (Corcoran et al., 2013) Ireland	Observational or cohort	OTC analgesics (other self-poisoning drugs)	Presentations to three hospital Eds that were identified as meeting the definition of deliberate self-harm used by the National Registry of Deliberate Self Harm over a continuous 6-month period (dates unspecified). Included self-harm presentations where there was information about whether the patient had a prescription for a psychotropic medication	288	<30 = 38.5% 30-44 = 38.2% 45+ = 23.3%	100%	**Access:** Psychotropic medications were more likely to be involved in intentional self-poisoning cases with prescriptions for these drugs, whereas analgesics were more common in cases without a prescription for psychotropic medication (significant for paracetamol, paracetamol, salicylate and NSAIDs/other analgesics, but not salicylate compounds)
Gilbertson (1996) (Gilbertson et al., 1996) UK & USA	Cross-sectional	Paracetamol	School students aged 13-16 years in UK and 12-19 years in US	582 UK students; 565 US students	UK: M = 14.8, range = 13-16 US: M = 14.3, range = 12-19	N/A (General population sample)	**Access:** 94% of students from the UK and 86% from the US reported having paracetamol at home with no sex or age differences **Knowledge:** UK students demonstrated increasing knowledge of side effects and toxicity with age, with 6% of 13-year-olds and 22% of 16-year-olds correctly identifying 'sickness and vomiting' and 'organ damage' as adverse effects. US students demonstrated decreasing knowledge with age, with 18% of 12-year-olds correctly identifying 'sickness and vomiting' and 'organ damage' compared to only 2% of 17-year-olds. A similar pattern was seen for 'damage to body parts/ organs. Erroneous belief that paracetamol could cause 'sleepiness and sedation' was common among students, and more common among UK than US students. In UK students, this belief increased with age, from 24% at 12 years to 46% at 16 years, but no age trend was identified for US students. 99% of students from the UK and 94% from the US answered that paracetamol in sufficient quantities can 'harm' you. 58% of UK students and 41% of US

First author (Year) Region, Country	Study type	Medication(s) examined (comparison medications)	Population description	Sample Size	Age (years)	Proportion Intentional	Key Findings
							students overestimated the 'harmful' dose at 20 or more 500 mg tablets, and approximately half of these students vastly overestimated the harmful dose, at 50 tablets or more tablets. 97% of UK students and 89% of US students recognised that a paracetamol overdose could kill. 75% of UK students and 62% from US overestimated the lethal dose at 50 or more tablets, while 45% of UK and 41% of US students vastly overestimated the dose of paracetamol required to kill at 100 or more tablets
Hawton (1995) (K. Hawton et al., 1995) England, UK	Qualitative	Paracetamol	Consecutive patients with self-poisoning who were admitted to the John Radcliffe Hospital, Oxford, from September 1992 to March 1993	80	13+	Not reported	**Method choice:** Availability was the most common reason for choosing paracetamol (63%), although 36% chose it because they knew it was dangerous. 5% chose it because it was cheap. **Access:** 48% obtained the paracetamol for medical purposes, while 52% obtained it specifically for intentional self-harm **Knowledge:** 78% thought a paracetamol overdose could cause death, 20% thought it could cause permanent damage or harm, 10% thought it could have harmful but short-lasting effects and 2.5% thought it could have mild, short-lived effects. 43% knew that paracetamol could cause damage or failure of the liver. Most participants thought any harmful effects would show fairly quickly; only 23% realised the effects would take > 24 hours to appear. 52% participants had expected paracetamol to cause unconsciousness
Hawton (1996) (K. Hawton et al., 1996) England, UK	Qualitative	Paracetamol	Consecutive self-poisoning patients who were admitted to the John Radcliffe Hospital in Oxford between September 1992 and March 1993, having taken overdoses of paracetamol or paracetamol-containing compounds, or both	80	13-20 = 40% 21-35 = 40% 36+ = 20%	Not reported	**Planning:** 41% of participants reported obtaining the tablets less than an hour before ingestion, 14% between 1 and 24 hours beforehand, 9% 1-7 days beforehand, and 31% more than a week beforehand **Access:** 53% participants obtained the tablets specifically for taking an overdose, while the remaining participants obtained them for another reason, such as pain relief **Impulsivity:** 41% seriously contemplated intentional self-poisoning for less than one hour beforehand, 33% for 1-3 hours, 6% for 3-24 hours and 20% for more than one day **Packaging:** In 60% cases tablets had been in a blister pack. More of those who took tablets from a loose preparation consumed 25 or more tablets (69%) than those who used a blister-pack preparation (40%) **Rapid consumption of tablets:** 45% ingested tablets in less than 5 minutes, 34% 5-60 minutes, 21% >60 minutes **Access:** 40% of tablets were from a chemist, 24% other type of shop, 13% family member, and 11% GP **Motives:** 75% escape intolerable situation, 66% gain relief from an unbearable state of mind, 66% to make other people understand how desperate they felt, 36% to seek help, 31% to influence other people, 26% to make other people sorry, 16% to find if someone cared for them, 11% to show how much they loved someone **Factors that might deter overdoses:** 66% participants said they would still have taken paracetamol in spite of knowing that it can cause death; 35% would still take it knowing that there is a delay in effects and likely to remain conscious; only 25% of participants thought a warning label would have stopped them from self-poisoning; of the participants who had taken >12 tablets, 37% said that they would either have taken a smaller overdose or no overdose at all if

First author (Year) Region, Country	Study type	Medication(s) examined (comparison medications)	Population description	Sample Size	Age (years)	Proportion Intentional	Key Findings
							paracetamol had only been available in small packets of 12 tablets. 7% said they would have taken some other substance; If paracetamol was just available on prescription from a GP 20% would still have self-poisoned, 34% would take a different substance, 6% would use another method of self-harm, 35% would not have self-poisoned; 64% would not have self-poisoned with paracetamol if paracetamol contained an antidote to stop the harms of an overdose.
Hedeland (2013) (Hedeland et al., 2013) Denmark	Case-control	Paracetamol	Admissions to the Paediatric Department of Hillerød Hospital because of suicide attempts with paracetamol between January 2006 and July 2011 (identified through ICD10 diagnoses DT39, DT390, DT398 & DT398A)	107 cases (+ 59 aged- and gender-matched healthy controls)	Cases: M = 13.5, range = 11-15 Controls: M = 13.4, range = 11-15	100%	**Planning:** 12.5% of attempts were planned. Those who planned their attempt did not consume more paracetamol than those with an unplanned attempt **Motive:** 32.5% wanted to die; 31% wanted relief from thoughts; 20.5% wanted to show how badly they felt; 16% had other reasons (e.g., punish others, get attention, etc). The main reason for the attempt for those with a dissociated relationship with their parent was to die. Most common reasons were problems with parents (19.5%), problems with boyfriends/girlfriends (14%), and problems with friends (13.5%) **Perceived support:** 40% of children had attempted to speak with their parents/other adults about their problems prior to their attempt but felt that they were not heard/understood, and that they did not receive necessary help/support to cope with problems **Relationship with parents:** 28.25% of cases vs. 73% of controls described a close relationship with parents; 30.25% of cases vs. 25% of controls described an intermediate relationship with parents; 41.5% of cases vs. 2% of controls described a dissociated relationship with parents **Relationship with friends:** 15.5% of study group stated they had no friends with whom they could share their problems; 16.5% described an intermediate relationship with friends; 65.5% had one or several close friendships
Hedeland (2016) (Hedeland et al., 2016) Denmark	Case-control	Paracetamol	Adolescents admitted to a Denmark paediatric department after a suicide attempt with paracetamol between November 2011 and August 2014. All 17 paediatric departments in Denmark and the Medical Department of Bornholms hospital participated	381 (+ 296 aged- and gender-matched healthy controls)	Cases: M = 14.8, range = 10-17 Controls: M = 14.6, range = 11-17	100%	**Motive:** 46.5% stated that the purpose of their suicide attempt was to die, 28.5% wanted to obtain relief from thoughts, and 18.5% wanted to show how bad they were feeling. The most common reasons for the suicide attempts were problems with parents (66%), problems with boyfriends/girlfriends (17%), non-academic problems in school (e.g., bullying; 17%), problems with friends (14.5%) and loneliness (12%) **Planning:** 21% of suicide attempts were planned for more than 24 hrs **Relationship with parents/siblings/friends:** 23% of cases reported having a close relationship with their parents compared to 76% of the control group; 41.5% of cases vs. 4% of controls reported a dissociated relationship or no contact with their parents; 54% of cases vs. 82% of controls felt they had at least one friend they could turn to for help; 18% of cases vs. 1% of controls had dissociated/no friendships; 35% of cases vs. 57.5% of controls had a close relationship with their siblings; 35.5% of cases vs. 6% of controls had a dissociated relationship or no contact with siblings **Perceived support:** 62% of cases reported that, when they attempted to talk to their parents or other adults about their problems up to two months prior to their suicide attempt, they felt either not heard or not understood

First author (Year) Region, Country	Study type	Medication(s) examined (comparison medications)	Population description	Sample Size	Age (years)	Proportion Intentional	Key Findings
Larson (2022) (Larson et al., 2022) Oregon, US	Observational or cohort	OTC medications (other prescription medications used in self-poisonings)	Patients seen by the Doernbecher Child and Adolescent Psychiatry Consultation-Liaison Service for intentional ingestion between the years 2015-2017	434 (n = 240 for OTC drug overdoses)	M = 15; range = 11-17	100%	**Access:** 65.8% OTC medication available in the home, 11.7% acquired elsewhere, 22.5% source unclear
Lo (2003) (Lo et al., 2003) Vancouver, Canada	Observational or cohort	OTC medications (other prescription medications used in self-poisonings)	Patients who presented at St Paul's Hospital from 1 August 1997 to 31 July 1998 with a discharge diagnosis of medication overdoses. Patients were excluded if they had accidental poisoning or overdose	95 (OTC drug use in overdose = 28; no OTC drug use in overdose = 67)	Overall: M = 43, SD = 13 OTC drug OD: M = 35, SD = 9 Other OD: M = 42, SD = 14	100%	**Access:** Those using OTC drugs in intentional self-poisoning less likely to possess prescription medication compared to those using prescription drugs in overdose
Makin (2000) (Makin & Williams, 2000) London, UK	Observational or cohort	Paracetamol	Patients treated for paracetamol-induced severe hepatoxicity in the Liver Failure Unit of King's College Hospital during the 7-year period between January 1987 and December 1993	553	<30 = 54% 30-50 = 37% >50 = 9%	93.1%	**Motive:** 60% self-poisoned impulsively in response to an adverse life event; 36% did so as a result of depression (i.e., patient was receiving treatment for depression, or they were described as depressed by next of kin or family practitioner)
Pezzia (2017) (Pezzia et al., 2017) USA	Cross-sectional survey	Paracetamol	Patients hospitalised for paracetamol-related acute liver failure or injury, enrolled at one of eight different study sites between February 2007 and June 2013 who consented to participate in a questionnaire	95 (44 intentional, 51 unintentional)	Total: Median = 35, IQR = 28-46 Unintentional: Median = 34, IQR = 28-46 Intentional: Median = 35, IQR = 27-46	46.3%	**Impulsivity:** Levels of impulsivity were similar between intentional and unintentional groups
Schmidt (2001) (Schmidt, 2001) Denmark	Observational or cohort	Paracetamol	The charts of all patients with paracetamol poisoning admitted to Copenhagen University Hospital, Denmark, between 1994 and 2000, were reviewed	110	Range = 12-19	91%	**Motive:** Among participants with suicidal intent (44% of cases), 37% had a known psychiatric disorder, 20% new depression diagnosis, 43% social problems (family problems, drug abuse, school related problems). Among participants with parasuicidal intent (deliberate act of impulse, not premediated), 47% had a row with their boy (girl) friend, 29% had a row with parents, 4% experienced bereavement, 20% reported other or gave no reason
Simkin (2012) (Simkin et al., 2012) England, UK	Qualitative	Paracetamol	General hospital patients at John Radcliffe Hospital in Oxford. Patients were eligible for inclusion if they had taken an overdose of more than 16 pure paracetamol tablets, were aged at least16 years and had received a psychosocial assessment by a member of the clinical self-harm team in the	60	Females: M = 29.9, SD = 13.2, range = 16-65 Males: M = 33.3, SD = 14.9, range = 19-65	100%	**Planning:** 25% spent 0-<15 mins planning, 25% spent 15-<60 mins, 23.3% 1-<24hours, 15% 1-<7 days, 11.7% 1 week+. People who took impulsively (within an hour of thinking about it) more likely to take tablets already in the home (63.3%) **Access:** 53.3% already in the home, 28.3% pharmacy, 35% supermarket, 13.3% local shop, 11.7% other outlet (e.g., garage and internet). 30% bought the paracetamol from at least two different outlets. 58.3% bought tablets specifically for self-poisoning **Anticipated effects:** 6.7% Harmful but short-lasting effects, 18.3% permanent damage or harm, 70% could cause death, 80% knew could harm the liver

First author (Year) Region, Country	Study type	Medication(s) examined (comparison medications)	Population description	Sample Size	Age (years)	Proportion Intentional	Key Findings
			Department of Psychological Medicine at the hospital				**Knowledge:** 70% thought they would lose consciousness. Of these people, 54.8% would not have taken overdose if had known they would not lose consciousness and effects would not be immediate. 20% did not know how many tablets could cause death **Factors that might deter overdoses:** 48.3% noticed warning on packet about dangers of overdose but this did not affect decision for 79.3% cases. Of those who didn't see the warning 80% would still have done it if they had. 89.7% still would have taken overdose if packets were smaller **Motives:** 76.7% wanted to die, 75% to get relief from a terrible state of mind, 73.3% escape an unbearable situation, 53.3% show how desperate they were feeling, 43.3% to get help, 15% to find out whether someone really loved them, 15% to make someone feel sorry, 5% to influence someone **Method choice:** 38.3% knew someone else who had self-poisoned with paracetamol, 35% read/seen in media, 13% used internet to get info on methods. 38.3% took paracetamol as it was already in the household, 20% bought paracetamol as it was cheap and readily available, 27% chose paracetamol because they knew it was effective, 8% used it as they had self-poisoned with paracetamol in the past **Future self-harm:** 70.9% (39/55, 5 participants were unsure) said they would not intentionally self-poison using paracetamol again. The main reason given for not taking another paracetamol overdose was the unpleasant effects (38%), 23% wouldn't self-poison using any drug, 15% would not self-poison using paracetamol again as they were now aware of the dangers, 23% wouldn't do it again because it wasn't quick or effective. Those who would take paracetamol again would do so as it would be effective (19%), is easy to obtain or readily available in the house (44%), habit or what they know (19%)

Notes. M = Mean, SD = Standard deviation, IQR = Inter-quartile range, OTC = over-the-counter, ICU = Intensive care unit, A & E = Accident and Emergency, ED = Emergency department.

Table 33. Studies examining the effect of restricting medication accessibility on overdoses and method substitution to other drugs (ordered based on restriction type)

First author (Year) Region, Country	Details of Restriction	Medication(s) and Comparator(s)	Sample Type	Key Outcomes: Restricted medication	Key Outcomes: Comparator
Turvill (2000) (Turvill et al., 2000) UK	**Type:** Pack size limit **Year:** 1998 **Medication affected:** Paracetamol, aspirin or both substances **Description:** Legislation reduced pack size to 32 tablets (pharmacies) and 16 tablets (other retail outlets). In addition, warnings were placed on packs about the danger of overdose and paracetamol became available almost exclusively in blister packs	**Restricted medication:** Paracetamol **Comparator:** Benzodiazepine	Reported on total number of overdoses	**Paracetamol:** For the 3 years leading up to the legislation change, the occurrence of paracetamol overdoses at the Royal Free Hospital, London, was consistent. In the year following the introduction there was a 21% reduction in all paracetamol overdoses and 64% reduction in severe overdoses.	**Benzodiazepine:** The frequency of overdoses remained stable over the study period.
Hawton (2004) (K. Hawton et al., 2004) UK	**Type:** Pack size limit **Year:** 1998 **Medication affected:** Paracetamol, aspirin or both substances **Description:** Legislation reduced pack size to 32	**Restricted medication:** Paracetamol; salicylates (either alone or in combination with	Deaths reported are for suicides, open verdicts and accidental poisonings. Findings were similar when	**Paracetamol alone:** Reduced deaths (suicides, open verdicts and accidental poisonings) in the year after the legislation (29%) sustained in subsequent two years (34%). Reduced presentations to hospital for non-fatal paracetamol overdoses in the first year (15% reduction), but no reduction in subsequent	**Ibuprofen**: All deaths increased 2.2-fold and suicide/open verdict deaths increased 2.1-fold following legislation change, however actual numbers were small (4

First author (Year) Region, Country	Details of Restriction	Medication(s) and Comparator(s)	Sample Type	Key Outcomes: Restricted medication	Key Outcomes: Comparator
	tablets (pharmacies) and 16 tablets (other retail outlets). In addition, warnings were placed on packs about the danger of overdose and paracetamol became available almost exclusively in blister packs	other drugs (excludes co-proxamol) **Comparator:** Ibuprofen	restricted to suicides and open verdicts however data was not shown.	years. Number of tablets taken in overdoses decreased post-legislation. Large paracetamol overdoses (>32 tablets) decreased in the year after legislation was introduced and was sustained. 30% reduction in the number of people admitted to liver units due to paracetamol-induced hepatoxicity, those listed for liver transplant and actual transplantations in the first two years post-legislation **Salicylates alone:** Reduced deaths (suicides, open verdicts and accidental poisonings) in the year after legislation (46%), sustained in subsequent two years (70%). No change in non-fatal salicylate overdoses with introduction of legislation. Number of tablets taken in overdoses decreased post-legislation.	accidental and 7 open verdict/suicide in the 5 years before legislation; 4 accidental and 9 open verdict/suicide in the 3 years following legislation). Number of ibuprofen overdoses increased by 27% in the second and third years after the legislation was introduced. No major change in the number of tablets taken in non-fatal overdoses with ibuprofen alone. Large ibuprofen overdoses (>32 tablets) did not change significantly following legislation change.
Morgan (2005) (O. Morgan et al., 2005) England and Wales, UK	**Type:** Pack size limit **Year:** 1998 **Medication affected:** Paracetamol, aspirin or both substances **Description:** Legislation reduced pack size to 32	**Restricted medication:** Paracetamol **Comparator:** Paracetamol compounds, all other drugs excluding	Intentionality of deaths or overdoses leading to hospital admission was not assessed.	**Paracetamol:** Modelling showed a decreasing trend in age-standardised mortality rates for deaths involving pure paracetamol over time, but some of this decrease was speculated to be the result of natural variation in rates. There was a modest decline in hospital admissions due to paracetamol (trend not significant).	**Compound paracetamol:** Deaths due to compound paracetamol remained relatively constant. **All poisonings:** There was a decreasing trend for age standardised mortality

First author (Year) Region, Country	Details of Restriction	Medication(s) and Comparator(s)	Sample Type	Key Outcomes: Restricted medication	Key Outcomes: Comparator
	tablets (pharmacies) and 16 tablets (other retail outlets). In addition, warnings were placed on packs about the danger of overdose and paracetamol became available almost exclusively in blister packs	paracetamol and opioids	Across the whole study period 47% of all paracetamol only deaths were classified as intentional self-poisoning, and 33% were of underdetermined intent.		rates for deaths due to all poisoning excluding opioids and paracetamol.
Morgan (2007) (O. W. Morgan et al., 2007) England and Wales, UK	**Type:** Pack size limit **Year:** 1998 **Medication affected:** Paracetamol, aspirin or both substances **Description:** Legislation reduced pack size to 32 tablets (pharmacies) and 16 tablets (other retail outlets). In addition, warnings were placed on packs about the danger of overdose and paracetamol became available almost	**Restricted medication:** Paracetamol; aspirin **Comparator:** Paracetamol compounds, antidepressants, or non-drug poisoning suicide	Intentional and unintentional self-poisoning considered. 75% of all paracetamol only deaths were classified as suicide.	**Paracetamol:** Age-standardised mortality rates for deaths involving paracetamol increased until 1997, and then showed a decrease over time after the restriction was introduced. **Aspirin:** Trends in age-standardised mortality rate similar to paracetamol (increasing until 1997 and then declining).	**Paracetamol compounds, antidepressants:** Trends in the age-standardised mortality rate for aspirin, paracetamol compounds, and antidepressants were similar to paracetamol (increasing until 1997 and then declining). **Non-drug poisoning suicide:** Non-drug poisoning suicide also declined during the study period.

First author (Year) Region, Country	Details of Restriction	Medication(s) and Comparator(s)	Sample Type	Key Outcomes: Restricted medication	Key Outcomes: Comparator
	exclusively in blister packs				
Balit (2002) (Balit et al., 2002) Australia	**Type**: Recall causing lack of supply **Year**: 2000 **Medication affected**: Paracetamol **Description**: Two recalls of paracetamol products from 16 March – 21 May 2000 and 6 June – 23 August 2000 due to extortion and spiking with strychnine	**Restricted medication:** Paracetamol **Comparator:** Ibuprofen, aspirin	Intentional poisoning considered, except for paediatric calls.	**Paracetamol:** No significant change in deliberate self-harm calls to NSW PIC related to paracetamol during recall periods. First recall period had slight non-significant reduction for paracetamol deliberate self-harm. No significant change in proportion of deliberate self-harm presentations to HATS related to paracetamol (or ibuprofen) during the recall period. Regarding accidental paediatric poisoning, there was no significant change in calls for paracetamol.	**Aspirin:** No significant change in deliberate self-harm calls to NSW PIC related to aspirin during recall periods. Significant increase in the proportion of deliberate self-harm presentations to HATS related to aspirin. Regarding accidental paediatric poisoning, there was no significant change in calls for aspirin. **Ibuprofen:** Significant increase in the proportion of calls about ibuprofen, suggesting means substitution. No significant change in proportion of deliberate self-harm presentations to HATS related to ibuprofen during the recall period. Regarding accidental

First author (Year) Region, Country	Details of Restriction	Medication(s) and Comparator(s)	Sample Type	Key Outcomes: Restricted medication	Key Outcomes: Comparator
					paediatric poisoning, there was a significant increase in calls related to ibuprofen.
Kisely (2003) (Kisely et al., 2003) Western Australia, Australia	**Type**: Recall causing lack of supply **Year**: 2000 **Medication affected**: Paracetamol **Description**: Two recalls of paracetamol products from 16 March – 21 May 2000 and 6 June – 23 August 2000 due to extortion and spiking with strychnine	**Restricted medication:** Paracetamol **Comparator:** Aspirin, ibuprofen, other poisoning agents	Intentional deaths not considered separately	**Paracetamol:** Decrease in admission rate for paracetamol poisoning when sales were restricted in 2000.	**Aspirin, ibuprofen, other non-paracetamol agents:** No increase in hospital admissions from overdoses using aspirin, ibuprofen or other non-paracetamol agents during paracetamol recall period.
Sandilands (2008) (Sandilands & Bateman, 2008) Scotland, UK	**Type**: Withdrawal **Year**: 2005 **Medication affected**: Co-proxamol **Description**: Withdrawal from the UK market	**Restricted medication**: Co-proxamol **Comparator:** Co-codamol, co-dydramol, tramadol, dihydrocodeine, codeine, paracetamol	Intentional deaths not considered separately	**Co-proxamol:** Significant reduction in the proportion of poisoning deaths due to co-proxamol (mean 2000-2004, 37 deaths (21.8% total poisoning deaths) compared to 2006, 10 (7.8%)). A shift in age distribution of deaths was observed following legislation, particularly in younger patients (where there was a marked decrease in cases).	**Other commonly prescribed analgesics:** No evidence of increased mortality for co-codamol, paracetamol or any other commonly prescribed analgesics, despite steady rise in co-codamol and paracetamol prescriptions since legislation.

First author (Year) Region, Country	Details of Restriction	Medication(s) and Comparator(s)	Sample Type	Key Outcomes: Restricted medication	Key Outcomes: Comparator
Hawton (2009) (K. Hawton et al., 2009) England and Wales, UK	**Type**: Withdrawal **Year**: 2005 **Medication affected**: Co-proxamol **Description**: Withdrawal from the UK market	**Restricted medication:** Co-proxamol **Comparator:** Paracetamol; NSAIDs; Codeine; co-codamol, co-dydramol, dihydrocodeine, tramadol	**S**uicide (with open verdict deaths) and also in combination with unintentional deaths	**Co-proxamol:** Before 2005, co-proxamol deaths accounted for 19.5% of suicides by drug poisoning, whereas between 2005-2007, they accounted for 6.4%. Co-proxamol withdrawal was associated with a major reduction in deaths involving co-proxamol compared with the expected number of deaths (an estimated 295 fewer suicides (115 approx.. 62%) and 349 fewer deaths, including accidental poisonings (115 approx.. 61%)). Prescriptions of co-proxamol decreased by 59% in the three years post intervention.	**Other analgesics:** No statistical evidence of an increase in deaths involving other analgesics or drugs. Prescribing of some other analgesics (co-codamol, paracetamol, co-dydramol, and codeine) increased significantly during this time (20%, 13%, 12%, 8% respectively), however prescriptions for dihydrocodeine decreased by approximately 6%. **NSAIDs:** Prescriptions decreased by approximately 19%.
Hawton (2011) (K. Hawton et al., 2011) Oxford, Derby & Leeds, UK	**Type**: Withdrawal **Year**: 2005 **Medication affected**: Co-proxamol **Description**: Withdrawal from the UK market	**Restricted medication:** Co-proxamol **Comparator:** co-codamol, codeine, co-dydramol, dihydrocodeine, tramadol, NSAIDs, paracetamol	All patients presented with self-harm (intentional self-poisoning)	**Co-proxamol:** Significant decrease in level and slope for non-fatal self-poisoning for co-proxamol was associated with the restriction. This equated to an approximate decrease of 62% over 2005-2007, when compared to prior to the restriction.	**Other analgesics: N**o significant change in the level or slope of non-fatal self-poisoning involving five often prescribed analgesics (co-codamol, codeine, co-dydramol, dihydrocodeine, and tramadol) and no change in level or slope of self-

First author (Year) Region, Country	Details of Restriction	Medication(s) and Comparator(s)	Sample Type	Key Outcomes: Restricted medication	Key Outcomes: Comparator
					poisoning involving all other analgesics (co-codamol, codeine, co-dydramol, dihydrocodeine, NSAIDS, paracetamol, and tramadol).
Hawton (2012) (K. Hawton et al., 2012) UK	**Type**: Withdrawal **Year**: 2005 **Medication affected**: Co-proxamol **Description**: Withdrawal from the UK market	**Restricted medication:** Co-proxamol **Comparator:** Co-codamol, codeine, co-dydramol, dihydrocodeine, NSAIDs, paracetamol, tramadol	**S**uicide (with open verdict deaths) and also in combination with unintentional deaths.	**Co-proxamol:** During 2005 – 2010 there was a 61% reduction in deaths by suicide (and open verdict deaths) and 62% reduction when accidental deaths included for co-proxamol poisoning. During the same period, there was a 53% reduction in prescribing of co-proxamol.	**Other analgesics:** There was a significant increase in the prescribing of co-codamol (23%), paracetamol (16%), codeine (10%), co-dydramol (6%), and tramadol (19%). The number of deaths involving other analgesics did not appear to change markedly during this study period.
Corcoran (2010) (Corcoran et al., 2010) Ireland	**Type**: Withdrawal **Year:** 2006 **Medication affected**: Co-proxamol (Distalgesic) **Description**: Withdrawal from Irish market	**Restricted medication:** Co-proxamol (Distalgesic) **Comparator:** Any paracetamol containing medication, solpadeine, 'other	Intentional self-poisoning	**Co-proxamol (Distalgesic):** The rate of intentional self-poisoning presentations to hospital involving co-proxamol in 2006-2008 was 84% lower than in the three years before it was withdrawn.	**Other prescription compound analgesics:** There was a 44% increase in the rate of intentional self-poisoning presentations involving other prescription compound analgesics, but the magnitude of this rate

First author (Year) Region, Country	Details of Restriction	Medication(s) and Comparator(s)	Sample Type	Key Outcomes: Restricted medication	Key Outcomes: Comparator
		prescription compound analgesics' (kapake, paramol, solpadol, syndol, tylex)			increase was five times smaller than the magnitude of the decrease in distalgesic-related intentional self-poisoning presentations. **Any paracetamol-containing medication:** Overall, there was a 16% decrease in presentations for any paracetamol-containing medication after restriction. **Sales data:** Between 2005-2006, 48% jump in sales of other prescription compound analgesics, 11% increase in solpadeine and 22% increase in sales of other paracetamol-containing medicines.
Birchall (2021) (Birchall et al., 2021) Ireland	**Type**: Sale guidelines for pharmacists **Year**: 2010 **Medication affected**: Codeine **Description**: Guidelines for pharmacists included	**Restricted medication:** Codeine **Comparator:** Non-opioid analgesics, other opiates, all drugs	All patients presenting with self-harm (intentional self-poisoning)	**Codeine:** Rate of codeine related intentional overdose was 20% lower in the post-guidance period compared to the pre-guidance period. Reduction in codeine-related intentional overdoses was more pronounced in females (-24%) than males (-13%), and in >65 year olds (-44%) compared to 25–64 year olds (-14%)	**Comparator:** There was an overall reduction in intentional overdoses with all drugs other than codeine. The rate of intentional overdose with non-opioid analgesics

First author (Year) Region, Country	Details of Restriction	Medication(s) and Comparator(s)	Sample Type	Key Outcomes: Restricted medication	Key Outcomes: Comparator
	specific criteria for sale of codeine reiterating its pre-existing classification as Schedule 5 (available OTC under pharmacist supervision)			and <25 year olds (-23%). In the over 65 year olds and 25–44 year olds, decreases were significant only for females, but in the <25 year olds, decreases were seen for both males and females.	reduced by 11%, but no change was identified for other opiates.
Morthorst (2020) (Morthorst et al., 2020) Denmark	**Type**: Age restriction and pack size limit **Year**: 2011 (age restriction) and 2013 (pack size limit) **Medication affected**: OTC non-opioid analgesics **Description**: Age restriction to ensure that only persons aged 18 years or older can purchase non-opioid analgesics. Legislation reduced pack size to 20 tablets	**Restricted medication:** Paracetamol, Aspirin, non-steroidal anti-inflammatory medication **Comparator: O**ther pharmacological poisonings, violent self-harm methods	Intentional and accidental poisoning combined for analysis. Considered suicide and accidental deaths separately however numbers too small for analysis	**Over-the-counter non-opioid analgesics:** No change in the overall number of emergency department presentations/hospital admissions for non-opioid analgesic poisonings (intentional/accidental) following age restriction, but there was a substantial reduction following pack size restriction (estimated 18.5% reduction). When stratified by age, there was a 17% reduction in non-opioid analgesic poisonings following the age restriction among those aged 10-17 years. No changes were observed in other age groups following the age restriction. No change in accidental poisoning deaths and suicides by non-opioid analgesics following pack size restriction (numbers too small for analysis). No change in suicide deaths involving other substances following pack size restriction (numbers too small for analysis).	**Other pharmacological poisonings:** Emergency department presentations/ hospital admissions with poisoning by substances other than non-opioid analgesics reduced by 10% and 11% following age and pack size restrictions, respectively. When stratified by age, there was a 18% reduction in other poisonings following age restriction among those aged 10-17 years. No changes observed in other age groups following the age restriction. **Violent self-harm methods:** No change in violent self-harm methods when comparing pre-

First author (Year) Region, Country	Details of Restriction	Medication(s) and Comparator(s)	Sample Type	Key Outcomes: Restricted medication	Key Outcomes: Comparator
					intervention vs. interim period trends (i.e., period between age restriction and pack size restriction); however, the pack size restriction was followed by a significant reduction in suicide attempts using violent methods.
Cairns (2020) (Cairns et al., 2020a) Australia	**Type**: Up-scheduling **Year**: 2018 **Medication affected**: Low-strength codeine products **Description**: Up scheduling from Schedule 3 (pharmacist	**Restricted medication:** Codeine **Comparator:** Oxycodone; tramadol, tapentadol, morphine, hydromorphone, fentanyl, buprenorphine,	Calls were for intentional misuse of medication	**Codeine:** Monthly calls related to intentional codeine poisoning reduced significantly after rescheduling with similar findings seen for all codeine poisoning calls. The change was driven by a reduction in calls for low-strength codeine (which was rescheduled) but not high-strength products (for which scheduling was unchanged). Codeine dose (mg) taken in intentional exposures did not differ	**Other pharmaceutical opioids and OTC products:** Calls about other pharmaceutical opioids and OTC products with misuse potential did not increase, suggesting no evidence of substitution.

First author (Year) Region, Country	Details of Restriction	Medication(s) and Comparator(s)	Sample Type	Key Outcomes: Restricted medication	Key Outcomes: Comparator
	only) to Schedule 4 (prescription only)	methadone, loperamide, dextromethorphan, dihydrocodeine		significantly. Sales of low-strength codeine preparations decreased following rescheduling.	
Harris (2020) (Harris et al., 2020) Australia	**Type**: Up-scheduling **Year**: 2018 **Medication affected**: Low-strength codeine products **Description**: Up-scheduling from Schedule 3 (pharmacist only) to Schedule 4 (prescription only)	**Restricted medication:** Codeine **Comparator:** Alternative opioid-related medications	Presentations included deliberate self-poisonings and recreational exposure	**Codeine:** The number of codeine-related presentations was 53% lower in the 12 months after rescheduling: there were 163 presentations before and 77 presentations after rescheduling. A similar number of presentations for 30mg codeine products (unaffected by rescheduling) were observed (52 before, 60 after rescheduling). A decrease in the number of presentations for codeine products affected by rescheduling (<30mg codeine) was observed (111 presentations before, 17 presentations after, 85% lower).	**Alternative opioid-related medications:** The decline in codeine-related presentations was not associated with a rise in alternative opioid-related presentations (185 alternative opioid-related presentations before, 178 after re-scheduling).

Notes. OTC = over-the-counter

5. Conclusions

Australians purchase around a thousand tonnes of paracetamol each year, and it is undoubtedly the most widely used analgesic. It is very safe in therapeutic use, and a first line analgesic in pain guidelines for many conditions. It is very widely available for purchase in quantities that would be harmful if ingested in intentional self-poisoning. It is also very commonly taken in intentional self-poisoning, especially by children/adolescents. Many (but not all) countries have responded to this problem by various restrictions on availability to reduce the size of overdoses, while maintaining ready access for the public to self-manage minor painful conditions.

The contemporary Australian data and the research literature are broadly in agreement about the nature of intentional self-poisoning in children, adolescents and adults. However, the social and psychiatric aspects of this problem within Australia have not been substantially addressed in recent years. We are short of information from within Australia about the use, and knowledge of paracetamol in the self-harming population. There is a need to look at age/gender differences in motivations, planning and perceived preventative actions. Further qualitative and quantitative research could investigate knowledge around the risks, nature, dosage knowledge, and potential perceived preventative strategies to self-harm, particularly in young women. There is particular merit in focussing efforts on young people. They have the highest rates of self-harm generally, and particularly in paracetamol, and these rates have greatly increased in recent years.(Cairns et al., 2019; Chitty, Raubenheimer, Cairns, Kirby, & Buckley, 2022) Paracetamol may often be the first means of self-harm used. The consequences of self-harm continue across the lifespan, and may well be ameliorated by early prevention and intervention. The use of means restriction of these (and other) toxic over-the-counter agents is likely to have the greatest impact in this group.

Over the last decade in Australia, there has been an increase in the use of paracetamol in adolescents and young adults. Importantly, the age at which children and adolescents are using this method has lowered. More children and very young teens use this method more frequently than previously recorded.

This represents a significant change in the pattern of use, the causes of which are not clear. We don’t know if it will continue or become worse, but the consequences of this change will need to be addressed. If the current pattern continues, we will see an increasing proportion of young people affected at younger ages, a long-term increase in suicide rates and attempts over the lifespan of users, higher prevalence of mental illness and ill effects that often accompany immediate and subsequent attempts, resulting in increased health utilisation, increased pressure on schools and families and ultimately reduced economic productivity.

One implication is that more effort should be directed to understanding the societal and environmental pressures that might be causing these changes. In the immediate short term, means restriction may be the best measure we have to counter this trend in young people. Means restriction is a strong preventative strategy, that might be particularly effective for young cohorts, because of its universal coverage, where we do not have effective ‘identifiers’ of risk prior to an attempt being made.

Looking after young people after a paracetamol self-poisoning should also be a high priority. Effective post care and treatment is critical, as treatments using dialectical behaviour therapy (DBT) are highly effective (Zalsman et al., 2016) if they can be accessed. Priority in access to treatment for young people might be considered as a health priority. Recent research has established the effectiveness of online and digital 'self-help' approaches (Torok et al., 2020) which may assist when clinician access is limited. Yet to be published research evaluating LifeSpan in Australia,(F. Shand et al., 2020) has demonstrated some positive effects from systems wide approaches that incorporate means restriction, community and school programs and health systems. However, access to psychiatric and psychological treatment is critical.

There may be some benefit to better education of the public and health professionals, in order to assist in harm minimisation at a population level. We are fully cognisant of the potential ill effects of publicising any methods for suicide or suicide attempt, and particularly for paracetamol, although the mortality risk is lower than many other medications or methods. However, a considered approach to educating the community about its dangers might be worthwhile. This could be approached by generic messages around keeping medications out of harm's way because of their potential inadvertent risk to children and adults. Effective strategies to assist in reducing danger are to keep medications in safe places, keep low doses of medication, and not to stockpile potentially hazardous medicines. This approach would need to first ascertain the current (lack of) knowledge of the community, and then ensure that the messages were carefully pretested.

We found that the research literature we identified had not been substantially refreshed for decades. Aside from the issue of not understanding the causes of the rising risk of paracetamol use in children and adolescents, we are short of information from within Australia about how our population understands the nature and risks of paracetamol (and self-poisoning more generally). There is a need to look at age/gender differences in motivations, planning and perceived preventative actions. Further qualitative and quantitative research could investigate knowledge around the risks, nature, dosage knowledge, and potential perceived preventative strategies to self-harm, particularly in older children, adolescents and women.

6. Recommendations to the TGA and to inform scheduling deliberations

6.1 Recommendations

Means restriction and harm minimisation interventions

Means restriction of highly toxic agents is a very effective suicide prevention strategy (Lim, Buckley, Chitty, Moles, & Cairns, 2021). Restrictions on moderately toxic over-the-counter medicines like paracetamol might prevent some suicide deaths. However, given the extremely widespread appropriate therapeutic use of paracetamol the main aim might be better framed as harm minimisation. Various restrictions will limit the average and maximum size of the overdose, or cause diversion to less toxic more easily purchased agents. This might limit the amount available for impulsive access in most homes and also limit the amount purchased specifically to self-harm, each of these scenarios reported as contributing roughly equally to deliberate paracetamol overdosing events.

There are four potential areas to consider based on overseas experience and regulation:

Recommendation 1: Pack size restrictions

Changes in scheduling to reduce the pack sizes that may be purchased in grocery and convenience sales or in a pharmacy without a prescription or consultation with the pharmacist are both possible strategies, and scheduling entries frequently depend on pack size. The current unscheduled pack size limit is 20 x 500 mg paracetamol tablets, and this is the main item sold in grocery and convenience stores. This could be reduced to 12 or 16 tablets and be expected to have a modest effect on overdose size (Donohoe, Walsh, & Tracey, 2006). However, the majority of paracetamol is purchased in pharmacies in Australia, and most paracetamol ingested is sourced from paracetamol already in the home. More benefit is likely from reducing the S2 pack size limit to 24 or 48 or 50 x 500 mg tablets. The 50-pack size limit would equate to a paracetamol quantity of 25 g, greater than the median dose taken intentionally in overdose. However, overdoses of 25 g or lower are easier to treat compared to overdoses more than 25 g, which disproportionately cause severe liver toxicity. The larger pack sizes would then become S3, and presumably become much less purchased generally.

Recommendation 2: Pack number limits

Most (~95%) sales of paracetamol tablets involve the purchase of 1 or 2 packs. Making this the maximum number of packs that can be purchased in one transaction would almost certainly reduce home stockpiles, and likely also reduce the number of very large overdoses, which have much higher morbidity and risk of death. Such restrictions would also inconvenience relatively few people. Purchasing limits on many pharmaceutical agents and other items have been widely used and shown to be implementable in the recent COVID-19 pandemic.

The TGA should consider whether scheduling is the appropriate mechanism to implement pack number limits. We observe that in the current Poisons Standard there is no precedent for making the scheduling status of a substance dependent on the number of packs purchased. As

such, it would need to be determined how, if at all, pack number limits in the Poisons Standard could be implemented, including monitoring and enforcement, under State and Territory legislation. Other approaches to enforcing pack number limits may need to be considered.

Recommendation 3: MR paracetamol restrictions

MR paracetamol (664 mg) is the largest tablet size registered in Australia, and it is associated with much more morbidity and larger typical overdoses (Cairns et al., 2019; Chiew, Isbister, et al., 2018). Such products are not registered in the EU or UK. The S3 scheduling of MR paracetamol does not appear to have had much impact. This product is designed to aid adherence with long-term use (e.g., for osteoarthritis), rather than for acute pain. Prescription only (S4) scheduling would be expected to reduce casual use of this more dangerous product and therefore overdoses, as shown recently for codeine (Cairns, Schaffer, Brown, Pearson, & Buckley, 2020b) and should be considered.

Recommendation 4: Age restrictions

There is research from Denmark (Morthorst et al., 2020) showing that an 18+ age restriction on the purchasing of over-the-counter non-opioid analgesics resulted in a significant decrease in non-opioid analgesic poisonings among 10-17 year-olds. Given that paracetamol self-poisoning is most common among adolescents and young people, an age restriction on paracetamol and similar over-the-counter non-opioid analgesics should be considered. However, any effect of such restrictions would be modest, as most paracetamol ingested in self-poisoning is already purchased and present in the home. Moreover, whereas scheduling based on the age for whom medicines are indicated is common, it would need to be determined whether scheduling based on the age of the person to whom a medicine is sold in real time is feasible.

Non-medication specific recommendations to reduce self-poisoning

Recommendation 5: Use safe reporting guidelines for any communication around the harms associated with paracetamol overdose

Any communication around the potential harms of paracetamol must comply with safe reporting guidelines for self-harm and suicide (e.g., Mindframe guidelines)(Mindframe Media Advisory Group, 2020) and be rigorously evaluated prior to implementation. This will enable any unintended consequences of the communication to be identified, such as an increase in self-harming behaviour.

Recommendation 6: Maintain and expand support for aftercare services

It is important to ensure that those reaching the emergency departments of hospitals following self-poisoning are treated quickly and respectfully. All should be offered appropriate care and Australian recommendations for aftercare (follow-up care and support after self-harm) implemented (F. Shand, Vogl, & Robinson, 2018). Previous research has identified that the period immediately after discharge from psychiatric inpatient care is associated with very high risk of death by suicide (F. Shand et al., 2019).

Recommendation 7: Safer storage of medicines and reduced stockpiling of unwanted medicines

Public health sites in Australia already provide messages around keeping medications and chemicals out of harm's way to reduce the risks of accidental poisoning. These typically target parents of young children, and don't mention the potential risk for older children and adolescents (Raising Children Network, 2021). Similar preventative messages targeting older children and adults could be delivered to the public so that medications are kept safely. Strategies to assist in increasing medication safety could include keeping medications in a secure location (e.g., locked or hard to reach cupboard), keeping low doses of medication, and avoiding stockpiling potentially hazardous medications. Further research would be required to examine the effects of these messages before larger campaigns

6.2 Other considerations

6.2.1 Considerations related to current knowledge and data gaps

This report has revealed that understanding the nature of the problem of intentional self-poisoning with paracetamol and recommending actions to address it are hampered by limited availability of relevant data. The gaps in the current knowledge fall under the following four themes, which further research could address.

Motivations and behaviours of young Australians who have taken paracetamol (and other medicines) for deliberate self-harm or attempted suicide

Much of the research identified in the current review pertaining to the motivations and behaviours of people who self-poison with paracetamol was dated and none of the studies were conducted in Australia, and thus none can be used to understand the doubling in self-harm in children and adolescents over the last decade. As such, commissioning research to undertake qualitative interviews with young Australians who have taken paracetamol for deliberate self-harm or attempted suicide would fill an important knowledge gap. Further research is also needed to understand how online purchasing behaviour including bulk buying through online supermarket and pharmacy retailers may impact the accessibility and availability of paracetamol in the home for self-harm. Research could also be commissioned to examine the health literacy of the public around paracetamol and its storage in the home.

Trends in self-harm with paracetamol over time to identify changing risks

Whether changes to paracetamol availability are made or not, monitoring ongoing trends in self-poisoning with paracetamol and other medicines would enable any new trends, such as age/gender trends or changes in response to COVID-19, to be effectively identified and monitored. The only current national real-time monitoring option is through poisons information centres, and this is also the only source likely to provide high quality information on specific medicines, doses or products ingested. This would be complemented by other sources such as the AIHW NMDS and NCIS, but increasing the currency of data and quality of coding of poisoning information would make these sources much more useful to regulators and policy makers.

There would also be benefits in research to better understand the public's current knowledge of paracetamol poisoning (population sample) and that of youth (not just those that have already self-harmed) to inform preventative practices, that could improve safety but not have adverse impacts on appropriate use. This research might also help understand how to reach

the large number of individuals at risk of self-harm who do not come to the attention of clinicians or educators.

Long-term outcomes after non-fatal self-harm to identify changing risks

There is a need for contemporary Australian data to better understand whether the long-term outcomes after self-harm are changing, in line with the changing rates. There is also much better access to routinely collected data for data linkage to enable comprehensive long-term follow-up. There are several examples of such studies from overseas (Jollant, Goueslard, Hawton, & Quantin, 2022) and one recent study focussed on admissions preceding suicide from Victoria, Australia. (Fernando, Clapperton, & Berecki-Gisolf, 2022). In this study, the top 2, and 5 of the top 7, admission diagnosis codes associated with subsequent suicide were for various poisonings. Non-opioid analgesic poisoning (T39.*) was in 5th place with a standardised mortality ratio for suicide in the year following this poisoning of 66.0 (95% CI: 45.6–92.5). However, this study was not sufficiently large to explore sub-groups (e.g., children/adolescents), and focussed only on suicide in one year period following the admission. Larger, more comprehensive, and longer-term studies utilising linked data are required. For example, the Victorian data might be usefully expanded and combined with the larger similar study that has yet to report on such preceding risk factors (Chitty et al., 2020). There is also a linked NSW poisoning data cohort that has been established yet to report, that might examine outcomes other than suicide (Rose Cairns, personal communication). Facilitated use of the National Integrated Health Services Information (NIHSI) Analysis Asset through the AIHW would allow even more comprehensive studies (Briffa, Jorm, Jackson, Reid, & Chew, 2019).

Medical and psychiatric management of paracetamol self-poisoning

Paracetamol poisoning remains the most common cause of acute liver failure and causes liver injury and many deaths after arrival in hospital. This indicates there is still a need to research methods to improve medical management. This could potentially include simply using current treatments more effectively, by ensuring translation of current guidelines into practice. There are also a number of new antidotes in development, of which the most promising is fomepizole. This is an approved treatment for methanol and ethylene glycol poisoning. It may also work for paracetamol poisoning by completely blocking production of the toxic metabolite NAPQI. Other mechanisms may be in play, as it appears to be effective even when administered with considerable delay. Current evidence is largely limited to animal models and small uncontrolled series with kinetic data. More rigorous randomised clinical trials will be required to meet regulatory and evidence-based guideline standards.

There is strong evidence that psycho-social interventions post self-poisoning are likely to help in reducing suicide reattempt. Increased monitoring and better implementation of effective aftercare services is still needed (F. Shand et al., 2019). New treatments for suicidality have emerged, such as the use of ketamine (Witt et al., 2020) which shows promising outcomes. A focus on reaching people preventatively, before they self-harm, may require innovative social media or mobile apps (Torok et al., 2022), some of which target young people. Effective school based programs should also be introduced in all Australian schools as part of the curriculum (McGillivray et al., 2021).

6.2.2 Forward outlook

Tablet size

The TGA may in future be confronted with a question around permitting larger tablet sizes (1000 mg), which have been developed and registered overseas but not to date in Australia. These appear to lead to larger overdoses (Martinez-De la Torre et al., 2020). While it is possible smaller tablet sizes (e.g., 250 mg) might lead to smaller overdoses, this would require 4 tablets per 1000 mg therapeutic dose and we do not expect this would be acceptable to key stakeholders and patient groups.

Substitution and OTC analgesics

Ibuprofen is much less toxic in overdose but has more adverse drug effects in therapeutic use. Aspirin is roughly equally toxic in overdose to paracetamol but is much less commonly used as an analgesic, and it also has more adverse drug effects with therapeutic use. Were the access to paracetamol following this report changed, an overall shift in the preferred over-the-counter analgesic may not be desirable. However, our review of the literature does not indicate that method substitution is likely. Nevertheless, if new data becomes available showing substitution of paracetamol with other over-the-counter analgesic medications, there may in future be a need to consider analogous pack size restrictions and/or purchasing limits for these. In this context, messaging about appropriate medicine use, and potential harms from stockpiling are relevant across the class of over-the-counter analgesic medications, such as ibuprofen and aspirin, and also where appropriate other NSAIDS that are S2 (e.g., naproxen).

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Appendices

Appendix A: Detailed longitudinal AIHW data in Tables

Data sub-groups of data that includes: Hospital separations with reported ICD-10-AM principal diagnosis codes or any external cause codes as per Table S.1.

Principal diagnosis and external causes as per the ICD-10-AM edition relevant for reference years (financial years).

Excludes:

- Separations for which the care type was reported as Newborn (without qualified days), and records for Hospital boarders or Posthumous organ procurement.
- Hospitalisations in WA with a contracted patient status of 'Inter-hospital contracted patient to private sector hospital', to adjust for separations recorded on both sides of contractual care arrangements.
    - ICD-10-AM codes relevant for reference years:
    - 2009-10: ICD-10-AM 6th edition
    - 2010-11 to 2012-13: ICD-10-AM 7th edition
    - 2013-14 to 2014-15: ICD-10-AM 8th edition
    - 2015-16 to 2016-17: ICD-10-AM 9th edition
    - 2017-18 to 2018-19: ICD-10-AM 10th edition
    - 2019-20: ICD-10-AM 11th edition.
- For analysis of injury or poisoning related separations, a record with an injury or poisoning principal diagnosis/external causes of injury from Table S1 is usually excluded (i.e. is out of scope) where:
    - Transfer_flag=1 (admitted patient transferred from another hospital). This adjusts for overstatement of injury separations arising from some episodes being treated in more than one hospital ; or
    - Rehabilitation_Flag =1 (ICD-10-AM code Z50 - Care involving the use of rehabilitation procedures reported in additional diagnosis). This adjusts for changes to rehabilitation coding and to reflect the number of injury separations where the primary clinical intent is acute care and not rehabilitation.
- Caution should be used in comparing diagnosis, procedure and external cause data over time, as the classifications and coding standards for those data can change over time. Please refer to the Chronicle of the ICD-10-AM First edition to Eleventh edition (ICD-10-AM/ACHI/ACS Chronicle) for information on changes in classifications and coding standards over time and ICD-10-AM editions.

Table S1. List of ICD-10-Am codes for scoping of the extract (provided by client).

Principle diagnoses: T36-T50: Poisoning by drugs, medicaments and biological substances T51-T65: Toxic effects of substances chiefly nonmedical as to source T88.7: Unspecified adverse effect of drug or medicament T96: Sequelae of poisoning by drugs, medicaments and biological substances T97: Sequelae of toxic effects of substances chiefly nonmedical as to source. F10-F19: Mental and behavioural disorders due to psychoactive substance use J68: Respiratory conditions due to inhalation of chemicals, gases, fumes and vapours. J69.1: Pneumonitis due to oils and essences N14: Drug and heavy-metal-induced tubule-interstitial and tubular conditions L27: Dermatitis due to substances taken internally F55: Harmful use of nondependence-producing substances
External causes: X20-X29: Contact with venomous animals and plants X40-X49: Accidental poisoning by and exposure to noxious substances X60-X69: Intentional self-harm (poisoning codes only) X85-X90: Assault (poisoning codes only) Y10-Y19: Event of undetermined intent (poisoning codes only) Y40-Y59: Drugs, medicaments and biological substances causing adverse effects in therapeutic use Y90-Y91: Evidence of alcohol involvement

Paracetamol poisoning admissions in Australia (AIHW NHMD 2009-2020

Ref year	00-04	05--09	10--14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80+	Grand Total
9-10	145	18	302	1759	1265	845	766	806	723	694	448	296	206	100	82	58	104	8617
10-11	163	9	322	1955	1209	818	728	776	694	606	445	307	196	119	70	61	126	8604
11-12	146	16	374	2221	1325	866	740	833	730	599	410	308	198	113	93	61	125	9158
12-13	146	14	650	2469	1230	824	762	780	675	678	497	321	213	131	103	62	157	9712
13-14	182	15	511	2310	1227	849	744	750	654	676	540	340	242	161	113	74	196	9584
14-15	164	26	482	2181	1379	950	872	797	804	656	586	394	260	174	100	83	177	10085
15-16	180	18	537	2509	1482	1107	907	828	805	784	690	380	265	181	118	107	224	11122
16-17	179	12	656	2971	1605	1088	836	818	751	798	651	394	290	218	129	100	201	11697
17-18	179	12	526	2498	1456	1047	732	673	634	650	572	346	269	149	125	106	212	10186
18-19	170	16	496	2199	1358	915	709	561	550	572	531	357	240	169	156	97	231	9327
19-20	156	20	494	1988	1274	874	635	554	476	581	366	373	262	192	120	134	224	8723

Paracetamol deliberate self-poisoning admissions in Australia (AIHW NHMD 2009-2020)

Ref year	<10	10--14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80+	Grand Total
9-10	<5	259	1474	1031	661	630	625	585	565	346	217	153	67	39	30	47	6730
10-11	<5	277	1679	969	624	562	613	559	488	353	235	130	83	44	22	61	6700
11-12	<5	316	1922	1094	693	559	658	568	456	316	231	139	60	54	40	57	7164
12-13	<5	592	2217	1029	670	568	616	541	521	367	242	145	78	64	34	46	7731
13-14	<5	469	2062	994	679	563	598	514	526	423	242	174	104	59	36	80	7524
14-15	0	437	1951	1160	774	651	606	634	480	469	274	163	98	48	37	63	7845
15-16	0	492	2277	1239	890	696	619	626	612	534	290	181	105	63	43	81	8748
16-17	0	613	2756	1373	889	640	631	565	619	481	299	192	127	75	40	81	9381
17-18	<5	495	2291	1261	856	578	513	484	490	426	257	168	86	52	49	69	8078
18-19	<5	466	2050	1188	737	570	408	427	448	395	264	173	98	64	40	75	7404
19-20	0	464	1852	1126	726	498	402	367	440	284	265	164	112	64	59	95	6918

Paracetamol poisoning admissions in Australia – Females

Ref year	00-04	05--09	10--14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80+	Grand Total
9-10	60	9	269	1382	908	560	518	536	507	505	302	209	118	54	44	26	62	6069
10-11	71	3	293	1594	884	541	485	507	474	418	286	199	109	70	35	34	76	6079
11-12	76	9	343	1864	932	636	476	593	477	408	293	198	123	64	49	33	75	6649
12-13	63	6	618	2044	851	565	493	538	459	485	336	204	135	70	66	37	113	7083
13-14	82	<5	483	1946	905	590	488	536	433	486	364	217	145	93	67	45	141	7025
14-15	74	14	439	1785	1013	640	576	531	543	453	394	258	159	106	59	60	117	7221
15-16	82	8	498	2065	1038	743	575	555	535	512	468	247	163	110	71	68	153	7891
16-17	73	7	601	2468	1141	732	528	546	502	540	424	259	173	134	76	66	125	8395
17-18	77	6	484	1990	1074	737	472	432	440	429	403	204	185	89	72	77	138	7309
18-19	77	6	449	1802	1013	638	484	333	370	394	371	199	148	91	95	63	149	6682
19-20	74	7	448	1653	920	626	408	355	321	420	249	230	162	115	77	86	125	6276

Paracetamol poisoning admissions in Australia – Males

Ref year	00-04	05--09	10--14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80+	Grand Total
9-10	85	9	33	377	357	285	248	270	216	189	146	87	88	46	38	32	42	2548
10-11	92	6	29	361	325	277	243	269	220	188	159	108	87	49	35	27	50	2525
11-12	70	7	31	357	393	230	264	240	251	191	117	110	75	49	44	28	50	2507
12-13	83	8	32	425	379	259	269	242	216	193	161	117	78	61	37	25	44	2629
13-14	100	11	28	364	322	259	256	214	221	190	176	123	97	68	46	29	55	2559
14-15	90	12	43	396	366	310	296	266	261	203	192	136	101	68	41	23	60	2864
15-16	98	10	39	444	444	364	332	273	270	272	222	133	102	71	47	39	71	3231
16-17	106	5	55	503	464	356	308	272	249	258	225	135	117	84	53	34	76	3300
17-18	102	6	42	508	382	310	260	241	194	221	169	137	84	60	53	29	74	2872
18-19	93	10	45	392	345	277	225	228	180	178	160	158	92	78	61	34	82	2638
19-20	82	13	46	331	354	248	227	199	155	161	117	143	100	77	43	48	99	2443

Liver injury from hospitalised paracetamol poisoning admissions in Australia by age group (AIHW NHMD 2009-2020)

Ref year	0-19	20-30	30-50	50+	Total
9-10	14	31	61	43	149
10-11	29	27	64	35	155
11-12	17	28	70	46	161
12-13	24	30	88	42	184
13-14	32	37	71	55	195
14-15	29	31	87	76	223
15-16	26	39	92	63	220
16-17	39	46	75	75	235
17-18	30	34	69	91	224
18-19	24	41	72	67	204
19-20	25	30	66	78	199

Note: Death data not detailed as most annual numbers by any age group are <5.

Changes in total medicine poisoning admissions in Australia (AIHW NHMD 2009-2020)

Ref year	00-04	05--09	10--14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80+	Grand Total
9-10	1498	169	697	4317	4408	3759	3548	3966	3556	3353	2344	1661	1294	870	829	834	1858	38961
10-11	1353	167	667	4658	4264	3642	3455	3709	3515	2995	2426	1659	1269	937	830	859	1911	38316
11-12	1234	172	770	5073	4465	3719	3619	3773	3678	3103	2441	1751	1292	947	838	846	1987	39708
12-13	1206	149	1209	5496	4165	3493	3464	3487	3417	3157	2491	1778	1370	1060	877	882	1910	39611
13-14	1258	182	1011	5180	4185	3578	3479	3430	3280	3157	2628	1837	1417	1176	940	876	1930	39547
14-15	1264	177	999	5296	4729	3696	3717	3624	3831	3211	2839	2087	1504	1319	1062	936	2036	42327
15-16	1258	186	1144	5840	5152	4347	3952	3926	3886	3565	3023	2193	1578	1297	1024	1067	2169	45607
16-17	1371	212	1305	6624	5339	4276	3957	3811	3786	3786	3093	2284	1706	1342	1172	1106	2156	47327
17-18	1298	197	1205	5976	4882	4009	3443	3479	3428	3361	2854	2229	1626	1334	1174	1038	2270	43807
18-19	1283	215	1172	5542	4885	3959	3397	3262	3228	3259	2824	2203	1697	1340	1223	1057	2220	42766
19-20	1340	216	1206	5560	4990	3926	3357	3224	2974	3105	2546	2067	1593	1333	1180	1084	2216	41920

Note: ICD codes: T36-T50: Poisonings by drugs, medicaments and biological substances.

Changes in intentional medicine poisoning admissions in Australia (AIHW NHMD 2009-2020)

Ref year	00-04	05--09	10--14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80+	Grand Total
9-10		6	506	3272	3081	2542	2465	2764	2610	2384	1584	998	711	342	200	205	304	23974
10-11		8	492	3613	2947	2435	2274	2602	2484	2152	1681	1048	675	401	257	186	321	23576
11-12		6	583	4066	3118	2492	2407	2624	2558	2176	1646	1062	693	358	239	197	336	24561
12-13		<5	999	4491	3002	2432	2272	2450	2402	2244	1639	1087	731	438	252	210	316	24968
13-14		12	852	4260	2968	2414	2282	2344	2238	2195	1706	1118	714	460	276	200	302	24341
14-15		7	827	4301	3395	2552	2387	2428	2623	2186	1873	1190	765	530	295	202	335	25896
15-16		<5	952	4884	3714	2979	2560	2493	2578	2409	2031	1312	816	521	303	250	367	28172
16-17		<5	1104	5624	3919	2968	2623	2485	2539	2579	2043	1321	869	536	364	241	436	29655
17-18		7	1016	5029	3560	2786	2259	2251	2196	2190	1789	1259	773	489	347	237	385	26573
18-19		9	983	4663	3652	2742	2331	2040	2077	2174	1799	1295	813	563	352	233	391	26117
19-20		<5	999	4574	3712	2650	2163	1987	1859	1988	1602	1203	778	505	335	255	455	25069

Annual totals of combinations of paracetamol and opiates in Australia (by age group) (AIHW NHMD 2009-2020)

Ref year	<10	10--14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80+	Grand Total
9-10	28	32	313	298	251	294	296	260	279	162	116	84	26	21	17	10	2487
10-11	22	49	332	302	256	273	278	243	211	141	101	69	38	9	14	24	2362
11-12	20	47	376	327	265	248	295	243	243	145	106	68	30	19	18	15	2465
12-13	13	70	435	301	279	233	282	233	230	180	102	67	34	21	26	28	2534
13-14	20	54	342	335	250	253	299	240	268	198	102	71	64	29	15	30	2570
14-15	30	72	362	357	281	299	276	312	219	237	142	79	57	30	16	26	2795
15-16	21	49	466	412	379	312	284	297	287	241	125	74	51	29	26	33	3086
16-17	18	80	499	433	314	274	286	278	298	239	138	97	73	35	24	35	3121
17-18	16	55	389	334	271	229	230	205	234	160	122	80	37	22	23	28	2435
18-19	18	33	243	249	177	155	137	143	172	129	94	73	51	38	18	33	1763
19-20	17	23	168	210	160	140	121	114	129	123	111	63	38	21	28	45	1511

Monthly totals of paracetamol poisoning admissions in Australia (by age group) (AIHW NHMD 2009-2020)

	<15	15--19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70+	Total
Jul-09	47	124	101	80	55	58	68	50	35	31	19	9	19	696
Aug-09	47	164	105	67	57	79	64	59	33	24	13	5	17	734
Sep-09	37	141	97	71	65	71	61	57	33	13	15	10	19	690
Oct-09	46	159	114	64	68	55	75	66	32	23	16	6	20	744
Nov-09	47	151	103	74	69	71	59	66	43	25	18	4	26	756
Dec-09	34	108	99	69	62	56	71	55	46	25	14	10	24	673
Jan-10	27	141	112	69	64	80	64	65	50	29	22	6	17	746
Feb-10	40	146	126	95	56	65	59	46	29	28	18	11	14	733
Mar-10	34	160	111	76	74	63	39	64	42	30	15	2	23	733
Apr-10	28	146	104	50	74	70	58	51	45	27	20	12	21	706
May-10	41	159	91	63	62	55	47	63	29	17	19	13	14	673
Jun-10	34	142	86	57	58	71	48	48	28	16	13	9	15	625
Jul-10	37	147	87	71	65	73	47	48	29	20	13	9	18	664
Aug-10	69	204	92	76	79	71	47	51	36	19	16	<5	20	783
Sep-10	51	156	106	56	49	71	62	52	29	24	18	7	19	700
Oct-10	55	164	107	70	65	65	62	46	29	21	10	12	21	727
Nov-10	29	154	99	72	70	60	62	60	45	23	22	7	23	726
Dec-10	33	133	98	69	50	61	54	43	39	28	14	13	24	659
Jan-11	31	139	112	69	61	72	68	59	37	34	11	13	24	730
Feb-11	45	146	100	67	46	64	57	55	34	23	21	9	20	687
Mar-11	42	177	126	74	72	75	76	47	40	27	17	9	11	793
Apr-11	39	166	79	67	61	43	42	41	40	18	13	10	18	637
May-11	32	183	112	58	49	58	54	53	41	37	18	13	16	724
Jun-11	28	178	89	61	55	58	58	36	38	26	18	9	35	689
Jul-11	34	159	90	56	55	56	40	40	21	18	17	13	22	621
Aug-11	43	190	88	62	71	57	60	44	29	19	11	8	23	705
Sep-11	37	142	101	56	68	66	67	50	35	29	14	6	18	689

Oct-11	40	202	113	70	61	68	58	54	38	24	18	5	21	772
Nov-11	49	182	125	97	66	74	67	43	40	27	14	6	25	815
Dec-11	33	134	113	68	50	84	54	64	45	31	7	8	19	710
Jan-12	29	189	136	78	67	77	61	46	31	28	16	16	26	800
Feb-12	58	172	97	78	64	80	71	57	49	28	13	13	29	809
Mar-12	56	202	125	75	56	82	69	63	34	24	20	4	30	840
Apr-12	35	189	117	66	46	72	70	48	20	24	26	4	21	738
May-12	58	259	107	83	61	58	47	41	35	22	24	8	19	822
Jun-12	57	182	108	71	66	56	53	45	29	23	9	15	14	728
Jul-12	56	174	85	70	58	59	47	55	48	22	9	16	17	716
Aug-12	61	208	85	69	61	59	49	55	37	29	12	11	22	758
Sep-12	69	203	91	58	60	73	51	44	45	27	24	10	28	783
Oct-12	92	240	115	58	72	59	61	50	46	23	14	15	20	865
Nov-12	70	231	113	75	60	69	61	61	43	21	19	14	24	861
Dec-12	57	150	99	73	55	72	54	55	46	34	21	11	27	754
Jan-13	55	170	104	66	72	84	56	55	38	23	26	12	21	782
Feb-13	73	201	96	64	62	54	57	57	41	16	23	6	32	782
Mar-13	80	212	108	96	65	53	66	60	33	27	14	14	28	856
Apr-13	69	209	110	69	64	68	62	75	41	25	18	<5	29	843
May-13	77	240	102	64	65	59	47	55	46	36	19	6	30	846
Jun-13	49	215	96	52	55	54	57	47	25	27	13	11	32	733
Jul-13	73	215	96	60	58	51	49	57	38	20	16	9	28	770
Aug-13	68	231	109	67	61	54	54	42	48	32	17	7	43	833
Sep-13	75	196	112	56	67	60	54	66	39	32	24	20	37	838
Oct-13	67	208	91	58	63	60	41	56	50	28	26	18	30	796
Nov-13	62	181	89	84	52	64	62	59	49	27	11	14	27	781
Dec-13	40	153	102	64	52	58	55	55	55	24	27	15	30	730
Jan-14	53	149	74	70	59	69	46	49	43	32	15	12	35	706
Feb-14	46	180	102	71	55	60	61	54	49	28	21	13	33	773

Mar-14	60	234	130	87	77	89	68	60	43	32	25	18	30	953
Apr-14	58	171	109	74	72	66	52	65	41	28	10	10	22	778
May-14	56	189	113	74	62	58	59	53	36	22	21	11	35	789
Jun-14	47	178	88	74	56	47	52	42	43	31	24	12	17	711
Jul-14	52	173	103	69	68	58	56	37	44	31	21	9	28	749
Aug-14	66	210	111	71	82	50	57	57	50	26	19	21	25	845
Sep-14	48	172	116	89	74	59	70	58	50	26	9	19	22	812
Oct-14	71	197	95	70	58	77	57	53	48	36	22	13	32	829
Nov-14	68	196	106	80	72	66	59	50	59	33	21	16	28	854
Dec-14	38	146	126	71	75	66	80	60	48	40	23	16	34	823
Jan-15	38	153	131	84	73	72	67	53	48	39	27	13	26	824
Feb-15	44	191	114	77	70	86	72	71	45	28	26	15	36	875
Mar-15	60	183	122	83	78	74	65	48	51	31	25	9	31	860
Apr-15	45	142	126	87	62	53	65	48	49	30	24	12	29	772
May-15	69	228	124	74	71	63	70	62	37	34	19	10	30	891
Jun-15	64	168	98	84	83	62	70	44	50	32	15	16	33	819
Jul-15	54	187	119	75	70	64	55	62	55	26	28	8	31	834
Aug-15	66	217	124	79	65	58	54	68	49	32	11	16	34	873
Sep-15	74	174	97	90	66	60	61	58	56	33	16	13	31	829
Oct-15	57	240	122	89	75	76	90	52	59	35	16	9	37	957
Nov-15	58	228	143	90	78	75	63	52	51	32	21	14	37	942
Dec-15	44	140	121	100	68	80	73	67	52	34	22	16	41	858
Jan-16	53	173	121	107	89	55	75	75	59	21	28	22	42	920
Feb-16	56	212	117	114	89	76	77	57	64	34	34	17	31	978
Mar-16	65	219	119	92	92	99	76	87	75	43	24	15	41	1047
Apr-16	56	205	119	78	75	63	59	60	46	30	20	15	41	867
May-16	69	266	136	97	77	49	58	64	76	20	13	15	32	972
Jun-16	77	228	126	82	48	71	50	74	37	30	30	16	33	902
Jul-16	54	246	113	96	69	65	61	46	50	32	19	17	28	896

Aug-16	83	258	129	65	64	70	46	61	54	37	25	8	16	916
Sep-16	55	226	145	83	83	80	65	74	51	26	26	19	51	984
Oct-16	72	237	111	102	76	61	75	72	44	24	33	23	32	962
Nov-16	70	242	140	100	72	65	67	49	63	32	20	21	50	991
Dec-16	61	178	132	92	66	64	53	59	51	37	21	18	30	862
Jan-17	57	200	139	86	63	65	69	57	45	32	35	27	41	916
Feb-17	60	247	143	90	58	71	63	61	67	26	21	11	51	969
Mar-17	101	330	152	102	84	76	83	92	56	36	18	21	39	1190
Apr-17	65	243	136	84	65	69	51	69	57	46	24	16	28	953
May-17	85	272	137	90	71	62	58	78	51	24	21	16	29	994
Jun-17	80	269	132	88	59	55	58	76	54	37	18	21	28	975
Jul-17	62	217	110	78	75	70	45	63	38	33	24	8	30	853
Aug-17	64	254	123	66	70	50	62	55	51	24	12	13	40	884
Sep-17	67	200	130	70	61	62	52	34	53	29	24	5	32	819
Oct-17	69	263	123	88	58	65	71	67	41	38	28	11	33	955
Nov-17	70	235	176	97	56	49	51	61	47	27	24	10	40	943
Dec-17	51	159	107	99	68	69	52	72	74	21	20	11	45	848
Jan-18	42	166	122	107	67	66	61	45	49	35	14	9	47	830
Feb-18	54	173	109	86	72	48	61	58	54	24	29	19	29	816
Mar-18	63	212	117	98	57	41	40	57	38	25	26	13	36	823
Apr-18	49	186	104	107	62	52	39	37	41	28	19	14	31	769
May-18	69	194	114	69	34	52	52	43	48	25	24	20	39	783
Jun-18	55	225	105	78	49	45	40	45	31	31	18	9	40	771
Jul-18	54	183	98	70	48	54	52	46	33	37	24	12	37	748
Aug-18	90	181	124	96	56	43	40	43	58	27	21	8	53	840
Sep-18	67	186	104	85	82	55	42	44	38	32	20	10	36	801
Oct-18	62	220	119	80	51	39	45	55	45	24	19	19	31	809
Nov-18	55	208	117	70	55	59	47	60	37	31	17	19	33	808
Dec-18	48	154	113	68	58	52	55	37	40	28	19	10	35	717

Jan-19	41	155	117	79	74	36	52	44	45	45	26	10	37	761
Feb-19	52	149	116	62	62	44	32	43	50	25	22	20	44	721
Mar-19	54	191	112	88	54	52	52	57	56	34	20	18	47	835
Apr-19	47	182	132	76	55	45	47	53	47	28	19	11	40	782
May-19	56	185	96	76	67	38	42	43	43	20	19	17	38	740
Jun-19	54	191	110	62	45	41	41	39	37	26	12	11	42	711
Jul-19	48	161	109	68	49	48	39	54	25	39	22	11	40	713
Aug-19	65	164	86	70	59	47	37	38	33	33	17	17	46	712
Sep-19	60	179	109	78	63	36	33	59	36	35	24	19	32	763
Oct-19	50	172	113	79	55	47	47	44	30	31	24	17	23	732
Nov-19	49	169	116	80	58	39	44	37	31	23	26	16	34	722
Dec-19	35	133	114	69	42	53	40	48	25	29	22	11	50	671
Jan-20	48	142	120	82	46	68	36	48	28	25	31	14	43	731
Feb-20	65	183	94	55	58	42	50	41	36	35	21	13	46	739
Mar-20	76	173	102	84	47	52	45	65	35	31	17	18	38	783
Apr-20	52	142	83	62	44	38	26	50	23	30	20	13	37	620
May-20	51	181	120	80	60	38	38	50	36	25	21	21	36	757
Jun-20	64	175	91	56	45	38	37	37	22	30	13	16	32	656

'Other NSAID' poisonings in Australia (by age group) (AIHW NHMD 2009-2020)

Total T393	0-19	20-30	30-50	50+	Total
9-10	320	289	308	82	999
10-11	388	298	309	101	1096
11-12	406	375	315	97	1193
12-13	595	343	320	84	1342
13-14	473	324	331	115	1243
14-15	521	394	395	140	1450
15-16	628	484	450	132	1694
16-17	766	515	418	148	1847
17-18	618	478	441	145	1682
18-19	618	488	421	153	1680
19-20	539	453	410	153	1555

'Other NSAID' poisonings in combination with 'other opiates' in Australia (by age group) (AIHW NHMD 2009-2020).

T393 + T402	0-19	20-30	30-50	50+	Total
9-10	95	110	165	41	411
10-11	109	107	140	37	393
11-12	104	150	148	19	421
12-13	149	135	142	33	459
13-14	111	129	162	39	441
14-15	133	144	173	77	527
15-16	150	181	189	57	577
16-17	197	169	169	70	605
17-18	148	145	183	53	529
18-19	103	119	125	36	383
19-20	63	99	107	60	329

Appendix B: Detailed longitudinal NSW PIC data in Tables

Changes in poisoning exposure events, overall, for paracetamol and for comparable categories. (NSW PIC 2011-2021)

All exposures	Unintentional	Intentional	Other/Unknown
2011	63400	11190	258
2012	62069	12252	631
2013	60995	12867	453
2014	60213	13221	368
2015	61805	13609	353
2016	60768	14092	411
2017	59192	14448	465
2018	58991	14637	438
2019	62587	15443	601
2020	65151	17780	699
2021	65945	19361	753
Medicines			
2011	26417	10151	172
2012	26681	11076	444
2013	25760	11582	310
2014	26536	10484	244
2015	28749	10695	247
2016	28380	11099	285
2017	28387	11430	312
2018	27892	11497	306
2019	29988	11948	406
2020	29972	13642	473
2021	31307	14762	505
Analgesics			
2011	4804	2669	33
2012	4878	3000	103
2013	4764	3286	84
2014	5443	3943	59
2015	6020	4127	73
2016	5804	4370	85
2017	5875	4844	101
2018	5697	4448	101
2019	6388	4638	118
2020	5855	5365	134
2021	5852	6057	134
Paracetamol			
2011	1286	1469	11
2012	1335	1637	41
2013	1300	1833	45
2014	1385	1814	28

2015	1536	1834	22
2016	1580	1970	28
2017	1553	2248	34
2018	1579	2226	40
2019	1890	2334	49
2020	1807	3049	53
2021	1810	3575	54

Note single ingredient paracetamol exposures only. "Intentional" includes a grouping of deliberate self-poisoning, intentional:other, and recreational exposure types.

Single ingredient and combination product paracetamol poisoning exposure events. (NSW PIC 2011-2021).

2011	5--19	Others	Total single ingredient	5--19	Others	Total combination products
Jan	69	146	215	14	101	115
Feb	65	150	215	15	98	113
Mar	95	179	274	33	104	137
Apr	60	132	192	22	83	105
May	90	172	262	34	92	126
Jun	79	143	222	30	122	152
Jul	68	137	205	19	111	130
Aug	97	149	246	30	104	134
Sep	82	168	250	20	113	133
Oct	77	139	216	26	121	147
Nov	79	169	248	21	92	113
Dec	74	147	221	21	113	134
2012						
Jan	71	166	237	22	114	136
Feb	79	142	221	26	90	116
Mar	87	142	229	23	94	117
Apr	74	154	228	32	78	110
May	101	150	251	27	117	144
Jun	99	159	258	31	105	136
Jul	104	165	269	20	90	110
Aug	125	148	273	37	121	158
Sep	97	175	272	25	119	144
Oct	110	152	262	35	98	133
Nov	111	163	274	34	116	150
Dec	72	167	239	17	93	110
2013						
Jan	68	196	264	25	86	111
Feb	99	166	265	21	89	110
Mar	84	181	265	28	100	128
Apr	105	163	268	17	93	110
May	113	156	269	34	101	135

Jun	103	142	245	34	95	129
Jul	109	170	279	29	102	131
Aug	120	180	300	36	117	153
Sep	99	154	253	23	103	126
Oct	115	150	265	28	104	132
Nov	110	152	262	19	102	121
Dec	85	158	243	21	100	121
2014						
Jan	80	164	244	20	113	133
Feb	72	169	241	26	96	122
Mar	109	212	321	19	112	131
Apr	78	179	257	36	127	163
May	79	180	259	34	97	131
Jun	86	180	266	28	128	156
Jul	81	183	264	34	113	147
Aug	96	178	274	24	133	157
Sep	91	198	289	26	121	147
Oct	96	194	290	27	102	129
Nov	98	178	276	29	121	150
Dec	60	186	246	23	131	154
2015						
Jan	72	178	250	20	136	156
Feb	75	199	274	24	106	130
Mar	75	178	253	29	111	140
Apr	70	168	238	23	137	160
May	99	159	258	36	148	184
Jun	78	198	276	30	114	144
Jul	93	198	291	26	164	190
Aug	147	218	365	39	159	198
Sep	112	205	317	28	132	160
Oct	97	193	290	31	155	186
Nov	98	218	316	37	148	185
Dec	69	195	264	22	134	156
2016						
Jan	79	191	270	22	127	149
Feb	89	210	299	39	129	168
Mar	90	225	315	25	125	150
Apr	85	171	256	25	138	163
May	119	185	304	32	134	166
Jun	103	161	264	33	116	149
Jul	101	202	303	37	163	200
Aug	144	226	370	61	140	201
Sep	109	204	313	39	178	217
Oct	115	207	322	25	133	158
Nov	103	178	281	31	112	143

Dec	87	194	281	25	163	188
2017						
Jan	73	214	287	26	150	176
Feb	108	186	294	36	153	189
Mar	127	206	333	28	158	186
Apr	98	180	278	28	152	180
May	115	190	305	36	109	145
Jun	109	218	327	24	153	177
Jul	118	209	327	49	159	208
Aug	157	223	380	39	171	210
Sep	118	224	342	48	163	211
Oct	122	224	346	29	164	193
Nov	117	231	348	25	177	202
Dec	79	189	268	30	128	158
2018						
Jan	73	188	261	23	137	160
Feb	109	194	303	26	114	140
Mar	101	199	300	28	126	154
Apr	107	238	345	15	118	133
May	115	210	325	37	102	139
Jun	123	218	341	23	109	132
Jul	90	197	287	22	108	130
Aug	130	207	337	23	105	128
Sep	134	213	347	27	132	159
Oct	109	208	317	30	107	137
Nov	144	243	387	37	123	160
Dec	94	201	295	26	102	128
2019						
Jan	101	211	312	27	117	144
Feb	100	212	312	21	116	137
Mar	126	261	387	31	112	143
Apr	117	227	344	25	127	152
May	123	215	338	33	130	163
Jun	121	228	349	44	113	157
Jul	117	236	353	37	141	178
Aug	149	251	400	36	153	189
Sep	158	258	416	37	129	166
Oct	125	216	341	31	125	156
Nov	129	228	357	28	103	131
Dec	102	262	364	32	116	148
2020						
Jan	104	269	373	19	116	135
Feb	134	240	374	17	108	125
Mar	138	230	368	28	124	152
Apr	97	214	311	17	112	129

May	130	284	414	23	106	129
Jun	156	252	408	26	118	144
Jul	145	247	392	30	117	147
Aug	203	285	488	45	104	149
Sep	161	313	474	29	103	132
Oct	160	280	440	22	112	134
Nov	188	258	446	28	112	140
Dec	145	276	421	22	119	141
2021						
Jan	125	264	389	22	130	152
Feb	165	269	434	38	116	154
Mar	217	292	509	30	104	134
Apr	183	297	480	37	92	129
May	247	240	487	46	117	163
Jun	211	269	480	40	128	168
Jul	194	267	461	36	113	149
Aug	222	241	463	40	98	138
Sep	161	250	411	40	83	123
Oct	199	279	478	29	97	126
Nov	205	244	449	39	111	150
Dec	145	253	398	26	96	122

Intentional single ingredient paracetamol poisoning exposure events. (NSW PIC 2011-2021)

	Child (5 to 14 years)	Adolescent (15 - 19 years)	Unspecified child/ adolescent	Adult (20 to 74 years)	Elderly (>75 years)	Unknown
Female						
2011	79	298	<5	583	<5	<5
2012	119	392	<5	585	6	<5
2013	157	466	<5	668	13	<5
2014	143	411		732	13	10
2015	139	407		787	11	5
2016	180	493		735	12	14
2017	219	528		859	7	10
2018	217	525		846	14	
2019	216	568		884	19	
2020	352	824		1092	17	
2021	577	1050		1123	30	
Male						
2011	12	54		276	7	
2012	12	94		240	<5	<5
2013	15	74	<5	313	6	
2014	24	75		352	<5	
2015	17	88		344	<5	
2016	25	89		374	6	<5
2017	31	131		412	11	<5

2018	28	134		439	9	
2019	32	134		442	19	
2020	47	142		543	13	
2021	54	194		495	19	

Non-intentional single ingredient paracetamol poisoning exposure events in those aged ≥ 5. (NSW PIC 2011-21)

	Child (5 to 14 years)	Adolescent (15 - 19 years)	Unspecified child/ adolescent	Adult (20 to 74 years)	Elderly (>75 years)	Unknown
Female						
2011	151	64	13	413	73	
2012	142	51	15	443	73	
2013	136	40	19	474	69	
2014	138	41	<5	561	91	<5
2015	161	45		608	103	<5
2016	184	37		611	110	
2017	155	44		589	131	
2018	149	40		603	152	
2019	184	49		737	169	
2020	150	38		757	201	
2021	152	33		739	197	
Male						
2011	174	14	18	231	28	
2012	163	35	15	264	31	
2013	187	19	14	249	31	
2014	152	25		322	38	
2015	191	28		338	46	
2016	172	31		368	53	
2017	196	20		348	60	<5
2018	192	23		344	68	
2019	232	33		407	73	<5
2020	159	25		405	70	
2021	163	27		415	78	

Intentional paracetamol combination product poisoning exposures generating calls. (NSW PIC 2011-21)

	Child (5 to 14 years)	Adolescent (15 - 19 years)	Unspecified child/ adolescent	Adult (20 to 74 years)	Elderly (>75 years)	Unknown
Females						
2011	79	298	<5	583	<5	<5
2012	119	392	<5	585	6	<5
2013	157	466	<5	668	13	<5
2014	143	411		732	13	10
2015	139	407		787	11	5

2016	180	493		735	12	14
2017	219	528		859	7	10
2018	217	525		846	14	
2019	216	568		884	19	
2020	352	824		1092	17	
2021	577	1050		1123	30	
Males						
2011	12	54		276	7	
2012	12	94		240	<5	<5
2013	15	74	<5	313	6	
2014	24	75		352	<5	
2015	17	88		344	<5	
2016	25	89		374	6	<5
2017	31	131		412	11	<5
2018	28	134		439	9	
2019	32	134		442	19	
2020	47	142		543	13	
2021	54	194		495	19	

Non-intentional paracetamol combination product poisoning exposures generating calls. (NSW PIC 2011-21)

	Child (5 to 14 years)	Adolescent (15 - 19 years)	Unspecified child/ adolescent	Adult (20 to 74 years)	Elderly (>75 years)	Unknown
Females						
2011	151	64	13	413	73	
2012	142	51	15	443	73	
2013	136	40	19	474	69	
2014	138	41	<5	561	91	<5
2015	161	45		608	103	<5
2016	184	37		611	110	
2017	155	44		589	131	
2018	149	40		603	152	
2019	184	49		737	169	
2020	150	38		757	201	
2021	152	33		739	197	
Males						
2011	174	14	18	231	28	
2012	163	35	15	264	31	
2013	187	19	14	249	31	
2014	152	25		322	38	<5
2015	191	28		338	46	
2016	172	31		368	53	<5
2017	196	20		348	60	
2018	192	23		344	68	
2019	232	33		407	73	

2020	159	25	405	70	
2021	163	27	415	78	

Annual NSW PIC calls about intentional paracetamol poisoning, showing the change in d the reported dose ingested (2011-2021). (Note data from ingestions of combination products are not included)

	<5 g	5 to <10 g	10 to <15g	15 to <20 g	20 to <30 g	30 to <40 g	40 to <60 g	60 g +	Unknown
2011	323	381	287	103	111	39	22	13	190
2012	321	414	349	124	122	52	42	18	195
2013	397	489	331	133	137	62	43	20	221
2014	373	481	325	134	163	55	52	28	203
2015	393	460	337	157	169	60	52	25	181
2016	368	518	333	158	198	64	64	26	241
2017	412	526	435	190	249	93	91	36	216
2018	498	555	296	204	252	112	104	28	177
2019	550	570	346	212	245	101	112	34	164
2020	703	744	459	285	298	136	131	44	249
2021	825	849	584	343	376	168	128	57	245

Annual NSW PIC calls about intentional paracetamol poisoning, showing the change in the reported dose ingested (2011-2021) x age group (Note data from ingestions of combination products are not included)

	<5 g	5 to <10 g	10 to <15g	15 to <20 g	20 to <30 g	30 to <40 g	40 to <60 g	60 g +	Unknown
5-19 years									
2011	120	131	88	31	26	12	4	3	52
2012	149	174	149	57	45	17	9	5	50
2013	190	219	150	42	49	23	10	7	67
2014	156	207	102	46	53	17	11	9	59
2015	164	188	127	58	55	13	11	1	39
2016	163	246	136	65	65	21	15	6	72
2017	189	255	175	95	93	28	25	7	49
2018	216	243	129	88	107	38	33	11	44
2019	267	257	137	90	71	39	35	12	45
2020	336	362	240	132	135	52	35	12	65
2021	460	465	330	192	190	85	60	23	87
other age groups									
2011	203	250	199	72	85	27	18	10	138
2012	172	240	200	67	77	35	33	13	145
2013	207	270	181	91	88	39	33	13	154
2014	217	274	223	88	110	38	41	19	144
2015	229	272	210	99	114	47	41	24	142
2016	205	272	197	93	133	43	49	20	169
2017	223	271	260	95	156	65	66	29	167

2018	282	312	167	116	145	74	71	17	133
2019	283	313	209	122	174	62	77	22	119
2020	367	382	219	153	163	84	96	32	184
2021	365	384	254	151	186	83	68	34	158

Annual NSW PIC calls about intentional paracetamol poisoning, showing the change in IR vs MR paracetamol (2011-2021).

	IR			MR			Total
	5 to 19	others	total IR	5 to 19	others	total MR	
2011	452	929	1381	15	73	88	1469
2012	621	888	1509	34	94	128	1637
2013	706	975	1681	51	101	152	1833
2014	597	1016	1613	63	138	201	1814
2015	590	997	1587	66	181	247	1834
2016	703	1024	1727	86	157	243	1970
2017	827	1177	2004	89	155	244	2248
2018	823	1168	1991	86	149	235	2226
2019	874	1216	2090	79	165	244	2334
2020	1259	1440	2699	110	240	350	3049
2021	1762	1484	3246	130	199	329	3575

Single ingredient product by intent

2011	5--19	Others	All single intentional	5--19	Others	All single accidental
Jan	23	94	117	46	50	96
Feb	34	77	111	30	71	101
Mar	46	100	146	47	78	125
Apr	32	66	98	28	66	94
May	44	91	135	46	80	126
Jun	39	84	123	40	59	99
Jul	33	65	98	35	72	107
Aug	43	75	118	53	74	127
Sep	46	85	131	36	83	119
Oct	47	84	131	30	55	85
Nov	48	101	149	31	68	99
Dec	32	80	112	42	66	108
2012						
Jan	35	80	115	34	83	117
Feb	43	82	125	35	58	93
Mar	47	71	118	38	68	106
Apr	41	82	123	33	69	102
May	69	86	155	32	63	95
Jun	49	81	130	50	76	126
Jul	52	88	140	50	76	126
Aug	76	75	151	48	72	120
Sep	55	83	138	41	91	132
Oct	77	90	167	31	58	89
Nov	73	80	153	37	80	117
Dec	38	84	122	33	79	112
2013						
Jan	44	105	149	24	80	104
Feb	59	98	157	38	65	103
Mar	48	103	151	36	77	113
Apr	72	82	154	33	77	110
May	82	90	172	29	61	90
Jun	68	90	158	34	52	86
Jul	72	89	161	37	81	118
Aug	65	100	165	55	79	134
Sep	59	81	140	39	71	110
Oct	74	75	149	39	70	109
Nov	63	80	143	47	70	117
Dec	51	83	134	32	74	106
2014						
Jan	46	92	138	34	68	102
Feb	56	82	138	16	84	100
Mar	74	126	200	34	84	118
Apr	52	88	140	26	90	116

May	49	90	139	30	89	119
Jun	56	84	140	29	94	123
Jul	49	109	158	31	73	104
Aug	59	81	140	37	95	132
Sep	62	113	175	28	84	112
Oct	64	103	167	32	88	120
Nov	58	94	152	40	83	123
Dec	35	92	127	24	92	116
2015						
Jan	47	93	140	24	85	109
Feb	52	93	145	22	103	125
Mar	43	98	141	32	77	109
Apr	34	75	109	36	93	129
May	63	93	156	36	64	100
Jun	51	105	156	26	93	119
Jul	50	105	155	43	92	135
Aug	73	113	186	74	105	179
Sep	68	101	169	44	101	145
Oct	69	83	152	28	106	134
Nov	67	117	184	31	100	131
Dec	39	102	141	30	91	121
2016						
Jan	56	103	159	22	88	110
Feb	50	101	151	39	107	146
Mar	62	120	182	28	103	131
Apr	55	78	133	30	93	123
May	80	98	178	38	84	122
Jun	74	80	154	28	79	107
Jul	64	101	165	36	101	137
Aug	81	97	178	62	126	188
Sep	62	106	168	45	98	143
Oct	79	103	182	36	103	139
Nov	65	96	161	37	78	115
Dec	61	98	159	26	93	119
2017						
Jan	53	121	174	20	93	113
Feb	82	88	170	26	95	121
Mar	103	113	216	23	91	114
Apr	61	87	148	36	92	128
May	78	100	178	36	87	123
Jun	79	130	209	30	85	115
Jul	73	105	178	44	102	146
Aug	89	108	197	67	113	180
Sep	69	112	181	49	110	159
Oct	86	130	216	36	88	124

Nov	90	122	212	27	107	134
Dec	53	116	169	26	70	96
2018						
Jan	51	98	149	22	89	111
Feb	71	104	175	37	88	125
Mar	78	100	178	19	98	117
Apr	68	124	192	39	112	151
May	72	91	163	43	114	157
Jun	81	120	201	42	96	138
Jul	64	97	161	24	96	120
Aug	97	117	214	32	89	121
Sep	94	111	205	38	102	140
Oct	80	109	189	28	98	126
Nov	98	131	229	44	110	154
Dec	55	115	170	37	82	119
2019						
Jan	78	99	177	22	107	129
Feb	61	94	155	38	116	154
Mar	87	150	237	38	110	148
Apr	76	118	194	41	106	147
May	82	94	176	40	119	159
Jun	63	113	176	58	113	171
Jul	66	103	169	50	129	179
Aug	98	125	223	50	123	173
Sep	102	121	223	54	135	189
Oct	97	109	206	24	104	128
Nov	79	118	197	48	104	152
Dec	64	137	201	37	124	161
2020						
Jan	73	148	221	28	115	143
Feb	102	129	231	29	111	140
Mar	95	132	227	41	94	135
Apr	81	124	205	15	89	104
May	103	158	261	27	124	151
Jun	111	134	245	43	115	158
Jul	116	117	233	26	126	152
Aug	170	155	325	31	128	159
Sep	131	156	287	29	153	182
Oct	138	147	285	22	129	151
Nov	144	141	285	42	115	157
Dec	105	139	244	39	136	175
2021						
Jan	107	138	245	18	123	141
Feb	145	152	297	20	114	134
Mar	179	159	338	38	130	168

Apr	153	151	304	30	140	170
May	194	120	314	51	117	168
Jun	177	134	311	34	131	165
Jul	164	155	319	30	110	140
Aug	181	115	296	39	122	161
Sep	138	139	277	22	110	132
Oct	176	157	333	22	113	135
Nov	159	130	289	46	114	160
Dec	119	133	252	25	111	136

Combination product by intent

2011	**5--19**	**Others**	**All combination intentional**	**5--19**	**Others**	**All combination accidental**
Jan	7	63	70	7	36	43
Feb	5	52	57	9	45	54
Mar	17	58	75	16	46	62
Apr	13	41	54	9	41	50
May	13	48	61	21	44	65
Jun	16	67	83	14	52	66
Jul	13	56	69	6	55	61
Aug	11	54	65	18	50	68
Sep	11	63	74	8	50	58
Oct	15	80	95	11	41	52
Nov	16	61	77	5	30	35
Dec	10	61	71	11	52	63
2012						
Jan	10	74	84	11	40	51
Feb	13	60	73	13	30	43
Mar	11	55	66	11	38	49
Apr	20	52	72	11	25	36
May	14	57	71	13	56	69
Jun	13	67	80	18	38	56
Jul	7	46	53	13	43	56
Aug	19	65	84	18	52	70
Sep	13	87	100	12	31	43
Oct	26	54	80	9	42	51
Nov	23	71	94	11	42	53
Dec	14	58	72	3	32	35
2013						
Jan	14	48	62	10	34	44
Feb	11	46	57	10	42	52
Mar	16	57	73	12	42	54
Apr	9	55	64	8	36	44
May	23	63	86	11	37	48
Jun	23	58	81	11	35	46

Jul	14	61	75	14	40	54
Aug	19	72	91	17	45	62
Sep	16	64	80	7	37	44
Oct	21	69	90	7	35	42
Nov	10	65	75	9	33	42
Dec	11	58	69	10	42	52
2014						
Jan	11	65	76	9	45	54
Feb	14	57	71	12	39	51
Mar	10	66	76	9	45	54
Apr	22	78	100	13	49	62
May	20	54	74	14	42	56
Jun	16	72	88	11	54	65
Jul	17	66	83	17	46	63
Aug	15	68	83	9	64	73
Sep	14	66	80	12	54	66
Oct	12	63	75	14	37	51
Nov	15	71	86	14	49	63
Dec	12	76	88	11	55	66
2015						
Jan	14	66	80	6	68	74
Feb	16	52	68	8	52	60
Mar	20	58	78	8	48	56
Apr	16	75	91	7	61	68
May	25	94	119	11	54	65
Jun	14	53	67	15	59	74
Jul	15	91	106	11	71	82
Aug	23	76	99	14	81	95
Sep	16	68	84	12	62	74
Oct	21	89	110	9	62	71
Nov	22	85	107	15	60	75
Dec	14	83	97	8	48	56
2016						
Jan	16	86	102	5	40	45
Feb	20	70	90	19	57	76
Mar	18	81	99	7	42	49
Apr	18	77	95	7	60	67
May	20	73	93	11	59	70
Jun	19	62	81	14	53	67
Jul	27	87	114	10	75	85
Aug	38	61	99	23	79	102
Sep	26	102	128	13	75	88
Oct	17	78	95	8	52	60
Nov	14	64	78	17	45	62
Dec	12	93	105	13	66	79

2017						
Jan	17	92	109	9	55	64
Feb	22	88	110	14	63	77
Mar	21	96	117	7	59	66
Apr	19	93	112	9	55	64
May	23	63	86	13	46	59
Jun	18	80	98	6	72	78
Jul	23	72	95	26	86	112
Aug	24	80	104	15	90	105
Sep	28	79	107	20	83	103
Oct	19	98	117	9	62	71
Nov	21	106	127	3	70	73
Dec	18	74	92	12	52	64
2018						
Jan	20	85	105	3	51	54
Feb	17	69	86	9	45	54
Mar	18	64	82	10	61	71
Apr	11	57	68	4	59	63
May	25	38	63	12	63	75
Jun	9	41	50	12	66	78
Jul	16	38	54	6	67	73
Aug	22	36	58	1	66	67
Sep	22	63	85	5	69	74
Oct	21	49	70	9	57	66
Nov	26	56	82	11	66	77
Dec	19	48	67	7	53	60
2019						
Jan	25	56	81	2	59	61
Feb	16	51	67	5	64	69
Mar	23	54	77	7	57	64
Apr	18	55	73	7	70	77
May	20	57	77	11	73	84
Jun	22	52	74	22	61	83
Jul	20	56	76	16	83	99
Aug	16	67	83	20	85	105
Sep	20	53	73	17	75	92
Oct	23	56	79	8	68	76
Nov	14	45	59	13	56	69
Dec	22	57	79	9	59	68
2020						
Jan	12	53	65	7	62	69
Feb	12	50	62	5	57	62
Mar	18	69	87	10	53	63
Apr	13	62	75	4	50	54
May	18	61	79	5	45	50

Jun	18	53	71	8	64	72
Jul	19	46	65	11	70	81
Aug	37	58	95	7	44	51
Sep	19	47	66	8	54	62
Oct	15	60	75	7	49	56
Nov	18	50	68	10	60	70
Dec	19	54	73	3	63	66
2021						
Jan	21	69	90	1	58	59
Feb	28	63	91	10	50	60
Mar	21	49	70	9	51	60
Apr	24	39	63	12	50	62
May	35	54	89	11	61	72
Jun	30	59	89	10	68	78
Jul	27	60	87	9	52	61
Aug	34	49	83	5	48	53
Sep	31	51	82	9	32	41
Oct	26	55	81	3	42	45
Nov	32	56	88	7	52	59
Dec	15	47	62	11	44	55

Intentional ibuprofen poisoning events per month (by age group), and change in total and proportion due to ibuprofen combinations after 2018 codeine S4 scheduling

	Child/adolescent	Adult/elderly/unknown	Total	Combination products
Jan-11	11	35	46	5
Feb-11	15	58	73	17
Mar-11	21	52	73	12
Apr-11	18	41	59	9
May-11	19	37	56	10
Jun-11	21	56	77	24
Jul-11	11	39	50	8
Aug-11	16	60	76	15
Sep-11	26	38	64	10
Oct-11	26	47	73	13
Nov-11	28	34	62	12
Dec-11	16	40	56	10
Jan-12	19	54	73	15
Feb-12	27	45	72	11
Mar-12	27	41	68	14
Apr-12	22	34	56	12
May-12	24	48	72	14
Jun-12	25	54	79	7
Jul-12	23	45	68	13

Aug-12	31	46	77	17
Sep-12	36	41	77	11
Oct-12	45	56	101	17
Nov-12	37	41	78	16
Dec-12	24	56	80	11
Jan-13	33	54	87	17
Feb-13	28	46	74	12
Mar-13	26	41	67	14
Apr-13	41	41	82	6
May-13	46	45	91	16
Jun-13	32	35	67	9
Jul-13	33	45	78	14
Aug-13	37	55	92	15
Sep-13	29	50	79	14
Oct-13	28	41	69	11
Nov-13	39	41	80	12
Dec-13	18	44	62	11
Jan-14	14	53	67	10
Feb-14	22	40	62	13
Mar-14	40	75	115	14
Apr-14	26	53	79	11
May-14	33	50	83	13
Jun-14	25	51	76	18
Jul-14	32	41	73	10
Aug-14	40	38	78	9
Sep-14	39	40	79	9
Oct-14	41	53	94	14
Nov-14	29	58	87	15
Dec-14	18	67	85	14
Jan-15	32	37	69	0
Feb-15	21	57	78	12
Mar-15	48	40	88	14
Apr-15	26	47	73	12
May-15	40	54	94	14
Jun-15	31	40	71	19
Jul-15	23	56	79	8
Aug-15	41	48	89	11
Sep-15	32	55	87	12
Oct-15	34	49	83	16
Nov-15	49	58	107	17
Dec-15	27	50	77	17
Jan-16	35	64	99	14
Feb-16	37	37	74	0

Mar-16	32	63	95	9
Apr-16	23	37	60	8
May-16	42	58	100	9
Jun-16	55	49	104	7
Jul-16	46	50	96	11
Aug-16	45	55	100	11
Sep-16	36	64	100	12
Oct-16	41	52	93	15
Nov-16	35	63	98	16
Dec-16	28	51	79	13
Jan-17	40	59	99	19
Feb-17	53	43	96	11
Mar-17	41	47	88	0
Apr-17	30	51	81	13
May-17	57	51	108	6
Jun-17	39	53	92	17
Jul-17	39	50	89	11
Aug-17	47	45	92	13
Sep-17	39	48	87	16
Oct-17	45	70	115	11
Nov-17	46	49	95	13
Dec-17	24	63	87	13
Jan-18	32	70	102	13
Feb-18	29	49	78	8
Mar-18	22	49	71	11
Apr-18	31	53	84	0
May-18	46	52	98	13
Jun-18	45	62	107	9
Jul-18	39	53	92	3
Aug-18	58	54	112	5
Sep-18	48	47	95	4
Oct-18	37	47	84	6
Nov-18	50	61	111	5
Dec-18	37	71	108	5
Jan-19	48	60	108	3
Feb-19	34	50	84	4
Mar-19	48	79	127	9
Apr-19	37	55	92	5
May-19	49	50	99	0
Jun-19	41	61	102	4
Jul-19	31	50	81	2
Aug-19	38	64	102	3
Sep-19	54	39	93	3

Oct-19	54	51	105	1
Nov-19	49	56	105	4
Dec-19	28	61	89	2
Jan-20	35	67	102	1
Feb-20	49	71	120	0
Mar-20	57	65	122	2
Apr-20	45	60	105	1
May-20	48	65	113	3
Jun-20	65	49	114	0
Jul-20	69	60	129	0
Aug-20	76	66	142	8
Sep-20	71	66	137	2
Oct-20	73	65	138	5
Nov-20	69	68	137	4
Dec-20	52	55	107	5
Jan-21	52	80	132	2
Feb-21	80	66	146	3
Mar-21	77	64	141	3
Apr-21	70	54	124	4
May-21	118	70	188	1
Jun-21	84	62	146	1
Jul-21	72	55	127	0
Aug-21	89	58	147	2
Sep-21	82	68	150	3
Oct-21	84	74	158	1
Nov-21	90	75	165	0
Dec-21	40	48	88	7

Appendix C: Tabulated data on Australian paracetamol sales from 2017 to 2021

Unit sales (millions) of non-prescription analgesics, IQVIA 2017-2021

Year	Paracetamol	Other paracetamol combinations	Ibuprofen	Aspirin	Other non-Rx analgesics	Others
2017	31.72	16.78	9.78	4.91	4.48	1.99
2018	32.39	11.26	10.44	4.84	4.90	0.27
2019	33.70	11.48	11.75	4.60	4.89	0.18
2020	33.64	8.59	11.08	4.72	4.99	0.13
2021	33.64	9.27	11.69	4.76	5.42	0.12

Pharmacy unit sales (millions) of non-prescription paracetamol by schedule, IQVIA 2017-21

Year	Schedule 3	Schedule 2	Not scheduled
2017	21.12	23.69	3.69
2018	15.53	24.49	3.62
2019	15.71	25.57	3.89
2020	15.04	23.44	3.75
2021	14.59	24.79	3.53

Pharmacy sales of non-prescription paracetamol, IQVIA 2017-21 by pack size (million units)

Year	1	10	12	20	24	40	48	96	100	Others	Grand Total
2017	3.65	0.39	0.73	2.15	3.58	2.56	1.60	7.68	6.56	0.77	29.68
2018	3.56	0.37	1.65	1.99	3.45	0.98	1.90	8.12	7.57	1.29	30.89
2019	3.72	0.43	1.63	2.04	3.63	1.09	1.99	8.16	7.76	1.48	31.95
2020	3.21	0.29	1.43	2.26	2.21	1.26	1.58	8.30	7.57	1.47	29.59
2021	3.41	0.42	1.38	2.13	2.46	1.18	1.48	7.61	7.51	1.78	29.36

Pharmacy sales of non-prescription paracetamol, IQVIA 2017-21 by pack size (tonnes of paracetamol)

Year	1	10	12	20	24	40	48	96	100	Others	Grand Total
2017	1.46	1.50	3.27	17.59	38.01	44.52	32.36	312.90	213.25	15.79	680.65
2018	1.44	1.43	7.41	16.30	36.52	15.78	38.04	340.29	249.29	26.22	732.71
2019	1.53	1.64	7.23	16.83	38.61	17.51	39.94	350.00	260.42	33.74	767.45
2020	1.25	1.01	6.31	17.39	22.03	19.94	28.91	375.05	268.64	36.91	777.45
2021	13.81	1.51	5.90	17.14	25.25	19.13	29.14	344.73	267.15	48.86	772.63

Proportion getting more than one paracetamol item by unit pack size, IQVIA 2017-21

Year	1	10	12	20	24	40	48	96	100	Average
2017	0.15	0.16	0.14	0.13	0.17	0.1	0.13	0.1	0.07	0.12
2018	0.15	0.16	0.13	0.15	0.17	0.14	0.14	0.1	0.07	0.14
2019	0.14	0.16	0.12	0.16	0.16	0.15	0.14	0.09	0.06	0.11
2020	0.18	0.19	0.13	0.18	0.21	0.15	0.2	0.1	0.07	0.15
2021	0.15	0.22	0.13	0.17	0.18	0.13	0.15	0.08	0.06	0.13

Unit sales (millions) of non-prescription analgesics in grocery stores, IRI2017-2021

Year	Paracetamol	Other paracetamol combinations	Ibuprofen	Aspirin
2017	22.67	0.30	16.86	2.53
2018	22.21	1.10	18.75	2.55
2019	21.40	1.68	20.13	2.40
2020	22.97	2.19	20.81	2.44
2021	24.04	2.34	22.26	2.29

Grocery sales of non-prescription paracetamol, IRI2017-21, million units

Year	12	16	20	Total
2017	2.0	0.1	20.9	23.0
2018	1.9	0.1	21.3	23.3
2019	1.7	0.1	21.3	23.1
2020	1.8	0.1	23.2	25.2
2021	2.2	0.0	24.2	26.4

Grocery sales of non-prescription paracetamol, IRI2017-21, tonnes of paracetamol

Year	12	16	20	Total
2017	11.79	0.45	208.89	221.13
2018	11.41	0.39	213.07	224.88
2019	10.31	0.39	212.65	223.36
2020	11.02	0.53	231.90	243.46
2021	12.98	0.03	242.06	255.07

Grocery sales of non-prescription paracetamol, IRI2017-21, number of packs purchased when more than one item purchased

Year	2 Units	3 Units	4 Units	5 Units	6 Units	7 Units	8 Units	9 Units	10+ Units
2017	17.17	2.81	1.17	0.26	0.16	0.03	0.03	0.01	0.06
2018	18.05	3.06	1.31	0.29	0.18	0.03	0.03	0.01	0.06
2019	18.37	3.17	1.35	0.30	0.19	0.03	0.03	0.01	0.06
2020	20.62	3.25	1.46	0.32	0.19	0.03	0.04	0.01	0.06
2021	19.61	3.21	1.36	0.30	0.17	0.03	0.03	0.01	0.05

Total sales (all states and territories) of paracetamol-containing products (single or multiple ingredients) by pack size at grocery/convenience stores.

Proportion of single pack sales, by pack size

Pack size	2017	2018	2019	2020	2021
20	87.80%	90.26%	90.43%	91.49%	92.29%
12	7.26%	4.00%	3.44%	3.92%	3.38%
10	4.95%	5.74%	6.13%	4.59%	4.33%

Proportion of occasions where this pack size is sold with at least one other paracetamol-containing product

Pack size	2017	2018	2019	2020	2021
20	0.64%	0.68%	0.72%	0.73%	0.66%
12	4.47%	5.50%	7.04%	8.67%	8.74%
10	8.00%	9.60%	9.55%	10.92%	11.01%

Appendix D: Combined Australian PIC data in Tables

National PIC calls about paracetamol exposures - Trends by age 2017-21

Year	<5	5--14	15-19	20-74	75+	All
2017	5172	1546	1950	7498	493	16690
2018	4934	1351	1752	6838	515	15406
2019	5297	1516	1969	7396	568	16779
2020	4431	1567	2272	7395	649	16341
2021	4941	2128	2911	7552	720	18293

National PIC calls about paracetamol exposures - Trends by Intent 2017-21

Year	DSPs	Accidental	Therapeutic errors	Others
2017	5910	3347	6197	1119
2018	5462	3054	6067	823
2019	5767	2914	7148	950
2020	6629	2294	6402	1018
2021	7729	2167	7259	1141

National PIC calls about deliberate self poisoning with paracetamol - Trends by Age 2017-21

Year	<5	5--14	15-19	20-74	75+	All
2017	0	473	1450	3299	44	5293
2018	0	502	1477	3421	47	5460
2019	0	502	1641	3518	78	5767
2020	0	840	2001	3698	51	6615
2021	0	1291	2607	3705	85	7725

Comparison of numbers of patients providing relevant data from the four PICs, 2017-21

All exposure calls	QLD	WA	VIC	NSW	Total
2017	28363	28497	33211	74105	164176
2018	26276	28818	33695	74066	162855
2019	27478	30285	34684	78631	171078
2020	29613	30440	33553	83630	177236
2021	29418	29430	35949	86059	180856

Paracetamol exposures					
2017	2688	2860	3040	7985	16573
2018	2356	2735	2964	7351	15406
2019	2467	3124	3085	8103	16779
2020	2676	2950	2477	8240	16343
2021	2876	3051	3404	8965	18296
Intentional paracetamol					
2017	983	943	1053	2931	5910
2018	844	935	998	2685	5462
2019	856	1038	1082	2791	5767
2020	1148	1143	1001	3337	6629
2021	1226	1176	1417	3910	7729
Child/adolescent paracetamol					
2017	590	695	573	1638	3496
2018	455	548	537	1563	3103
2019	497	645	604	1739	3485
2020	613	732	515	1979	3839
2021	750	848	857	2584	5039

Note Intentional paracetamol exposures refers to deliberate self-poisonings only

Appendix E: Supplementary data on Scheduling overseas and international comparisons

Methodology for scheduling comparison

The categorisation of paracetamol in each overseas jurisdiction was determined by the TGA in one of two ways.

1) Reference to a substance-based categorisation legislative instrument (akin to the Poisons Standard in Australia) or other document, if one could be located; or
2) If no instrument could be located, by inferring the categorisation thresholds for paracetamol based on an assessment of individual paracetamol product market authorisations (for example, for the UK).

To make a comparison between the foreign categorisation and the scheduling in Australia of paracetamol, either a 'forward' or 'reverse' mapping approach was taken. The forward approach started with identifying an overseas jurisdiction's access category for particular paracetamol preparations, and then mapping each of those to one or more Schedules in the Australian Poisons Standard. The reverse approach started with paracetamol preparations in a given Schedule of the Australian Poisons Standard, and then determining in which foreign jurisdiction category or categories they are placed. The steps in the process are detailed in the following table.

Approach	Foreign Source	Process
Forward	Instrument	1. Particular paracetamol preparations are identified in the foreign jurisdiction's instrument, along with its corresponding category ('schedule'). 2. The Poisons Standard was then searched to find in what schedule(s) each of those preparations would fall.
Forward	Individual product market authorisations	1. Individual medicinal product market authorisations in the oversees jurisdiction were retrieved for different paracetamol preparations. 2. The access categories of those products were noted from the market authorisations. 3. The trend for what types of paracetamol preparations are assigned to which foreign access categories was determined. 4. The Poisons Standard was then searched to determine in which schedule(s) those different preparations fall.
Reverse	Individual product market authorisations	1. The Poisons Standard was searched to identify each distinct paracetamol preparation with a given scheduling status. 2. For each of these, a corresponding product was identified in the foreign jurisdiction's database of medicinal product marketing authorisations. 3. The categorisation of that product ('schedule') was identified based on its marketing authorisation.

Notes on data underlying Figure 39 on scheduling

Canada:

- IR tabs/caps – no pack size limits were found

Ireland:

- 500 mg =< 12 tabs = General sale
- 500 mg =< 24 tabs = Pharmacy only
- 500 mg > 24 tabs = Prescription Only
- No equivalent S2/S3 categorisation – the *pharmacy only* sits in between S2 and S3 where it is more restrictive than S2 but less restrictive than S3

Singapore:

- 500 mg or MR – no pack size limits were found
- The database does not provide information on pack size in order to determine what pack sizes fall into the respective schedule in the Poisons Standard.
- No equivalent S2/S3 – *Pharmacy Only Medicine* classification states, "sold from any pharmacy by or under supervision of a pharmacist".

UK:

- Can purchase up to 100 non-effervescent tabs from pharmacies which in practice is a maximum of 96 (3 x 32).
- A pack size of between 16 to 20 tablets would be unscheduled in Australia, however a pack size above 16 would make is a pharmacy medicine in the UK.

USA:

- IR / MR – no pack size limits were found

Comparison of equivalent scheduling status in oversees jurisdictions.

Equivalent Status (if applicable) in oversees jurisdictions						
Australian Scheduling Status	Canada	Ireland	New Zealand	Singapore	UK	USA
Unscheduled	**Unscheduled**	**General Sale**	**General Sale**	**General Sales List**	**General Sales List^**	**Over-the-counter**
	Can be sold without professional supervision.	*Can, with reasonable safety, be sold without the supervision of a pharmacist.*	*Freely available from both pharmacies and other retail outlets*	*Sold or supplied to the public without restriction.*	*Available as self-selection items for sale in registered pharmacies. Can also be sold in other retail outlets that can 'close so as to exclude the public'.*	*No further clarification of any restrictions to this category was found.*
Schedule 2	**Schedule 3**		**Pharmacy Only**	**Pharmacy Only Medicine***	n/a	n/a
	Sold from the self-selection area of the pharmacy which is operated under the direct supervision of the pharmacist.	**Pharmacy-Only*** *Available only under the supervision of a pharmacist.*	*Can be sold in licensed pharmacies and sales can be made by any salesperson.*		*n/a*	n/a
Schedule 3	**Schedule 2**		**Restricted**	*Sold from any pharmacy by or under the supervision of a pharmacist*	**Pharmacy Medicine**	n/a
	Require professional intervention from the pharmacist at the point of sale and possible referral to a practitioner.		*Is not available for self-selection from pharmacy shelves, and the sale must be made by a pharmacist.*		*Can be sold from a registered pharmacy premises by a pharmacist or a person acting under the supervision of a pharmacist.*	n/a
Schedule 4	**Schedule 1**	**Prescription**	**Prescription**	**Prescription Only Medicine**	**Prescription Only Medicine**	**Prescription Only**
	Require a prescription for sale.	n/a	*Available on prescription only and cannot be purchased without a valid prescription.*	Sold or supplied to public on prescription only.	*Legally available only with a valid prescription from a prescriber.*	n/a

*No exact equivalent however, allows for supply by or under supervision of a pharmacist hence placed across Australian S2 and S3.
^No exact equivalent however, available from pharmacy and non-pharmacy outlets without restriction.

Selected Tables/Figures (source data) from publications referenced under international comparisons

Pack size restrictions and non-pharmacy sale restrictions in European countries in 2015/2016.(1)

Table 1.

European PICs, their year of establishment, pack size restriction on paracetamol in pharmacies and sales in non-pharmacy outlets by country.

	Poisons Information Centers (PIC)	Year of establishment of PIC	Area of coverage	Over the counter pharmacy sales (g)	Non-pharmacy outlet sales (g)
Countries with restriction (n = 14)					
Austria	Poisons Information Center Vienna	1975	National	30	No sale
Belgium	Anti-Poison Center of Belgium	1963	National	10	No sale
Denmark	Danish Poisons Information Center	2006	National	10	5
France	Toxic vigilance Coordination Committee and Association of French Poison Centers	1999	National	8	No sale
Finland	Finnish Poison Center	1961	National	15	No sale
Germany/ Munich	Poison Information Center Munich	1968	Regional	10	No sale
Iceland	Iceland Poison Center	1994	National	15	No sale
Ireland	National Poison Information Center Ireland	1966	National	12	6
Italy	Florence Poison Center & Pavia Poison Control Center	1991	National	15	No sale
Norway	Norwegian Poisons Information Center		National	10	5
Slovenia	Poison Control Centre, Division of Internal Medicine, Ljubljana	1973	National	10	No sale
Sweden	Swedish Poisons Information Center	1960	National	10	No sale[1]
Switzerland	Tox Info Suisse	1966	National	8	No sale
UK	National Poison Information Services England (Toxbase 1982)	1962	National	16	8
Countries without restriction (n = 7)					
Croatia	Poison Control Center Zagreb	1970	National	Unlimited	No sale
Czech Republic	Toxicological Information Center of Czech Republic (TIC)	1964	National	Unlimited	6
The Netherlands	Dutch Poison Information Center	1959	National	Unlimited	No sales
Lithuania	Poison Information Bureau	2012	National	Unlimited	No sale
Poland/Lodz	Poison Information Center	1967	Regional	Unlimited	6
Russian Federation/ Moscow	Research and Applied Toxicology Center of Medical and Biological Agency	1993	Regional	Unlimited	Unlimited
Slovakia	Research and Applied Toxicology Center of Medical and Biological Agency	1968	National	Unlimited	No sale

[1]In 2015, Sweden withdrew sales of mild analgesics including paracetamol (10 g) from non-pharmacy outlets sold as regular tablets leaving only effervescent tablets on the market.

US PIC paracetamol (acetaminophen) data from Gummin 2021(2).

Pharmaceuticals Total:	1,446,011	889,952	379,687	56,223	93,054	322,509	1,009	32,069	5,401	636,505	208,073	3,615	30,352	289,107	173,893	109,304	72,620	18,434	1,507
GRAND TOTAL (Nonpharmaceuticals + Pharmaceuticals):	2,557,819	1,866,592	859,042	112,878	133,388	635,580	4,229	105,443	16,032	1,532,146	246,310	17,847	48,893	433,106	321,798	262,086	105,617	21,547	1,957

Table 22B. Demographic profile of SINGLE SUBSTANCE Pharmaceuticals exposure cases by generic category

			Age							Reason				Treated in Health Care Facility	Outcome				
	No. of Case Mentions	No. of Single Exposures	<=5	6-12	13-19	>=20	Unknown Child	Unknown Adult	Unknown Age	Unint	Int	Other	Adv Rxn		None	Minor	Moderate	Major	Death
Analgesics																			
Acetaminophen Alone																			
Acetaminophen Alone, Adult	50,580	33,443	7,034	1,469	8,945	14,751	19	1,013	212	15,443	16,980	11	525	20,894	8,730	5,951	3,208	995	109
Acetaminophen Alone, Pediatric	15,849	14,467	13,072	1,049	145	167	15	11	8	14,069	253	8	70	1,712	2,989	253	50	14	0
Acetaminophen Alone, Unknown if Adult or Pediatric	9,092	5,207	1,229	254	1,323	2,207	6	135	53	2,286	2,656	4	75	3,442	1,358	942	568	242	44
Acetaminophen Combinations																			
Acetaminophen in Combination with Other Drugs, Adult Formulations	5,533	3,241	636	167	1,460	897	2	59	20	1,075	2,060	5	60	2,245	705	909	539	51	2
Acetaminophen in Combination with Other Drugs, Pediatric Formulations	240	205	173	23	5	3	0	1	0	201	4	0	0	12	46	10	0	0	0
Acetaminophen with Codeine	2,316	1,042	113	18	125	711	0	60	15	466	449	0	97	557	231	210	102	22	0
Acetaminophen with Diphenhydramine	6,016	3,546	554	92	707	2,072	1	88	32	1,196	2,241	0	65	2,425	676	794	758	134	5
Acetaminophen with Hydrocodone	9,798	4,258	499	94	413	3,010	5	202	35	2,065	1,853	14	233	2,390	985	867	526	168	17
Acetaminophen with Other Narcotics or Narcotic Analogs	185	101	13	1	9	73	0	5	0	40	48	1	7	51	22	17	12	10	0
Acetaminophen with Oxycodone	6,232	2,942	289	23	365	2,087	0	147	31	1,069	1,651	24	138	1,959	525	516	462	464	14
Acetaminophen with Propoxyphene	20	12	1	0	4	6	0	1	0	4	7	0	1	6	4	1	1	0	0
Acetylsalicylic Acid Alone																			
Acetylsalicylic Acid Alone, Adult Formulations	4,914	2,625	1,023	112	469	947	0	56	18	1,394	1,119	2	68	1,392	621	360	407	47	7
Acetylsalicylic Acid Alone, Pediatric Formulations	1,192	545	339	35	60	100	2	5	4	403	125	0	7	195	147	41	24	4	0
Acetylsalicylic Acid Alone, Unknown if Adult or Pediatric Formulations	9,329	4,188	1,273	163	812	1,804	3	87	46	1,884	2,026	3	96	2,619	935	670	795	117	13

Longitudinal trends in the same data from the US are shown from Hopkins and demonstrate a rise in children/adolescents roughly corresponding to the timing of the rise in Australia(3)

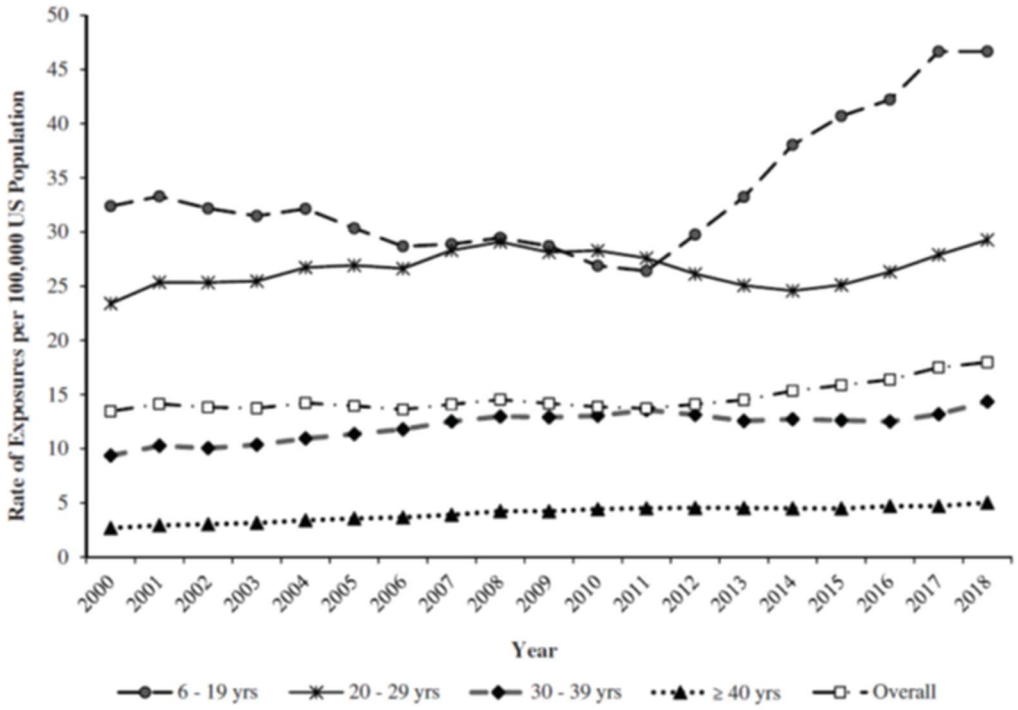

FIGURE 1 Annual rate of suicide-related exposures to over-the-counter analgesic medications per 100 000 US population by age group, NPDS 2000-2018

Edinburgh & Newcastle toxicology treatment centre outcomes for paracetamol overdose.(4)

Table 2
Frequency of liver injury after paracetamol overdose. Patients are grouped by hospital and NAC treatment regimen. RIE = Royal Infirmary of Edinburgh, RVI = Royal Victoria Infirmary, Newcastle. STH = St Thomas' Hospital London. 21 h regimen is the conventional NAC treatment, 12 h regimen is the SNAP regimen. Data from the 2 regimens are compared by presenting the absolute difference in percentage of patients with the defined degree of liver injury and 95% confidence intervals of that difference. All patients are included from the 3 hospital sites.

	RIE 21 h regimen	RIE 12 h regimen	RIE Absolute % difference (95% CI)	STH & RVI 21 h regimen	STH & RVI 12 h regimen	STH & RVI Absolute % difference (95% CI)	21 h v 12 h overall absolute % difference (95% CI)
Number of patients starting NAC	1075	1137	–	413	715	–	–
Extended treatment beyond 21 h (N, (%))	113 (11)	131 (12)	1.0 (−1.6 to 3.6)	47 (11)	40 (6)	−5.8 (−9.5 to 2.5)	−1.5 (−3.6 to 0.5)
Peak ALT > 100 U/L (N, (%))	131 (12)	141 (12)	0.2 (−2.5 to 3.0)	48 (12)	77 (11)	−0.9 (−4.8 to 2.8)	−0.3 (−2.5 to 1.9)
Peak ALT > 150 U/L (N, (%))	108 (10)	109 (10)	0.5 (−3.0 to 2.0)	18 (4)	56 (8)	3.5 (0.5 to 6.2)	0.4 (−1.5 to 2.3)
Peak ALT > 1000 U/L (N, (%))	47 (4)	44 (4)	−0.5 (−2.2 to 1.2)	17 (4)	23 (3)	−0.9 (−3.5 to 1.3)	−0.7 (−2.1 to 0.6)
Peak INR > 2 (N, (%))	35 (3)	37 (3)	0 (−1.5 to 1.5)	10 (2)	23 (3)	0.8 (−1.4 to 2.7)	0.2 (−1.0 to 1.4)
Peak INR > 3 (N, (%))	16 (2)	17 (2)	0 (−1.1 to 1.1)	3 (1)	9 (1)	0.5 (−1.0 to 1.7)	0.1 (−0.7 to 0.9)

Australian toxicology treatment centre overall outcomes for paracetamol overdose.(5)

Table 5
Outcome Table for all paracetamol overdose ingestion types. ALT= Alanine transaminase, INR=international normalized ratio. There was no significant difference between outcomes when comparing the treatment regimens.

	2 bag regimen, $n = 1300$	3 bag regimen, $n = 911$	Absolute difference% (95% CI)
Peak ALT > 150 U/L, n (%)	183 (14)	115 (13)	1 (−1.4,4.3)
ALT > 1000 U/L, n(%)	96 (7.4)	76 (8.3)	−0.9 (−1.3,3.3)
Peak INR > 2, n (%)	63 (4.8)	40 (4.4)	0.4 (−1.3,2.2)
Fulminant hepatic failure, n (%)	12 (0.9)	11 (1.2)	−0.3 (−1.2,0.6)
Mortality, n (%)	2 (0.1)	1 (0.1)	0.04 (−0.3,0.4)

1. Morthorst BR, Erlangsen A, Nordentoft M, Hawton K, Hoegberg LCG, Dalhoff KP. Availability of Paracetamol Sold Over the Counter in Europe: A Descriptive Cross-Sectional International Survey of Pack Size Restriction. Basic Clin Pharmacol Toxicol. 2018;122(6):643-9.

2. Gummin DD, Mowry JB, Beuhler MC, Spyker DA, Bronstein AC, Rivers LJ, et al. 2020 Annual Report of the American Association of Poison Control Centers' National Poison Data System (NPDS): 38th Annual Report. Clin Toxicol (Phila). 2021;59(12):1282-501.

3. Hopkins AG, Spiller HA, Kistamgari S, Zhu M, Michaels NL, Funk AR, et al. Suicide-related over-the-counter analgesic exposures reported to United States poison control centers, 2000-2018. Pharmacoepidemiol Drug Saf. 2020;29(9):1011-21.

4. Pettie JM, Caparrotta TM, Hunter RW, Morrison EE, Wood DM, Dargan PI, et al. Safety and Efficacy of the SNAP 12-hour Acetylcysteine Regimen for the Treatment of Paracetamol Overdose. EClinicalMedicine. 2019;11:11-7.

5. Wong A, Isbister G, McNulty R, Isoardi K, Harris K, Chiew A, et al. Efficacy of a two bag acetylcysteine regimen to treat paracetamol overdose (2NAC study). EClinicalMedicine. 2020;20:100288.

Appendix F: Literature review methodology

Methods

Search terms and strategy

A series of search terms were devised and combined, as outlined below, to identify the literature most relevant to the research questions presented above. The databases searched using this strategy included Medline, Embase, PsycInfo, and Cinahl (nursing and allied health).

1. exp paracetamol/
2. exp Acetaminophen/
3. (paracetamol or acetaminophen).ti,ab.
4. 1 or 2 or 3
5. exp ibuprofen/ or Ibuprofen.mp. or Promethazine.mp. or exp promethazine/ or exp doxylamine/ or Doxylamine.mp. or Naproxen.mp. or exp naproxen/ or Aspirin.mp. or exp acetylsalicylic acid/
6. exp analgesic agent/ or exp Analgesics/ or analgesic*.ti,ab.
7. exp non prescription drug/ or exp Nonprescription Drugs/ or "over the counter".ti,ab. or OTC.ti,ab. or "non prescription".ti,ab. or nonprescription.ti,ab.
8. 6 and 7
9. 5 or 8
10. exp *Pharmaceutical Preparations/ or (Pharmaceutical adj2 (drug* or substanc* or preparation*)).ti,ab.
11. 4 or 9 or 10
12. exp suicide/ or exp suicide attempt/ or exp Suicide, Attempted/ or exp suicidal ideation/ or exp self poisoning/ or exp Self-Injurious Behavior/
13. (suicid* or "self poison*" or (Intention* adj2 (overdos* or poison*)) or (deliberat* adj2 (overdos* or poison*))).ti,ab.
14. 12 or 13
15. exp epidemiology/ or exp incidence/ or exp prevalence/ or exp trend study/ or exp disease burden/ or exp longitudinal study/ or exp drug classification/ or exp Longitudinal Studies/ or exp "Cost of Illness"/
16. (predictor* or trend* or epidemiology or incidence or prevalence or characteristic*).ti,ab.
17. 15 or 16
18. exp Choice Behavior/ or exp Decision Making/ or exp motivation/

19. (planning or planned or opportunism or intent* or intentional* or Premeditate* or opportunistic or Opportunity or Impulsiv*).ti,ab.
20. 18 or 19
21. ((Packet* or pack or package* or packaging) adj3 (dimension or dimensions or size or concentration or volume or design or number or quantity or restrict* or limit* or availability or access or accessibility or chang* or regulat* or prohibit* or tablet*)).ti,ab.
22. (restrict* or limit* or availab* or access* or regulat* or prohibit* or ban or banned or banning or bans or schedul* or upschedul* or reschedul* or substitut*).ti,ab.
23. 21 or 22
24. 17 or 20 or 23
25. exp Australia/ or exp Austria/ or exp Belgium/ or exp Bulgaria/ or exp Canada/ or exp Croatia/ or exp Cyprus/ or exp Czech Republic/ or exp Denmark/ or exp Estonia/ or exp Finland/ or exp France/ or exp Germany/ or exp Greece/ or exp Hungary/ or exp Iceland/ or exp Ireland/ or exp Italy/ or exp Latvia/ or exp Lithuania/ or exp Luxembourg/ or exp Malta/ or exp Netherlands/ or exp New Zealand/ or exp Norway/ or exp Poland/ or exp Portugal/ or exp Romania/ or exp Slovakia/ or exp Slovenia/ or exp Spain/ or exp Sweden/ or exp Switzerland/ or exp United Kingdom/ or exp United States/
26. (Australia* or Austria or Belgium or Bulgaria or Canada or Croatia or Cyprus or Czech Republic or Denmark or Estonia or Finland or France or Germany or Greece or Hungary or Iceland or Ireland or Italy or Latvia or Lithuania or Luxembourg or Malta or Netherlands or "New Zealand" or Norway or Poland or Portugal or Romania or Slovakia or Slovenia or Spain or Sweden or Switzerland or "United Kingdom" or UK or "United states" or USA).af.
27. 25 or 26
28. 11 and 14 and 24 and 27
29. remove duplicates from 28
30. limit 29 to English language

Inclusion and exclusion criteria

The inclusion and exclusion criteria differed for each of the two research questions.

Question 1. Characteristics and behaviours of people engaging in self-harm via paracetamol or other non-opioid analgesics

Studies were considered for inclusion in the first research question of the review if they:

a. Examined participant characteristics, motivations, or behaviours associated with self-poisoning via paracetamol. Studies that did not purely assess paracetamol, but rather assessed all self-poisoning drugs, were included if the information provided on characteristics, motivations, and/or behaviours was broken down by drug type, and

included information available for paracetamol or a medication category containing paracetamol (e.g., over-the-counter analgesics);

b. Were conducted in a country of interest (Australia, Austria, Belgium, Bulgaria, Canada, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, New Zealand, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, Switzerland, United Kingdom (UK), United States of America (USA)). These countries were selected as they are predominantly high-income Western countries that are somewhat comparable to Australia;

c. Reported on primary data; and

d. Were published in an English language peer-reviewed journal from 1990 onwards.

No limits were placed on study design. For this question in the review, we focused specifically on intentional self-harm, therefore studies that did not differentiate between participant characteristics, motivations and behaviour for intentional versus non-intentional self-poisoning were excluded.

Question 2. The effect of restricting paracetamol or other medications on method substitution

Studies were considered for inclusion in the second research question of the review if they:

a. Examined the effect of restricting access to paracetamol or other medications on the use of the restricted medication or other methods in contributing to injury, hospitalisation or death. Outcomes could include prescription rates, number of tablets consumed, number of self-poisonings, number of hospitalisations or injuries (e.g., liver injury), number of calls to poisons information centres, and/or number of deaths due to suicide and/or accidental overdose;

b. Included the restriction of a medication of interest, including paracetamol, ibuprofen, promethazine, naproxen, aspirin, quetiapine, sertraline, fluoxetine, oxycodone, escitalopram, diazepam, pregabalin, co-proxamol, and codeine. These medications were selected as they are most commonly ingested in deliberate self-poisoning cases as identified by the New South Wales (NSW) Poisons Information Centre (PIC);

c. Were conducted in a country of interest (Australia, Austria, Belgium, Bulgaria, Canada, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, New Zealand, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, Switzerland, United Kingdom (UK), United States of America (USA)); and

d. Were published in an English language peer-reviewed journal.

No limits were placed on study design or publication year. Studies were excluded if there was no explicit assessment of the effect of the restriction on method substitution. Studies were permitted to report on outcomes for both intentional and unintentional poisonings or all

poisonings. This allowed a broader number of studies to be considered, given the limited research conducted in this area, and the relevance of both intentional and non-intentional poisoning outcomes to be considered for method substitution.

Screening and data extraction process

Figure 40 presents a PRISMA flow-diagram for the review process. A total of 2,408 abstracts were identified and independently screened for inclusion by one reviewer. A second reviewer independently double-screened 20% of the abstracts (Interrater Reliability results revealed 91% agreement). This screening process resulted in 241 abstracts being identified for full-text review. Full-text articles were collected for all but one abstract and reviewed for inclusion by two reviewers. This process resulted in 81 included studies for which relevant data was then extracted.

For each included study relevant to research question one, data was extracted on: first author name, year of publication, country/setting, study type, sample size, participant age, population and medication(s) assessed and key findings. For studies associated with research question two, information was also extracted about the type of restriction assessed (e.g., pack size reduction, medication withdrawal, up-scheduling). Data extraction was performed using Covidence software.

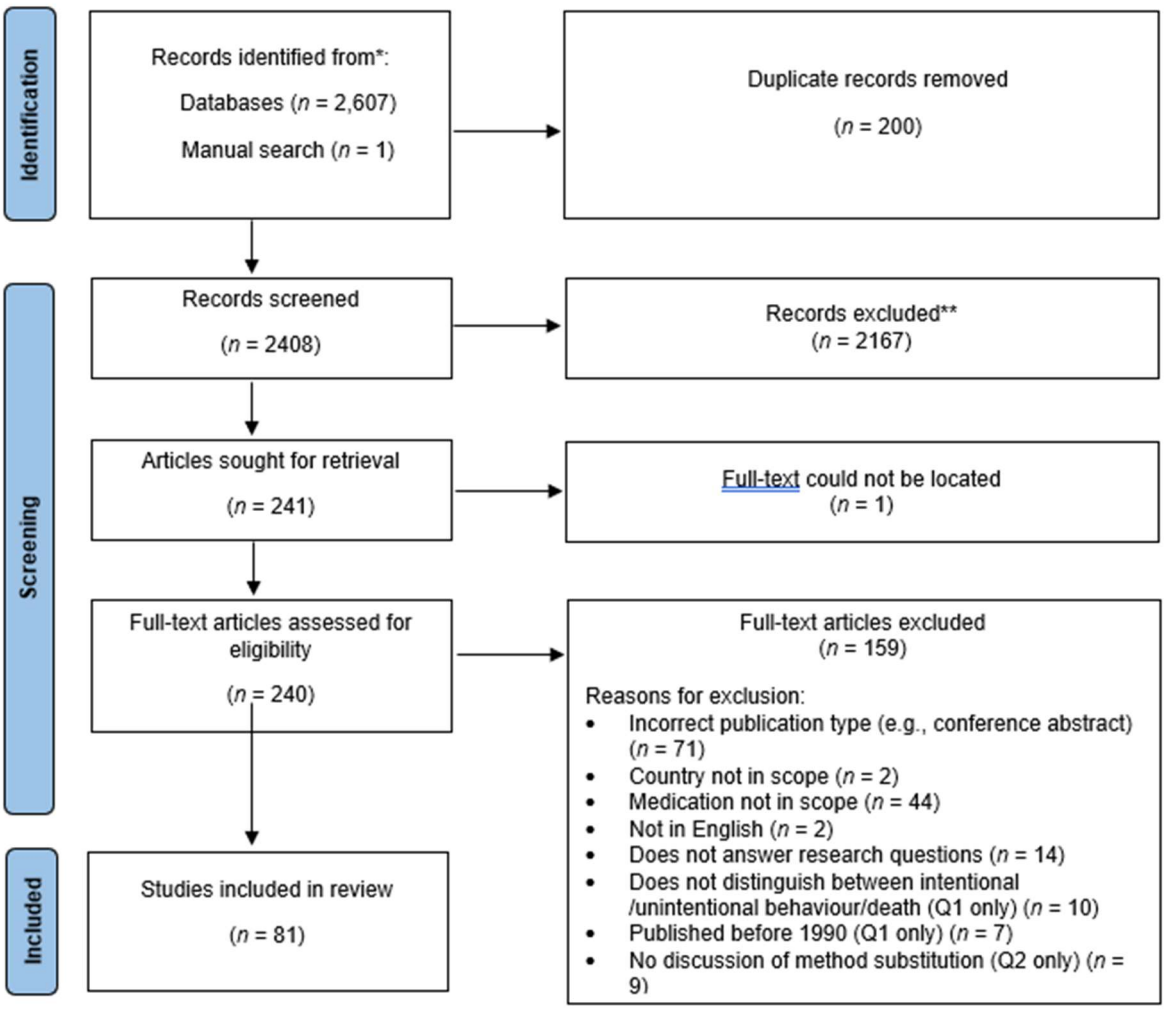

Figure 40. PRISMA flow diagram for study selection process