Risks of intentional self-poisoning with **paracetamol**: Independent expert findings and consultation on possible access and purchasing controls

Adj Prof Robyn Langham AM
Chief Medial Adviser,
Therapeutic Goods Administration

Adj Prof John Skerritt
Deputy Secretary,
Department of Health and Aged Care

The report

- Commissioned in response to concerns of increasing prevalence of intentional paracetamol poisoning in the last decade
  - especially among young people, and involving paracetamol obtained via general sale in supermarkets and convenience stores.

- To guide the Advisory Committee on Medicines Scheduling (ACMS) and the decision-maker for poisons scheduling in their consideration of whether any changes to the scheduling of paracetamol may be warranted

What the panel sought to do

Critical analysis of primary data and international literature

- the incidence of overdosing, including morbidity and mortality
  - Poisons information centre reports, hospital admissions, adverse health outcomes and deaths attributable to paracetamol misuse in Australia
- medicine overdosing behaviour
  - systematic review of available published data
- the balance of benefits and risks of current paracetamol access on the Australian market, and recommendations to the TGA

Who are the panel members?

Professor Nick Buckley (toxicology and pharmacology)

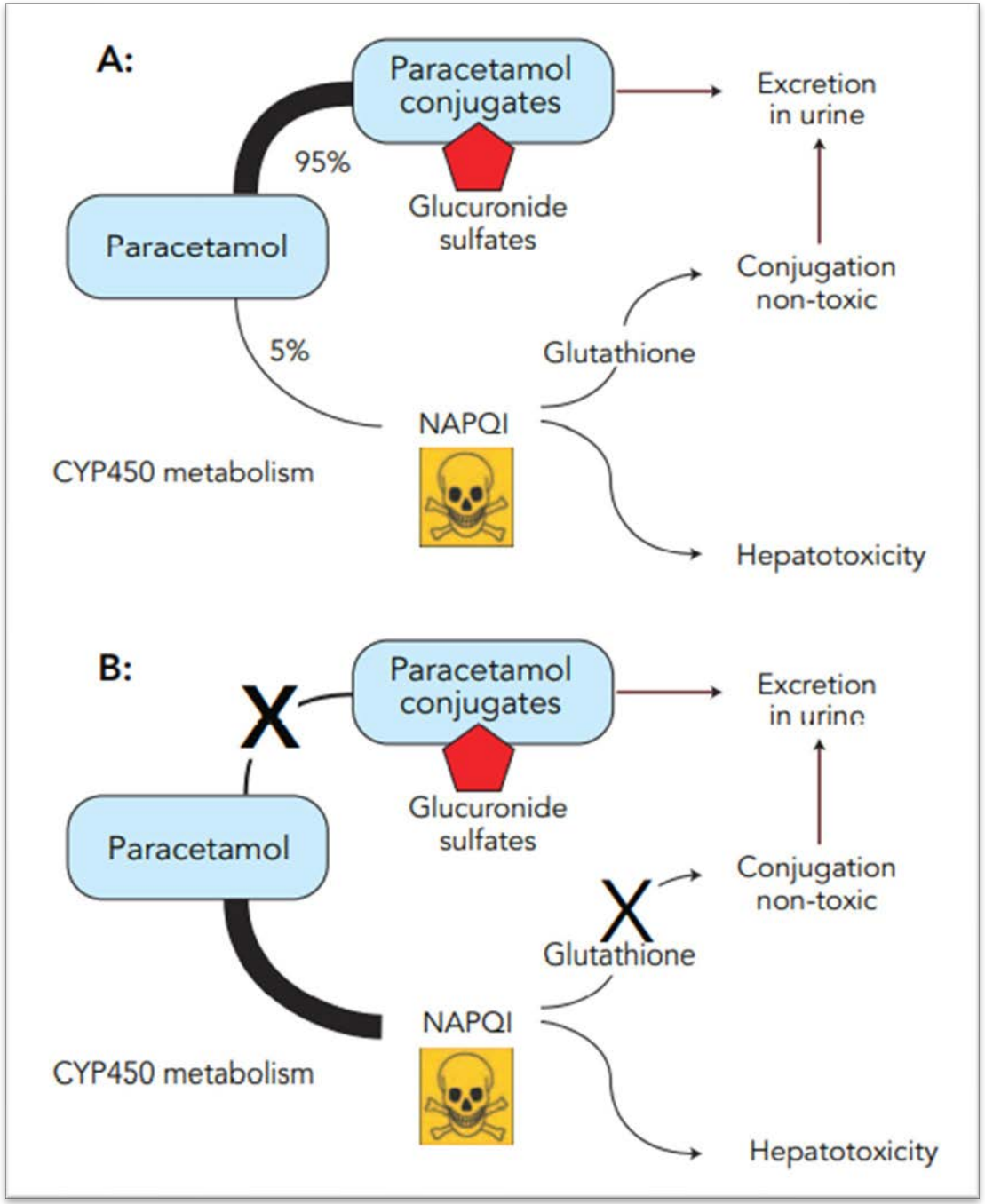
- Professor of Clinical Pharmacology at the University of Sydney and a practicing clinical toxicologist consulting at the RPA Hospital and through all the Poisons Centres in Australia.

Professor Alison Calear (mental health)

- Co-Head of the Centre for Mental Health Research at the Australian National University and works in the areas of youth mental health, e-health and the prevention and early intervention of anxiety, depression, and suicide

Professor Helen Christensen AO (mental health)

- Professor of Mental Health at UNSW and Board Director at the Black Dog Institute who is an international leader in the use of technology to both detect poor mental health and to deliver quality evidence-based therapies.

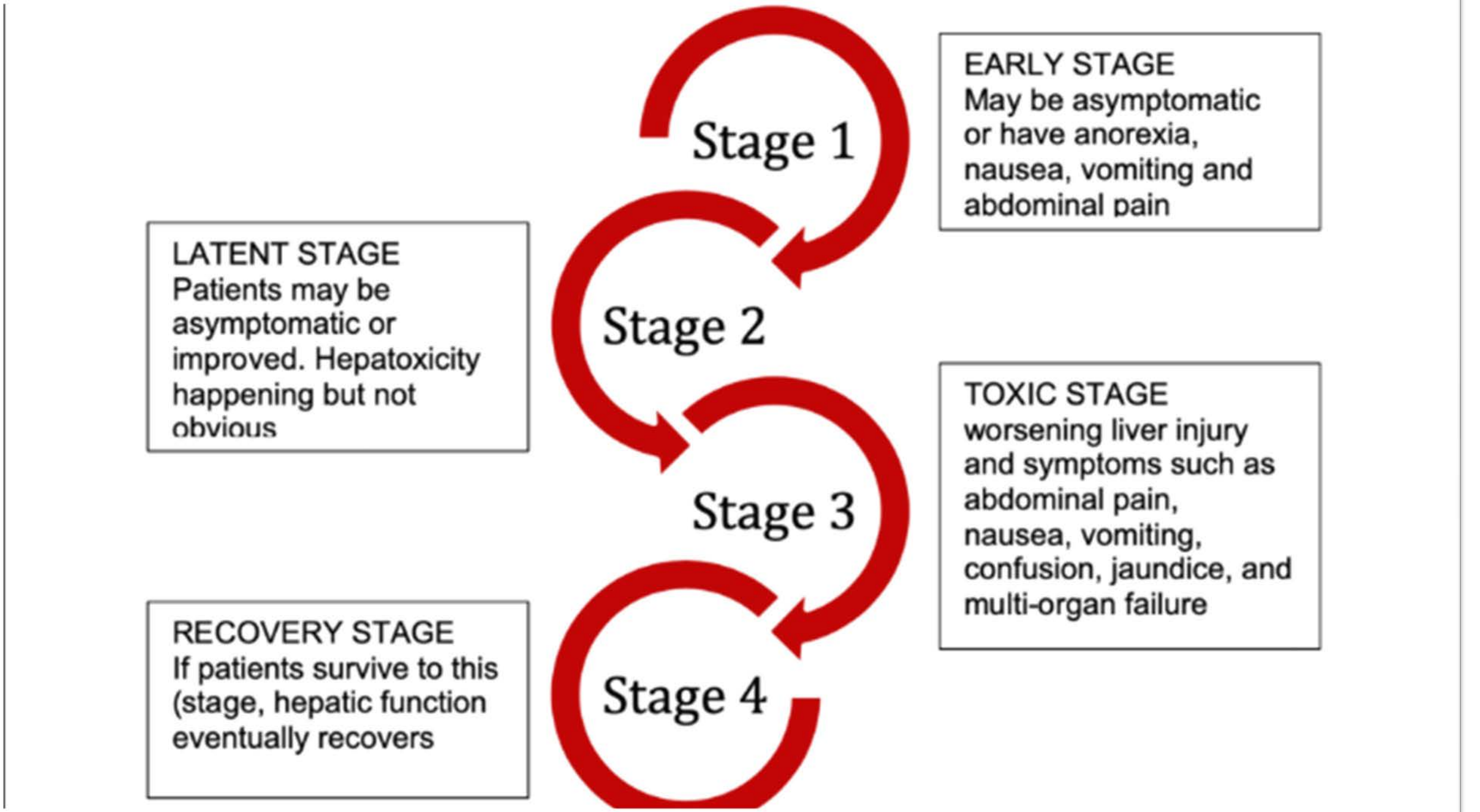


Mechanism of toxicity

With excess paracetamol, non-toxic pathways are saturated, with increased NAPQI

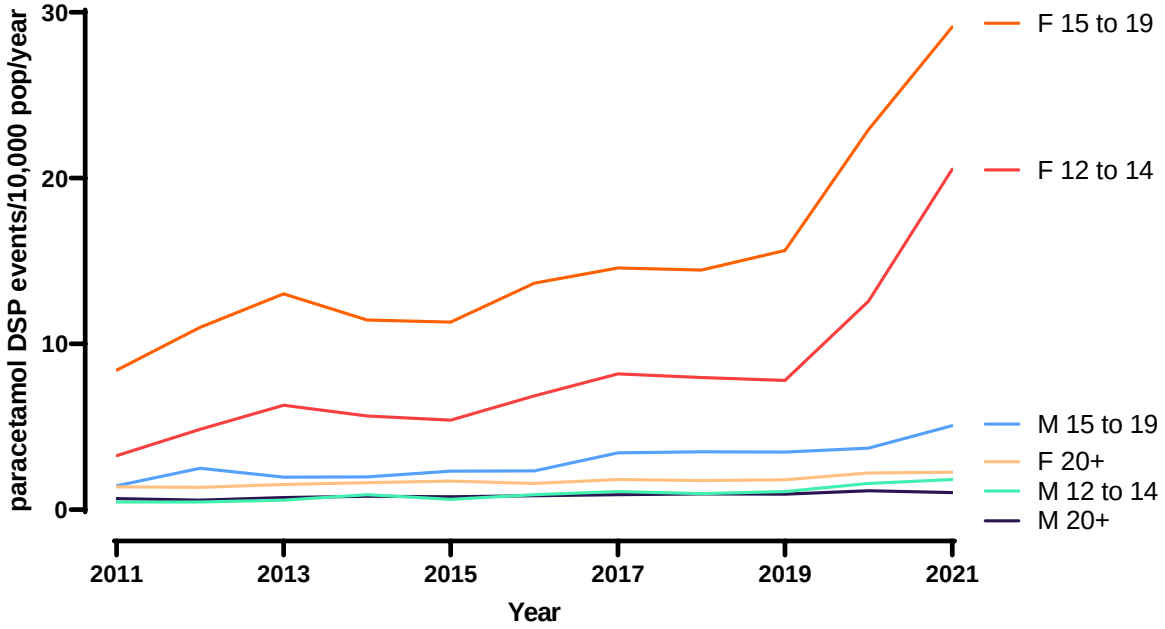
Glutathione depletion
N-Acetyl Cysteine as a substrate

John S Lubel et al. , Med J Aust 2007; 186 (7): 371-372.


Stage 1
EARLY STAGE
May be asymptomatic or have anorexia, nausea, vomiting and abdominal pain
LATENT STAGE
Patients may be asymptomatic or improved. Hepatoxicity happening but not obvious
Stage 2
Stage 3
TOXIC STAGE
worsening liver injury and symptoms such as abdominal pain, nausea, vomiting, confusion, jaundice, and multi-organ failure
RECOVERY STAGE
If patients survive to this (stage, hepatic function eventually recovers
Stage 4

Key findings: paracetamol self-poisoning, hospitalisation & deaths

- Intentional paracetamol overdose events increasing -- highest among adolescents and young adults & more common among females
    - Incidence of intentional self-poisoning increasing generally
- Severe liver injury (2-5%; ~9 people per million) and death (0.2-0.5%; ~2 people per million) from paracetamol poisoning – decreasing or plateau; current treatments usually effective
- Single ingredient and immediate release paracetamol mostly used in self-poisoning, but treatment of overdoses
  is more challenging following ingestion of modified release (MR) preparations



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

Key findings: characteristics and behaviour of patients intentionally overdosing

- Majority of paracetamol self-poisonings in all age groups are impulsive with suicidal intent
  - Repeated episodes of self-harm are common
  - No prior psychiatric diagnosis or mental health symptoms is common
  - Pack warnings unlikely to deter self-poisoning

- Over approximately half the time, the paracetamol taken was already present in the home
  - Only around 10% reported recently purchasing paracetamol (usually on that day)

- The pack size ingested most often and in roughly equal proportions were 20/24s and 96/100s.
  - At least 25-30% of ingestions were of unscheduled products
  - Product sourced from pharmacies and supermarket/convenience both used in self-poisoning

Key findings: international regulation

- Recent rises in child/adolescent female poisonings have been reported overseas; trends overall parallel those in Australia
- Scheduling of paracetamol varies considerably within OECD countries
- Evidence that reductions in pack size reduces deaths from poisonings

Key findings: purchasing of paracetamol

How has self-poisoning trended compared to population and paracetamol sales?

- Largest pack sizes in supermarket/convenience (20 tablets) and pharmacies (96/100 tablets) are favored by consumers
- Multiple pack purchases are common (10-20% of transactions)
- Per million head of population:
    - Units sold decreased between 2017 and 2018 (could be attributed to the rescheduling of codeine to S4), thereafter increasing
    - Poisonings increased, but hospital admissions decreased, with liver injury admissions remaining constant
- Per million units paracetamol sold
    - ~100 deliberate self-poisonings and appearing to increase over time
    - 3 hospitalisations with liver injury and <1 death

1. reducing the **size of packs** of paracetamol sold in supermarkets and convenience stores, and in pharmacies without the advice of a pharmacist

2. limiting the **number of packs** of paracetamol products that can be purchased in one transaction to 1 or 2 packs to reduce home stockpiles of paracetamol

3. making **modified-release paracetamol**, which is designed for long-term use rather than for acute pain, available only with a prescription

4. restricting the purchasing of paracetamol without a prescription to individuals aged **18 years and older**

Expert panel recommendations

Means restriction and harm minimisation

5 improving the **communication** around the potential harms from paracetamol

6 maintaining and expanding **follow-up care** and support after self-harm

7 increasing **awareness about safer storage of medicines and reducing stockpiling** of unwanted medicines.

Expert panel recommendations

Non-medication specific recommendations

Paracetamol re-scheduling options – what are they?

Adjunct Prof, John Skerritt

Deputy Secretary
Australian Department of Health and Aged Care
Head, Therapeutic Goods Administration

What is scheduling?

- A national classification system that **controls ACCESS to medicines and chemicals**
- Medicines and chemicals are classified into Schedules according to the **level of regulatory control over their availability required to protect public health and safety**
- **Schedules are published** in the Poisons Standard and while it is made by the Commonwealth, it is given legal effect through state and territory legislation
- **Decisions are made by a Senior Medical Officer at the TGA**, usually following public consultation and on the advice of the Advisory Committee on Medicines Scheduling

What products are in scope?

The focus of the consultation is on possible changes to scheduling of medicines containing paracetamol

Single ingredient paracetamol medicines are the main focus

- But if limits to maximum paracetamol amounts in general sale or S2 products were introduced, some products containing other ingredients (such as some cold and flu medicines) may also be affected

Current scheduling of single ingredient paracetamol (in brief)

Schedule 4 (Prescription only)

- modified release tablets or capsules > 665 mg
- non-modified release tablets or capsules > 500 mg
- in individually wrapped powders or granules > 1000 mg
- packs of more than 100 tablets or 50 powders or sachets
- for injection

Schedule 3 (Pharmacist only)

- modified release tablets/ capsules containing 665 mg or less paracetamol in a pack of 100 or less

Current scheduling of single ingredient paracetamol (in brief)

Schedule 2 (Pharmacy only)

- liquid preparations containing a maximum of 10 g
- in tablets or capsules enclosed in a primary pack containing not more than 100 tablets or capsules
- in individually wrapped powders /granules in a pack of not more than 50

General sale (supermarkets, convenience stores)

- tablets or capsules in packs of not more than 10 g (20 x 500 mg tablets or capsules)

How does this compare with overseas?

UK and Europe – much tighter rules on paracetamol availability

UK rules

- General sale - 16 x 500 mg tablet limits, 2 pack purchase limits
- Pharmacy - 32 tablet pack limits, no supply of MR paracetamol.

Other European countries (rules vary)

- Many (12) countries do not allow any sales outside of pharmacies
- 6 other countries have a 5-8 g limit on general sale pack size
- Lower limits on pharmacy pack sizes (14 countries have 8-30 g limits)

US and Canada - few controls on pack size and access

- e.g. in Canada - controls for children only, modified release paracetamol on general sale in packs under 50 units

NZ tends to follow Australia

This is an open consultation

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

Several options – or no options at all – could be implemented

The TGA (including the decision maker) have NOT formed a view at this time as to which option(s) if any should be implemented

Potential controls discussed by the review team and ACMS and their rationale

- ***Requirement for blister packs*** **-** it is slower to consume tablets or capsules from blister packs as compared to bottles - reduce harm from impulsive attempts to self-poison
- ***Pack size restrictions*** **-** to reduce the amount of paracetamol purchased at once or held in homes and thus numbers of very large overdoses in impulsive self-poisonings
- ***Pack number limits*** **-** to reduce home stockpiles, and also numbers of large overdoses
- ***Sale from behind the counter*** **–** to discourage impulsive purchasing by those vulnerable to overdosing with paracetamol at general retail outlets
- ***Modified Release paracetamol*** **-** prescription only scheduling may reduce inappropriate use of this product which is harder to treat in overdose
- ***Age restrictions*** **-** An 18+ purchase rule may reduce poisonings among 10-17 year-olds

Q&A

Specific options that feedback is being sought on – 1

Option 1: Blister packs for tablets and capsules

- no change (no requirement for blister packs), OR
- for general sale preparations only, OR
- for general sale and pharmacy preparations only, OR
- for prescription, pharmacist only, pharmacy and general sale preparations

Option 2: Maximum pack size reductions

- no change, OR
- for general sale preparations, to be reduced to 10 x 500 mg tablets/capsules or 5 individually wrapped sachets, AND / OR
- for pharmacy only medicines, to be reduced to 32 x 500 mg tablets/capsules or 16 individually wrapped sachets

Q&A

Specific options that feedback is being sought on – 2

Option 3: Allowing only one pack to be purchased at a time

- no change, OR
- when purchased without a prescription in pharmacies, AND/OR
- when purchased in outlets other than pharmacies

Option 4: Sale from behind the counter

- no change, OR
- display and self-selection of paracetamol in non-pharmacy outlets to no longer be permitted

Q&A

Specific options that feedback is being sought on – 3

Option 5: Age restrictions

- no change, OR
- purchase to be restricted to those 18 years and over in pharmacies AND/OR
- purchase to be restricted to those 18 years and over only in outlets other than pharmacies (general sale)

Option 6: Modified release paracetamol

- no change, OR
- all modified release paracetamol is rescheduled from Schedule 3 to Schedule 4, without change to maximum pack size

What about other analgesics?

Paracetamol in combination with other analgesics (e.g. ibuprofen, codeine) already more heavily restricted so changes are not in scope

Other OTC analgesics on general sale are not in scope

- **Toxic (and fatal) doses of paracetamol are considerably lower** than the other two main OTC analgesics, ibuprofen and aspirin:
  - one-quarter of paracetamol overdoses died after 30 g (3 general sale packs)
  - in contrast, fatal doses of aspirin range from 34-56 g (5-8 general sale packs) and some ibuprofen fatalities after 36-105 g (7.5-22 general sale packs)
- Coroners Court of Victoria report on **Victorian overdose deaths** (2011-20)
  - average of 36 paracetamol overdose deaths annually reported in Victoria alone
  - In contrast, 4 ibuprofen overdose deaths per year and no reports for aspirin

Q&A

The process and timeframes for considering possible rescheduling are specified in regulation

- **Public consultation** on possible options - closes 14 October
- Submissions considered and discussed at **Advisory Committee on Medicines Scheduling** – November 2022
- **Interim Delegate's Decision**
- **Second round** of public consultation – early 2023
- **Further consultation** with Advisory Committee on Medicines Scheduling as required
- **Final Delegates' decision** – mid 2023
- **Implementation** – late 2023 or 2024?

Q&A

Questions

Adj Prof John Skerritt

Deputy Secretary

Department of Health and Aged Care

Adj Prof Robyn Langham AM

Chief Medial Adviser

Therapeutic Goods Administration

Q&A

More information

TGA website	www.tga.gov.au
TGA Facebook	www.facebook.com/TGAgovau/
TGA Twitter	www.twitter.com/TGAgovau
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TGA topics blog	www.tga.gov.au/blogs/tga-topics
TGA Linkedin	www.linkedin.com/company/therapeutic-goods-administration/
TGA Instagram	www.instagram.com/tgagovau/?hl=en

Australian Government

Department of Health and Aged Care

Therapeutic Goods Administration

Key data sets used in the report

- Australian Poisons Information Centre (PIC) call data (NSW, QLD, VIC, WA)
- National Coronial Information System (NCIS) mortality data
- IQVIA, IRI and Quantium sales data (pharmacy, convivence store and grocery sales data)
- The Australian Institute of Health and Welfare (AIHH) - access to the National Hospital Morbidity Database
- Literature review
  - burden of paracetamol poisoning internationally (including regulatory changes)
  - options for and effectiveness of restrictions to reduce harm
  - intent and underlying social/psychiatric issues experienced by those engaging in paracetamol self-poisoning

AIHW data

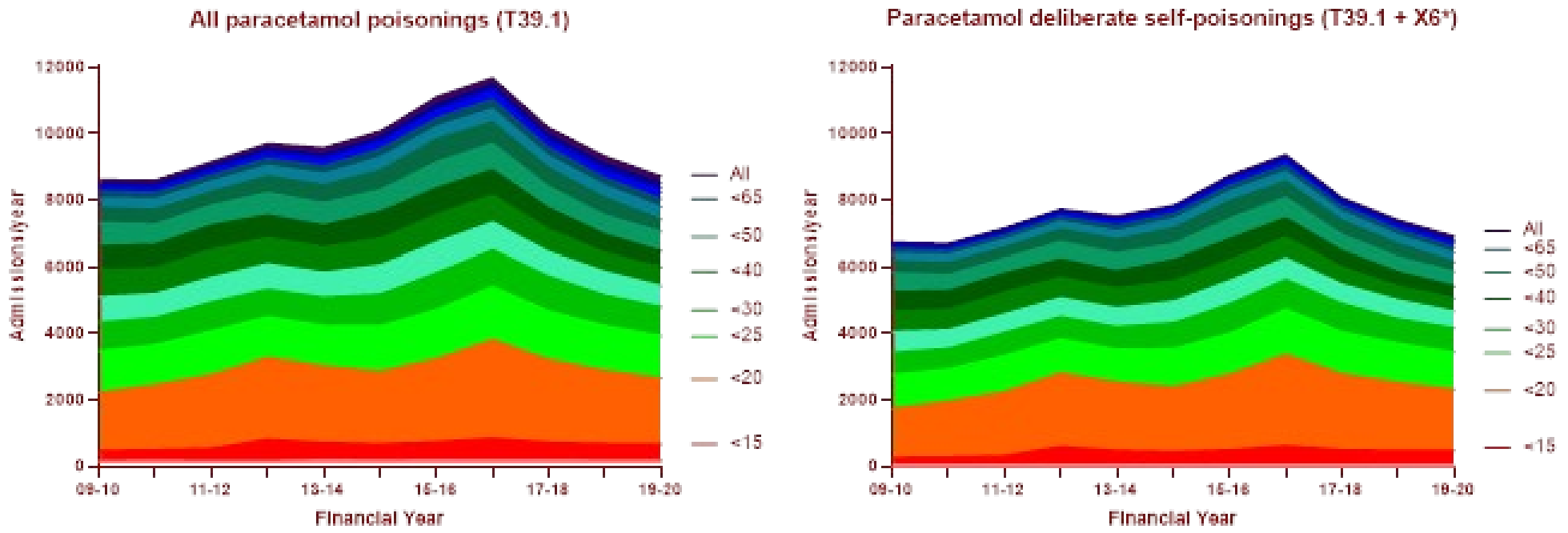


Figure 3 Paracetamol poisoning admissions and deliberate self-poisoning admissions in Australia (AIHW NHMD 2009-2020)

AIHW data

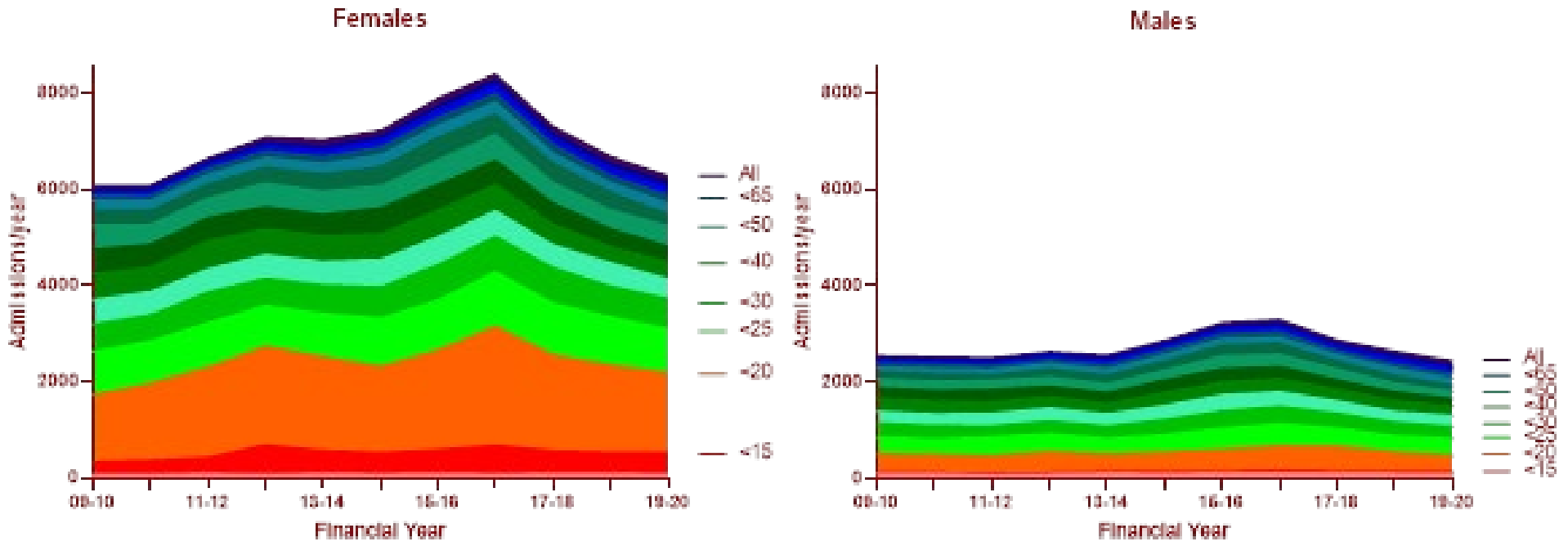


Figure 4 Paracetamol poisoning admissions in Australia – males vs females (AIHW NHMD 2009-2020)

AIHW data

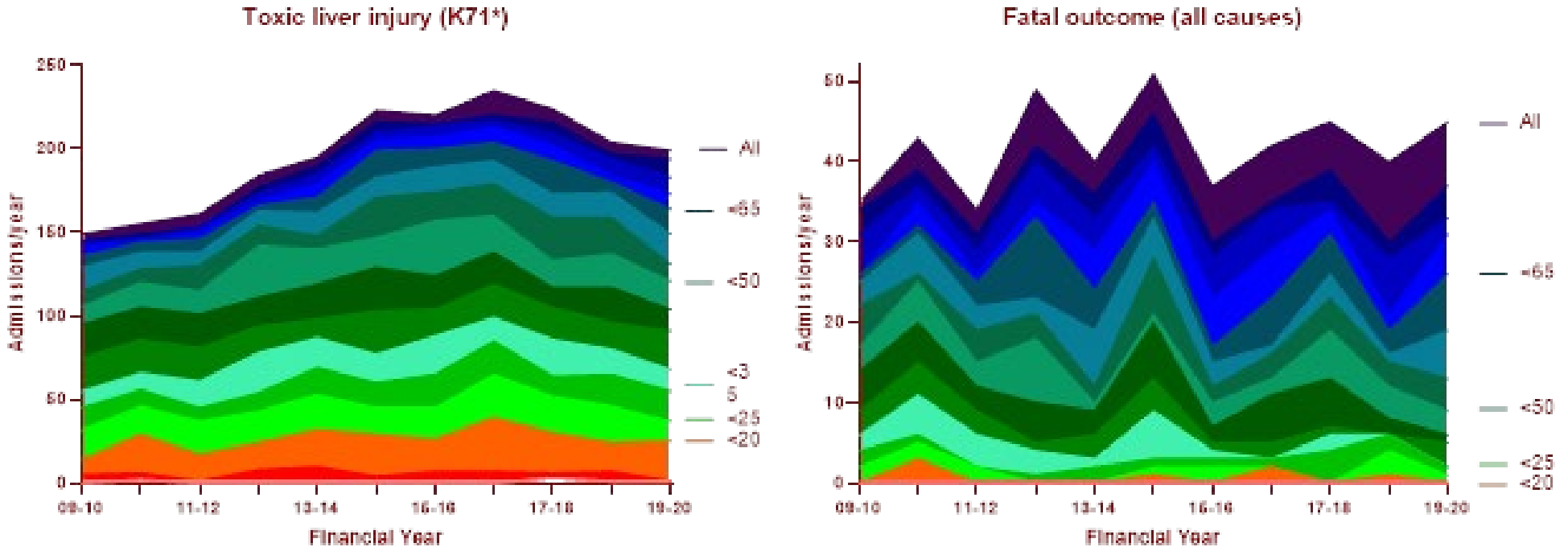


Figure 5 Harms from hospitalised paracetamol poisoning admissions in Australia (AIHW NHMD 2009-2020)

AIHW data

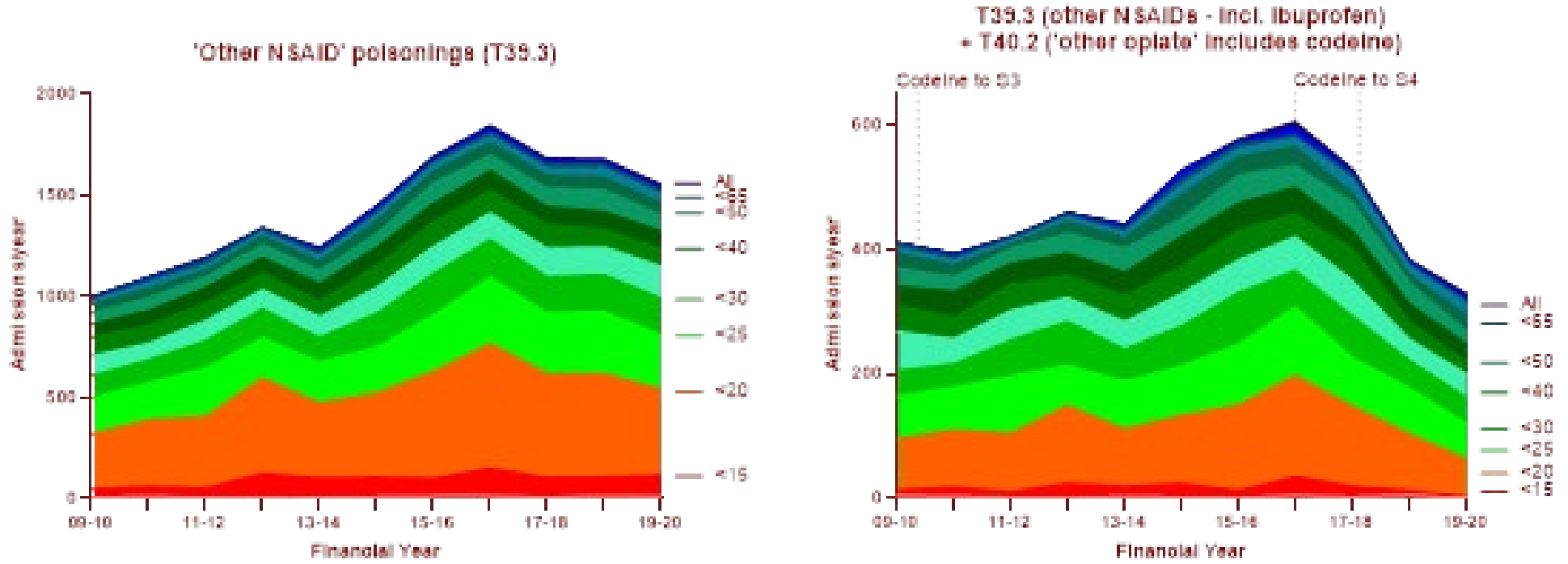


Figure 9. 'Other NSAID' poisonings in Australia (by age group) (AIHW NHMD 2009-2020) – total and those in combination with 'other opiates'.

NCIS data

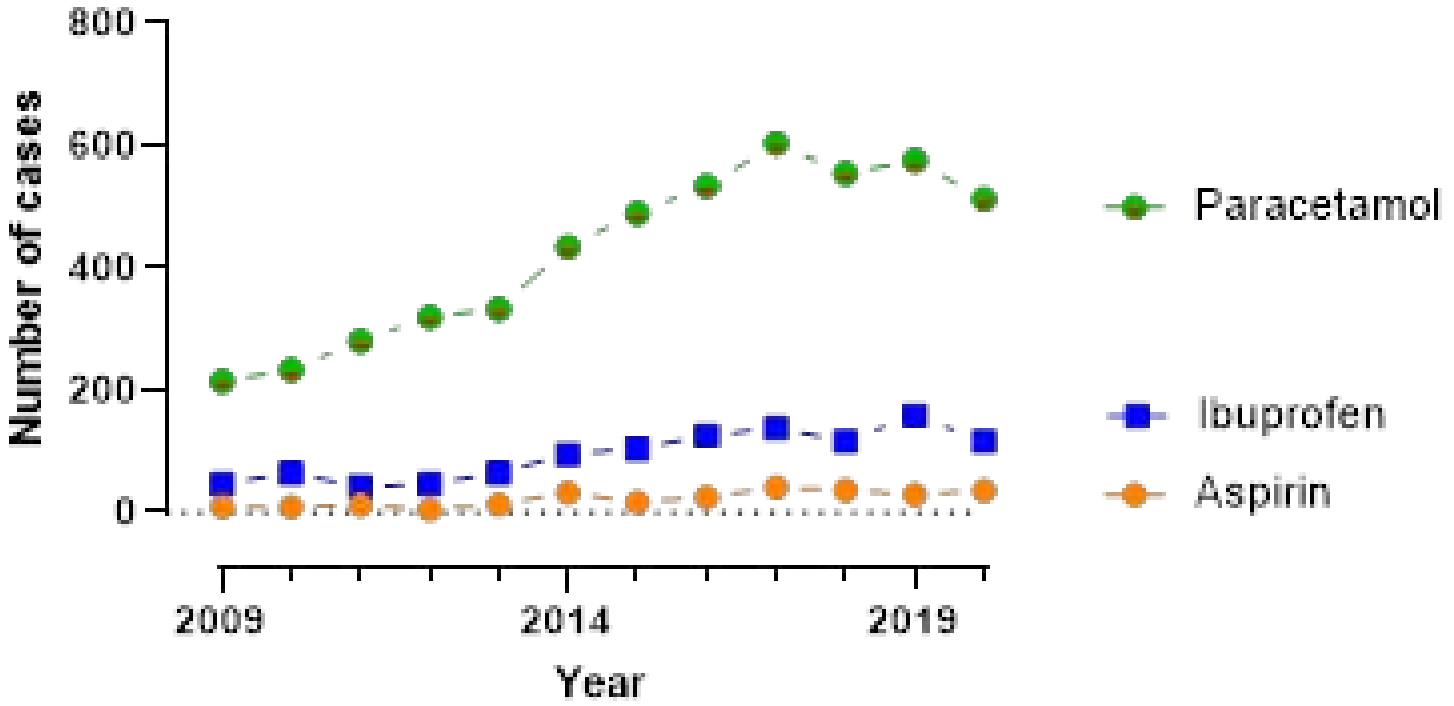


Figure 10. NCIS deaths where OTC analgesics are listed as 'pharmaceutical agents causing injury'

NCIS data

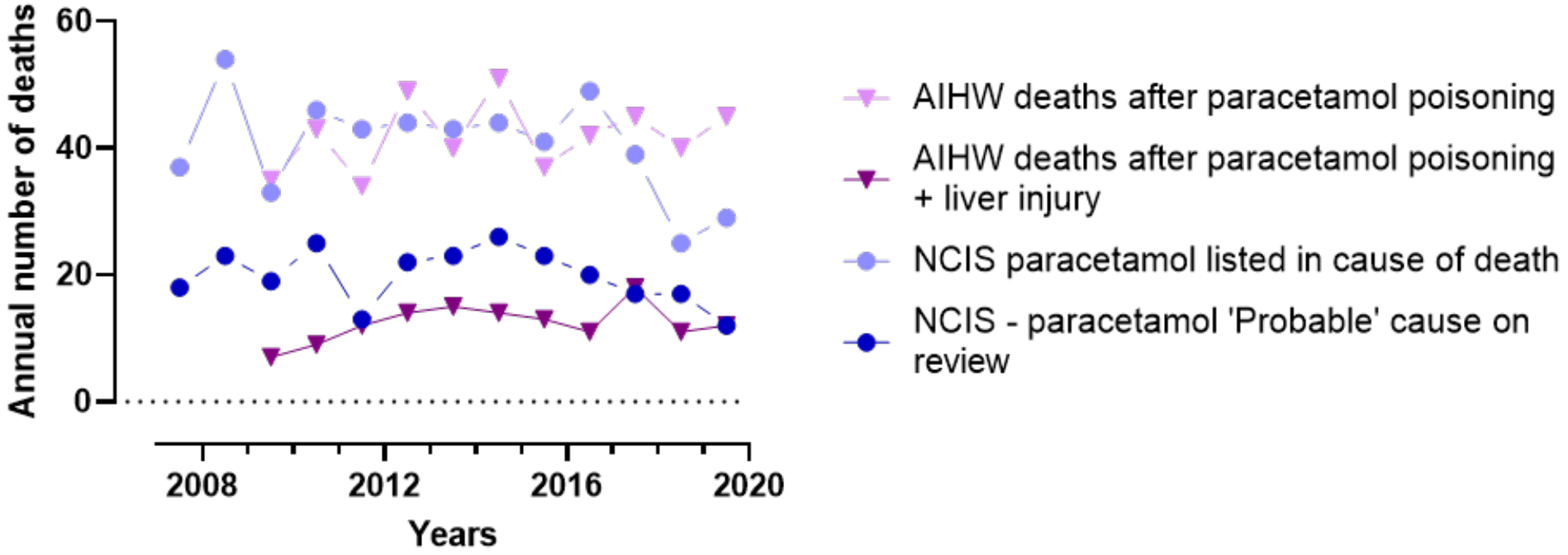


Figure 11. High and low estimates on in-hospital (AIHW) and total (NCIS) deaths

NSW PIC data

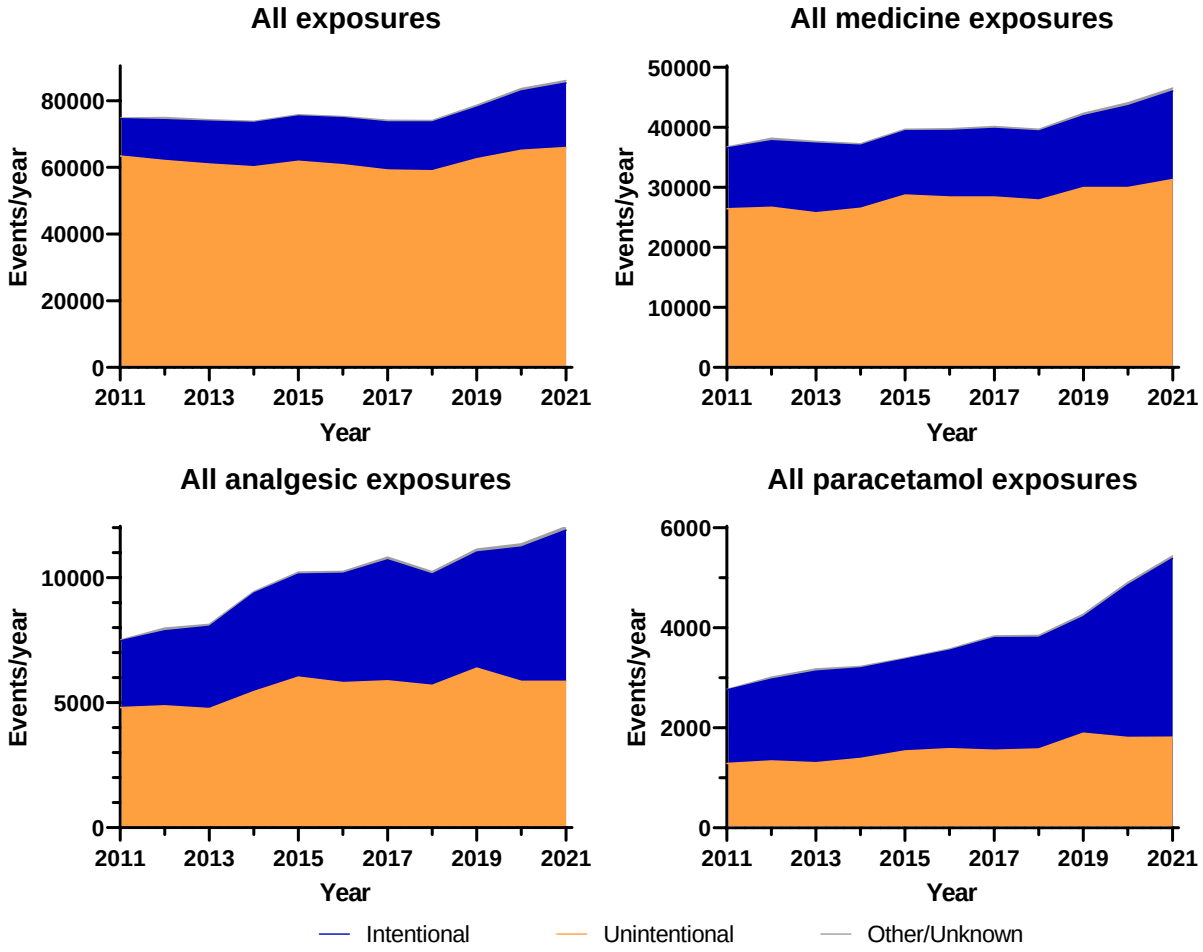


Figure 12 Changes in poisoning exposure events, overall, for paracetamol and for comparable categories. (NSW PIC 2011-2021)

NSW PIC data

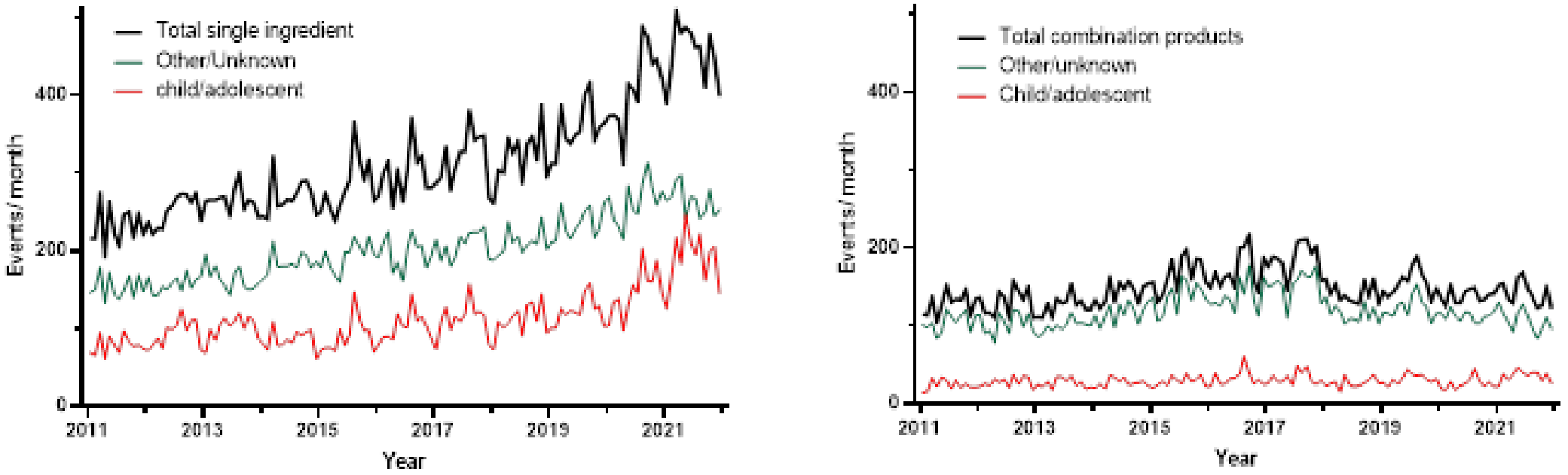


Figure 13 Single ingredient and combination product paracetamol poisoning exposure events. (NSW PIC 2011-2021)

NSW PIC data

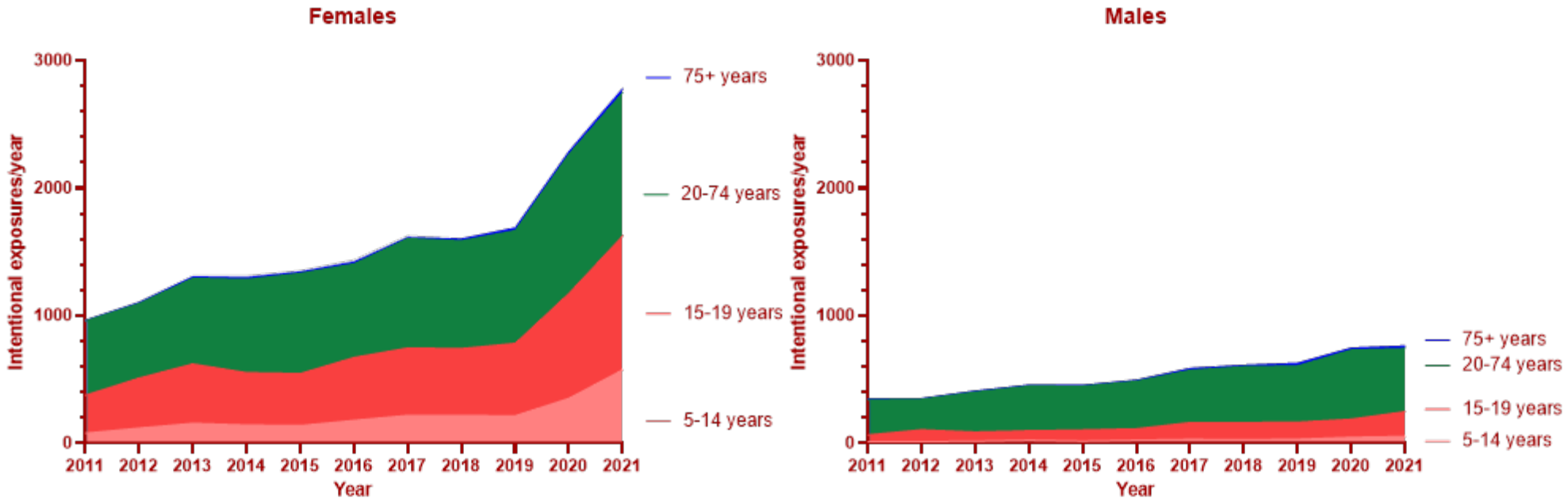


Figure 14 Intentional single ingredient paracetamol poisoning exposure events (NSW PIC 2011-2021)

NSW PIC data

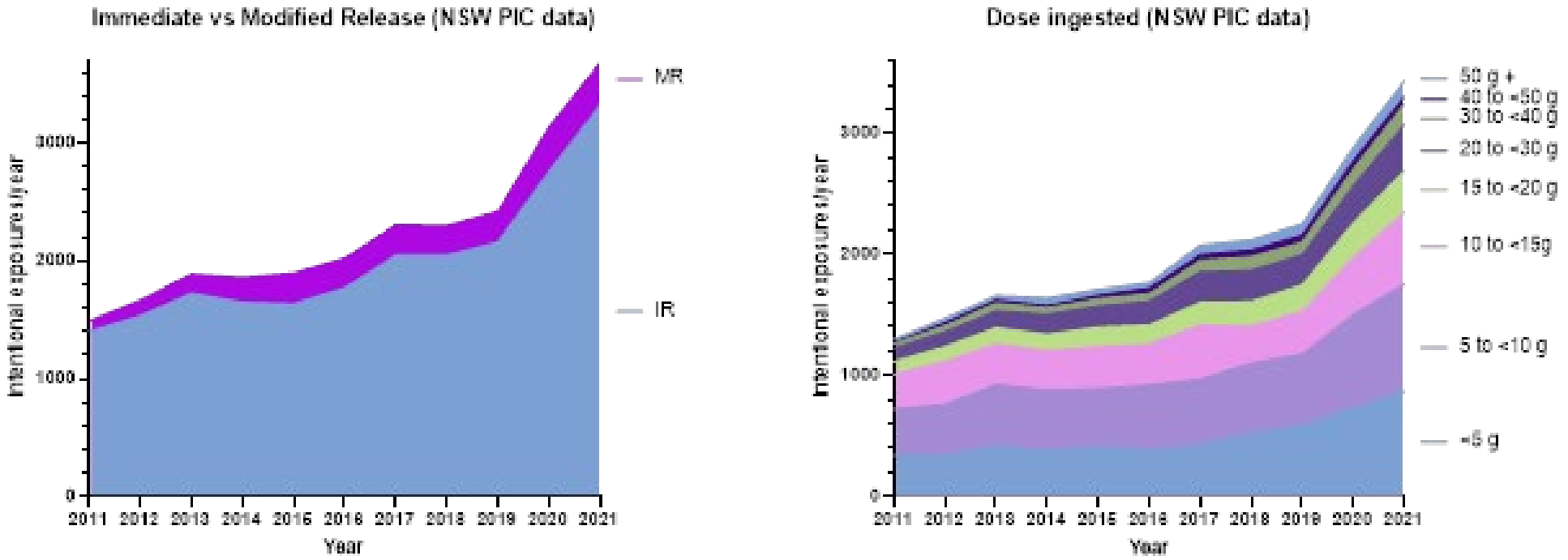
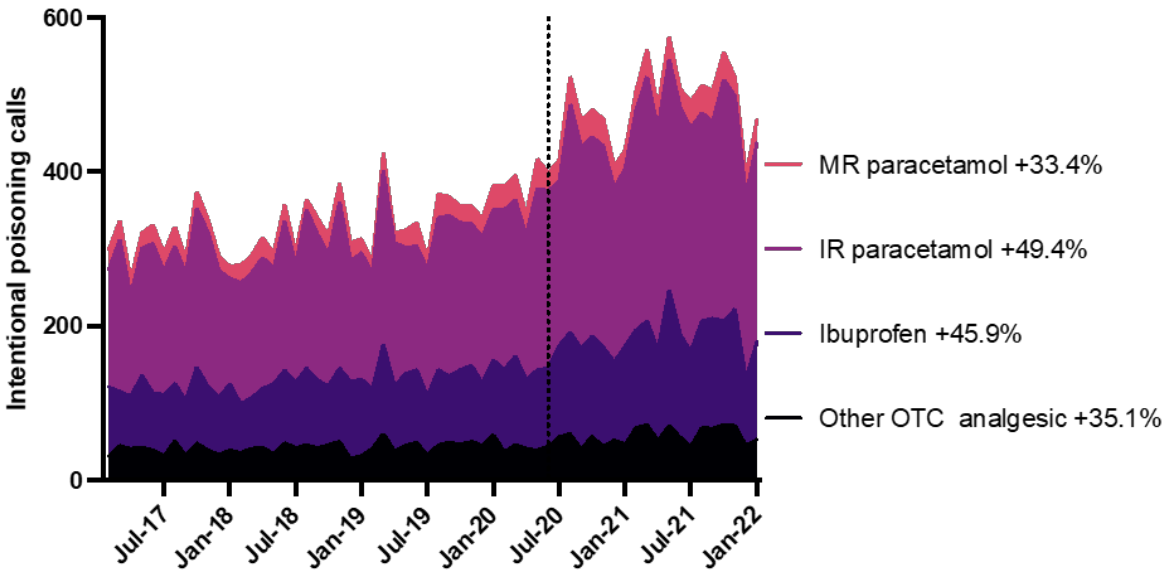


Figure 18. Annual NSW PIC calls about intentional paracetamol poisoning, showing the change in MR paracetamol and the reported dose ingested (2011-2021)

NSW PIC data



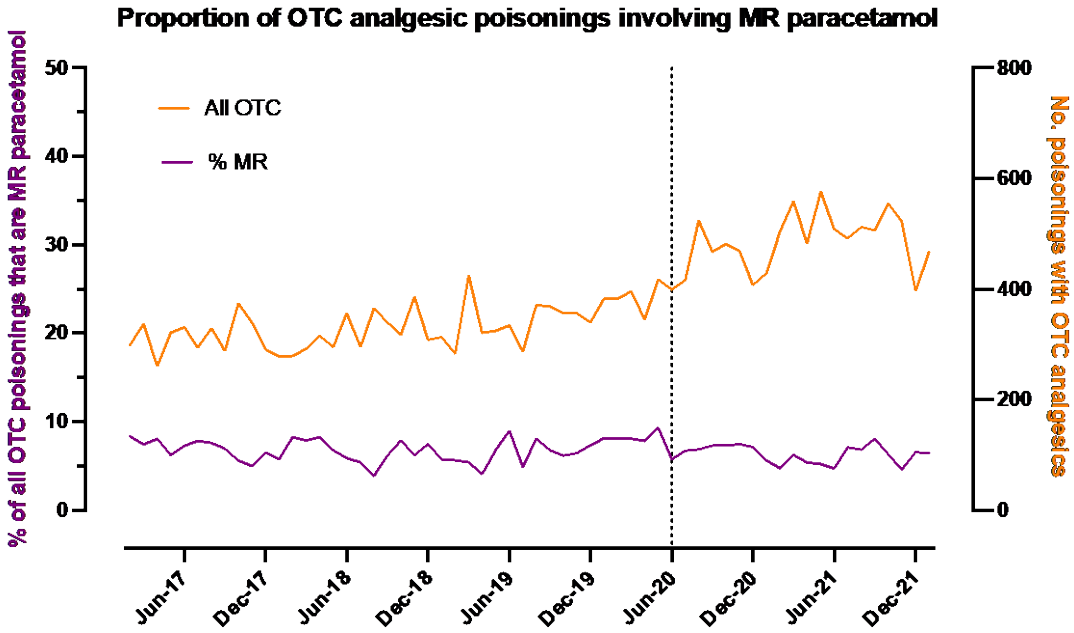


Figure 23. Monthly NSW PIC calls about OTC available analgesic poisonings per month and change in total and proportion due to MR paracetamol (2017-1/2022)