UNIVERSITY of OTAGO
Te Whare Wānanga o Otāgo
NEW ZEALAND

Intentional overdoses: risk assessment & pearls from a clinical toxicologist

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National Poisons Centre
Te Pokapū Mātauranga Tāoke

toxinz

Objectives

- Describe 3 key concepts underpinning medical/clinical toxicology
- Discuss how to optimally risk assess any overdose
- Identify National Poisons Centre as source of real-time support for clinical professionals

What do these patients have in common?

- 2 year old girl with bloody vomiting
- 15 year old boy with fever, delirium, and dilated pupils
- 33 year old depressed woman in cardiac arrest
- 45 year old chrome plater with recurring nosebleeds
- 52 year old woman with seizures after a gas release
- 61 year old man with blue-green vomit and a bright red rash
- 82 year old woman with dizziness and trouble breathing

Medical (clincal) toxicology

- A clinical subspecialty focused on the diagnosis, management, and prevention of poisoning/toxicity and other adverse health effects due to medications, chemicals, occupational and environmental toxins (including radiation) and biological hazards.

Key concept #1

“Poisoning” is not a precise clinical term, it simply denotes harm from exposure to a substance.

Harm

An injury, damage, or disruption of normal physiologic functioning to:

- Cells
- Tissues
- Organs
- Individuals

Exposure

- External to body
  - Direct contact with epithelial surfaces
  - Skin, mucosa, eye, GI tract, etc

- Internal to body
  - Absorbed into bloodstream
  - Distributed to tissue compartments
  - Intracellular or extracellular spaces

Routes of exposure

- Ingestion
- Inhalation
- Eye
- Topical (skin)
- Oral/mouth
- Parenteral
- Other (insufflation, bite/sting, etc)

Substance

Literally any chemical substance

Lots of potential poisons

- ~ 40,000-60,000 industrial chemicals in global commerce
- > 6,000 approved drugs
- > 730 new psychoactive substances
- ~ 2,000 poisonous plant species
- ~ 1,200 poisonous or venous animals
- Countless household and industrial products

Poisoning is a significant public health problem and cause of injury morbidity and mortality in NZ and globally

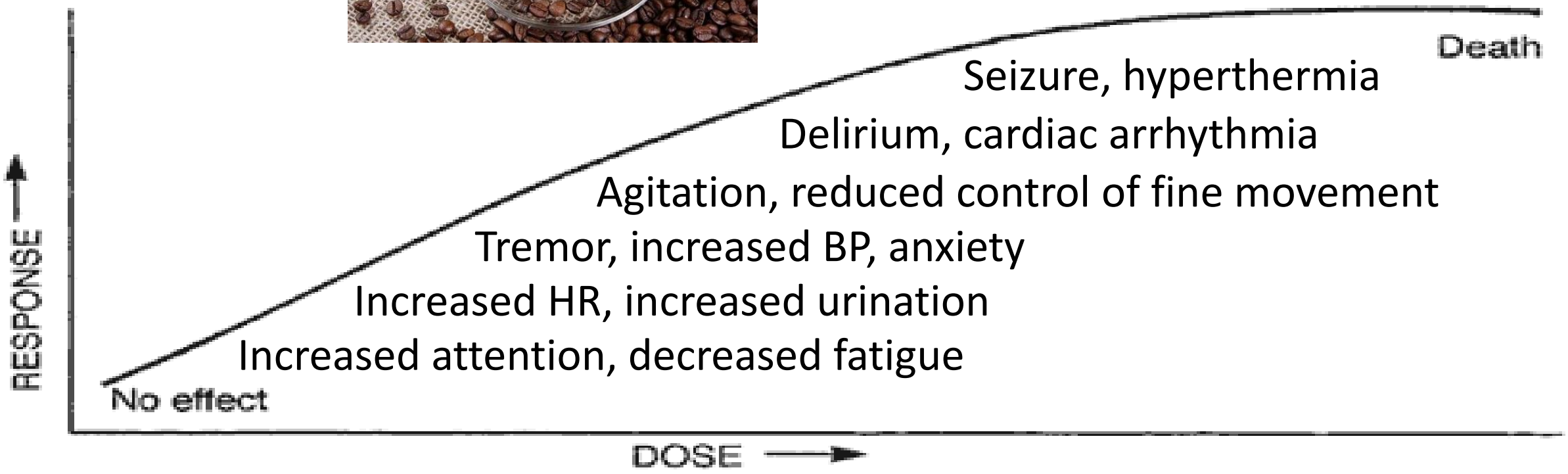
Key concept #2

All things are poison and not without poison; only the dose makes a thing not a poison.

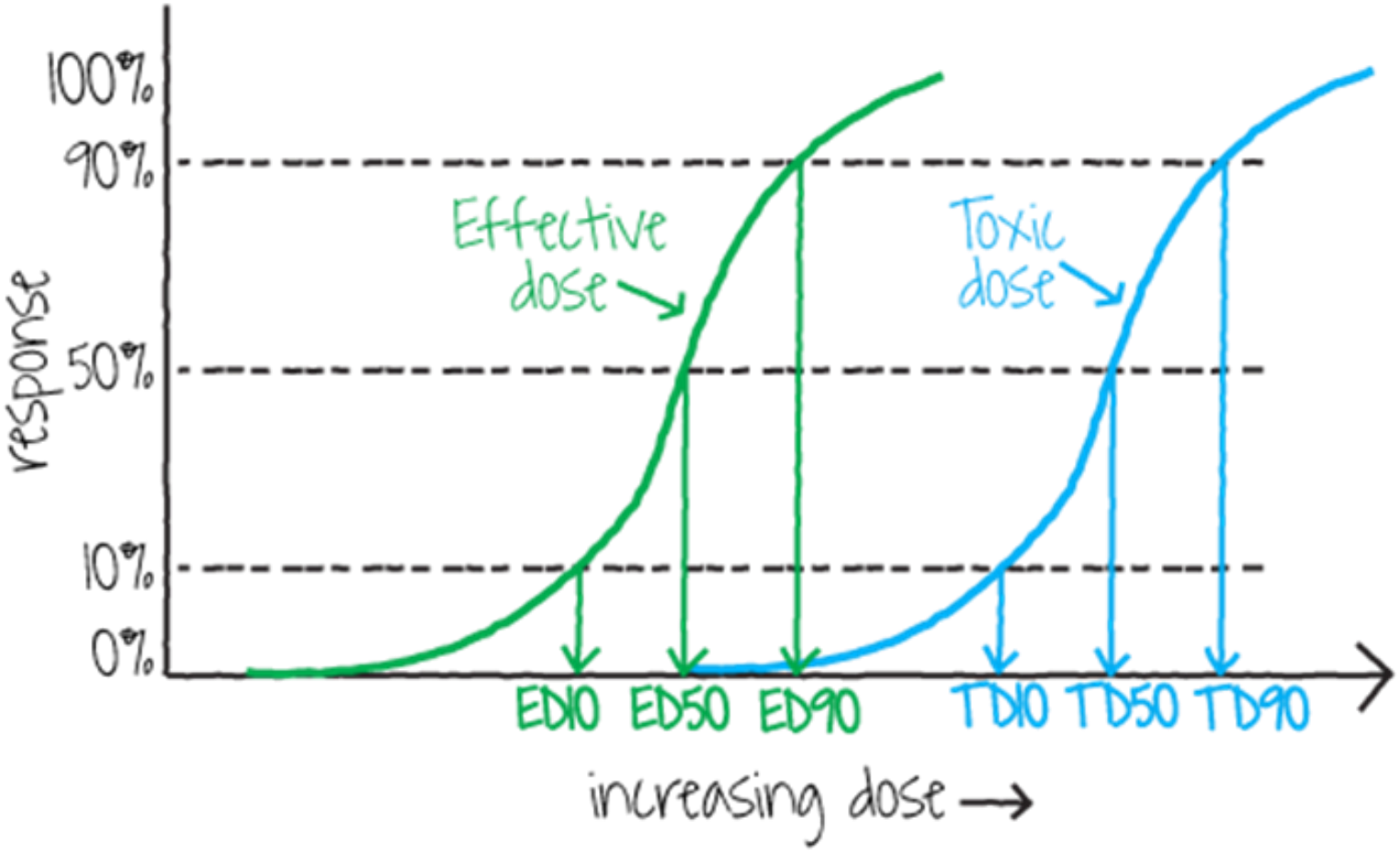
-Paracelsus

https://upload.wikimedia.org/wikipedia/commons/4/4a/Paracelsus.jpg

Caffeine

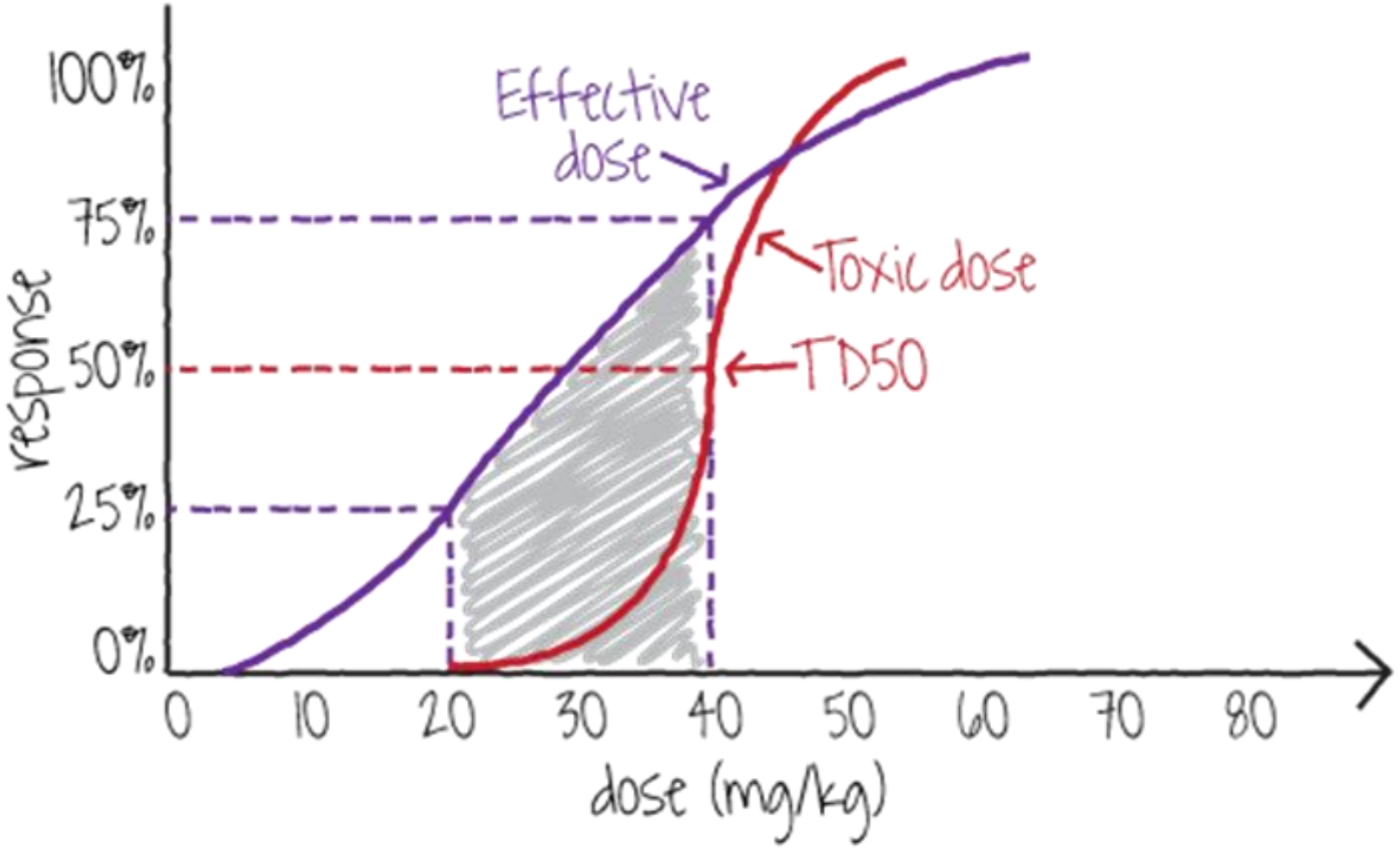

Death
Seizure, hyperthermia
Delirium, cardiac arrhythmia
Agitation, reduced control of fine movement
Tremor, increased BP, anxiety
Increased HR, increased urination
Increased attention, decreased fatigue
No effect
RESPONSE
DOSE

Therapeutic index – wide



https://toxtutor.nlm.nih.gov/02-004.html

Therapeutic index – narrow



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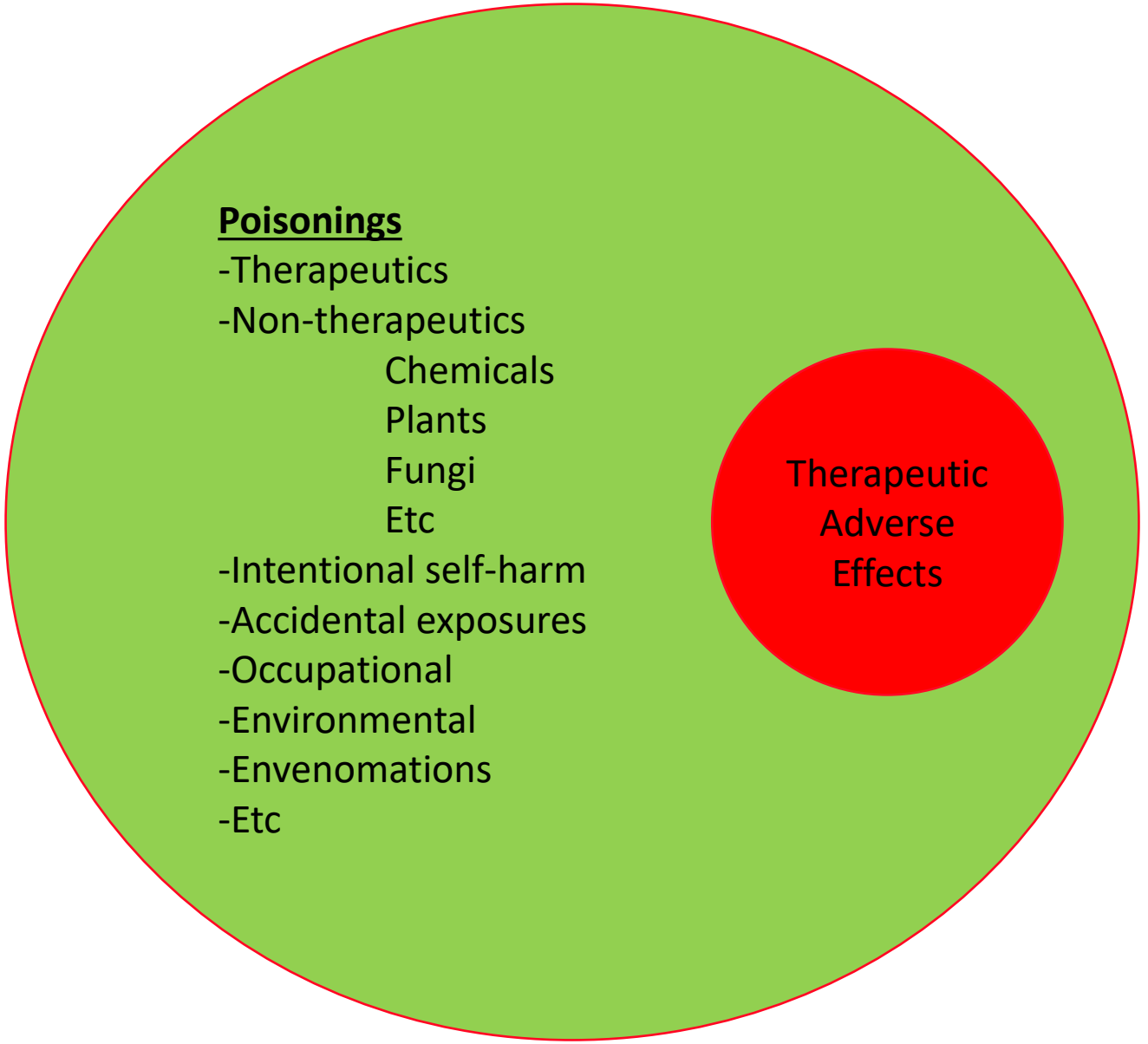

Poisonings
-Therapeutics
-Non-therapeutics
Chemicals
Plants
Fungi
Etc
-Intentional self-harm
-Accidental exposures
-Occupational
-Environmental
-Envenomations
-Etc
Therapeutic Adverse Effects

Key concept #3

The performance of a well-informed clinical toxicity risk assessment is imperative for management and dictates the optimal care setting.

Components of clin tox risk assessment

Patient

- Age
- Weight
- Comorbidities
- Genetic PK/PD factors
- Vital signs & Exam
- Symptoms
- Medication use hx

Substance(s)

- Chemical identity
- Physical properties
- PK/PD properties

Exposure

- Dose
- Route
- Timing
- Reason
- Co-ingestions

Investigations

- Blood glucose
- ECG
- Organ function & metabolic status
- Drug concentrations

Risk assessment pitfalls

“She wouldn’t have eaten that much; it doesn’t taste good”

Do not rely on perceived unpalatability to rule out risk of toxicity

“She seems fine at the moment.”

The absence of symptoms does not rule out developing toxicity

“She didn’t bring the product in with her.”

Products can appear very similar but contain different substances

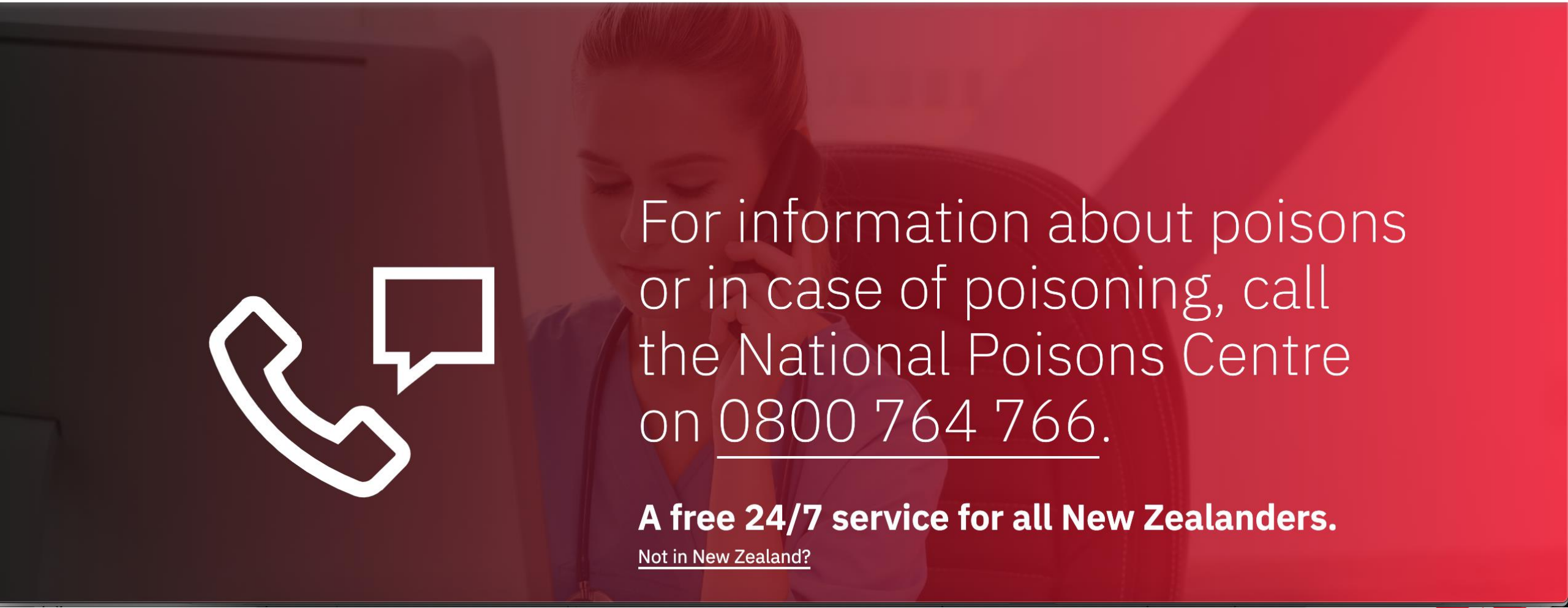
Red flags

- Altered mental status
- Abnormal vital signs
- Access to high-risk substances
- Self-harm behavior
  - Period of observation for developing toxicity
  - Paracetamol blood test
  - Psychiatric assessment

Where can I find good information to enhance my risk assessment?

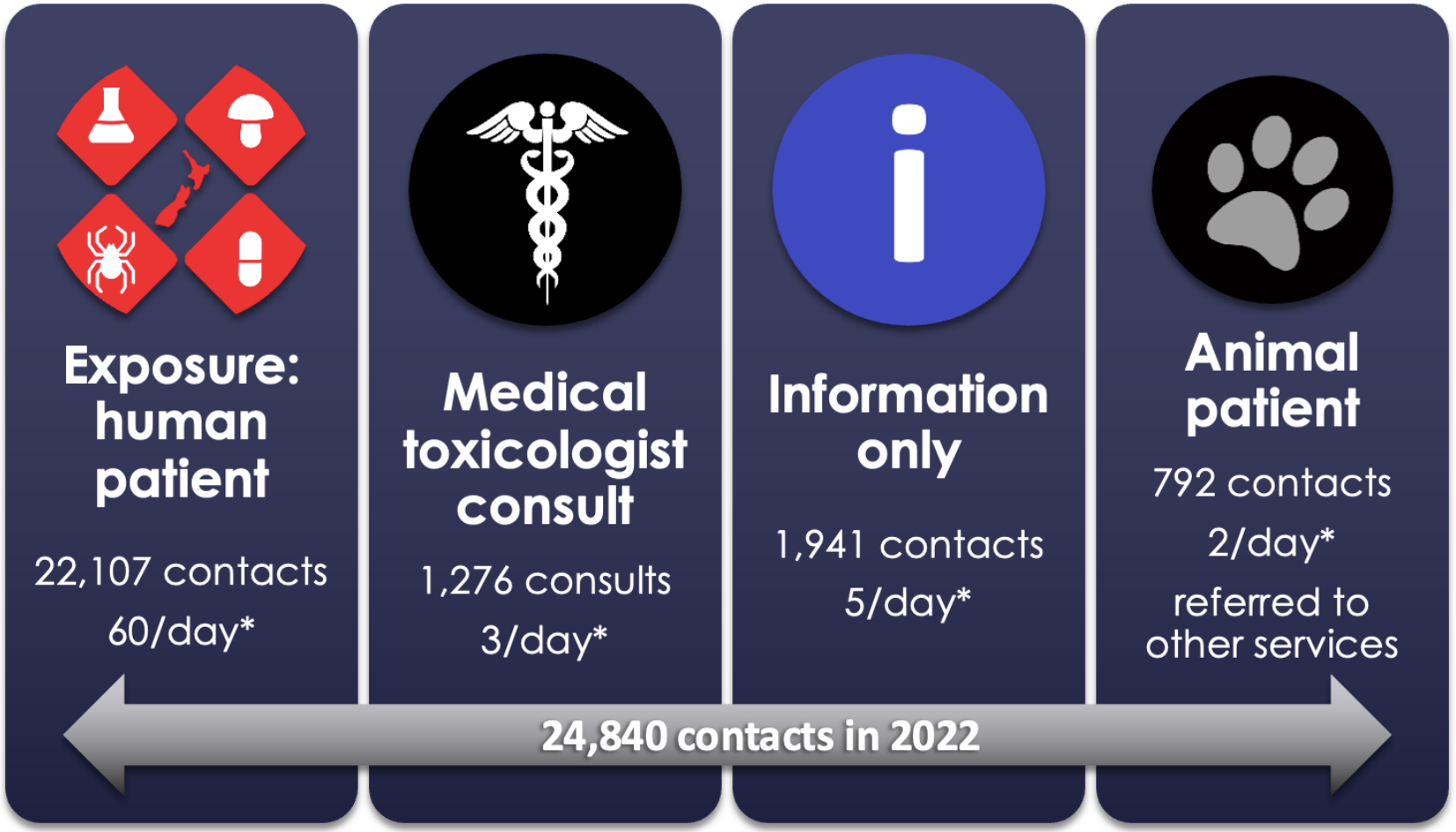
National Poisons Centre
Te Pokapū Mātauranga Tāoke

0800 764 766 | Poisons Centre Info | Contact | First Aid | Resources | Articles & Info | News | KIDS! ZONE



www.poisons.co.nz

24/7 national clinical telehealth



*Daily numbers of contacts presented are median values of all similar daily contacts in 2022.

NPC activity domains

24/7 national clinical telehealth

Poisons information & specialist expertise

Research

Education

Liaising with broad stakeholder range

Public health

M-Eslon

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Print

- Description
- Intervention Criteria
- Treatment
- Signs And Symptoms
- Toxicity
- Therapeutic Drug Information
- Identification
- Specification Information
- References

DESCRIPTION

SUBSTANCE NAME

Morphine

SUBSTANCE CLASS

Opioid

Access www.toxinz.com using a browser on a Te Whatu Ora network device

PRODUCT INFORMATION

Tablets range from 5 to 200 mg morphine. Sustained release formulations are available.

Formulations for injection range from 0.4 to 80 mg/mL morphine.

Oral solutions range from 1 to 10 mg/mL morphine.

Oral concentrates range from 20 to 50 mg/mL morphine.

The packaging of each trade product will include information on the exact quantity of morphine and whether the formulation is sustained release.

ACTIVE INGREDIENT

M-Eslon SR Capsule
10 mg, 15 mg, 30 mg, 60 mg, 100 mg, 200 mg Morphine

Recent NPC data on intentional self-harm exposures

Rates of intentional exposure records of females (A) and males (B) in contacts with NZNPC by age groups, 2019-2022.

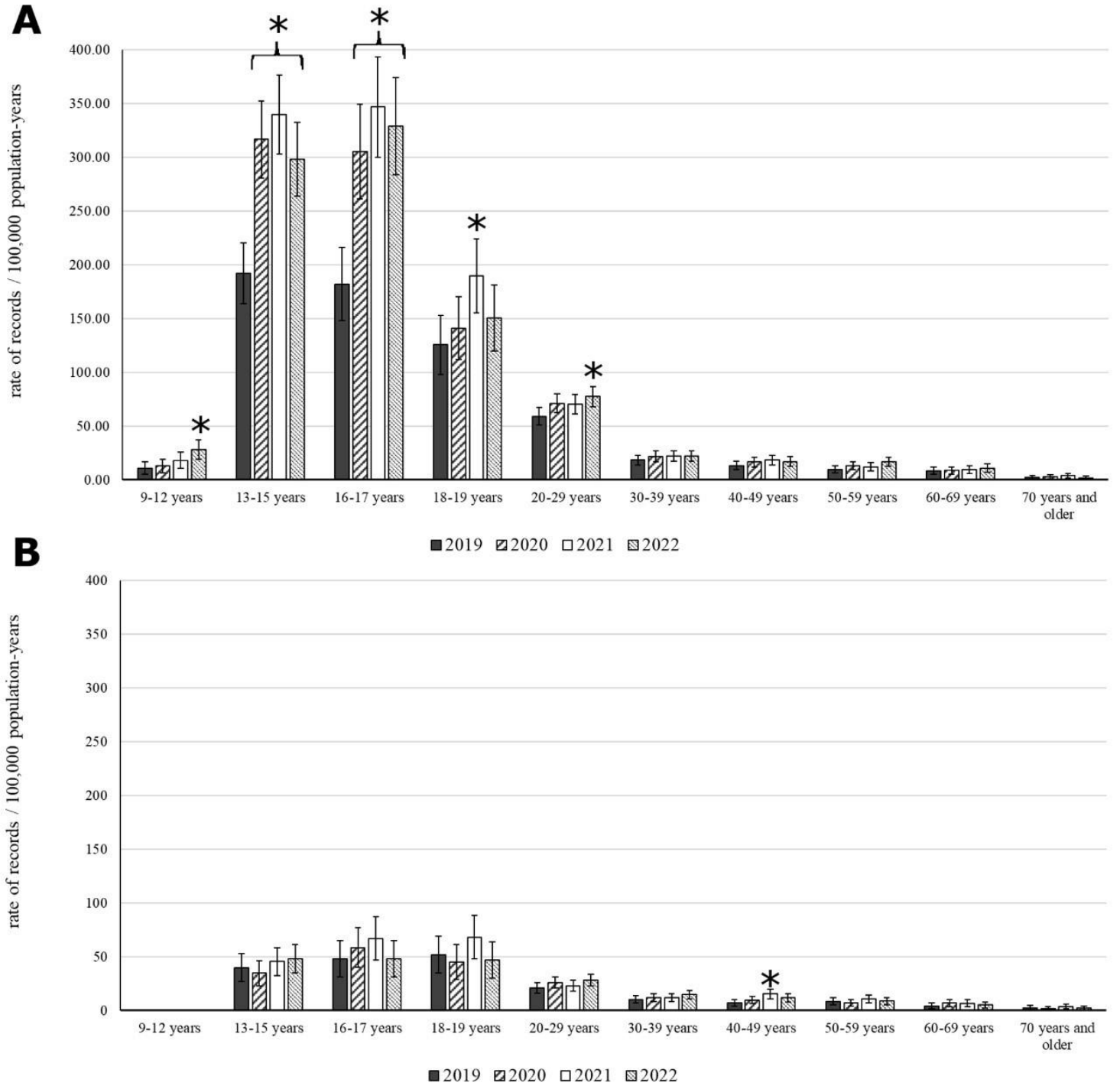

Figure from manuscript currently in preparation for journal submission

Table 3: Ten most frequent medicine exposures and reasons for exposures by age group in human patients exposed to at least one therapeutic product and assisted by the NZNPC in 2018–2020.

Therapeutic substance exposures; n (% of row total) Substance name (ATC code)	Reason for therapeutic product exposure/individual substances						
	All exposure reasons	Child exploratory[a]	Unintentional	Therapeutic error	Intentional[b]	Substance abuse[c]	Other and unknown reason
0–12 years of age or unknown child	**17,348 (100%)**	**13,253 (76%)**	**635 (4%)**	**3,341 (19%)**	**63 (0.4%)**	**4 (0.02%)**	**52 (0.3%)**
1) paracetamol (N02BE01)	2,937 (100%)	1,298 (44%)	59 (2%)	1,550 (53%)	21 (1%)	-	9 (0.3%)
2) ibuprofen (M01AE01, M02AA13)	1,068 (100%)	739 (69%)	14 (1%)	305 (29%)	6 (1%)	-	4 (0.4%)
3) choline salicylate,ethanol (N02BA03)	388 (100%)	367 (95%)	8 (2%)	12 (3%)	-	-	1 (0.3%)
4) diclofenac (M01AB05, M02AA15)	336 (100%)	327 (97%)	3 (1%)	6 (2%)	-	-	-
5) zinc oxide (A12CB, D02AB)	304 (100%)	293 (96%)	10 (3%)	1 (0.3%)	-	-	-
6) loratadine (R06AX13)	271 (100%)	170 (63%)	5 (2%)	92 (34%)	1 (0.4%)	-	3 (1%)
7) levothyroxine (H03AA01)	267 (100%)	261 (98%)	1 (0.4%)	3 (1%)	1 (0.4%)	-	1 (0.4%)
8) codeine (R05DA04)	264 (100%)	255 (97%)	7 (3%)	1 (0.4%)	-	-	1 (0.4%)
9) amoxicillin (J01CA04)	240 (100%)	110 (46%)	8 (3%)	122 (51%)	-	-	-
10) potassium iodate (H03CA)	234 (100%)	233 (99.6%)	1 (0.4%)	-	-	-	-

Kumpula EK, Paterson DA, Pomerleau AC. A retrospective analysis of therapeutic drug exposures in New Zealand National Poisons Centre data 2018-2020. Aust N Z J Public Health. 2023 Apr;47(2):100027. doi: 10.1016/j.anzjph.2023.100027. Epub 2023 Mar 10. PMID: 36907001.

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	All exposure reasons	Child exploratory[a]	Unintentional	Therapeutic error	Intentional[b]	Substance abuse[c]	Other and unknown reason
13-19 years of age	**3,301 (100%)**	**22 (1%)**	**399 (12%)**	**545 (17%)**	**2,008 (61%)**	**130 (4%)**	**197 (6%)**
1) paracetamol (N02BE01)	696 (100%)	2 (0.3%)	75 (11%)	80 (11%)	508 (73%)	2 (0.3%)	29 (4%)
2) ibuprofen (M01AE01)	292 (100%)	1 (0.3%)	31 (11%)	37 (13%)	214 (73%)	2 (1%)	7 (2%)
3) fluoxetine (N06AB03)	143 (100%)	1 (1%)	16 (11%)	14 (10%)	102 (71%)	2 (1%)	8 (6%)
4) sertraline (N06AB06)	134 (100%)	-	18 (13%)	23 (17%)	79 (59%)	4 (3%)	10 (7%)
5) quetiapine (N05AH04)	117 (100%)	-	9 (8%)	13 (11%)	85 (73%)	2 (2%)	8 (7%)
6) citalopram + escitalopram	116 (100%)	-	16 (14%)	16 (14%)	70 (60%)	4 (3%)	10 (9%)
a) citalopram (N06AB04)	67 (100%)	-	5 (7%)	10 (15%)	43 (64%)	2 (3%)	7 (10%)
b) escitalopram (N06AB10)	49 (100%)	-	11 (22%)	6 (12%)	27 (55%)	2 (4%)	3 (6%)
7) codeine (R05DA04)	87 (100%)	-	10 (11%)	8 (9%)	55 (63%)	8 (9%)	6 (7%)
8) tramadol (N02AX02)	81 (100%)	-	12 (15%)	8 (10%)	40 (49%)	17 (21%)	4 (5%)
9) iron-only supplements (B03AA)	72 (100%)	-	2 (3%)	7 (10%)	55 (76%)	-	8 (11%)
10) methylphenidate (N06BA04)	69 (100%)	-	-	33 (48%)	15 (22%)	9 (13%)	12 (17%)

Kumpula Aust N Z J Public Health. 2023.

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Therapeutic substance exposures; n (% of row total) Substance name (ATC code)	Reason for therapeutic product exposure/individual substances						
	All exposure reasons	Child exploratory[a]	Unintentional	Therapeutic error	Intentional[b]	Substance abuse[c]	Other and unknown reason
20-64 years of age	**8,801 (100%)**	**48 (1%)**	**1,479 (17%)**	**4,421 (50%)**	**2,415 (27%)**	**105 (1%)**	**315 (4%)**
1) paracetamol (N02BE01)	974 (100%)	3 (0.3%)	207 (21%)	338 (35%)	385 (40%)	2 (0.2%)	39 (4%)
2) ibuprofen (M01AE01)	425 (100%)	2 (0.5%)	101 (24%)	198 (47%)	109 (26%)	-	15 (4%)
3) quetiapine (N05AH04)	343 (100%)	3 (1%)	35 (10%)	88 (26%)	193 (56%)	6 (2%)	18 (5%)
4) zopiclone (N05CF01)	254 (100%)	-	58 (23%)	53 (21%)	119 (47%)	4 (2%)	20 (8%)
5) codeine (R05DA04)	225 (100%)	-	68 (30%)	55 (24%)	86 (38%)	4 (2%)	12 (5%)
6) tramadol (N02AX02)	224 (100%)	-	55 (25%)	60 (27%)	89 (40%)	8 (4%)	12 (5%)
7) citalopram + escitalopram	221 (100%)	1 (0.5%)	18 (8%)	107 (48%)	83 (38%)	3 (1%)	9 (4%)
a) citalopram (N06AB04)	142 (100%)	-	12 (8%)	69 (49%)	56 (39%)	1 (1%)	4 (3%)
b) escitalopram (N06AB10)	79 (100%)	1 (1%)	6 (8%)	38 (48%)	27 (34%)	2 (3%)	5 (6%)
8) venlafaxine (N06AX16)	153 (100%)	-	5 (3%)	70 (46%)	70 (46%)	-	8 (5%)
9) sertraline (N06AB06)	152 (100%)	2 (1%)	7 (5%)	79 (52%)	59 (39%)	-	5 (3%)
10) lorazepam (N05BA06)	148 (100%)	-	28 (19%)	23 (16%)	79 (53%)	3 (2%)	15 (10%)

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	All exposure reasons	Child exploratory[a]	Unintentional	Therapeutic error	Intentional[b]	Substance abuse[c]	Other and unknown reason
65 years of age or older	3,792 (100%)	12 (0.3%)	348 (9%)	3,273 (86%)	106 (3%)	1 (0.03%)	52 (1%)
1) paracetamol (N02BE01)	247 (100%)	3 (1%)	42 (17%)	182 (74%)	16 (6%)	-	4 (2%)
2) metoprolol (C07AB02)	207 (100%)	-	12 (6%)	191 (92%)	2 (1%)	-	2 (1%)
3) dabigatran (B01AE07)	172 (100%)	-	5 (3%)	165 (96%)	1 (1%)	-	1 (1%)
4) cilazapril (C09AA08)	122 (100%)	-	3 (2%)	115 (94%)	2 (2%)	-	2 (2%)
5) omeprazole (A02BC01)	110 (100%)	-	4 (4%)	103 (94%)	2 (2%)	-	1 (1%)
6) atorvastatin (C10AA05)	109 (100%)	-	3 (3%)	103 (94%)	2 (2%)	-	1 (1%)
7) acetylsalicylic acid (B01AC06, N02BA01)	109 (100%)	-	1 (1%)	105 (96%)	2 (2%)	-	1 (1%)
8) diltiazem (C08DB01)	70 (100%)	-	1 (1%)	67 (96%)	2 (3%)	-	-
9) furosemide (C03CA01)	67 (100%)	-	1 (1%)	66 (99%)	-	-	-
10) warfarin (B01AA03)	62 (100%)	-	1 (2%)	60 (97%)	1 (2%)	-	-

Kumpula Aust N Z J Public Health. 2023.

A few quick pearls

When to restart therapeutic medicines?

Patient overdosed on 40x 40mg fluoxetine yesterday.

Observed in ED and medically cleared.

Assessed by EPS and psychiatrically cleared for discharge home.

When should they re-start their fluoxetine?

When to r…nes?

Therapeutic Advances i…

Review

Restarting a medication a… need for evi…

Emma Tay…, Andreas Sc… and Richard O. Day

Ther Adv Psychopharmacol

2019, Vol. 9: 1–19

DOI: 10.1177/2045125319836889

https://www.ncbi.nlm…

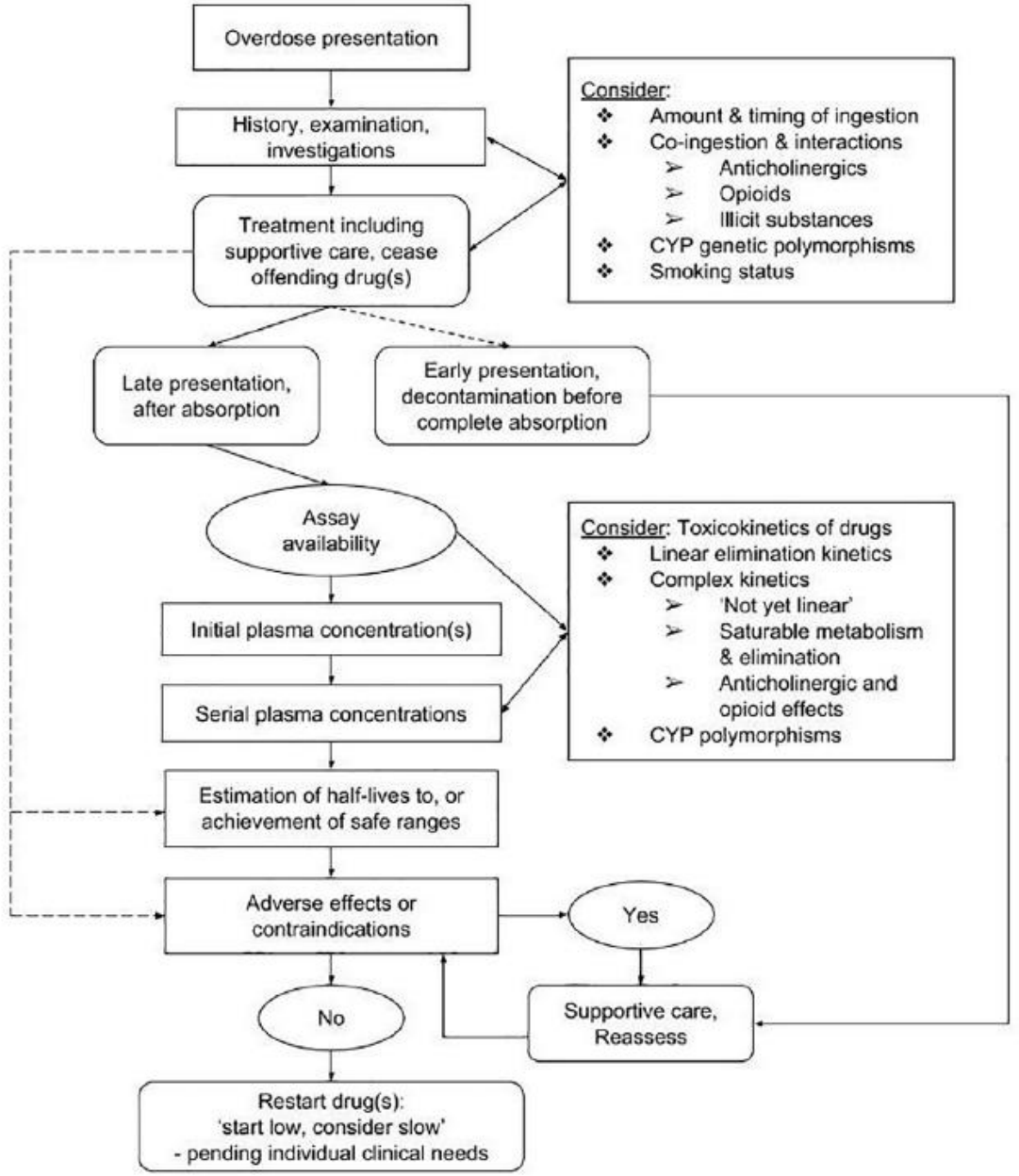

Figure 3. Flowchart summarizing recommendations for restarting psychoactive medications following overdose.
Solid arrows (→) depict our recommendations. Dashed arrows (⇢) depict typical pathways without plasma concentration measurements.
CYP, cytochrome P450 enzyme.

When to restart therapeutic medicines?

- There is no evidence-based or consensus approach
- Principles to keep in mind
  - Use a tailored approach unique for each patient
  - Assess risk of not restarting and define endpoints to avoid (e.g. withdrawal)
  - Very few drugs have readily available serum measurements with rapid TAT
  - PK ≠ PD → 5 half-life approach not always required
  - Treat the patient, not a drug concentration
  - Close clinical observation required during re-introduction
    - Good to establish objective findings before re-introducing medicine so these can be reassessed later → particularly for serotonergic agents

Insulin overdose

- Risk assessment
  - Accidental vs intentional?
  - What type of insulin(s)?
- Elimination kinetics in overdose ≠ therapeutic dose PK
- Treatment
  - Close monitoring, frequent BSL checks
  - If hypoglycemia → glucose, glucose….and more glucose
  - Empiric approach to duration of treatment and monitoring → absence of hypoglycemia

Paracetamol overdose

Most common intentional overdose, can be fatal (but rarely)

Risk stratification can be tricky

No early clinical signs can definitively rule out developing toxicity

→ blood test is essential for risk stratification

Risk increases with delayed presentation for treatment

Once liver injury starts, takes up to 4 days to determine recovery vs ALF

Once recovered, no matter how bad injury was, there is no evidence of long-term liver damage

<u>Always</u> consider blood paracetamol test in context of self-harm exposures

Take home messages

Poisoning = harm from exposure to a substance

Dose makes the poison

Well-informed tox risk assessment imperative for management and dictates optimal care setting

Use toxinz – www.toxinz.com

Call NPC any time at 0800 764 766 for real-time support managing your patients

Questions?

adam@poisons.co.nz