

A retrospective analysis of therapeutic drug exposures in New Zealand National Poisons Centre data 2018–2020

Eeva-Katri Kumpula,^{1*} Daniel A. Paterson,² Adam C. Pomerleau¹

¹National Poisons Centre, University of Otago, Dunedin, New Zealand

²School of Pharmacy, University of Otago, Dunedin, New Zealand

Submitted: 13 July 2022; Revision requested: 24 November 2022; Accepted: 11 December 2022

Abstract

Objective: The New Zealand National Poisons Centre advises the general public and health professionals on management of exposures to various substances. The epidemiology of medicine exposures was used to characterise inappropriate use of medicines across age groups.

Methods: Data from contacts in 2018–2020 were analysed: patient demographics (age, gender), number of therapeutic substances, and advice given. The most frequent individual therapeutic substance exposures across age groups and the reasons for these occurring were determined.

Results: A total of 76% of children's (aged 0–12 or unknown child) exposures were exploratory in nature, involving a variety of medicines. Youth (aged 13–19) had frequently engaged in intentional self-poisoning (61% of their exposures), and most commonly by exposure to paracetamol, antidepressants, and quetiapine. Adults (aged 20–64) and older adults (aged 65 and over) were frequently affected by therapeutic errors (50% and 86% of their exposures, respectively). Adults were most frequently exposed to paracetamol, codeine, tramadol, antidepressants, and hypnotics, while older adults were exposed to paracetamol and various cardiac medications.

Conclusions: Types of inappropriate medicine exposures vary in different age groups.

Implications for public health: Poisons centre data add to pharmacovigilance monitoring of potential harm from medicines and inform medication safety policies and interventions.

Key words: poison control, pharmacovigilance, medication safety

Introduction

Exposures to medicines in ways which were not intended are a significant cause of morbidity, mortality, and suboptimal pharmacotherapy. Surveillance of harm from medicines is a vital part of pharmacovigilance, as some adverse effects may not be observed in clinical trial stages, and some potential harm from intentional or unintentional improper use would not be expected to become apparent until medicines have been in everyday use by large populations. Information about drug-harm incidents can be obtained from reporting to specific pharmacovigilance centres, hospital presentation datasets, and from treatment-advising units such as poisons centres and toxicology units in hospitals.^{1,2} While large datasets of hospital presentations will—for administrative reasons among others—be about 1–2 years old by the time they can be

analysed for emerging trends, poisons centre data have the potential to be available for monitoring much sooner.^{2,3} Studies of poison centre data have investigated medication errors overall,^{4–7} specifically outside hospital settings,^{8,9} and in specific age groups such as the elderly³ and children,¹⁰ or specific pharmacovigilance-related issues such as adverse drug reactions¹¹ and iatrogenic incidents,¹² depending on each poison centre's scope of practice. Since poisons centres generally advise in all kinds of substance exposures, not just therapeutic errors, they have opportunities to characterise a variety of improper medication use, including use for self-harm or substance abuse. Poisons centre exposure data can contribute to pharmacovigilance as a source of information not captured by other means of surveillance, thus complementing other data. This can broaden understanding of various harms from medicines and add to pharmacist and prescriber awareness of risks and inform local drug safety policy development.

Abbreviations

ATC, Anatomical Therapeutic Chemical [classification]; IQR, inter-quartile range; ISP, intentional self-poisoning; NZNPC, New Zealand National Poisons Centre; SSRI, selective serotonin reuptake inhibitor.

*Correspondence to: Eeva-Katri Kumpula, National Poisons Centre, University of Otago, PO Box 56, Dunedin, 9054, New Zealand. Tel.: +64 3 479 8227.

e-mail: eeva-katri.kumpula@otago.ac.nz.

© 2023 The Authors. Published by Elsevier B.V. on behalf of Public Health Association of Australia. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Aust NZ J Public Health. 2023; Online; <https://doi.org/10.1016/j.anzjph.2023.100027>

Table 1: Descriptives in the records of human patients exposed to at least one therapeutic product and who were assisted by the NZNPC in 2018–2020.

| | |
|---|---------------------------------------|
| Records with at least one therapeutic product | 29,677 (100%) |
| Median age in years (IQR) | 4.0 (2.0–27.0) |
| Patient record age group | Number of records (% of total) |
| 0–12 + unknown child | 16,328 (55%) |
| 13–19 | 2,536 (9%) |
| 20–64 | 6,119 (21%) |
| 65 and over | 2,295 (8%) |
| Unknown adult | 2,118 (7%) |
| Unknown age | 281 (1%) |
| Patient gender | |
| Female | 16,047 (54%) |
| Male | 12,731 (43%) |
| Other, diverse, or unknown | 900 (3%) |
| Number of products^a involved in the exposure incident | |
| 1 | 25,340 (85%) |
| 2 | 2,628 (9%) |
| 3 | 853 (3%) |
| 4 or more | 857 (3%) |
| Median number of products (IQR) | 1 (1–1) |

IQR = inter-quartile range; NZNPC = New Zealand National Poisons Centre.

^aMay also involve products containing other substances than therapeutic agents, except in single-product exposures.

The New Zealand (NZ) population of 5 million is served by the NZ National Poisons Centre (NZNPC) for enquiries relating to various substance exposures (“poisonings”) through a 24/7 toll-free telephone helpline. Contacts to NZNPC from the general public and healthcare professionals cover a broad range of exposure scenarios including accidents, therapeutic errors, incidents of intentional self-harm, and others. Similarly, there is a broad range of substances involved in exposures including pharmaceuticals, chemicals, and commercial or industrial products.

This study was designed to describe the contacts to NZNPC involving human patients exposed to therapeutics, with information about specific therapeutic substances across different age groups, and reasons for the exposures occurring. This was done with the aim of providing additional information about inappropriate use of medicines in New Zealand beyond therapeutic errors.

Methods

Contacts to the NZNPC occurring between 1 January 2018 and 31 December 2020 were extracted from the NZNPC patient data management system in a de-identified format. A contact may involve an information request only (no exposure), or an exposure to a substance involving an animal or human patient or multiple patients, and all contacts result in staff recording case details in a structured electronic form that goes through peer and managerial review before completion. As a result, there is one record per each patient (or information request) following a contact. All substances/products involved in the exposure are coded separately in the patient record and counted as product exposures. Any record of a human patient exposed to at least one therapeutic product (coded in Anatomical Therapeutic Chemical [ATC] codes) was included in further analysis. It should be noted that if there are multiple contacts made to the NZNPC about the same patient and exposure incident, a unique patient and exposure incident can be represented by multiple patient records on the system, in “linked records”. Due to technical limitations of the system, “linked records” cannot be collapsed into one representative record, and therefore, substances in such exposures are counted multiple times (over counted). For this reason, this study does not aim to describe true poisoning prevalence rates but simply aims to describe numbers of records relating to exposures to specific ATC classification system groups and most frequent individual substances. The rate of linked records was determined for reference. Any human patient records with no therapeutic product involved in the exposure incident and contacts involving animal patients were excluded from analysis.

Data extracted included patient age and gender, number and identity of substances involved in the exposure, site of exposure incident, NZNPC medical toxicologist involvement (yes/no), whether NZNPC recommended medical assessment or not, and reasons for exposure incidents (child exploratory, unintentional, therapeutic error, intentional, substance abuse, other reason, unknown reason). These data variables were compared across age groups (those aged 0–12 or “unknown child”, 13–19, 20–64, 65 and over, “unknown adult”, and “unknown age”). Median patient age in years (where known) and median number of substances involved were determined. Therapeutic substance data were converted into ATC codes by one author (DAP, a pharmacist) according to the 2021 coding instructions manual¹³ and cross-checked by another author (EKK, a pharmacist). The 10 most frequent specific substances and reasons for exposures

Table 2: Triage advice given in the records of human patients exposed to at least one therapeutic product and assisted by the NZNPC in 2018–2020.

| n (% row total) Patient age group in record | All records | Medical referral | No referral advised | Referral to other service | Further info required ^a | NZNPC medical toxicologist consulted |
|--|---------------|------------------|---------------------|---------------------------|------------------------------------|--------------------------------------|
| 0–12 (+ unknown child) | 16,328 (100%) | 2,012 (12%) | 13,852 (85%) | 32 (0.2%) | 432 (3%) | 339 (2%) |
| 13–19 | 2,536 (100%) | 1,721 (68%) | 723 (29%) | 17 (1%) | 75 (3%) | 388 (15%) |
| 20–64 | 6,119 (100%) | 2,627 (43%) | 3,331 (54%) | 45 (1%) | 116 (2%) | 866 (14%) |
| 65 and over | 2,295 (100%) | 680 (30%) | 1,570 (68%) | 8 (0.3%) | 37 (2%) | 270 (12%) |
| Unknown adult | 2,118 (100%) | 1,358 (64%) | 628 (30%) | 34 (2%) | 98 (5%) | 151 (7%) |
| Unknown age | 281 (100%) | 185 (66%) | 65 (23%) | 4 (1%) | 27 (10%) | 25 (9%) |
| All ages | 29,677 (100%) | 8,583 (29%) | 20,169 (68%) | 140 (0.5%) | 785 (3%) | 2,039 (7%) |

NZNPC = New Zealand National Poisons Centre.

^aNot enough information available at the time of the contact to assign an advice category yet.

to them were determined for selected age groups to characterise trends in these exposures.

Results

There were 25,347 contacts to NZNPC in 2018, 26,144 in 2019, and 26,619 in 2020, for a total of 78,110 contacts. Of this total, 65,892 contacts (84%) involved at least one human patient with an exposure. These contacts relating to humans resulted in 68,404 patient records. Of these records, 29,677 (43%) involved at least one therapeutic product, while a total of 372 records (0.5% of the 68,404) with unidentified products, but no named therapeutics were excluded and may potentially have been missed from further analysis if they did contain unidentified therapeutics. A total of 2,761 of the therapeutic records (9% of all 29,677) were “linked” to another record. The exposure incident occurred in residential settings in 27,849 records (94% of all 29,677). Most exposures involving at least one therapeutic involved one product only (85%; Table 1).

A total of 29% of patient records included advice to seek medical assessment, while 68% were advised that no such assessment was necessary and that either no action was needed or the person could be monitored and/or cared for at home (“no referral required”; Table 2). These proportions varied by patient age group, with records of children aged 0–12 or of unknown age with 12% medical referral rates, and records of those aged 13–19 with 68%.

The 29,677 records of human patients exposed to at least one therapeutic product contained a total of 36,539 therapeutic product exposures. These substance exposures in the records of those aged 0–12 or unknown child, 13–19, 20–64, and 65 and over, are summarised in Table 3, with paracetamol (ATC code N02BE01) the most common medicine in all of these age groups. The most common reasons for paracetamol exposures varied by age group, with 53% of children’s paracetamol exposures due to therapeutic errors and 44% due to child exploratory behaviours, and 74% of older adults’ exposures due to therapeutic errors. Intentional exposures were the most common reasons for paracetamol exposures in those aged 13–19 and 20–64.

Discussion

The patient population assessed by NZNPC during the study period was generally very young, with over half of the records about exposures to therapeutics being for children. This is in line with observations for all substance exposures from other poisons centres that serve the general public as well as healthcare professionals, such as the Australian,¹⁴ American,¹⁵ and Israeli centres¹⁶ but somewhat lower than for the Saudi Arabian centre.¹⁷ Therapeutic products were frequently involved in exposures reported to the NZNPC, with 43% of all patient records indicating the presence of at least one such product.

Drugs primarily affecting the nervous system (ATC class N) were frequently seen in exposures reported in this study. This may be because people exposed to these medicines may experience central nervous system–related effects that prompt them or their carers to contact the NZNPC for advice, or in the case of analgesics, also due to being commonly used in the New Zealand community. The most common therapeutic substance across all age groups was paracetamol. It is available in New Zealand and Australia from non-pharmacy retailers and pharmacies without a prescription, with limits

on pack sizes but not quantities of packs purchased. The Australian Therapeutic Goods Administration is currently conducting a review of risks of intentional misuse of paracetamol in the context of limits on access to it.¹⁸ Labelling of paracetamol products was recently reviewed in New Zealand, and the medication safety regulator Medsafe made changes to labelling requirements, to be implemented in 2022–2023, to assist safe use and to prevent accidental paracetamol overdoses.¹⁹ Such safety reviews may benefit from inclusion of poisons centre surveillance data of relevant exposures or even be triggered via public health agencies by trends noted by poisons centres. There appear to be significant stocks of paracetamol commonly present in New Zealand households²⁰ where it could be accessed for various purposes besides its intended therapeutic use.

Roughly half of paediatric exposures to paracetamol in this study were due to child exploratory behaviours, and half were therapeutic errors. Paracetamol has been commonly involved in paediatric therapeutic errors reported to other poison centres as well.⁷ In New Zealand, previous efforts to reduce inappropriate paracetamol exposures in children have included prescribing and labelling advice for health professionals as well as dosing tables and advice for caregivers.²¹ The overall medical referral rate for children in our study was only 12%, and the previously noted rate of medical referrals in paediatric therapeutic errors reported to the NZNPC was only 4%,⁵ which together suggest that most paediatric exposures that the centre advises on may be managed at home with appropriate guidance. This highlights potential health service resource savings, if this advice is given over the phone by the poisons centre rather than through a presentation at the emergency department or a general practice clinic, for example.²²

Young people (aged 13–19) were also frequently exposed to paracetamol and other ATC class N medicines, but their exposures were mostly due to intentional self-poisoning (ISP). With the exception of methylphenidate where therapeutic errors were more common, ISP was the most common reason for exposures to the 10 most commonly encountered medicines in this age group. The substances seen in this study match those seen in ISP managed at New Zealand emergency departments, though that study investigated those aged 16 and over as one group only.²³ This information about use in ISP can add to safety profiling of these substances and help inform prescribers about the risk of improper use of the medicines they prescribe in this age group. There were four selective serotonin reuptake inhibitors (SSRIs) frequently encountered in the therapeutic substance exposures of this young age group. SSRIs as a group are generally less toxic than older antidepressants, but citalopram and its S-enantiomer escitalopram have the potential to cause seizures, QT prolongation, and clinically significant cardiac arrhythmias in overdose.²⁴ The evidence base for using SSRIs in people younger than 18 is not clear, and their use in adolescents necessitates careful monitoring of any emerging or worsening suicidal ideation or self-harming behaviours.²⁵ A child and adolescent psychiatrist should be consulted before treatment initiation where possible,²⁶ but a recent Australian large-scale safety review did not find grounds for limiting antidepressant prescribing in adolescents to psychiatrists only.²⁷ As ISP incidents often involve medicines prescribed to the patient^{23,28} and quick, impulsive decisions about proceeding with the act,²⁹ amounts of SSRIs in a single dispensing may need to be limited to prevent access to significant amounts quickly. In New Zealand, SSRIs can be prescribed and then dispensed

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%) | - | - | - | - |
| 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%) |
| 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%) |
| 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%) | - | - |

NZNPC = New Zealand National Poisons Centre.

^aAge-appropriate exploratory behaviour.

^bIntentional self-harm, misuse for greater therapeutic effect.

^cFor psychotropic effects.

in one-off (“statim”) quantities of 3- or 6-month supply, but also trial quantities of a month’s supply can be prescribed, or the prescriber or even the community pharmacist can specify time intervals when aliquots of the whole prescribed quantity are dispensed if the patient could be at risk of ISP.^{26,30,31} Research into the actual quantities of antidepressants dispensed to young people in unique dispensing events could further characterise and help assess the risk of ISP from SSRIs and other antidepressants as this information has not been published previously due to complexities and limitations of routinely collected pharmaceutical dispensing data.³²

The therapeutic errors causing methylphenidate exposures in the 13–19 age group suggest that further investigation of the causes of such exposures is warranted. Iron-only supplements were also frequently encountered in intentional exposures in youth: such overdoses may be clinically significant, requiring extensive interventions such as whole bowel irrigation and antidote therapy.^{33,34} While there is evidence to suggest unintentional/exploratory iron exposures in young children could be reduced by introduction of dose-unit packaging,³⁵ it is unclear whether such measures would work in preventing ISP by iron supplement ingestion in youth. Reducing pack sizes and introducing dose-unit packaging may have reduced large paracetamol overdoses in the United Kingdom, but these effects were not necessarily robust or sustained.³⁶ Iron supplements are available over-the-counter in pharmacies in New Zealand, and therefore, further studies into their inappropriate use and possible interventions that could mitigate such use are needed.

Adults aged 20–64 frequently had exposures to codeine and tramadol and particularly in ISP incidents. While the management of overdose with both of these opioids is well established, their case fatality ratios in ISP are higher than, for example, for paracetamol.³⁷ Tramadol in particular carries risk of inducing potentially severe adverse effects such as serotonin syndrome or seizures in overdose.³⁸ For most of the study period, codeine was available in New Zealand without prescription in combination products but only from pharmacies. All codeine-containing products became prescription only in New Zealand on 5 November 2020.³⁹ Australia implemented a similar legislation change in February 2018, and initial analyses appeared to show a reduction in contacts to the New South Wales poisons centre regarding exposures to low-dose codeine combination products, which had been rescheduled to prescription only.⁴⁰ While it is unclear for how long any benefits from a change in medicine availability may be sustained³⁶ or whether unintended substitution to misuse and/or abuse of other medicines and potential means of harm occurs, it will be of public health interest to monitor codeine and other analgesic exposure prevalence in New Zealand after the recent codeine legislative change.

Those aged 65 and over had exposures to cardiac drugs from ATC class C frequently, and metoprolol and cilazapril were the most common specific substances. This, however, highlights an important limitation in interpreting poisons centre and other surveillance data: These medicines are by far the most prescribed in their respective therapeutic classes in New Zealand,⁴¹ and therefore not necessarily the most harmful of all similar medicines, but frequently encountered in poisons centre reports due at least in part to frequent use in the community. The use of these two medicines “near-exclusively” in New Zealand has resulted in warnings about over-reliance on them and the likely impacts of possible sourcing issues.⁴² Eventually a

prohibition on starting new patients on cilazapril, instead favouring other acetylcholine esterase (ACE) inhibitors was decreed from 1 May 2021.⁴³ The effects of such changes may be reflected in prevalence of reports to NZNPC in the future.

As most therapeutic exposures occurred in residential settings, this highlights the importance of ongoing efforts to promote and refine consumer awareness of risks of storing medicines in the home in places where children, or indeed people from any age groups, might gain unsupervised and unintended access. Convenience of access, a storage place serving as a reminder for taking the medicine, and keeping medicines away from children’s reach were important factors deciding where New Zealanders stored medicines in their households.⁴⁴ Medicines no longer acutely required or already expired were often kept “just in case,”⁴⁵ which may lead to accumulation in the household and cause added risk if there is unintended access by children or others. Public health campaigns should target these issues through simple, clear, and practical messaging.

Study limitations

Poisons centre data are limited by the accuracy and reliability of what is reported by the person contacting the service.⁴⁶ Exposures in the vast majority of contacts are not objectively confirmed by laboratory analysis. There may not be suitable samples or tests available for all analytes or testing may not be feasible. Further, if a healthcare professional is managing a case with multiple substances involved, but is concerned and seeking advice about only one of them, unless they disclose the other products as well, they may be missed. The substance data presented here are therefore also subject to these potential reporting biases, which may vary to an unknown degree from case to case. This is impossible to control for, as the main function of a poisons centre is to provide risk assessments and give advice accordingly, and the focus would be on advising about the substance(s) the caller is enquiring about. Further, the NZNPC’s main task is advising on the management of various substance exposures, and as such specific details of root causes of exposures are not collected, but only to a degree that assists acute patient management, and where such details are available. As contacting the centre is voluntary, NZNPC data will always only capture an unknown subset of all exposures occurring in the New Zealand community. Due to the variation in and unpredictability of what information is available about the exposure incident background from the person contacting the poisons centre for advice, reasons for exposures occurring coded in NZNPC data may not capture all nuances of what actually transpired. Poisons centre data can therefore add to pharmacovigilance data but should be interpreted in conjunction with data from other sources that may capture other types of misuse and errors in use of medications. Further, as NZNPC does not routinely follow up cases, eventual outcomes including any harm or absence of it from exposures presented here cannot be determined from these data.

As some products in the dataset were unidentified, some cases involving an exposure to a therapeutic product may have been missed from the analysis. The rate of this potential undercount occurring is low, with 372 records of 68,404 (0.5%) potentially affected; however, other products may have been missed from reporting. A total of 2,761 of the 29,678 records (9%) with at least one

therapeutic product were linked to another record about the same patient and incident. Due to technical limitations of the NZNPC data system, these are unable to be collapsed into “single representative records” of the incidents, and the products involved in these records are therefore over counted, representing product exposures reported, rather than unique incidents. These results do not therefore attempt to describe true prevalence of unique poisoning incidents and should be interpreted with this limitation in mind.

Conclusion

NZNPC frequently advised on management of medicine exposures involving drugs affecting the nervous system. All age groups were frequently exposed to paracetamol, while youth and adults were also frequently exposed to psychiatric medicines, and older adults to cardiac medicines. Youth and adults had more intentional exposures compared to children and older adults who frequently had unintentional exposures and exposures due to therapeutic errors. The epidemiological data on exposures reported in contacts with the NZNPC can increase our understanding about different types of inappropriate use of specific medicines in different age groups. Poisons centre data can be used in conjunction with other toxicovigilance and pharmacovigilance data to obtain a more comprehensive picture of various harms from use of medicines that can be used to inform medication safety monitoring and public health interventions.

Data availability statement

Raw data are not available due to confidentiality issues, but summary data may be available from the corresponding author upon reasonable request.

Funding

No funding was received for the preparation of this article.

Ethical approval

The study was approved by the University of Otago Human Research Ethics Committee (ref# HD19/064).

Acknowledgements

NZNPC Poisons Information Officers for serving callers and collecting the data used in this study as part of their routine documentation practice.

Conflicts of interest

E-K Kumpula, DA Paterson, and AC Pomerleau declare that they have no conflict of interest.

References

- Bell JC, Bentley JP, Downie C, Cairns R, Buckley NA, Katelaris A, et al. Accidental pharmacological poisonings in young children: population-based study in three settings. *Clin Toxicol* 2018. <https://doi.org/10.1080/15563650.2017.1422509>.
- Naun CA, Olsen CS, Dean JM, Olson LM, Cook LJ, Keenan HT. Can poison control data be used for pharmaceutical poisoning surveillance? *J Am Med Inf Assoc* 2011. <https://doi.org/10.1136/jamia.2010.004317>.
- Hayes BD, Klein-Schwartz W, Gonzales LF. Causes of therapeutic errors in older adults: evaluation of National Poison Center data. *J Am Geriatr Soc* 2009. <https://doi.org/10.1111/j.1532-5415.2008.02166.x>.
- Brophy T, Spiller H, Casavant M, Chounthirath T, Smith M, Xiang H. Medication errors reported to US poison control centers. *Clin Toxicol* 2014;2000–12. <https://doi.org/10.3109/15563650.2014.953168>.
- Yang NY, Pomerleau AC, Shieffelbien LM, Kunac DL, Braund R. Therapeutic errors captured by the New Zealand National Poisons Centre: a retrospective audit. *J Prim Health Care* 2021. <https://doi.org/10.1071/HC20066>.
- Lavon O, Ben-Zeev A, Bentur Y. Medication errors outside healthcare facilities: a national poison centre perspective. *Basic Clin Pharmacol Toxicol* 2014. <https://doi.org/10.1111/bcpt.12150>.
- Cassidy N, Duggan E, Williams DJ, Tracey JA. The epidemiology and type of medication errors reported to the National Poisons Information Centre of Ireland. *Clin Toxicol* 2011. <https://doi.org/10.3109/15563650.2011.587193>.
- Urban M, Leššo R, Pelclová D. Unintentional pharmaceutical-related medication errors caused by laypersons reported to the toxicological information centre in the Czech Republic. *Basic Clin Pharmacol Toxicol* 2016. <https://doi.org/10.1111/bcpt.12578>.
- Shah K, Barker KA. Out-of-hospital medication errors: a 6-year analysis of the national poison data system. *Pharmacoepidemiol Drug Saf* 2009. <https://doi.org/10.1002/pds.1823>.
- Taylor DMCD, Robinson J, MacLeod D, MacBean CE, Braitberg G. Therapeutic errors among children in the community setting: nature, causes and outcomes. *J Paediatr Child Health* 2009. <https://doi.org/10.1111/j.1440-1754.2008.01462.x>.
- Saheb Sharif-Askari F, Saheb Sharif-Askari N, Javadi M, Gholami K. Adverse drug reactions reported to the drug and poison information center of Tehran, Iran. *PLoS One* 2017. <https://doi.org/10.1371/journal.pone.0185450>.
- Leonard JB, Minhaj FS, Klein-Schwartz W. An analysis of fatal iatrogenic therapeutic errors reported to United States poison centers. *Clin Toxicol* 2021. <https://doi.org/10.1080/15563650.2020.1766691>.
- WHO Collaborating Centre for Drug Statistics Methodology. *Guidelines for ATC classification and DDD assignment 2021*. Oslo: WHO Collaborating Centre for Drug Statistics Methodology; 2020.
- Huynh A, Cairns R, Brown JA, Lynch AM, Robinson J, Wylie C, et al. Patterns of poisoning exposure at different ages: the 2015 annual report of the Australian Poisons Information Centres. *Med J Aust* 2018. <https://doi.org/10.5694/mja17.01063>.
- Gummin DD, Mowry JB, Beuhler MC, Spyker DA, Bronstein AC, Rivers LJ, et al. Annual report of the American association of poison control centers' national poison data system (NPDS): 38th annual report. *Clin Toxicol* 2020. <https://doi.org/10.1080/15563650.2021.1989785>.
- Bentur Y, Lurie Y, Cahana A, Bloom-Krasik A, Kovler N, Neuman G, et al. Poisoning in Israel: annual report of the Israel poison information center. *Isr Med Assoc J* 2017;21(3):175–82. 2019.
- Al-Mousa FA, Gado AM, Attia AM, Tammam HG. Medical toxicology experience: poisoning consultations cases registry in Saudi Ministry of Health - 2020 annual report. *Toxicol Rep* 2021. <https://doi.org/10.1016/j.toxrep.2021.07.024>.
- Therapeutic Goods Administration. *Independent expert report on the risks of intentional self-poisoning with paracetamol*. 9 May 2022. Available from, <https://www.tga.gov.au/how-we-regulate/ingredients-and-scheduling-medicines-and-chemicals/poisons-standard-and-scheduling-medicines-and-chemicals/scheduling/independent-expert-report-risks-intentional-self-poisoning-paracetamol>.
- Medsafe. *Outcome of the consultation on the proposed changes to paracetamol warning and advisory statements*. 29 March 2021. Available from, <https://www.medsafe.govt.nz/consultations/paracetamol-warning-statements-outcome.asp>.
- Kumpula E-K, Norris P, Pomerleau AC. Stocks of paracetamol products stored in urban New Zealand households: a cross-sectional study. *PLoS One* 2020. <https://doi.org/10.1371/journal.pone.0233806>.
- Health Navigator New Zealand. *Paracetamol for babies and children*. July 2018. Available from: <https://www.healthnavigator.org.nz/media/5078/paracetamol-safe-use-of-paracetamol-for-children-july-2018.pdf>.
- Nicholls E, Sullivan T, Zeng J, et al. Staying at home: the potential cost savings related to triage advice provided by the New Zealand National Poisons Centre. *Clin Toxicol* 2022;60(1):115–21.
- Kumpula E-K, Lambie B, Quigley P, Nada-Raja S, Norris P. Prescribers aware: a cross-sectional study from New Zealand emergency departments on the substances used in intentional self-poisoning and their sources. *J Prim Health Care* 2020. <https://doi.org/10.1071/HC20017>.
- Isbister GK, Bowe SJ, Dawson A, Whyte IM. Relative toxicity of selective serotonin reuptake inhibitors (SSRIs) in overdose. *Clin Toxicol* 2004. <https://doi.org/10.1081/CLT-120037428>.
- Malhi GS, Bell E, Bassett D, Boyce P, Bryant R, Hazell B, et al. The 2020 Royal Australian and New Zealand College of Psychiatrists clinical practice guidelines for mood disorders. *Aust N Z J Psychiatr* 2021. <https://doi.org/10.1177/0004867420979353>.
- Best Practice Advocacy Centre. *The role of medicines for the treatment of depression and anxiety in patients aged under 18 years*. *Best Pract J* 2016; (74):19–26.
- Buykx P, Loxley W, Dietze P, Ritter A. Medications used in overdose and how they are acquired—an investigation of cases attending an inner Melbourne emergency department. *Aust N Z J Publ Health* 2010. <https://doi.org/10.1111/j.1753-6405.2010.00573.x>.
- Kessel N, McCulloch W. Repeated acts of self-poisoning and self-injury. *Proc Roy Soc Med* 1966:89–92.

29. Australian Therapeutic Goods Administration Advisory Committee on Medicines. In: *ACM meeting statement, meeting 29, 30 September – 1 October 2021*; 17 January 2022. Available from, <https://www.tga.gov.au/resources/publication/meeting-statements/acm-meeting-statement-meeting-29-30-september-1-october-2021>.
30. PHARMAC. *Rules of the schedule*. 1 July 2022. Available from, <https://pharmac.govt.nz/pharmaceutical-schedule/general-rules-section-a/>.
31. Best Practice Advocacy Centre. Piles of pills: prescribing appropriate quantities of medicines. *Best Pract J* 2015;69:10–7.
32. Ministry of Health. *Patterns of antidepressant drug prescribing and intentional self-harm outcomes in New Zealand: an ecological study*. Wellington: Ministry of Health; 2007.
33. Chang TP-Y, Rangan C. Iron poisoning: a literature-based review of epidemiology, diagnosis, and management. *Pediatr Emerg Care* 2011. <https://doi.org/10.1097/PEC.0b013e3182302604>.
34. Bateman DN, Eagling V, Sandilands EA, Jackson G, Crawford C, Hawkins L, et al. Iron overdose epidemiology, clinical features and iron concentration-effect relationships: the UK experience 2008–2017. *Clin Toxicol* 2018. <https://doi.org/10.1080/15563650.2018.1455978>.
35. Tenenbein M. Unit-dose packaging of iron supplements and reduction of iron poisoning in young children. *Arch Pediatr Adolesc Med* 2005. <https://doi.org/10.1001/archpedi.159.6.557>.
36. Bateman DN. Pack size and paracetamol overdose: 16 years later. *Clin Toxicol* 2014. <https://doi.org/10.3109/15563650.2014.952432>.
37. Hawton K, Ferrey A, Casey D, Wells C, Fuller A, Bankhead C, et al. Relative toxicity of analgesics commonly used for intentional self-poisoning: a study of case fatality based on fatal and non-fatal overdoses. *J Affect Disord* 2019. <https://doi.org/10.1016/j.jad.2019.01.002>.
38. Hassamal S, Miotto K, Dale W, Danovitch I. Tramadol: understanding the risk of serotonin syndrome and seizures. *Am J Med* 2018. <https://doi.org/10.1016/j.amjmed.2018.04.025>.
39. Medsafe. *Codeine-containing medicines to be reclassified*. Ministry of Health; 2020. Media release 22 October 2020, <https://www.health.govt.nz/news-media/media-releases/codeine-containing-medicines-be-reclassified>. [Accessed 17 December 2021].
40. Cairns R, Schaffer AL, Brown JA, Pearson SA, Buckley NA. Codeine use and harms in Australia: evaluating the effects of re-scheduling. *Addiction* 2020. <https://doi.org/10.1111/add.14798>.
41. Tomlin AM, Woods DJ, Reid JJ, Tilyard MW. Trends in prescription medicine use by older people in New Zealand 2010–2015: a national population-based study. *N Z Med J* 2020;133(1513):61–6.
42. Medlicott R. *Over-reliance in cardiovascular treatment*. 29 November 2017. Available from: <https://pharmac.govt.nz/medicine-funding-and-supply/medicine-notices/cilazapril/over-reliance-in-cardiovascular-treatment-a-supply-risk-that-needs-to-change/>.
43. PHARMAC. *Cilazapril: No new patients from 1 May 2021*. 29 November 2017. Available from: <https://pharmac.govt.nz/medicine-funding-and-supply/medicine-notices/cilazapril/>.
44. Hewson C, Shen CC, Strachan C, Norris P. Personal medicines storage in New Zealand. *J Prim Health Care* 2013. <https://doi.org/10.1071/HC13146>.
45. Braund R, Peake BM, Shieffebien L. Disposal practices for unused medications in New Zealand. *Environ Int* 2009. <https://doi.org/10.1016/j.envint.2009.04.003>.
46. Hoffman RS. Understanding the limitations of retrospective analyses of poison center data. *Clin Toxicol* 2007. <https://doi.org/10.1080/15563650701233370>.