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# Availability of antidotes for drug poisonings and doctors' perspectives thereof

Drug poisoning is an important area of study in South Africa as a treatable cause of mortality. While research has been conducted on poisoning, there is a paucity of literature on the availability of antidotes in South Africa. The objectives of this study were to assess the availability of antidotes in selected teaching hospitals in the Southern Gauteng City-Region and to explore doctors' experiences of antidote supply. The availability of antidotes in the emergency departments (EDs) and pharmacies was assessed and recorded using a data sheet that was completed in person at each of the teaching hospitals. A questionnaire exploring experiences of antidote supply was distributed to 126 doctors working in the EDs. Our results indicate that N-acetylcysteine, atropine, diazepam, clonazepam, sodium bicarbonate, vitamin K, calcium gluconate, naloxone, ethanol, and pyridoxine were present in all EDs; activated charcoal was present in 80%; lorazepam, glycopyrrolate, and calcium chloride in 60%; freeze-dried plasma in 40%; glucagon and desferrioxamine in 20%; and fresh frozen plasma, hydroxocobalamin, sodium nitrite, sodium thiosulfate, sodium calcium edetate, and intralipid were not present in any of the EDs. Doctors reported organophosphate poisoning and paracetamol overdose as the most common drug poisonings (81.7% and 14.3% of 126 respondents, respectively). Most doctors experienced no supply issues for N-acetylcysteine, calcium gluconate, sodium bicarbonate, or pyridoxine (85.7%, 83.3%, 87.3%, and 75.4% of 126 respondents, respectively). The antidotes to the most common poisonings reported by doctors were present in all EDs. However, concerns were raised about consistency of supply, which will be an important avenue for further research.

#### Significance:

- These findings highlight the lack of uniform availability of antidotes to common and critical drug poisonings in emergency departments.
- The experiences of doctors in Gauteng concerning the most commonly encountered poisonings contrast with existing literature from South Africa, suggesting regional differences within the country.

## Introduction

Poisoning, both accidental and intentional, is a significant problem in South Africa.<sup>1-7</sup> Accidental poisoning was reported to comprise 2.7% of external causes of accidental injury, which made up 66.5% of non-natural deaths in South Africa in 2016. Intentional self-harm, of which poisoning is one of multiple causes, is reported as 0.8% of non-natural deaths. Consequently, poisonings altogether account for approximately 2% of non-natural deaths in South Africa.<sup>8</sup> Despite a low mortality, poisoning is a common presentation to emergency departments (EDs). Self-poisoning accounted for 8.3% of all ED admissions over a 6-month period at Khayelitsha District Hospital in the Western Cape<sup>3</sup>, while Pelonomi Regional Hospital in Bloemfontein in the Free State had 260 incidents of deliberate self-poisoning in an 18-month study from January 2010 to July 2011<sup>7</sup>. Antidotes are agents directed at treating or reversing the effects of specific poisons. While many poisons can be treated adequately with supportive care alone, there are some which benefit from specific antidotes.<sup>9</sup>

Globally, antidote availability has been shown to be of concern. Studies in Canada revealed that most hospitals did not stock all of the antidotes that were considered.<sup>10,11</sup> A study in the UK similarly showed that while over 90% of hospitals sampled had the most commonly used antidotes, the less commonly used antidotes were less reliably stocked.<sup>12</sup> In a Massachusetts (USA) survey, while 9.8% of the hospitals had stock of all antidotes assessed, fewer had a sufficient supply to treat even one adult.<sup>13</sup> A Sri Lankan study of essential medicine availability in primary and secondary hospitals found none of the hospitals had 100% of the antidotes assessed available, with atropine, DL-methionine, and naloxone being the most reliably stocked.<sup>14</sup> In South Africa, a study on antidote availability reported tertiary public hospitals stocking only 46% of antidotes considered, with secondary-level and private hospitals stocking less.<sup>15</sup>

While the types of poisoning cases that present to South African EDs have been documented in various regional studies, there is a paucity of studies about the availability of antidotes. This paucity presents challenges in determining whether there are shortages in supply that need to be addressed and whether this impacts patient mortality. There is also a lack of published data on the poisoning presentations seen in EDs in Gauteng as compared to other provinces. Therefore, in this study, we aimed to assess the availability of antidotes to poisonings, and doctors' experiences thereof, in a selection of EDs in teaching hospitals in the Southern Gauteng City-Region of South Africa.

## Methods

This cross-sectional observational and interrogative study took place from December 2020 to March 2021 in the EDs and pharmacies of five purposively selected teaching hospitals in the Southern Gauteng City-Region, namely Charlotte Maxeke Johannesburg Academic Hospital (CMJAH), Chris Hani Baragwanath Academic Hospital (CHBAH), Helen Joseph Hospital (HJH), Tambo Memorial Hospital (TMH) and Thelle Mogoerane Regional Hospital



(TMRH). These hospitals were chosen for their status as teaching hospitals including regional, tertiary, and central academic facilities, providing a cross-section of the variety of cases seen and ED total patient numbers. Their status as teaching hospitals is important in that it both provides a spectrum of doctors' experience levels and because teaching hospitals have previously been found to be more likely to adequately stock antidotes.<sup>11,16</sup>

The antidotes assessed in this study were selected based on reports in the literature on the most common poisons implicated in ED presentations in South Africa (Table 1). The poisons were evaluated to isolate those with specific antidotes (Table 1).<sup>9</sup> Activated charcoal and benzodiazepines were included as they are required for gut decontamination and treatment of seizures resulting from many poisons.<sup>9</sup> Additionally, antidotes which are less commonly used but are still necessary to stock were identified using the World Health Organization (WHO) Model List of Essential Medicines.<sup>17</sup> These antidotes include methylene blue, pyridoxine, sodium nitrite, sodium thiosulfate, hydroxocobalamin, sodium calcium edetate, and ethanol (fomepizole, the alternative antidote to toxic alcohol poisoning, was not included in this study as it is available only on a named patient basis from Equity pharmaceutical company after approval from the South African Health Products Regulatory Authority (SAHPRA)).<sup>17,18</sup> Intralipid, the antidote for local anaesthetic toxicity, was included as local anaesthetics are widely used in EDs.<sup>19</sup>

Data collection took place in two stages. The first stage involved assessing the presence of antidotes in the EDs and pharmacies through completing one data sheet per hospital across five separate days in December 2020. The second stage explored the experiences of doctors through the use of a questionnaire administered in hard copy to the doctors working in the respective EDs from December 2020 to March 2021. Doctors were approached at academic meetings or at shift handover times and questionnaires were completed in the presence of the first author to ensure that there was no collaboration between respondents. Participants were given an information sheet before their participation and were made aware that they could withdraw their participation at any time.

The study population for the questionnaires consisted of any doctor in each ED who had worked there for more than 1 month. The temporal requirement addressed biases that might have arisen from respondents not yet having experienced the specific poisonings common to that ED. Part-time doctors were excluded from the study as they work less often in the specific ED and would thus be less accurate in attributing poisoning trends to an individual hospital. The study population was thus 168 doctors, with the sample size required to achieve a confidence interval of 95% with a margin of error of 5% being 118 doctors.<sup>20</sup>

The information from the data sheet and the data obtained from the questionnaires were captured on two separate spreadsheets. The variables considered in this study were: the most common poisonings, the presence or absence of specific antidotes, the quantity of each antidote, restrictions in access to each antidote, and doctors' experiences of supply issues.

Data were manually classified and thereafter assessed using means, ranges, and percentages to draw comparisons between poisonings, antidotes, and the different hospitals. When analysing the section of the questionnaire on causes of shortages, if a range was given, the lower value was captured (for example, 4–5 was captured as 4). Frequency distributions were used to explore the results of Likert-style questions. Relationships between potentially associated factors were assessed using Pearson's correlation coefficient, following confirmation that the data were normally distributed.

Ethics approval was granted by the University of the Witwatersrand Human Research Ethics Committee (Medical); clearance certificate number M200628 MED20-05-134.

## Results

### Demographics

A total of 126 respondents completed the questionnaire; 40 (31.7%) from HJH, 22 (17.5%) from CMJAH, 12 (9.5%) from TMRH, 27 (21.4%) from CHBAH, and 25 (19.8%) from TMH. The levels of expertise represented

**Table 1:** Poisons commonly implicated in emergency department presentations in South Africa and their antidotes

| Poison                                                                  | Management                                | Antidote                                                                  | References    |
|-------------------------------------------------------------------------|-------------------------------------------|---------------------------------------------------------------------------|---------------|
| Paracetamol                                                             | Specific                                  | N-acetylcysteine                                                          | 1,2,3,5,7     |
| Benzodiazepines                                                         | Specific/supportive                       | Flumazenil*                                                               | 1,2,7         |
| Antihistamines                                                          | Supportive                                |                                                                           | 1,2,3,4       |
| Anticholinesterases                                                     | Specific                                  | Atropine/glycopyrrolate                                                   | 1,2,3,4,5,6,7 |
| Irritants/corrosive agents                                              | Supportive                                |                                                                           | 1,2,3,5,7     |
| Anticoagulant pesticides                                                | Specific                                  | Vitamin K/fresh frozen plasma (FFP)/freeze-dried plasma (FDP)/Haemosolvex | 1,2,3,4       |
| Tricyclic antidepressants                                               | Specific                                  | Sodium bicarbonate                                                        | 1,2,6         |
| Other antidepressants (SSRIs, SNRIs)                                    | Supportive                                |                                                                           | 1,4,7         |
| Antihypertensives (includes beta blockers and calcium channel blockers) | Specific/supportive                       | Calcium chloride/gluconate glucagon                                       | 3,4,7         |
| Antiretroviral drugs                                                    | Supportive                                |                                                                           | 5,7           |
| Other analgesics                                                        | NSAIDs – supportive<br>Opioids – specific | Naloxone                                                                  | 1,3,4,7       |
| Volatile solvents                                                       | Supportive                                |                                                                           | 1,2,4,7       |
| Antibiotics                                                             | Supportive                                |                                                                           | 3,7           |
| Iron tablets                                                            | Specific                                  | Desferrioxamine                                                           | 3,7           |

\*Flumazenil was not included in this study due to concerns regarding safety in poly-pharmacy overdose and the risk of precipitating seizures.<sup>9</sup>



were consultants (10; 7.9%), registrars (24; 19.0%), medical officers (MOs; 52; 41.3%), community service medical officers (CSMOs; 12; 9.5%) and interns (28; 22.2%) (Table 2). The duration of time spent by respondents in each ED was predominantly 1–6 months, but with longer time periods well represented (Table 2).

### Presence of antidotes

The number of listed antidotes present in the ED ranged from 12 (48.0%) at TMH to 15 (60.0%) at TMRH. The pharmacy with the largest number of the listed antidotes available was at HJH with 18 (72.0%); the fewest antidotes (13; 52.0%) were available at the pharmacy of CMJAH.

N-acetylcysteine, atropine, clonazepam, calcium gluconate, naloxone, and pyridoxine were present in all EDs and pharmacies (Figure 1). Diazepam, vitamin K, ethanol, and sodium bicarbonate were present in all EDs but not all pharmacies, while glycopyrrolate, lorazepam and desferrioxamine were present in all pharmacies but not all EDs. Hydroxycobalamin, sodium nitrite, sodium thiosulfate, and sodium calcium edetate were absent in all EDs and pharmacies; pharmacists were asked about the individual drugs as well as the combination – Tripac-cyano – and they confirmed that none was stocked in any form. Haemosolvex, methylene blue, and intralipid were absent in all EDs but were present in some pharmacies.

The two regional hospitals (TMH and TMRH) did not have calcium chloride but they did have greater quantities of calcium gluconate than the other hospitals. Desferrioxamine was available at all of the hospital pharmacies, but only in the ED at TMRH. Similarly, methylene blue was available in four of the five hospital pharmacies but not stocked in any of the EDs. Intralipid was present in two of the pharmacies and in none of the EDs.

All the hospitals in this study have access to a blood bank from which fresh frozen plasma can be issued. Freeze-dried plasma was available in the ED at HJH and TMRH, in the pharmacy but not the ED at TMH, and was not available at CMJAH and CHBAH.

### Antidote location within EDs

Benzodiazepines, all of which are schedule 5 drugs, are kept in locked cupboards (Table 3).<sup>18</sup> Atropine, which is schedule 2, is kept in unlocked areas in all hospitals as 0.5 mg and 1 mg vials (Table 3).<sup>18</sup> By contrast, the 100 mg vials are kept in locked cupboards in all EDs which stock this dose.

### Perceived relative frequency of poisonings

The majority of respondents, both overall and at each hospital, named organophosphate poisoning as the most recent case ( $\bar{x} = 74.6\%$ ;  $n = 126$ ; range: 58.3% at TMRH to 86.4% at CMJAH; Figure 2). Paracetamol poisoning was the second most commonly noted as the most recent case at HJH and CMJAH. At CMJAH, this frequency is shared with polypharmacy, which is also the second most commonly noted as recent at CHBAH and TMH. The same number of doctors at TMH reported tricyclic antidepressant poisonings as the most recently experienced polypharmacy cases. Paracetamol poisoning was not reported as most recently experienced by any respondents at TMRH, CHBAH or TMH.

The majority of respondents reported organophosphate poisoning ( $\bar{x} = 81.7\%$ ;  $n = 126$ ; range: 72.5% at HJH to 96.3% at CHBAH; Figure 3) as the most common poisoning. It was ranked second most common by 12 (9.5%) respondents, third by 7 (5.6%), fourth by 2 (1.6%), and fifth by 1 (0.8%) respondent.

Paracetamol is the second most frequently reported poisoning as most common ( $\bar{x} = 14.3\%$ ;  $n = 126$ ; range: 0.0% at TMRH to 25.0% at HJH; Figure 3) and is most commonly reported as second most common across all hospitals ( $\bar{x} = 44.4\%$ ;  $n = 126$ ; range: 33.3% at TMRH to 74.1% at CHBAH; Figure 3). From third ranked onwards, there is more variety in poisonings reported and more varied dominance.

The relationship between the responses for the most recent poisoning and the first-ranked poisoning for organophosphate poisoning across hospitals demonstrated a very weak, statistically insignificant, correlation ( $r = 0.02$ ,  $p = 0.9768$ ). Of 103 doctors who reported organophosphate poisoning as first ranked, 82 experienced it as their most recent. There is a stronger, but statistically insignificant, correlation for paracetamol ( $r = 0.66$ ,  $p = 0.2302$ ) and polypharmacy ( $r = 0.08$ ,  $p = 0.9044$ ). The rest of the poisonings that were listed as the first most common were not mentioned by any respondent as the most recent, therefore no correlation could be calculated.

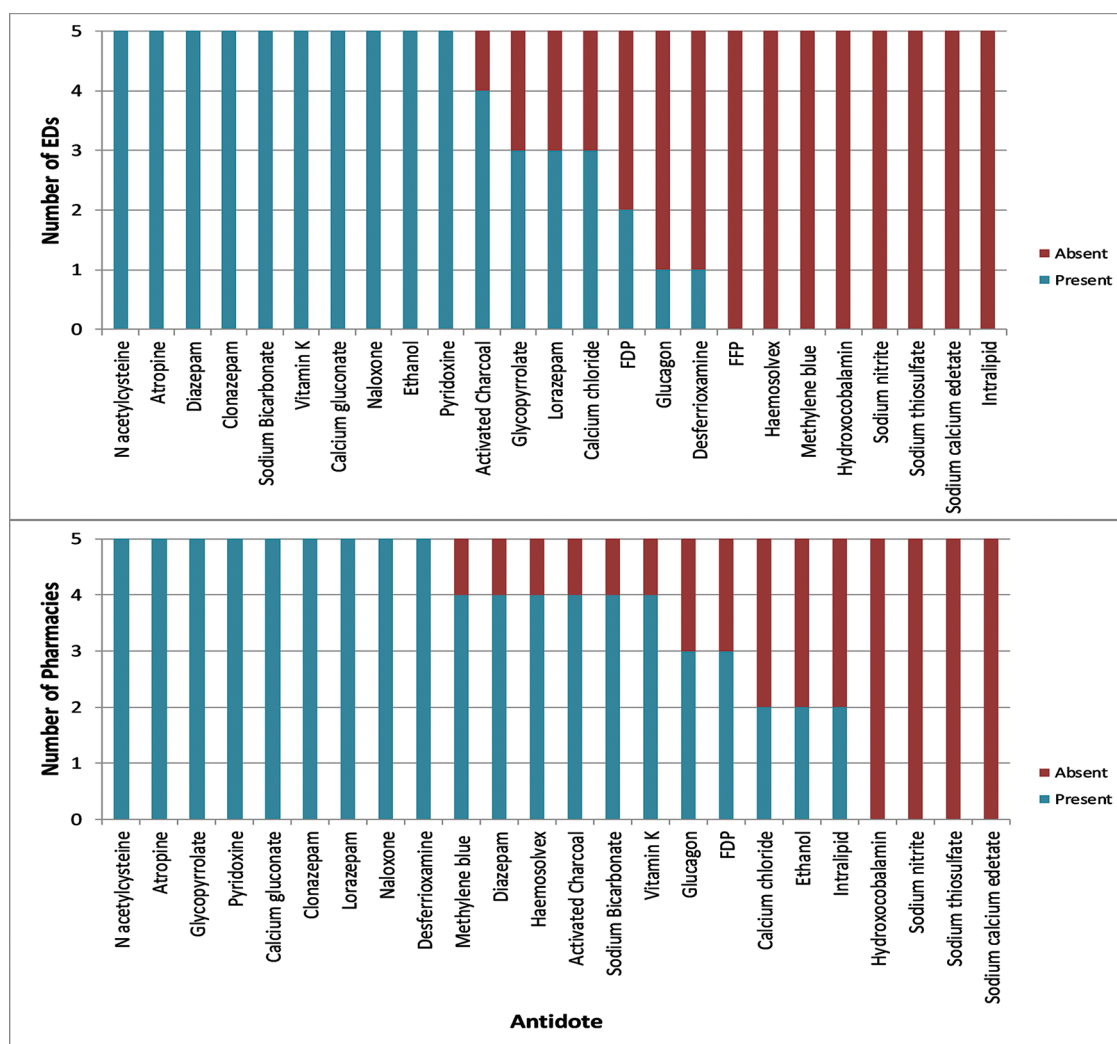
### Shortages of antidotes

Doctors predominantly reported no supply issues for N-acetylcysteine, calcium gluconate, sodium bicarbonate, and pyridoxine, which is in keeping with the finding that all four of these antidotes were present in all the hospitals' EDs (Figures 1 and 4). Sodium bicarbonate was the treatment most reliably reported as having no supply issues ( $\bar{x} = 87.3\%$ ;  $n = 126$ ; range: 77.7% at CHBAH to 100% at TMRH; Figure 4). Supply

**Table 2:** Doctors' current roles and durations working in the emergency department (ED)

|                                   | All        | HJH        | CMJAH      | TMRH      | CHBAH      | TMH        |
|-----------------------------------|------------|------------|------------|-----------|------------|------------|
| <b>Duration in this ED</b>        |            |            |            |           |            |            |
| 1–6 months                        | 66 (52.4%) | 23 (57.5%) | 11 (50.0%) | 8 (66.7%) | 12 (44.4%) | 12 (48.0%) |
| 6–12 months                       | 17 (13.5%) | 4 (10.0%)  | 4 (18.2%)  | 1 (8.3%)  | 4 (14.8%)  | 4 (16.0%)  |
| 1–2 years                         | 17 (13.5%) | 6 (15.0%)  | 2 (9.1%)   | 2 (16.7%) | 3 (11.1%)  | 4 (16.0%)  |
| 2–5 years                         | 14 (11.1%) | 4 (10.0%)  | 3 (13.6%)  | 0 (0.0%)  | 5 (18.5%)  | 2 (8.0%)   |
| >5 years                          | 12 (9.5%)  | 3 (7.5%)   | 2 (9.1%)   | 1 (8.3%)  | 3 (11.1%)  | 3 (12.0%)  |
| <b>Current role</b>               |            |            |            |           |            |            |
| Consultant                        | 10 (7.9%)  | 4 (10.0%)  | 2 (9.1%)   | 1 (8.3%)  | 2 (7.4%)   | 1 (4.0%)   |
| Registrar                         | 24 (19.0%) | 4 (10.0%)  | 8 (36.4%)  | 2 (16.7%) | 7 (25.9%)  | 3 (12.0%)  |
| Medical Officer                   | 52 (41.3%) | 20 (50.0%) | 7 (31.8%)  | 5 (41.7%) | 14 (51.9%) | 6 (24.0%)  |
| Community Service Medical Officer | 12 (9.5%)  | 3 (7.5%)   | 3 (13.6%)  | 3 (25.0%) | 0 (0.0%)   | 3 (12.0%)  |
| Intern                            | 28 (22.2%) | 9 (22.5%)  | 2 (9.1%)   | 1 (8.3%)  | 4 (14.8%)  | 12 (48.0%) |

HJH, Helen Joseph Hospital; CMJAH, Charlotte Maxeke Johannesburg Academic Hospital; TMRH, Thelle Mogoerane Regional Hospital; CHBAH, Chris Hani Baragwanath Academic Hospital; TMH, Tambo Memorial Hospital



**Figure 1:** Antidote availability in emergency departments and pharmacies in five teaching hospitals in the Southern Gauteng City-Region of South Africa.

issues for atropine were reported by more than 20% of respondents at all hospitals except for TMH, where 25 (100%) respondents reported no supply issues (Figure 4). This finding is, however, not in keeping with the finding of atropine being stocked in all the hospitals' EDs and pharmacies (Figure 1).

Lorazepam was the drug for which the greatest number of respondents reported supply issues ( $\bar{x}$  = 42%;  $n$  = 126; range: 33.3% at TMRH to 50% at CMJAH), while clonazepam and diazepam had fewer responses indicating lack of supply – a result which is reflected by the finding that while diazepam and clonazepam were present in all of the hospitals' EDs, lorazepam was only present in three of the five (60%) (Figures 1 and 4). Methylene blue, sodium nitrite, sodium thiosulfate, sodium calcium edetate and glucagon had supply issues reported as unknown by the majority of respondents as they had not needed to use them (Figure 4).

### Perceived reasons for supply issues

Inadequate stock from the pharmacy was ranked as the most frequent cause of supply problems (rank 5;  $\bar{x}$  = 29.4%;  $n$  = 126; range: 25.0% at HJH to 33.3% at TMRH and CHBAH; Figure 5). Second most commonly rated as most frequent was that the antidote was not stocked ( $\bar{x}$  = 25%;  $n$  = 126; range: 13.6% at CMJAH to 45.5% at TMRH). The cause ranked as least common for supply issues (rank 1) was patient load ( $\bar{x}$  = 26.4%;  $n$  = 126; range: 22.7% at CMJAH to 33.3% at TMRH; Figure 5).

### Key experiences of access

The most commonly experienced issue regarding access to antidotes related to atropine. Atropine 100 mg vials require section 21 forms to be

completed, which leads to difficulties accessing stock at times. While smaller vials were available at all hospitals, these can be time-consuming to use when a severe organophosphate poisoning case is treated.

Another common challenge raised by respondents was that of timeous replacement of the drugs after use, both when the pharmacies are closed after hours when the on-call pharmacist would have to assist and on a day-to-day basis when there is delayed ordering of stock by ED staff. A further concern raised was that of infrequently used antidotes not being stocked as they expire before use.

## Discussion

Globally, the availability of antidotes for poisonings is reported as inadequate, both in variety and quantity.<sup>10-14,21</sup> Antidotes for poisonings common within the populations studied are reported to be more reliably stocked.<sup>12,14,21</sup> Similarly, in this study, none of the EDs had stock of all the antidotes surveyed, but the antidotes for the most common poisonings, as reported by the doctors, were present in all the EDs. However, when considering the reliability of supply, there were no antidotes for which all the doctors in any of the EDs reported having never experienced a supply issue. This suggests that, at times, the quantity of antidotes ordered is not adequate for the needs of the EDs. The authors of a prior study performed in Khayelitsha in the Western Cape reported that 79% of the poisoning cases had presented after hours, which reinforces the need highlighted in this study for an adequate supply of antidotes in the ED.<sup>3</sup> As the presence of antidotes in the EDs and pharmacies was assessed on a single day in each hospital, prior shortages could be overlooked, which may reflect the doctors' experiences reported in the

**Table 3:** Antidote location within the emergency departments (EDs) of five teaching hospitals in the Southern Gauteng City-Region of South Africa

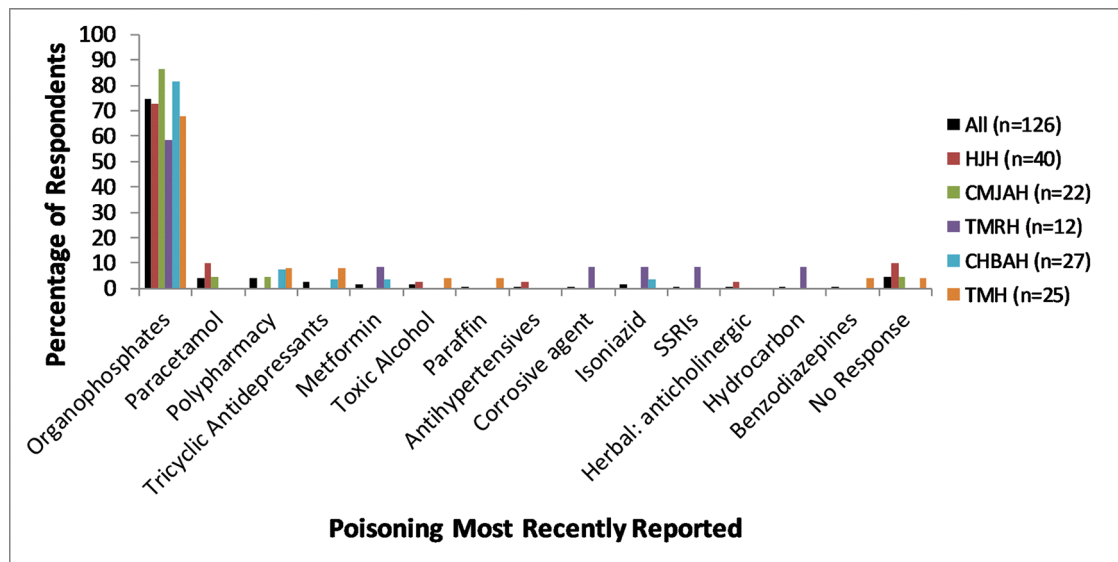
| Antidote               | Schedule | Number of EDs with barriers to access ( <i>N</i> = 5) |                               |                                      |                      |
|------------------------|----------|-------------------------------------------------------|-------------------------------|--------------------------------------|----------------------|
|                        |          | No lock                                               | Key with senior nurse on duty | Key/access code with doctors on duty | Antidote not present |
| N-acetylcysteine       | S2       | 4                                                     | 1                             |                                      |                      |
| Atropine               | S2       | 5 (0.5 & 1 mg)                                        | 1 (100 mg)                    | 3 (100 mg)                           | 1 (100 mg)           |
| Glycopyrrolate         | S2       | 2                                                     |                               | 1                                    | 2                    |
| Lorazepam              | S5       | 2 (fridge)                                            | 2 (fridge)                    |                                      | 1                    |
| Diazepam               | S5       |                                                       | 5                             |                                      |                      |
| Clonazepam             | S5       |                                                       | 5                             |                                      |                      |
| Activated charcoal     | N/A      | 4                                                     |                               |                                      | 1                    |
| Sodium bicarbonate     | N/A      | 5                                                     |                               |                                      |                      |
| Vitamin K              | S3       | 4                                                     | 1                             |                                      |                      |
| Fresh frozen plasma    | S4       | Blood bank                                            |                               |                                      |                      |
| Freeze-dried plasma    | S4       | 1                                                     | 1                             |                                      | 3                    |
| Haemosolvex            | S4       |                                                       |                               |                                      | 5                    |
| Calcium gluconate      | S3       | 5                                                     |                               |                                      |                      |
| Calcium chloride       | S1       | 3                                                     |                               |                                      | 2                    |
| Glucagon               | N/A      |                                                       | 1                             |                                      | 4                    |
| Naloxone               | S4       | 5                                                     |                               |                                      |                      |
| Desferrioxamine        | S4       |                                                       |                               | 1                                    | 4                    |
| Ethanol                | N/A      |                                                       | 2                             | 3                                    |                      |
| Methylene blue         | N/A      |                                                       |                               |                                      | 5                    |
| Pyridoxine             | S0       | 4                                                     |                               | 1                                    |                      |
| Hydroxocobalamin       | N/A      |                                                       |                               |                                      | 5                    |
| Sodium nitrite         | S1       |                                                       |                               |                                      | 5                    |
| Sodium thiosulfate     | S1       |                                                       |                               |                                      | 5                    |
| Sodium calcium edetate | N/A      |                                                       |                               |                                      | 5                    |
| Intralipid             | S3       |                                                       |                               |                                      | 5                    |

questionnaire. Furthermore, the mere presence of the antidote does not ensure there is a sufficient quantity to treat the patient population; for example, the 7.7 g of pyridoxine available at CMJAH would potentially only be sufficient to treat one patient if the maximum dose of 5 g was required.<sup>22,23</sup> This finding mirrors the results of a study in Massachusetts which found that, while 9.8% of the hospitals surveyed had stock of the antidotes assessed, fewer had sufficient supply to treat even one adult.<sup>13</sup>

To ensure that the appropriate antidotes are stocked in EDs in South Africa, various departments have input. If the antidote is not already available in the ED, or not on the essential drug list for the hospital level, a consultant or similar appropriate healthcare worker should motivate for the antidote to be ordered. If approved by the hospital pharmaceutical and therapeutics committee, the pharmacy will then order the appropriate drug if it is available at a reasonable cost. If the drug is unavailable or unregistered in South Africa, it may have to be ordered or sourced internationally using a section 21 form – the SAHPRA form for unregistered medicines.<sup>24</sup> The perception of doctors that the most common reason for poor antidote supply is that there is inadequate stock from the pharmacy is in contrast to the finding that most antidotes were present in the pharmacies. The problem might lie in communication between the EDs and the pharmacies in terms of what

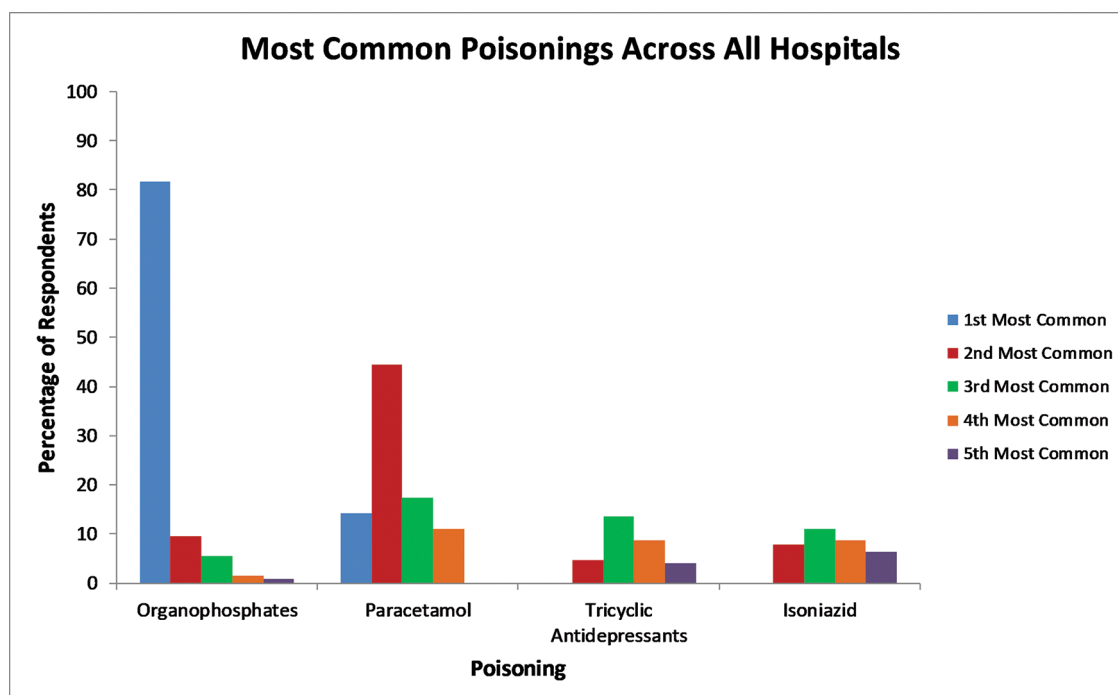
is needed and the quantities thereof. At TMRH, the doctors reported a lack of stock of antidotes as a reason for the lack of supply in far greater proportion than a lack of stock from the pharmacy, perhaps reflecting better communication between the ED and pharmacy at this hospital.

Studies done from 2003 to 2015 in other provinces in South Africa have reported the most common poisoning cases presenting to South African EDs as paracetamol, antihistamines, antihypertensives, and corrosive chemicals.<sup>1-5,7</sup> Data from Gauteng and KwaZulu-Natal reported from eight hospitals show paraffin to be the most common poisoning presenting in 2005, but, of note, the two provinces were not compared in the study.<sup>25</sup> A study reporting calls received over a 1-year period spanning 2008 to 2009 by the Tygerberg Poisons Information Centre, reflecting 42% of calls from the Western Cape and the remainder from the other provinces, noted irritants/corrosive substances to be the most commonly reported poisoning, followed by paracetamol, benzodiazepines, and then cholinesterase inhibitors.<sup>1</sup> The linked study of patients presenting to Tygerberg Academic Hospital in the Western Cape during the same time span reported paracetamol as the most common poisoning presentation, followed by amitriptyline (a tricyclic antidepressant), antihistamines, irritants/corrosive agents and then organophosphates, and notably that the most common poisoning cases



HJH, Helen Joseph Hospital; CMJAH, Charlotte Maxeke Johannesburg Academic Hospital; TMRH, Thelle Mogoerane Regional Hospital; CHBAH, Chris Hani Baragwanath Academic Hospital; TMH, Tambo Memorial Hospital

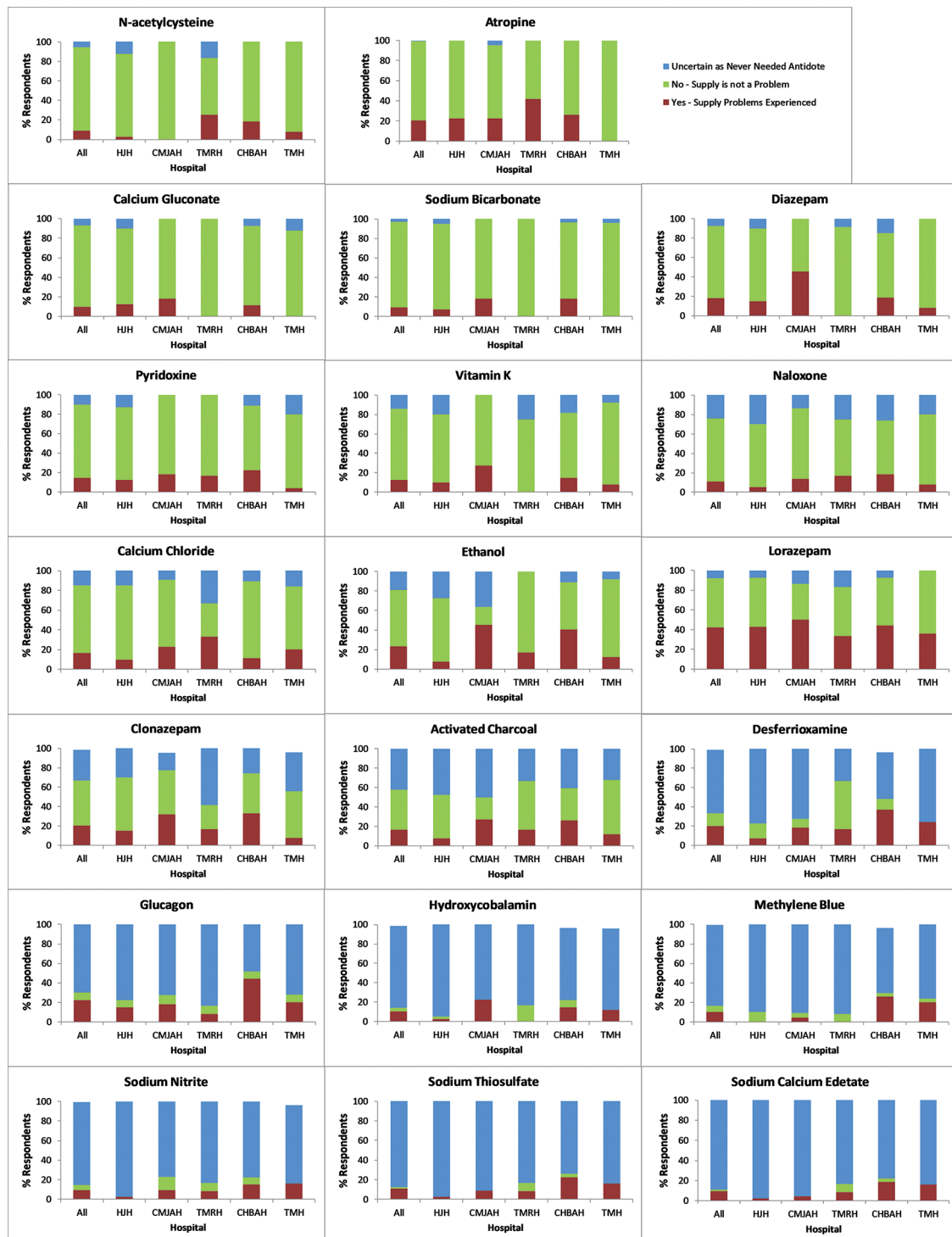
**Figure 2:** Most recent poisonings reported by doctors working in five teaching hospitals in the Southern Gauteng City-Region of South Africa.



**Figure 3:** Most common poisonings reported by doctors working in the emergency departments of five teaching hospitals in the Southern Gauteng City-Region of South Africa.

requiring ICU admission were amitriptyline and organophosphates.<sup>2</sup> Similarly, a study based in the ICU and high-care area in an Eastern Cape hospital reported tricyclic antidepressants and organophosphates as the most common poisoning admissions for the 1-year study period spanning 2014 to 2015.<sup>6</sup> A further study performed from 2014 to 2015 in a tertiary hospital in the Western Cape reported ingestion of prescription medication to be the most common poisoning presentation followed by non-prescription medication and other poisons being less common.<sup>26</sup> Deliberate self-poisoning cases presenting to Pelonomi Hospital in Bloemfontein from 2010 to 2011 were reported as most commonly paracetamol followed by household chemicals.<sup>7</sup> A recent study based in a Durban hospital's ICU from 2015 to 2017 reported tricyclic antidepressants, antiepileptics, ethylene glycol, and isoniazid as the most commonly implicated poisons, while a prior study of patients

presenting to a regional hospital in Northern KwaZulu-Natal from 2012 to 2013 reported paracetamol overdose as the most common, followed by antiretroviral drugs and then organophosphates.<sup>5,27</sup> In contrast to the data reported by these studies, organophosphate poisoning was reported as most common and as most recent by the majority of doctors in this study (Figure 6). The lack of a statistically significant correlation between the response of the most common and the most recent being organophosphate poisoning suggests that doctors are not being biased in their responses by what they had most recently treated. The contrast of the findings of this study with prior regional studies outside of Gauteng reporting organophosphate poisoning to be less common is also reflected in the National Institute for Communicable Diseases Notifiable Medical Condition reporting for agricultural or stock remedy poisoning (this category includes organophosphates) for March and April of 2023,

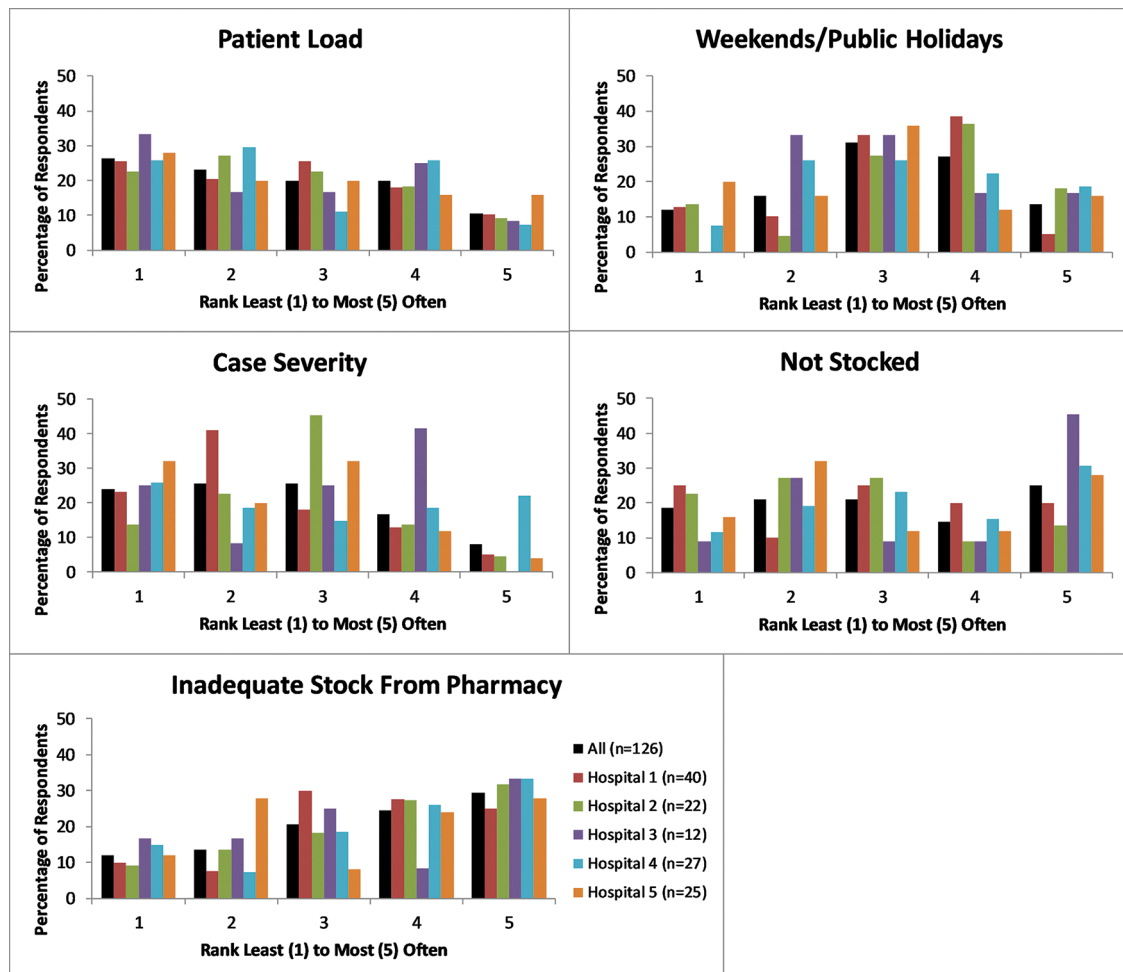


HJH, Helen Joseph Hospital; CMJAH, Charlotte Maxeke Johannesburg Academic Hospital; TMRH, Thelle Mogoerane Regional Hospital; CHBAH, Chris Hani Baragwanath Academic Hospital; TMH, Tambo Memorial Hospital

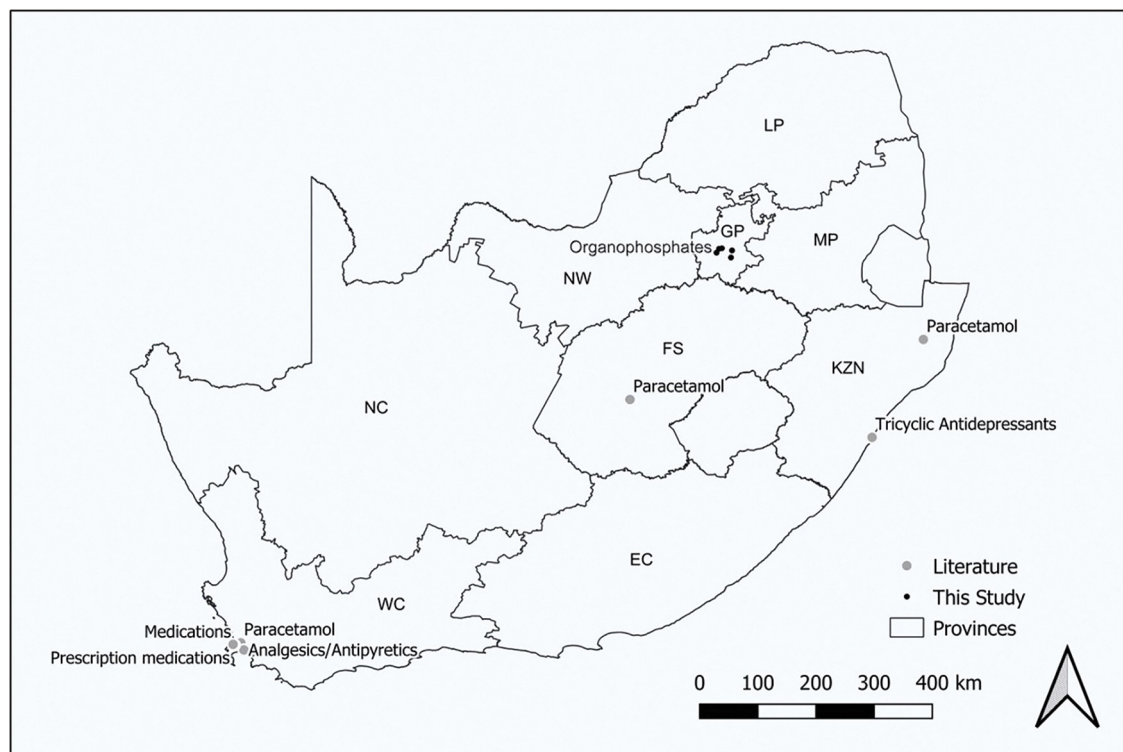
**Figure 4:** Experiences of antidote supply issues reported by doctors working in the emergency departments of five teaching hospitals in the Southern Gauteng City-Region of South Africa.

noting that 44 of the 66 cases and 50 of the 75 cases for March and April, respectively, were from Gauteng.<sup>28,29</sup> Regional differences in the common poisoning presentations (Figure 6) necessitate more specific local guidelines in terms of antidote supply, as needs would vary. Both studies reporting on ICU admissions specifically reported organophosphate poisoning as a common reason for ICU admission, which raises concern about the burden on ICU beds in Gauteng and the need for critical care in the ED for the larger proportion of patients presenting with this poisoning.<sup>2,6</sup>

Atropine, the antidote to the muscarinic effects of organophosphates, was present in all the EDs on the days on which data collection was performed. However, consistency of supply is of concern, as over 20% of doctors across the five EDs reported that supply problems had been experienced with this antidote. N-acetylcysteine, as the antidote for the second most common poisoning reported, had fewer supply issues reported by doctors, and was present in all EDs at the time of data collection – a finding that is in keeping with another study in South Africa that found N-acetylcysteine was well supplied.<sup>15</sup>



**Figure 5:** Reasons for antidote supply issues as ranked by respondents from the emergency departments of five teaching hospitals in the Southern Gauteng City-Region of South Africa.



LP, Limpopo; NW, North West; GP, Gauteng; MP, Mpumalanga; NC, Northern Cape; FS, Free State; KZN, KwaZulu-Natal; EC, Eastern Cape; WC, Western Cape

**Figure 6:** Map indicating the most prevalent cases of poisoning in South African provinces based on information from the literature<sup>2-5,7,25,26</sup> and this study.

Cyanide antidotes were absent in all hospitals as they are not listed in the South African Essential Drugs List.<sup>23</sup> However, 'Tripac-Cyano', which is a cyanide antidote kit containing amyl nitrite for inhalation, sodium nitrite, and sodium thiosulphate, is listed in the South African Medicines Formulary, suggesting that it should be accessible.<sup>18</sup> For all of the cyanide antidotes, the majority of respondents reported not knowing whether they were present as they had never needed them, suggesting that cyanide poisoning is not a common presentation to the hospitals in question or that the diagnosis is not actively pursued. Methylene blue, while present in many pharmacies, was absent in all EDs; this could be due to the worldwide shortage of methylene blue due to supply issues from the manufacturer.<sup>30</sup> Intralipid was similarly absent from all the EDs and present in only two of the pharmacies; in this study we did not assess whether it was present in the operating theatres, which would be a helpful location to access.

Calcium chloride is not on code for regional hospitals, but calcium gluconate is listed on the Essential Drugs List for primary hospitals as well as higher levels of care.<sup>18</sup> While calcium chloride contains a higher amount of elemental calcium than calcium gluconate (272 mg vs 92 mg), there is a risk of damage to veins, or to the tissue if there is extravasation.<sup>19</sup> This risk leads to the recommendation that calcium chloride be administered through central venous access when feasible.<sup>19</sup> By contrast, calcium gluconate may be administered safely through any intravenous access.

Certain poisonings have more than one antidote, leading to differences in what is stocked in each ED. The EDs that have freeze-dried plasma in addition to fresh frozen plasma in their blood bank are both mixed EDs that receive trauma cases as well as medical and surgical cases. That this antidote is more commonly ordered as a trauma resuscitation fluid than as an antidote for anticoagulant poisoning is reflected in the abundance of literature on freeze-dried plasma in the trauma setting.<sup>31,32</sup> Despite fresh frozen plasma and freeze-dried plasma being very similar substances, fresh frozen plasma is issued by the blood bank and freeze-dried plasma by the pharmacy. As learned from personal communication with pharmacists at HJH, these substances are charged to different parts of the hospital's budget (blood products, including fresh frozen plasma, are charged via the provincial budget and freeze-dried plasma is charged directly via the hospital pharmacy budget), which raises further logistical and cost considerations which may deter hospitals from ordering freeze-dried plasma.

Across all the hospitals' EDs there are a few distinct locations where antidotes were found, between open shelves in the areas where poisoned patients are treated, cupboards to which senior nurses hold the key, and cupboards to which doctors have access. This allows for treatment to be easily located once each new staff member to the unit is orientated to the specific ED. Certain drugs are kept in areas where access is tightly controlled in order to regulate use. Reasons for this include the potential for abuse, notably for the benzodiazepines and alcohol, and the need for section 21 motivation for 100 mg atropine vials.

Limitations of this study include the period across which the questionnaires were administered to the doctors, as experiences could change at different times of the year. In terms of data collection on the presence of antidotes in each hospital, a better comparison could have been made if data were collected on the same day at all the hospitals, as stock amounts are likely affected by day of the week and time of the month. Efforts were made to mitigate this limitation by ensuring that data collection was conducted on weekdays only, and during the same month to limit variation between months. The potential for recall bias when asking respondents for the most common poisoning is also a potential limitation. This limitation was accounted for by also asking respondents for the most recent case, with the lack of correlation between the responses for what is recent and what is common suggesting that recall bias was not a significant factor.

## Conclusion

We aimed to assess the availability of antidotes and how this relates to doctors' experiences of antidote supply. The teaching hospitals

surveyed stock the appropriate antidotes for the poisoning cases that are common in the population groups they serve, as reported by the doctors working in the EDs. Consistency of supply is of concern, especially for atropine and lorazepam, and more regular restocking or protocols surrounding minimum acceptable amounts of antidotes could help to prevent supply problems from occurring. Further research to quantify the prevalent poisoning cases and determine whether the less common poisonings are experienced more frequently than is perceived by doctors in this study could further inform the development of antidote stocking guidelines. In addition, a longitudinal study could offer valuable insights into the temporal changes in antidote availability.

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## Data availability

The ethical clearance granted was on the basis that data would be accessible only to the researchers. Data are available on request from the authors, subject to secondary ethical clearance.

## Declaration of AI use

There was no use of AI in the writing of this article.

## Authors' contributions

M.P.F.: Conceptualisation, data collection, data analysis and writing – the initial draft, writing – revisions. P.M.S.: Conceptualisation, writing – revisions, student supervision. C.M.L.: Conceptualisation, writing – revisions, student supervision. All authors read and approved the final manuscript.

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## Competing interests

M.P.F. and P.M.S. currently work in hospital emergency departments in Gauteng, there were no material conflicts of interest and no external funding sources.

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# QUESTIONNAIRE

## E2(26) Part 1 of 2

### Availability of antidotes for drug poisonings and doctors' perspectives thereof

#### INSTRUCTIONS

- Read through the article and answer the multiple-choice questions provided below.
- **Some questions may have more than one correct answer;** in which case you must mark **all** the correct answers.

#### Introduction

**Question 1:** According to the 2016 South African mortality data, what percentage of non-natural deaths did poisonings altogether account for?

- A: 0.8%
- B: 2.0%
- C: 2.7%
- D: 8.3%

**Question 2:** What percentage of all emergency department admissions did self-poisoning account for at Khayelitsha District Hospital over a 6-month period?

- A: 2.7%
- B: 9.8%
- C: 8.3%
- D: 12.5%

**Question 3:** Which of the following two findings were reported in global studies on antidote availability?

- A: Most Canadian hospitals stocked all antidotes that were considered
- B: Over 90% of UK hospitals had the most commonly used antidotes
- C: In Massachusetts, 9.8% of hospitals had stock of all antidotes assessed
- D: Sri Lankan hospitals had 100% of assessed antidotes available

**Question 4:** In a previous South African study, what percentage of antidotes did tertiary public hospitals stock?

- A: 46%
- B: 56%
- C: 86%
- D: 96%

**Question 5: TRUE or FALSE?**

"There is abundant data published on poisoning presentations seen in emergency departments in Gauteng compared to other provinces."

- A: TRUE
- B: FALSE

**Question 6:** What were the **TWO** main aims of this study?

- A: To assess antidote availability in selected teaching hospitals in Southern Gauteng
- B: To determine mortality rates from drug poisoning
- C: To evaluate emergency department patient loads
- D: To explore doctors' experiences of antidote supply

#### Methods

**Question 7:** Which of the following hospitals were **NOT** included in this study?

- A: Charlotte Maxeke Johannesburg Academic Hospital
- B: Chris Hani Baragwanath Academic Hospital
- C: Tygerberg Academic Hospital
- D: Helen Joseph Hospital

**Question 8:** What criteria were used for excluding doctors from the study population?

- A: Doctors working night shifts only
- B: Doctors who had worked in the ED for less than 1 month
- C: Part-time doctors
- D: Doctors who had not experienced poisoning cases

#### Results

**Question 9:** Which three antidotes were absent in **ALL** emergency departments and pharmacies surveyed?

- A: Hydroxocobalamin
- B: Sodium thiosulfate
- C: Sodium calcium edetate
- D: N-acetylcysteine

**Question 10: TRUE or FALSE?**

"Methylene blue was present in all emergency departments surveyed in this study."

- A: TRUE
- B: FALSE

**THE END**

## QUESTIONNAIRE

### E2(26) Part 2 of 2

#### Availability of antidotes for drug poisonings and doctors' perspectives thereof

##### INSTRUCTIONS

- Read through the article and answer the multiple-choice questions provided below.
- **Some questions may have more than one correct answer;** in which case you must mark **all** the correct answers.

**Question 1:** What did the majority of doctors in this study report as the most recent cases of poisoning?

- A: Paracetamol overdose
- B: Organophosphate poisoning
- C: Benzodiazepine overdose
- D: Tricyclic antidepressant poisoning

**Question 2:** Which antidote had the greatest number of respondents reporting supply issues?

- A: N-acetylcysteine
- B: Atropine
- C: Diazepam
- D: Lorazepam

**Question 3:** What was the most commonly perceived reason for antidote supply problems?

- A: Patient load
- B: Inadequate stock from the pharmacy
- C: The antidote was not stocked
- D: Budget constraints

**Question 4:** Which specific issue regarding atropine access was commonly experienced by doctors?

- A: The drug was too expensive
- B: Section 21 forms were required for 100 mg vials
- C: The drug was not on the essential medicines list
- D: Pharmacies refused to stock it

##### Discussion

**Question 5:** What percentage of poisoning cases in a prior Khayelitsha study presented after hours, reinforcing the need for adequate ED antidote supply?

- A: 46%
- B: 66%
- C: 79%
- D: 87%

**Question 6: TRUE or FALSE?**

According to studies from 2003 to 2015 in other South African provinces, organophosphate poisoning was reported as the most common poisoning presenting to emergency departments.

- A: TRUE
- B: FALSE

**Question 7:** According to the National Institute for Communicable Diseases data for March and April 2023, how many of the agricultural or stock remedy poisoning cases were from Gauteng?

- A: 44 of 66 cases in March and 50 of 75 cases in April
- B: All cases were from Gauteng
- C: Less than 25% of cases were from Gauteng
- D: Equal distribution across all provinces

**Question 8:** What is a limitation of this study mentioned by the authors?

- A: The sample size was too small
- B: The period across which questionnaires were administered, as experiences could change at different times of the year
- C: Too many hospitals were included
- D: The study was conducted regionally

##### Conclusion

**Question 9:** According to the conclusion, which antidotes had consistency of supply concerns reported by doctors?

- A: N-acetylcysteine
- B: Lorazepam
- C: Atropine
- D: Diazepam

**Question 10:** What type of future research did the authors suggest would offer valuable insights?

- A: International comparative studies
- B: Studies on antidote costs
- C: Studies on pharmaceutical company supply chains
- D: A longitudinal study on temporal changes in antidote availability

**THE END**



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### ANSWER SHEET

#### E2(26)

Availability of antidotes for drug poisonings and doctors' perspectives thereof

| *Time spent on activity                                      |   |   |   |   |   |        |   |   |   |   |   | hour min |   |   |   |   |   |    |   |   |   |   |   |
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| PART 1                                                       |   |   |   |   |   | PART 2 |   |   |   |   |   |          |   |   |   |   |   |    |   |   |   |   |   |
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| 4                                                            |   |   |   |   |   | 9      |   |   |   |   |   | 4        |   |   |   |   |   | 9  |   |   |   |   |   |
| 5                                                            |   |   |   |   |   | 10     |   |   |   |   |   | 5        |   |   |   |   |   | 10 |   |   |   |   |   |

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