Supplementary Table 1: All drugs, compounds and metabolites that can be identified by the Emerging Drugs Network of Australia, stratified into illicit, novel psychoactive substances, pharmaceutical and other.

*Please see excel spreadsheet.*

Supplementary Table 2: Drug and associated metabolites identified in analysis of blood samples.

|  |  |
| --- | --- |
| **Drug included in count** | **Metabolite** |
| Amitriptyline | Nortriptyline\* |
| Clonazepam | 7-aminoclonazepam |
| Clonazolam | 8-aminoclonazolam |
| Cocaine | Benzoylecgonine, cocaethylene, norcocaine, ecgonine methyl ester |
| Codeine | Norcodeine, morphine\* |
| Diazepam | Desmethyldiazepam, nordiazepam, oxazepam\*, temazepam\* |
| Fluoxetine | Norfluoxetine |
| Heroin (6-O-monoacetylmorphine) | Morphine\*, acetylcodeine† |
| Ketamine | Norketamine |
| Mdma | Mda\* |
| Methylamphetamine | Amphetamine\* |
| Naltrexone | Naltrexol |
| Nitrazepam | 7-aminonitrazepam |
| Risperidone | Paliperidone\*, 9-hydroxyrispiridone |
| Tramadol | O-desmethyltramadol, n-desmethyltramadol, Desmethyltramadol |
| Venlafaxine | O-desmethylvenlafaxine\* |

\*Counted as a separate drug if blood sample analysis did not also include the associated drug.

†Acetylcodeine is not a metabolite, but is an impurity from the manufacturing of heroin and is therefore used as evidence for the use of heroin if found in the blood sample.

Abbreviations: MDMA, 3,4-methyl​enedioxy​methamphetamine; MDA, 3,4-methyl​enedioxy​amphetamine.

Supplementary Table 3: Analytically confirmed drugs, detected in the analysis of blood samples within presentations with severe and/or unusual toxicity features to Western Australian Emergency Departments, April 2020-December 2021.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Drug (metabolite) detected** | **Drug type** | **Count in full cohort n=434 (%)** | **Count in cohort with full clinical management data n=383 (%)** | **Proportion of drug detected also used within pre- or in-hospital setting** | **%** |
| Metamfetamine (methylamphetamine) | Illicit | 201 (58.6) | 175 (45.7) | 0 | 0.0 |
| Gamma-hydroxybutyrate | Illicit | 30 (8.7) | 29 (7.6) | 0 | 0.0 |
| 6-O-monoacetylmorphine | Illicit | 23 (6.7) | 21 (5.5) | 0 | 0.0 |
| 3,4-methylendioxymethamphetamine | Illicit | 21 (6.1) | 6 (1.6) | 0 | 0.0 |
| Cocaine (benzoylecgonine, ecgonine methyl ester, cocaethylene) | Illicit | 8 (2.3) | 8 (2.1) | 0 | 0.0 |
| 3,4-methylenedioxyamphetamine | Illicit | 6 (1.8) | 6 (1.6) | 0 | 0.0 |
| Lysergic acid diethyamide | Illicit | 6 (1.8) | 4 (1.0) | 0 | 0.0 |
| Psilocine | Illicit | 1 (0.3) | 1 (0.3) | 0 | 0.0 |
| Clonazolam (8-aminoclonazolam) | Novel psychoactive substance | 12 (3.5) | 12 (3.1) | 0 | 0.0 |
| Etizolam | Novel psychoactive substance | 7 (2.0) | 7 (1.8) | 0 | 0.0 |
| Flualprazolam | Novel psychoactive substance | 7 (2.0) | 6 (1.6) | 0 | 0.0 |
| Methcathinone | Novel psychoactive substance | 4 (1.2) | 3 (0.8) | 0 | 0.0 |
| Dimethyltryptamine | Novel psychoactive substance | 3 (0.9) | 2 (0.5) | 0 | 0.0 |
| 2,5-dimethox-4-bromophenethylamine | Novel psychoactive substance | 2 (0.6) | 2 (0.5) | 0 | 0.0 |
| Akb48 | Novel psychoactive substance | 2 (0.6) | 2 (0.5) | 0 | 0.0 |
| Methylone | Novel psychoactive substance | 2 (0.6) | 2 (0.5) | 0 | 0.0 |
| Bromazolam | Novel psychoactive substance | 2 (0.6) | 1 (0.3) | 0 | 0.0 |
| 3,4-methylenedioxyethylamphetamine | Novel psychoactive substance | 1 (0.3) | 1 (0.3) | 0 | 0.0 |
| 5f-cumyl-p7aica | Novel psychoactive substance | 1 (0.3) | 1 (0.3) | 0 | 0.0 |
| 5f-cumyl-pinaca | Novel psychoactive substance | 1 (0.3) | 1 (0.3) | 0 | 0.0 |
| Am-1248 | Novel psychoactive substance | 1 (0.3) | 1 (0.3) | 0 | 0.0 |
| Mdmb-4en-pinaca | Novel psychoactive substance | 1 (0.3) | 1 (0.3) | 0 | 0.0 |
| Flubromazolam | Novel psychoactive substance | 1 (0.3) | 0 (0.0) | 0 | 0.0 |
| Xlr-11 | Novel psychoactive substance | 1 (0.3) | 0 (0.0) | 0 | 0.0 |
| Amphetamine\* | Other | 14 (4.1) | 13 (3.4) | 0 | 0.0 |
| Acetylcodeine§ | Other | 1 (0.3) | 1 (0.3) | 0 | 0.0 |
| Amyl nitrite | Other | 1 (0.3) | 2 (0.3) | 0 | 0.0 |
| Nicotine | Other | 1 (0.3) | 3 (0.3) | 0 | 0.0 |
| Diazepam (nordiazepam, desmethyldiazepam) | Pharmaceutical | 158 (46.1) | 142 (37.1) | 42 | 29.6 |
| Midazolam | Pharmaceutical | 95 (27.7) | 78 (20.4) | 74 | 94.9 |
| Paracetamol | Pharmaceutical | 86 (25.1) | 81 (21.1) | 38 | 46.9 |
| Clonazepam (7-aminoclonazepam) | Pharmaceutical | 49 (14.3) | 45 (11.7) | 5 | 11.1 |
| Ondansetron | Pharmaceutical | 45 (13.1) | 40 (10.4) | 32 | 80.0 |
| Droperidol | Pharmaceutical | 38 (11.1) | 30 (7.8) | 30 | 100.0 |
| Olanzapine | Pharmaceutical | 36 (10.5) | 32 (8.4) | 18 | 56.3 |
| Lignocaine¶ | Pharmaceutical | 33 (9.6) | 27 (7.1) | 1 | 3.7 |
| Quetiapine | Pharmaceutical | 29 (8.5) | 26 (6.8) | 4 | 15.4 |
| Mirtazapine | Pharmaceutical | 27 (7.9) | 25 (6.5) | 4 | 16.0 |
| Amitriptyline | Pharmaceutical | 25 (7.3) | 21 (5.5) | 3 | 14.3 |
| Codeine§ | Pharmaceutical | 24 (7.0) | 22 (5.7) | 0 | 0.0 |
| Sertraline | Pharmaceutical | 22 (6.4) | 21 (5.5) | 4 | 19.0 |
| Tramadol (desmethyltramadol) | Pharmaceutical | 22 (6.4) | 17 (4.4) | 3 | 17.6 |
| Citalopram (norcitalopram) | Pharmaceutical | 19 (5.5) | 19 (5.0) | 7 | 36.8 |
| Methadone | Pharmaceutical | 18 (5.2) | 16 (4.2) | 4 | 25.0 |
| Fentanyl | Pharmaceutical | 17 (5.0) | 14 (3.7) | 13 | 92.9 |
| Naloxone | Pharmaceutical | 15 (4.4) | 15 (3.9) | 15 | 100.0 |
| Ketamine | Pharmaceutical | 15 (4.4) | 14 (3.7) | 14 | 100.0 |
| Nortriptyline\* | Pharmaceutical | 15 (4.4) | 14 (3.7) | 0 | 0.0 |
| Fluoxetine (norfluoxetine) | Pharmaceutical | 15 (4.4) | 11 (2.9) | 1 | 9.1 |
| Promethazine | Pharmaceutical | 13 (3.8) | 13 (3.4) | 0 | 0.0 |
| Quinine | Pharmaceutical | 13 (3.8) | 13 (3.4) | 0 | 0.0 |
| Venlafaxine | Pharmaceutical | 12 (3.5) | 12 (3.1) | 2 | 16.7 |
| Morphine§ | Pharmaceutical | 11 (3.2) | 10 (2.6) | 3 | 30.0 |
| Tapentadol | Pharmaceutical | 11 (3.2) | 10 (2.6) | 2 | 20.0 |
| Buprenorphine | Pharmaceutical | 10 (2.9) | 10 (2.6) | 0 | 0.0 |
| Aripiprazole | Pharmaceutical | 10 (2.9) | 9 (2.3) | 3 | 33.3 |
| Quinidine | Pharmaceutical | 9 (2.6) | 9 (2.3) | 0 | 0.0 |
| Paliperidone | Pharmaceutical | 8 (2.3) | 8 (2.1) | 0 | 0.0 |
| Levetiracetam | Pharmaceutical | 7 (2.0) | 7 (1.8) | 5 | 71.4 |
| Methorphan | Pharmaceutical | 7 (2.0) | 7 (1.8) | 0 | 0.0 |
| Desmethylvenlafaxine\* | Pharmaceutical | 7 (2.0) | 6 (1.6) | 0 | 0.0 |
| Doxylamine | Pharmaceutical | 7 (2.0) | 6 (1.6) | 0 | 0.0 |
| Pholcodine | Pharmaceutical | 7 (2.0) | 6 (1.6) | 0 | 0.0 |
| Metoclopramide | Pharmaceutical | 7 (2.0) | 5 (1.3) | 3 | 60.0 |
| Pregabalin | Pharmaceutical | 7 (2.0) | 5 (1.3) | 1 | 20.0 |
| Pantoprazole | Pharmaceutical | 6 (1.8) | 6 (1.6) | 3 | 50.0 |
| Modafinil | Pharmaceutical | 6 (1.8) | 5 (1.3) | 0 | 0.0 |
| Lamotrigine | Pharmaceutical | 5 (1.5) | 5 (1.3) | 1 | 20.0 |
| Oxycodone | Pharmaceutical | 5 (1.5) | 4 (1.0) | 1 | 25.0 |
| Sildenafil | Pharmaceutical | 5 (1.5) | 4 (1.0) | 0 | 0.0 |
| Meloxicam | Pharmaceutical | 5 (1.5) | 3 (0.8) | 0 | 0.0 |
| Ephedrine | Pharmaceutical | 4 (1.2) | 4 (1.0) | 1 | 25.0 |
| Alprazolam | Pharmaceutical | 4 (1.2) | 3 (0.8) | 0 | 0.0 |
| Metronidazole | Pharmaceutical | 4 (1.2) | 3 (0.8) | 2 | 66.7 |
| Oxazepam† | Pharmaceutical | 4 (1.2) | 3 (0.8) | 0 | 0.0 |
| Paroxetine | Pharmaceutical | 4 (1.2) | 3 (0.8) | 0 | 0.0 |
| Lorazepam | Pharmaceutical | 3 (0.9) | 3 (0.8) | 0 | 0.0 |
| Naltrexone (naltrexol) | Pharmaceutical | 3 (0.9) | 3 (0.8) | 0 | 0.0 |
| Risperidone (9-hydroxyrispiridone) | Pharmaceutical | 3 (0.9) | 3 (0.8) | 1 | 33.3 |
| Temazepam† | Pharmaceutical | 3 (0.9) | 3 (0.8) | 0 | 0.0 |
| Zuclopenthixol | Pharmaceutical | 3 (0.9) | 3 (0.8) | 1 | 33.3 |
| Carbamazepine | Pharmaceutical | 3 (0.9) | 2 (0.5) | 1 | 50.0 |
| Propanolol | Pharmaceutical | 3 (0.9) | 2 (0.5) | 0 | 0.0 |
| Atenolol | Pharmaceutical | 2 (0.6) | 2 (0.5) | 0 | 0.0 |
| Celecoxib | Pharmaceutical | 2 (0.6) | 2 (0.5) | 0 | 0.0 |
| Chlorpheniramine | Pharmaceutical | 2 (0.6) | 2 (0.5) | 0 | 0.0 |
| Dihydrocodeine§ | Pharmaceutical | 2 (0.6) | 2 (0.5) | 0 | 0.0 |
| Duloxetine | Pharmaceutical | 2 (0.6) | 2 (0.5) | 1 | 50.0 |
| Loratadine | Pharmaceutical | 2 (0.6) | 2 (0.5) | 1 | 50.0 |
| Methylphenidate (ritalinic acid) | Pharmaceutical | 2 (0.6) | 2 (0.5) | 0 | 0.0 |
| Nitrazepam (7-aminonitrazepam) | Pharmaceutical | 2 (0.6) | 2 (0.5) | 0 | 0.0 |
| Omeprazole | Pharmaceutical | 2 (0.6) | 2 (0.5) | 0 | 0.0 |
| Topiramate | Pharmaceutical | 2 (0.6) | 2 (0.5) | 0 | 0.0 |
| Zopiclone | Pharmaceutical | 2 (0.6) | 2 (0.5) | 0 | 0.0 |
| Amisulpride | Pharmaceutical | 1 (0.3) | 1 (0.3) | 1 | 100.0 |
| Benztropine | Pharmaceutical | 1 (0.3) | 1 (0.3) | 0 | 0.0 |
| Chlorpromazine | Pharmaceutical | 1 (0.3) | 1 (0.3) | 0 | 0.0 |
| Clomipramine | Pharmaceutical | 1 (0.3) | 1 (0.3) | 1 | 100.0 |
| Clozapine | Pharmaceutical | 1 (0.3) | 1 (0.3) | 0 | 0.0 |
| Cotinine | Pharmaceutical | 1 (0.3) | 1 (0.3) | 0 | 0.0 |
| Doxepin | Pharmaceutical | 1 (0.3) | 1 (0.3) | 0 | 0.0 |
| Fluvoxamine | Pharmaceutical | 1 (0.3) | 1 (0.3) | 0 | 0.0 |
| Gliclazide | Pharmaceutical | 1 (0.3) | 1 (0.3) | 0 | 0.0 |
| Hydrocodone§ | Pharmaceutical | 1 (0.3) | 1 (0.3) | 0 | 0.0 |
| Hydroxychloroquine | Pharmaceutical | 1 (0.3) | 1 (0.3) | 0 | 0.0 |
| Irbesartan | Pharmaceutical | 1 (0.3) | 1 (0.3) | 0 | 0.0 |
| Isopropylbenzylamine | Pharmaceutical | 1 (0.3) | 1 (0.3) | 0 | 0.0 |
| Moclobemide | Pharmaceutical | 1 (0.3) | 1 (0.3) | 0 | 0.0 |
| Prilocaine | Pharmaceutical | 1 (0.3) | 1 (0.3) | 0 | 0.0 |
| Pseudoephedrine | Pharmaceutical | 1 (0.3) | 1 (0.3) | 0 | 0.0 |
| Salbutamol | Pharmaceutical | 1 (0.3) | 1 (0.3) | 1 | 100.0 |
| Tamoxifen | Pharmaceutical | 1 (0.3) | 1 (0.3) | 0 | 0.0 |
| Telmisartan | Pharmaceutical | 1 (0.3) | 1 (0.3) | 1 | 100.0 |
| Trihexyphenidyl | Pharmaceutical | 1 (0.3) | 1 (0.3) | 0 | 0.0 |
| Warfarin | Pharmaceutical | 1 (0.3) | 1 (0.3) | 0 | 0.0 |
| Zolpidem | Pharmaceutical | 1 (0.3) | 1 (0.3) | 0 | 0.0 |
| Haloperidol | Pharmaceutical | 1 (0.3) | 0 (0.0) | 0 | 0.0 |
| Noscapine | Pharmaceutical | 1 (0.3) | 0 (0.0) | 0 | 0.0 |

\*Metabolite is recorded as separate drug detected when parent drug is not detected in the same sample.

† Drug recorded separately when diazepam was not detected in the same sample

§ Recorded any time this drug was detected regardless if it was a metabolite or the detected drug.

¶ Lignocaine is inconsistently recorded in medical records and therefore it is difficult to determine if this drug was used within the emergency department presentation.

Supplementary Table 4: Frequency and type of illicit drugs or novel psychoactive substances within presentations with severe and/or unusual toxicity features to Western Australian Emergency Departments between April 2020 and December 2021 stratified by type of management used pre- or in-hospital.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Managed with Benzodiazepines** | **Managed without Benzodiazepines** | **Managed with naloxone** | **Managed without naloxone** | **Intubated** | **Not intubated** | **Total** |
| Total Cohort (N) | 205 | 178 | 86 | 297 | 51 | 332 | 383 |
| Number of illicit drugs or novel psychoactive substances per presentation |  |  |  |  |  |  |  |
| 1 | 91 (44.4) | 72 (40.5) | 37 (43.0) | 126 (42.4) | 18 (35.3) | 145 (43.7) | 163 (42.6) |
| 2 | 23 (11.2) | 30 (16.9) | 23 (26.7) | 30 (10.1) | 10 (19.6) | 43 (13.0) | 53 (13.8) |
| 3 | 3 (1.5) | 8 (4.5) | 4 (4.7) | 7 (2.4) | 2 (3.9) | 9 (2.7) | 11 (2.9) |
| 4 | 1 (0.5) | 0 (0.0) | 0 (0.0) | 1 (0.3) | 0 (0.0) | 1 (0.3) | 1 (0.3) |
| Identified illicit drug or novel psychoactive substances |  |  |  |  |  |  |  |
| Metamfetamine (Methylamphetamine) | 93 (78.8) | 82 (73.9) | 49 (76.5) | 126 (76.3) | 24 (80.0) | 151 (75.9) | 175 (76.8) |
| Gamma-hydroxybutyrate | 8 (6.8) | 21 (18.9) | 18 (28.1) | 11 (6.7) | 10 (33.3) | 19 (9.5) | 29 (12.7) |
| Heroin | 8 (6.8) | 13 (11.7) | 17 (26.6) | 4 (2.4) | 1 (3.3) | 20 (10.1) | 21 (9.2) |
| MDMA | 12 (10.2) | 8 (7.2) | 1 (1.6) | 19 (11.5) | 1 (3.3) | 19 (9.5) | 20 (8.8) |
| Cocaine | 2 (1.7) | 6 (5.4) | 1 (1.6) | 7 (4.2) | 1 (3.3) | 7 (3.5) | 8 (3.5) |
| LSD | 4 (3.4) | 0 (0.0) | 0 (0.0) | 4 (2.4) | 0 (0.0) | 4 (2.0) | 4 (1.8) |
| Psilocine | 0 (0.0) | 1 (0.9) | 0 (0.0) | 1 (0.6) | 0 (0.0) | 1 (0.5) | 1 (0.4) |
| Number of novel psychoactive substances detected per presentation |  |  |  |  |  |  |  |
| 1 | 16 (7.8) | 16 (9.0) | 9 (10.5) | 23 (7.7) | 7 (13.7) | 25 (7.5) | 32 (8.4) |
| 2 | 1 (0.5) | 4 (2.2) | 0 (0.0) | 5 (1.8) | 0 (0.0) | 5 (1.5) | 5 (1.3) |

Abbreviations: 3,4-methyl​enedioxy​methamphetamine; LSD, lysergic acid diethyamide.