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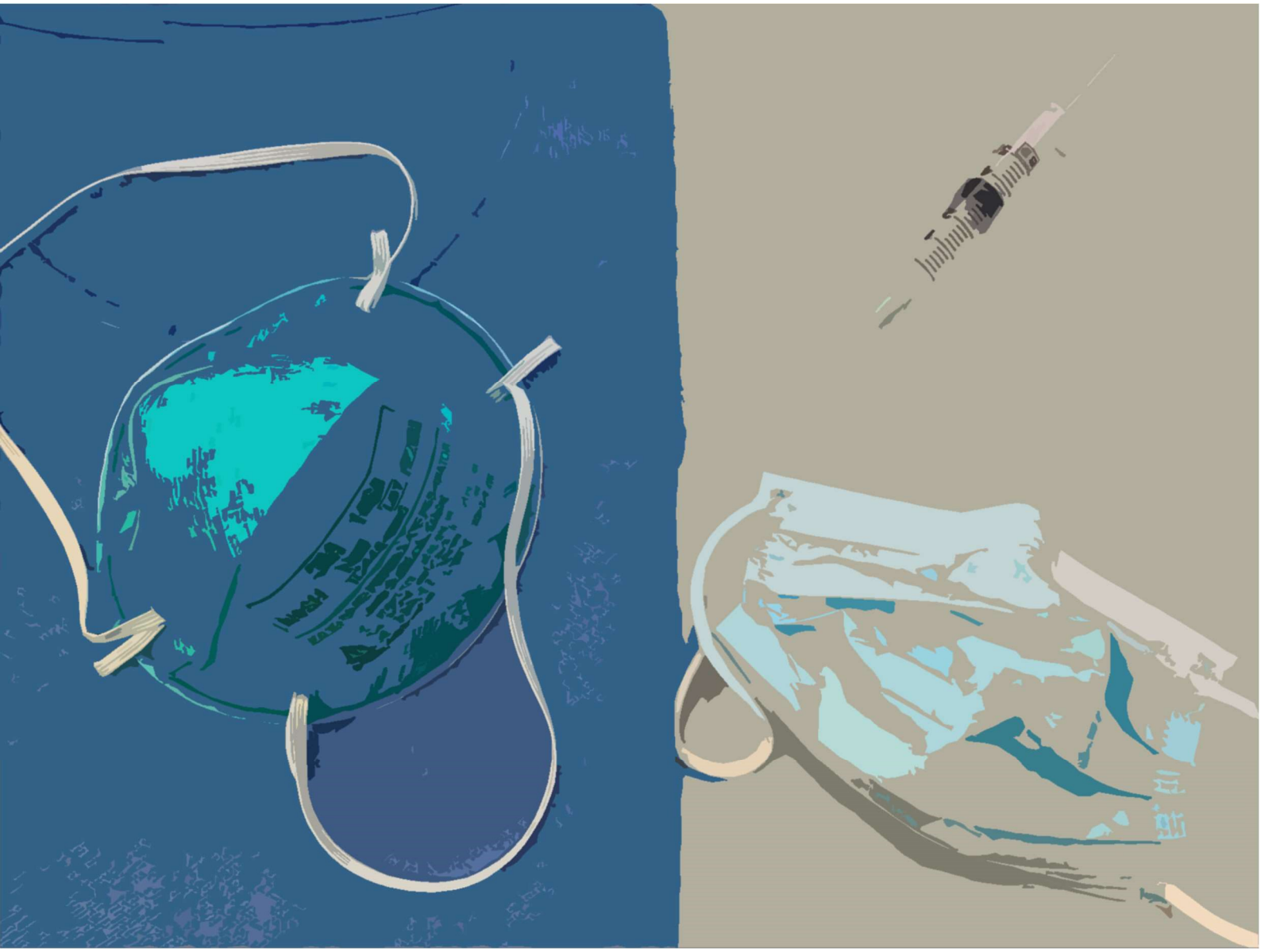

The impact of the COVID-19 pandemic on acute toxicity related to recreational drug abuse presenting to emergency departments

Dr Rex Pui Kin Lam
The University of Hong Kong

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Final Research Report

Project Title
The impact of the COVID-19 pandemic on acute toxicity related to recreational drug abuse presenting to emergency departments

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Principal Investigator
Dr Rex Pui Kin Lam
Clinical Associate Professor of Practice, Department of Emergency Medicine, School of Clincial Medicine, Li Ka Shing Faculty of Medicine, The University of Hong Kong

Co-Investigators
Dr Man Li Tse
Director, Hong Kong Poison Information Centre, United Christian Hospital, Hopsital Authority

Dr Chi Keung Chan
Associate Consultant, Hong Kong Poison Information Centre, United Christian Hospital, Hospital Authority

Dr Eric Ho Yin Lau
Honorary Assistant Professor, School of Public Health, The University of Hong Kong

Professor Timothy Hudson Rainer
Clinical Professor, Department of Emergency Medicine, School of Clincial Medicine, Li Ka Shing Faculty of Medicine, The University of Hong Kong

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Executive summary (English)

Unprecedented in history, the COVID-19 pandemic had wide-ranging impacts on drug demand, supply and distribution. We conducted this study to characterise the trends, patterns, and clinical and psychosocial management of acute toxicity related to amphetamines, cocaine, cannabis, heroin and ketamine abuse presenting to emergency departments in Hong Kong during the pandemic. We also evaluated the impact of social and recreational venue closure and social distancing measures on recreational drug-related toxicity.

We analysed 1,453 episodes of acute toxicity involving the above five drugs reported to the Hong Kong Poison Information Centre by public emergency departments between 23 January 2017 and 22 January 2023. The number of acute toxicities reported did not correlate with the Central Registry of Drug Abuse data or drug seizure data, except for heroin. Acute toxicities involving methamphetamine, cannabis and heroin increased at the outset of the pandemic but then dropped faster than the pre-pandemic period. Ketamine toxicities also increased but the trend remained the same during the pandemic. No significant changes in the number and trend of acute cocaine toxicities were observed during the pandemic. Overall, closure of social and recreational venues had a limited impact on acute drug toxicities. Strict social distancing measures reduced the number of acute heroin poisonings.

Several changes in the patterns of drug abuse and clinical presentations are noteworthy. Compared with the pre-pandemic period, during the pandemic, more patients with acute methamphetamine toxicity presented with agitation, injury and self-harm behaviours; required invasive treatment and intensive care unit admission; and developed major effects or died. More acute myocardial injuries and major effects were seen in patients with acute cocaine toxicity during the pandemic than before. Notably, more female patients with acute cannabis toxicities were seen in emergency departments during the pandemic than before. Compared to before, during the pandemic, more heroin abusers used methamphetamine, presented with agitation, confusion, or hallucinations; or required chemical restraints. As for ketamine, polydrug abuse with other stimulants such as cocaine was common, and more alcohol co-ingestion was observed during the pandemic. Overall, presenting during the COVID-19 pandemic was not significantly associated with severe complications of acute toxicities, after adjusting for other known factors for poor clinical outcomes. Neither clinical nor psychosocial interventions changed significantly during the pandemic. However, the referral network to social workers and non-governmental organisation drug rehabilitation and treatment services can be further strengthened.

The study shows that the reduction in the number of acute toxicities involving methamphetamine and heroin during the pandemic did not translate into a lower severity of poisoning. The increased combination of heroin and methamphetamine, in particular, is alarming. Education focused on existing heroin users should be further strengthened to avoid

concurrent misuse of methamphetamine. The increase in cocaine-related acute myocardial injury is also noteworthy, especially when the global supply of cocaine is increasing. Acute cannabis toxicity increased during the pandemic, particularly among female drug users. The number of ketamine users also increased during the pandemic and many of them were multi-stimulant abusers. Public education on the harms of cocaine, cannabis and ketamine should be targeted at young people and tailored to specific gender needs.

The findings of this study call for continued vigilance against drug use and related acute toxicity during and in the aftermath of the COVID-19 pandemic. Coming out of the pandemic, we must monitor the evolving trends in drug abuse and toxicity and the impact of the combination of traditional illicit drugs. The role of gender in cannabis abuse and toxicity needs further studies.

Executive summary (Chinese) 研究摘要

2019 冠狀病毒病大流行對毒品需求、供應和販毒影響深遠，並無先例可循。這項研究的主要目的是探討疫情期間因吸食安非他明 (冰毒)、可卡因、大麻、海洛英及氯胺酮而引致急性中毒到香港急症室就診的趨勢，吸毒者濫藥模式、臨床及心理社會管理，並評估關閉社交及娛樂場所以及實施社交距離措施對吸毒所引致急性中毒的影響。

我們分析了 1,453 宗於 2017 年 1 月 23 日到 2023 年 1 月 22 日期間，公立醫院急症室向香港中毒諮詢中心呈報涉及上述五類主要毒品的急性中毒個案。除海洛英外，香港中毒諮詢中心的急性中毒數據與藥物濫用資料中央檔案室吸毒人數統計和緝獲毒品數據並沒有關聯性。涉及冰毒、大麻和海洛英的中毒個案在疫情開始時有所增加，但隨後以比疫情前更快的速度下降。氯胺酮的中毒個案也有所增加，並在疫情期間趨勢保持不變。急性可卡因中毒的數量和趨勢在疫情期間並沒有顯著的變化。關閉社交及娛樂場所對吸毒所引致的急性中毒影響有限。嚴格的社交距離措施減少了涉及海洛英急性中毒個案。

這項研究顯示出數個值得留意的濫藥模式和臨床表現。與疫情前相比，疫情期間有更多的急性冰毒中毒的病人躁動不安，受傷及自殘，需要更多入侵性的治療及重症監護病房治療，並嚴重中毒甚至死亡。疫情期間，更多急性可卡因中毒的病人出現急性心肌受損和嚴重中毒。值得注意的是，更多在急症室的女性吸毒者在疫情期間出現急性大麻中毒。對比疫情前後，我們發現更多吸食海洛英的病人同時濫用冰毒，並出現躁動不安、意識模糊、幻覺及需要鎮靜藥物。至於氯胺酮，吸食者同時濫用多種其他危害精神毒品如可卡因等情況普遍，在疫情期間有更多同時吸食氯胺酮及喝酒的情況。總括而言，經統計及分析，2019 冠狀病大流行並未對個別毒品引致急性中毒後出現嚴重併發症的機會率有明顯的影響，亦未對病人住院期間心理以及戒毒服務的轉介帶來顯著的變化。然而，數據指出相關社工和非政府戒毒康復和治療服務的轉介網絡可以進一步加強。

這項研究顯示，疫情涉及期間冰毒和海洛英的急性中毒個案的減少並未減緩相關中毒的嚴重程度。同時濫用冰毒和海洛英個案的增多更令人擔憂。針對現時海洛英吸毒者的教育應予進一步加強，以免其同時濫用冰毒。對於可卡因引發急性心肌受損的增加亦值得關注，尤其現時全球可卡因供應量正在增加。在疫情期間，急性大麻中毒的個案有所上升，特別是女性大麻吸毒者。氯胺酮的吸毒者亦有所上升，他們很多都是同時濫用氯胺酮及多種危害精神藥物。我們須加強對年輕人的公共教育，以幫助其認識濫用可卡因、大麻和氯胺酮的禍害，並針對不同性別的需要調整相關的內容。

這項研究的結果印證我們須要在疫情期間和過後，持續對本地吸毒以及由此引起的急性中毒問題保持警惕。走出疫情，我們必須繼續監察本地濫用藥物和中毒的趨勢，和密切關注同時吸食多種傳統毒品的影響。而性別在濫用大麻和中毒的角色亦需要進一步的研究。

Abstract

Introduction and background

The COVID-19 pandemic has had an unprecedented impact on every aspect of people's lives. However, its impact on the trends, characteristics and management of acute toxicity related to amphetamines, cocaine, cannabis, heroin and ketamine in Hong Kong is not clear. The impact of social and recreational venue closure and social distancing measures on recreational drug-related toxicity is not well studied.

Objectives

The objectives of this study were to (1) characterise the trends and patterns of acute toxicity related to amphetamines, cocaine, cannabis, heroin and ketamine abuse presenting to emergency departments (EDs) in Hong Kong during the COVID-19 pandemic and (2) evaluate the practice of ED interventions, including psychosocial interventions, and referrals to substance abuse services during the pandemic.

Methods

This was a retrospective study of all consecutive patients reported to the Hong Kong Poison Information Centre (HKPIC) by public EDs in Hong Kong between 23 January 2017 and 22 January 2023 for acute toxicity related to the recreational use of methamphetamine, cocaine, cannabis, heroin or ketamine. The electronic medical records of the included cases were reviewed, with data extracted in parallel by trained research personnel according to a standardised coding manual. The severity of acute toxicity was ranked using the Poison Severity Score, and the patient outcome was rated by clinical toxicologists with reference to the American Association of Poison Control Centers' National Poison Data System.

We studied the trends in acute toxicity using Poisson regression/negative binominal models, accounting for the concurrent drop in ED attendance volume during the pandemic. We also evaluated the correlation between the trends of acute toxicities involving individual drugs and the number of reported abusers of the respective drugs in the Central Registry of Drug Abuse (CRDA) published by the Government and drug seizure data from law enforcement agencies. Interrupted time series (ITS) analysis was performed to evaluate the impact of the COVID-19 pandemic, closure of social and recreational venues and social distancing measures, as measured by the Oxford COVID-19 Government Response Tracker (OxCGRT) Stringency Index, on the monthly incidence of acute toxicities involving individual drugs. Patient demographics, patterns of drug use, clinical presentations and outcomes, and clinical and psychosocial interventions before and during the pandemic were compared for individual drugs. Multivariable logistic regression was performed to evaluate the association between

the pandemic and severe complications for individual drugs, after adjusting for known independent predictors for poor clinical outcomes.

Results

In total, 1,453 episodes were analysed. From 2018 to 2022, the median incidence rates of methamphetamine-, cocaine-, cannabis-, heroin- and ketamine-related ED visits were 1.69, 0.65, 0.43, 0.79 and 0.35 per 100,000 population, respectively. No significant correlations were observed between the number of acute toxicities reported to the HKPIC and CRDA or drug seizure data for any of the study drugs, except that the number of acute heroin toxicities was significantly correlated with the fall in the number of heroin abusers in the CRDA (Spearman's rho 0.89, p = 0.045). Acute toxicities involving methamphetamine, cannabis and heroin increased shortly after the beginning of the pandemic but then decreased faster than the pre-pandemic period. Acute toxicities involving ketamine increased and followed a similar trend as before the pandemic. As for cocaine, no significant changes in the number and trend of acute toxicities were observed during the pandemic. Overall, closure of social and recreational venues during the pandemic had a limited impact on acute drug toxicities. The Stringency Index was associated with decreased acute heroin toxicities.

Compared with the pre-pandemic period, a significantly higher proportion of patients with acute methamphetamine toxicity during the pandemic presented with agitation (40.7% vs 30.1%, p = 0.004), injury (18.5% vs 12.9%, p = 0.042) and self-harm behaviours (16.0% vs 10.2%, p = 0.024); required invasive treatment and intensive care unit (ICU) admission; and developed major effects or died (p = 0.012). Significantly more acute myocardial injuries (12.7% vs 4.9%, p = 0.015), drowsiness (25.4% vs 14.6%, p = 0.019), and major effects (p = 0.025) were seen in acute cocaine toxicity during the pandemic than before. For cannabis, more female patients with acute cannabis toxicity (35.5% vs 18.4%, p = 0.01) were seen during the pandemic than before. Episodes involving heroin were characterised by a significantly higher proportion with concurrent use of methamphetamine (25.7% vs 15.4%, p = 0.023); more agitation, confusion, or hallucination; and more need for chemical restraints during the pandemic compared to before. As for ketamine, polydrug abuse with stimulants such as cocaine was common, and more alcohol co-ingestion (18.8% vs 6.0%, p = 0.011) was observed during the pandemic than before. In multivariable logistic regression, presenting during the COVID-19 pandemic was not significantly associated with severe complications of acute toxicity, after adjusting for known independent predictors for poor clinical outcomes for the respective drugs.

Conclusions

The COVID-19 pandemic has had multiple impacts on local patterns of drug abuse and associated toxicities. For acute toxicity related to amphetamines, cocaine, cannabis, heroin

and ketamine abuse presenting to EDs in Hong Kong during the COVID-19 pandemic, social and recreational venue closure had no apparent significant impact on drug abuse and toxicity. Social distancing measures during the pandemic were significantly associated with decreased number of acute heroin toxicities. However, the reduction in acute toxicities involving methamphetamine and heroin during the pandemic did not translate into a lower severity of poisoning, and the increased combination of heroin and methamphetamine is alarming. The increase in cocaine-related acute myocardial injury is also noteworthy in the face of increasing cocaine supply and abuse internationally. Acute cannabis toxicity slightly increased in number during the pandemic, particularly among female drug users for the former. The number of ketamine users also showed an increase and many of them were also multi-substance abusers. Further studies are warranted to monitor the trends in drug abuse and toxicity in the aftermath of the pandemic, the impact of combinations of traditional illicit drugs, and the role of gender in cannabis abuse and toxicity.

Declaration

The following work was completed by the research team led by the principal investigator, Dr Rex Pui Kin Lam at the Department of Emergency Medicine, School of Clinical Medicine, Li Ka Shing Faculty of Medicine, The University of Hong Kong with collaboration with the Hong Kong Poison Information Centre of the Hospital Authority and the School of Public Health of The University of Hong Kong.

The current study was approved by the Institutional Review Board of The University of Hong Kong/Hong Kong West Cluster of the Hospital Authority (HA; reference no. UW 22–544) and the Research Ethics Committee of the Kowloon Central/Kowloon East Cluster of the HA (reference no. KC/KE-22-0138/ER-4). Our previous study (Project Reference No. BDF190053) was approved by these two ethics committees (HKU/HKW IRB no. UW20-597; KEC IRB no. KC/KE-20-0270/ER-2).

The study was conducted in full compliance with the Declaration of Helsinki and the Principles of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use–Good Clinical Practice.

No work resembling the current study has been published before. We certify that we have reviewed and approved the content of the report.

Acknowledgements

The research team would like to express our heartfelt gratitude to Ms Crystal Tsz Yu Tang and Mr Michael Chun Kai Lau for their help in data collection and preparation of the manuscript.

We sincerely thank our colleagues working in emergency departments and public hospitals of Hong Kong and the Hong Kong Poison Information Centre for their expert care of the patients described in this study. We dedicate this study to them all for their tireless efforts in looking after patients with acute toxicity from recreational drug use.

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List of abbreviations

1P-LSD	1-Propionyl-d-lysergic acid diethylamide
2C-B	4-bromo-2,5-dimethoxyphenethylamine
2F-DCK	2-Fluoro-deschoroketamine
2-FEA	2-Fluoroethylamphetamine
3-FEA	3-Fluoroethylamphetamine
4-FA	4-Fluoroamphetamine
5F-MDMB-PICA	Methyl-2-[[1-(5-fluoropentyl) indole-3-carbonyl]amino]-3,3-dimethyl-butanoate
5-MeO-DET	5-methoxy-*N,N*-diethyltryptamine
5-MeO-DIPT	5-methoxy-*N,N*-diisopropyltryptamine
5-MeO-MiPT	5-Methoxy-*N,N*-methylisopropyltryptamine
2-oxo-PCE	Deschloro-*N*-ethyl-ketamine
A&E	Accident and Emergency Department
AAPCC	American Association of Poison Control Centers
ACS	Acute coronary syndrome
AKI	Acute kidney injury
ALP	Alaine phosphatase
ALT	Alaine aminotransferase
AMI	Acute myocardial infarction
ARDS	Adult respiratory distress syndrome
AST	Aspartate aminotransferase
CDARS	Clinical Data Analysis and Reporting System
CI	Confidence interval
CK	Creatine kinase
CMS	Clinical Management System
COVID-19	Coronavirus disease 2019
CRDA	Central Registry of Drug Abuse
DAWN	Drug Abuse Warning Network
DCK	Deschloroketamine
DIC	Disseminated intravascular coagulation
DILI	Drug-induced liver injury
ECMO	Extracorporeal membrane oxygenation
ED	Emergency department
EMW	Emergency medicine ward
Euro-DEN	European Drug Emergencies Network
GCS	Glasgow Coma Scale
GGT	γ-glutamyl transferase
HA	Hospital Authority
HKPIC	Hong Kong Poison Information Centre
ICU	Intensive care unit
IQR	Interquartile range
ITS	Interrupted time series

KDIGO	Kidney Disease: Improving Global Outcomes
LOS	Length of stay
LSD	Lysergic acid diethylamide
MDMA	3,4-methylenedioxy-methamphetamine
MSM	Men who have sex with men
N/A	Not applicable
NGO	Non-governmental organisation
NPS	Novel psychoactive substances
NSTEMI	Non-ST-elevation myocardial infarction
OR	Odds ratio
OxCGRT	Oxford Coronavirus Government Response Tracker
PI	Principal investigator
PICMS	Poison Information and Clinical Management System
PMA	Paramethoxyamphetamine
PMMA	Paramethoxymethamphetamine
PSS	Poison Severity Score
RR	Relative risk
SPSS	Statistical Package for the Social Sciences
STEMI	ST-elevation myocardial infarction
STROBE	Strengthening the Reporting of Observational Studies in Epidemiology
TFMPP	1–(3-trifluoromethylphenyl)piperazine
TRL	Toxicology Reference Laboratory
ULN	Upper limit of normal
UNODC	United Nations Office on Drugs and Crime
URL	Upper reference limit
US	United States

1. Introduction

1.1. Background

The coronavirus disease 2019 (COVID-19) pandemic, unprecedented in scale, magnitude and duration, has had a major impact on lives and livelihoods around the world. Because of the social distancing measures and travel restrictions implemented in different societies, the pandemic has brought many changes in illicit drug production, trafficking and consumption,[1] disrupting not only the conventional drug markets but also crypto markets on the dark web.[2] According to the United Nations Office on Drugs and Crime (UNODC), party drugs such as 3,4-methylenedioxy-methamphetamine (MDMA), lysergic acid diethylamide (LSD) and cocaine have been used less due to the closing of recreational venues during the pandemic. By contrast, the use of cannabis and non-medical use of pharmaceutical drugs such as benzodiazepines are rising because of increased stress, more free time, boredom and changes in the financial conditions of drug users.[1] Further complicating the problem is the limited access to drug rehabilitation services and treatment because of social distancing measures and other disruptions brought by the pandemic, forcing the drug users to become more isolated and hidden.

Notably, however, the shift in drug use patterns appears to be heterogeneous across different regions and lockdown periods. Different research methodologies also seem to come to different conclusions. In Europe, an online survey of 36,538 adult substance users from 21 countries early in the pandemic showed that most respondents reported no change in substance use, but both tobacco and cannabis use increased.[3] In Australia, a survey of 800 users of ecstasy/MDMA and other illicit stimulants showed that 70% cited reduced use of MDMA, and almost half reported less use of cocaine, ketamine, methamphetamine and nitrous oxide. As for cannabis, 40% of the respondents reported increasing use, and another 40% reported no change in use.[4] A global survey of 185 addiction medicine professionals from 77 countries showed an increase in perceived alcohol, cannabis, prescription opioid and sedative/hypnotic use among drug users, whereas the perceived use of amphetamines, cocaine and opiates declined during the pandemic.[5]

Laboratory studies provide another perspective. Serial hair analysis of a small group of vulnerable drug users in Italy showed that the use of heroin, cocaine, MDMA and cannabis fell considerably during the lockdown, but this consumption resumed to pre-lockdown levels when the confinement was over. Notably, the consumption of benzodiazepines and alcohol had remained high throughout the confinement period, presumably due to better access during lockdowns and self-medication to replace illicit drugs that were no longer readily available.[6] Wastewater analysis in seven European cities showed heterogeneous results for different substances across different locations, making it difficult to evaluate the effect of the COVID-19 pandemic on illicit drug use.[7] In the United States (US), despite a drop in the

overall drug testing volume during the pandemic, test positivity rose by 35% for non-prescribed fentanyl and 44% for heroin compared with before the pandemic.[8] So far, studies in the emergency department (ED) looking at the trends and patterns of acute recreational drug toxicity during the pandemic are lacking.

Hong Kong witnessed the first confirmed case of COVID-19 on 23 January 2020. Since then, multiple social distancing and travel restriction measures have been implemented at different times in response to the various waves of the pandemic.[9] It is unclear how these public health measures have affected the local drug supply chain and pattern of drug use. It is noteworthy that during the pandemic, Hong Kong has witnessed the largest seizure of cannabis in a decade.[10,11] Our previous research titled 'Acute toxicity related to psychoactive substance abuse and the impact of emergency department interventions on drug-related reattendance' (Project Number BDF 190053) has demonstrated a significant association between the number of acute cannabis toxicities reported to the HKPIC and the market value of cannabis seized by law enforcement in the same year before the pandemic. It is uncertain that whether such an association persisted during the pandemic when the mode of drug trafficking might change. However, the rising trend of cannabis seized by law enforcement, together with its legalisation in some Western countries, lower perceived harm among users compared to other illicit drugs and the busting of more and more cannabis dens in Hong Kong,[12] still raises concerns about the increasing use of cannabis in the community. Particularly concerning is the rising trend in cannabis abuse among youths found in surveys. The 2017/18 Student Survey revealed that 13,600 had tried cannabis, compared with 8,600 in 2014/2015.[13]

1.2. Knowledge gaps

In summary, knowledge gaps exist in the following areas:

1. The impact of the COVID-19 pandemic on the trends and characteristics of patients who present to EDs with acute toxicity related to the abuse of amphetamines, cocaine, cannabis, heroin or ketamine in Hong Kong.

2. The impact of the COVID-19 pandemic on ED interventions, including psychosocial intervention and referral to substance abuse services, for patients with acute toxicity due to the recreational use of these drugs.

There is a need to monitor the most recent trends and patterns in recreational drug abuse during the COVID-19 pandemic to inform a timely adaptation of public education strategy and drug-control interventions. As demonstrated by our previous work, ED-based drug surveillance studies provide important complementary information about the drug harms and patterns of health service utilisation in detail, which is otherwise not available based on the

current CRDA statistics. To the best of our knowledge, local studies to fill these knowledge gaps are currently lacking.

The COVID-19 pandemic also provides a unique opportunity to observe the impact of various public health measures, such as the closure of bars and leisure venues and restriction of social gatherings, on patterns of drug abuse and the occurrence of associated acute toxicity. The findings will provide important insights into where and how these recreational drugs reach users and whether shutting down venues has had any impact on usage and the associated harms. This information will have significant implications for future drug-control policy by showing where to target interventions for individual drugs as we return to normalcy or adapt to a new normal in the aftermath of the COVID-19 pandemic.

2. Study objectives and purpose

The objectives of this study are:

1. To characterise the trends and patterns in acute toxicity related to amphetamine, cocaine, cannabis, heroin and ketamine abuse presenting to EDs in Hong Kong during the COVID-19 pandemic.

2. To evaluate the practice of ED interventions, including psychosocial interventions, and referral to substance abuse services during the COVID-19 pandemic.

3. Methods

3.1. Study design

This was a retrospective observational study of consecutive patients who were reported to the Hong Kong Poison Information Centre (HKPIC) by all the Accident and Emergency Departments (A&Es) of Hong Kong over 6 years between 23 January 2017 and 22 January 2023. The study period covered the first 3 years of the COVID-19 pandemic in Hong Kong (from 23 January 2020 to 22 January 2023).

For acute toxicity episodes that involved methamphetamine, cocaine and cannabis, our study team had collected data in a previous study supported by the Beat Drugs Fund Association (project reference no. BDF190053), which covered 10 years from 1 January 2010 to 31 December 2019. We collected additional data in this study from 1 January 2020 to 22 January 2023 for episodes that involved these three drugs.

Acute toxicity episodes involving heroin and ketamine were not covered by our previous study. Therefore, the data collection period was from 23 January 2017 to 22 January 2023. We collected data covering 3 years before and 3 years after the commencement of the COVID-19 pandemic to identify significant changes brought by it.

We followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies in reporting the findings of this study.[14]

3.2. Research ethics

The study was approved by the Institutional Review Board of The University of Hong Kong/Hong Kong West Cluster of the Hospital Authority (HA; reference no. UW 22–544) and the Research Ethics Committee of the Kowloon Central/Kowloon East Cluster of the HA (reference no. KC/KE-22-0138/ER-4). Our previous study was approved by these two ethics committees (HKU/HKW IRB no. UW20-597; KEC IRB no. KC/KE-20-0270/ER-2).

Informed consent from the recruited subjects was waived because of the retrospective study design and the analysis of anonymised data. The study was conducted in full compliance with the Declaration of Helsinki and the Principles of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use–Good Clinical Practice.

3.3. Study setting and data sources

Our data source was HKPIC, which is the only poison control centre in Hong Kong and a central information hub on poisoning. Data on poisoning come from two major sources: records from a round-the-clock phone consultation service to local health care professionals and voluntary reporting from all public A&Es in our city.[15] Data on each poisoning case, received from either consultation or reporting, are entered prospectively into the Poison Information and Clinical Management System (PICMS) by health care staff trained in clinical toxicology and routinely verified by senior clinical toxicologists. Quality assurance was maintained by regular audits and team discussion of individual cases. The database contains territory-wide data that are representative of the local recreational drug use patterns.

3.4. Study population

All patients with acute toxicity related to amphetamines, cocaine, cannabis, heroin or ketamine within the study period were included. Drug use was defined based on clinical diagnosis with or without confirmation by urine toxicology immunoassay or hospital laboratory toxicology screen.

The exclusion criteria were:

1. Unintentional exposure

2. Malicious exposure in which the patients were victims of another person's intention to harm them

3. 'Body packing' of amphetamines, cocaine, cannabis, heroin or ketamine; however, individuals who had swallowed drugs hastily to avoid law enforcement arrest ('body stuffers') were still included because they were considered likely to be drug abusers.

4. Unrelated cases in which clinical presentations were explained by alternative medical or psychiatric diagnoses, or social or non-medical reasons

5. Confirmed non-exposure, with objective evidence that the initially suspected involvement of amphetamines, cocaine, cannabis, heroin or ketamine had not occurred

6. Non-ED cases

In addition, we excluded duplicate records from the PICMS and cases reported outside the study period.

3.5. Data collection

Eligible poisoning episodes were identified from the PICMS in HKPIC through a poison code search (Appendix 1). Electronic medical records were retrieved from the HA Clinical Management System (CMS) and reviewed for determination of inclusion. The CMS is a central repository of the clinical, laboratory and outcome data of patients treated in all public hospitals in Hong Kong. To ensure accuracy, all data were collected independently by two research assistants in parallel using a standardised data entry manual (Appendix 2). Each research assistant undertook lectures and data entry training with 100 sample cases before commencing data collection. The principal investigator crosschecked all data, resolved all discrepancies in data entry and determined the inclusion of individual cases. We collected the following data from the PICMS and HA CMS:

1. Demographic data, including age, gender, and social allowance status

2. Poison data, including the type of drug, dose, route, time, place, and reason for exposure

3. Clinical data, including triage category, clinical features and investigation results. Triage clinical variables include Glasgow Coma Scale (GCS), blood pressure, pulse rate, respiratory rate, oxygen saturation, body temperature and pupil sizes

4. Management data, including the use of supportive treatment, decontamination, antidotes and other specific treatments, such as mechanical ventilation, electrical therapy and renal replacement therapy

5. Data on severe complications, including acute coronary syndrome, heart failure, shock, respiratory failure, acute kidney injury, rhabdomyolysis, liver derangement, seizure, coma, intracranial bleeding and hyperthermia

6. Outcome data, including hospitalisation, intensive care unit (ICU) admission, psychiatric admission, length of stay and episode death

7. ED interventions, including psychiatry consultation and referral to social worker and non-governmental organisation (NGO) drug treatment and rehabilitation services

We evaluated the whole clinical course of each case and graded the severity of toxicity using the Poison Severity Score (PSS), which classifies the severity of poisoning into five categories: (0) none, (1) minor, (2) moderate, (3) severe and (4) fatal poisoning, based on the most severe clinical features. We checked the occurrence of a particular symptom or sign against the PSS chart (Appendix 3) and assigned a severity grade for each case.[16] PSS is

commonly used in similar studies on substance abuse in the literature, and it has been validated.[17,18] It allows comparison of the severity of acute recreational drug toxicity across different centres. All grading was performed by the principal investigator, who is an emergency medicine specialist with post-graduate training in clinical toxicology.

The outcome of acute poisoning is routinely classified by HKPIC staff into five categories: no effect, mild effect, moderate effect, major effect or death, with reference to the American Association of Poison Control Centers' National Poison Data System before the study (Appendix 4).[19] The relationship between the exposure to the poison and the clinical outcomes is graded as definite, probable, possible, not related or undetermined/not applicable according to the judgement of the clinical toxicologists in HKPIC.

3.6. Sample size calculation

According to the HKPIC database, 48 cases of cannabis, 51 cases of cocaine, 132 cases of methamphetamine, 66 cases of heroin, and 43 cases of ketamine were reported from January 2020 to January 2021. Assuming similar figures in 2021 to 2023, the number of cases in the first 3 years of the COVID-19 pandemic would be around 900, considering that some might involve polysubstance abuse and duplicate entries. For cannabis, methamphetamine and cocaine, we already had data on 534 episodes, covering 23 January 2017 to 31 December 2019, from our previous study. Additional data from 1 January 2020 to 22 January 2023 during the COVID-19 pandemic were collected for cannabis, methamphetamine and cocaine. For heroin and ketamine, we extended data collection back to 23 January 2017 and reviewed episodes involving them up to 23 January 2023. Therefore, in total, the estimated sample size was more than 1,800 episodes after pooling all data, including 1,300 additional episodes reviewed in this study. This sample size was sufficient for trend analysis and comparative analysis before and during the pandemic.

3.7. Definitions

3.7.1. Definition of the pre-COVID-19 and COVID-19 pandemic periods

The first case of COVID-19 was officially confirmed by the health authority on 23 January 2020.[20] We defined the period from 23 January 2017 to 22 January 2020 as the 'pre-pandemic period' and the period 23 January 2020 to 22 January 2023 as the 'pandemic period'.

3.7.2. Definition of poor clinical outcome

Similar to our previous study, we defined poor clinical outcome as a composite outcome of severe complications, including cardiac arrest, acute myocardial injury, myocardial infarction, ventricular dysrhythmia, heart failure, shock, respiratory failure, seizure, coma, acute kidney injury (AKI), liver injury, rhabdomyolysis, acute ischaemic stroke, intracranial bleeding that was not due to injury and disseminated intravascular coagulation. The details of the definition of individual complications are given in Table 1.

We did not include the need for ICU admission in the definition because non-clinical factors such as ICU bed availability and the admission policies of individual hospitals affect such decisions. Likewise, the provision of certain invasive treatments, such as mechanical ventilation or renal replacement therapy, was also not included in the definition of poor clinical outcome because the accessibility of such treatments varies across different hospitals and periods and the medical conditions for which these invasive procedures are indicated are already covered in the definition.

Table 1. Definition of severe complications related to drug abuse

Condition	Definition
Acute myocardial injury	Elevated cardiac troponin value above the 99th percentile of the upper reference limit, with a rise and fall of the value, according to the Fourth Universal Definition of Myocardial Infarction.[21]
Myocardial infarction	As documented in the medical notes.
Ventricular dysrhythmia	As documented in the medical notes.
Heart failure	As documented in the medical notes.
Shock	Systolic blood pressure < 90 mmHg or mean arterial blood pressure < 65 mmHg or clinical diagnosis of circulatory shock in the clinical notes when the blood pressure readings were above the cut-off points.[22]
Respiratory failure	As documented in the medical notes.
Seizure	As documented in the medical notes.
Coma	As documented in the medical notes.
Acute ischaemic stroke	As documented in the medical notes.
Intracranial bleeding	As documented in the medical notes.
Drug-induced liver injury (DILI)	(a) Alanine transferase (ALT) value ≥ 5 × upper limit of normal (ULN), (b) alanine phosphatase (ALP) value ≥ 2 × ULN, or (c) ALT value ≥ 3 × ULN and total bilirubin ≥ 2 × ULN[23] after excluding concurrent rhabdomyolysis.[24] Only patients with concurrently elevated bilirubin or γ-

	glutamyl transferase (GGT) levels, which are inconsistent with isolated muscle injury, were considered to be suffering from DILI in this study.[25] Patients with an alternative explanation of liver derangement, such as hepatitis C infection, were also not considered to have DILI in our study.
Acute kidney injury (AKI)	Based on the Kidney Disease: Improving Global Outcomes (KDIGO) Clinical Practice Guidelines for Acute Kidney Injury.[26]
Rhabdomyolysis	Creatine kinase (CK) level > 1,000 IU/L in the absence of myocardial infarction/CK elevation with cardiac aetiology, chronic renal failure or neuromuscular disease with myopathy.[27] We did not include symptoms in this definition because many patients were intoxicated at the time of presentation, and they might not have been able to accurately report muscle pain or weakness.
Disseminated intravascular coagulation	As documented in the medical notes.

3.7.3. Definition of social and recreational venues

To evaluate the impact of the closure of social and recreational venues such as bars and party rooms on drug use and acute toxicities, we followed the definitions in the Prevention and Control of Disease (Requirements and Directions) (Business and Premises) Regulation (Cap. 599F) for different premises.[28] We classified these premises into two broad groups for analysis (Table 2), based on the presumed likelihood of exposure to recreational drugs and different times of closure of these premises throughout the COVID-19 pandemic. We believe that drug exposure was more likely in Group 2 premises, which include bars, pubs, party rooms, nightclubs and karaoke. These premises were generally closed for a longer period during the pandemic.

Table 2. Classification of social and recreational venues

Group	Premises
Group 1	1. Amusement game centres 2. Places of amusement 3. Places of public entertainment 4. Fitness centres 5. Sports premises 6. Beauty parlours 7. Club-houses 8. Mahjong-tin kau premises 9. Massage establishments 10. Cinemas
Group 2	1. Bars or pubs 2. Nightclubs 3. Karaoke establishments 4. Party rooms 5. Bathhouses

3.8. Data analysis

3.8.1. Annual incidence and correlation analyses

Descriptive statistics were used to analyse the distribution of characteristics of the study population. Missing values were not imputed. We calculated the median annual incidence of drug-related visits per 100,000 ED attendances and the median annual incidence of ED visits for drug-related problems per 100,000 population for each of the drugs of interest over the study period. The mid-year population estimates were based on the data published by the Census and Statistics Department of the Government of the Hong Kong Special Administrative Region.[29] We then evaluated the correlation between the number of patients with acute recreational drug toxicity reported to the HKPIC and the number of respective drug abusers reported in the CRDA.[30] We also performed a similar correlation analysis between the HKPIC data and the amount and market value of the drugs seized by the Customs and Excise Department of the Hong Kong Special Administrative Region in the same year, up to 2021 (The drug seizure data in 2022 was not yet published at the time of writing of this report).[31–34] We did not include 2017 or 2023 in the estimation of annual incidence and correlation analyses because we did not have complete data for the whole year.

Concerning MDMA and novel psychoactive substances (NPS) identified during data collection, the number of acute toxicities was too small for meaningful incidence and correlation analyses. We only reported the number of acute toxicity episodes involving them each year separately.

3.8.2. Interrupted time series analyses of the trends in drug toxicities

To evaluate the impact on the trends in drug toxicities of the COVID-19 pandemic, closure of different social and recreational venues and social distancing measures during the pandemic, we performed interrupted time series (ITS) analyses. We divided the whole study period into 72 months, with each monthly interval spanning from the 23rd day of a month to the 22nd day of the following month, since the first COVID-19 case was officially confirmed on 23rd January 2020. The dependent variables were the number of acute toxicities of methamphetamine, cocaine, cannabis, heroin and ketamine reported to the HKPIC per month.

The whole 72-month study period covered at six seasonal cycles, which was long enough for modelling complex time series and seasonality. These monthly data allowed us to assess the seasonality, trends and the impact of the COVID-19 pandemic, closure of different social and recreational venues as well as social distancing measures introduced during the different waves of the pandemic.

We were aware that the period of closure of some venues did not fit exactly well into the defined monthly time intervals. For instance, the start date of closure did not fall exactly on the 23rd day of a month. In that case, we evaluated the period of closure of these premises in the involved monthly intervals. If the closure lasted longer than 50% of a particular monthly interval, we defined the premises as ‘closed’ in that particular monthly interval, and the opposite if the closure was shorter.

We evaluated the impact of the COVID-19 pandemic by including it as a dummy variable in the analysis (‘pre-pandemic period’ = 0 and ‘pandemic period’ = 1). Social distancing measures implemented during the different waves of the COVID-19 pandemic were quantified using the Stringency Index from the Oxford Coronavirus Government Response Tracker (OxCGRT) project. The OxCGRT Stringency Index is a composite measure of nine

metrics: school closures; workplace closures; cancellation of public events; restrictions on public gatherings; closure of public transport; stay-at-home requirements; public information campaigns; restrictions on internal movements; and international travel controls.[35] The Index ranges from 0 to 100, with a high score indicating a stricter government response. The Index has been widely used in studies on the impact of government responses during the COVID-19 pandemic on various health outcomes.[36-38]

We then evaluated the trend using Poisson regression/negative binomial models (depending on model stability and dispersion of variance) with the logarithm of total ED attendance of the same year as the offset term. We retrieved the total ED attendance in each of the included months from the Clinical Data Analysis and Reporting System (CDARS) of the HA. We included month, the pandemic, social and recreational venue closure, Stringency Index into the model as interactive terms to evaluate the change in level and trend in acute toxicities of each study drug during the pandemic.

3.8.3. The impact of the pandemic on drug use pattern and clinical outcome

We stratified patients into groups who presented during the pre-pandemic period and pandemic period for each drug. Pearson's chi-square test or Fisher's exact test, where appropriate, were used to study the differences in proportions between groups. For variables in a normal distribution, we compared the mean values of the variables of interest across different groups using Student's t-test. For variables that did not follow a normal distribution, we calculated the median and interquartile range (IQR) and used non-parametric test for comparison of the median values. Furthermore, univariate and multivariable logistic regression analyses were performed to evaluate whether presentation during the pandemic period was associated with a poor clinical outcome, after controlling for known confounding factors identified in our previous and current work.

The Statistical Package for the Social Sciences (SPSS) version 27.0 (IBM Corp., Armonk, NY, USA) for Windows version 27.0 and R version 4.2.1 or later (R Foundation for Statistical Computing, Vienna, Austria) were used for data analysis. A two-tailed p value < 0.05 was considered statistically significant.

4. Results

During the study period, 1,714 episodes of acute toxicity were identified from the PICMS in the HKPIC, based on the predefined search criteria. Of these, 261 episodes were excluded after case review, and 1,453 episodes were included for analysis (Figure 1). These 1,453 episodes included 534 episodes of acute toxicity involving methamphetamine, cocaine, or cannabis included in the previous project (project reference no. BDF190053). Figure 1 shows the patient flow diagram and the reasons for exclusion.

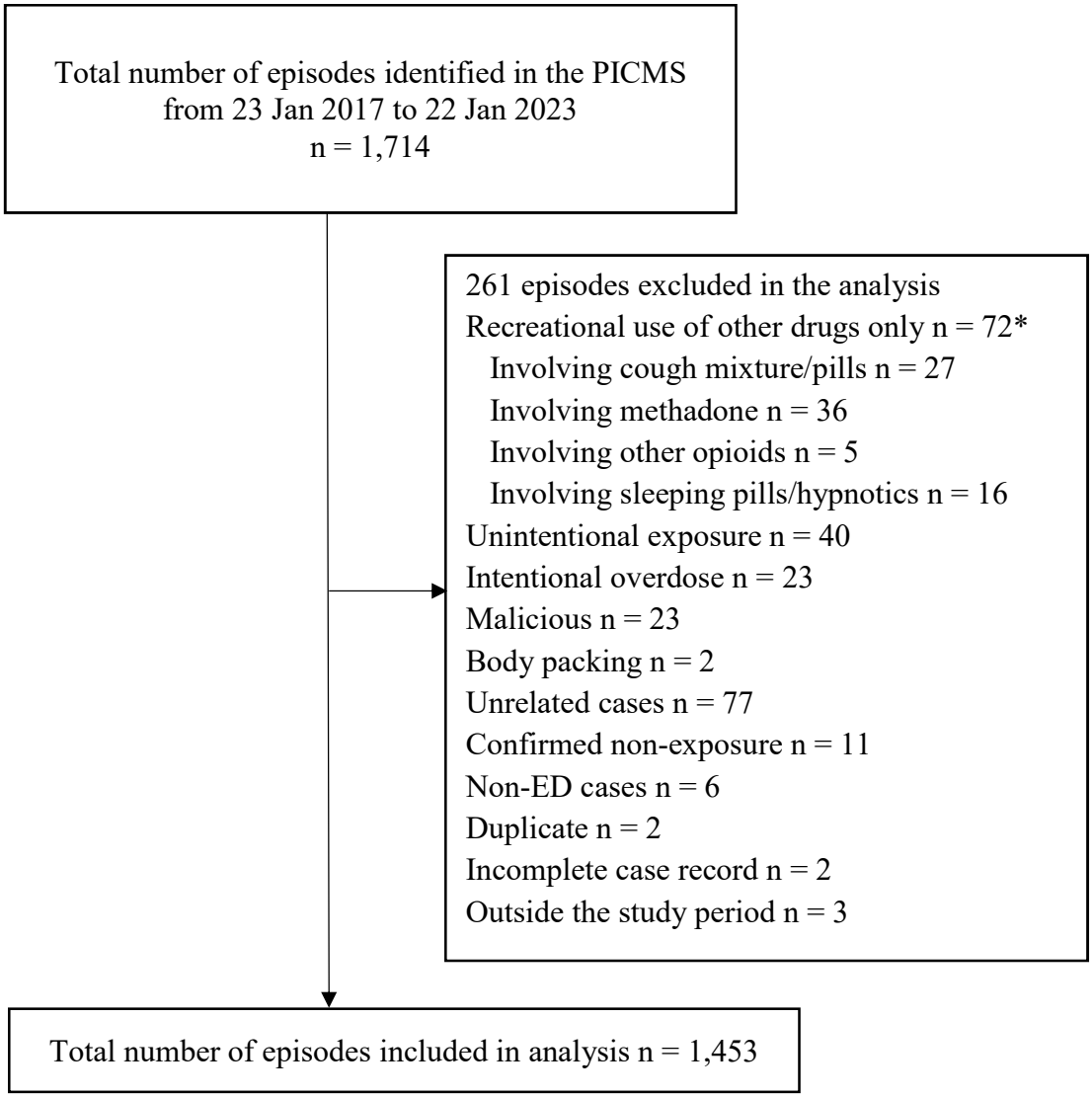


Figure 1. Patient flow diagram and reasons for exclusion
*Footnote
The sum of the number of episodes involving cough mixture/pills, methadone, other opioids and sleeping pills/hypnotics was greater than 72 because of polysubstance abuse.

4.1. Annual incidence and correlation analyses

4.1.1. Overall analysis

From 2018 to 2022, the median annual incidence of acute toxicity related to methamphetamine, cocaine, cannabis, heroin and ketamine were 6.01 (IQR 4.36–7.16), 2.65 (IQR 2.36–3.17), 1.50 (IQR 1.26–2.39), 3.15 (IQR 1.22–3.65) and 1.24 (IQR 1.07–2.27) per 100,000 ED attendances, respectively. The median incidence rates of methamphetamine-, cocaine-, cannabis-, heroin-, and ketamine-related ED visits were 1.69 (IQR 1.02–1.73), 0.65 (IQR 0.59–0.78), 0.43 (IQR 0.32–0.54), 0.79 (IQR 0.28–0.95) and 0.35 (IQR 0.26–0.51) per 100,000 population, respectively. Figure 2 shows the number of acute toxicities related to methamphetamine, cocaine, cannabis, heroin and ketamine reported to the HKPIC from 2018 to 2022.

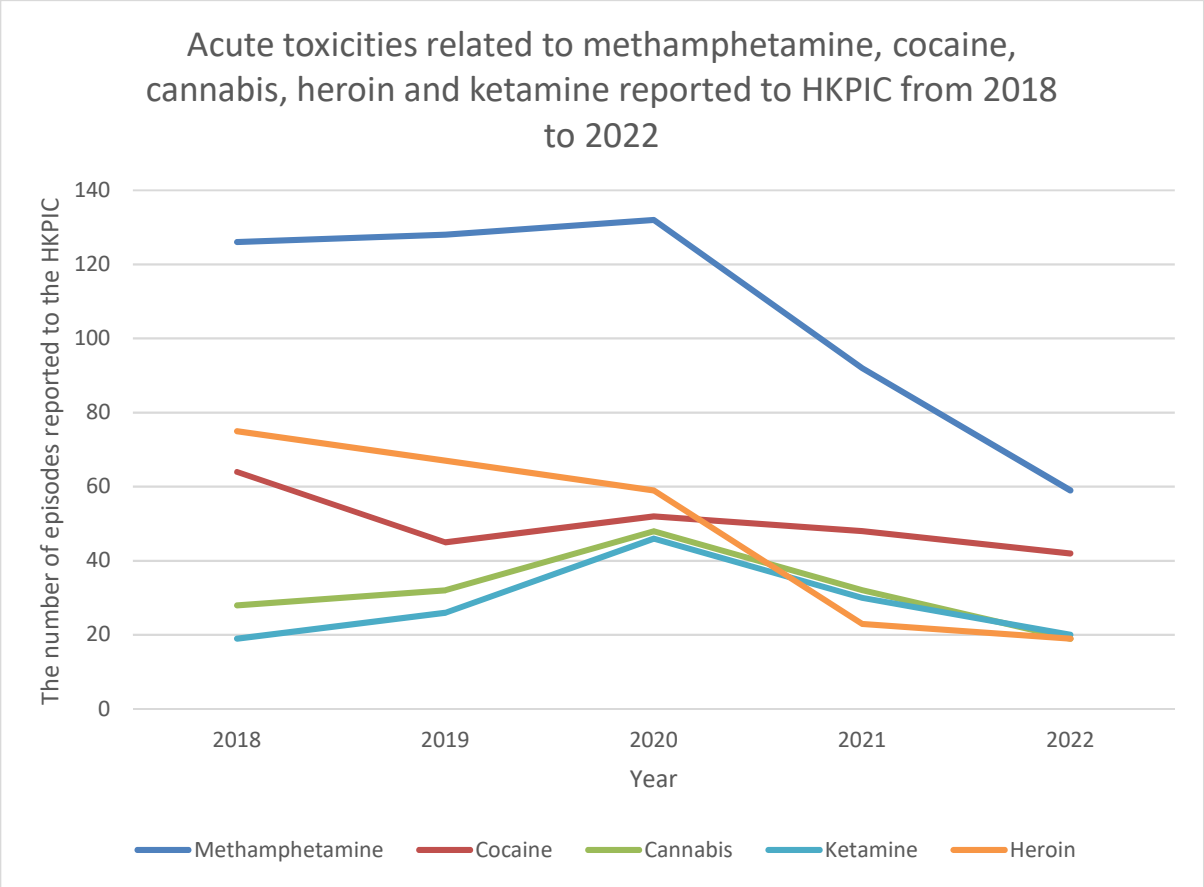


Figure 2. The number of acute toxicities related to methamphetamine, cocaine, cannabis, heroin and ketamine reported to the HKPIC from 2018 to 2022.

During the study period, 56 episodes of acute toxicity involving MDMA, 21 episodes involving LSD and 46 episodes involving NPS were reported to the HKPIC. Table 3 shows the distribution of these episodes throughout the study period. A detailed discussion of each individual NPS is given in Appendix 5.

Table 3. The number of acute toxicities related to 3,4-methylenedioxy-methamphetamine and novel psychoactive substances reported to the HKPIC from 2017 to 2023.

	2017 (from 23 Jan 2017)	2018	2019	2020	2021	2022	2023 (up to 22 Jan 2023)
MDMA	12	5	9	16	6	8	0
Phenylethylamines							
PMMA/PMA	2	0	0	2	0	0	0
2-FEA/3-FEA/4-FA	0	0	1	0	0	0	0
2C-B	0	0	0	1	0	0	0
Synthetic cathinones							
N-cyclohexylmethylone/ Dibutylone/ Ethylone/ Eutylone/ Pentylone	1	1	1	4	0	0	1
Tryptamines							
5-MeO-MiPT/ 5-MeO-DET	0	1	0	0	0	0	0
Psilocin (magic mushroom)	0	0	0	0	1	0	0
Piperazines							
TFMPP	1	0	0	0	0	0	0
Phencyclidines							
2-oxo-PCE	20	2	0	2	0	0	0
DCK	0	0	0	2	0	0	0
Fluoro-2-oxo-PCE	0	0	0	0	0	0	1
2F-DCK	0	0	0	3	0	0	0
Tiletamine	0	0	1	0	4	2	0
Novel benzodiazepines							
Etizolam	0	0	0	1	0	0	0
Novel opioids							
Fentanyl	0	0	0	0	0	1	0
Protonitazene	0	0	0	0	0	1	0
Synthetic cannabinoids							
5F-MDMB-PICA	1	0	0	0	0	0	0
Other substances							
1P-LSD	0	0	1	0	0	0	0

Abbreviations: 2C-B, 4-bromo-2,5-dimethoxyphenethylamine; DCK, deschloroketamine; 2F-DCK, 2-fluoro-deschoroketamine; 4-FA, 4-fluoroamphetamine; 2-FEA, 2-fluoroethylamphetamine; 3-FEA, 3-fluoroethylamphetamine; 5F-MDMB-PICA, methyl (2S)-2-{[1-(5-fluoropentyl)-1H-indole-3-carbonyl]amino}-3,3-dimethylbutanoate; MDMA, 3,4-methylenedioxy-methamphetamine; 5-MeO-DET, 5-methoxy-*N,N*-diethyltryptamine; 5-MeO-MiPT, 5-Methoxy-*N,N*-methylisopropyltryptamine; 2-oxo-PCE, deschloro-*N*-ethyl-norketamine; 1P-LSD, 1-propionyl-d-lysergic acid diethylamide; PMA, paramethoxyamphetamine; PMMA, paramethoxymethamphetamine; TFMPP, 1-(3-trifluoromethylphenyl)piperazine

4.1.2. Number of acute toxicities involving methamphetamine

Figures 3–5 show the plots of the numbers of acute toxicities of methamphetamine against the reported number of methamphetamine abusers in the CRDA, as well as the quantity and estimated market value of methamphetamine seized by law enforcement in the same year. Both the HKPIC and CRDA showed a decline in the reported numbers from 2018 to 2022, but their correlation was not statistically significant (Spearman's rho 0.60, p = 0.29). No correlation was found between the quantity (Spearman's rho -0.20, p = 0.80) and the estimated market value (Spearman's rho -0.20, p = 0.80) of methamphetamine seized by law enforcement with the respective data in HKPIC on methamphetamine. Both increased considerably from 2018 to 2022.

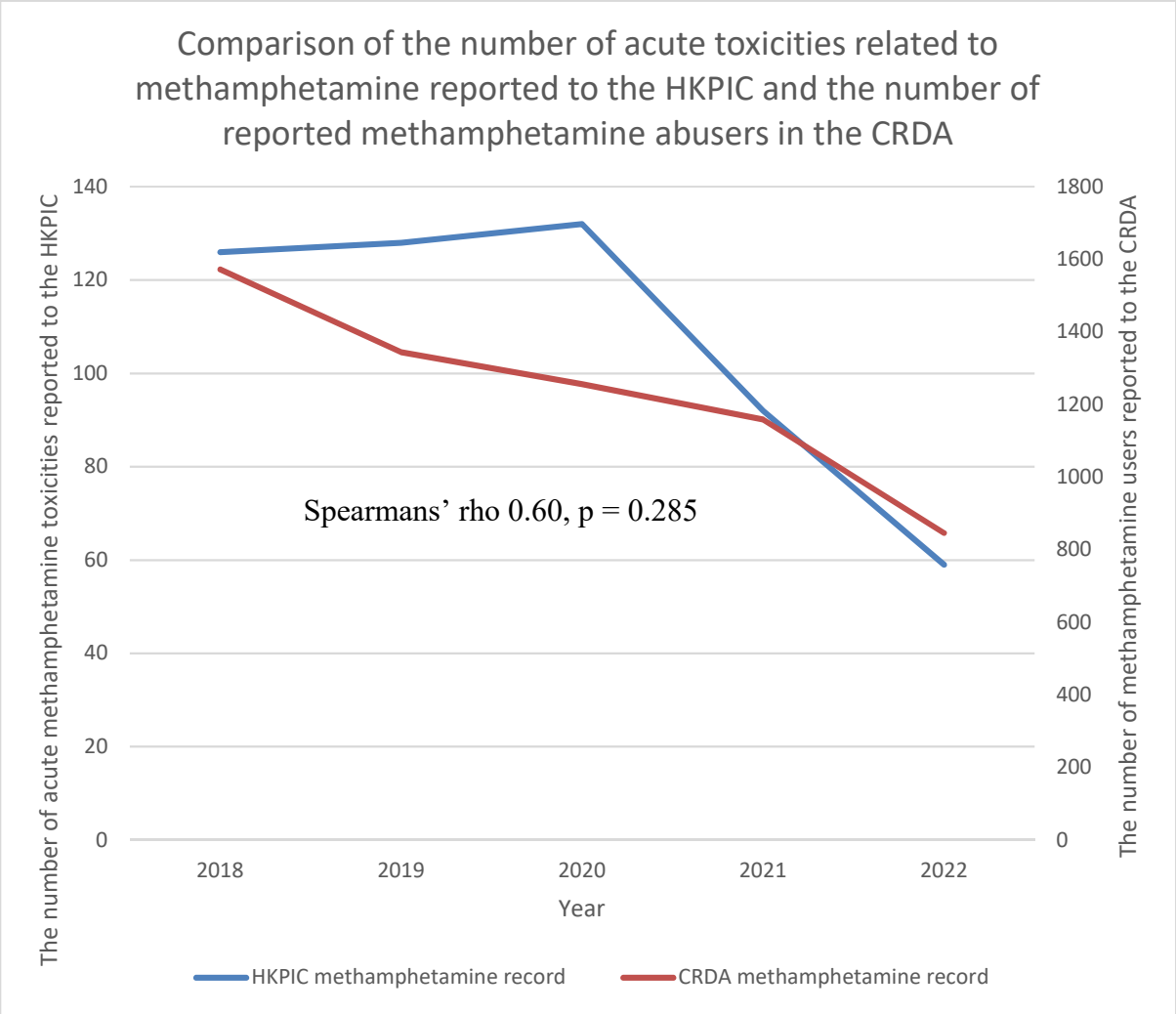


Figure 3. Comparison of the number of acute toxicities related to methamphetamine reported to the HKPIC and the number of reported methamphetamine abusers in the CRDA.

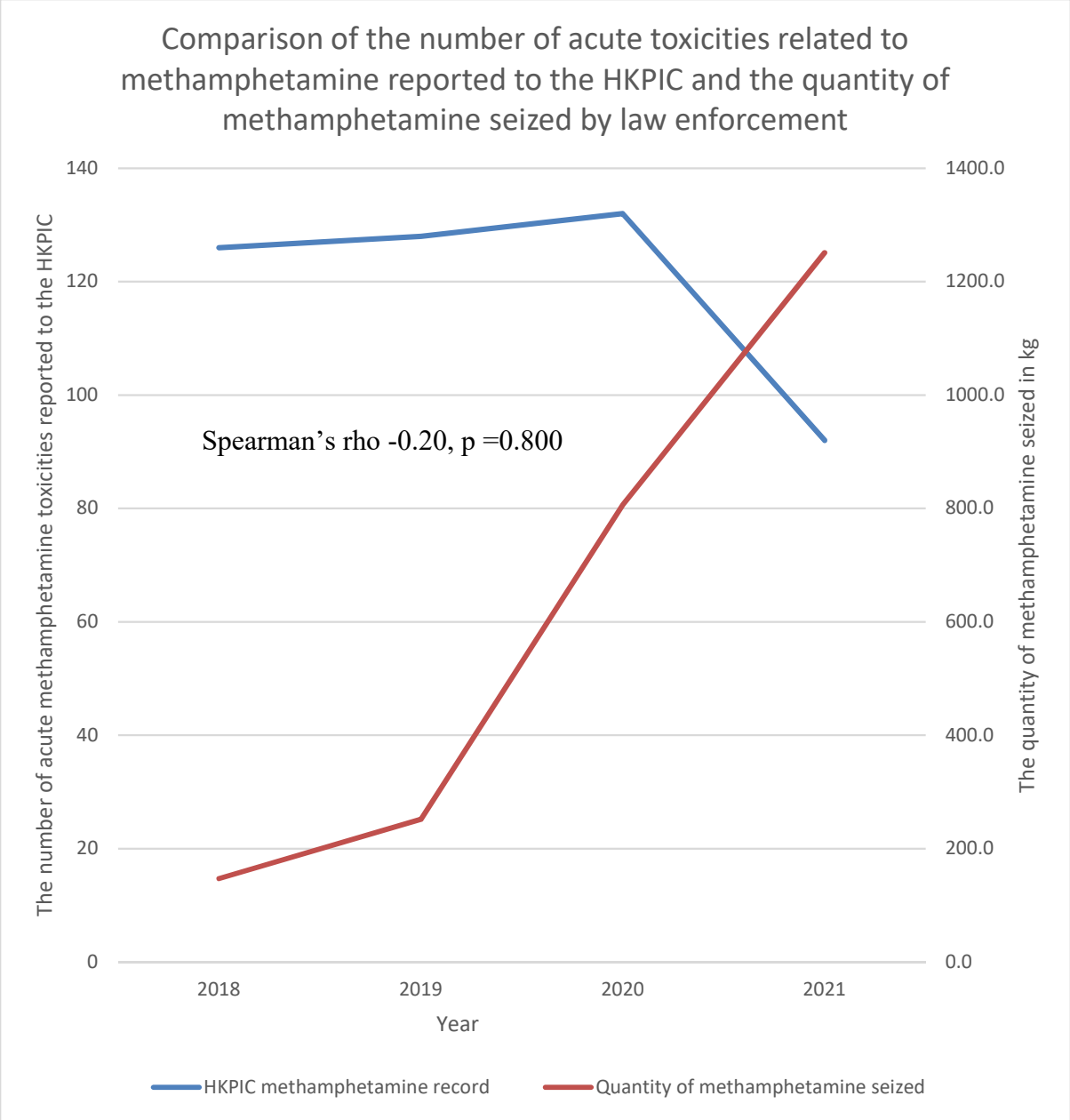


Figure 4. Comparison of the number of acute toxicities related to methamphetamine reported to the HKPIC and the quantity of methamphetamine seized by law enforcement.

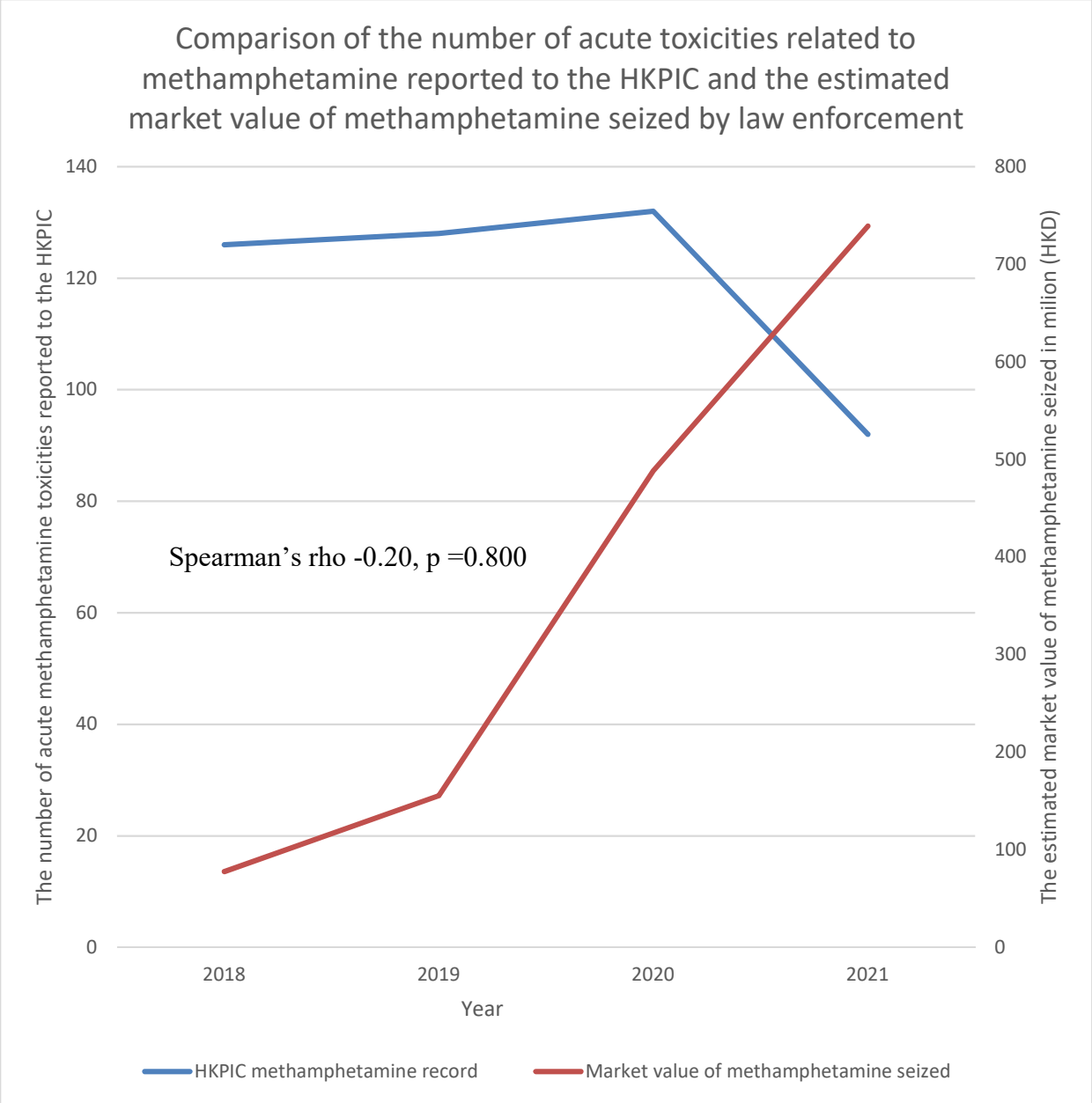


Figure 5. Comparison of the number of acute toxicities related to methamphetamine reported to the HKPIC and the estimated market value of methamphetamine seized by law enforcement.

4.1.3. Number of acute toxicities involving cocaine

Figures 6–8 show the number of acute toxicities related to cocaine reported to the HKPIC compared with the reported number of cocaine abusers in the CRDA, as well as the quantity and estimated market value of cocaine seized by law enforcement in the same year. No significant correlations existed between these reported numbers.

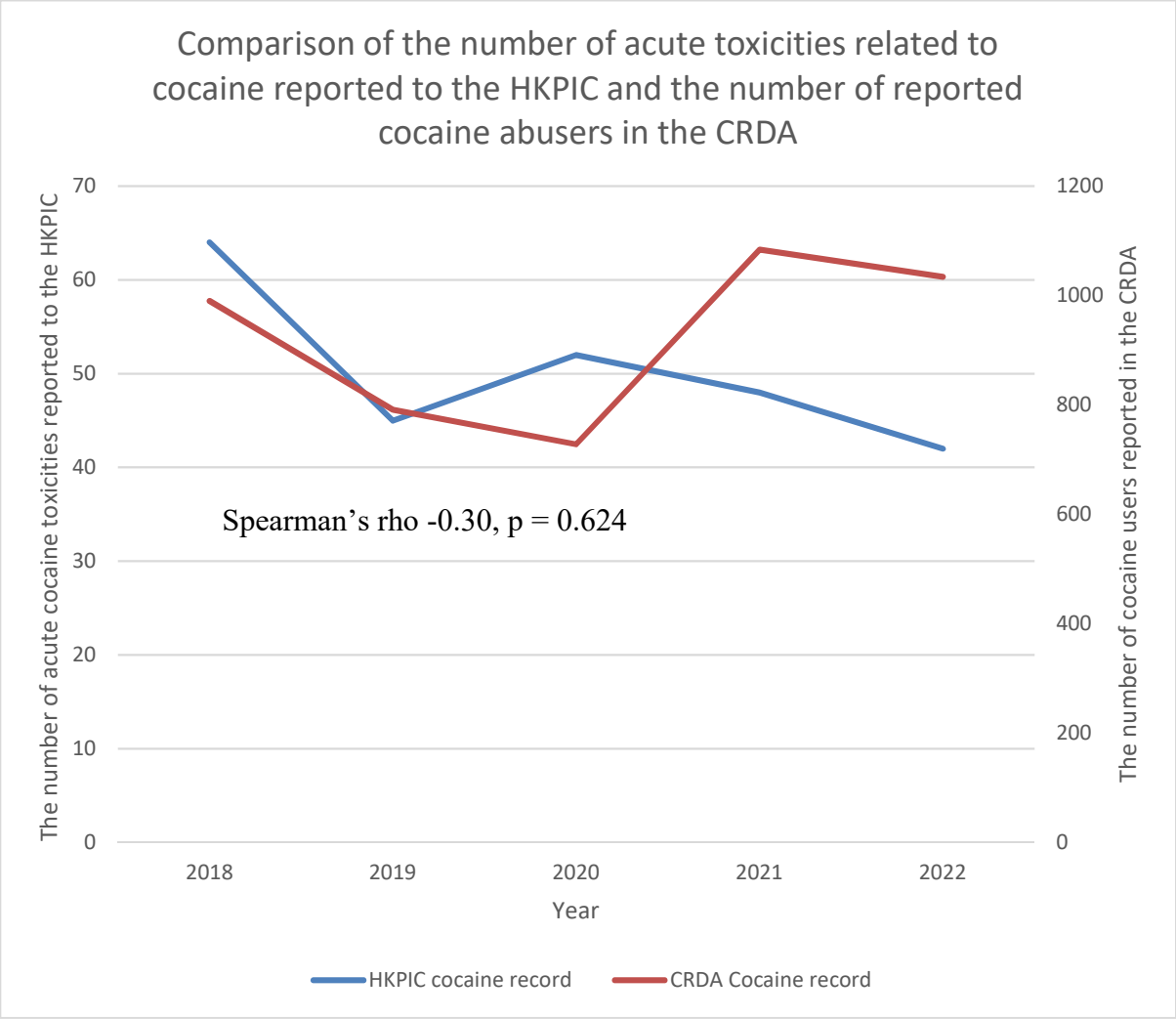


Figure 6. Comparison of the number of acute toxicities related to cocaine reported to the HKPIC and the number of reported cocaine abusers in the CRDA.

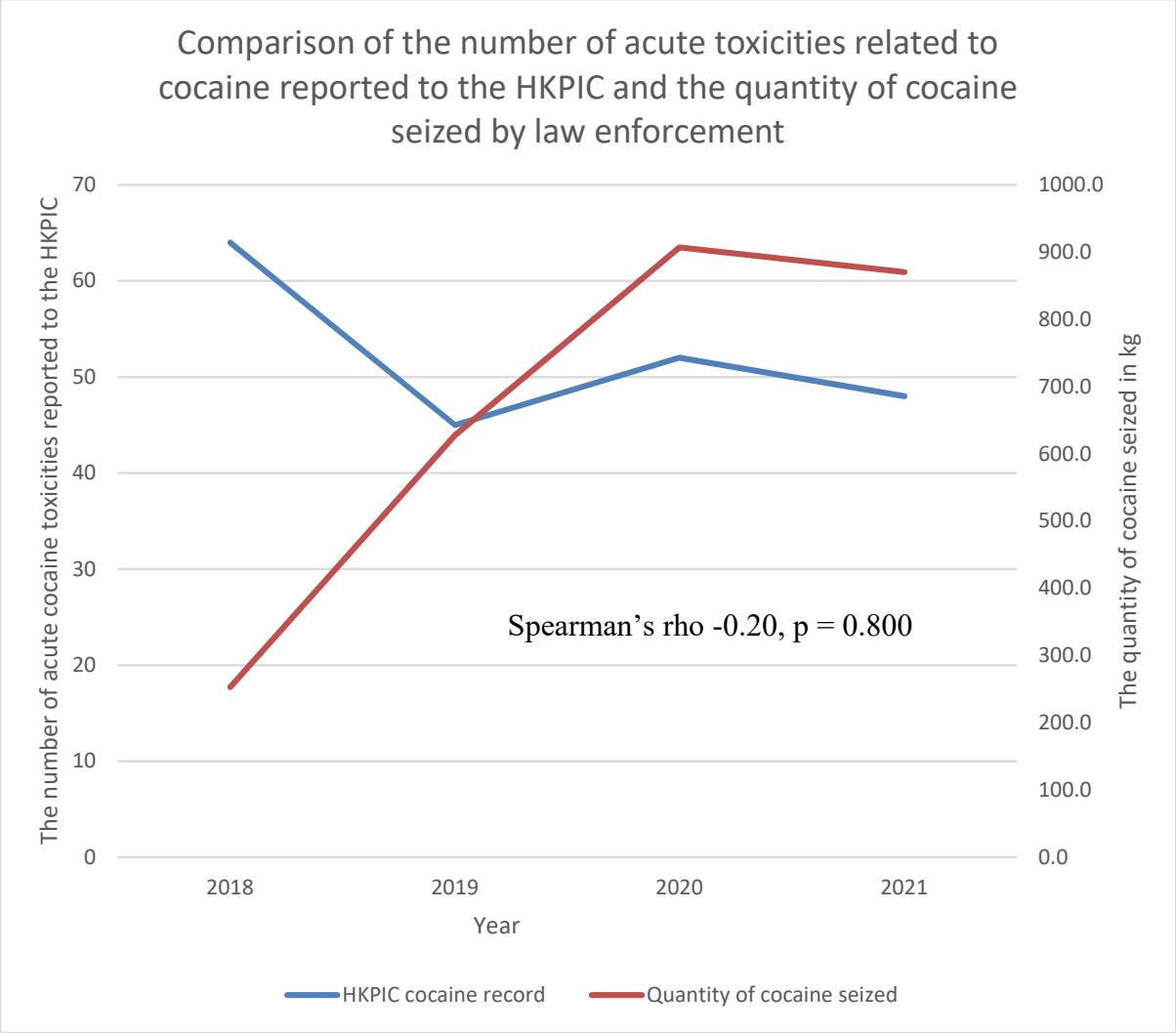


Figure 7. Comparison of the number of acute toxicities related to cocaine reported to the HKPIC and the quantity of cocaine seized by law enforcement.

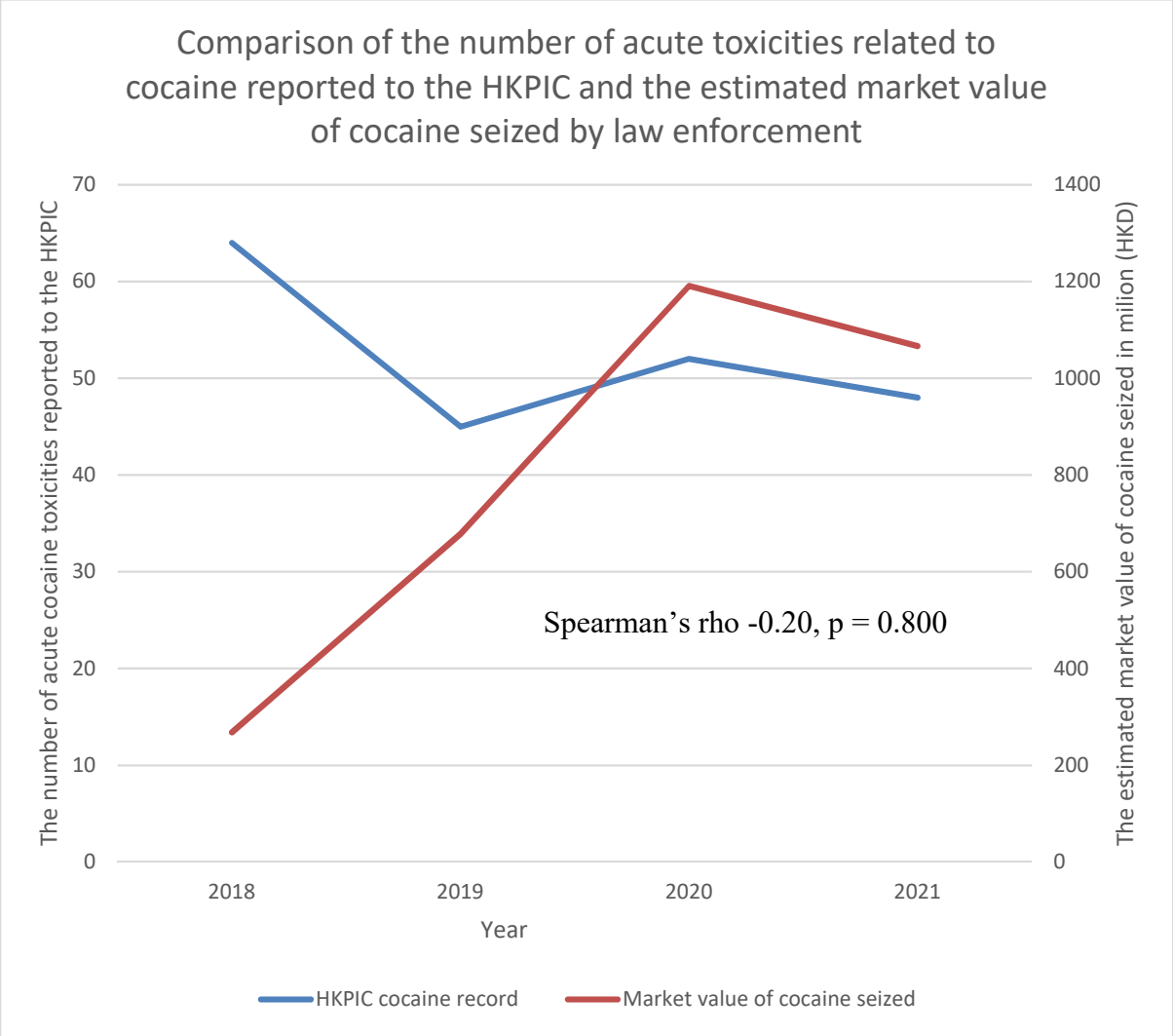


Figure 8. Comparison of the number of acute toxicities related to cocaine reported to the HKPIC and the estimated market value of cocaine seized by law enforcement.

4.1.4. Number of acute toxicities involving cannabis

The HKPIC data and CRDA data showed a peak in the reported number of related acute toxicities and the number of cannabis abusers in 2020 and 2021, respectively, followed by a decline in both in 2022 (Figure 9). The correlation between the HKPIC and CRDA data was not statistically significant (Spearman's rho 0.05, p = 0.94). The quantity and the estimated market value of the cannabis seized by law enforcement were also not correlated significantly with the number of acute toxicities reported to the HKPIC in the same year (Figures 10 and 11).

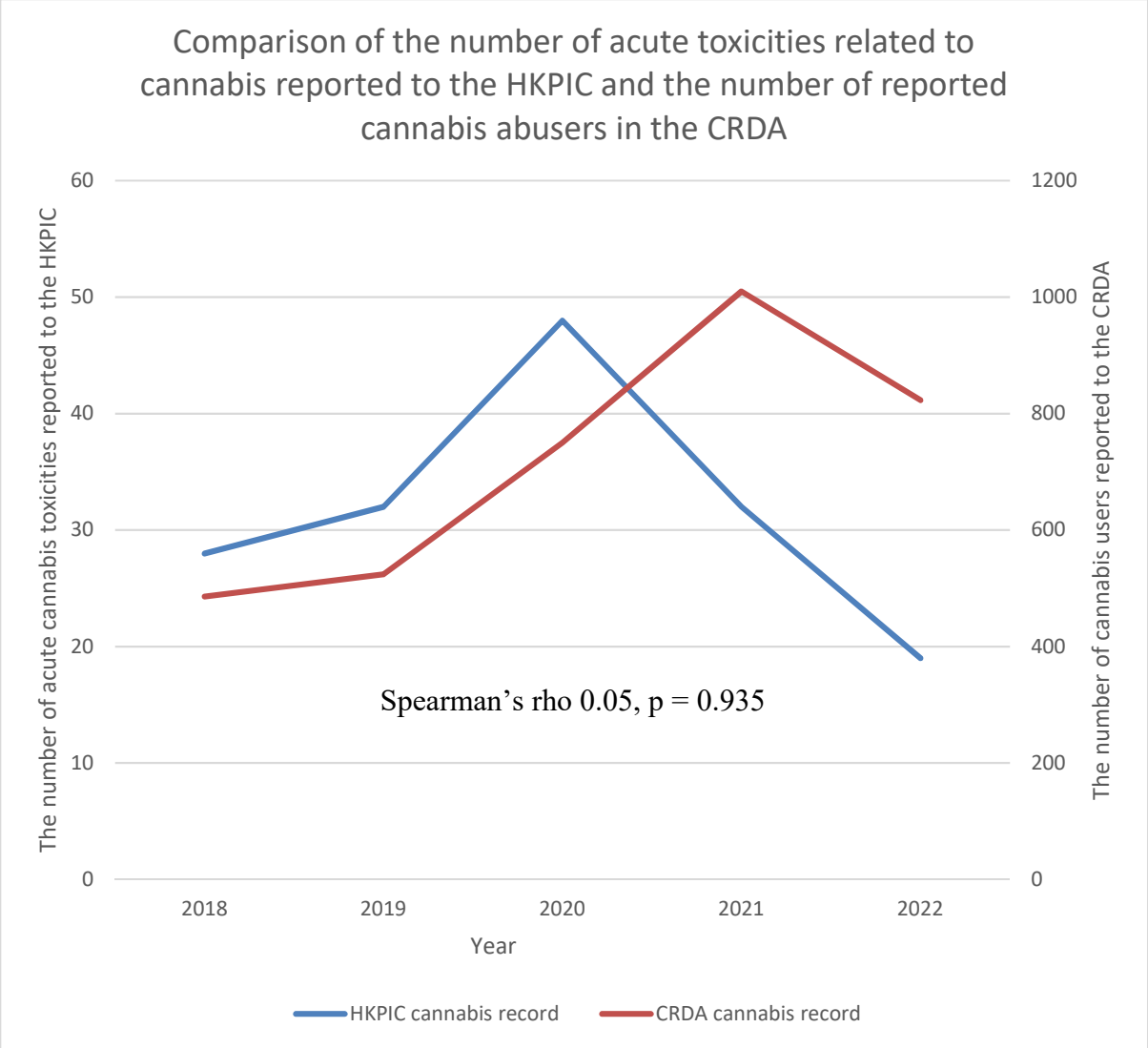


Figure 9. Comparison of the number of acute toxicities related to cannabis reported to the HKPIC and the number of reported cannabis abusers in the CRDA.

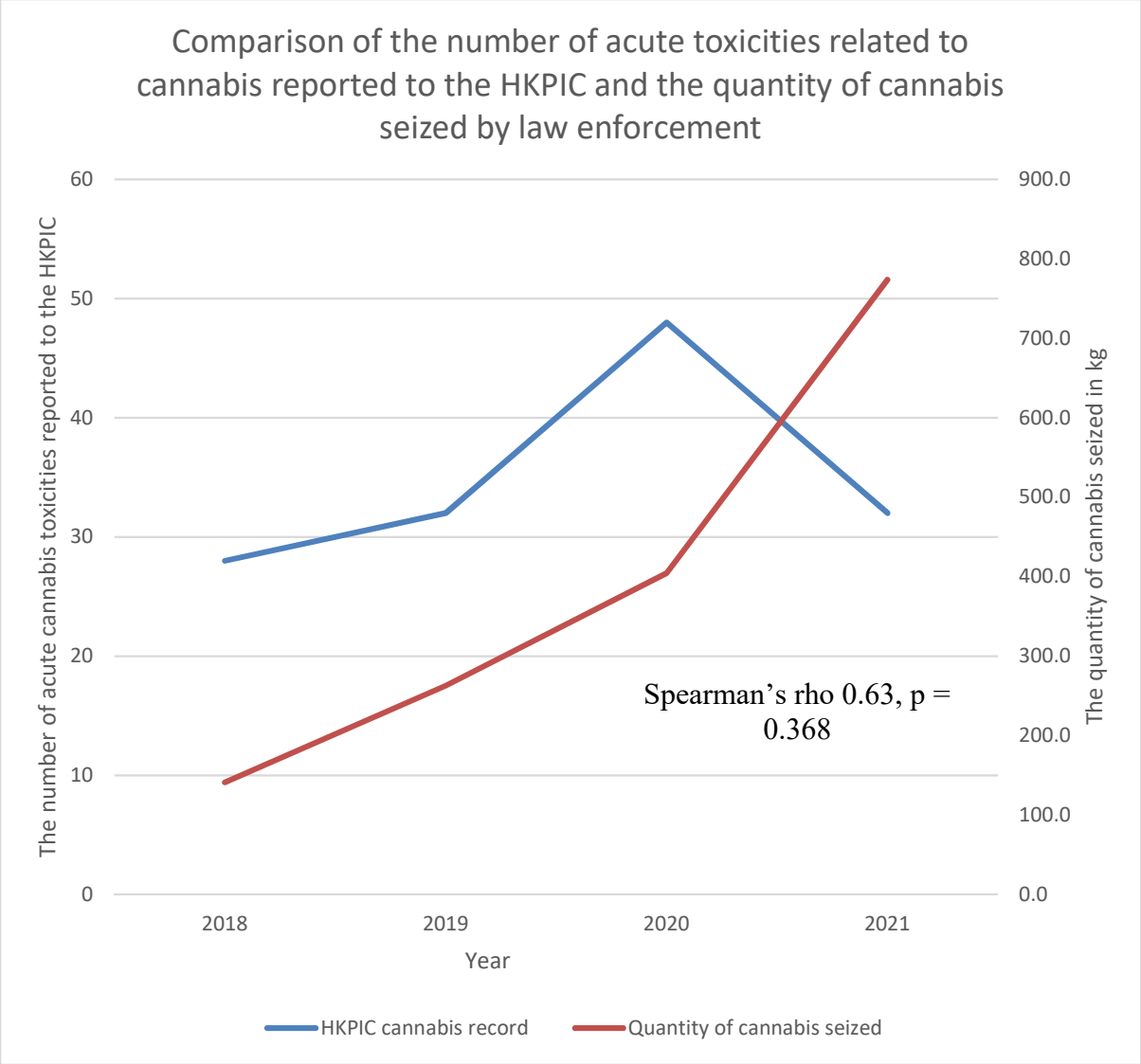


Figure 10. Comparison of the number of acute toxicities related to cannabis reported to the HKPIC and the quantity of cannabis seized by law enforcement.

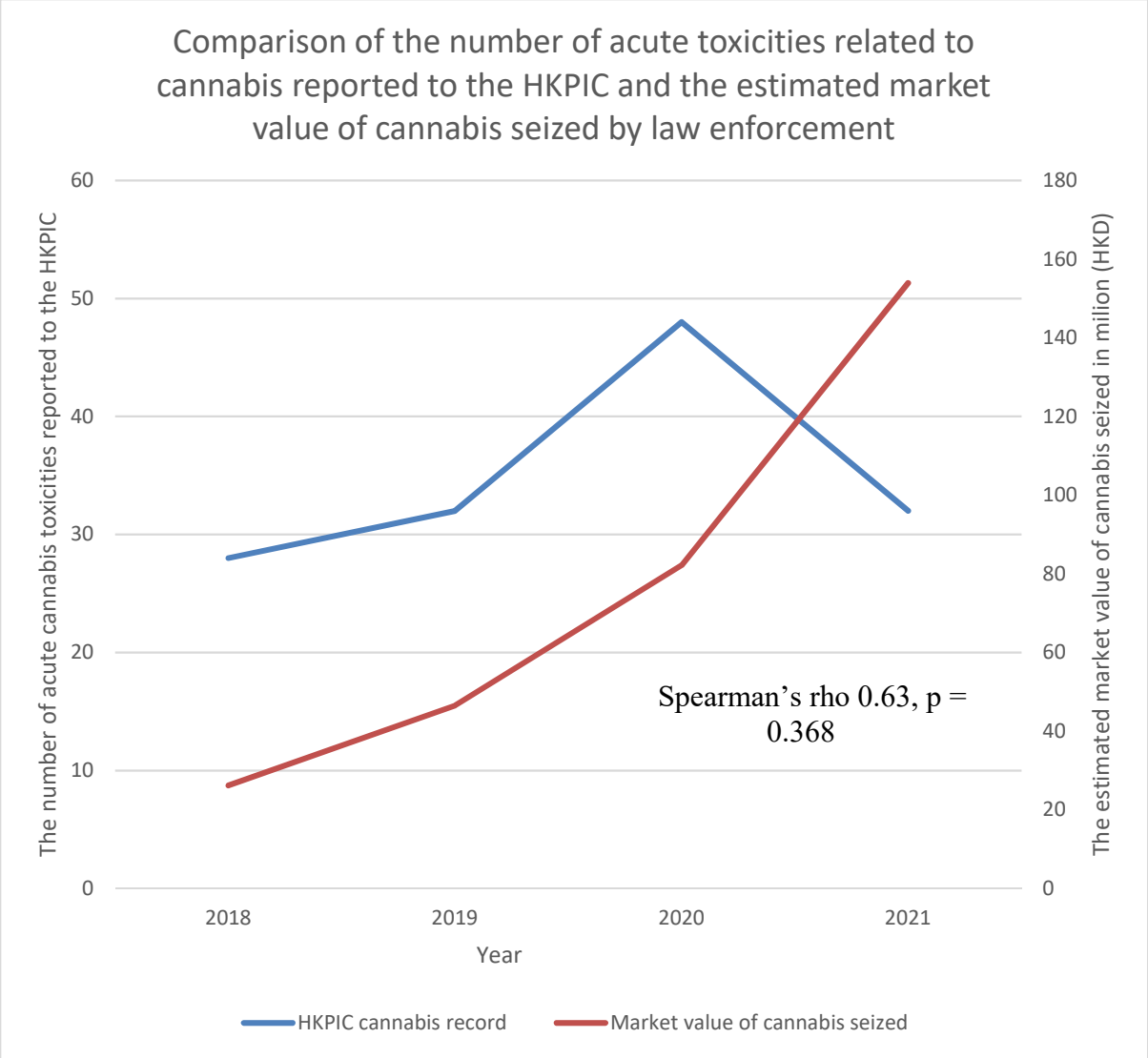


Figure 11. Comparison of the number of acute toxicities related to cannabis reported to the HKPIC and the estimated market value of cannabis seized by law enforcement.

4.1.5. Number of acute toxicities involving heroin

For heroin, Figure 12 shows that both the HKPIC and CRDA data showed a general decline trend from 2018 to 2022, with a significant correlation with them (Spearman's rho 0.89, p = 0.045). In contrary, both the quantity and the estimated market value of the heroin seized by law enforcement increased, which did not correlate with the HKPIC data (Figures 13 and 14).

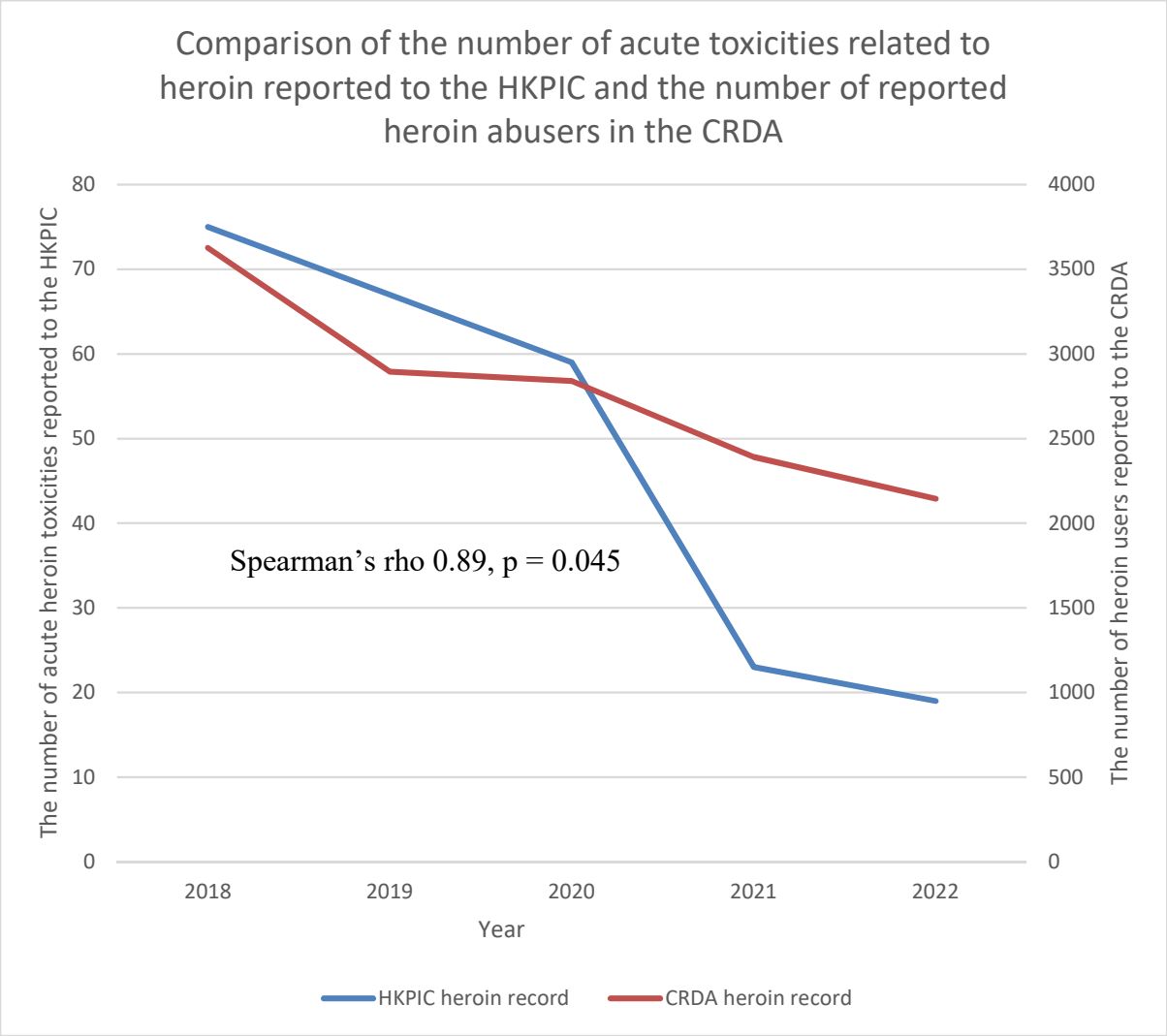


Figure 12. Comparison of the number of acute toxicities related to heroin reported to the HKPIC and the number of reported heroin abusers in the CRDA.

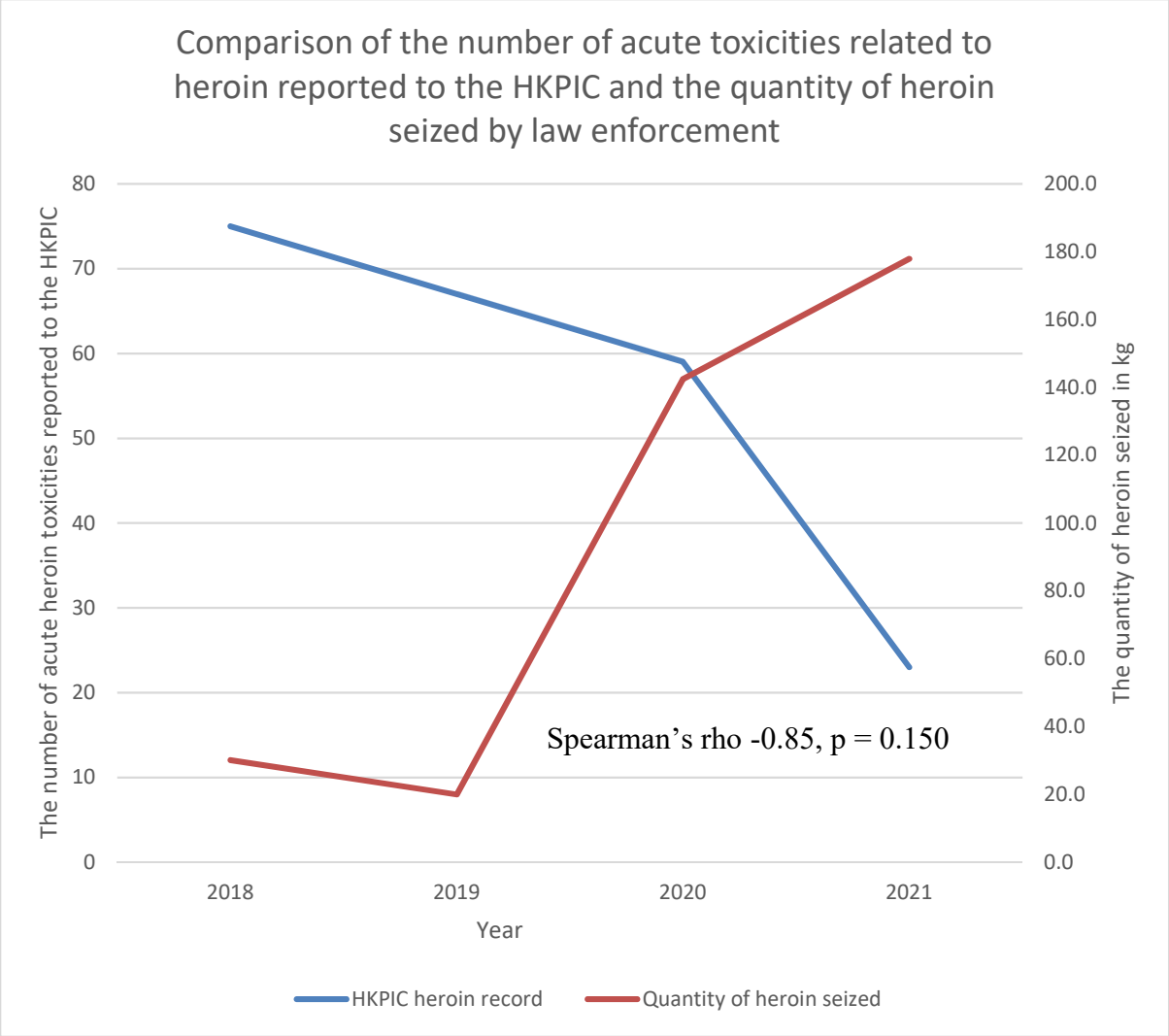


Figure 13. Comparison of the number of acute toxicities related to heroin reported to the HKPIC and the quantity of heroin seized by law enforcement.

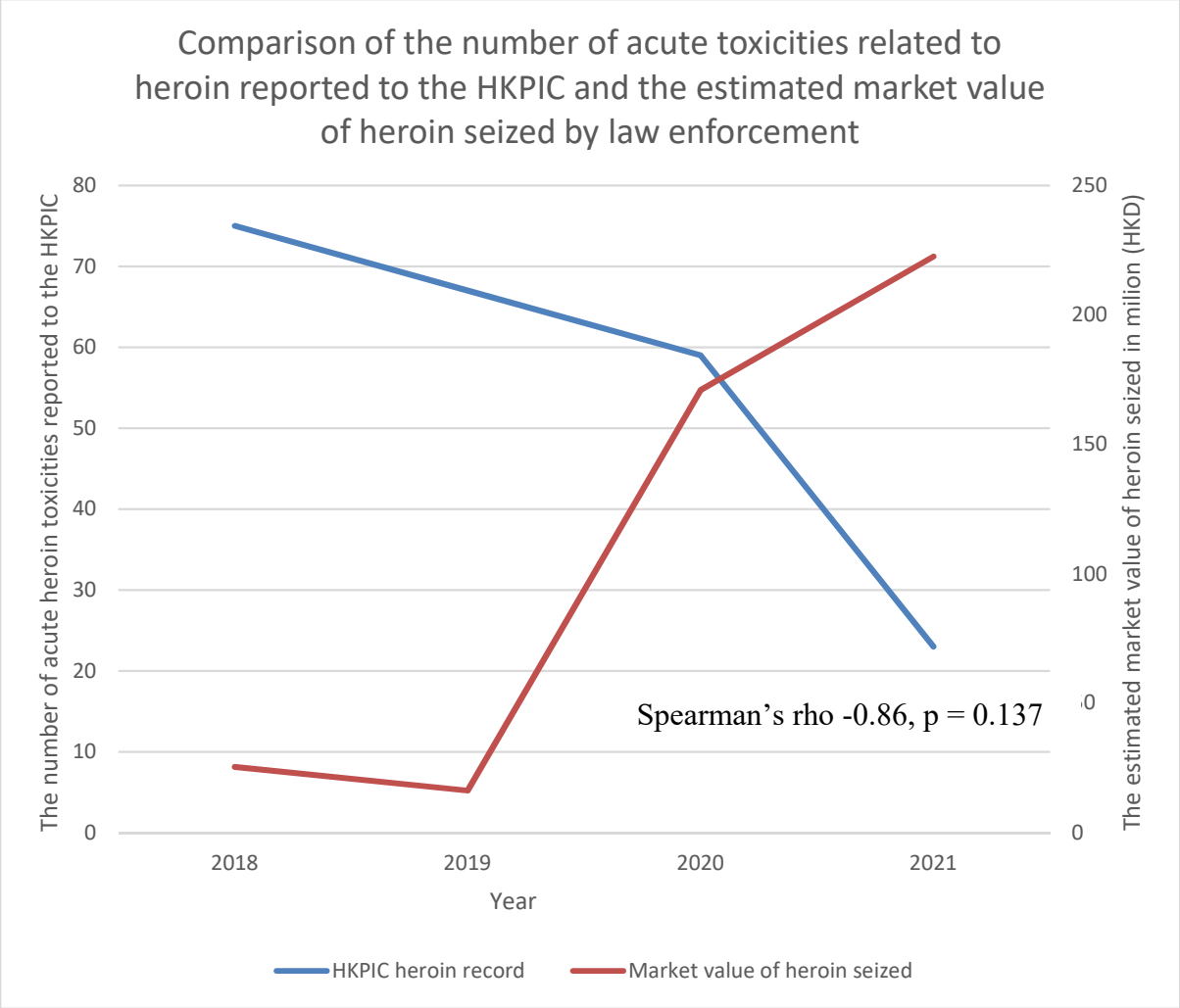


Figure 14. Comparison of the number of acute toxicities related to heroin reported to the HKPIC and the estimated market value of heroin seized by law enforcement.

4.1.6. Number of acute toxicities involving ketamine

Similar to cannabis, the peaks in the number of acute toxicities related to ketamine reported to the HKPIC and the number of ketamine abusers in the CRDA appeared in 2020 and 2021, respectively. A drop in both figures occurred in 2022 (Figure 15), and the correlation between these two figures was not statistically significant (Spearman's rho 0.50, p = 0.391). Notably, both the quantity and the estimated market value of the ketamine seized by law enforcement rose from 2018 to 2021, with a lack of correlation between the drug seizure data and the data from HKPIC (Figures 16 and 17).

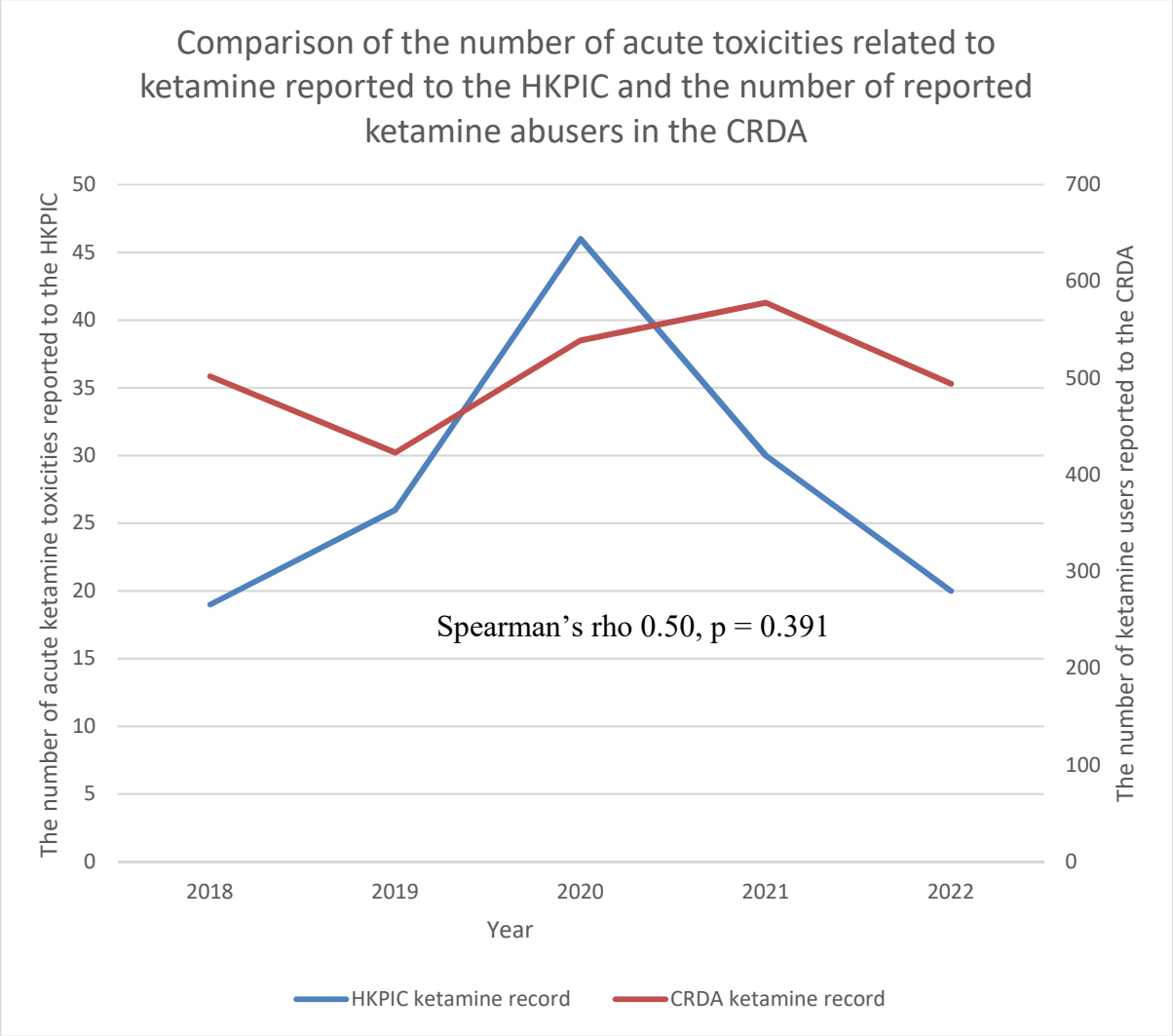


Figure 15. Comparison of the number of acute toxicities related to ketamine reported to the HKPIC and the number of reported ketamine abusers in the CRDA.

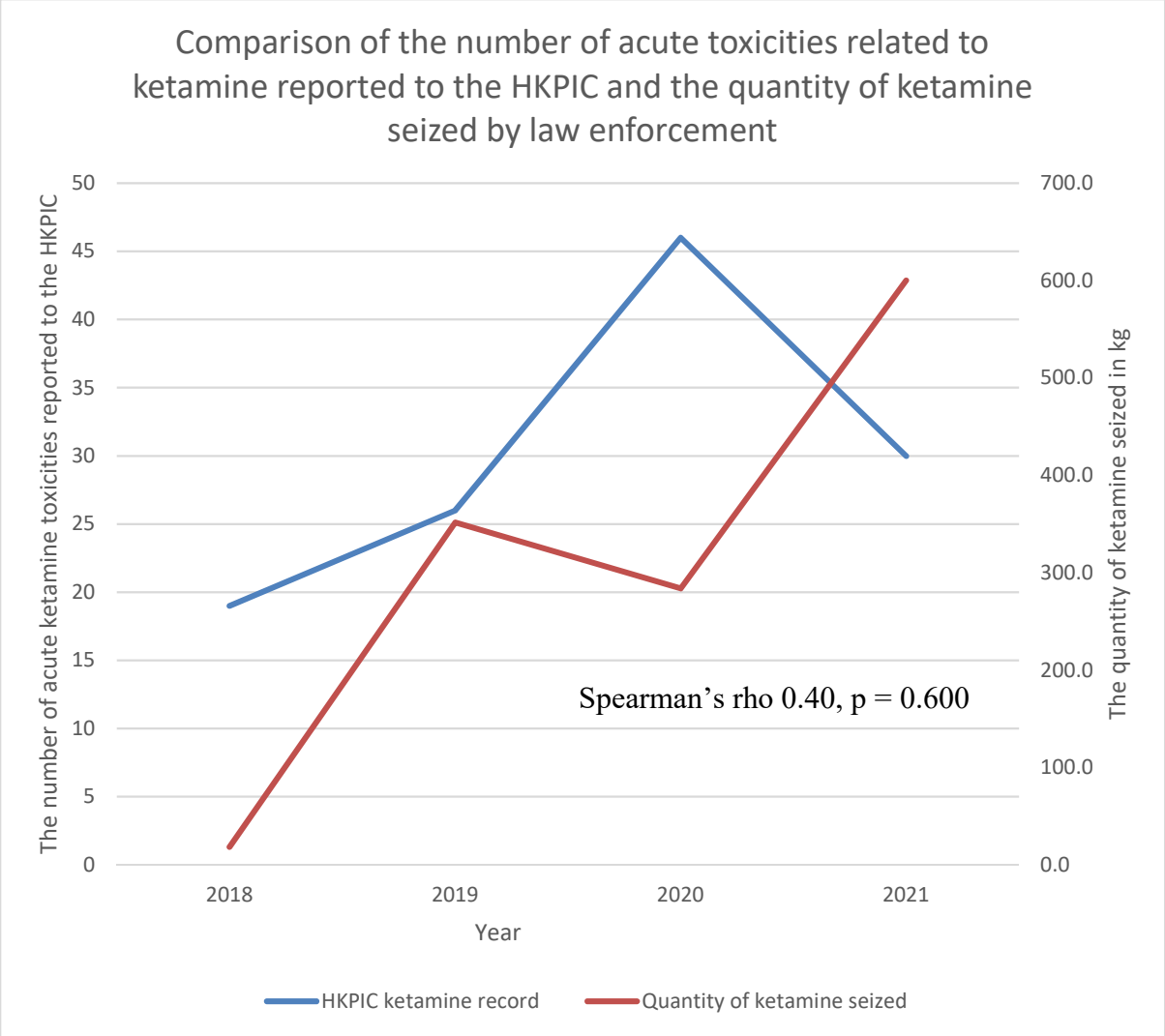


Figure 16. Comparison of the number of acute toxicities related to ketamine reported to the HKPIC and the quantity of ketamine seized by law enforcement.

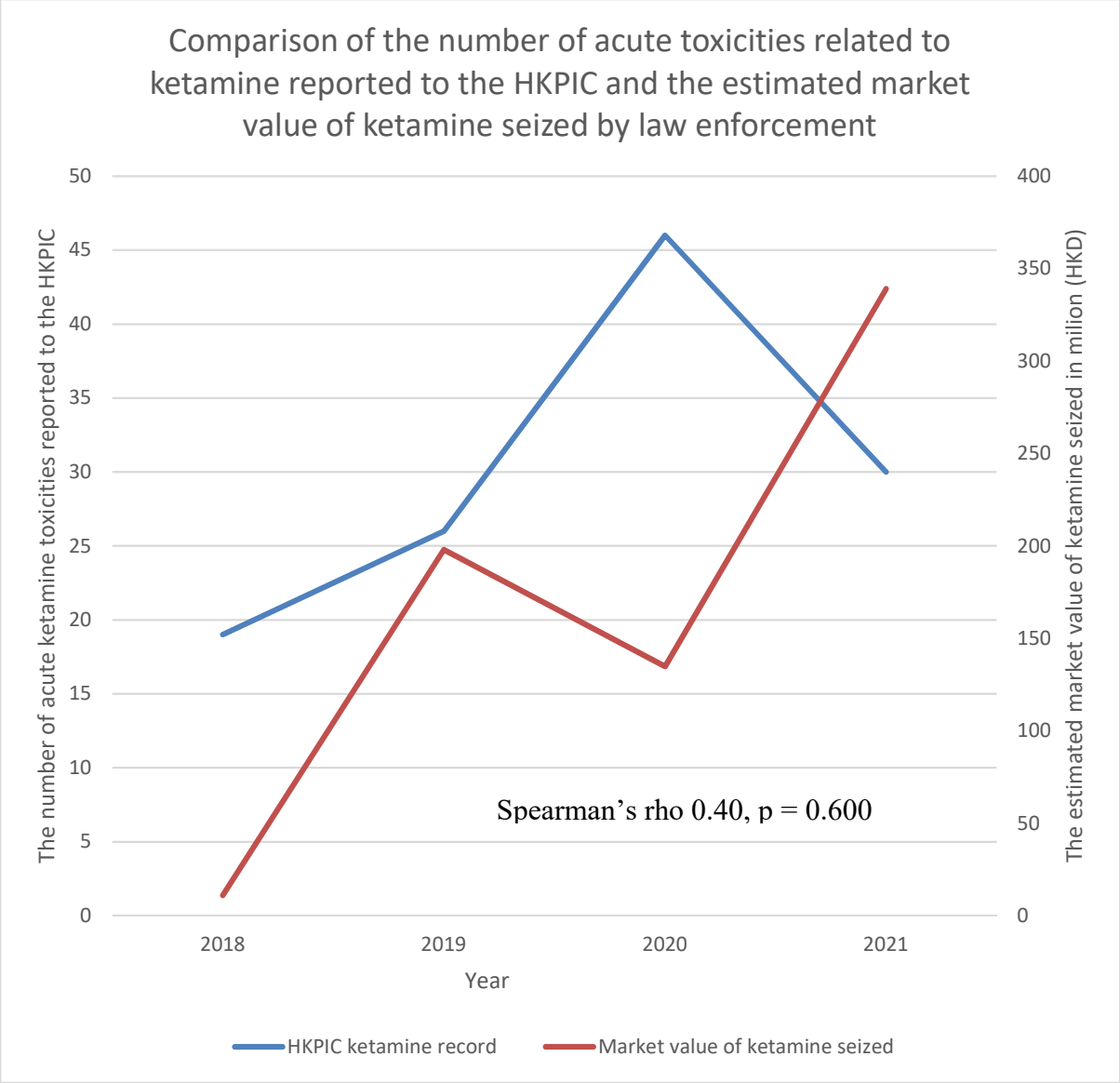


Figure 17. Comparison of the number of acute toxicities related to ketamine reported to the HKPIC and the estimated market value of ketamine seized by law enforcement.

4.1.7. Number of acute drug toxicities of patients under 21 years of age

For drug abusers under 21 years of age, the correlations between the number of acute toxicities reported to the HKPIC, the reported number of respective drug users in the CRDA and the drug seizure data are summarised in Table 4.

	Acute toxicities related to methamphetamine reported to HKPIC		Acute toxicities related to cocaine reported to HKPIC		Acute toxicities related to cannabis reported to HKPIC		Acute toxicities related to heroin reported to HKPIC		Acute toxicities related to ketamine reported to HKPIC	
	ρ (rho)	P value	ρ (rho)	P value	ρ (rho)	P value	ρ (rho)	P value	ρ (rho)	P value
Reported number of the respective drug abusers in CRDA	0.47	0.420	-0.45	0.450	0.20	0.747	0.71	0.182	-0.47	0.420
Quantity of the respective drug seized	-0.11	0.895	-0.11	0.895	0.80	0.200	-0.26	0.742	0	>0.99
Estimated market value of the respective drug seized	-0.11	0.895	-0.11	0.895	0.80	0.200	-0.26	0.742	0	>0.99

Table 4. Correlation between the HKPIC, CRDA and drug seizure data on drug abusers of methamphetamine, cocaine, cannabis, heroin and ketamine under the age of 21 years.

4.2. Interrupted time series analyses on the trends in drug toxicities and the impact of COVID-19, closure of social and recreational venues and social distancing measures

4.2.1. Overall trends

Figures 18–22 show the trends in acute toxicities involving methamphetamine, cocaine, cannabis, heroin and ketamine from January 2017 to January 2023. The pandemic period is shaded light grey and the periods of closure of Group 2 social and recreational premises are shaded dark grey in each diagram. The orange line represents the OxCGRT Stringency Index.

Figure 18. The trends in acute toxicities involving methamphetamine before and during the COVID-19 pandemic.

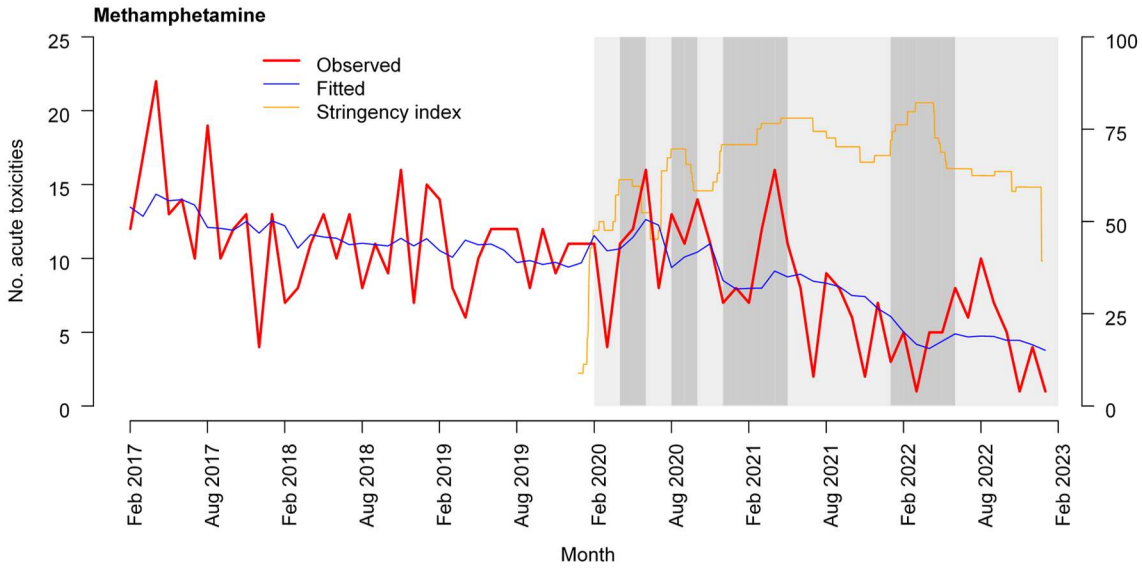


Figure 19. The trends in acute toxicities involving cocaine before and during the COVID-19 pandemic.

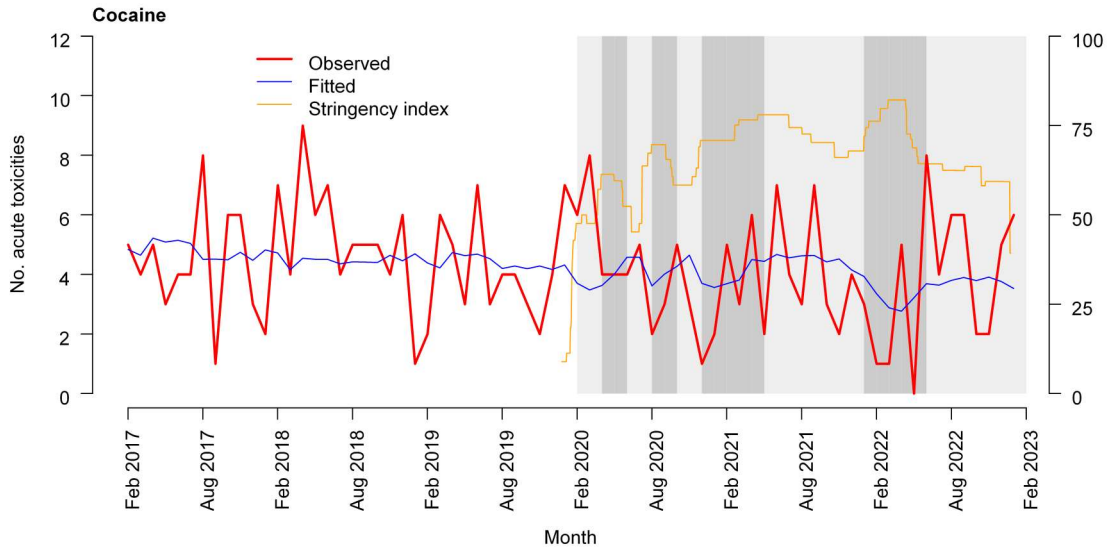


Figure 20. The trends in acute toxicities involving cannabis before and during the COVID-19 pandemic.

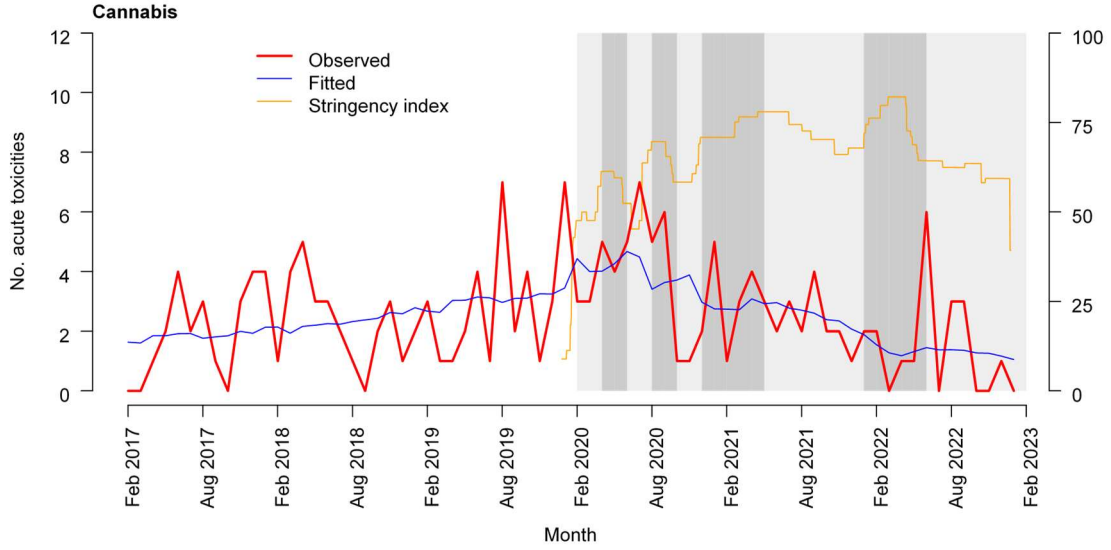


Figure 21. The trends in acute toxicities involving heroin before and during the COVID-19 pandemic .

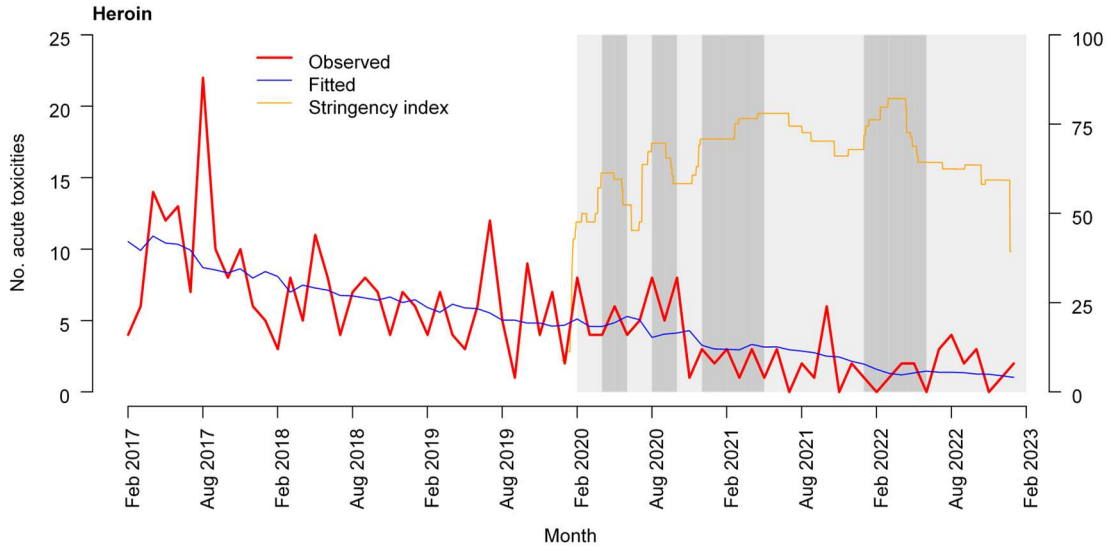
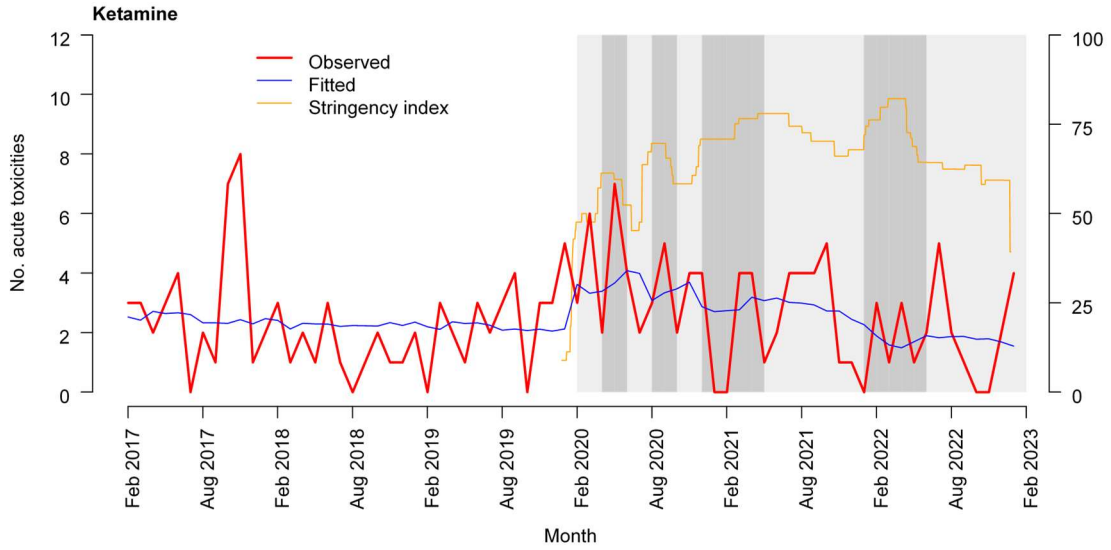


Figure 22. The trends in acute toxicities involving ketamine before and during the COVID-19 pandemic.



4.2.2. The impact of the COVID-19 pandemic

The impact of the COVID-19 pandemic on acute drug toxicities after accounting for long-term time trends and concurrent changes in ED attendance is summarised in Table 5. Acute toxicities involving methamphetamine, cannabis and heroin increased shortly at the outset of the COVID-19 pandemic but then decreased faster than the pre-pandemic period. Acute toxicities involving ketamine increased shortly after the pandemic and followed a similar

trend during the pandemic. As for cocaine, no significant changes in level and trend were observed during the pandemic.

Table 5. The impact of the COVID-19 pandemic on the levels and trends of acute drug toxicities

Acute toxicities	Level change		Trend change	
	RR	P value	RR	P value
Methamphetamine	5.11	<0.001	0.97	<0.001
Cocaine*	1.49	0.410	1.00	0.769
Cannabis	23.57	<0.001	0.93	<0.001
Heroin	4.77	0.011	0.97	0.045
Ketamine	6.50	0.003	0.98	0.122

Abbreviation: RR, relative risk

* Poisson regression was used due to instability of the negative binomial model

4.2.3. The impact of the pandemic and social and recreational venues closure

Table 6 summarises the combined impact of the COVID-19 pandemic and closure of Group 2 social and recreational venues on acute toxicities involving methamphetamine, cocaine, cannabis, heroin and ketamine, after accounting for the long-term time trend and concurrent changes in ED attendance. Since the closures of Group 1 social and recreational venues were too short during the pandemic, given the lower likelihood of drug exposure in Group 1 premises, we did not further analyse the impact of Group 1 premises on acute drug toxicities.

Table 6. The impact of the COVID-19 pandemic and closure of Group 2 social and recreational venues on acute drug toxicities.

Acute toxicities	Level change		Trend change		Group 2 social and recreational closure	
	RR	P value	RR	P value	RR	P value
Methamphetamine	4.50	<0.001	0.97	<0.001	1.16	0.242
Cocaine*	2.05	0.151	0.99	0.530	0.69	0.055
Cannabis	20.05	<0.001	0.94	<0.001	1.21	0.363
Heroin	4.72	0.016	0.97	0.048	1.01	0.952
Ketamine	6.45	0.005	0.98	0.127	1.01	0.969

Abbreviation: RR, relative risk

* Poisson regression was used due to instability of the negative binomial model

Similar increased acute toxicities involving methamphetamine, cannabis and heroin immediately were observed after the pandemic, followed by more rapid downtrends during the pandemic than before. Again, acute toxicities involving ketamine increased shortly after the beginning of the pandemic with no significant change in trend during the pandemic. No significant changes in the level and trend of cocaine toxicities were observed before and during the pandemic. Closure of Group 2 social and recreational venues did not have a significant impact on acute toxicities involving any of the study drugs.

4.2.4. The impact of the pandemic and social distancing measures

The impact of the COVID-19 pandemic and social distancing measures, as measured by the OxCGRT Stringency Index, on acute toxicities involving methamphetamine, cocaine, cannabis, heroin and ketamine is shown in Table 7. Figures 18–22 show that the most stringent peroid in early 2022 coincided with the lowest levels of acute drug toxicity of all study drugs.

After accounting for the long-term time trend and concurrent changes in ED attendance, we found that acute toxicities involving heroin increased shortly after the beginning of the pandemic, and decreased signficantly when social distancing measures were more stringent during the pandemic. Acute toxicities involving ketamine increased significantly shortly after the pandemic. However, social distancing measures did not have a signficant impact on ketamine toxicities during the pandemic

Table 7. The impact of the COVID-19 pandemic and social distancing measures on acute drug toxicities.

Acute toxicities	**Level change**		**OxCGRT**	
	RR	**P value**	**RR**	**P value**
Methamphetamine	1.33	0.383	1.00	0.311
Cocaine*	1.88	0.120	0.99	0.274
Cannabis	0.77	0.679	1.02	0.060
Heroin	4.38	0.003	0.98	0.012
Ketamine	3.70	0.026	1.00	0.545

Abbreviation: RR, relative risk

* Poisson regression was used due to instability of the negative binomial model

4.3. Drug use pattern and clinical presentations before and during the COVID-19 pandemic

4.3.1. Methamphetamine abuse before and during the COVID-19 pandemic

There were 412 episodes of acute toxicity related to methamphetamine before the COVID-19 pandemic and 275 episodes during the pandemic. The clinical features and drug use patterns of patients with recreational use of methamphetamine who presented before and during the COVID-19 pandemic are summarised in Table 8.

Compared with the pre-pandemic episodes, methamphetamine abusers were older (median age 39 years vs 37 years, p = 0.042), more likely to be male (82.9% vs 71.1%, p = 0.001) and more likely to be social allowance recipients (32.0% vs 24.0%, p = 0.021). No episodes involving non-local residents who abused methamphetamine were reported to the HKPIC during the COVID-19 pandemic. More patients used three or more different drugs during the pandemic than before (20.0% vs 11.4%). More patients used cannabis in addition to methamphetamine during the pandemic than before (4.7% vs 1.9%, p = 0.038), although the number remained low.

Table 8. Clinical features and drug use pattern of methamphetamine abusers before and during the COVID-19 pandemic.

	Before COVID-19 pandemic n = 412	During COVID-19 pandemic n = 275	P value
Age—median (IQR), year	37.0 (28.0–44.0)	39.0 (33.0–45.0)	0.042#
Sex—n (%)			
Female	117 (28.4)	47 (17.1)	0.001*
Male	293 (71.1)	228 (82.9)	
Transgender	2 (0.5)	0 (0)	
Social allowance—n (%)	99 (24.0)	88 (32.0)	0.021*
Ambulance case—n (%)	333 (80.8)	218 (79.3)	0.617*
Police involved—n (%)	125 (30.3)	85 (30.9)	0.874*
Non-local resident—n (%)	15 (3.6)	0 (0)	0.002*
MSM—n (%)	31 (7.5)	26 (9.5)	0.369*
Pregnant at the time of presentation—n (%)	2 (0.5)	1 (0.4)	>0.99**
Number of drugs abused—n (%)			
1	221 (53.6)	140 (50.9)	0.006*
2	144 (35.0)	80 (29.1)	
≥ 3	47 (11.4)	55 (20.0)	
Drug also abused at presentation—n (%)			
Cocaine	48 (11.7)	31 (11.3)	0.879*
Cannabis	8 (1.9)	13 (4.7)	0.038*

Heroin	40 (9.7)	26 (9.5)	0.912*
Ketamine	22 (5.3)	21 (7.6)	0.223*
MDMA	4 (1.0)	7 (2.5)	0.127**
Cough mixture or pills	40 (9.7)	29 (10.5)	0.721*
Zopiclone or zolpidem	29 (7.0)	28 (10.2)	0.143*
Benzodiazepine	25 (6.1)	18 (6.5)	0.800*
GHB	10 (2.4)	7 (2.5)	0.922*
Sildenafil	17 (4.1)	11 (4.0)	0.935*
Novel psychoactive substances	5 (1.2)	5 (1.8)	0.532**
Co-ingestion of alcohol—n (%)	25 (6.1)	25 (9.1)	0.135*
Inhalation as the primary route of exposure—n (%)	301 (73.1)	195 (70.9)	0.538*
Triage category—n (%)			
Category 1—Critical	43 (10.4)	42 (15.3)	0.201*
Category 2—Emergent	121 (29.4)	85 (30.9)	
Category 3—Urgent	228 (55.3)	138 (50.2)	
Category 4—Semi-urgent	20 (4.9)	10 (3.6)	
Category 5—Non-urgent	0 (0)	0 (0)	
Acute myocardial injury	30 (7.3)	28 (10.2)	0.180*
Myocardial infarction	1 (0.2)	0 (0)	>0.99**
Coma	14 (3.4)	13 (4.7)	0.380*
Seizure	12 (2.9)	9 (3.3)	0.788*
Agitation	124 (30.1)	112 (40.7)	0.004*
Confusion	165 (40.0)	120 (43.6)	0.350*
Drowsiness	71 (17.2)	63 (22.9)	0.066*
Any hallucination	82 (19.9)	72 (26.2)	0.053*
Any delusion	61 (14.8)	42 (15.3)	0.867*
Severe hyperthermia (temperature> 40°C)	4 (1.0)	7 (2.5)	0.127**
Acute kidney injury—n (%)	55 (13.3)	39 (14.2)	0.756*
Rhabdomyolysis—n (%)	81 (19.7)	58 (21.1)	0.647*
Overall PSS—median (IQR)	2.0 (2.0–2.0)	2.0 (2.0–2.0)	0.158#
AAPCC outcome classification			
Death	3 (0.7)	3 (1.1)	0.012*
Major effect	12 (2.9)	21 (7.6)	
Moderate effect	134 (32.5)	105 (38.2)	
Minor effect	256 (62.1)	141 (51.3)	
No effect	7 (1.7)	5 (1.8)	
Associated injury—n (%)	53 (12.9)	51 (18.5)	0.042*
Associated infection—n (%)	5 (1.2)	7 (2.5)	0.238**
Deliberate self-harm—n (%)	42 (10.2)	44 (16.0)	0.024*
Violent behaviours to others—n (%)	53 (12.9)	31 (11.3)	0.533*

Abbreviations: AAPCC, American Association of Poison Control Centers; GHB, gamma-hydroxbutyrate; IQR, interquartile range; MDMA, 3,4-methylenedioxy-methamphetamine; MSM, men having sex with men; PSS, Poison Severity Score

Footnotes: *Pearson Chi-square test, **Fisher's Exact test, #non-parametric test

During the pandemic, more patients than before presented with agitation after methamphetamine abuse (40.7% vs 30.1%, p = 0.004), with associated injury (18.5% vs 12.9%, p = 0.042) and with deliberate self-harm behaviours (16.0% vs 10.2%, p = 0.024). The proportions of patients who died and had major effects from methamphetamine exposure were significantly higher during the pandemic compared with the pre-pandemic period, although the overall PSS did not differ significantly.

Table 9 summarises the clinical management and psychosocial interventions provided to patients with methamphetamine misuse before and during the COVID-19 pandemic. Although the use of supportive treatment and physical and chemical restraints did not differ significantly, higher proportions of methamphetamine users required invasive treatment, such as intubation and mechanical ventilation (6.9% vs 3.2%, p = 0.022) and renal replacement therapy (1.8% vs 0.2%, p = 0.040) during the pandemic compared to the pre-pandemic period. More patients were admitted to general wards (50.5% vs 35.7%, p < 0.001) and ICUs (10.2% vs 4.9%, p = 0.007), with a significantly longer length of hospital stay (median 3.15 days vs 1.93 days, p = 0.006). During the pandemic period, more patients were referred to see social workers during the index hospitalisation (28.4% vs 19.4%, p = 0.006) compared with the pre-pandemic period. The proportions of patients who received psychiatric consultations and NGO referrals for drug rehabilitation and treatment services did not differ significantly between the pre-pandemic and pandemic periods.

Table 9. Clinical management and psychosocial interventions of acute toxicities related to methamphetamine before and during the COVID-19 pandemic.

	Before COVID-19 pandemic n = 412	During COVID-19 pandemic n = 275	P value
Physical restraint—n (%)	160 (38.8)	112 (40.7)	0.619*
Chemical restraint—n (%)	110 (26.7)	73 (26.5)	0.964*
Diazepam	100 (24.3)	44 (16.0)	0.009*
Lorazepam	14 (3.4)	15 (5.5)	0.189*
Midazolam	49 (11.9)	43 (15.6)	0.158*
Haloperidol	18 (4.4)	6 (2.2)	0.126*
Dexmedetomidine	6 (1.5)	5 (1.8)	0.762**
Propofol	6 (1.5)	5 (1.8)	0.762**
Gastrointestinal decontamination—n (%)	2 (0.5)	6 (2.2)	0.065**
Gastric lavage	0 (0)	1 (0.4)	0.400**
Activated Charcoal	2 (0.5)	5 (1.8)	0.123**
Intravenous fluid—n (%)	216 (52.4)	134 (48.7)	0.342*
Inotrope—n (%)	8 (1.9)	5 (1.8)	0.907*
Supplemental oxygen—n (%)	57 (13.8)	53 (19.3)	0.057*
Intubation and mechanical ventilation—n (%)	13 (3.2)	19 (6.9)	0.022*
Administration of anti-arrhythmic—n (%)	0 (0)	1 (0.4)	0.400**
Electric therapy for arrhythmia—n (%)	1 (0.2)	1 (0.4)	>0.99*
Cardiopulmonary resuscitation—n (%)	3 (0.7)	0 (0)	0.279**
Renal replacement therapy—n (%)	1 (0.2)	5 (1.8)	0.040**
ECMO—n (%)	0 (0)	0 (0)	N/A
Direct discharge from the ED—n (%)	17 (4.1)	6 (2.2)	0.165*
Discharge against medical advice/patient walked away before or after consultation—n (%)	65 (15.8)	51 (18.5)	0.343*
Managed in emergency medicine ward or observation ward in the ED—n (%)	242 (58.7)	112 (40.7)	<0.001
General ward admission—n (%)	147 (35.7)	139 (50.5)	<0.001*
ICU admission—n (%)	20 (4.9)	28 (10.2)	0.007*
Psychiatry ward/hospital admission—n (%)	103 (25.0)	77 (28.0)	0.381*
Total length of hospital stay—median (IQR), day^	1.93 (0.83–9.76)	3.15 (1.35–14.36)	0.006#
Psychiatric consultation during the index episode—n (%)	274 (66.5)	199 (72.4)	0.104*
Referral to social worker—n (%)	80 (19.4)	78 (28.4)	0.006*
Referral to NGO drug treatment and rehabilitation service—n (%)	28 (6.8)	29 (10.5)	0.081*

Abbreviations: ECMO, extracorporeal membrane oxygenation; ED, emergency department; ICU, intensive care unit; LOS, length of stay, NGO, non-governmental organisation

Footnotes: *Pearson Chi-square test, **Fisher's Exact test, #non-parametric test

^calculated only for those hospitalised patients

4.3.2. Cocaine abuse before and during the COVID-19 pandemic

The number of reported acute toxicities related to cocaine was 164 during the pre-pandemic period and 142 during the pandemic period, as summarised in Table 10. The patient age, sex and drug use pattern of cocaine users did not differ significantly between the periods. More cocaine abusers co-used ketamine during the pandemic than before (26.1% vs 17.1%, p = 0.055), but the difference did not reach statistical significance. More patients received social allowances (9.2% vs 3.7%, p = 0.047) and fewer patients were non-local residents (1.4% vs 9.8%, p = 0.003) during the pandemic than before. Notably, significantly higher proportions of cocaine users developed acute myocardial injury (12.7% vs 4.9%, p = 0.015) and drowsiness (25.4% vs 14.6%, p = 0.019) during the pandemic than in the pre-pandemic period. More patients had major effects of acute toxicities (10.6% vs 1.8%, p = 0.025) and associated infection (2.8% vs 0%, p = 0.045) during the pandemic than before.

Table 10. Clinical features and drug use pattern of cocaine users before and during the COVID-19 pandemic.

	Before COVID-19 pandemic n = 164	During COVID-19 pandemic n = 142	P value
Age—median (IQR), year	31.0 (26.0–38.0)	32.0 (27.0–38.0)	0.535#
Sex—n (%)			
Female	50 (30.5)	40 (28.2)	0.657
Male	114 (69.5)	102 (71.8)	
Social allowance—n (%)	6 (3.7)	13 (9.2)	0.047*
Ambulance case—n (%)	110 (67.1)	103 (72.5)	0.300*
Police involved—n (%)	41 (25.0)	44 (31.0)	0.244*
Non-local resident—n (%)	16 (9.8)	2 (1.4)	0.003*
MSM	1 (0.6)	0 (0.0)	>0.99**
Pregnant at the time of presentation—n (%)	2 (1.2)	1 (0.7)	>0.99**
Number of drugs abused—n (%)			
1	59 (36.0)	54 (38.0)	0.232*
2	73 (44.5)	51 (35.9)	
≥ 3	32 (19.5)	37 (26.1)	
Drug abused at presentation—n (%)			
Methamphetamine	48 (29.3)	31 (21.8)	0.138*
Cannabis	14 (8.5)	11 (7.7)	0.801*
Heroin	5 (3.0)	4 (2.8)	>0.99**
Ketamine	28 (17.1)	37 (26.1)	0.055*
MDMA	15 (9.1)	14 (9.9)	0.832*
Cough mixture or pills	8 (4.9)	10 (7.0)	0.422*
Zopiclone or zolpidem	10 (6.1)	12 (8.5)	0.427*
Benzodiazepine	11 (6.7)	6 (4.2)	0.345*
Novel psychoactive substances	13 (7.9)	7 (4.9)	0.290*
Co-ingestion of alcohol—n (%)	37 (22.6)	31 (21.8)	0.878*
Insufflation as the primary route of exposure—n (%)	73 (44.5)	62 (43.7)	0.881*
Triage category—n (%)			

Category 1—Critical	16 (9.8)	20 (14.1)	0.540*
Category 2—Emergent	53 (32.3)	50 (35.2)	
Category 3—Urgent	85 (51.8)	65 (45.8)	
Category 4—Semi-urgent	10 (6.1)	7 (4.9)	
Category 5—Non-urgent	0 (0)	0 (0)	
Acute myocardial injury	8 (4.9)	18 (12.7)	0.015*
Myocardial infarction	0 (0)	0 (0)	N/A
Coma	4 (2.4)	5 (3.5)	0.738**
Seizure	8 (4.9)	8 (5.6)	0.767*
Agitation	42 (25.6)	42 (29.6)	0.438*
Confusion	41 (25.0)	46 (32.4)	0.153*
Drowsiness	24 (14.6)	36 (25.4)	0.019*
Any hallucination	14 (8.5)	17 (12.0)	0.321*
Any delusion	10 (6.1)	8 (5.6)	0.863*
Severe hyperthermia (temperature> 40°C)	2 (1.2)	2 (1.4)	>0.99**
Acute kidney injury—n (%)	13 (7.9)	18 (12.7)	0.170*
Rhabdomyolysis—n (%)	19 (11.6)	20 (14.1)	0.513*
Overall PSS—median (IQR)	2.0 (1.0–2.0)	2.0 (1.0–2.0)	0.004#
AAPCC outcome classification			
Death	2 (1.2)	1 (0.7)	0.025*
Major effect	3 (1.8)	15 (10.6)	
Moderate effect	45 (27.4)	40 (28.2)	
Minor effect	109 (66.5)	83 (58.5)	
No effect	5 (3.0)	3 (2.1)	
Associated injury—n (%)	26 (15.9)	27 (19.0)	0.466*
Associated infection—n (%)	0 (0)	4 (2.8)	0.045**
Deliberate self-harm—n (%)	23 (14.0)	29 (20.4)	0.137*
Violent behaviours to others—n (%)	14 (8.5)	15 (10.6)	0.546*

Abbreviations: AAPCC, American Association of Poison Control Centers; IQR, interquartile range; MDMA, 3,4-methylenedioxy-methamphetamine; MSM, men having sex with men; PSS, Poison Severity Score

Footnotes: *Pearson Chi-square test, **Fisher's Exact test, #non-parametric test

Overall, the supportive and invasive treatment for acute toxicities related to cocaine use did not differ significantly between the pre-pandemic and pandemic periods. However, more patients were admitted to general wards (48.6% vs 25.6%, $p < 0.001$) and ICUs (12.7% vs 4.3%, $p = 0.007$) during the pandemic than before, with a significantly longer hospital length of stay (median 1.93 days vs 0.97 days, $p = 0.001$). However, more patients discharged against medical advice or left before or after consultation during the pandemic period (33.8% vs 19.5%, $p = 0.005$). The practice of psychiatric consultation and referral to social workers and NGO drug rehabilitation and treatment services did not change significantly (Table 11).

Table 11. Clinical management and psychosocial interventions of acute toxicities related to cocaine abuse before and during the COVID-19 pandemic.

	Before COVID-19 pandemic n = 164	During COVID-19 pandemic n = 142	P value
Physical restraint—n (%)	50 (30.5)	36 (25.4)	0.319*
Chemical restraint—n (%)	39 (23.8)	28 (19.7)	0.391*
Diazepam	37 (22.6)	28 (19.7)	0.544*
Lorazepam	6 (3.7)	5 (3.5)	0.949*
Midazolam	24 (14.6)	17 (12.0)	0.495*
Haloperidol	1 (0.6)	6 (4.2)	0.052**
Dexmedetomidine	0 (0)	3 (2.1)	0.099**
Propofol	2 (1.2)	0 (0)	0.501**
Gastrointestinal decontamination—n (%)	4 (2.4)	3 (2.1)	>0.99**
Gastric lavage	1 (0.6)	0 (0)	>0.99**
Activated Charcoal	3 (1.8)	3 (2.1)	>0.99**
Intravenous fluid—n (%)	88 (53.7)	64 (45.1)	0.134*
Inotrope—n (%)	4 (2.4)	5 (3.5)	0.738**
Supplemental oxygen—n (%)	24 (14.6)	33 (23.2)	0.054*
Intubation and mechanical ventilation—n (%)	5 (3.0)	8 (5.6)	0.264*
Renal replacement therapy—n (%)	1 (0.6)	3 (2.1)	0.340**
Administration of anti-arrhythmic—n (%)	0 (0)	0 (0)	N/A
Electric therapy for arrhythmia—n (%)	1 (0.6)	0 (0)	>0.99**
Cardiopulmonary resuscitation—n (%)	2 (1.2)	1 (0.7)	>0.99**
ECMO—n (%)	0 (0)	0 (0)	N/A
Direct discharge from the ED—n (%)	16 (9.8)	11 (7.7)	0.537*
Discharge against medical advice/patient walked away before or after consultation—n (%)	32 (19.5)	48 (33.8)	0.005*
Managed in emergency medicine ward or observation ward in the ED—n (%)	97 (59.1)	54 (38.0)	<0.001*
General ward admission—n (%)	42 (25.6)	69 (48.6)	<0.001*
ICU admission—n (%)	7 (4.3)	18 (12.7)	0.007*
Psychiatry ward/hospital admission—n (%)	15 (9.1)	18 (12.7)	0.321*
Total length of hospital stay—median (IQR), day^	0.97 (0.48–2.96)	1.93 (0.89–4.87)	0.001
Psychiatric consultation during the index episode—n (%)	73 (44.5)	77 (54.2)	0.090*
Referral to social worker—n (%)	29 (17.7)	32 (22.5)	0.289*
Referral to NGO drug treatment and rehabilitation service—n (%)	6 (3.7)	6 (4.2)	0.799*

Abbreviations: ED, emergency department; ICU, intensive care unit; LOS, length of stay, NGO, non-governmental organisation

Footnotes: *Pearson Chi-square test, **Fisher's Exact test, #non-parametric test

^calculated only for those hospitalised patients

4.3.3. Cannabis abuse before and during the COVID-19 pandemic

The number of acute toxicities that involved cannabis before and during the COVID-19 pandemic were 87 and 93, respectively (Table 12). During the pandemic, more female patients with acute cannabis toxicities (35.5% vs 18.4%, p = 0.01), more ambulance transport (77.4% vs 63.2%, p = 0.037) and less co-ingestion of alcohol (10.8% vs 25.3%, p = 0.011) were observed compared with the pre-pandemic period. No significant difference was found in drug use patterns, clinical presentations or outcomes of patients with acute cannabis toxicities between the pre-pandemic and pandemic periods. Table 13 summarises the clinical and psychosocial interventions given to patients with cannabis use before and during the pandemic, which did not change significantly except that more patients were admitted to general wards during the pandemic (46.2% vs 27.6%, p = 0.01).

Table 12. Clinical features and drug use pattern of cannabis users before and during the COVID-19 pandemic.

	Before COVID-19 pandemic n = 87	During COVID-19 pandemic n = 93	P value
Age—median (IQR), year	25.0 (19.8–31.5)	25.0 (19.8–31.0)	0.891#
Sex—n (%)			
Female	16 (18.4)	33 (35.5)	0.010*
Male	71 (81.6)	60 (64.5)	
Social allowance—n (%)	4 (4.6)	4 (4.3)	>0.99**
Ambulance case—n (%)	55 (63.2)	72 (77.4)	0.037*
Police involved—n (%)	21 (24.1)	25 (26.9)	0.673*
Non-local resident—n (%)	5 (5.7)	0 (0)	0.060**
MSM	1 (1.1)	1 (1.1)	>0.99**
Pregnant at the time of presentation—n (%)	0 (0)	0 (0)	N/A
Number of drugs abused—n (%)			
1	55 (63.2)	53 (57.0)	0.424*
2	25 (28.7)	27 (29.0)	
≥ 3	7 (8.0)	13 (14.0)	
Drug abused at presentation—n (%)			
Methamphetamine	8 (9.2)	13 (14.0)	0.318*
Cocaine	14 (16.1)	11 (11.8)	0.408*
Heroin	1 (1.1)	0 (0)	0.483**
Ketamine	2 (2.3)	6 (6.5)	0.280**
MDMA	2 (2.3)	4 (4.3)	0.683**
Cough mixture or pills	5 (5.7)	2 (2.2)	0.266**
Zopiclone or zolpidem	1 (1.1)	1 (1.1)	>0.99**
Benzodiazepine	0 (0)	1 (1.1)	>0.99**
Novel psychoactive substances	2 (2.3)	2 (2.2)	>0.99**
Co-ingestion of alcohol—n (%)	22 (25.3)	10 (10.8)	0.011*

Inhalation as the primary route of exposure—n (%)	58 (66.7)	67 (72.0)	0.434*
Triage category—n (%)			
Category 1—Critical	6 (6.9)	7 (7.5)	0.959*
Category 2—Emergent	22 (25.3)	22 (23.7)	
Category 3—Urgent	54 (62.1)	60 (64.5)	
Category 4—Semi-urgent	5 (5.7)	4 (4.3)	
Category 5—Non-urgent	0 (0)	0 (0)	
Acute myocardial injury	1 (1.1)	7 (7.5)	0.065**
Myocardial infarction	0 (0)	0 (0)	N/A
Coma	1 (1.1)	4 (4.3)	0.369**
Seizure	2 (2.3)	3 (3.2)	>0.99**
Agitation	23 (26.4)	24 (25.8)	0.923*
Confusion	23 (26.4)	33 (35.5)	0.190*
Drowsiness	7 (8.0)	13 (14.0)	0.206*
Any hallucination	11 (12.6)	9 (9.7)	0.527*
Any delusion	5 (5.7)	7 (7.5)	0.632*
Severe hyperthermia (temperature> 40°C)	0 (0)	1 (1.1)	>0.99**
Acute kidney injury—n (%)	8 (9.2)	9 (9.7)	0.912*
Rhabdomyolysis—n (%)	12 (13.8)	11 (11.8)	0.693*
Overall PSS—median (IQR)	2.0 (1.0–2.0)	2.0 (1.0–2.0)	0.207#
AAPCC outcome classification			
Death	0 (0)	1 (1.1)	0.360*
Major effect	3 (3.4)	3 (3.2)	
Moderate effect	24 (27.6)	29 (31.2)	
Minor effect	60 (69.0)	57 (61.3)	
No effect	0 (0)	3 (3.2)	
Associated injury—n (%)	13 (14.9)	14 (15.1)	0.983*
Associated infection—n (%)	0 (0)	2 (2.2)	0.498**
Deliberate self-harm—n (%)	11 (12.6)	5 (5.4)	0.087*
Violent behaviours to others—n (%)	7 (8.0)	6 (6.5)	0.680*

Abbreviations: AAPCC, American Association of Poison Control Centers; IQR, interquartile range; MDMA, 3,4-methylenedioxy-methamphetamine; MSM, men having sex with men; PSS, Poison Severity Score

Footnotes: *Pearson Chi-square test, **Fisher's Exact test, #non-parametric test

Table 13. Clinical management and psychosocial interventions of acute toxicities related to cannabis before and during the COVID-19 pandemic.

	Before COVID-19 pandemic n = 87	During COVID-19 pandemic n = 93	P value
Physical restraint—n (%)	32 (36.8)	23 (24.7)	0.079*
Chemical restraint—n (%)	22 (25.3)	19 (20.4)	0.437*
Diazepam	19 (21.8)	17 (18.3)	0.551*
Lorazepam	0 (0)	5 (5.4)	0.060**
Midazolam	16 (18.4)	12 (12.9)	0.310*
Haloperidol	0 (0)	2 (2.2)	0.498**
Dexmedetomidine	1 (1.1)	3 (3.2)	0.622**
Propofol	1 (1.1)	0 (0)	0.483**
Gastrointestinal decontamination—n (%)	2 (2.3)	3 (3.2)	>0.99**
Gastric lavage	0 (0)	0 (0)	N/A
Activated Charcoal	2 (2.3)	3 (3.2)	>0.99**
Intravenous fluid—n (%)	44 (50.6)	44 (47.3)	0.662*
Inotrope—n (%)	0 (0)	0 (0)	N/A
Supplemental oxygen—n (%)	10 (11.5)	7 (7.5)	0.363*
Intubation and mechanical ventilation—n (%)	2 (2.3)	4 (4.3)	0.683**
Renal replacement therapy—n (%)	0 (0)	1 (1.1)	>0.99**
Administration of anti-arrhythmic—n (%)	0 (0)	0 (0)	N/A
Electric therapy for arrhythmia—n (%)	0 (0)	0 (0)	N/A
Cardiopulmonary resuscitation—n (%)	0 (0)	0 (0)	N/A
ECMO—n (%)	0 (0)	0 (0)	N/A
Direct discharge from the ED—n (%)	9 (10.3)	8 (8.6)	0.690*
Discharge against medical advice/patient walked away before or after consultation—n (%)	14 (16.1)	21 (22.6)	0.272*
Managed in emergency medicine ward or observation ward in the ED—n (%)	46 (52.9)	37 (39.8)	0.078*
Admission to the general ward—n (%)	24 (27.6)	43 (46.2)	0.010*
ICU admission—n (%)	3 (3.4)	7 (7.5)	0.333**
Admission to psychiatry ward/hospital—n (%)	9 (10.3)	10 (10.8)	0.929*
Total length of hospital stay—median (IQR), day^	0.89 (0.50–2.74)	1.61 (0.60–3.70)	0.072#
Psychiatric consultation during the index episode—n (%)	40 (46.0)	46 (49.5)	0.640*
Referral to social worker—n (%)	12 (13.8)	22 (23.7)	0.091*
Referral to NGO drug treatment and rehabilitation service—n (%)	2 (2.3)	7 (7.5)	0.171**

Abbreviations: ED, emergency department; ICU, intensive care unit; LOS, length of stay, NGO, non-governmental organisation

Footnotes: *Pearson Chi-square test, **Fisher's Exact test, #non-parametric test

^calculated only for those hospitalised patients

4.3.4. Heroin abuse before and during the COVID-19 pandemic

Heroin was involved in 259 and 101 episodes of acute toxicities reported to the HKPIC before and during the COVID-19 pandemic, respectively. Notably, more heroin abusers also used methamphetamine (25.7% vs 15.4%, p = 0.023) and benzodiazepine (26.7% vs 15.8%, p = 0.018) during the pandemic period than before. A significantly higher proportion of patients presented with agitation (15.8% vs 7.7%, p = 0.021), confusion (27.7% vs 15.8%, p = 0.010) and hallucination (6.9% vs 1.9%, p = 0.043) during the pandemic compared to the pre-pandemic period (Table 14).

Table 14. Clinical features and drug use pattern of heroin abusers before and during the COVID-19 pandemic.

	Before COVID-19 pandemic n = 259	During COVID-19 pandemic n = 101	P value
Age—median (IQR), year	50.0 (43.8–61.0)	53.0 (43.0–64.0)	0.149#
Sex—n (%)			
Female	16 (6.2)	11 (10.9)	0.127*
Male	243 (93.8)	90 (89.1)	
Social allowance—n (%)	134 (51.7)	56 (55.4)	0.527*
Ambulance case—n (%)	248 (95.8)	91 (90.1)	0.040*
Police involved—n (%)	51 (19.7)	23 (22.8)	0.516*
Non-local resident—n (%)	1 (0.4)	1 (1.0)	0.477**
MSM	1 (0.4)	0 (0)	>0.99**
Pregnant at the time of presentation—n (%)	0 (0)	0 (0)	N/A
Number of drugs abused—n (%)			
1	167 (64.5)	55 (54.5)	0.197*
2	61 (23.6)	29 (28.7)	
≥ 3	31 (12.0)	17 (16.8)	
Drug abused at presentation—n (%)			
Methamphetamine	40 (15.4)	26 (25.7)	0.023*
Cocaine	5 (1.9)	4 (4.0)	0.275**
Cannabis	1 (0.4)	0 (0)	>0.99**
Ketamine	0 (0)	0 (0)	N/A
MDMA	0 (0)	0 (0)	N/A
Cough mixture or pills	19 (7.3)	4 (4.0)	0.239*
Zopiclone or zolpidem	18 (6.9)	4 (4.0)	0.287*
Benzodiazepine	41 (15.8)	27 (26.7)	0.018*
Novel psychoactive substances	0 (0)	0 (0)	N/A
Co-ingestion of alcohol—n (%)	13 (5.0)	7 (6.9)	0.477*
Parental route as the primary route of exposure—n (%)	166 (64.1)	60 (59.4)	0.409*
Triage category—n (%)			
Category 1—Critical	71 (27.4)	26 (25.7)	0.964*
Category 2—Emergent	108 (41.7)	41 (40.6)	
Category 3—Urgent	75 (29.0)	32 (31.7)	

Category 4—Semi-urgent	5 (1.9)	2 (2.0)	
Category 5—Non-urgent	0 (0)	0 (0)	
Acute myocardial injury	21 (8.1)	8 (7.9)	0.953*
Myocardial infarction	0 (0)	0 (0)	N/A
Coma	49 (18.9)	15 (14.9)	0.364*
Seizure	5 (1.9)	1 (1.0)	>0.99**
Agitation	20 (7.7)	16 (15.8)	0.021*
Confusion	41 (15.8)	28 (27.7)	0.010*
Drowsiness	148 (57.1)	50 (49.5)	0.191*
Any hallucination	5 (1.9)	7 (6.9)	0.043**
Any delusion	3 (1.2)	3 (3.0)	0.355**
Severe hyperthermia (temperature> 40°C)	1 (0.4)	0 (0)	>0.99**
Acute kidney injury—n (%)	31 (12.0)	17 (16.8)	0.223*
Rhabdomyolysis—n (%)	30 (11.6)	10 (9.9)	0.648*
Overall PSS—median (IQR)	2.0 (1.0–2.0)	2.0 (2.0–2.0)	0.827#
AAPCC outcome classification			
Death	7 (2.7)	5 (5.0)	0.357*
Major effect	11 (4.2)	4 (4.0)	
Moderate effect	104 (40.2)	47 (46.5)	
Minor effect	132 (51.0)	45 (44.6)	
No effect	5 (1.9)	0 (0)	
Associated injury—n (%)	40 (15.4)	15 (14.9)	0.888*
Associated infection—n (%)	14 (5.4)	9 (8.9)	0.222*
Deliberate self-harm—n (%)	6 (2.3)	1 (1.0)	0.678**
Violent behaviours to others—n (%)	5 (1.9)	2 (2.0)	>0.99**

Abbreviations: AAPCC, American Association of Poison Control Centers; IQR, interquartile range; MDMA, 3,4-methylenedioxy-methamphetamine; MSM, men having sex with men; PSS, Poison Severity Score
Footnotes: *Pearson Chi-square test, **Fisher's Exact test, #non-parametric test

Compared to the pre-pandemic period, more heroin abusers required chemical restraints (9.9% vs 4.2%, p = 0.040). Three patients with heroin abuse required anti-arrhythmic medication during the pandemic compared with none required before the pandemic. During the pandemic, more heroin users were admitted to general wards (57.4% vs 30.5%, p < 0.001), with a longer hospital length of stay (median 1.63 days vs 1.00 days, p = 0.002). A significantly higher proportion received psychiatric consultation during the index hospitalisation (35.6% vs 20.5%, p = 0.003, Table 15).

Table 15. Clinical management and psychosocial interventions of acute toxicities related to heroin before and during the COVID-19 pandemic.

	Before COVID-19 pandemic n = 259	During COVID-19 pandemic n = 101	P value
Physical restraint—n (%)	36 (13.9)	17 (16.8)	0.481*
Chemical restraint—n (%)	11 (4.2)	10 (9.9)	0.040*
Naloxone administration—n (%)	154 (59.5)	50 (49.5)	0.087*
Gastrointestinal decontamination—n (%)	2 (0.8)	2 (2.0)	0.314**
Gastric lavage	0 (0)	0 (0)	N/A
Activated Charcoal	1 (0.4)	2 (2.0)	0.191**
Intravenous fluid—n (%)	101 (39.0)	41 (40.6)	0.780*
Inotrope—n (%)	5 (1.9)	3 (3.0)	0.691**
Supplemental oxygen—n (%)	122 (47.1)	48 (47.5)	0.943*
Intubation and mechanical ventilation—n (%)	13 (5.0)	8 (7.9)	0.291*
Renal replacement therapy—n (%)	4 (1.5)	0 (0)	0.580**
Administration of anti-arrhythmic—n (%)	0 (0)	3 (3.0)	0.022**
Electric therapy for arrhythmia—n (%)	0 (0)	1 (1.0)	0.281**
Cardiopulmonary resuscitation—n (%)	3 (1.2)	4 (4.0)	0.100**
ECMO—n (%)	0 (0)	0 (0)	N/A
Direct discharge from the ED—n (%)	29 (11.2)	1 (1.0)	0.002*
Discharge against medical advice/patient walked away before or after consultation—n (%)	73 (28.2)	39 (38.6)	0.055*
Managed in emergency medicine ward or observation ward in the ED—n (%)	123 (47.5)	27 (26.7)	<0.001*
Admission to the general ward—n (%)	79 (30.5)	58 (57.4)	<0.001*
ICU admission—n (%)	14 (5.4)	6 (5.9)	0.842*
Admission to psychiatry ward/hospital—n (%)	15 (5.8)	6 (5.9)	0.957*
Total length of hospital stay—median (IQR), day^	1.00 (0.62–3.27)	1.63 (0.75–6.05)	0.002#
Psychiatric consultation during the index episode—n (%)	53 (20.5)	36 (35.6)	0.003*
Referral to social worker—n (%)	17 (6.6)	12 (11.9)	0.094*
Referral to NGO drug treatment and rehabilitation service—n (%)	2 (0.8)	2 (2.0)	0.312**

Abbreviations: ED, emergency department; ICU, intensive care unit; LOS, length of stay, NGO, non-governmental organisation

Footnotes: *Pearson Chi-square test, **Fisher's Exact test, #non-parametric test

^calculated only for those hospitalised patients

4.3.5. Ketamine abuse before and during the COVID-19 pandemic

Ketamine was involved in 83 reported episodes before the pandemic and 96 episodes during the pandemic. As shown in Table 16, ketamine users with acute toxicities during the pandemic were older (median 35.0 years vs 31.0 years, p = 0.021). More patients used alcohol (18.8% vs 6.0%, p = 0.011) and fewer patients used benzodiazepine (1.0% vs 9.6%, p = 0.013) in addition to ketamine during the pandemic than before. More violent behaviours towards others among ketamine abusers were recorded during the pandemic than before (8.3% vs 1.2%, p = 0.039). The clinical management and psychosocial interventions did not differ between the pre-pandemic and pandemic periods, except that more ketamine users required supplemental oxygen (19.8% vs 8.4%, p = 0.032) during the pandemic than before (Table 17).

Table 16. Clinical features and drug use pattern of ketamine abusers before and during the COVID-19 pandemic.

	Before COVID-19 pandemic n = 83	During COVID-19 pandemic n = 96	P value
Age—median (IQR), year	31.0 (27.0–36.0)	35.0 (29.0–39.0)	0.021#
Sex—n (%)			
Female	29 (34.9)	31 (32.3)	0.708*
Male	54 (65.1)	65 (67.7)	
Social allowance—n (%)	5 (6.0)	10 (10.4)	0.290*
Ambulance case—n (%)	69 (83.1)	73 (76.0)	0.243*
Police involved—n (%)	22 (26.5)	26 (27.1)	0.931*
Non-local resident—n (%)	3 (3.6)	0 (0)	0.104**
MSM	1 (1.2)	0 (0)	0.464**
Pregnant at the time of presentation—n (%)	0 (0)	1 (1.0)	>0.99**
Number of drugs abused—n (%)			
1	33 (39.8)	32 (33.3)	0.299*
2	31 (37.3)	32 (33.3)	
≥ 3	19 (22.9)	32 (33.3)	
Drug abused at presentation—n (%)			
Methamphetamine	22 (26.5)	21 (21.9)	0.470*
Cocaine	28 (33.7)	37 (38.5)	0.505*
Cannabis	2 (2.4)	6 (6.3)	0.289**
Heroin	0 (0)	0 (0)	N/A
MDMA	7 (8.4)	12 (12.5)	0.378*
Cough mixture or pills	4 (4.8)	7 (7.3)	0.492*
Zopiclone or zolpidem	2 (2.4)	2 (2.1)	>0.99**
Benzodiazepine	8 (9.6)	1 (1.0)	0.013**
Novel psychoactive substances	13 (15.7)	10 (10.4)	0.296*
Co-ingestion of alcohol—n (%)	5 (6.0)	18 (18.8)	0.011*
Insufflation as the primary route of exposure—n (%)	49 (59.0)	61 (63.5)	0.537*

Triage category—n (%)			
Category 1—Critical	13 (15.7)	13 (13.5)	0.560*
Category 2—Emergent	34 (41.0)	33 (34.4)	
Category 3—Urgent	33 (39.8)	48 (50.0)	
Category 4—Semi-urgent	3 (3.6)	2 (2.1)	
Category 5—Non-urgent	0 (0)	0 (0)	
Acute myocardial injury	4 (4.8)	4 (4.2)	>0.99**
Myocardial infarction	1 (1.2)	0 (0)	0.464**
Coma	3 (3.6)	3 (3.1)	>0.99**
Seizure	1 (1.2)	3 (3.1)	0.625**
Agitation	15 (18.1)	28 (29.2)	0.083*
Confusion	29 (34.9)	39 (40.6)	0.435*
Drowsiness	25 (30.1)	36 (37.5)	0.299*
Any hallucination	10 (12.0)	6 (6.3)	0.175*
Any delusion	9 (10.8)	4 (4.2)	0.086*
Severe hyperthermia (temperature> 40°C)	0 (0)	2 (2.1)	0.500**
Acute kidney injury—n (%)	5 (6.0)	8 (8.3)	0.553*
Rhabdomyolysis—n (%)	9 (10.8)	13 (13.5)	0.583*
Overall PSS—median (IQR)	2.0 (1.0–2.0)	2.0 (1.0–2.0)	0.760#
AAPCC outcome classification			
Death	1 (1.2)	0 (0)	0.354*
Major effect	3 (3.6)	7 (7.3)	
Moderate effect	19 (22.9)	28 (29.2)	
Minor effect	60 (72.3)	60 (62.5)	
No effect	0 (0)	1 (1.0)	
Associated injury—n (%)	12 (14.5)	21 (21.9)	0.202*
Associated infection—n (%)	1 (1.2)	4 (4.2)	0.375**
Deliberate self-harm—n (%)	9 (10.8)	14 (14.6)	0.456*
Violent behaviours to others—n (%)	1 (1.2)	8 (8.3)	0.039**

Abbreviations: AAPCC, American Association of Poison Control Centers; IQR, interquartile range; MDMA, 3,4-methylenedioxy-methamphetamine; MSM, men having sex with men; PSS, Poison Severity Score

Footnotes: *Pearson Chi-square test, **Fisher's Exact test, #non-parametric test

Table 17. Clinical management and psychosocial interventions of acute toxicities related to ketamine before and during the COVID-19 pandemic.

	Before COVID-19 pandemic n = 83	During COVID-19 pandemic n = 96	P value
Physical restraint—n (%)	21 (25.3)	25 (26.0)	0.910*
Chemical restraint—n (%)	13 (15.7)	22 (22.9)	0.222*
Diazepam	9 (10.8)	18 (18.8)	0.140*
Lorazepam	1 (1.2)	5 (5.2)	0.218**
Midazolam	9 (10.8)	11 (11.5)	0.896*
Haloperidol	1 (1.2)	2 (2.1)	>0.99**
Dexmedetomidine	0 (0)	0 (0)	N/A
Propofol	0 (0)	0 (0)	N/A
Gastrointestinal decontamination—n (%)	3 (3.6)	2 (2.1)	0.664**
Gastric lavage	1 (1.2)	0 (0)	0.464**
Activated Charcoal	2 (2.4)	2 (2.1)	>0.99**
Intravenous fluid—n (%)	24 (28.9)	38 (39.6)	0.135*
Inotrope—n (%)	1 (1.2)	1 (1.0)	>0.99**
Supplemental oxygen—n (%)	7 (8.4)	19 (19.8)	0.032*
Intubation and mechanical ventilation—n (%)	4 (4.8)	5 (5.2)	>0.99**
Renal replacement therapy—n (%)	0 (0)	2 (2.1)	0.500**
Administration of anti-arrhythmic—n (%)	1 (1.2)	1 (1.0)	>0.99**
Electric therapy for arrhythmia—n (%)	1 (1.2)	0 (0)	0.464**
Cardiopulmonary resuscitation—n (%)	1 (1.2)	0 (0)	0.464**
ECMO—n (%)	0 (0)	0 (0)	N/A
Direct discharge from the ED—n (%)	10 (12.0)	10 (10.4)	0.730*
Discharge against medical advice/patient walked away before or after consultation—n (%)	28 (33.7)	30 (31.3)	0.723*
Managed in emergency medicine ward or observation ward in the ED—n (%)	33 (39.8)	37 (38.5)	0.868*
Admission to the general ward—n (%)	25 (30.1)	37 (38.5)	0.238*
ICU admission—n (%)	4 (4.8)	9 (9.4)	0.242*
Admission to psychiatry ward/hospital—n (%)	10 (12.0)	13 (13.5)	0.766*
Total length of hospital stay—median (IQR), day^	1.29 (0.65–5.95)	1.72 (0.60–5.97)	0.605#
Psychiatric consultation during the index episode—n (%)	41 (49.4)	54 (56.3)	0.360*
Referral to social worker—n (%)	9 (10.8)	20 (20.8)	0.070*
Referral to NGO drug treatment and rehabilitation service—n (%)	1 (1.2)	5 (5.2)	0.218**

Abbreviations: ED, emergency department; ICU, intensive care unit; LOS, length of stay, NGO, non-governmental organisation

Footnotes: *Pearson Chi-square test, **Fisher's Exact test, #non-parametric test

^calculated only for those hospitalised patients

4.4. Predictors of severe complications and their associations with the COVID-19 pandemic

4.4.1. Methamphetamine

Among 687 episodes of acute toxicities related to methamphetamine during the whole study period, severe complications were observed in 226 episodes (32.9%). In our previous study (project reference no. BDF190053), seven factors were identified as independent predictors of severe complications in patients with acute methamphetamine toxicity: a triage temperature > 39°C, agitation, diaphoresis, a triage ranking of higher acuity, sluggish or non-reactive pupils, tachycardia > 120 beats per minute and auditory hallucination. Multiple logistic regression was performed to adjust for the confounding effects of these seven factors (Table 18). We found that presentation during the COVID-19 pandemic was not significantly associated with severe complications (OR 1.05, 95% CI 0.70–1.58, p = 0.810).

Table 18. Multivariable logistic regression analysis of factors associated with severe complications of acute methamphetamine toxicity in the emergency department.

Factor	Adjusted OR (95% CI)	P value
Triage temperature > 39 °C	8.23 (0.99–68.11)	0.051
Agitation	2.01 (1.32–3.05)	0.001
Triage category	1.79 (1.37–2.34)	<0.001
Diaphoresis	1.39 (0.72–2.69)	0.334
Tachycardia > 120 beats per minute	1.38 (0.89–2.16)	0.152
Sluggish or non-reactive pupils	1.37 (0.78–2.44)	0.277
Auditory hallucination	0.66 (0.36–1.19)	0.163
Presenting during the COVID-19 pandemic	1.05 (0.70–1.58)	0.810

Abbreviations: CI, confidence interval; OR, odds ratio

4.4.2. Cocaine

For cocaine, severe complications occurred in 82 out of 306 episodes (26.8%) throughout the study period. Three predictors of severe complications of cocaine abuse were reported in our previous study (project reference no. BDF190053): tachycardia > 120 beats per minute, shortness of breath and a higher triage acuity. After adjusting the effects of these known predictors in a multivariable logistic regression model, presenting during the COVID-19 pandemic was not significantly associated with severe complications (OR 1.45, 95% CI 0.84–2.50, p = 0.184, Table 19).

Table 19. Multivariable logistic regression analysis of factors associated with severe complications of acute cocaine toxicity in the emergency department.

Factor	Adjusted OR (95% CI)	P value
Tachycardia > 120 beats per minute	2.26 (1.24–4.12)	0.008
Triage category	2.45 (1.71–3.52)	< 0.001
Shortness of breath	0.56 (0.25–1.28)	0.172
Presenting during the COVID-19 pandemic	1.45 (0.84–2.50)	0.184

Abbreviations: CI, confidence interval; OR, odds ratio

4.4.3. Cannabis

Severe complications occurred in 36 out of 180 episodes (20.0%) of acute toxicity that involved cannabis. Paranoid delusion, diaphoresis, agitation and associated injury were identified as independent predictors of severe complications of cannabis abuse in our previous report (project reference no. BDF190053). In multivariable logistic regression, presenting during the COVID-19 pandemic was not associated with severe complications (OR 1.33, 95% CI 0.59–3.02, p = 0.491) after adjusting for these four predictive variables (Table 20).

Table 20. Multivariable logistic regression analysis of factors associated with severe complications of acute cannabis toxicity in the emergency department.

Factor	Adjusted OR (95% CI)	P value
Associated injury	6.22 (2.44–15.82)	<0.001
Agitation	2.77 (1.17–6.58)	0.021
Diaphoresis	1.36 (0.38–4.87)	0.634
Paranoid delusion	1.30 (0.27–6.33)	0.743
Presenting during the COVID-19 pandemic	1.33 (0.59–3.02)	0.491

Abbreviations: CI, confidence interval; OR, odds ratio

4.4.4. Heroin

Since our previous study did not include heroin as a target drug of analysis, we performed univariate analysis, followed by multivariable logistic regression, to identify independent predictors of severe complications in heroin use. In this study, severe complications occurred in 160 out of the total 360 episodes of acute toxicity (44.4%) involving heroin. In univariate analysis, 16 variables were significantly associated with severe complications (Appendix 6, Supplementary Table 1). In multivariable logistic regression, four variables remained

independent predictors of severe complications in heroin abuse (Appendix 6, Supplementary Table 2): tachycardia > 120 beats per minute (OR 5.61, 95% CI 2.02–15.55, p = 0.001), triage category of a higher acuity (OR 2.42, 95% CI 1.65–3.56, p < 0.001), previous detoxification treatment (OR 2.06, 95% CI 1.19–3.58, p = 0.010) and drowsiness (OR 0.28, 95% CI 0.16–0.49, p < 0.001). After adjusting for these four independent predictors for severe complications of heroin abuse in the ED, presenting during the COVID-19 pandemic was not significantly associated with severe complications in heroin abuse (OR 0.82, 95% CI 0.48–1.39, p = 0.453, Table 21).

Table 21. Multivariable logistic regression analysis of factors associated with severe complications of acute heroin toxicity in the emergency department.

	Adjusted OR (95% CI)*	P value
Tachycardia > 120 beats per minute	3.68 (1.77–7.68)	0.001
Triage category	2.48 (1.81–3.40)	< 0.001
Previous detoxification treatment	1.73 (1.07–2.80)	0.025
Drowsiness	0.31 (0.19–0.50)	< 0.001
Presenting during the COVID-19 pandemic	0.82 (0.48–1.39)	0.453

Abbreviations: CI, confidence interval; OR, odds ratio

4.4.5. Ketamine

Similar to heroin, we performed univariate and multivariable analyses to first identify independent predictors of severe complications of ketamine abuse in the ED (Appendix 6, Supplementary Tables 1 and 3). Two clinical variables were independent predictors of severe complications in ketamine abuse in the ED: triage temperature > 38ºC (OR 20.51, 95% CI 3.04–138.32, p = 0.002) and tachycardia > 120 beats per minute (OR 5.02, 95% CI 1.63–15.49, p = 0.005).

In this study, severe complications occurred in 37 out of the total 179 episodes of ketamine abuse (20.7%). After adjusting for the independent predicting variables in multivariable logistic regression, presenting during the COVID-19 pandemic was not significantly associated with a poor clinical outcome (OR 1.42, 95% CI 0.61–3.29, p = 0.417, Table 22).

Table 22. Multivariable logistic regression analysis of factors associated with severe complications of acute ketamine toxicity in the emergency department.

	Adjusted OR (95% CI)*	P value
Temperature > 38ºC	14.31 (3.28-62.53)	< 0.001
Tachycardia > 120 beats per minute	4.32 (1.80-10.40)	0.001
Presenting during the COVID-19 pandemic	1.42 (0.61-3.29)	0.417

Abbreviations: CI, confidence interval; OR, odds ratio

5. Discussion

Globally, COVID-19 has had a wide-ranging yet heterogeneous impact on drug demand, supply and distribution.[1,39,40] In Hong Kong, our study showed acute toxicities involving methamphetamine, cannabis, heroin increased shortly after the beginning of the pandemic but then followed a downtrend trend during the pandemic. Acute toxicities involving ketamine increased at the outset of the pandemic and the trend did not change significantly throughout the past 3 years. Apparently, acute toxicities involving cocaine were not significantly affected by the pandemic. Overall, closure of social and recreational venue closure and social distancing measures during the pandemic had a limited impact on the monthly incidence of acute toxicities involving these recreational drugs. We observed several significant changes in demographics, drug use patterns, clinical presentations and outcomes for individual drugs before and during the pandemic, but the pandemic did not negatively impact psychosocial interventions provided to drug abusers. These findings have important implications for drug-control policy, clinical management and future research as we return to normalcy.

5.1. Overall incidence and trends of acute drug toxicities during the COVID-19 pandemic

Over the past six years, methamphetamine has remained the most frequently encountered drug of abuse reported to the HKPIC, followed by heroin, cocaine, cannabis and ketamine. The respective median incidence rates per 100,000 population were 1.69, 0.79, 0.65, 0.43, and 0.35, respectively. Overall, the incidence rates of methamphetamine, cocaine, cannabis and heroin were much lower than those reported by the ED-based Drug Abuse Warning Network (DAWN) in the US in 2021 and 2022.[41,42] The difference was likely due to differences in data sources, reporting mechanisms and methods of data analysis. Since DAWN did not provide data for ketamine, such a comparison for ketamine was not possible. Population-level estimates were not available from the ED-based European Drug Emergencies Network (Euro-DEN Plus).[43] Relevant data published from Asian countries for comparison was also lacking.

The current estimate for methamphetamine is similar to our previous estimate of 1.63 per 100,000 population (project reference no. BDF190053). Importantly, the number of acute methamphetamine toxicities decreased since 2017, especially after 2020. Despite the initial increased number of acute toxicities at the beginning of the pandemic, methamphetamine toxicities decreased at a faster rate during the pandemic than before. The overall decline in acute methamphetamine toxicities was consistent with the reduction in the number of methamphetamine abusers reported in the CRDA.[30] However, we did not find a significant correlation between them. This can probably be explained by a steeper fall in the number of acute toxicities after 2020 compared to the drop in the number of methamphetamine users. For heroin, similar pattern of trend in the number of acute toxicities occurred during the

pandemic. The decreased number of acute toxicities involving heroin correlated significantly with the decreased number of heroin abusers in the CRDA.

Surprisingly, the increase in the number of cocaine abusers in the CRDA[30] did not translate into a rise in acute cocaine toxicity during the study period. Two explanations are possible. One is that the overall quantity of cocaine used decreased, despite an increasing number of abusers, because of drug shortages and few opportunities for drug use at socialising events during the pandemic. This resulted in a lower probability of acute toxicities that warranted ED presentations. The other explanation is the avoidance of ED utilisation among cocaine abusers during the pandemic because of the fear of contracting the infection in the hospital. Some overdose events with mild presentations were possibly unattended, as reported by many drug users in previous studies.[44] Since measuring the exact drug quantity used by cocaine users was not possible, the likelihood for the first explanation is not clear. The second explanation is supported by published evidence of a reduction in ED utilisation by patients with substance abuse disorders, especially during the early phases of the pandemic,[45,46] as well as the higher proportion of cocaine users who discharged against medical advice or left before or after consultation during the pandemic than before in our study.

For cannabis, the number of acute toxicities increased at the beginning of the pandemic but then it followed a downward trend during the pandemic, despite the increase in the number of cannabis users in the CRDA.[30] Similar to cocaine, during the pandemic, cannabis might become less available to some users and cannabis users might avoid hospitals for mild toxicities. The decreasing trend of acute cannabis toxicity might also indicate the effectiveness of the current drug-control strategy and public education about the harms of cannabis abuse in recent years.

Notably, acute toxicities involving ketamine increased at the beginning of the pandemic and the trend remained unchanged during the pandemic, indicating on overall increase in ketamine use during the pandemic. It is unclear whether such an increase represented better access to ketamine in the drug market during the pandemic or resurgence of the popularity of ketamine among drug users. No significant correlation existed between the number of toxicities involving ketamine reported to the HKPIC and the number of users in the CRDA or the quantity or market value of ketamine seized by law enforcement. There is a need to continue data monitoring from multiple sources to understand the current trend in ketamine abuse. As for ketamine analogues, apart from the surge of cases related to deschloro-*N*-ethyl-norketamine (2-oxo-PCE) in 2021,[47,48] their use remained low in subsequent years.

The use of MDMA and NPS remained low in Hong Kong. The use of new drug combinations in the form of mixtures of controlled drugs, such as ‘happy water’ (a mixture that typically

contains amphetamines, e.g. MDMA, cocaine and ketamine, but the exact composition varies), is worth further monitoring. In our study, six of the eight patients who reported the ingestion of 'happy water' presented in 2020.

From 2018 to 2022, the quantity and market value of methamphetamine, cocaine, cannabis, heroin and ketamine seized by law enforcement increased dramatically. In our study, no correlation was found between the drug seizure data and acute toxicities related to any of the study drugs. According to the UNODC, the COVID-19 pandemic accelerated new patterns in drug trafficking, including larger shipment sizes, increased use of private aircraft, increased use of waterway routes and contactless methods of drug delivery to end-users because of border closures and reductions in commercial flights.[1] Many of the drugs seized might come from shipments transiting Hong Kong, which were not intended for the local drug market. Increased drug seizures also might have reduced drug availability in the local market.

For patients aged under 21 years, we could not identify any significant correlations between the number of acute toxicities related to any of the study drugs and CRDA or drug seizure data.

5.2. Impact of COVID-19, closure of social and recreational venues and social distancing measures on drug toxicities

The COVID-19 pandemic provided a unique opportunity as a natural experiment in public health to evaluate the impact of social and recreational venue closure on drug abuse and harm, which would otherwise not be possible. However, literature specifically looking into the issue is lacking. In our study, ITS analysis showed that such closures apparently did not have a significant impact on the number of acute toxicities related to methamphetamine, cocaine, cannabis, heroin or ketamine, indicating alternative venues where psychotropic substance abusers could still obtain and use drugs.

According to the UNODC, the drug markets were resilient to the disruption brought about by the pandemic.[1] Despite the disruption of street-based retail drug markets in the initial lockdowns, market adaptations during the pandemic included increased use of encrypted messaging services, social media applications, online sources, and mail and home delivery services.[49] We are not sure how these new trends in drug trafficking impacted drug distribution in Hong Kong when social gathering was restricted. From our data, the closure of social and recreational venues did not seem to be effective in reducing drug exposure and the associated harms.

Other explanations for the lack of impact of social and recreational venue closure on drug abuse are the location and reasons of drug use reported by the abusers. According to the CRDA, 59% of the reported drug abusers took drugs at home or a friend's home only (56% in 2020), and 22% (24% in 2020) took drugs only in other places such as recreational areas, disco, karaoke, clubhouses or bars. In 2021, the commonest reasons for drug abuse were 'to relieve boredom/depression/stress', 'to avoid discomfort of its absence', and 'peer influence/to identify with peers'.[50,51] The increase in boredom and stress during the pandemic might have led to more hidden use of drugs at home despite few opportunities for socialising during the closure of social and recreational venues. Therefore, their closures had limited impact on drug abuse and toxicities.

Studies have shown increased illicit drug use due to the boredom, stress and loneliness of drug users during the pandemic.[52–55] That also explained the increased number of acute toxicities involving methamphetamine, cannabis, heroin and ketamine early in the pandemic when drug users might still have stock of these recreational drugs. The subsequent social distancing measures might decrease drug availability and the resultant number of acute toxicities. This argument is supported by the significant association between the Stringency Index and decreased heroin toxicities in the ITS analysis. Although the Stringency Index did not have a significant impact on acute toxicities involving methamphetamine, cocaine, cannabis and ketamine in ITS analysis, the lowest number of toxicities involving these drugs coincided with the time when social distancing measures were the strictest in early 2022.

5.3. Impact of COVID-19 on drug use pattern and clinical outcome

5.3.1. Methamphetamine

Published data on the impact of the COVID-19 pandemic on methamphetamine-related ED presentations have been conflicting. Fry et al. reported a 15% fall in methamphetamine-related ED presentations in 2020 compared to the same period in 2019 in a clinical toxicology unit in Australia.[56] Redona Jr. et al. showed an increase in methamphetamine-related presentations to Victorian EDs during the pandemic.[57] Our study adds to the literature by demonstrating a fall in the number of acute methamphetamine toxicities in Hong Kong during the pandemic.

Despite the reduced number of acute methamphetamine toxicities during the pandemic, our study showed that more methamphetamine users used three or more different drugs; presented with agitation, injury and deliberate self-harm; and developed major effects or died during the pandemic, necessitating more invasive treatment such as intubation and mechanical ventilation, renal replacement therapy and ICU admission. However, in multivariable logistic regression, presenting during the COVID-19 pandemic was not

associated with a poor clinical outcome in acute methamphetamine toxicity, after adjusting for known predictors for severe complications. These findings suggest that the observed differences in major effects and deaths were not due to the pandemic per se but the different patterns of drug use and presentations of methamphetamine abusers during the pandemic. The higher proportion of general ward admission, which was also seen across different study drugs, was likely the result of role changes in the emergency medicine ward (EMW) in many hospitals during the pandemic instead of a major change in clinical management.

Our study showed that during the pandemic, patients with acute methamphetamine toxicity were slightly older and were more likely receiving social allowances than before, which reflected the adverse socioeconomic conditions of methamphetamine users imposed by COVID-19. A higher proportion of social worker referrals for methamphetamine users also was noted during the pandemic. Since the reasons for social worker referrals were not consistently documented in clinical notes, it is not clear how many of these were related to the arrangement of detoxification services and how many were for social allowance applications.

5.3.2. Cocaine

Compared with the pre-pandemic period, only a slight reduction occurred in the number of acute cocaine toxicities during the pandemic in Hong Kong. Our finding is consistent with an Australian study that showed no significant difference in ED presentations of people who used cocaine during the pandemic.[57] However, in Hong Kong, we found that more cocaine users developed acute myocardial injury, drowsiness and major toxicity effects, and required ICU admission during the pandemic compared with the pre-pandemic period. After adjusting for known predictors of severe complications in multivariable analysis, presenting during the COVID-19 pandemic per se was not significantly associated with a poor outcome. Comparing drug use patterns before and during the pandemic did not reveal any significant differences. Taken together, although we could not ascertain the exact dose of cocaine in each episode, these findings suggest that cocaine users who presented to the ED with acute toxicity during the pandemic might have taken larger doses.

Notably, more cocaine users discharged against medical advice or left before or after consultation during the pandemic than before, posing additional risks because of incomplete assessment and treatment. We found no significant differences in the psychiatric consultation, referrals to social worker and referral to NGO drug treatment and rehabilitation services before and during the pandemic for cocaine users.

5.3.3. Cannabis

During the pandemic, we observed a slight increase in the number of acute toxicity episodes that involved cannabis. Notably, significantly more female cannabis users presented to the ED during the pandemic compared with the pre-pandemic period. This is consistent with the observation of female patients surpassing their male counterparts in US cannabis-involved ED visits in mid-2020.[58] Although previous studies have shown differential impacts of the COVID-19 pandemic on cannabis use in different age groups,[59,60] large-scale surveys have consistently demonstrated that female gender was correlated with increased cannabis use during the pandemic.[61–63] More local research is needed to evaluate the role of gender in cannabis abuse and to explore the reasons for increased cannabis use by female users during the pandemic.

In a Canadian study on substance use-related ED visits among adolescents and young adults during the pandemic, Kim et al. showed a significant increase in emergent and life-threatening triage levels (Canadian Triage and Acuity Scales 1 and 2) in cannabis-related ED visits.[64] In Hong Kong, we did not observe a higher ED triage acuity in episodes related to cannabis, although the local triage system is different from the Canadian system. The PSS score and AAPCC outcome classification also did not differ significantly before and during the pandemic, along with the proportions of patients who required invasive treatment or ICU admission. In multivariable logistic regression, presenting during the COVID-19 pandemic was not significantly associated with a poor outcome, after adjusting for known predictors of severe complications. In summary, we found no evidence of more severe cannabis toxicity during the pandemic period compared with the pre-pandemic period.

Regarding psychosocial interventions including psychiatric consultation, or referral to social workers or NGO drug treatment and rehabilitation services, no significant differences existed before and during the pandemic for cannabis users.

5.3.4. Heroin

The number of acute heroin toxicities reported to the HKPIC more than halved during the pandemic period compared with the pre-pandemic period. In contrast, increased opioid-related ED visits were reported in North America during the pandemic,[65–72] but many of these studies did not provide a breakdown of the type of opioids used. Fentanyl and prescription opioids other than heroin are more popular in North America. Analysis of drug test results before and during the pandemic showed an overall increase in heroin use in the US but the changes were not consistent across different studies.[73–75]

In our study, the most striking feature of acute heroin toxicity during the pandemic was the increased concurrent use of benzodiazepine and methamphetamine with heroin. The increased combination of heroin with methamphetamine during the pandemic might explain the more frequent agitation, confusion, hallucination, chemical restraint and psychiatric consultation observed among heroin users during the pandemic. Methamphetamine is often used as an opioid substitute when heroin became less available and more expensive during the pandemic.[76] It is also used to achieve a synergistic high with heroin or to balance out the effects of opioids to maintain daily function.[77] This high-risk pattern of heroin and methamphetamine use has been increasingly reported as 'twin epidemics' in the US, especially among those with injection drug use and serious mental illness.[77,78] It complicates the clinical presentations by masking opioid and sympathomimetic toxidromes from one another,[79] which may lead to misdiagnosis. Reversing opioid toxidrome with naloxone may unmask the underlying methamphetamine toxicity, which may cause cardiac dysrhythmias in excessive reversal.[80] Opioid overdose deaths involving methamphetamine increased dramatically in the US[81,82] In our study, tachycardia > 120 beats per minute, which is not expected in pure opioid toxidrome and was likely due to concurrent stimulant use, was identified as an independent predictor of severe complication in multivariable analysis, whereas presenting during the pandemic per se was not. It is important to closely monitor the trend of this high-risk combination of heroin and methamphetamine abuse.

5.3.5. Ketamine

During the pandemic, a small increase occurred in the number of episodes of acute toxicity that involved ketamine compared with the pre-pandemic period, with a significantly higher proportion of patients with alcohol co-ingestion and violent behaviours to others. It is noteworthy that in these episodes that involved ketamine, only one third involved ketamine alone, and two thirds involved more than one drug. The commonest drug concurrently used was cocaine, followed by methamphetamine and MDMA. No significant changes in these drug combinations were seen before and during the pandemic, indicating that concurrent use of ketamine with other stimulants is now common and increased use with alcohol has emerged during the pandemic. Increased use of dissociative drugs, and ketamine in particular, has been reported by other countries during the pandemic,[83,84] with 'dealing with boredom' quoted as a motivator for dissociative drug use.[84] Given the increased number of acute toxicities that involved ketamine, we must monitor any local rebound in ketamine abuse and any major shift in the pattern of ketamine use with other stimulants.

On the whole, clinical management and psychosocial interventions did not differ significantly before and during the pandemic for acute ketamine toxicity. In multivariable analysis, we found that a temperature > 38ºC and tachycardia > 120 beats per minute, but not presenting during the COVID-19 pandemic, were independent predictors of severe complications. Both hyperthermia and tachycardia were likely related to concurrent stimulant abuse, highlighting the detrimental effect of concurrent stimulant use on patient outcomes.

6. Strengths and limitations of the study

6.1. Strengths

To the authors' knowledge, this study is the first local study to evaluate the impact of the COVID-19 pandemic on the occurrence, drug use patterns, clinical presentations and outcomes of acute toxicities related to the recreational use of methamphetamine, cocaine, cannabis, heroin and ketamine. The territory-wide database in HKPIC that involves all public A&Es is representative of the contemporary drug use pattern in Hong Kong and provides population-level estimates, which are lacking in Asia. The collection of data that covered 3 years before and the first 3 years of the pandemic, during which the HKPIC reporting mechanism remained consistent, allowed us to study the impact of the whole pandemic on drug abuse on a time scale long enough to account for the long-term time trend and seasonality.

Unlike other poison centre-based studies, we were able to access the electronic health records of all recruited cases through the HA CMS. The detailed information on individual cases allowed us to analyse the changes in demographics, drug use patterns, clinical presentations, and outcomes before and during the pandemic in detail, which would otherwise not be possible with other study methods that use administrative data or diagnostic codes alone. The quality of data was also ensured by the parallel data entry method and manual verification by qualified clinicians with training in clinical toxicology.

6.2. Limitations

This study has several limitations, similar to our previous study (project reference no. BDF190053). First, the retrospective study design was limited by missing data, errors in recording, misinterpretation and information bias. Clinicians usually only document the presence or absence of important clinical features. We could only assume their absence when they were not documented in the clinical notes.

Second, we relied on the clinical judgement of the treating clinicians and clinical toxicologists in HKPIC in determining the relationship between drug exposure and clinical presentations, with subsequent vetting during data collection and verification. Given the absence of a standardised protocol for toxicology screening across different A&Es in Hong Kong, under-reporting of drug toxicities was possible, especially when history from the patients was not forthcoming or the treating clinical team did not consider drug use in the differential diagnosis. The use of NPS was also likely under-reported since screening for NPS was not part of the routine toxicology screening.

Third, not all poisoning cases related to recreational drugs in local A&Es were reported to the HKPIC. The reported cases were likely to be more severe or complicated, warranting a consultation with the HKPIC, and they were more likely from A&Es where compliance with reporting was higher. Given that the reporting mechanism did not change significantly during the pandemic, the HKPIC data was useful in gauging the change in drug use and toxicity patterns over time.

Fourth, we did not study the impact of the COVID-19 pandemic on the use of different forms of drugs (e.g. powder vs crack cocaine[85]), or the quantity, time, or location of drug use because relevant information was often poorly documented in clinical notes. Including these factors in our regression models was not possible.

Fifth, polysubstance use was common, and teasing out the toxic effects of other drugs used concurrently by patients was difficult. Analysing patients with exposure to a single drug at one time would have greatly reduced the sample size and power of the study. We believe that the current analysis method for individual drugs that included concurrent drugs reflects the real clinical situations better when polysubstance abuse predominates.

Sixth, we could not quantify the severity of addiction using validated tools, such as the Addiction Severity Index,[86] because of the retrospective study design. We do not know the differentiated impact of the COVID-19 pandemic on the clinical presentations of casual drug users and patients with drug dependence disorder, who might have different sources of drugs and behavioural changes in response to the pandemic and the associated social distancing measures.

Finally, we regarded the whole pandemic period as a homogeneous period without further studying the impact of its individual waves on drug use and toxicities. Given the ever-changing virulence and prevalence of the virus, future waves, if present, are likely to be different from previous waves. Studying the impact of previous waves on drug use and toxicities is less relevant for drug control policy and clinical management in future waves. We focused our effort on studying the impact of social and recreational venue closure and social distancing measures because they might be re-introduced in future waves of the COVID-19 pandemic or other different epidemics.

7. Implications of the research

Despite the limitations, this study provides real-world territory-wide data on acute toxicities related to methamphetamine, cocaine, cannabis, heroin and ketamine collected 3 years before and 3 years during the COVID-19 pandemic, with implications for future drug-control policy, clinical management and research.

7.1. Implications for drug-control policy

The COVID-19 pandemic has multifaceted impacts on drug use and associated toxicities. The closure of social and recreational venues did not appear to have an impact on drug toxicities during the pandemic, indicating that drug-control measures solely targeting these places may not be very effective in curbing drug use and reducing harm. The drug market has demonstrated remarkable adaptability under stringent social distancing measures during the pandemic. This underscores the importance of continued vigilance and a consistent anti-drug policy irrespective of the drastic changes brought about by pandemics or other social events.

During the pandemic, the number of acute toxicity episodes that involved methamphetamine and heroin decreased, but this reduction did not translate into a lower severity of poisoning when drug users presented to the ED. The increased combination of heroin and methamphetamine during the pandemic is worrying. More education should target existing heroin users and focus on the harm of combining heroin and methamphetamine.

For cocaine, despite a slight decrease in the number of acute toxicities, more myocardial injuries and major effects were seen during the pandemic, indicating potentially a higher dose of abuse in patients presenting to the ED. According to the UNODC, ‘the world is currently experiencing a prolonged surge in both supply and demand of cocaine’.[40] With the increasing number of cocaine abusers recorded in the CRDA, closely monitoring the local trends in cocaine abuse and associated harm is imperative.

As for cannabis and ketamine, the number of acute toxicities increased slightly during the pandemic. Although increased cannabis consumption may be fuelled by legalisation in many other countries,[87] the increased reported of ketamine toxicity, especially in combination with other stimulants, may represent a resurgence of the popularity of ketamine among local drug users. More public education about the harms of cocaine, cannabis and ketamine should be targeted at young people.

7.2. Implications for clinical management

Overall, our study did not show major changes in the clinical management of acute toxicity related to methamphetamine, cocaine, cannabis, heroin and ketamine before and during the pandemic. The increased use of invasive treatment and ICU admission for methamphetamine toxicity and chemical restraint for heroin toxicity was likely the result of differences in drug use patterns and clinical presentations during the pandemic. The shift of care location from EMW run by emergency doctors and nurses to general wards during the pandemic was likely due to the reassigned role of EMWs in many hospitals to cope with COVID-19. Since more health care professionals in general wards were involved in the care of patients with acute recreational drug toxicities during the pandemic, there is a need to continue staff education on the management of acute recreational drug toxicity across different specialties.

A few emerging developments are noteworthy for health care professionals. First, the concurrent use of heroin and methamphetamine may mask the opioid toxidrome and sympathomimetic toxidrome from one another. Reversing opioid toxidrome with naloxone may unmask underlying methamphetamine toxicity, which might lead to the misdiagnosis of acute withdrawal of heroin or cardiac dysrhythmias in excessive reversal. Second, clinicians should be aware of cocaine-related cardiovascular complications, which can be acute or chronic and include ischaemic and non-ischaemic events.[88,89]

Although this study did not show a negative impact of the COVID-19 pandemic on psychosocial interventions, the referral rate to social workers and NGO drug rehabilitation and treatment services remained suboptimal across different study drugs. There is a need to strengthen the referral network of different service providers in the hospital.

7.3. Implications for future research

It is unclear whether the pattern of drug abuse and the associate toxicities would change after the COVID-19 pandemic when all social distancing measures are lifted. Some of the changes in the pattern of drug abuse and toxicities brought about by the pandemic may continue or further develop after its end. ED-based surveillance data are valuable in complementing the current CRDA statistics and gauging the severity of acute toxicities related to recreational drugs in the aftermath of the pandemic.

The impact of combining heroin and methamphetamine warrants further investigations. The results will have implications for appropriate antidote use and clinical management in mixed opioid and sympathomimetic toxidromes.

Additionally, the increase in female presentations with acute cannabis toxicity during the pandemic calls for further qualitative study to explore the reasons for the increased cannabis use and toxicity among female drug users. The findings will have important implications in tailoring future anti-drug strategy and education to the specific needs of different genders.

8. Conclusions

The COVID-19 pandemic had multiple impacts on local patterns of drug abuse and associated toxicities. The closure of social and recreational venues did not apparently have a significant impact on drug abuse and toxicity. Social distancing measures during the pandemic were significantly associated with decreased number of acute heroin toxicities. However, the reduction in acute toxicities involving methamphetamine and heroin during the pandemic did not translate into a lower severity of poisoning, and the increased combination of heroin and methamphetamine is alarming. The increase in cocaine-related acute myocardial injury is also noteworthy in the face of increasing cocaine supply and abuse internationally. Both acute cannabis and ketamine toxicity increased during the pandemic, particularly among female drug users for the former and multi-stimulant abusers for the latter. Further studies are warranted to monitor the trend of drug abuse and toxicity in the aftermath of the pandemic, the impact of combinations of traditional illicit drugs and the role of gender in cannabis abuse and toxicity.

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Appendices

Appendix 1. Search method used in identifying eligible episodes in the Poison Information Clinical Management System.

Time: 23/1/2017 to 22/1/2023

Toxins: Poison category

A16a to e (Abusive opioids)

A19a (Amphetamines)

A19b (Cannabis)

A19c (Cocaine)

A19f (Ketamine)

Appendix 2. Data Entry Coding Manual

The University of Hong Kong
Emergency Medicine Unit
Beats Drug Fund Project BDF 190053/210069
Acute toxicity related to psychoactive substance abuse and the impact of emergency department interventions on drug-related re-attendance
The impact of the COVID-19 pandemic on acute toxicity related to recreational drug abuse presenting to emergency departments
Data Entry Coding Manual version 1.2

General rules

1. Retrospective chart review requires a careful review of medical records. Clinicians may not document every symptoms or signs in the clinical notes. Some symptoms and signs require interpretation. The reviewer should be familiarize themselves with how symptoms and signs are recorded as follows:
'cough **+**' – it means the patient had cough
'pain**+++**' – it means the patient had severe pain, with the number of '+' representing the severity of that particular symptoms
'vomiting**o**' – it means the patient did not vomit
2. Sometimes, a symptom is not mentioned specifically in the clinical notes but one can deduce from the information documented in the record. For instance, 'no respiratory symptoms' – it means the patient did not have any respiratory symptoms. So even cough was not mentioned at all in the notes, the review should code the absence of cough.
3. For dichotomized variables (yes/no), enter '1' for yes and '0' for no.
4. For any missing values, enter '999'.
5. For triage vital signs, enter the first set of readings if more than 1 reading are recorded.
6. For date/time variables, follow the format of '**dd/mm/yyyy hh:mm'**.
7. If you are not certain, please highlight the cell with yellow colour and seek advice from the investigators.
8. Data extraction will run in parallel to ensure accuracy of coding.
9. For patients with repeated ED attendance within the study period, the first attendance will be treated as the 'index presentation'.

Variables no. (excel column)	Variable name	Value	Definition
A	Coder 1	Coder initials	The initials of coder 1's name
B	Caseno.	Study code	Assigned study code on the master list
C	Hospital	AHNH	Alice Ho Miu Ling Nethersole Hospital
		CMC	Caritas Medical Centre
		KWH	Kwong Wah Hospital
		NDH	North District Hospital
		NLTH	North Lantau Hospital
		POH	Pok Oi Hospital
		PMH	Princess Margaret Hospital
		PWH	Prince of Wales Hospital
		PYNEH	Pamela Youde Nethersole Eastern Hospital
		QEH	Queen Elizabeth Hospital
		QMH	Queen Mary Hospital
		RH	Ruttonjee Hospital
		SJH	St John Hospital
		TKOH	Tseung Kwan O Hospital
		TMH	Tuen Mun Hospital
		TSH	Tin Shui Wai Hospital
		UCH	United Christian Hospital
		YCH	Yan Chai Hospital
		Others (free text)	Other hospital or clinic
D	HKID	HK ID number	**HK ID number – NOT NEED to enter bracket (to be erased after data collection)**
E	AENum	AE number	AE number on the A&E record - **NOT NEED to enter bracket**
F	Age	Age in years	Patient's age in years at the time of A&E presentation
G	Gender	0	Female
		1	Male
DM	Date and time	dd/mm/yyyy hh:mm	Date and time of A&E registration
DN	Year of presentation	yyyy	Year of A&E registration
DO	Ambulance case	0	Not transported by ambulance
		1	Transported by ambulance
DP	Police case	0	Not a police case
		1	Police case / brought in by police
DQ	On CSSA?	0	Not on comprehensive social allowance
		1	Receiving social allowance
DR	Triage Category	1	Triage Category 1 'immediate'
		2	Triage Category 2 'emergent'

		3	Triage Category 3 'urgent'
		4	Triage Category 4 'semi-urgent'
		5	Triage Category 5 'non-urgent'
DS	SBP	Systolic blood pressure	Triage systolic blood pressure in mmHg
DT	DBP	Diastolic blood pressure	Triage diastolic blood pressure in mmHg
DU	Pulse	Pulse rate	Triage pulse rate in beats per minute
DV	RR	Respiratory rate	Triage respiratory rate
DW	SaO2	Oxygen Saturation	Triage oxygen saturation in %
DX	O2 flow rate	The flow rate of supplemental oxygen given to the patient	Triage supplemental oxygen flow rate in L/min (If oxygen is not given – **input '0')**
DY	Temp	Temperature	Triage temperature
DZ	APVU	A	Alert
		V	Response to verbal command
		P	Response to pain only
		U	Unresponsive
EA	GCS	Glasgow coma score	The first reading documented in the AED notes
EB	Pupil size	Pupil size	Triage pupil size in mm (e.g. 3/2 – it means the right pupil was 3 mm and the left pupil 2 mm)
EC	Pupil reactivity	1	Pupils reactive to light or '+' following the documented pupil size in the notes. (e.g. +/+ means both pupils were reactive)
		0	Pupils not reactive to light or 'fixed' or '-ve' or '-' or 'sluggish' following the documented pupil size in the notes. (e.g. -/- means both pupils were non-reactive)
ED	Self-reported **Methamphetamine**	1	Clinical history or toxicology assays **suggested exposure to methamphetamine** before A&E presentation.
		0	Clinical history or toxicology assays **NOT suggestive of exposure to methamphetamine** before A&E presentation.
EE	Self-reported **MDMA**	1	Clinical history or toxicology assays **suggested exposure to MDMA** before A&E presentation.

		0	Clinical history or toxicology assays **NOT suggestive of exposure to MDMA** before A&E presentation.
EF	Self-reported **Other amphetamines** – free text	Free text	
EG	Self-reported **Cocaine**	1	Clinical history or toxicology assays **suggested exposure to cocaine** before A&E presentation.
		0	Clinical history or toxicology assays **NOT suggestive of exposure to cocaine** before A&E presentation.
EH	Self-reported **Cannabis**	1	Clinical history or toxicology assays suggested **exposure to cannabis** before A&E presentation.
		0	Clinical history or toxicology assays **NOT suggestive of exposure to cannabis** before A&E presentation.
EI	Self-reported **Heroin**	1	Clinical history or toxicology assays suggested **exposure to heroin** before A&E presentation.
		0	Clinical history or toxicology assays **NOT suggestive of exposure to heroin** before A&E presentation.
EJ	Self-reported **Other opioids**	Free text	
EK	Self-reported **Ketamine**	1	Clinical history or toxicology assays suggested **exposure to ketamine** before A&E presentation.
		0	Clinical history or toxicology assays **NOT suggestive of exposure to ketamine** before A&E presentation.
EL	Self-reported **Other drugs**	Free text	
EM	**Alcohol**	1	Clinical history or toxicology assays suggested **exposure to alcohol** before A&E presentation.
		0	Clinical history or toxicology assays **NOT suggestive of exposure to alcohol** before A&E presentation
EN	Time of exposure	dd/mm/yyyy hh:mm	
EO	Route of exposure	1	**Smoking/inhalation**

		2	**Snorting/mucosal**
		3	Oral ingestion
		4	Intravenous injection
		5	Others with free text
EP	Recreational use	1	Recreational use was the reason of exposure
		0	Other reasons of exposure
EQ	Other reason of use	Free text	
ER	Site of use	1	Home
		2	Workplace
		3	School
		4	Public space
		999	Unknown
ES	Music festival/ event	1	Drug use in music festival or event
		0	Drug use not associated with music festival or event
ET	Cross-border drug use	1	Drug use across the border with Shenzhen
		0	Drug use in Hong Kong
EU	Use with E-cigarette	1	Drug use associated with E-cigarette
		0	Drug use NOT associated with E-cigarette
EV	Tourist/non-local resident	1	The patient is a tourist or not a HK resident
		0	The patient is HK resident
EW	History of drug abuse	1	The patient has a history of drug abuse
		0	The patient has no history of drug abuse
EX	Known drugs being used in the past	Free text	Name of each drug reported abused in the past
EY	History of drug-induced psychosis	1	The patient has a history of drug-induced psychosis in the past
		0	The patient has NO history of drug-induced psychosis in the past
EZ	Previous medical FU for drug-related problem	1	The patient has previous follow up appointment for drug-related problem, defined as outpatient appointment records in epr including psychiatric consultation
		2	The patient defaulted previous medical follow up appointments for drug-related problem. **Only recent default is counted.**
		0	The patient has no previous follow up appointment for drug-related problem

FA	Previous Psy FU remarks	Free text	
FB	SAC FU	1	Follow up by substance abuse clinic
		0	No follow up by substance abuse clinic
FC	Previous medical treatment for drug-related problem	1	The patient received medication for drug-related problem in the past, including medications for psychiatric symptoms
		2	The patient received non-pharmacological treatment for drug-related problem in the past, including psychotherapy
		3	The patient defaulted treatment for drug-related problem in the past. **Only recent default is counted.**
		0	The patient did not receive any treatment in the past for drug-related problem
FD	Previous detox treatment	1	The patient received professional detoxification treatment in the past
		0	The patient did not receive professional detoxification treatment in the past
FE	History of refusal of detox	1	The patient refused detoxification treatment in the past
		0	The patient did not refuse detoxification treatment in the past
FF	Case followed up by social worker	1	The patient had already been followed by a social worker before the index presentation, e.g. brought in by social worker
		0	The patient had NOT been followed by a social worker before the index presentation
FG	History of refusal of social worker	1	The patient refused social worker follow up before explicitly in the medical notes.
		0	There is no history of refusal to see a social worker before.
FH	Case followed up by NGO	1	The patient had already been followed by a NGO before the index presentation
		0	The patient had NOT been followed by a NGO before the index presentation
FI	History of refusal of NGO service	1	The patient refused NGO drug treatment service before explicitly in the medical notes.

		0	There is no history of refusal to NGO drug treatment service before.
FJ	Good past health	1	The patient had good past health (physical health), not including drug-induced psychosis in the past before the index presentation. Input '0' to FK to FY if FJ is 1.
		0	The patient had chronic medical disease in the patient before the index presentation.
FK	Phx Asthma	1	The patient had a history of asthma.
		0	The patient did not have a history of asthma.
FL	Phx Thyroid disease	1	The patient had a history of thyroid disease.
		0	The patient did not have a history of thyroid disease.
FM	Phx IHD	1	The patient had a history of ischaemic heart disease.
		0	The patient did not have a history of ischaemic heart disease.
FN	Phx HT	1	The patient had a history of hypertension.
		0	The patient did not have a history of hypertension.
FO	Phx DM	1	The patient had a history of diabetes mellitus.
		0	The patient did not have a history of diabetes mellitus.
FQ	Phx Hyperlipidemia	1	The patient had a history of hyperlipidemia disease.
		0	The patient did not have a history of hyperlipidemia.
FR	Phx Depression	1	The patient had a history of depression.
		0	The patient did not have a history of depression.
FS	Phx Anxiety disorder	1	The patient had a history of anxiety disorder, including panic disorder or obsessive compulsive disorder.
		0	The patient did not have a history of anxiety disorder.
FT	Phx Borderline personality disorder	1	The patient had a history of borderline personality disorder.
		0	The patient did not have a history of borderline personality disorder.
FU	Phx Antisocial personality disorder	1	The patient had a history of antisocial personality disorder.

		0	The patient did not have a history of antisocial personality disorder.
FV	Phx Bipolar affective disorder	1	The patient had a history of bipolar affective disorder.
		0	The patient did not have a history of bipolar affective disorder.
FW	Phx HBV	1	The patient had a history of hepatitis B infection.
		0	The patient did not have a history of hepatitis B infection.
FX	Phx HCV	1	The patient had a history of hepatitis C infection.
		0	The patient did not have a history of hepatitis C infection.
FY	Phx HIV	1	The patient had a history of HIV infection.
		0	The patient did not have a history of HIV infection.
FZ	Other medical history	Free text	
GA (by doctor)	GIPSS	0-3	Gastrointestinal toxicity as graded with PSS
GB	Nausea	1	The presence of nausea during A&E or hospital admission
		0	The absence of nausea during A&E or hospital admission
GC	Vomiting	1	The presence of vomiting during A&E or hospital admission
		0	The absence of vomiting during A&E or hospital admission
GD	Diarrhoea	1	The presence of diarrhoea during A&E or hospital admission
		0	The absence of diarrhoea during A&E or hospital admission
GE	Abdominal pain	1	The presence of abdominal pain during A&E or hospital admission
		0	The absence of abdominal pain during A&E or hospital admission
GF	GI other symptoms	Free text	
GG (by doctor)	RespPSS	0-3	Respiratory toxicity as graded with PSS
GH	SOB	1	The presence of other 'SOB', 'Shortness of Breath', 'dyspnoea' during A&E or hospital admission

		0	The absence of other 'SOB', 'Shortness of Breath', 'dyspnoea' during A&E or hospital admission
GI	Pneumothorax	1	The presence of pneumothorax during A&E or hospital admission
		0	The absence of pneumothorax during A&E or hospital admission
GJ	Pneumomediastinum	1	The presence of pneumomediastinum during A&E or hospital admission
		0	The absence of pneumomediastinum during A&E or hospital admission
GK	Respiratory failure	1	The presence of respiratory failure or mechanical ventilation during A&E or hospital admission
		0	The absence of respiratory failure or mechanical ventilation during A&E or hospital admission
GL	Other respiratory symptoms	Free text	Free text of any respiratory symptoms
GM (by doctor)	CNSPSS	0-3	Neurological toxicity as graded with PSS
GN	Agitation	1	The presence of 'agitation', 'aggressiveness', 'violent act' during A&E or hospital admission
		0	The absence of 'agitation', 'aggressiveness', 'violent act' during A&E or hospital admission
GO	Coma	1	The presence of 'coma', or a GCS<8 during A&E or hospital admission
		0	The absence of 'coma', or a GCS<8 during A&E or hospital admission
GP	Dizziness	1	The presence of 'dizziness', 'fainting', 'lightheadedness' during A&E or hospital admission
		0	The absence of 'dizziness', 'fainting', 'lightheadedness' during A&E or hospital admission
GQ	Headache	1	The presence of 'headache' during A&E or hospital admission
		0	The absence of 'headache' during A&E or hospital admission

GR	Seizure	1	The presence of 'seizure', 'convulsion', 'fit' during A&E or hospital admission
		0	The absence of 'seizure', 'convulsion', 'fit' during A&E or hospital admission
GS	Unstable emotion	1	The presence of 'unstable emotion' during A&E or hospital admission
		0	The absence of 'unstable emotion' during A&E or hospital admission
GT	Visual hallucination	1	The presence of 'visual hallucination' during A&E or hospital admission
		0	The absence of 'visual hallucination' during A&E or hospital admission
GU	Auditory hallucination	1	The presence of 'auditory hallucination' during A&E or hospital admission
		0	The absence of 'auditory hallucination' during A&E or hospital admission
GV	Paranoid delusion	1	The presence of 'paranoid' or 'persecutory' delusion during A&E or hospital admission
		0	The absence of 'paranoid' or 'persecutory' delusion during A&E or hospital admission
GW	Other CNS symptoms	Free text	
GX	Ischaemic stroke	1	The presence of ischaemic stroke during index presentation
		0	The absence of ischaemic stroke during index presentation
GY	Haemorrhagic stroke	1	The presence of haemorrhagic stroke during index presentation
		0	The absence of haemorrhagic stroke during index presentation
GZ (by doctor)	CVSPSS	0-3	Cardiovascular toxicity as graded with PSS
HA	Shock	1	The presence of 'shock', 'hypotension', 'SBP<90' or 'MAB<65' during A&E or hospital admission
		0	The absence of 'shock', 'hypotension', 'SBP<90' or 'MAB<65' during A&E or hospital admission

HB	VT	1	The presence of 'ventricular fibrillation', 'ventricular tachycardia', 'VF', VT', 'Torsade de pointees' during A&E or hospital admission
		0	The absence of 'ventricular fibrillation', 'ventricular tachycardia', 'VF', VT', 'Torsade de pointees' during A&E or hospital admission
HC	AF	1	The presence of new-onset atrial fibrillation, irrespective of rate, during A&E or hospital admission
		0	The absence of new-onset atrial fibrillation, irrespective of rate, during A&E or hospital admission
HD	AMI	1	The presence of 'acute myocardial infarction', 'STEMI', 'non-STEMI' during A&E or hospital admission
		0	The absence of 'acute myocardial infarction', 'STEMI', 'non-STEMI' during A&E or hospital admission
HE	ACS	1	The presence of 'acute coronary syndrome', 'ACS', 'angina' during A&E or hospital admission
		0	The absence of 'acute coronary syndrome', 'ACS', 'angina'during A&E or hospital admission
HF	Highest Troponin level	Number (specify I or T in brackets)	e.g. 38 (I) – the highest troponin I level was 38 during the index hospitalization.
HG	Heart failure	1	The presence of 'heart failure' during A&E or hospital admission
		0	The absence of 'heart failure' during A&E or hospital admission
HH	Chest pain	1	The presence of 'chest pain' during A&E or hospital admission
		0	The absence of 'chest pain' during A&E or hospital admission
HI	Palpitation	1	The presence of 'palpitation' during A&E or hospital admission
		0	The absence of 'palpitation' during A&E or hospital admission
HJ	Cardiac arrest	1	The presence of 'cardiac arrest' during A&E or hospital admission
		0	The absence of 'cardiac arrest' during A&E or hospital admission
HK	Other CVS symptoms	Free text	
HL	Metabolic PSS	0-3	Metabolic toxicity as graded with PSS

HM	Hyperkalaemia	1	The presence of 'hyperkalaemia' or HIGH potassium level (K+ > 5) during A&E or hospital admission that warranted medical interventions
		0	The absence of 'hypokalaemia' or HIGH potassium level during A&E or hospital admission
HN	Hypokalaemia	1	The presence of 'hyperkalaemia' or LOW potassium level (K+ < 3.5) during A&E or hospital admission that warranted medical interventions
		0	The absence of 'hypokalaemia' or LOW potassium level during A&E or hospital admission
HO	Highest/lowest K level		
HP	Hypernatremia	1	The presence of 'hypernatraemia' or HIGH sodium level (Na+ > 150) during A&E or hospital admission that warranted medical interventions
		0	The absence of 'hypernatraemia' of HIGH sodium level during A&E or hospital admission
HQ	Hyponatraemia	1	The presence of 'hyponatraemia' or LOW sodium level (Na+ < 135) during A&E or hospital admission that warranted medical interventions
		0	The absence of 'hyponatraemia' or LOW sodium level during A&E or hospital admission
HR	Highest/lowest Na level		
HS	Hyperglycaemia	1	The presence of 'hyperglycaemia' or HIGH blood glucose level (Glucose > 10) during A&E or hospital admission that warranted medical interventions
		0	The absence of 'hyperglycaemia' or HIGH blood glucose level during A&E or hospital admission
HT	Hypoglycaemia	1	The presence of 'hypoglycaemia' or LOW blood glucose level (Glucose < 3.5) during A&E or hospital admission that warranted medical interventions

		0	The absence of 'hypoglycaemia' or LOW blood glucose level during A&E or hospital admission
HU	Highest/lowest glucose level		
HV	Metabolic acidosis	1	The presence of 'metabolic acidosis' during A&E or hospital admission
		0	The absence of 'metabolic acidosis' during A&E or hospital admission
HW	Lowest pH		
HX	Blood gas pattern		
HY	Hyperthermia	1	The presence of 'hyperthemia' or 'temperature > 38ºC' during index presentation
		0	The absence of 'hyperthemia' or 'temperature > 38ºC' during index presentation
HZ	Highest Temperature		
IA	Other metabolic symptoms	Free text	Free text of other metabolic symptoms
IC	Liver PSS	0-3	Liver toxicity as graded with PSS
ID	KidneyPSS	0-3	Kidney toxicity as graded with PSS
IE	Elevated serum creatinine	1	Serum creatinine was ABOVE the upper limit in laboratory analysis.
		0	Serum creatinine was BELOW the upper limit in laboratory analysis.
IF	Peak serum creatinine		The peak serum creatinine level during the index hospitalisattion.
IG	Baseline creatinine		
IH	Acute kidney injury (KDIGO AKI criteria)	1	The presence of AKI during A&E or hospital admission
		0	The absence of AKI during A&E or hospital admission
II	BloodPSS	0-3	Haematological toxicity as graded with PSS
IJ	DIC	1	The presence of disseminated intravascular coagulation during A&E or hospital admission
		0	The absence of disseminated intravascular coagulation during A&E or hospital admission
IK	Muscle pain or cramp or rigidity	1	The presence of 'muscle pain', 'muscle cramp', or 'muscle rigidity' during A&E or hospital admission
		0	The absence of 'muscle pain', 'muscle cramp', or 'muscle rigidity' during A&E or hospital admission
IL	Peak CK level		

IM	Rhabdomyolysis	1	The presence of rhabdomyolysis during A&E or hospital admission
		0	The absence of rhabdomyolysis during A&E or hospital admission
IN	Compartment syndrome	1	The presence of compartment syndrome during A&E or hospital admission
		0	The absence of compartment during A&E or hospital admission
IO	Muscle PSS	0-3	Muscle toxicity as graded with PSS
IP	LocalPSS	0-3	Skin or local toxicity as graded with PSS
IQ	Sweating	1	The presence of sweating during A&E or hospital admission
		0	The absence of sweating during A&E or hospital admission
IR	Shivering	1	The presence of shivering during A&E or hospital admission
		0	The absence of shivering during A&E or hospital admission
IS	Other complications	Free text	
IT	Other PSS	0-3	Other toxicity as grade with PSS with free text
IU	Overall PSS	0-3	Overall Poison Severity Score
IV	Injury	1	The presence of any physical injury or trauma during the index presentation
		0	The absence of any physical injury or trauma during the index presentation
IW	Injury	Free text	
IX	Abrasion	1	The presence of abrasion during A&E or hospital admission
		0	The absence of abrasion during A&E or hospital admission
IY	Laceration	1	The presence of laceration during A&E or hospital admission
		0	The absence of laceration during A&E or hospital admission
IZ	Contusion	1	The presence of contusion during A&E or hospital admission
		0	The absence of contusion during A&E or hospital admission
JA	Fracture	1	The presence of fracture during A&E or hospital admission
		0	The absence of fracture during A&E or hospital admission
JB	Aggressive act to self	1	Any evidence of physical harm to oneself, including any form of self-

			inflicted injuries and overdose of medications
		0	No evidence of aggressive act to oneself
JC	Nature of self-harm	Free text	
JD	Aggressive act to other	1	Aggressive act to another person
		0	No evidence of aggressive act to another person
JE	Nature of aggressive act to other	Free text (Who?)	
JF	Associated infection	1	The presence of infection associated with recreational drug use during the index presentation
		0	The absence of infection associated with recreational drug use during the index presentation
JG	Associated with psychiatric complaints	1	The presence of psychotic symptoms associated with recreational drug use during the index presentation, **defined as the presence of any hallucinations, delusions or clinical diagnosis of psychosis**
		0	The absence of psychotic symptoms associated with recreational drug use during the index presentation
JH	Urine immunoassay	1	'ABON' or 'ACON' test kit for urine drug screen ordered
		0	No 'ABON' or 'ACON' test kit ordered for urine drug screen
JI	Methamphetamine detected with bedside kit?	1	Methamphetamine detected with 'ABON' or 'ACON' urine kit
		0	Methamphetamine NOT detected with 'ABON' or 'ACON' urine kit
JJ	MDMA detected with bedside kit?	1	MDMA detected with 'ABON' or 'ACON' urine kit
		0	MDMA NOT detected with 'ABON' or 'ACON' urine kit
JK	Cocaine detected with bedside kit?	1	Cocaine detected with 'ABON' or 'ACON' urine kit
		0	Cocaine NOT detected with 'ABON' or 'ACON' urine kit
JL	Cannabis detected with bedside kit?	1	Cannabis detected with 'ABON' or 'ACON' urine kit
		0	Cannabis NOT detected with 'ABON' or 'ACON' urine kit

JM	Heroin detected with bedside kit?	1	'MOP' detected with 'ABON' or 'ACON' urine kit
		0	'MOP' NOT detected with 'ABON' or 'ACON' urine kit
JN	Ketamine detected with bedside kit?	1	Ketamine detected with 'ABON' or 'ACON' urine kit
		0	Ketamine NOT detected with 'ABON' or 'ACON' urine kit
JO	Other drugs detected with bedside kit?	Free text	Free text of other drugs detected with bedside kit
JP	Hospital laboratory toxicology screen done?	1	Hospital laboratory toxicology screen was performed
		0	Absence of hospital laboratory toxicology screening
JQ	Which specimens were analyzed in the hospital lab?	1	Urine
		2	Serum
		3	Both urine and serum
		4	Others
JR	Methamphetamine detected in hospital lab?	1	Methamphetamine detected in hospital lab
		0	Methamphetamine NOT detected in hospital lab
JS	MDMA detected in hospital lab?	1	MDMA detected in hospital lab
		0	MDMA NOT detected in hospital lab
JT	Cocaine detected in hospital lab?	1	Cocaine detected in hospital lab
		0	Cocaine NOT detected in hospital lab
JU	Cannabis detected in hospital lab?	1	Cannabis detected in hospital lab
		0	Cannabis NOT detected in hospital lab
JV	Heroin detected in hospital lab?	1	Heroin detected in hospital lab
		0	Heroin NOT detected in hospital lab
JW	Ketamine detected in hospital lab?	1	ketamine detected in hospital lab
		0	Ketamine NOT detected in hospital lab
JX	Other drugs detected in hospital lab?	Free text	Free text of other drugs detected in hospital lab
JY	Toxicology Reference Laboratory assay done?	1	Specimen sent to the Toxicology Reference Lab for analysis

		0	Specimen NOT sent to the Toxicology Reference Lab for analysis
JZ	Which specimens were analyzed in the TRL lab?	1	Urine
		2	Serum
		3	Both urine and serum
		4	Others
KA	Methamphetamine detected in TRL?	1	Methamphetamine detected in TRL
		0	Methamphetamine NOT detected in TRL
KB	MDMA detected in TRL?	1	MDMA detected in TRL
		0	MDMA NOT detected in TRL
KC	Cocaine detected in TRL?	1	Cocaine detected in TRL
		0	Cocaine NOT detected in TRL
KD	Cannabis detected in TRL?	1	Cannabis detected in TRL
		0	Cannabis NOT detected in TRL
KE	Heroin detected in TRL?	1	Heroin detected in TRL
		0	Heroin NOT detected in TRL
KF	Ketamine detected in TRL?	1	Ketamine detected in TRL
		0	Ketamine NOT detected in TRL
KG	Other drugs detected in TRL (Free text)	Free text	Free text of other drugs detected in TRL
KH	ED Physical restraint?	1	Physical restraint needed in the ED
		0	Physical restraint NOT needed in the ED
KI	ED Chemical restraint?	1	Chemical restraint needed in the ED
		0	Chemical restraint NOT needed in the ED
KJ	ED IV fluid	1	Intravenous fluid infused in the ED
		0	Intravenous fluid NOT needed in the ED
KK	ED Supplemental O2	1	Supplemental O2 given in the ED
		0	Supplemental O2 NOT given in the ED
KL	ED GI decontamination	1	Gastrointestinal decontamination performed in the ED
		0	Gastrointestinal decontamination NOT performed in the ED
KM	ED Gastric lavage	1	Gastric lavage performed in the ED
		0	Gastric lavage NOT performed in the ED

KN	ED Activated charcoal	1	Activated charcoal administered in the ED
		0	Activated charcoal NOT administered in the ED
KO	ED Antidote	1	Antidote administered in the ED
		0	Antidote NOT administered in the ED
KP	Diazepam (Valium) given in the ED	1	Diazepam/Valium administered in the ED
		0	Diazepam/Valium NOT administered in the ED
KQ	Midazolam (Dormicum) given in the ED	1	Midazolam/Dormicum administered in the ED
		0	Midazolam/Dormicum NOT administered in the ED
KR	Lorazepam (Ativan) given in the ED	1	Lorazepam/Ativan administered in the ED
		0	Lorazepam/Ativan NOT administered in the ED
KS	Naloxone (Narcane) given in the ED	1	Naloxone/Narcane administered in the ED
		0	Naloxone/Narcane NOT administered in the ED
KT	Flumazenil (Annexate) given in the ED	1	Flumazenil/Annexate administered in the ED
		0	Flumazenil/Annexate NOT administered in the ED
KU	Haloperidol (Haldol) given in the ED	1	Haloperidol/Haldol administered in the ED
		0	Haloperidol/Haldol NOT administered in the ED
KV	Dexmedetomidine (Precedex) given in the ED	1	Dexmedetomidine/Precedex administered in the ED
		0	Dexmedetomidine/Precedex NOT administered in the ED
KW	Propofol given in the ED	1	Propofol administered in the ED
		0	Propofol NOT administered in the ED
KX	Other antidote?	Free text if yes	The name(s) of the antidote given in the ED
KY	ED Antidote given time	Dd/mm/yyyy hh:mm	The time of the **FIRST dose** of the antidote given
KZ	ED antiarrhythmic	free text	Amiodarone or other antiarrhythmic administered in the ED
LA	ED Electrical shock	1	Electrical therapy given in the ED
		0	Electrical therapy NOT given in the ED
LB	ED Electrical shock	Free text if yes	Defibrillation (D) or DC synchronised cardioversion (CD)

LC	ED CPR	1	Chest compression was performed in the ED
		0	Chest compression was NOT performed in the ED
LD	ED Inotrope	Free text if yes	Inotrope infused in the ED
LE	ED Renal replacement therapy	Free text if yes	CVVH/ HD/ HF/ CAPD
LF	ED Intubation and mechanical intubation	1	Intubation performed in the ED, including RSI
		0	Intubation NOT performed in the ED
LG	ED ECMO	1	Extracorporeal Membrane Oxygenation initiated in the ED
		0	Extracorporeal Membrane Oxygenation NOT initiated in the ED
LH	ED ATT	1	Anti-tetanus toxoid administered in the ED
		0	Anti-tetanus toxoid NOT administered in the ED
LI	ED Wound dressing	1	Wound dressing performed in the ED
		0	Wound dressing NOT performed in the ED
LJ	ED Suturing/Sterile strip	1	Suturing/sterile strips performed in the ED
		0	Suturing/sterile strips NOT performed in the ED
LK	ED Thiamine	1	Thiamine administered in the ED
		0	Thiamine NOT administered in the ED
LL	ED KCl supplement	1	Potassium supplement (IV or oral) administered in the ED
		0	Potassium supplement NOT administered in the ED
LM	ED D50	1	Dextrose solution administered in the ED
		0	Dextrose solution NOT administered in the ED
LN	ED NaHCO3	1	Sodium Bicarbonate administered in the ED
		0	Sodium bicarbonate NOT administered in the ED
LO	ED Alkaline diuresis	1	Alkaline diuresis administered in the ED
		0	Alkaline diuresis NOT administered in the ED
LP	Other treatment	Free text	

LQ	Hospital Physical restraint?	1	Physical restraint needed in the hospital.
		0	Physical restraint NOT needed in the hospital
LR	Hospital Chemical restraint?	1	Chemical restraint needed in the hospital
		0	Chemical restraint NOT needed in the hospital
LS	Hospital IV fluid	1	Intravenous fluid infused in the hospital.
		0	Intravenous fluid NOT needed in the hospital
LT	Hospital Supplemental O2	1	Supplemental O2 given in the hospital
		0	Supplemental O2 NOT given in the hospital
LU	Hospital GI decontamination	1	Gastrointestinal decontamination performed in the hospital
		0	Gastrointestinal decontamination NOT performed in the hospital
LV	Hospital Gastric lavage	1	Gastric lavage performed in the hospital
		0	Gastric lavage NOT performed in the hospital
LW	Hospital Activated charcoal	1	Activated charcoal administered in the hospital
		0	Activated charcoal NOT administered in the hospital
LX	Hospital Antidote	1	Antidote administered in the hospital
		0	Antidote NOT administered in the hospital
LY	Diazepam (Valium) given in the hospital	1	Diazepam/Valium administered in the hospital
		0	Diazepam/Valium NOT administered in the hospital
LZ	Midazolam (Dormicum) given in the hospital	1	Midazolam/Dormicum administered in the hospital
		0	Midazolam/Dormicum NOT administered in the hospital
MA	Lorazepam (Ativan) given in the hospital	1	Lorazepam/Ativan administered in the hospital
		0	Lorazepam/Ativan NOT administered in the hospital
MB	Naloxone (Narcane) given in the hospital	1	Naloxone/Narcane administered in the hospital
		0	Naloxone/Narcane NOT administered in the hospital

MC	Flumazenil (Annexate) given in the hospital	1	Flumazenil/Annexate administered in the hospital
		0	Flumazenil/Annexate NOT administered in the hospital
MD	Haloperidol (Haldol) given in the hospital	1	Haloperidol/Haldol administered in the hospital
		0	Haloperidol/Haldol NOT administered in the hospital
ME	Dexmedetomidine (Precedex) given in the hospital	1	Dexmedetomidine/Precedex administered in the hospital
		0	Dexmedetomidine/Precedex NOT administered in the hospital
MF	Propofol given in the hospital	1	Propofol administered in the hospital
		0	Propofol NOT administered in the hospital
MG	Hospital Other antidote?	Free text if yes	The name(s) of the antidote given in the hospital
MH	Hospital Antidote given time	Dd/mm/yyyy hh:mm	The time of the **FIRST dose** of the antidote given in the hospital
MI	Hospital antiarrhythmic	free text	Amiodarone or other antiarrhythmic administered in the hospital
MJ	Hospital Electrical shock	1	Electrical therapy given in the hospital
		0	Electrical therapy NOT given in the hospital
MK	Hospital Electrical shock	Free text if yes	Defibrillation (D) or DC synchronised cardioversion (CD) in the hospital
ML	Hospital CPR	1	Chest compression was performed in the hospital
		0	Chest compression was NOT performed in the hospital
MM	Hospital Inotrope	Free text if yes	Inotrope infused in the hospital
MN	Hospital Renal replacement therapy	Free text if yes	CVVH/ HD/ HF/ CAPD given in the hospital
MO	Hospital Intubation and mechanical intubation	1	Intubation performed in the hospital, including RSI, but NOT including intubation for operation
		0	Intubation NOT performed in the hospital
MP	Hospital ECMO	1	Extracorporeal Membrane Oxygenation initiated in the hospital
		0	Extracorporeal Membrane Oxygenation NOT initiated in the hospital
MQ	Hospital Wound dressing	1	Wound dressing performed in the hospital

		0	Wound dressing NOT performed in the hospital
MR	Hospital Suturing/Sterile strip	1	Suturing/sterile strips performed in the hospital
		0	Suturing/sterile strips NOT performed in the hospital
MS	Hospital Thiamine	1	Thiamine administered in the hospital
		0	Thiamine NOT administered in the hospital
MT	Hospital KCl supplement	1	Potassium supplement (IV or oral) administered in the hospital
		0	Potassium supplement NOT administered in the hospital
MU	Hospital D50	1	Dextrose solution administered in the hospital
		0	Dextrose solution NOT administered in the hospital
MV	Hospital NaHCO3	1	Sodium Bicarbonate administered in the hospital
		0	Sodium bicarbonate NOT administered in the hospital
MW	Hospital Alkaline diuresis	1	Alkaline diuresis administered in the hospital
		0	Alkaline diuresis NOT administered in the hospital
MX	Hospital treatment	Free text	
MY	ED Disposition**	1	Discharge
		2	Observation or admission to the Emergency Medicine Ward
		3	Admission to general ward
		4	Intensive care unit
		5	Psychiatry ward
		6	Transfer to other hospital
		7	Referral to psychiatric specialist outpatient clinic (SOPC)
		8	Referral to other specialist outpatient clinic
		9	Left before being see
		10	Disappeared after being seen
		11	Discharge against medical advice
		12	Death
MZ	EMW admission	1	Admission to the Emergency Medicine Ward or Observation Ward
		0	Not admitted to the Emergency Medicine Ward or Observation Ward

NA	Date and time of EMW admission	dd/mm/yyyy hh:mm	
NB	Date and time of EMW discharge	dd/mm/yyyy hh:mm	
NC	LOSED	Not need to fill	Automatic calculation by excel formula
ND	ICU/CCU/PICU admission	1	Admission to the Intensive Care Unit, Cardiac Care Unit or Paediatric Intensive Care Unit
		0	Not admitted to the Intensive Care Unit, Cardiac Care Unit or Paediatric Intensive Care Unit
NE	Date and time of ICU admission	dd/mm/yyyy hh:mm	
NF	Date and time of ICU discharge	dd/mm/yyyy hh:mm	
NG	LOSICU	No need to fill	Automatic calculation by excel formula
NH	General ward admission	1	Admission to the General Ward
		0	Not admitted to the General Ward
NI	Date and time of general ward admission	dd/mm/yyyy hh:mm	
NJ	Date and time of general ward discharge	dd/mm/yyyy hh:mm	
NK	LOS in general ward	No need to fill	Automatic calculation by excel formula
NL	Psychiatric ward admission	1	Admission to the Psychiatry Ward
		0	Not admitted to the Psychiatry Ward
NM	Date and time of psychiatry ward admission	dd/mm/yyyy hh:mm	
NN	Date and time of psychiatry ward discharge	dd/mm/yyyy hh:mm	
NO	LOS Psychiatry ward	No need to fill	Automatic calculation by excel formula
NP	LOS hospital	No need to fill	Automatic calculation by excel formula
NQ	Psychiatric consultation during index presentation	1	Psychiatrist was consulted during index presentation
		0	Psychiatrist was NOT consulted during index presentation
NR	Refusal to psychiatric consultation	1	Documented patient's refusal to psychiatric consultation
		0	No refusal to psychiatric consultation

NS	Referral to psychiatrist OPD	1	The patient was referred to psychiatrist upon hospital discharge.
		0	The patient was NOT referred to psychiatrist upon hospital discharge.
NT	Referral to SAC	1	The patient was referred to substance abuse clinic upon hospital discharge.
		0	The patient was NOT referred to substance abuse clinic upon hospital discharge
NU	Refusal to psychiatric FU	1	Documented patient's refusal to psychiatric outpatient follow-up
		0	No refusal to psychiatric outpatient follow-up
NV	MSW referral during index presentation	1	The patient was referred to see medical social worker during index presentation
		0	The patient was NOT referred to see medical social worker during index presentation
NW	Refusal to MSW referral	1	Documented patient's refusal to MSW referral
		0	No refusal to MSW referral
NX	NGO referral during index presentation	1	The patient was referred to non-governmental organization for follow up during index presentation
		0	The patient was NOT referred to non-governmental organization for follow up during index presentation
NY	Refusal to NGO referral	1	Documented patient's refusal to NGO referral
		0	No refusal to NGO referral
NZ	Compulsory detox/prison	1	The patient was sent to compulsory detoxification centre on count order or prison upon hospital discharge.
		0	The patient was NOT sent to compulsory detoxification centre on count order or prison upon hospital discharge.
OA	Episode death?	1	The patient died in the episode
		0	The patient survived in the episode

**How to record ED disposition
If a patient was first admitted to the EMW, then transferred to the ICU, followed by general ward and then psychiatric ward admission and then DAMA, it should be coded as 2,4,3,5,11

Appendix 3. Poison Severity Score (adapted from Persson et al.)

ORGAN	NONE	MINOR	MODERATE	SEVERE	FATAL
	0	1	2	3	4
	No symptoms or signs	Mild, transient and spontaneously resolving symptoms or signs	Pronounced or prolonged symptoms or signs	Severe or life-threatening symptoms or signs	Death
GI-tract		• Vomiting, diarrhoea, pain • Irritation, 1st degree burns, minimal ulcerations in the mouth • Endoscopy: erythema, oedema	• Pronounced or prolonged vomiting, diarrhoea, pain, ileus • 1st degree burns of critical localization or 2nd and 3rd degree burns in restricted areas • Dysphagia • Endoscopy: ulcerative transmucosal lesions	• Massive haemorrhage, perforation • More widespread 2nd and 3rd degree burns • Severe dysphagia • Endoscopy: ulcerative transmural lesions, circumferential lesions, perforation	
Respiratory system		• Irritation, coughing, breathlessness, mild dyspnoea, mild bronchospasm • Chest X-ray: abnormal with minor or no symptoms	• Prolonged coughing, bronchospasm, dyspnoea, stridor, hypoxemia requiring extra oxygen • Chest X-ray: abnormal with moderate symptoms	• Manifest respirator insufficiency (due to e.g. severe bronchospasm, airway obstruction, glottal oedema, pulmonary oedema, ARDS, pneumonitis, pneumonia, pneumothorax) • Chest X-ray: abnormal with severe symptoms	

ORGAN	NONE	MINOR	MODERATE	SEVERE	FATAL
	0	1	2	3	4
	No symptoms or signs	Mild, transient and spontaneously resolving symptoms or signs	Pronounced or prolonged symptoms or signs	Severe or life-threatening symptoms or signs	Death
Nervous system		• Drowsiness, vertigo, tinnitus, ataxia	• Unconsciousness with appropriate response to pain	• Deep coma with inappropriate response to pain or unresponsive to pain	
			• Brief apnoea, bradypnoea	• Respiratory depression with insufficiency	
		• Restlessness	• Confusion, agitation, hallucinations, delirium	• Extreme agitation	
			• Infrequent, generalized or local seizures	• Frequent, generalized seizures, status epilepticus, opisthotonus	
		• Mild extrapyramidal symptoms	• Pronounced extrapyramidal symptoms		
		• Mild cholinergic/anticholinergic symptoms	• Pronounced cholinergic/anticholinergic symptoms		
		• Paraesthesia	• Localized paralysis not affecting vital functions	• Generalized paralysis or paralysis affecting vital functions	
		• Mild visual and auditory disturbances	• Visual and auditory disturbances	• Blindness, deafness	

Appendix 4. American Association of Poison Control Centers' National Poison Data System definition of medical outcome (adapted from Mowry et al.)

Outcome	Description
No effect	The patient did not develop any signs or symptoms as a result of the exposure.
Minor effect	The patient developed some signs or symptoms as a result of the exposure, but they were minimally bothersome and generally resolved rapidly with no residual disability or disfigurement. A minor effect is often limited to the skin or mucus membranes (e.g., self-limited gastrointestinal symptoms, drowsiness, skin irritation, firstdegree dermal burn, sinus tachycardia without hypotension, and transient cough).
Moderate effect	The patient exhibited signs or symptoms as a result of the exposure that were more pronounced, more prolonged, or more systemic in nature than minor symptoms. Usually, some form of treatment is indicated. Symptoms were not life-threatening, and the patient had no residual disability or disfigurement (e.g., corneal abrasion, acidbase disturbance, high fever, disorientation, hypotension that is rapidly responsive to treatment, and isolated brief seizures that respond readily to treatment).
Major effect	The patient exhibited signs or symptoms as a result of the exposure that were life-threatening or resulted in significant residual disability or disfigurement (e.g., repeated seizures or status epilepticus, respiratory compromise requiring intubation, ventricular tachycardia with hypotension, cardiac or respiratory arrest, esophageal stricture, and disseminated intravascular coagulation).
Death	The patient died as a result of the exposure or as a direct complication of the exposure.

Appendix 5. Brief description of novel psychoactive substances reported to HKPIC from 2017–2023 from local emergency departments.

Novel psychoactive substance	Brief description
Phenylethylamines	
Paramethoxymethamphetamine (PMMA) and paramethoxyamphetamine (PMA)	PMMA and PMA are synthetic methoxylated derivatives of methamphetamine and amphetamine, respectively. PMA can be a PMMA metabolite. PMMA and PMA are abused as a MDMA substitute but the toxicity is substantially higher than that of MDMA, earning the street name 'Death'. Severe toxicities, including acute respiratory distress, hyperthermia, cardiac arrest, convulsions, sudden collapse, acute kidney injury, hepatic injury, rhabdomyolysis, coagulopathy, cardiac ischaemia, and/or multiple organ failure have been reported.[90–92] Psychotic presentations have been reported after ingesting 'instant coffee sachets' that contained PMMA and other stimulants in Taiwan.[93]
4-Fluoroamphetamine (4-FA)	4-Fluoroamphetamine is a halogenated amphetamine with modes of action similar to those of MDMA and amphetamine.[94,95] Severity toxicity including fatalities, cerebral haemorrhage, inverted Takotsubo cardiomyopathy, myocardial infarction and acute heart failure have been reported.[96,97]
2-/3-Fluoroethylamphetamine (2-/3-FEA)	2-/3-Fluoroethylamphetamine are fluorinated analogues of ethylamphetamine that produce entactogenic and stimulant effects. Information about its pharmacological and toxicological effects is limited.[98]
4-bromo-2,5-dimethoxyphenethylamine (2C-B)	2C-B is a ring-substituted phenethylamine in the 2C family of phenethylamines. Reported symptoms after exposure include mydriasis, euphoria, agitation or aggression, hallucinations, confusion, anxiety, hypertension, tachycardia, serotonin toxicity, hyperthermia, and seizures.[99–101]
Synthetic cathinones	
***N*-cyclohexylmethylone**	*N*-cyclohexylmethylone is a synthetic cathinone ith a cyclohexyl substituent attached to the amino group.[102] Limited information exist regarding its exact toxicity. Clinical presentations after exposure may be similar to other synthetic cathinones.
Dibutylone	Dibutylone, also known as bk-DMBDB, bk-MMBDB or methylbutylone is a synthetic cathinone within limited information on toxicities. Deaths have been reported after dibutylone exposure.[103]
Ethylone	Ethylone is a N-ethyl form of methylone, a synthetic cathinone. Synthetic cathinones are

	emerging drugs of abuse with both amphetamine-like properties and the ability to modulate serotonin.[104] Fatalities related to ethylone use have been reported.[105]
Eutylone	Eutylone, also known as bk-EBDB, is a synthetic cathinone first reported in Poland in 2014.[106] Clinical presentations after exposure include delirium, agitation, tachycardia, hypertension, hyperthermia, rhabdomyolysis, seizure, and cardiac arrest.[107]
Pentylone	Pentylone, also known as bk-EDBP or ephylone is a new synthetic cathinone. Hyperthermia, elevated troponins, rhabdomyolysis, hypoglycaemia, hepatic and renal injury, respiratory failure, metabolic acidosis, disseminated intravascular coagulation and deaths have been reported after exposure to *N*-ethyl pentylone derived from pentylone.[108,109]
Tryptamines	
5-Methoxy-*N,N*-methylisopropyltryptamine (5-MeO-MiPT) and 5-methoxy-*N,N*-diethyltryptamine (5-MeO-DET)	5-Methoxy-*N,N*-methylisopropyltryptamine and 5-methoxy-*N,N*-diethyltryptamine are synthetic active hallucinogenic tryptamine derivatives and 5-HT2 receptor agonists that are structurally similar to 5-MeO-DIPT with presumably similar toxic effects. Clinical toxic effects of 5-MeO-DIPT include agitation, hallucinations, tachycardia, hypertension, confusion, tremor and seizure.[110,111]
Psilocin (magic mushroom)	Psilocin is the pharmacologically active metabolite of psilocybin, a naturally-occurring tryptamine found in Psilocybe mushrooms ('magic' or 'hallucinogenic' mushrooms).[111] Common toxic effects include mydriasis, hallucinations, agitation and tachycardia.[112]
Piperazines	
1-(3-trifluoromethylphenyl)piperazine (TFMPP)	TFMPP is a non-selective serotonin receptor agonist of piperazine family with hallucinogenic effect. Combination with 1-benzylpiperzine has been reported in the literature to achieve MDMA-like effects and TFMPP has been found in street ecstasy.[113, 114] Adverse reactions to TFMPP include agitation, bruxism and tachycardia.[115]
Phencyclidine-type NPS	
Deschloro-*N*-ethyl-norketamine (2-oxo-PCE)	2-oxo-PCE is an arylcyclohexylamine analogue with ketamine-like dissociative effects. The main clinical symptoms associated with 2-oxo-PCE include impaired consciousness, confusion, abnormal behaviour, hypertension, tachycardia, and seizure.[116] In 2017, 2-oxo-PCE was detected in a

	cluster of patients, drug driving cases and in drug seizures in Hong Kong.[116,117]
Deschloroketamine (DCK)	Deschloroketamine is a ketamine analogue with a lack of information on its toxicity.[118] In animal model, its effects are comparable to that of ketamine but its duration of action is longer.[119]
Fluoro-2-oxo-PCE	Fluoro-2-oxo-PCE is a ketamine analogue in the arylcyclohexylamine class with little clinical toxicology data.
2-Fluoro-deschoroketamine (2F-DCK)	2F-DCK is a new ketamine analogue. Reported toxic effects include impaired consciousness, agitation, abnormal behaviours, hypertension, tachycardia etc. It is frequently detected together with ketamine and its analogues.[120]
Tiletamine	Tiletamine is a phencyclidine derivative and an NMDA antagonist with structural similarity with ketamine. Tiletamine is used as a dissociative veterinary anaesthetic agent in combination with zolazepam. Reported toxicities include involuntary choreatic movement, acute psychosis, coma and death.[121,122]
Novel benzodiazepines	
Etizolam	Etizolam is a novel benzodiazepine with structural similarity to pharmaceutical benzodiazepines. Reported effect during overdose include drowsiness, confusion and paradoxical agitation.[123,124]
Novel opioids	
Protonitazene	Protonitazene is a highly potent benzimidazole synthetic μ-opioid receptor agonist with heroin-like effects, including high risk of abuse and toxicity including central nervous system and respiratory depression.[125,126]
Synthetic cannabinoids	
Methyl (2S)-2-{[1-(5-fluoropentyl)-1H-indole-3-carbonyl]amino}-3,3-dimethylbutanoate (5F-MDMB-PICA)	5F-MDMB-PICA is a synthetic cannabinoid with potent agonist activity at CB1 and CB2 receptors. Observed adverse effects included balance deficiencies, ocular effects such as conjunctival injection, glassy eyes, delayed or unresponsive pupil light reaction, mood disturbances, aggression, confusion, erratic behaviour, mental leaps, slow reaction and slurred speech. Fatalities associated with its use have been reported.[127]
Other substances	
1-Propionyl-d-lysergic acid diethylamide (1P-LSD)	1P-LSD is a psychedelic substance structurally related to d-lysergic acid (LSD) with the addition of a propionyl group at the 1-position. It is the prodrug

	of LSD.[128] It produces LSD-like serotonergic in animal model but the psychoactive effects in human remains to be invesitgated.[129]

Appendix 6

Supplementary Table 1. Univariate analysis of factors associated with severe complications in acute heroin and ketamine toxicity.

	Episodes that involved heroin N = 360	Episodes that involved ketamine N = 179
Age—median, year	0.422#	0.848#
Sex	0.421*	0.875*
Transgender		
Social allowance	0.345*	0.516**
Ambulance case	0.291*	0.096*
Police case	0.448*	0.089*
Non-local resident	>0.99**	0.495**
Pregnant at the time of presentation	N/A	>0.99**
MSM	0.444**	0.207**
Methamphetamine	0.315*	0.631*
Cocaine	0.194**	0.080*
Cannabis	0.444**	0.365**
MDMA	N/A	0.234**
Ketamine	N/A	
Heroin		N/A
Cough mixture or pills	0.101*	>0.99**
Zopiclone or zolpidem	0.660*	>0.99**
Benzodiazepine	0.630*	0.688**
Novel psychoactive substances	N/A	0.096**
Co-ingestion of alcohol	0.681*	0.789**
Inhalation as the primary route of exposure	0.121*	0.284*
Insufflation as the primary route of exposure	>0.99**	0.030*
Parental as the primary route of exposure	0.318*	0.207**
Place of drug abuse		
Place outside Hong Kong	N/A	N/A
Past history of drug abuse	0.147**	0.614*
History of drug-induced psychosis	0.052*	0.929*
Schizophrenia	0.001*	>0.99**
Depression	0.569*	0.365**
Anxiety	0.444**	>0.99**
Bipolar affective disorder	N/A	>0.99**
Antisocial personality disorder	0.158*	N/A
Borderline personality disorder	0.446**	>0.99**
Good past health	0.101*	0.805*

Hypertension	0.024*	0.670**
Diabetes mellitus	0.055*	N/A
Ischaemic heart disease	0.092**	N/A
Previous psychiatry follow-up	0.677*	0.680*
Previous detoxification treatment	0.026*	0.315*
Followed-up by social worker	0.658*	0.067*
Followed-up by NGO service provider for drug abuse	0.175*	0.298*
Triage category	<0.001*	0.001*
Pulse rate—mean, beat per minute	<0.001^	0.006^
Temperature—median	0.944#	0.822#
Pupil size—median	0.945#	0.108#
Pupil reactivity	0.009*	0.008**
Tachycardia > 120 beats per minute	<0.001	<0.001*
Temperature > 40°C	0.444**	0.042**
Temperature > 39°C	0.197**	0.007**
Temperature > 38°C	0.924*	<0.001**
Chest pain/discomfort	0.312*	0.329**
Palpitation	0.257**	0.365**
Hypertension	0.465*	0.057*
Sinus tachycardia	<0.001*	0.004*
Agitation	<0.001*	0.027*
Confusion	0.719*	0.263*
Headache	0.548**	0.670**
Dizziness	0.016*	0.575**
Syncope	0.609*	0.516**
Drowsiness	<0.001*	0.310*
Weakness	0.723*	>0.99**
Numbness	N/A	0.503**
Restlessness	0.632**	>0.99**
Unstable emotion	0.548**	0.569**
Anxiety	>0.99**	0.585**
Auditory hallucination	0.010*	>0.99**
Visual hallucination	0.036**	0.347**
Tactile hallucination	N/A	0.207**
Paranoid delusion	>0.99**	>0.99**
Referential delusion	N/A	0.503**
Any hallucination	0.010*	>0.99**
Any delusion	>0.99**	0.733**
Nausea	0.697**	0.585**
Vomiting	0.658*	0.025**
Diarrhoea	>0.99**	>0.99**
Abdominal pain	>0.99**	>0.99**

Shortness of breath	0.844*	0.700**
Hyperventilation	0.444**	>0.99**
Cough	>0.99**	>0.99**
Bronchospasm	0.444**	>0.99**
Diaphoresis	>0.99**	0.058**
Deliberate self-harm	0.469**	0.010**
Violent behaviours to others	>0.99**	0.207**
Associated injury	0.647*	0.130*

Abbreviations: NGO, non-governmental organisation

Footnotes: *Pearson Chi-square test, **Fisher's Exact test, ^Student t-test, #non-parametric test

Supplementary Table 2. Multivariable logistic regression analysis of factors associated with severe complications of acute heroin toxicity in the emergency department

	Un-adjusted OR (95% CI)	P value	Adjusted OR (95% CI)*	P value
Tachycardia > 120 beats per minute	4.19 (2.14-8.22)	< 0.001	5.61 (2.02-15.55)	0.001
Triage category	2.49 (1.86-3.35)	< 0.001	2.42 (1.65-3.56)	<0.001
Previous detoxification treatment	1.61 (1.06-2.45)	0.026	2.06 (1.19-3.58)	0.010
Drowsiness	0.28 (0.18-0.44)	< 0.001	0.28 (0.16-0.49)	< 0.001
Hypertension	2.09 (1.09-4.00)	0.027		
Agitation	3.69 (1.72-7.90)	0.001		
Schizophrenia	3.94 (1.62-9.57)	0.002		
Pupil reactivity	1.82 (1.16-2.87)	0.009		
Dizziness	0.31 (0.11–0.84)	0.022		
Any hallucination	0.11 (0.01-0.85)	0.034		

Abbreviations: CI, confidence interval; OR, odds ratio

Supplementary Table 3. Multivariable logistic regression analysis of factors associated with severe complications of acute ketamine toxicity in the emergency department

	Un-adjusted OR (95% CI)	P value	Adjusted OR (95% CI)*	P value
Temperature > 38ºC	13.63 (3.40-54.70)	< 0.001	20.51 (3.04-138.32)	0.002
Tachycardia > 120 beats per minute	4.39 (1.98-9.76)	< 0.001	5.02 (1.63-15.49)	0.005
Pupil reactivity	5.23 (1.61-17.01)	0.006		
Vomiting	3.45 (1.19-10.00)	0.023		
Deliberate self-harm	3.68 (1.46-9.25)	0.006		
Agitation	2.37 (1.09-5.17)	0.030		
Triage category	2.36 (1.44-3.88)	0.001		

Abbreviations: CI, confidence interval; OR, odds ratio