


See discussions, stats, and author profiles for this publication at: <https://www.researchgate.net/publication/393952275>

Significant changes in preference of illicit drug use in a population of Hanoi, Vietnam—A 6-year wastewater study (2018–2023)

Article in *Addiction* · July 2025
DOI: 10.1111/add.70147

CITATION
1


11 authors, including:



Hue Thi Thanh Tran

6 PUBLICATIONS 56 CITATIONS

SEE PROFILE




Zhe Wang

The University of Queensland

17 PUBLICATIONS 165 CITATIONS

SEE PROFILE

READS
40




Hieu K.T. Ngo

The University of Queensland

15 PUBLICATIONS 47 CITATIONS

SEE PROFILE



Nguyen Thi Kieu Anh

Hanoi University of Pharmacy

11 PUBLICATIONS 539 CITATIONS







SEE PROFILE

RESEARCH REPORT

ADDICTION

SSA

Significant changes in preference of illicit drug use in a population of Hanoi, Vietnam—A 6-year wastewater study (2018–2023)

Tran Thi Thanh Hue^{1,2} | Hieu K. T. Ngo³  | Zhe Wang³  |
 Nguyen Thi Kieu Anh¹ | Vu Ngan Binh¹  | Ngo Quang Trung¹ |
 Pham Quoc Chinh⁴ | Hai Thanh Luong⁵ | Qiuda Zheng³  | Wayne Hall³  |
 Phong K. Thai³ 

¹Hanoi University of Pharmacy, Faculty of Analytical Chemistry and Drug Quality Control, Hanoi, Vietnam

²Department of Science and Training Management, National Institute of Drug Quality Control, Hanoi, Vietnam

³Queensland Alliance for Environmental Health Sciences (QAEHS), The University of Queensland, Woolloongabba, Australia

⁴Department of Toxins, National Institute of Forensic Medicine, Hanoi, Vietnam

⁵School of Criminology and Criminal Justice, Griffith University, Gravatt, Australia

Correspondence

Vu Ngan Binh, Hanoi University of Pharmacy, Faculty of Analytical Chemistry and Drug Quality Control, Hanoi, Vietnam.
 Email: binhvn@hup.edu.vn

Funding information

This study was partly supported by the National Foundation for Science and Technology Development (NAFOSTED), Vietnam (project no. 105.99-2020.22).

Abstract

Background and Aim: Illicit drug use causes great harm and economical loss to society, yet there is limited understanding of its prevalence in the population in low-income countries like Vietnam where survey resources are scarce. In this study, we used wastewater analysis as a cost-effective monitoring tool to measure illicit drug use in a population of Hanoi, Vietnam, a low-income country in Southeast Asia.

Design, setting and participants: This is a longitudinal observational study. Wastewater samples were collected at a sewage canal serving > 430 000 people, in Hanoi, Vietnam, over a six-year period (2018–2023).

Measurements: Drug biomarkers for amphetamine, methamphetamine, 3,4-Methylenedioxymethamphetamine (MDMA), ketamine, morphine, codeine and benzoylcegonine were measured using liquid chromatography-tandem mass spectrometry via direct injection. The results were used to back-estimate per capita drug consumption. Together with an evaluation of general temporal trend, an interrupted time series analysis using segmented linear regression was conducted to examine the potential changes in drug use associated with the post-COVID-19 restriction.

Findings: There was a statistically significant decrease in methamphetamine use, with annual averages declining from a peak value of 359.2 to 125.6 mg/day/1000 people between 2018 and 2023 ($P < 0.001$). In contrast, ketamine use increased statistically significantly, rising from 149.7 to 465.9 mg/day/1000 people over the study period ($P < 0.001$), making it the most commonly used illicit drug. Cocaine and heroin use levels remained relatively low, while MDMA use was relatively stable over time. In the post-COVID-19 restriction period, declines were observed in methamphetamine, MDMA, cocaine and codeine consumption; however, only cocaine [Coefficient (standard error, SE) = -1.9 (0.9), $P = 0.034$] and codeine [Coefficient (SE) = -42.4 (12.4), $P = 0.001$] showed statistically significant downward trends. In contrast, ketamine and heroin consumption exhibited slight but non-significant increases, suggesting limited disruption during the post-restriction period.

Tran Thi Thanh Hue and Hieu K.T. Ngo contributed equally to this work.

Conclusions: Wastewater analysis shows that the market of illicit drugs in Vietnam is dynamic and shifting toward synthetic drugs. Methamphetamine replaced heroin as the substance with the highest estimated per capita use in Vietnam from 2018 to 2020 and was subsequently overtaken by ketamine by the end of 2022. Wastewater analysis can provide information on population use of multiple substances, including changes due to different factors in a cost-effective way, which is essential in data-poor countries.

KEYWORDS

cocaine, Covid-19 pandemic, heroin, ketamine, methamphetamine, Vietnam

INTRODUCTION

East and Southeast Asia's drug market has been marked by a decade of growth in the production and trafficking of synthetic drugs, particularly amphetamine-type stimulants (ATS) and ketamine [1]. Vietnam is a developing country in Southeast Asia with an extensive border in mountainous areas, which has been recognized as a transnational trafficking hub and an active area of illicit drug consumption [2–4]. A better understanding of drug use in Vietnam is required to identify substance use beyond traditional opioids and to facilitate the treatment of substance use disorders in the country [5]. A major challenge in Vietnam's drug control efforts is the lack of data available on the prevalence and types of drugs being used [6–8].

In recent years, wastewater-based epidemiology (WBE) or wastewater analysis has significantly contributed to monitoring drug use in high-income countries [9, 10]. It has not been widely used in low-income countries where data on drug use are particularly lacking. Our pilot study in 2018 to 2020 has reported the emergence of ketamine in the illicit drug scene [11]. However, longitudinal data are needed to better understand changes in Vietnam's illicit drug market in response to transnational (organised) crimes, and changes in the modus operandi of drug trafficking groups in the Golden Triangle areas in shared borderland between Laos, Myanmar and Thailand [2, 3]. Objective information about the prevalence of illicit drug use in the population from longitudinal WBE can inform the formulation of effective supply, demand and harm reduction policies [12]. WBE provides data on population drug use, distinguishing it from data on seizures, which may reflect the dynamic trafficking activities in regions such as Vietnam.

WBE is officially supported and integrated into national drug monitoring frameworks across many countries, such as Australia and European unions [10, 13, 14]. While WBE studies have been widely conducted during and after the Covid-19 pandemic [15], low-income countries often face barriers to implementing WBE studies because of poor sewage infrastructure [16, 17]. However, WBE could still be a better surveillance tool in these settings because developing countries do not have the resources to conduct the large-scale drug use surveys and data linkage studies [18, 19] while illicit drug use can have a greater negative impact on the society in the absence of social support services. WBE could be more important in Vietnam and other Asian countries, given that family dynamics and stigma may lead to underreporting of illicit drug use [20].

During the coronavirus disease 2019 (COVID-19) pandemic, Vietnam implemented targeted lockdowns and a wide range of containment measures, including school and workplace closures, restaurants and bars closed or limited hours opening and suspension of domestic and international travel [21]. These interventions might disrupt both the supply and demand dynamics of illicit drug market. However, limited evidence exists on how these activities during the COVID-19 pandemic affected population-level drug use, especially in the period following the easing of restrictions. Most existing studies in Vietnam have focused on high-risk groups. For example, a qualitative study found that people who inject drugs (PWID) increased methamphetamine use in group settings to cope with lockdown-related stress and boredom [22]. In contrast, a survey of 780 PWID observed decreased use of non-injected drugs—such as amphetamine and ecstasy—during the restriction period, while no significant change was observed for methamphetamine or cocaine use [23]. For understanding drug use in the broader population, WBE provides a low-cost and effective monitoring tool that can capture drug use dynamics over time and identify any disruptions because of the pandemic.

In this study, we used WBE to evaluate temporal trends in licit and illicit drug use in a population of Hanoi, the capital of Vietnam. Our objectives were to: (i) assess the long-term trends in the use of dominant illicit drugs over 6 years (2018–2023); and (ii) evaluate changes in drug consumption patterns following the lifting of COVID-19 restrictions, with a particular focus on long-term post-restriction effects. This is the first long-term WBE study of its kind conducted in a low- and middle-income country (LMIC). By demonstrating the feasibility of WBE in a context where traditional drug monitoring is limited, our findings offer proof for future WBE applications in similar LMIC settings. Moreover, this study provides evidence-based information to support intervention planning and inform national public health policy.

MATERIALS AND METHODS

Sample collection and preparation

Wastewater samples were collected at the site located 500 m from the wastewater treatment plant (WWTP) in one of the main sewage canals in Hanoi, the Kim Nguu River (Figure S1). The canal receives domestic wastewater from the center of the city with a mean daily volume of approximately 85 000 m³/day (based on the data from the Hanoi

sewage and drainage company). The estimated population size, obtained from daily flow rate and per capita discharge rate, was approximately 430 000 inhabitants [11]. Details of chemicals, reagents, analytical samples, and Quality Assurance/Quality Control (QA/QC) are provided in the Supporting Information (Tables S1–S3).

Wastewater samples were collected with a sampling volume of 500 mL by compositing several grab samples within a period of 1 hour. Collection was conducted in multiple 1-month periods over 6 consecutive years, starting in September 2018 and ending in November 2023 (Table S4). Moreover, to assess the impact of diurnal variation of drug concentrations in wastewater in low-resource settings, hourly samples were collected in 3 consecutive days (from 7 PM on 31 October 2022 to 6 PM on 3 November 2022). After collection, all samples were acidified immediately to pH 2 using 1 M hydrochloric acid and transported to the Hanoi University of Pharmacy for processing. Wastewater samples were vortexed well and filtered using 0.45 µm regenerated cellulose syringe filter (Finetech, Taiwan). One millilitre of filtrate was transferred to the 2-mL glass amber vials and was frozen at −70°C before being shipped on ice to the Queensland Alliance for Environmental Health Sciences (QAEHS), The University of Queensland and then kept at −20°C until analysis.

Back estimation of drug consumption

The consumption of targeted drugs in this study was estimated using the back-calculation method reported previously [10, 24] as shown in equation 1 below:

$$\text{Consumption of drug (mg/d/1000 pp)} = \frac{C_i \times F}{P \times E_i} \times \frac{M_{\text{Par}}}{M_{\text{Met}}} \times 1000 \quad (1)$$

where C_i is the concentration of the target compound i in the influent (µg/L). F is the average value of daily volume of wastewater (m³/day). P is the population of the WWTP catchment (people), E_i is the excretion factor of the target analyte (%), M_{Par} is the molecular weight of the parent compound and M_{Met} is the molecular weight of the metabolite (or target analyte). The excretion factor (E_i) of the targeted compounds is listed in Table 1.

The consumption of heroin was calculated based on the mass load of morphine and codeine (Text S1), as morphine measured in wastewater samples originates from the metabolism of both codeine and heroin [31]. For amphetamine, consumption was determined by measuring the mass load of amphetamine and subtracting the amount excreted from methamphetamine metabolism [26]. Cocaine consumption levels were calculated using the mass load of its primary metabolite, benzoylecgonine. Methamphetamine consumption was directly estimated from its mass load, while ketamine and 3,4-methylenedioxymethamphetamine (MDMA) consumption were directly estimated from their respective mass loads.

Statistical analysis

Diurnal variation analysis

We conducted a separate diurnal variation analysis to evaluate hourly fluctuations in drug biomarker concentrations within a 24-hour cycle. Grab samples were collected every hour continuously for 72 hours at a single monitoring site. For each substance, we calculated the hourly deviation from the daily mean concentration and examined consistency across days. This analysis aimed to evaluate whether fixed-time daily sampling could provide a reliable approximation of average daily concentrations. This is particularly relevant for LMIC settings, where 24-hour composite sampling is often not feasible because of resource and infrastructure limitations.

Long-term trend analysis

To explore temporal trends in population-level drug use from 2018 to 2023, we performed simple linear regression models using 'decimal-year' as the continuous time variable for each drug. For visualization, both linear regression lines and locally estimated scatterplot smoothing (LOESS) curves were plotted to display overall and local patterns of drug use over time.

TABLE 1 Excretion factor used to estimate the consumption of drugs.

No.	Compound	Metabolites/biomarkers	Excretion factor (%)	References
1	Amphetamine	Amphetamine	36.3	Gracia-Lor <i>et al.</i> [25]
2	Methamphetamine	Methamphetamine	43	Gracia-Lor <i>et al.</i> [25]
		Amphetamine	9	Gao <i>et al.</i> [26]
3	MDMA	MDMA	22.5	Gracia-Lor <i>et al.</i> [25]
4	Heroin	Morphine	42	Du <i>et al.</i> [27]
5	Codeine	Morphine	6	Gracia-Lor <i>et al.</i> [25]
		Codeine	30	Thai <i>et al.</i> [28]
6	Ketamine	Ketamine	20	Du <i>et al.</i> [29]
7	Cocaine	Benzoylecgonine	29	Castiglioni <i>et al.</i> [30]

MDMA, 3,4-methylenedioxymethamphetamine.

Interrupted time series analysis

To evaluate changes in drug use associated with the post-COVID-19 restriction period, we conducted an interrupted time series analysis (ITSA) using segmented linear regression. The primary aim was to assess long-term changes in drug consumption following the onset of post-restriction conditions. During the COVID-19 pandemic, the city experienced its first lockdown in April 2020 and a prolonged lockdown from July to September 2021. Although no wastewater samples were collected during these strict lockdown phases, the models aimed to detect consumption shifts between the pre-pandemic and post-restriction periods. The intervention point was defined as 15 December 2020 representing the first available data point after the initial wave of COVID-19 lockdowns, allowing for the assessment of long-term post-restriction trends.

We implemented generalized least squares (GLS) with an autoregressive (AR) [1] correlation structure to account for serial autocorrelation in the residuals including the following variables: 'decimal_year' (a continuous time variable representing the pre-intervention trend), 'covid' (a binary variable, coded 1 from 15 December 2020 onward) and 'post_covid_time' (a continuous variable measuring time since the intervention).

A sequential time variable 'time-index' was constructed to represent the temporal order of observations. Model diagnostics included inspection of residuals, autocorrelation function (ACF) and partial autocorrelation function (PACF) plots and Durbin-Watson statistics to quantify autocorrelation in residuals.

As a sensitivity analysis, we re-estimated all models using a GLS framework with an AR [2] correlation structure. Model comparisons based on Akaike information criterion (AIC) and likelihood ratio tests showed that AR [1] provided a better overall fit in most cases. All statistical analyses were conducted using RStudio version 4.4. The analysis in this study was conducted without pre-registration; therefore, the findings should be considered exploratory.

RESULTS

Evaluation of diurnal variation of drug biomarkers in wastewater and its impact on WBE implementation

All target biomarkers for amphetamine, methamphetamine, MDMA, ketamine, benzoylecgonine, morphine and codeine were detected in the hourly grab samples collected over 3 days. The concentration differences of each target drug compared to the average concentration are shown in Figure S2. These figures illustrated that sampling around noon (from 11 AM–1 PM) consistently represented the average value (for methamphetamine, MDMA, codeine and morphine), but slightly under-represented levels for ketamine and benzoylecgonine.

Presence of drug biomarkers in wastewater over the 6-year monitoring

The concentrations of seven target drugs measured at the sampling site along the sewer canal over a 6-year monitoring period are summarised in Table 2. Six target drug biomarkers (methamphetamine, MDMA, ketamine, benzoylecgonine, morphine and codeine) were detected in over 60% of the samples. The detection frequency of amphetamine, a metabolite of methamphetamine and an illicit drug itself, decreased over time. Notably, it was not detected in the most recent two sampling periods. The ratio of concentrations between amphetamine and methamphetamine in 2018 to 2021 ranged from 0.11 to 0.15. Benzoylecgonine was also in the low concentration ranges, often close to the limit of quantification (LOQ) (ranging from the LOQ up to 0.06 µg/L). In the first three sampling periods before 2022, methamphetamine had the highest concentration among the target analytes, followed by morphine, codeine, ketamine and MDMA. However, in the later sampling period from 16 December 2022 to 15 January 2023, ketamine emerged as the substance with the highest concentration.

Trends of drug use over the 6 years

The findings revealed distinct trends in the consumption of different drugs in Hanoi between 2018 and 2023 (Figure 1). A statistically significant decrease was observed in methamphetamine, heroin and cocaine consumption (all $P < 0.001$), indicating an overall downward trajectory. Methamphetamine was the dominant illicit drug during 2018 to 2021, with a moderate decline in consumption from 414 to 285 mg/d/1000 pp. From 2022, methamphetamine use clearly decreased by half compared to the previous years, with the average value <130 mg/d/1000 pp. Cocaine and heroin also showed slight, but statistically significant decreasing trends over time. Cocaine consumption reached its peak level of 20.6 mg/d/1000 pp by the end of 2022 while heroin, previously the second-highest prevalence after methamphetamine in 2018 to 2019, decreased afterward and lost its second position (Table S5).

In contrast, ketamine use showed a statistically significant increase over time ($P < 0.001$) and surpassed methamphetamine as the most dominant detected substance by the end of the study period. MDMA use showed a slightly upward trend, but the change was not significant ($P = 0.715$). There was a downward trend in codeine consumption over time, although it was not statistically significant ($P = 0.364$). The variation in codeine mass measured in wastewater is consistent with import statistics of codeine to Vietnam in the same period (Figure S3). The consistency between two datasets underscores the utility of WBE in monitoring substance use at the population level.

TABLE 2 Concentration range (µg/L) and detection frequency of illicit drugs detected in this study.

Target compounds	09/2018 (n = 30)	12/2018- 01/2019 (n = 31)	12/2019- 01/2020 (n = 31)	12/2020- 01/2021 (n = 32)	09/2021- 10/2021 (n = 30)	12/2021- 01/2022 (n = 31)	03/2022- 04/2022 (n = 30)	06/2022- 07/2022 (n = 30)	12/2022- 01/2023 (n = 31)	10/2023- 11/2023 (n = 31)
AMP	Range 0.03-0.05 Mean* 0.11 DF (%) 100.0	0.04-0.15 0.10 48.4	<LOQ-0.13 - 48.4	<LOQ-0.08 0.04 90.6	<LOQ-0.21 - 40.0	<LOQ-0.05 - 9.7	- - 0.0	- - 0.0	- - 0.0	- - 0.0
METH	Range 0.28-1.09 Mean* 0.73 DF (%) 100.0	0.44-1.20 0.90 0.71	0.26-0.95 0.71 0.71	0.39-0.95 0.62 100.0	0.02-0.63 0.26 100.0	0.10-0.40 0.26 100.0	0.07-0.33 0.24 100.0	0.08-0.30 0.19 100.0	0.23-0.34 0.28 100.0	0.10-0.45 0.27 100.0
MDMA	Range 0.05-0.24 Mean* 0.15 DF (%) 100.0	0.09-0.31 0.19 0.20	<LOQ-0.31 0.20 96.8	0.16-0.30 0.22 100.0	<LOQ-0.20 0.10 96.7	0.05-0.20 0.13 100.0	0.07-0.22 0.16 100.0	0.03-0.22 0.14 100.0	0.24-0.41 0.29 100.0	0.05-0.25 0.15 100.0
KET	Range 0.04-0.20 Mean* 0.14 DF (%) 100.0	0.09-0.29 0.19 0.24	0.10-0.47 0.24 100.0	0.19-0.40 0.28 100.0	0.03-0.37 0.16 100.0	0.04-0.27 0.15 100.0	0.02-0.31 0.18 100.0	0.01-0.32 0.17 100.0	0.31-0.79 0.50 100.0	0.15-0.64 0.43 100.0
MOR	Range <LOQ-0.35 Mean* 0.25 DF (%) 96.7	<LOQ-0.53 0.35 96.8	0.10-0.42 0.31 100.0	0.15-0.32 0.23 100.0	<LOQ-0.26 0.15 86.7	0.09-0.31 0.20 100.0	0.08-0.41 0.28 100.0	<LOQ-0.32 0.22 90.0	0.22-0.41 0.33 100.0	<LOQ-0.24 0.16 100.0
COD	Range 0.05-0.21 Mean* 0.14 DF (%) 100.0	0.05-0.30 0.17 0.31	0.10-0.92 0.31 100.0	0.13-1.03 0.27 100.0	<LOQ-0.22 0.13 70.0	<LOQ-0.29 0.13 87.1	<LOQ-0.30 0.17 93.3	<LOQ-0.29 0.16 80.0	0.20-0.40 0.29 100.0	<LOQ-0.27 0.15 77.4
BEN	Range <LOQ-0.06 Mean* 0.02 DF (%) 90.0	<LOQ-0.02 0.01 96.8	0.01-0.06 0.03 100.0	0.01-0.05 0.01 100.0	<LOQ-0.03 0.01 90.0	<LOQ-0.03 0.01 64.5	<LOQ-0.02 0.02 93.3	<LOQ-0.04 0.01 70.0	0.02-0.06 0.03 100.0	- - 0.0

‘-’, not detected in all wastewater samples; AMP, amphetamine; BEN, benzoylcegonine; COD, codeine; DF, detection frequency; KET, ketamine; LOQ, limit of quantification; MDMA, 3,4-methylenedioxymethamphetamine; METH, methamphetamine; MOR, morphine.

*Mean only determined if more than 50% of sample was above the LOD.

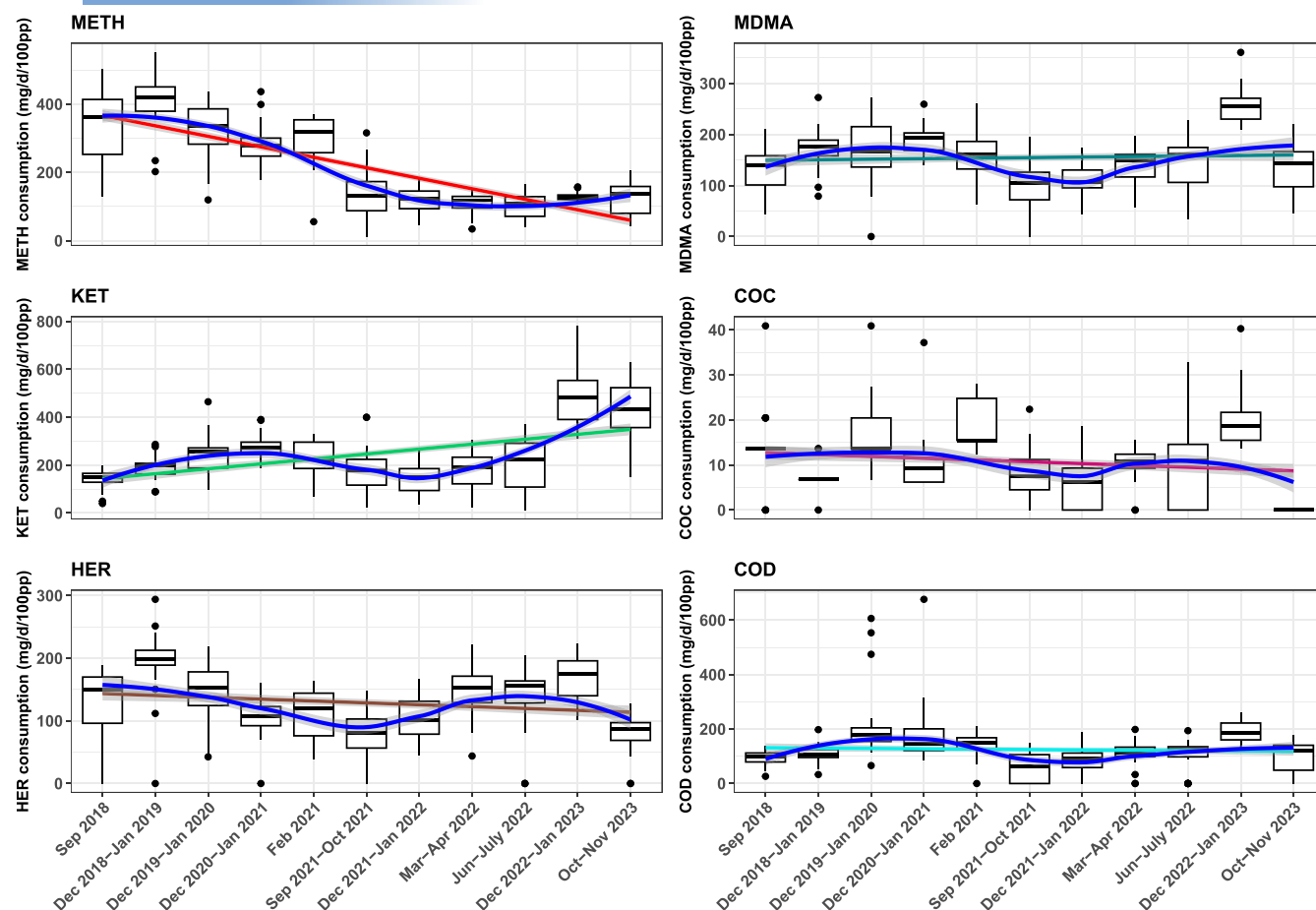


FIGURE 1 Trend of illicit drug and codeine use in Hanoi, Vietnam from 2018 to 2023. Locally estimated scatterplot smoothing (LOESS) curves (blue) show smoothed time trends, while linear regression lines (red or colored) illustrate overall directional tendencies.

TABLE 3 Segmented regression results estimating changes in drug consumption by the COVID-19 post-restrictions.

Coefficient (SE)	Methamphetamine	MDMA	Ketamine	Cocaine	Heroin	Codeine
Baseline level	24 456.2 (22 246.8)	-12 361.4 (14 331.9)	-22 833.4 (22 715.2)	-3080.8 (1733.4)	4467.6 (11 919.7)	-80 461.3 (23 188.6)*
Time	-12.0 (11.0)	6.1 (7.1)	11.3 (11.2)	1.5 (0.9)	-2.2 (5.9)	39.8 (11.5)*
Post-covid time	-8.4 (11.9)	-5.1 (7.6)	1.6 (11.9)	-1.9 (0.9)*	2.8 (6.4)	-42.4 (12.4)*

The post-intervention slope is calculated as the sum of the 'time' coefficient (representing the pre-intervention trend) and the 'post_covid_time' coefficient (representing the change in trend after the intervention).

* $P < 0.05$.

Illicit drug consumption post-COVID-19 restrictions

The results indicated that drug-specific patterns diverged in the post-restriction phase. Notably, a decline was observed in the consumption of methamphetamine, MDMA, cocaine and codeine after the lifting of restrictions; however, only the downward trends for cocaine ($P = 0.034$) and codeine ($P = 0.001$) were statistically significant. In contrast, slight but non-significant increases were observed for ketamine ($P = 0.896$) and heroin ($P = 0.659$). These findings suggest potential shifts in drug preference and availability in the aftermath of COVID-19 control measures (Table 3).

DISCUSSION

Evaluation of diurnal variation of drug biomarkers in wastewater and its impact on WBE implementation

Because of the limited resources in sewage infrastructure in low income countries like Vietnam, the use of autosamplers for collecting 24-h composite samples is often not feasible as recognised by Devault *et al.* [17]. The results of our diurnal sampling demonstrated that drug concentrations around noon (11 AM–1 PM) were generally representative of daily averages for most substances, although they slightly

underestimated levels of ketamine and benzoylecgonine. It means that a composite of multiple grab samples within an hour at a fixed time during the day could be used for the study of temporal trend in drug consumption because the systematic error is likely to be consistent over time. To minimize the bias of random large variation, we collected 30 samples for a period of sampling during the 6-year period.

Presence of drug biomarkers in wastewater over the 6-year monitoring

The high detection frequency of methamphetamine, ketamine, MDMA, codeine and morphine suggests their widespread use in the population of Hanoi. The detection frequency of amphetamine decreased, and it was not detected in the most recent two sampling periods. As a metabolite of methamphetamine and an illicit drug itself, in recent years, its low ratio relative to methamphetamine (ranging from 0.11–0.15 in 2018–2021) indicated that amphetamine measured in wastewater originated mainly from methamphetamine consumption [26]. Similarly, benzoylecgonine levels remained consistently low—often near the LOQ, suggesting limited cocaine use consistent with patterns observed in other Asian countries such as Malaysia [32] and China [33]. Notably, a significant shift in drug use was observed in the later sampling period from 16 December 2022 to 15 January 2023, when ketamine surpassed methamphetamine in measured concentration.

Trends of drug use over the 6 years

The findings showed that consumption in methamphetamine decreased significantly over time. This decline was consistent with a reported decrease in the proportion of drug users reporting methamphetamine use in Vietnam in 2022 [1]. This trend may be affected by recent national drug control efforts. The Vietnamese government implemented several anti-drug campaigns in recent years, with a strong focus on synthetic drugs, particularly methamphetamine, which has been a major drug of concern. According to the 'Country briefing' report by the Drugs Abuse Network for Asia and the Pacific (DAINAP, 2023), the percentage of registered drug users in Vietnam using ATS decreased from approximately 75% to 80% in 2019 and 2020 to 24% in 2022, much lower than in neighbouring countries (e.g. Philippines >90%; Malaysia >60%; Thailand >80% in 2022). This decline might be partly attributed to Vietnam's stringent 2021 drug law, which introduced compulsory testing for suspected ATS users and shifted focus from administrative sanctions to criminal penalties, effective from 1 January 2022. The enforcement of this law facilitated the detection of ATS use through observable behavioral indicators, associated with these substances in practice, mandatory testing procedures and more targeted policing strategies [4]. Seizures of methamphetamine also surged during this period, ranging from approximately 2.4 to 4.0 million tablets between 2020 and 2022, doubling compared to previous years (DAINAP, 2023). In response to the challenges of ATS usage and trafficking, law enforcement efforts have prioritized reducing

supply over implementing demand and harm reduction policies [34]. Meanwhile, MDMA use showed a slightly increasing trend over the 6-year period, but not significantly. The divergent trends between MDMA and methamphetamine use may reflect the difference in user profiles and usage contexts, even though they are both ATS. Methamphetamine use is associated with regular users. In contrast, MDMA is more commonly used in recreational settings, where it is sought for empathogenic effects [35].

In contrast to methamphetamine, ketamine use showed a statistically significant increase over time. By the end of 2022, ketamine had emerged as the highest estimated per capita consumption among the monitored substances, despite Vietnamese authorities reporting 'no seizures of ketamine' during the same period [1]. Classified as a Class III drug in Vietnam, ketamine can be legally used in healthcare and veterinary settings as an anesthetic. However, misuse of ketamine has increased because of its dissociative and hallucinogenic effects [36]. The emerging dominance of ketamine could be attributed to several factors, including its lower regulatory status, greater affordability, legitimate medical availability and unique psychoactive effects, all of which make it more accessible than more tightly controlled drugs like methamphetamine [37]. It should be noted that ketamine also appears to be replacing traditionally abused drugs in some Asian countries, potentially driven by stricter penalties and enforcement on other substances in recent years [38].

Cocaine and heroin showed slightly decreases over time. Cocaine consumption reached its peak level of 20.6 mg/d/1000 pp by the end of 2022, which remains significantly lower compared to levels observed in Western countries [10]. Heroin, which had the second-highest prevalence after methamphetamine in 2018 to 2019, decreased afterward and lost its second position. According to the United Nations Office on Drugs and Crime report [1], the quantity of heroin seizures in Vietnam had shown a clear decreasing trend from 2018 to 2020 and stabilized from 2020 to 2022. However, our data suggested that heroin still has the potential to make a comeback in Vietnam while law enforcement is focusing their attention on ATS.

There was a downward trend in codeine consumption over time, although it was not statistically significant. The consistency between codeine trends in wastewater and national import statistics (Figure S3) demonstrates the advantage of WBE in providing an accurate reflection of drug use prevalence compared to seizure or survey data, particularly during periods of restrictions or limited resources.

The influence of post-COVID-19 restrictions on illicit drug consumption

Our study revealed notable decreases in most studied illicit drugs following the onset of the post-COVID-19 restrictions period, although only cocaine and codeine show significant long-term declines. These findings are consistent with studies conducted in high-income countries, which reported temporary reductions in drug consumption during the pandemic [39–41]. Conversely, other studies found limited

or no impact of COVID-19 restrictions on drug use in certain populations [42–44].

Ketamine and heroin consumption increased slightly, but the upward trends were not statistically significant. This may indicate a rebound in drug supply chains or shifting drug preferences after the easing of restrictions. Notably, ketamine use appeared less affected in the long term, possibly reflecting its pre-existing upward trend. A recent WBE study in United States reported recorded levels of ketamine use during the COVID-19 pandemic [45]. Moreover, the pandemic's influence on drug use could have varied depending on the type of drug including social drugs declined because of gathering restrictions, while solitary-use drugs increased because of isolation [46].

In Vietnam, the level of illicit drug use during the COVID-19 pandemic was seriously impacted by the 'zero-tolerance lockdown' policy, which imposed stringent 'nothing-in-and-nothing-out' restrictions, including a ban on outdoor and indoor entertainment events [47]. While we were unable to collect wastewater samples during the lockdown periods, it is likely that these extreme measures significantly affected both drug availability and consumption. Mobility restrictions, border closures and a decline in global trade hindered the production and sale of illicit drugs, disrupted the supply chains of drug markets and the economic difficulties caused by COVID-19 may affect the drug consumption behaviour [48]. However, drug traffickers may also adapt to these challenges by trafficking and trading drugs via online platforms (particularly on the Dark web) and/or using maritime routes [49]. Therefore, the influence of the pandemic, either directly or indirectly, on the supply-and-demand process should be approached from multiple perspectives with adequate contextual information.

Our results demonstrate that in LMIC contexts with limited infrastructure WBE can generate reliable, population-level data that are otherwise difficult to obtain through conventional methods. In countries like Vietnam, where drug monitoring relies primarily on surveys and seizure statistics, and where community drug-checking programs are not available [50], WBE provides an effective and complementary approach for identifying emerging substances and tracking usage trends. It serves as a potentially transformative tool for evidence-based drug policy that can also function as an indirect early warning system. Moreover, integrating WBE into public health strategies in LMICs could enhance transparency regarding drug market dynamics and support the design of targeted, health-centered interventions [51].

Limitations

We acknowledge the following limitations of our study. First, the daily flow rate was not measured using a flow meter, but was instead estimated based on the average flow in the sewage river, as provided by the sewage company. Second, estimating heroin consumption from codeine and morphine concentrations in wastewater, while assuming negligible morphine use in the community, could introduce some

uncertainty. Third, we did not account for the degradation of biomarkers in septic tanks, which are part of the sewage system in the city, for chemicals such as morphine and codeine. These limitations may lead to an underestimate of the consumption of those drugs. However, the potential systematic errors would not affect the overall trend in illicit drug use observed in this study. Finally, although we cannot identify individual users or specific subpopulations, our study focused on a small, well-defined urban catchment area where wastewater flows into a localized canal. This minimized mixing from multiple sources and enabled the findings to reflect drug use trends more accurately within a specific community, supporting improved early warning systems and local public health monitoring.

CONCLUSIONS

This is the first study to investigate the long-term trend in illicit drug use in Vietnam over a 6-year period, including the impact of post-COVID-19 restrictions. The results indicated that the illicit drug market in Vietnam is dynamic. Methamphetamine replaced heroin as the substance with the highest estimated per capita use during the period of 2018 to 2020 and was subsequently overtaken by ketamine by the end of 2022. Ketamine use significantly increased over time, becoming the illicit drug with the highest estimated per capita use in recent years. Our data suggest that drug consumption patterns diverged after the lifting of COVID-19 restrictions, with cocaine declining, whereas other substances remained relatively stable. This study demonstrated that WBE can provide important information on population drug use in a cost-effective manner, particularly in low- and middle-income countries with limited resources.

AUTHOR CONTRIBUTIONS

Tran Thi Thanh Hue: Methodology (equal), formal analysis (equal), writing—original draft (equal), writing—review and editing (equal). **Hieu K.T. Ngo:** Methodology (equal), formal analysis (equal), writing—original draft (equal), writing—review and editing (equal). **Zhe Wang:** Methodology (equal), formal analysis (supporting), writing—review and editing (equal). **Nguyen Thi Kieu Anh:** Conceptualization (equal), resources (equal), funding acquisition (equal), supervision (equal). **Vu Ngan Binh:** Methodology (equal), writing—review and editing (equal), funding acquisition (equal), supervision (equal). **Ngo Quang Trung:** Methodology (equal). **Pham Quoc Chinh:** Methodology, writing—review and editing (equal). **Hai Thanh Luong:** Writing—review and editing (equal). **Qiuda Zheng:** Methodology (equal), writing—review and editing (equal). **Wayne Hall:** Writing—review and editing (equal). **Phong K. Thai:** Conceptualization (equal), methodology (equal), supervision (equal), writing—review and editing (equal).

ACKNOWLEDGEMENTS

This study was partly supported by the National Foundation for Science and Technology Development (project no. 105.99-2020.22). We thank the staff of the Faculty of Analytical Chemistry and Drug Quality control, Hanoi University of Pharmacy, Hanoi, Vietnam for

their sampling and analysing support. The Queensland Alliance for Environmental Health Sciences, The University of Queensland, gratefully acknowledges the financial support of Queensland Health, Australia. Q.Z. is the recipient of an ARC Discovery Early Career Researcher Award (DE250101412) and P.K.T. is the recipient of an ARC Mid-Career Industry Fellowship (IM240100018).

DECLARATION OF INTERESTS

None.

DATA AVAILABILITY STATEMENT

The data that supports the findings of this study are available in the supplementary material of this article.

ORCID

Hieu K. T. Ngo  <https://orcid.org/0000-0003-4949-2950>

Zhe Wang  <https://orcid.org/0000-0003-1266-7251>

Vu Ngan Binh  <https://orcid.org/0000-0003-1285-7514>

Qiuda Zheng  <https://orcid.org/0000-0002-6456-0926>

Wayne Hall  <https://orcid.org/0000-0003-1984-0096>

Phong K. Thai  <https://orcid.org/0000-0003-0042-3057>

REFERENCES

1. UNODC (United Nations Office on Drugs and Crime). Synthetic drugs in east and Southeast Asia. Latest developments and challenges 2023.
2. Luong HT. Drug trafficking in the mainland southeast Asian region: the example of Vietnam's shared borderland with Laos. *Int Ann Criminol*. 2020;58(1):130–51. <https://doi.org/10.1017/cri.2020.19>
3. Luong HT. Transnational crime and its trends in South-East Asia: a detailed narrative in Vietnam. *Int J Crime Justice Soc Democr*. 2020;9(2):88–101. <https://doi.org/10.5204/ijcjsd.v9i2.1147>
4. Tran MTN, Dunne MP, Minh Le G, Han HD, Nguyen TT, Luong HT, et al. Understanding Vietnam's drug policy for amphetamine-type stimulants misuse. *Harm Reduct J*. 2022;19(1):45. <https://doi.org/10.1186/s12954-022-00621-9>
5. Nong T, Capoccia V, Mulvey KP. Facing the future of substance use disorders treatment in Vietnam – A case study for international development and cooperation. *J Subst Abuse Treat*. 2022;134:108401. <https://doi.org/10.1016/j.jsat.2021.108401>
6. Luong H. T. Transnational drug trafficking across the Vietnam-Laos border; 2019, <https://doi.org/10.1007/978-3-030-15773-9>
7. Hieu DM, Gray B, Tuan DM, Colman BP. Facing drug addiction: Vietnam's struggle with opioids. *Drug Sci Pol Law*. 2021;7:20503245211034934. <https://doi.org/10.1177/20503245211034934>
8. Nguyen VT, Scannapieco M. Drug abuse in Vietnam: a critical review of the literature and implications for future research. *Addiction*. 2008;103(4):535–43. <https://doi.org/10.1111/j.1360-0443.2007.02122.x>
9. Gao Z, Gao M, Chen CH, Zhou Y, Zhan ZH, Ren Y. Knowledge graph of wastewater-based epidemiology development: a data-driven analysis based on research topics and trends. *Environ Sci Pollut Res Int*. 2023;30(11):28373–82. <https://doi.org/10.1007/s11356-023-25237-9>
10. González-Mariño I, Baz-Lomba JA, Alygizakis NA, Andrés-Costa MJ, Bade R, Bannwarth A, et al. Spatio-temporal assessment of illicit drug use at large scale: evidence from 7 years of international wastewater monitoring. *Addiction*. 2020;115(1):109–20. <https://doi.org/10.1111/add.14767>
11. Hue TTT, Zheng Q, Anh NTK, Binh VN, Trung NQ, Trang HT, et al. Prevalence of illicit drug consumption in a population of Hanoi: an estimation using wastewater-based epidemiology. *Sci Total Environ*. 2022;815:152724. <https://doi.org/10.1016/j.scitotenv.2021.152724>
12. Bruno R, Edirisinghe M, Hall W, Mueller JF, Lai FY, O'Brien JW, et al. Association between purity of drug seizures and illicit drug loads measured in wastewater in a south East Queensland catchment over a six year period. *Sci Total Environ*. 2018;635:779–83. <https://doi.org/10.1016/j.scitotenv.2018.04.192>
13. Lai FY, O'Brien JW, Thai PK, Hall W, Chan G, Bruno R, et al. Cocaine, MDMA and methamphetamine residues in wastewater: Consumption trends (2009–2015) in south east Queensland, Australia. *Sci Total Environ*. 2016;568:803–9. <https://doi.org/10.1016/j.scitotenv.2016.05.181>
14. Bijlsma L, Picó Y, Andreu V, Celma A, Estévez-Danta A, González-Mariño I, et al. The embodiment of wastewater data for the estimation of illicit drug consumption in Spain. *Sci Total Environ*. 2021;772:144794. <https://doi.org/10.1016/j.scitotenv.2020.144794>
15. Barcellos DS, Barquilha CER, Oliveira PE, Prokopiuk M, Etchepare RG. How has the COVID-19 pandemic impacted wastewater-based epidemiology? *Sci Total Environ*. 2023;892:164561. <https://doi.org/10.1016/j.scitotenv.2023.164561>
16. Shrestha S, Yoshinaga E, Chapagain SK, Mohan G, Gasparatos A, Fukushi K. Wastewater-based epidemiology for cost-effective mass surveillance of COVID-19 in low- and middle-income countries: challenges and opportunities. *Water*. 2021;13(20):2897. <https://doi.org/10.3390/w13202897>
17. Devault DA, Maguet H, Merle S, Péné-Annette A, Lévi Y. Wastewater-based epidemiology in low human development index states: bias in consumption monitoring of illicit drugs. *Environ Sci Pollut Res*. 2018;25(28):27819–38. <https://doi.org/10.1007/s11356-018-2864-7>
18. Gleij DA, Preston SH. Estimating the impact of drug use on US mortality, 1999–2016. *PLoS ONE*. 2020;15(1):e0226732. <https://doi.org/10.1371/journal.pone.0226732>
19. Degenhardt L, Webb P, Colledge-Frisby S, Ireland J, Wheeler A, Ottaviano S, et al. Epidemiology of injecting drug use, prevalence of injecting-related harm, and exposure to behavioural and environmental risks among people who inject drugs: a systematic review. *Lancet Glob Health*. 2023;11(5):e659–72. [https://doi.org/10.1016/S2214-109X\(23\)00057-8](https://doi.org/10.1016/S2214-109X(23)00057-8)
20. Thao Trang NH, Dang Thuy T. Silent struggles: Family dynamics and drug abuse reporting under harsh laws and stigmatizing perceptions. *Deviant Behav*. 2024;1–16.
21. Le TT, Vodden K, Wu J, Atiweh G. Policy responses to the COVID-19 pandemic in Vietnam. *Int J Environ Res Public Health*. 2021;18(2):559. <https://doi.org/10.3390/ijerph18020559>
22. Nguyen TT, Hoang GT, Nguyen DQ, Nguyen AH, Luong NA, Laureillard D, et al. How has the COVID-19 epidemic affected the risk behaviors of people who inject drugs in a city with high harm reduction service coverage in Vietnam? A qualitative investigation. *Harm Reduct J*. 2022;19(6):1–10.
23. Giang HT, Duc NQ, Molès J-P, Vinh VH, Nagot N, Thanh NTT, et al. Maintaining HIV and HCV prevention and care for people who inject drugs despite COVID-19 in Hai Phong, Vietnam. *Int J Drug Policy*. 2022;110:103870. <https://doi.org/10.1016/j.drugpo.2022.103870>
24. Lai FY, Bruno R, Hall W, Gartner C, Ort C, Kirkbride P, et al. Profiles of illicit drug use during annual key holiday and control periods in Australia: wastewater analysis in an urban, a semi-rural and a vacation area. *Addiction*. 2013;108(3):556–65. <https://doi.org/10.1111/add.12006>

25.

Gracia-Lor E, Zuccato E, Castiglioni S. Refining correction factors for back-calculation of illicit drug use. *Sci Total Environ.* 2016;573:1648–59. <https://doi.org/10.1016/j.scitotenv.2016.09.179>

26.

Gao J, Burgard DA, Tschärke BJ, Lai FY, O'Brien JW, Nguyen HD, et al. Refining the estimation of amphetamine consumption by wastewater-based epidemiology. *Water Res.* 2022;225:119182. <https://doi.org/10.1016/j.watres.2022.119182>

27.

Du P, Zhou Z, Bai Y, Xu Z, Gao T, Fu X, et al. Estimating heroin abuse in major Chinese cities through wastewater-based epidemiology. *Sci Total Environ.* 2017;605–606:158–65. <https://doi.org/10.1016/j.scitotenv.2017.05.262>

28.

Thai PK, Lai FY, Bruno R, van Dyken E, Hall W, O'Brien J, et al. Refining the excretion factors of methadone and codeine for wastewater analysis - combining data from pharmacokinetic and wastewater studies. *Environ Int.* 2016;94:307–14. <https://doi.org/10.1016/j.envint.2016.05.033>

29.

Du P, Zheng Q, Thomas KV, Li X, Thai PK. A revised excretion factor for estimating ketamine consumption by wastewater-based epidemiology - Utilising wastewater and seizure data. *Environ Int.* 2020;138:105645. <https://doi.org/10.1016/j.envint.2020.105645>

30.

Castiglioni S, Bijlsma L, Covaci A, Emke E, Hernández F, Reid M, et al. Evaluation of uncertainties associated with the determination of community drug use through the measurement of sewage drug biomarkers. *Environ Sci Technol.* 2013;47(3):1452–60. <https://doi.org/10.1021/es302722f>

31.

Du P, Thai PK, Bai Y, Zhou Z, Xu Z, Zhang X, et al. Monitoring consumption of methadone and heroin in major Chinese cities by wastewater-based epidemiology. *Drug Alcohol Depend.* 2019;205:107532. <https://doi.org/10.1016/j.drugalcdep.2019.06.034>

32.

Du P, Liu X, Zhong G, Zhou Z, Thomes MW, Lee CW, et al. Monitoring consumption of common illicit drugs in Kuala Lumpur, Malaysia, by wastewater-based epidemiology. *Int J Environ Res Public Health.* 2020;17(3):889. <https://doi.org/10.3390/ijerph17030889>

33.

Deng Y, Guo C, Zhang H, Yin X, Chen L, Wu D, et al. Occurrence and removal of illicit drugs in different wastewater treatment plants with different treatment techniques. *Environ Sci Eur.* 2020;32(1):28. <https://doi.org/10.1186/s12302-020-00304-x>

34.

Luong HT, Hoang LT, Le TQ, Hoang TA, Vu MT, Tran HQ, et al. 'We realised we needed a new approach': government and law enforcement perspectives on the implementation and future of the drug decriminalisation policy in Vietnam. *Int J Drug Policy.* 2021;87:102990. <https://doi.org/10.1016/j.drugpo.2020.102990>

35.

Bedi G, Hyman D, de Wit H. Is ecstasy an "empathogen"? Effects of \pm 3,4-methylenedioxymethamphetamine on prosocial feelings and identification of emotional states in others. *Biol Psychiatry.* 2010;68(12):1134–40. <https://doi.org/10.1016/j.biopsych.2010.08.003>

36.

Favretto D, Vogliardi S, Tucci M, Simoncello I, El Mazloum R, Snenghi R. Occupational exposure to ketamine detected by hair analysis: a retrospective and prospective toxicological study. *Forensic Sci Int.* 2016;265:193–9. <https://doi.org/10.1016/j.forsciint.2016.03.010>

37.

Patrycja K, Malgorzata Z. In: Nieves S-S, Manuel G-G, editors *An Update of Ketamine Illicit Use Ketamine Revisited*. Rijeka: IntechOpen; 2021 p. Ch. 18.

38.

Han E, Kwon N j, Feng L-Y, Li J-H, Chung H. Illegal use patterns, side effects, and analytical methods of ketamine. *Forensic Sci Int.* 2016;268:25–34. <https://doi.org/10.1016/j.forsciint.2016.09.001>

39.

Luo J, Bello D, Pagsuyoin S. Long-term wastewater-based surveillance and impacts of the COVID-19 pandemic on drug use trends in a U.S. northeast rural town. *Sci Total Environ.* 2023;877:162806. <https://doi.org/10.1016/j.scitotenv.2023.162806>

40.

Oertel R, Schubert S, Helm B, Mayer R, Dumke R, El-Armouche A, et al. Drug consumption in German cities and municipalities during the COVID-19 lockdown: a wastewater analysis. *Naunyn Schmiedebergs Arch Pharmacol.* 2023;396(5):1061–74. <https://doi.org/10.1007/s00210-022-02377-2>

41.

Bade R, Tschärke BJ, O'Brien JW, Magsarjav S, Humphries M, Ghetia M, et al. Impact of COVID-19 controls on the use of illicit drugs and alcohol in Australia. *Environ Sci Technol Lett.* 2021;8:799–804.

42.

Boogaerts T, Quireyns M, De prins M, Pussig B, De Loof H, Matheï C, et al. Temporal monitoring of stimulants during the COVID-19 pandemic in Belgium through the analysis of influent wastewater. *Int J Drug Policy.* 2022;104:103679. <https://doi.org/10.1016/j.drugpo.2022.103679>

43.

Psichoudaki M, Mina T, Savvidou M, Mina C, Michael C, Fatta-Kassinos D. Wastewater-based monitoring of illicit drugs in Cyprus by UPLC-MS/MS: the impact of the COVID-19 pandemic. *Sci Total Environ.* 2023;854:158747. <https://doi.org/10.1016/j.scitotenv.2022.158747>

44.

Estévez-Danta A, Bijlsma L, Capela R, Cela R, Celma A, Hernández F, et al. Use of illicit drugs, alcohol and tobacco in Spain and Portugal during the COVID-19 crisis in 2020 as measured by wastewater-based epidemiology. *Sci Total Environ.* 2022;836:155697. <https://doi.org/10.1016/j.scitotenv.2022.155697>

45.

Adhikari S, Kumar R, Driver EM, Bowes DA, Ng KT, Sosa-Hernandez JE, et al. Occurrence of Z-drugs, benzodiazepines, and ketamine in wastewater in the United States and Mexico during the Covid-19 pandemic. *Sci Total Environ.* 2023;857(Pt 2):159351. <https://doi.org/10.1016/j.scitotenv.2022.159351>

46.

Loi NM, Thorsteinnsson EB, Rice K, Rock AJ. Illicit drug use in Australia during the COVID-19 pandemic. *J Glob Health.* 2022;12:03026. <https://doi.org/10.7189/jogh.12.03026>

47.

Luong HT. Community-based policing in COVID-19: a 4-p's priorities of Vietnam's police. *Pol Soc.* 2021;31(10):1217–31. <https://doi.org/10.1080/10439463.2020.1860981>

48.

Conway FN, Samora J, Brinkley K, Jeong H, Clinton N, Claborn KR. Impact of COVID-19 among people who use drugs: a qualitative study with harm reduction workers and people who use drugs. *Harm Reduct J.* 2022;19(1):72. <https://doi.org/10.1186/s12954-022-00653-1>

49.

Reitano T, Shaw M. *Criminal contagion: How mafias, gangsters and scammers profit from a pandemic* Hurst Publishers; 2021.

50.

Wallace B, van Roode T, Pagan F, Hore D, Pauly B. The potential impacts of community drug checking within the overdose crisis: qualitative study exploring the perspective of prospective service users. *BMC Public Health.* 2021;21(1):1156. <https://doi.org/10.1186/s12889-021-11243-4>

51.

Brosky H, Prasek SM, Innes GK, Pepper IL, Miranda J, Brierley PE, et al. A framework for integrating wastewater-based epidemiology and public health. *Front Public Health.* 2024;12 2024:1418681. <https://doi.org/10.3389/fpubh.2024.1418681>

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Hue TTT, Ngo HKT, Wang Z, Anh NTK, Binh VN, Trung NQ, et al. Significant changes in preference of illicit drug use in a population of Hanoi, Vietnam—A 6-year wastewater study (2018–2023). *Addiction.* 2025. <https://doi.org/10.1111/add.70147>

View publication stats

13000443, 0, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/add.70147 by Hui Luong - University of Queensland, Wiley Online Library on [13/08/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License