



Weekend highs: Rising ketamine levels in Australian wastewater

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ABSTRACT

Ketamine is an anaesthetic drug with dissociative effects and is used in hospitals and for emergency treatment. Over the past four years, there has been increasing interest in the non-medical (recreational) use of ketamine in Australia. This study aimed to interrogate patterns in ketamine loads found in wastewater in Australia between December 2020 and April 2025. Daily influent wastewater samples were collected from up to 50 wastewater treatment plants over a week across state and territory capital city and regional sites every 4 months from all states and territories of Australia covering on average 53% of the total population. Wastewater was concentrated using solid phase extraction followed by quantitative analysis using liquid chromatography tandem mass spectrometry to determine concentrations of the metabolite norketamine, with final concentrations flow and population normalised to units of excreted mg/day/1000 people. Norketamine excreted mass loads were compared with regionality and socioeconomic status. Considering the intended application, substantially higher mass loads of norketamine on weekends compared to weekdays would suggest the non-medical use of ketamine at weekends. Nationally, norketamine mass loads were higher for sites located in major city areas compared to those in 'inner' and 'outer' regional Australia. In addition, sites with higher socioeconomic status had higher mass loads of norketamine. Overall, norketamine mass loads have been increasing in Australia from 2022 to 2025, particularly in sites with higher socioeconomic status. This study demonstrates the value of ongoing wastewater monitoring, revealing both within-week and long-term shifts in ketamine excreted loads in Australia.

1. Introduction

Ketamine ((RS)-2-(2-chlorophenyl)-2-(methylamino)cyclohexanone) is a pharmaceutical drug used as an anaesthetic, or to treat severe pain and depression. The S-enantiomer of ketamine, commonly known as esketamine, is specifically used as a nasal spray for treatment resistant depression (Australian Government Department of Health and Aged Care 2024). However, esketamine is still cost prohibitive for widespread use as it is not listed on the federally funded pharmaceutical benefits scheme (Australian Government Department of Health and Aged Care 2024). It has been suggested that media coverage about the medical use of ketamine and MDMA for the treatment of depression and post-traumatic stress disorder can influence some people to use these drugs non-medically (Palamar and Le, 2022). Despite its legitimate therapeutic application, prolonged or excessive use of ketamine can lead to severe acute and chronic health effects including impaired cognition, urinary cystitis, or cardiovascular and respiratory impairment (Corkery et al., 2021; Palamar et al., 2023). Internationally, deaths associated

with non-medical use of ketamine have been increasing since 2019, where fatalities are mostly caused by an impaired perception and a lack of awareness of risks (Corkery et al., 2021; Palamar et al., 2023).

In Australia, ketamine trends in the general population are monitored every 3 years in the National Drug Strategy Household survey, with recent results in 2023 indicating non-medical use of ketamine is on the rise, from 1.9% of people ever using ketamine in 2016 to 4.3% in 2023 (Australian Institute of Health and Welfare 2019). Wastewater-based epidemiology (WBE) is another method which can be used to determine population-scale use of substances such as ketamine between locations and over time. The principle involves measuring chemical residues that are excreted daily by people using drugs into the sewer system. After normalising for catchment population size and flow volumes, daily excreted loads can be determined (Zuccato et al., 2005). WBE ideally measures metabolites of drugs in municipal sewage, in effect serving as a community urine test to determine the relative amount in different communities. WBE has been used to measure substance use at a population level since 2005, typically reporting in units of

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population-normalised mass load, mg/day/1000 inhabitants (Zuccato et al., 2005). An advantage of the approach is the increased frequency and specificity of sampling by location which allows for greater spatiotemporal resolution of total community ketamine use. Using WBE, it is possible to distinguish drug levels between days of the week, where elevated mass loads on weekends may be indicative of non-medical use (Bade et al., 2021; Ter Laak et al., 2022). Medical use of pharmaceutical drugs or habitual use of other illicit substances typically show consistent mass loads across the 7 days (e.g., oxycodone or methamphetamine) (Boogaerts et al., 2023; Australian Criminal Intelligence Commission 2025). There have been no studies that have specifically investigated recreational patterns of ketamine use in Australia using long-term spatiotemporal monitoring programs. This study aimed to use WBE to track trends in norketamine excretion over time and determine the influence of urban level (remoteness) and socioeconomics of locations on mass loads of norketamine.

2. Materials and methods

2.1. Chemicals and reagents

Certified reference material of the ketamine metabolite, 2-amino-2-(2-chlorophenyl)cyclohexanone hydrochloride ((±) norketamine), ketamine 2-(2-chlorophenyl)-2-(methylamino)cyclohexan-1-one, and deuterated norketamine-d4 was produced by Cerilliant® Corporation, USA, purchased via Novachem, Victoria, Australia.

2.2. Sampling campaigns

For each sampling period, daily composite influent wastewater samples were collected for 7 consecutive days using autosamplers operated by wastewater treatment plant staff in a time or flow proportional manner, depending on the requirements of each specific site. Samples were collected every four months between December 2020 and April 2025 from wastewater treatment plants across capital cities of all Australian states and territories (N = 20) and regional sites and chilled immediately upon collection, with each state or territory represented by at least one site (N = 50 sites in total) (Table S1). Samples were unavailable from some sites for some collections. The collective population across all sites was more than 50% of the Australian population. Composite 24-hr wastewater samples (600 mL) were collected in PET bottles that contained sodium metabisulfite (0.5 g/L) and shipped frozen to the laboratory and stored at -20°C until analysis.

2.3. Sample preparation

The wastewater samples were thawed and filtered under vacuum using glass microfibre filter papers (GF/A 1.6 mm, Whatman, Kent, U.K). Solid phase extraction (SPE) was performed using 100 mL of wastewater using a validated method providing a 1000-fold concentration factor. Briefly, the wastewater samples were adjusted to pH 4.5-5 using acetic acid (10%), then extracted using UCT XRADH 506 SPE cartridges (UCT Inc. Bristol, PA, USA) as previously described (Bade et al., 2019). Samples were analysed using a Sciex Exion LC coupled to a Sciex QTrap 6500+ mass spectrometer for quantitation. Norketamine (metabolite) was monitored according to a validated method (Tables S2-3). The parent drug, ketamine was monitored qualitatively for direct disposal events. Further details of the analytical method and the results for method validation are provided in the supplementary material. Norketamine-d4 was used as an internal standard for norketamine.

2.4. Data analysis

Population-normalised excreted mass loads (PNML) were calculated by multiplying the concentration (obtained via LC-MS/MS) in ng/L by the daily flow volume in ML and dividing by the population in 1000 to

give final units of mg excreted/day/1000 people. When aggregating multiple sites into a mean value, a population-weighting approach was applied. Daily flow was obtained for each day from wastewater treatment plant personnel and census populations were calculated from the catchment maps and 2021 census units. Sampling sites were categorised by 3 levels of remoteness based on their location and socioeconomic index as previously described (Tscharke et al., 2024). The remoteness index describes the lowest to highest levels of relative geographic access to services, “Major Cities”, “Inner Regional”, and “Outer Regional to Remote”. The last category is a combination of “Outer Regional” and “Remote” categories due to a smaller number per category. The catchment-level socioeconomic index, the Index of Relative Socioeconomic Advantage and Disadvantage (IRSAD) for 2021 from the Australian Bureau of Statistics (ABS) was calculated by intersecting the smallest available unit of the census (statistical area level 1, SA1), with the catchment maps and calculating the population-weighted average of the intersected areas. The IRSAD ranks each area across Australia and provides a percentile ranking from 0% for most disadvantaged to 100% for most advantaged. The details of the number of sites within each remoteness and IRSAD category are in Table S4.

Each site was grouped by IRSAD quartile, and consumption was plotted over time, or across the entire study duration for comparison between categories. Temporal trends were visualised using a mixed effects model output and LOESS localised polynomial smoothed lines (R Statistical Software, v4.5.1; R Core Team [2025]). We analysed consumption patterns using robust linear mixed effects models with the `rlmer` function from the `robustlmm` package in R (Koller, 2016). Prior to analysis, the data was log-transformed to enable interpretation of model coefficients as percentage changes and reduce impacts of outliers. The analysis utilised all individual daily measurements (n = 2831) rather than aggregated period means to improve precision of trend estimates. Robust estimation approaches were used to minimise influence of outliers and account for non-normality and unequal variances between groups. The models incorporated random intercepts for each site to account for repeated observations over time and unmeasured site characteristics. The models included time since study commencement (Period), socioeconomic disadvantage (IRSAD quartiles), and geographic remoteness categories, with interaction terms between period and IRSAD quartile and period and remoteness to examine differences in consumption trends by grouping. Annual percentage change was calculated from the model time coefficients. The models were:

$$\log(\text{Consumption}) \sim (\text{Period} \times \text{Remoteness}) + (1|\text{Site_ID})$$

$$\log(\text{Consumption}) \sim (\text{Period} \times \text{IRSAD quartile}) + (1|\text{Site_ID})$$

Model validation focused on diagnostics specific to the robust modelling methods rather than traditional assumption tests. This involved checking model convergence, outlier downweighting (proportion with weights <0.95), residual patterns (correlation with fitted values), random effects distribution (± 2 SD thresholds), and the influence of observations (standardised residuals ≥ 3 SD). Model coefficients (β) were converted to percentage changes using $(\exp(\beta) - 1) \times 100\%$ for interpretation. Statistical significance was assessed at $\alpha = 0.05$ using robust standard errors. Analyses were performed in R using `robustlmm`, `lme4` (Bates et al., 2015), and `emmeans` (Searle et al., 1980) packages. Model validation confirmed adequate convergence and performance of robust estimation procedures with robust downweighting for outlier observations (~17% downweighting, indicating robust methods were necessary), adequate residual patterns, small amount of extreme random effects (2 sites and 4 sites for remoteness and IRSAD models, respectively), and no influential outliers (1% of observations classified as outliers).

Pairwise comparisons between IRSAD quartiles and remoteness categories were conducted using robust linear mixed effects models with the same robust estimation procedures as the main analysis to ensure consistency in handling outliers. Estimated marginal means were

calculated using the emmeans package with Holm's sequential Bonferroni adjustment.

3. Results

Ketamine was monitored by its urinary metabolite, norketamine. Throughout the remainder of the paper, reference to “ketamine” implies norketamine, and the term “mass load” infers excreted mass load. Norketamine was detected above LOD (0.3 ng/L) in 88% of samples, with detected concentrations ranging from 0.5 ng/L (LOQ) to 673 ng/L.

3.1. National ketamine trends

The average population normalised mass load (PNML) increased gradually over time, from approximately 2.7mg/day/1000 people in December 2020 to 5.8 mg/day/1000 people in April 2025, a ~ 2.2 fold increase over 4.5 years (Fig. 1).

3.2. Ketamine trends by remoteness

Norketamine PNML over time for all categories of remoteness increased over the sampling campaign (Fig. 2A). The PNML were not significantly different between each category when sites were grouped by remoteness with the population weighted average ranging between 4 and 5 mg/day/1000 people (Fig. 2B). The rising trend in excreted loads of norketamine increased more sharply from August 2022 to August 2025 collections compared with December 2020 to April 2022.

3.3. Ketamine trends by socioeconomics

When sites were grouped based on the catchment-level socioeconomic index (IRSAD), all quartiles increased in PNML of norketamine

(Fig. 3A). The PNML of norketamine was the highest in the most advantaged socioeconomic quartile (SE scores of 75-100%) with a population weighted average of 6 mg/day/1000 people compared to the other quartiles (3, 2 and 4 mg/day/1000 people for 0-25, 25-50 and 50-75 quartiles respectively) (Fig. 3B). Sites in the mid-range socioeconomic quartile (50-75 IRSAD) showed the greatest increase in norketamine in the study period (blue line) compared to steady trends for the 0-25 and 75-100 quartiles (Fig. 3A). The highest socioeconomic quartile showed a U-shape LOESS smoothed trend, whereby the latter part of the sampling campaign showed an increasing trend compared to the first (Fig. 3A). Due to the fewer number of sites that fell into the 75-100 IRSAD category, excreted mass loads varied, and trends were influenced largely by outliers. The PNML in the more advantaged quartiles also showed the greatest spread of site mass loads of norketamine in each sampling month.

3.4. Weekend to weekday ratio for ketamine

The average weekend to weekday ratio for norketamine is shown in Fig. 4 for all sites included in the study. The ratio of the highest two-day average loads representing Saturday and Sunday representative days compared to the remaining weekdays ranged from 1:1 to 16:1. In total, the overall average ratio for all sites across all collections was 2:1, of which 33% of all data points included in the study had a ratio greater than this. Of all data points with a ratio of greater than 2:1, 70% were in inner regional or outer regional and remote categories. The same proportion of data points (70%) with a ratio greater than 2:1 was in the lower socioeconomic quartiles (0-25 and 25-50). Weekly trends of norketamine were also grouped by location for whether they contained the central business district within the state or territory capital cities or not. There were significantly higher loads in central business district sites (on average 5.7 mg/d/1000 people, [95% CI: 5.2-6.2]) compared to

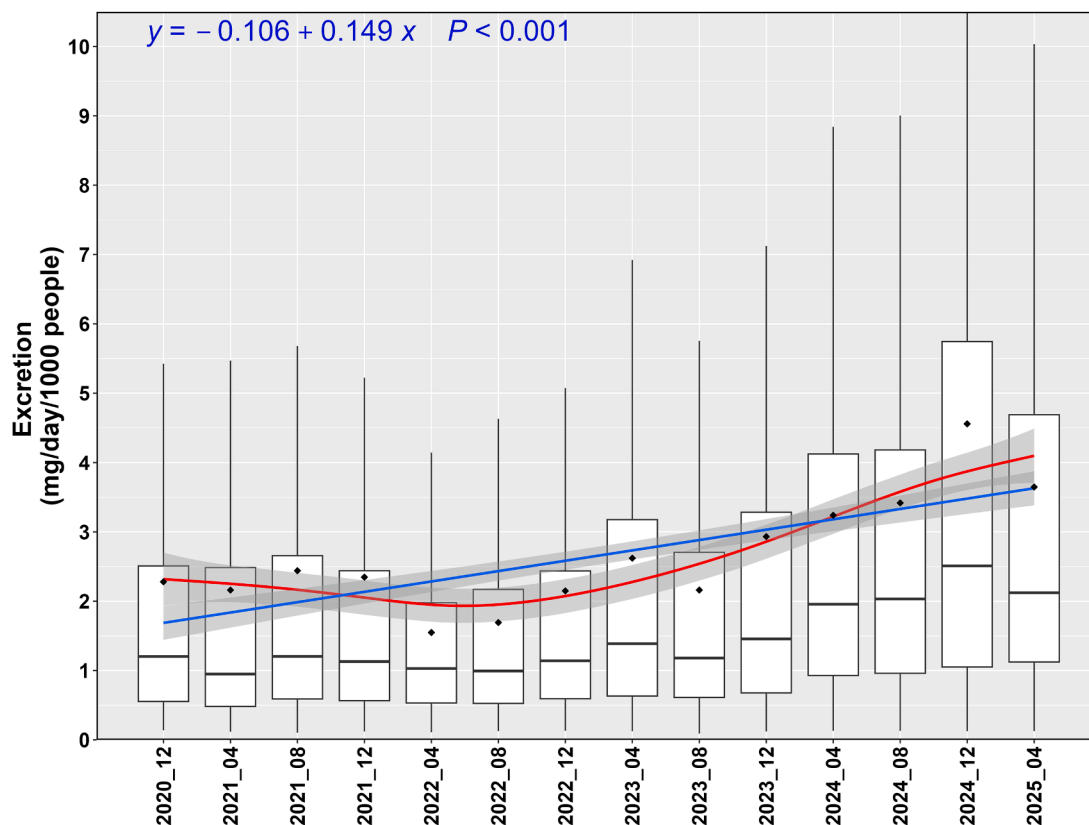


Fig. 1. Ketamine excreted population normalised mass loads from 2020 to 2025 in Australia. The black dots on the boxplots represent the mean, blue line the linear trend, and red line the loess smoothed trend, and the grey shading representing the uncertainty in the trend.

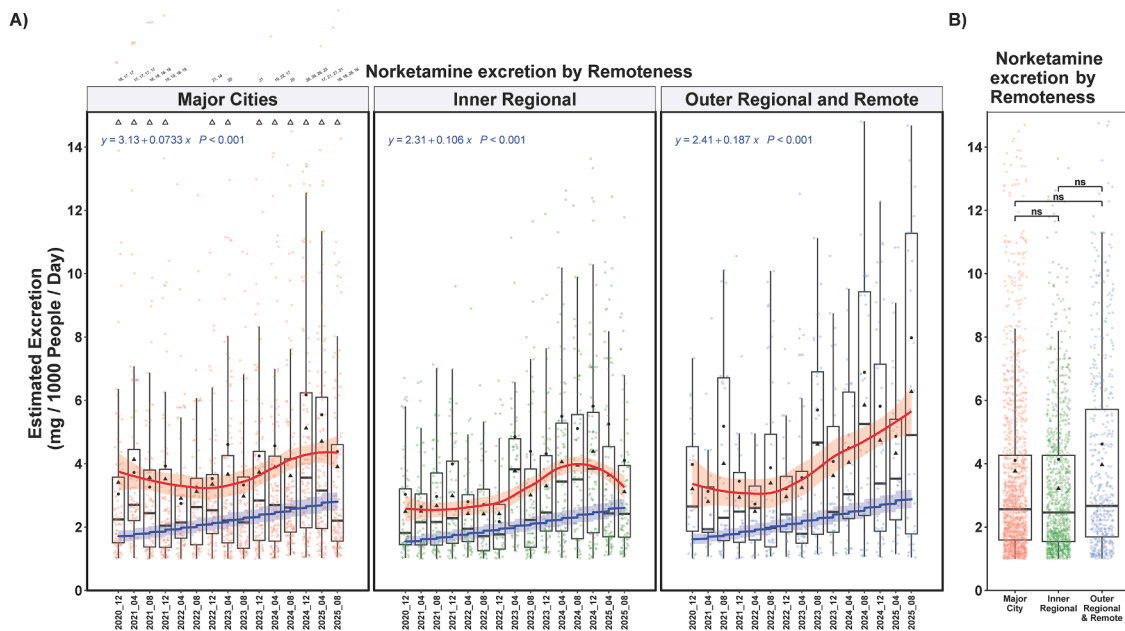


Fig. 2. Ketamine trends by remoteness. The black circles on the boxplots represent the population weighted mean, and the triangles represent the raw mean. The blue line represents the mixed effects model line of best fit, and red line the loess smoothed trend.

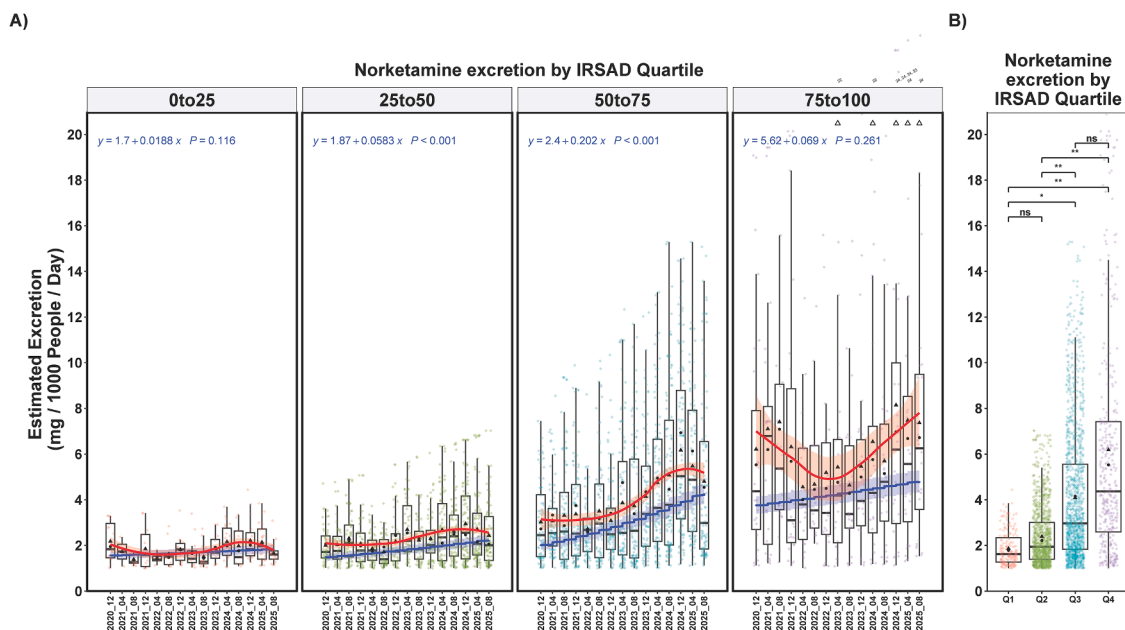


Fig. 3. Ketamine trends by Index of Relative Socioeconomic Advantage and Disadvantage (IRSAD). The black circles on the boxplots represent the population weighted mean, and the triangles represent the raw mean. The blue line represents the mixed effects model line of best fit, and red line the loess smoothed trend.

those that were not (on average 2.0 mg/d/1000 people, [95% CI: 1.9–2.2]) (Fig. S1).

4. Discussion

Long-term wastewater monitoring of substances with abuse potential is a complimentary approach to identify emerging spatiotemporal trends. In this study, ketamine trends were assessed by catchment attributes of remoteness category, inclusion of state capital city CBD area, as well as by socioeconomic status. Recent increasing trends in norketamine mass loads were observed for all remoteness categories. This was contrary to the variable trends observed when the data was categorised

based on socioeconomic status, with one category (50–75 IRSAD) showing a steep increase over the sampling period. A large number of the sites within that IRSAD category are major cities (11 of 16 sites for 50–75 IRSAD). The highest norketamine mass loads were observed in both the major city and highest IRSAD (75–100) categories and were also much higher in the state or territory capital CBD sites. Overall, this suggests higher consumption of ketamine in inner city locations with the greatest business activity. These locations tend to have higher socioeconomic status due to higher and more disposable income relative to the surrounding areas. The higher norketamine mass loads in these locations could be related to a proportionally larger number of hospitals/clinics where ketamine may be prescribed and used, and/or a higher

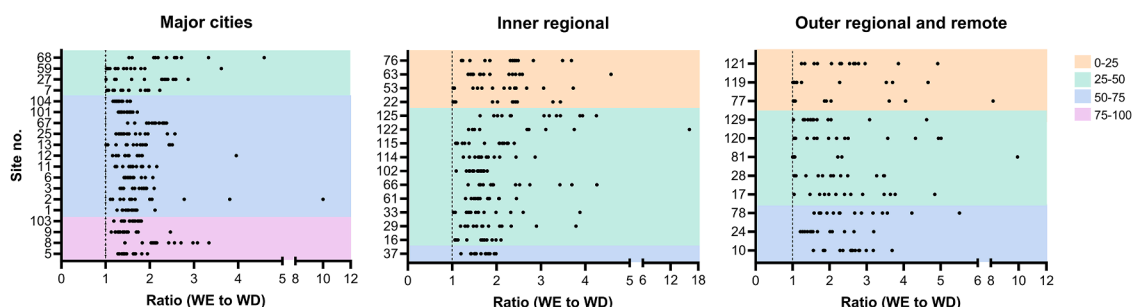


Fig. 4. Weekend (WE) to weekday (WD) ratio of norketamine excreted loads across the sampling campaign. Each black dot represents one collection. Sites that do not sample wastewater on weekends were excluded.

proportion of nightclubs, pubs, hotels and nightlife which may draw higher recreational use of psychoactive substances. Distribution and access to ketamine may also be easier in the central parts of cities. More dramatic increasing trends were observed more recently from mid-2022 (August 2022) across major city and inner regional areas.

Norketamine mass loads were variable across Australia, with some sites showing large differences between weekends and weekdays, suggestive of non-medical use on weekends. Alternative hypotheses for weekend increases could be ketamine use in first-line pain management for injury, which may increase on weekends, for example frequency of sports injury or car accidents, which may be greater on the weekend. However, this does not explain the fluctuating weekend/weekday ratio across the sampling period. The scale of ketamine use in Australia cannot be easily compared with other countries, as many researchers measure the parent drug, ketamine, as opposed to the metabolite (norketamine) that was monitored in this study. Norketamine is increasingly being recommended as the more suitable indicator of ketamine consumption as it reflects human consumption and is not influenced by drug disposal into the sewer (Van Wichelen et al., 2025). Most of the metabolite is excreted in urine within the first 24 h (Adamowicz and Kala, 2005). In Australia, sewer networks are mostly separate from storm water and agricultural run-off. Therefore, veterinary use of the drug for sedating large animals is unlikely have any effect on measured wastewater levels. Despite these differences, the excreted loads of ketamine in wastewater collected in Italy between 2011 and 2013 showed similar weekly trends, with increases observed on Sundays for most collections (Castiglioni et al., 2015) and generally higher on weekends in the United Kingdom (Rice et al., 2020). Wastewater studies in some other countries such as Colombia and China show no obvious ketamine weekend trend (Bijlsma et al., 2016; Zheng et al., 2021). Wastewater surveillance of ketamine and other drugs is considered an important, cost effective, least-intrusive method of measuring population scale drug use (Australian Criminal Intelligence Commission 2025). It is increasingly recognised as a component of drug early warning systems and to assist policy makers to show market resilience and create opportunities for coordinated strategies.

While wastewater analysis cannot distinguish the source of the ketamine use (e.g., legitimate pharmaceutical use in hospital settings versus recreational use of illicitly produced or diverted ketamine), it is clear that recent use has been increasing across Australia. Non prescribed ketamine use reported in surveys has also increased recently. The Ecstasy and Related Drugs Reporting System (EDRS) which surveys people who consume ecstasy, indicated over half of the national participants self-reported non-medical ketamine use in 2024 (53% of 740 participants), with most consuming infrequently in the previous 6 months (Sutherland et al., 2024). However, 12% of those who recently consumed ketamine reported using the drug on a weekly basis or greater (Sutherland et al., 2024). Longer term trends indicate there was a five-fold increase in ketamine use reported by EDRS participants between 2009–2021, but that trend has stabilised in the years following (Sutherland et al., 2024). The National Drug Strategy Household Survey

surveys the general population and has also reported an increase in ketamine use by participants recently from 1.9% to 4.3% ever used between 2016 and 2022–23, equating to around 900,000 people in the latest report (Australian Institute of Health and Welfare (AIHW) 2024). The age demographic of people who reported non-medical use of ketamine were between 20–29, which is similar to MDMA (Australian Institute of Health and Welfare 2024). Non-medical use of ketamine is often consumed in conjunction with other illicit substances such as MDMA to heighten feelings of euphoria and dissociation (Vari et al., 2022). In 2022/2023 The National Drug Early Warning System reported increased online mentions of ‘kitty flipping’ which refers to party related poly drug use of MDMA and ketamine (National Drug and Early Warning System (NDEWS) 2024). This has also been observed for a study of patrons at an Australian music festival, where all blood samples that tested positive for ketamine also detected MDMA, with some samples containing up to five substances (Syrjanen et al., 2024).

5. Conclusion

Long-term monitoring of norketamine mass loads demonstrated the drug trends were largely stable from December 2020 to April 2022, while subsequent results to April 2025 show increasing mass loads and evidence of emerging higher weekend use. This suggests that ketamine may be gaining popularity as a non-medically used substance. The wastewater results provide evidence suggesting the use of ketamine is significantly higher in locations with higher socioeconomic status in Australia.

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CRediT authorship contribution statement

Emma Keller: Writing – original draft, Visualization, Validation, Investigation, Formal analysis, Conceptualization. **Ben Tschärke:** Visualization, Data curation, Writing – review & editing. **Brock Peake:** Writing – original draft, Validation, Investigation, Formal analysis, Writing – review & editing. **Rory Verhagen:** Writing – review & editing, Resources. **Richard Bade:** Writing – review & editing. **Jake O’Brien:** Writing – review & editing, Resources. **Phong Thai:** Writing – review & editing, Conceptualization. **Kevin Thomas:** Writing – review & editing, Funding acquisition. **Jochen Mueller:** Writing – review & editing, Funding acquisition. **Jason White:** Writing – review & editing, Resources, Funding acquisition, Conceptualization. **Bradley Simpson:** Writing – review & editing, Project administration, Funding acquisition, Conceptualization. **Cobus Gerber:** Writing – review & editing, Visualization, Supervision, Resources, Project administration, Methodology,

Funding acquisition, Data curation, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Cobus Gerber reports financial support was provided by Australian Criminal Intelligence Commission. Cobus Gerber reports financial support was provided by SA Health.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.envadv.2026.100687](https://doi.org/10.1016/j.envadv.2026.100687).

Data availability

Data will be made available on request.

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