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TOXICOLOGICAL EFFECTS OF RECREATIONAL DRUG USE AND LONG-TERM HEALTH IMPLICATIONS: A SYSTEMATIC REVIEW

Original Research

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ABSTRACT

Background: Recreational drug use represents a major global health concern due to its well-documented acute toxic effects and growing evidence of long-term health implications. Although prior studies have addressed specific substance-related harms, there remains a lack of consolidated evidence evaluating both the immediate and chronic toxicological impacts across a wide range of recreational drugs. This gap underscores the need for a systematic review to provide a comprehensive synthesis of current knowledge.

Objective: This systematic review aims to evaluate the toxicological effects and long-term health consequences associated with recreational drug use, with a focus on synthesizing data across diverse substances and study designs to inform clinical and public health strategies.

Methods: A systematic review was conducted following PRISMA guidelines. Literature was searched across PubMed, Scopus, Web of Science, and Cochrane Library databases using predefined keywords. Inclusion criteria encompassed studies on human participants evaluating recreational use of psychoactive substances with reported toxicological or health outcomes. Exclusion criteria included non-English, animal, and unpublished studies. Two independent reviewers screened and extracted data, and risk of bias was assessed using the Cochrane Risk of Bias Tool and Newcastle-Ottawa Scale.

Results: Eight studies were included, comprising observational studies, reviews, and surveillance analyses. Key findings revealed frequent polysubstance use, underreporting of drug intake, and a wide range of acute effects (e.g., coma, cardiac arrest, psychosis) and chronic consequences (e.g., bone demineralization, neuropsychiatric disorders, hormonal dysfunction). Benzodiazepines, cannabis, synthetic cannabinoids, ketamine, and opioids were among the most implicated substances. Risk of bias was moderate, with variability in study designs limiting meta-analysis.

Conclusion: Recreational drug use is associated with significant toxicological risks and chronic health burdens. These findings underscore the need for enhanced clinical screening, public health surveillance, and targeted interventions. Future longitudinal research is warranted to clarify causal pathways and improve management strategies.

Keywords: Recreational Drug Use, Toxicology, Long-Term Health Effects, Substance Abuse, Systematic Review, Polysubstance Use.

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INTRODUCTION

Recreational drug use continues to be a significant global public health concern, with substantial implications for both individual and societal health. The toxicological consequences of these substances are wide-ranging, involving acute and chronic harm to multiple organ systems, and posing a growing challenge to healthcare services. Epidemiological data illustrate the scope of the problem: according to recent reports, emergency departments are increasingly managing cases involving polysubstance toxicity, with opioids, benzodiazepines, cannabis, synthetic cannabinoids, and stimulants among the most frequently detected drugs in toxicology screenings (1,2). Furthermore, recreational use of novel psychoactive substances (NPS) has led to emergent clinical presentations, including psychosis, cardiovascular toxicity, and even sudden cardiac death, highlighting the evolving landscape of substance abuse (3,4). Although the acute effects of many recreational drugs are well-documented, less is known about their long-term toxicological impact. Studies have demonstrated that prolonged exposure to substances such as cannabis, opioids, and stimulants can impair bone health, disrupt hormonal regulation, and lead to neuropsychiatric complications and cognitive decline (5,6). Despite these findings, comprehensive assessments that synthesize toxicological data across substances and timeframes are scarce. Given the dynamic and multifaceted nature of recreational drug use, a systematic review is necessary to critically evaluate and consolidate the current evidence on both the immediate and long-term health implications of commonly abused substances. This review aims to bridge existing gaps by examining the full toxicological spectrum of recreational drugs, thereby informing clinical practice, public health strategies, and future research directions (7,8).

The central research question guiding this systematic review is: "What are the toxicological effects and long-term health implications associated with the recreational use of psychoactive substances?" The review will focus on adult populations (P), evaluate the recreational use of psychoactive drugs (I), with no formal comparator (C), and explore both acute toxicological outcomes and long-term health impacts (O). To ensure comprehensive coverage, this review will include both observational and experimental studies published globally between 2010 and 2024. The included studies will span various regions and substance categories, encompassing traditional drugs like cannabis and opioids as well as emerging synthetic compounds. By synthesizing the current body of evidence, this review will contribute meaningfully to the literature by offering an updated, broad-spectrum analysis of drug toxicity, highlighting patterns of substance misuse, and identifying critical risks requiring targeted intervention. This systematic review is conducted in accordance with PRISMA guidelines to ensure methodological rigor and reproducibility.

METHODS

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to ensure methodological transparency and reproducibility. A comprehensive search strategy was employed using four major electronic databases: PubMed, Scopus, Web of Science, and the Cochrane Library. The search was performed using a combination of relevant medical subject headings (MeSH) and free-text keywords including: "recreational drug use," "toxicological effects," "long-term health outcomes," "drug abuse," "substance toxicity," and "health implications." Boolean operators such as “AND” and “OR” were used to refine the search (e.g., “recreational drug use AND long-term health effects”). In addition to database searches, reference lists of key retrieved articles were manually screened to identify potentially eligible studies not captured by the initial search. Eligibility criteria for study inclusion were established based on study design, population characteristics, type of exposure, and outcomes assessed. Eligible studies included randomized controlled trials, cohort studies, case-control studies, and cross-sectional studies that examined the toxicological effects and long-term health consequences of recreational drug use. Studies involving human participants of any age or gender were included, provided that the primary exposure was non-therapeutic, recreational use of substances such as opioids, stimulants, cannabis, hallucinogens, or novel psychoactive substances. Studies that reported on relevant clinical outcomes, including physical toxicity, psychological morbidity, and chronic disease associations, were included (9,10). Non-English articles, animal studies, editorials, commentaries, and unpublished data were excluded to maintain consistency and reliability in evidence synthesis.

The study selection process was undertaken in three stages: title screening, abstract review, and full-text analysis. Two independent reviewers screened all retrieved titles and abstracts to identify relevant articles. Full-text versions of potentially eligible studies were then assessed using pre-specified inclusion and exclusion criteria. Any disagreements between reviewers were resolved by consensus or

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third-party adjudication. Reference management was conducted using EndNote X9 software, which also facilitated the removal of duplicates. A PRISMA flow diagram was constructed to illustrate the study selection process from identification to inclusion. Data extraction was performed using a standardized, pre-piloted extraction form. Extracted data included study design, publication year, sample size, population characteristics, type of drug used, duration of use, measured toxicological outcomes, and long-term health effects. This process was carried out independently by two reviewers to ensure consistency and reduce data handling errors. To assess the methodological quality and potential bias in the included studies, two independent reviewers applied validated tools: the Cochrane Risk of Bias Tool for randomized controlled trials and the Newcastle-Ottawa Scale (NOS) for observational studies. Each study was assessed for potential selection bias, performance bias, detection bias, attrition bias, and reporting bias. Discrepancies in bias assessment were resolved through discussion and consensus. Given the anticipated heterogeneity in study designs, populations, and outcome measures, a qualitative synthesis was deemed most appropriate. Therefore, a narrative summary of findings was conducted to integrate and interpret results from the included studies. Where possible, patterns of similarity in toxicological outcomes and health consequences across different substances were identified and described.

RESULTS

A total of 1,238 records were initially retrieved from the database searches and manual reference checks. After duplicate removal and initial screening based on titles and abstracts, 184 articles were shortlisted for full-text assessment. Of these, 176 studies were excluded for not meeting the inclusion criteria due to reasons such as non-relevance to the population, intervention, or outcomes, as well as non-English language and lack of full text. Ultimately, eight studies were included in the final qualitative synthesis. This process was documented and illustrated using a PRISMA-compliant flowchart to maintain methodological transparency. The selected studies encompassed a diverse range of designs, including retrospective observational studies, reviews, surveillance data analysis, and case reports, as detailed in the accompanying table. Study populations were varied, with some focusing on emergency department patients presenting with acute drug toxicity, while others examined long-term users of substances such as cannabis, ketamine, and opioids. The clinical outcomes investigated ranged from immediate toxicological effects such as coma and cardiac arrest to chronic complications including neuropsychiatric disorders, hormonal dysregulation, and musculoskeletal damage. Risk of bias assessments revealed that retrospective and observational designs, while informative, were susceptible to reporting bias and selection bias due to the reliance on self-reported substance use and incomplete toxicology data. Several narrative reviews and case reports lacked comparative control groups, introducing limitations in internal validity. Nonetheless, the Newcastle-Ottawa Scale indicated that most included studies demonstrated acceptable methodological quality, particularly those employing structured data extraction and validated toxicological screening protocols.

Key findings consistently indicated a high prevalence of poly substance use among recreational drug users, often underreported by patients. In a retrospective analysis of 872 cases, laboratory findings revealed a median of three drug classes per patient, with significant underreporting of substances such as THC and benzodiazepines. This study also highlighted severe clinical outcomes including coma, cardiac arrest, and mortality ($p < 0.001$) (11). A study identified that chronic cannabis and opioid use impaired osteoblast function and disrupted endocrine regulation, raising the risk of fractures and bone density loss (12). A study provided a comprehensive synthesis of evidence linking ketamine abuse to urological dysfunction, liver enzyme abnormalities, and persistent psychiatric sequelae (13). Further corroborating these findings, a study described a spectrum of acute toxic effects associated with cannabis and synthetic drugs, such as hyperthermia, seizures, and cardiovascular collapse (14). A study demonstrated through real-time toxicology surveillance that methamphetamine, opioids, and synthetic cannabinoids were more commonly detected than initially suspected by clinicians, emphasizing the necessity for improved diagnostic protocols (15). Lastly, unique clinical presentations were documented in case studies. A study described a patient who developed persistent paranoid psychosis following chronic use of synthetic cathinones and ketamine, with minimal responsiveness to antipsychotics (16). Fischbach identified a clear link between stimulant use, particularly cocaine and amphetamines, and sudden cardiac death among young adults (17). Collectively, these findings underscore the multifaceted and severe nature of recreational drug toxicity, emphasizing the need for continued surveillance, comprehensive patient history, and robust toxicological screening to inform appropriate clinical and public health interventions.

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Table 1: Study Characteristics

Author	Year	Study Design	Sample Size	Intervention/Exposure	Main Outcomes
Zellner et al.	2024	Retrospective Observational	872	Recreational drug toxicity	Polysubstance ingestion, underreporting, coma, mortality
Gartenberg et al.	2024	Narrative Review	N/A	Cannabis, opioids, inhalants	Bone density, hormone dysregulation
PerÅ‚owski et al.	2024	Systematic Review	55 studies	Recreational ketamine use	Urological and neuropsychiatric toxicity
Schep et al.	2020	Narrative Review	N/A	Cannabis use	Toxicity, psychosis, cardiovascular issues
Wiens et al.	2019	Surveillance Pilot	963	Various recreational drugs	Surveillance data on ED visits, toxicology mismatch
Rehman et al.	2018	Review	N/A	Acute recreational drug use	Morbidity, mortality, acute effects
Dragogna et al.	2014	Case Report	1 patient	Synthetic cathinones and ketamine	Severe psychosis, poor antipsychotic response
Fischbach	2017	Review	N/A	Illicit drug use	Sudden cardiac death

DISCUSSION

This systematic review identified and synthesized evidence from eight studies examining the toxicological effects and long-term health implications of recreational drug use. The findings consistently indicated that recreational drug use is associated with a wide range of acute toxic effects, including central nervous system depression, psychosis, cardiovascular complications, and multi-organ toxicity, as well as chronic conditions such as hormonal disruption, neuropsychiatric disorders, and musculoskeletal degeneration. The overall strength of the evidence is moderate to strong, supported by well-documented toxicological analyses and real-time clinical surveillance data, although variations in study designs and sample populations must be considered when interpreting the results (18,19). When compared with previous literature, the results of this review are largely consistent with known acute effects of substances such as cannabis, opioids, stimulants, and synthetic drugs. Similar to earlier findings, cannabis was shown to contribute to neuropsychiatric morbidity and cardiovascular dysfunction (20,21), while synthetic cannabinoids and cathinones have been linked to psychosis and treatment-resistant agitation (22). The present review builds on existing literature by incorporating recent surveillance data showing a significant underreporting of drug use among patients presenting with overdose symptoms, particularly with substances like benzodiazepines and THC (23,24). Notably, the inclusion of evidence on ketamine's chronic urological and neuropsychiatric effects adds new dimensions to understanding its long-term toxicity profile (25).

A key strength of this review lies in its methodological rigor. A comprehensive search strategy encompassing four major databases and manual reference screening was employed, minimizing the risk of missing relevant studies. Additionally, the review adhered to PRISMA guidelines, incorporated independent study selection and data extraction by multiple reviewers, and used validated tools to assess risk of bias. These steps ensured transparency, reproducibility, and high-quality synthesis of findings. Despite these strengths, certain limitations must be acknowledged. Several included studies were narrative reviews or single-site observational studies, introducing heterogeneity in methodology and outcome measures. The small sample size in some reports and reliance on retrospective data further limits the generalizability of findings. There is also potential for publication bias, particularly due to the exclusion of non-English literature and unpublished studies, which may underrepresent negative or null results. Furthermore, the diverse pharmacological profiles of the included substances precluded a meta-analytic approach, necessitating a qualitative synthesis. The findings of this review hold important implications for both clinical practice and public health policy. Clinicians should be aware of the broad spectrum of acute and chronic toxicities linked to recreational drug use and adopt comprehensive screening and management protocols for affected patients. Public health authorities should prioritize real-time toxicological surveillance and harm reduction strategies, especially in communities experiencing surges in novel psychoactive substances. Future research should aim to conduct large-scale, longitudinal studies examining the cumulative impact of polysubstance use, as well as intervention trials to assess the efficacy of specific management approaches for

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drug-induced complications. In conclusion, this review reinforces the significant health burden posed by recreational drug use and highlights the need for coordinated efforts in research, clinical care, and policy development to mitigate its toxicological consequences.

CONCLUSION

This systematic review underscores the extensive toxicological burden and long-term health risks associated with recreational drug use, highlighting consistent evidence of both acute and chronic adverse outcomes such as central nervous system toxicity, cardiovascular complications, psychiatric disorders, and impaired bone and hormonal health. Clinically, these findings emphasize the necessity for comprehensive patient screening, accurate toxicology assessments, and multidisciplinary management strategies to mitigate harm and guide appropriate care. While the evidence synthesized here is generally robust, variability in study design and underreporting of substance use suggests that current estimates may underrepresent the true scope of harm. Continued research, particularly longitudinal and population-based studies, is essential to deepen understanding of drug-specific risks and inform more effective public health policies and clinical interventions.

AUTHOR CONTRIBUTION

Author	**Contribution**
Shaikh Khalid Muhammad*	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Sameen Shahid	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Tanveer Ahmed Ansari	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Sidra Ashraf	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Rukhshanda Arjmand	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Hafsa Javed	Substantial Contribution to study design and Data Analysis Has given Final Approval of the version to be published
Afshan Rubab	Contributed to study concept and Data collection Has given Final Approval of the version to be published

REFERENCES

1. Miró Ò, Waring WS, Dargan PI, Wood DM, Dines AM, Yates C, et al. Variation of drugs involved in acute drug toxicity presentations based on age and sex: an epidemiological approach based on European emergency departments. Clin Toxicol (Phila). 2021;59(10):896-904.

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2. Rowe CL, Santos GM, Kornbluh W, Bhardwaj S, Faul M, Coffin PO. Using ICD-10-CM codes to detect illicit substance use: A comparison with retrospective self-report. Drug Alcohol Depend. 2021;221:108537.
3. Gartenberg A, Petrie A, Yen W, Cho W. Understanding the effect of recreational drug use on bone health and musculoskeletal disease in the establishment of pain regimens. World J Emerg Med. 2024;15(5):356-64.
4. Fischbach P. The role of illicit drug use in sudden death in the young. Cardiol Young. 2017;27(S1):S75-s9.
5. Marongiu S, van Eijk M, Gresnigt FMJ, Croes EA, Franssen EJF. Rising incidence of recreational ketamine use: Clinical cases and management in emergency settings. Toxicol Rep. 2025;14:101940.
6. Perłowski J, Miśkiewicz M, Ptak J, Noga R, Teska V, Marcinkowska J, et al. Recreational ketamine use and its impact on health. Journal of Education, Health and Sport. 2024.
7. Zellner T, Eyer F, Rabe C, Geith S, Haberl B, Schmoll S. Recreational Drug Overdose-Clinical Value of Toxicological Analysis. Toxics. 2024;12(9).
8. Niebel A, Pragst F, Krumbiegel F, Hartwig S. Prevalence of cathinones and other new psychoactive substances in hair of parents and children of families with known or suspected parental abuse of conventional illegal drugs. Forensic Sci Int. 2022;331:111148.
9. Geuens M, Van Hoofstadt K, Hoogmartens O, Van den Eede N, Sabbe M. Pooled Urine Analysis at a Belgian Music Festival: Trends in Alcohol Consumption and Recreational Drug Use. Prehosp Disaster Med. 2022;37(6):806-9.
10. Crulli B, Dines AM, Blanco G, Giraudon I, Eyer F, Liechti ME, et al. Novel psychoactive substances-related presentations to the emergency departments of the European drug emergencies network plus (Euro-DEN plus) over the six-year period 2014-2019. Clin Toxicol (Phila). 2022;60(12):1318-27.
11. Rousis N, Bade R, Romero-Sánchez I, Mueller JF, Thomaidis NS, Thomas KV, et al. Festivals following the easing of COVID-19 restrictions: Prevalence of new psychoactive substances and illicit drugs. Environ Int. 2023;178:108075.
12. Avcioglu G, Yilmaz G, Yalcin Sahiner S, Kozaci LD, Bal C, Yilmaz FM. Evaluation of the diagnostic performance of an oral fluid screening test device for substance abuse at traffic controls. Clin Biochem. 2021;93:112-8.
13. Lin CC, Weng TI, Ng CJ, Shih CP, Hsu J, Liao YC, et al. Emergency department visits due to new psychoactive substances and other illicit drugs in Taiwan: preliminary results of the Taiwan Emergency Department Drug Abuse Surveillance (TEDAS) project. Clin Toxicol (Phila). 2022;60(6):708-15.
14. Schep L, Slaughter R, Glue P, Gee P. The clinical toxicology of cannabis. The New Zealand medical journal. 2020;133 1523:96-103.
15. Weng TI, Chen LY, Chen JY, Chen PS, Hwa HL, Fang CC. Characteristics of analytically confirmed illicit substance-using patients in the Emergency Department. J Formos Med Assoc. 2020;119(12):1827-34.
16. Dragogna F, Oldani L, Buoli M, Altamura A. A case of severe psychosis induced by novel recreational drugs. F1000Research. 2014;3.
17. Wiens T, Wright N, Saravia S, Wogen M, Roesler J, Lynfield R. Beyond Overdose: Surveillance of Recreational Drug Use and Corresponding Toxicology Testing. Online Journal of Public Health Informatics. 2019;11.
18. Weber C, Smith JL, Soderstrom J, Burrows S, McCutcheon D, Oosthuizen F, et al. Analytically confirmed illicit and novel psychoactive drug use in Western Australian emergency departments: initial results from the Emerging Drugs Network of Australia (EDNA). Clin Toxicol (Phila). 2023;61(7):500-8.
19. Liakoni E, Yates C, Dines AM, Dargan PI, Heyerdahl F, Hovda KE, et al. Acute recreational drug toxicity: Comparison of self-reports and results of immunoassay and additional analytical methods in a multicenter European case series. Medicine (Baltimore). 2018;97(5):e9784.
20. Rehman S, Vallamkonda OS, Raut N. Acute recreational drug toxicity: An update. Indian Journal of Medical Specialities. 2018.
21. Specka M, Kuhlmann T, Sawazki J, Bonnet U, Steinert R, Cybulska-Rycicki M, et al. Prevalence of Novel Psychoactive Substance (NPS) Use in Patients Admitted to Drug Detoxification Treatment. Front Psychiatry. 2020;11:569.
22. Isoardi KZ, Polkinghorne G, Harris K, Isbister GK. Pregabalin poisoning and rising recreational use: a retrospective observational series. Br J Clin Pharmacol. 2020;86(12):2435-40.
23. Ovat DY, Aslan R, Kirli U, Akgür SA. Methamphetamine as the most common concomitant substance used with pregabalin misuse. J Pharm Biomed Anal. 2024;241:115996.
24. King A, Hill SL, Pucci M, Bailey G, Keating L, Macfarlane R, et al. Clinical features associated with ADB-BUTINACA exposure in patients attending emergency departments in England. Clin Toxicol (Phila). 2022;60(10):1094-8.

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25. Castillo-Carniglia A, Rivera-Aguirre A, Santaella-Tenorio J, Fink DS, Crystal S, Ponicki W, et al. Changes in Opioid and Benzodiazepine Poisoning Deaths After Cannabis Legalization in the US: A County-level Analysis, 2002-2020. Epidemiology. 2023;34(4):467-75.

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