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REVIEW OPEN ACCESS

Contextualizing Mental Health Comorbidities in SUD Patients Leading to Increased Risk of Overdose: A Systematic Literature Review

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Introduction: Despite increased awareness of the risk associated with drug overdose, it remains a significant public health concern in North America. In the case of Substance Use Disorder (SUD), comorbid mental illness has been found to increase risk of overdose. This systematic review aims to identify, assess and contextualize common comorbidities associated with SUD that have contributed to overdose occurrences.
Methods: A comprehensive literature search was conducted to identify major comorbidities associated with SUD. PubMed, Embase, MEDLINE, and Web of Science were utilized. Peer-reviewed primary studies were included if they examined the prevalence of SUD in conjunction with a comorbidity involving mental illness. To establish a correlation with real-world overdose cases, the collected data was compared with coroner data to determine if current drug and comorbidity research in literature was reflective of the most prevalent forms of overdose in the general population. Results were summarized following the PRISMA guidelines.
Results: A total of 60 papers investigating SUD with a comorbidity involving mental illness comorbidity were identified. Alcohol and cannabis were the most frequently studied substances, while Depressive and Anxiety disorders were the most common mental illness comorbidities examined. Geographically, these findings were consistent with studies from the US. However, in Canada, opioids were the most extensively studied substances, with Depressive and Neurodevelopmental disorders being the most commonly investigated mental illness comorbidities.
Discussion: Comparison with coroner data suggests that greater research focus should be directed towards substances with greater potential for harm and fatal overdose. This emphasis on specific drugs can help improve overall mortality rates among SUD patients with comorbid mental illnesses. In Canada, this could involve conducting further research on stimulants such as cocaine and methamphetamine, and in the US with fentanyl.
Conclusion: A disconnect between the substances studied in the literature and their real-world impact was found. Bridging this gap is essential to develop evidence-based interventions for comorbid SUD. More research on SUD, mental health comorbidity and overdose trends are needed to improve relevance to real-world scenarios.

Keywords: substance use disorder; comorbidities; drug overdose; North America

Introduction

Substance use disorder (SUD) is a multifaceted medical condition characterized by problematic and/or excessive substance use, leading to significant health, social and legal issues [1]. This term encompasses both the use of illicit substances like heroin, cocaine and methamphetamine, as well as the misuse of legal substances such as alcohol, nicotine, cannabis and prescription or over-the-counter (OTC) medications. SUDs are among the most prevalent psychiatric disorders, in modern Western society, contributing to substantial morbidity and mortality rates [2]. In 2020 alone, drug-involved overdoses claimed the lives of nearly 100,000 individuals, in addition to causing extensive economic and public safety implications [2].

Comorbidities occur when multiple health conditions interact within an individual, synergistically or sequentially [3]. Studies have consistently demonstrated that there is a high prevalence of comorbid mental illnesses among individuals with SUDs [3]. Patients with SUDs often experience concurrent mental health conditions such as depression, anxiety disorders or post-traumatic stress disorder [4]. Moreover, SUD patients with comorbid mental illness face significantly worsened treatment outcomes and an increased risk of overdose [5]. Recognizing this intersection between SUD patients and comorbid mental illness is crucial to providing more comprehensive care and improving patient outcomes.

The presence of co-occurring mental health disorders and SUDs often leads to poorer health outcomes due to the mutually reinforcing effect that each has on the other. SUDs exacerbate symptoms associated with comorbid mental health disorders, and vice versa, resulting in positive

feedback loops that further deteriorate overall health outcomes. This creates unique challenges in terms of diagnosis development and effective care. A systematic literature review was chosen as the most appropriate method for comparing individuals with comorbid mental health disorders and SUDs, as systematic reviews synthesize existing evidence to provide comprehensive overviews of complex relationships. By exploring the bidirectional relationship between mental illnesses and SUDs, this systematic review aims to shed light on the intricate dynamics and implications for this patient population and their care. Furthermore, it will help identify gaps in current research and prioritize areas that require further investigation to enhance the overall understanding of comorbid disorders.

Although the connections between comorbidities and SUDs, as well as SUDs and overdose have been extensively documented, it remains unclear whether the amount of research being conducted on the most common SUDs and their associated mental illness comorbidities reflects the current prevalence of overdose in North America. This systematic literature review seeks to address this gap by examining the prevalence of comorbid SUDs and mental health disorders. The findings will then be compared to current coroner data to determine if the existing drug and comorbidity research in the literature aligns with the most common types of overdoses observed in the general population.

It is hypothesized that the current literature will not accurately represent the major patterns of SUDs and related comorbidities present in the general population. By highlighting this potential disparity, this paper aims to contribute to the ongoing advancement of current knowledge regarding individuals with comorbid SUDs and mental illness. These insights will allow for the informed and targeted development of interventions, treatment strategies, and comprehensive support systems, ultimately working towards reducing the societal consequences associated with these disorders.

Methods

Protocols

This systematic review adhered to the guidelines outline in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [6].

Search Strategy

On February 4th, 2023, a comprehensive primary search was conducted using Medical Subject Headings (MeSH) terms on the PubMed, Embase, MEDLINE, and Web of Science databases. The MeSH terms were related to SUD, comorbidity, drug overdose, epidemiology, and North America. Initially, 2338 papers were identified for further screening in Covidence. For a detailed version of the search terms, please refer to Appendix A.

Study Selection

The selection of studies was conducted in two stages. In the first stage, the authors screened based on titles and abstracts. Conflicts were resolved through the involvement of an unbiased third party. The second stage involved a full text review of the accepted papers, applying the same eligibility criteria as the title and abstract screening. Included studies focused on target populations aged 18 to 65, were written in English, were peer-reviewed, constituted primary literature, were based in treatment settings, and investigated the prevalence of substance abuse along with comorbidity. Exclusions were made for studies targeting prenatal, maternal, prisoner or veteran populations, those limited to describing clinical manifestations or effects of prescribed medication-based substance abuse, studies focused on the efficacy of specific tools or techniques, systematic reviews, grey literature, conference reports, or thesis reports.

Data Extraction

Eligible papers were tabulated based on the publication date, target population, major comorbidities mentioned, SUDs, and main findings. Common comorbidity themes were extracted and classified using DSM-V diagnostic criteria, while substances were grouped based on their common occurrence. Themes and core categories were extracted from each paper. Additionally, studies were organized chronologically to observe comorbidity and SUD trends.

The frequency of each category discussed was analyzed in relation to the publication year to identify trends in the prevalence of specific topics. Separate analyses were also conducted for Canada and the United States (US) to identify unique characteristics, trends, or patterns specific to each country. This analysis aimed to highlight strengths, challenges, or opportunities, given the varying degrees of economic, societal, and governmental differences in healthcare.

Coroner overdose data was used as a metric for the population level impact of SUDs and compared to the frequency of study on specific substances to observe the relationship between literature and real-world impact. The British Columbia Coroners Service Illicit Drug Toxicity Report [7] and the Provisional Drug Overdose Death Counts [8] were utilized to analyze Canadian and US overdose rates by drug class.

While the overdose rates of British Columbia are higher compared to the rest of Canada, the coroner data from this region was considered representative of the country due to a lack of comprehensive national overdose or coroner data available to the authors at the time of writing. Furthermore, the British Columbia coroner data provided detailed stratification of overdose cases based on specific substances, thus offering valuable insights.

Results

Out of the 2338 studies, 1629 were excluded during the title and abstract screening, and an additional 649 were excluded during the full-text review. Ultimately, 60 texts remained, focusing on the substance abuse in patients with mental illness comorbidities. Detailed descriptions of each of the 60 studies can be found in Appendix B. A summary of these papers based on the substances and comorbidities addressed can be found in Table 1.

Table 1. Summary of the prevalence of comorbidities and substances discussed

Themes	Core Categories	Number of Studies
Comorbidity	Depression	32
	Anxiety	26
	Pain	15
	Neurodevelopmental Disorders (ADHD)	13
	Schizophrenia Spectrum and Other Psychiatric Disorders	12
	Feeding and Eating Disorders	11
	Trauma and Stressor Related Disorders	13
	Personality Disorders	15
	Bipolar and Related Disorders	12
	Other Mental Disorders	13
Substance	Alcohol	41
	Cannabis	27
	Opioids	26
	Stimulants	25
	Nicotine	21
	Psychedelics	14
	Prescription Drug Use	13
	Ecstasy / MDMA	13
	Other	19

Studies ranged from publication dates of 1990 to 2023. A total of 199 substances and 162 comorbidities were mentioned. Graphical representation of results can be seen in Figure 1 and Figure 2 discussing the prevalence of various substances and comorbidities found among the 60 studies. It was found that alcohol (n = 41) and cannabis (n = 27) were the most researched substances and Depressive disorders (n = 32) and Anxiety disorders (n = 26) were the most prevalent mental illness comorbidities discussed. The least researched substances overall were prescription drug use (n = 13), ecstasy/MDMA (n = 13), and psychedelics (n = 14). The least researched mental health comorbidities were Feeding and Eating Disorders (n = 11), Schizophrenia Spectrum (n = 12) and Bipolar and Related Disorders (n = 12).

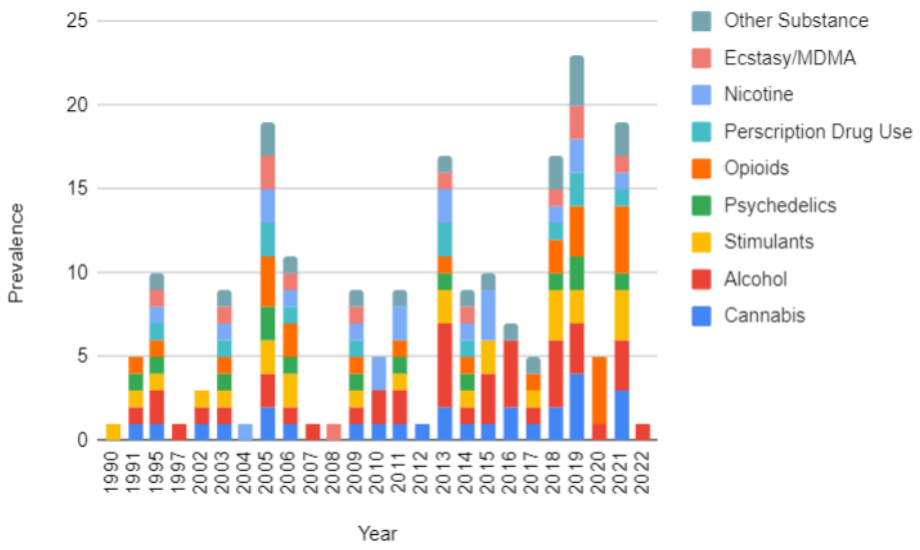

Figure 1. Prevalence of studies that discussed various substances in patients with mental illness comorbidities (made in Google Sheets).

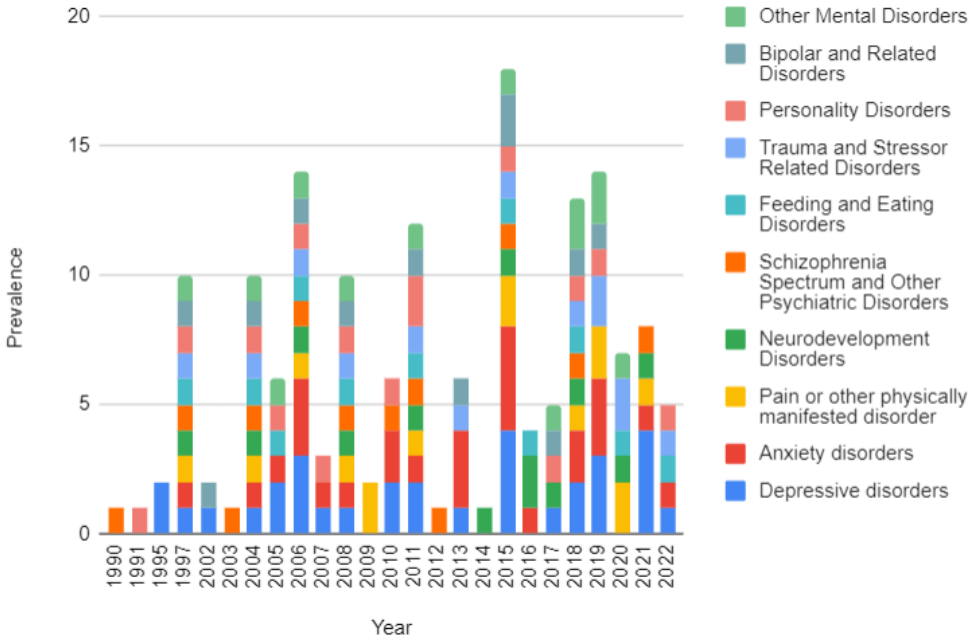

Figure 2. Prevalence of studies that discussed various mental health comorbidities among patients with SUD (made in Google Sheets).

Fifty-three studies were found with populations of interest from the US. Graphical representation of these results can be found in Figure 3 and Figure 4. Alcohol (n = 37) and cannabis (n = 23) were the most studied substances whereas prescription drugs (n = 11), ecstasy/MDMA (n = 11), and psychedelics (n = 12) were the least studied. Depressive disorders (n = 29) and Anxiety disorders (n = 26) were the most studied mental health comorbidity while Feeding and Eating Disorders (n = 9) as well as Neurodevelopmental Disorders (n = 10) were least studied.

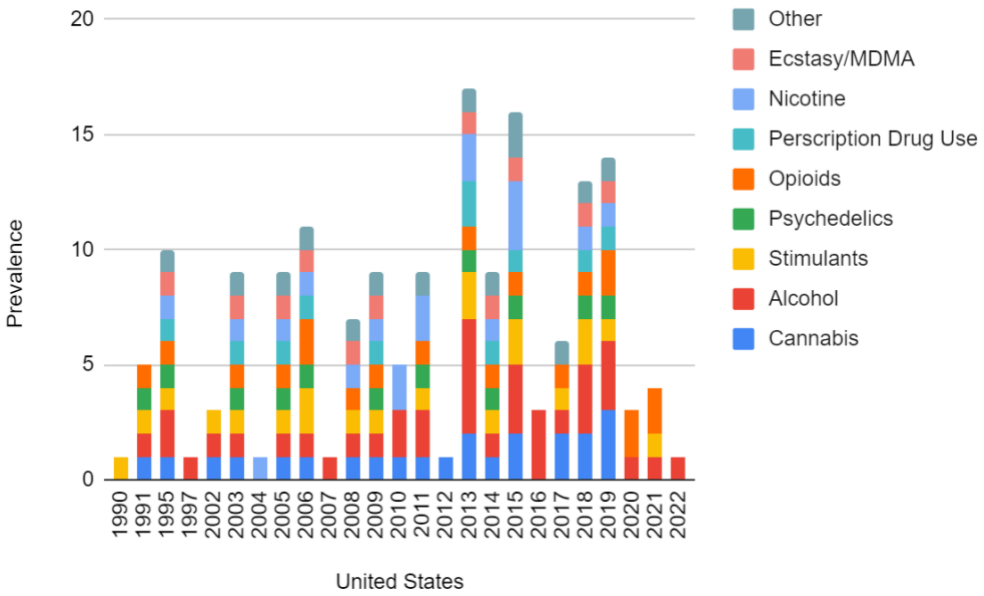

Figure 3. Prevalence of substances discussed in studies conducted in the US on patients with mental illness comorbidities (made in Google Sheets).

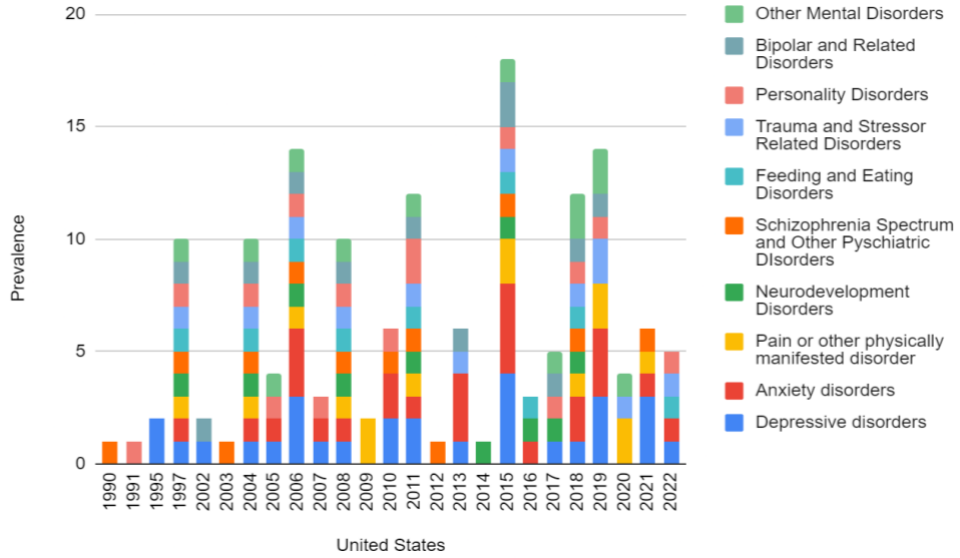

Figure 4. Prevalence of DSM-5 mental illnesses discussed in studies conducted in the US in patients with SUD (made in Google Sheets).

Seven studies were found with populations of interest from Canada. Graphical representation of these results can be found in Figure 5 and Figure 6. Opioids (n = 6) were the most common substances researched, with cannabis (n = 4), alcohol (n = 4) and stimulants (n = 4) following closely behind. Nicotine (n = 2), ecstasy/MDMA (n = 2), prescription drugs (n = 2) and psychedelics (n = 2) were the least studied substances. In terms of comorbidities, Depressive disorders (n = 4) was the most prevalent followed by Neurodevelopmental Disorders (n = 3).

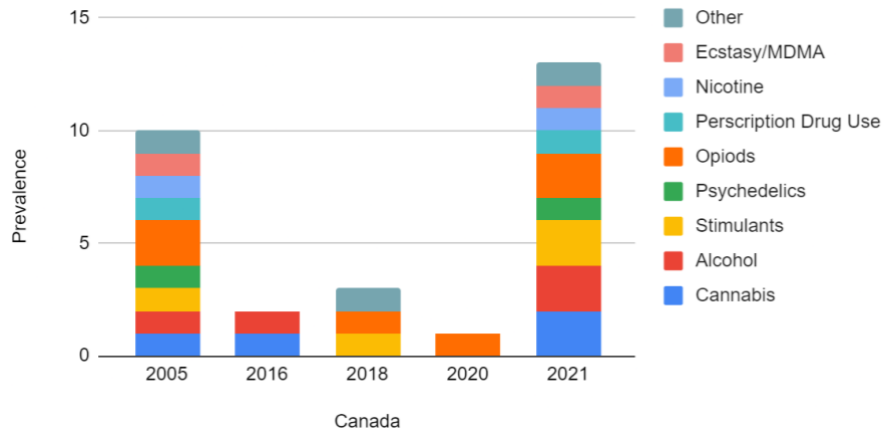

Figure 5. Prevalence of substances discussed in studies conducted in Canada on patients with mental illness comorbidities (made in Google Sheets).

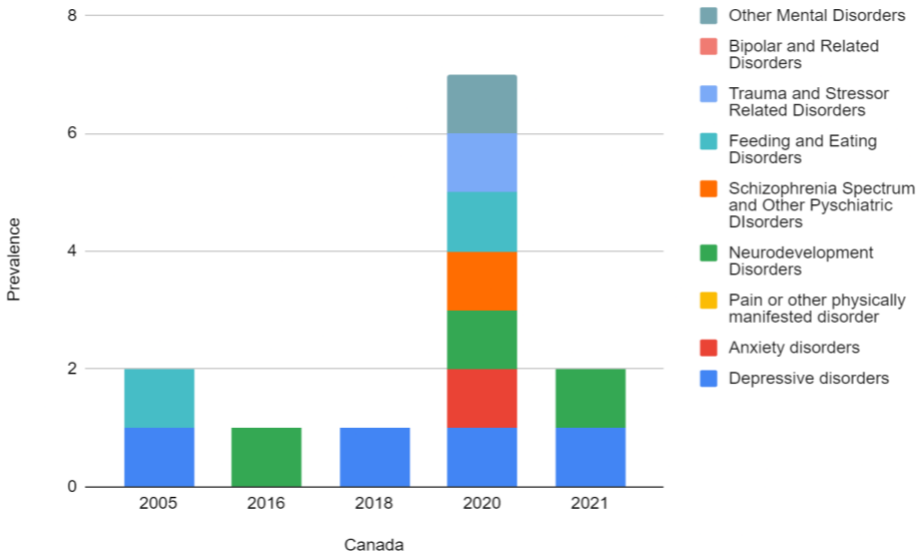

Figure 6. Prevalence of DSM-5 mental illnesses discussed in studies conducted in Canada in patients with SUD (made in Google Sheets).

Discussion

Coroner data was used to offer complementary insights into the population-level harms of SUDs. Coroner data sheds light on the specific substances involved in drug overdose serving as a resource for identifying emerging drug use trends and understanding patterns of drug toxicity. Specifically, rates of fatal overdose for each substance were compared to how prominently these substances were studied in the literature.

Coroner data for Canada was sourced from British Columbia and used as a representative sample for the rest of the country. The British Columbia Coroners Service Illicit Drug Toxicity Report from 2012-2022 was used to analyze trends [7]. According to the report, rates of methamphetamine toxicity have risen from 14% in 2012 to 42% in 2021 [7]. Additionally, cocaine use was responsible for 46% of illicit drug toxicity deaths, making it the second most prominent cause of overdose [7]. Despite stimulants making up a significant portion of drug overdoses, studies examining stimulants (cocaine and methamphetamine) are limited in number. This indicates that the drugs most associated with overdose are receiving limited research attention whereas drugs with lower rates of overdose (ex. alcohol, cannabis and opioids) are being extensively studied. It makes sense that these substances are the most extensively studied substances since they are generally the most widely used, however a greater focus should be placed on studying drugs with a greater potential for harm and fatal overdose as to improve overall mortality rates in SUD patients with mental illness comorbidities.

For the US, the Provisional Drug Overdose Death Counts from 2015-2022 was used to analyze overdose rates

by drug class [8]. The provisional report excluded data on the number of alcohol overdoses since it focused on illicit substances. Between 2015-2022 rates of synthetic opioid (specifically fentanyl) overdoses have been steadily rising whereas rates of natural and semi-synthetic opioids (ex. oxycodone, hydrocodone, and morphine) overdose have remained stagnant [8]. Most of the literature relating to opioids looks at opioid use disorder generally, or specifically examines prescription drug opioids [8]. There is limited research specifically looking at fentanyl despite its high potential for misuse and associated harms. More research into the patterns of fentanyl use and its associated comorbidities is essential for developing targeted interventions and harm reduction strategies.

Limitations and Future Research

There are several limitations concerning this systematic review. Currently, there is no comprehensive population-level data on the prevalence of mental health comorbidities in individuals with SUD. Thus, specific findings to compare the relationship between comorbidities, overdose, and specific substances is met with numerous obstacles. Further, the studies included in this review lacked a standardized metric for diagnosing patients with SUD or comorbidities. Since study populations, study methods, and outcome measurements differed between the studies, quantitative comparisons could not be made. Additionally, reporting bias may be present in the study table as only selective outcomes were recorded for individual studies.

Coroner data from British Columbia was deemed a sufficient proxy for the rest of Canada as it was the most comprehensive and representative data source, in comparison to other province-specific and overall Canadian coroner data, however this source is evidently not ideal and poses numerous limitations. To develop a comprehensive understanding of the relationship between literature frequency and population effects in Canada of SUD, a national coroner database of overdose with substance-specific stratification should be used. As previously mentioned, this was not available to the authors at the time of writing and as such, the British Columbia Coroners Service Illicit Drug Toxicity Report was used as a proxy since it provided said comprehensive analysis and stratification of data.

The lack of comprehensive population-level data on drug-related comorbidities, particularly those related to mental illness conditions, poses a significant challenge in comparing literature results to real-world findings. The lack of standardized diagnostic criteria among studies makes it difficult to collect data on the presence of a mental illness condition. Some studies relied only on self-reported symptoms, whereas others required a psychiatric assessment to determine the presence of a comorbidity. Diagnostic guidelines also vary depending on the geographic region and healthcare setting making it difficult to categorize each type of comorbidity. Furthermore, the subjective nature of mental illness conditions can contribute to patients underreporting, not recognizing, or inadequately disclosing their symptoms. These issues may be heightened by the presence of additional physical and cognitive impairments resulting from an individual's SUD. Additionally, limited access to mental health care can hinder the proper diagnosis of mental illness conditions. Many studies were conducted at patient treatment facilities in major cities, which are not accessible to many Canadians and Americans. The literature significantly underrepresented individuals residing in rural and low-income communities, thus limiting the available data necessary for targeted efforts to address comorbid SUD.

Recognizing and addressing these barriers is crucial for developing interventions that target patients with comorbid SUD and developing prevention strategies for at-risk populations. Overcoming these obstacles would allow researchers to better compare literature findings to real-world circumstances, ultimately enhancing health outcomes and quality of life for patients affected by SUD and mental illness conditions.

Conclusions

This systematic review examined the prevalence of discussion on various substances and comorbidities in the literature. These findings were compared to coroner data which determined that a disparity exists between the substances most studied in the literature and substances that exhibit a prominent real-world effect. It is essential to bridge this knowledge gap to support the development of evidence-based interventions that address the needs of individuals with comorbid SUD. Further research must be conducted on emerging drug use trends and specific substances involved in drug overdose deaths in order to improve the relevance and applicability of findings to real-world scenarios.

List of Abbreviations Used

MeSH: medical subject headings
PRISMA: preferred reporting items for systematic reviews and meta-analyses
SUD: substance use disorder
USA: United States of America

Conflicts of Interest

The authors declare that they have no conflict of interests.

Ethics Approval and/or Participant Consent

No ethics approval or participant consent was needed for this study.

Authors' Contributions

All authors contributed equally to the study.

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