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Global Patterns of Polysubstance Abuse and Overdose Mortality During the COVID-19 Pandemic

Aisha Katsina Isa
Igbinedion University Okada, Nigeria

* Corresponding Author: **Aisha Katsina Isa**

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Abstract
COVID-19 emerged at a time when many countries were already struggling with an escalating opioid crisis and increasingly complex patterns of polysubstance abuse. Although global attention focused on the spread of the virus, individuals with substance use disorders faced major disruptions in care, unstable drug supplies, and heightened socioeconomic pressures. This narrative review synthesizes peer-reviewed literature published through 2021 to examine how the pandemic affected overdose mortality, patterns of polysubstance use, and access to services across diverse settings. Evidence from epidemiological studies, clinical research, and qualitative reports shows that fatal overdoses increased during the pandemic, driven by treatment disruptions, isolation, changes in drug availability, and emotional distress. Polysubstance involvement, including combinations of opioids, stimulants, and sedatives, played a significant role. While telehealth expansion and more flexible medication policies helped sustain treatment for some, these adaptations were unevenly implemented and did not fully reach structurally disadvantaged groups. The findings underscore the necessity for robust public health strategies that guarantee continuity of treatment, safeguard harm reduction programs, and mitigate socioeconomic inequities during future emergencies.

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Keywords: COVID-19, Opioid Crisis, Polysubstance Abuse, Overdose Mortality, Treatment Disruptions, Drug Supply Changes

Introduction

The COVID-19 pandemic overlapped with ongoing global challenges related to opioid misuse and polysubstance abuse. In the years leading up to the pandemic, many countries observed rising fatalities involving synthetic opioids and mixtures of substances, including stimulants and benzodiazepines (Compton *et al*., 2021) [5]. These patterns created an unstable environment that made people who use drugs especially vulnerable when the pandemic began.

Once COVID-19 mitigation measures were implemented, treatment systems experienced immediate strain. Individuals who depended on routine clinic visits or supervised dosing encountered limited access to services. Evidence from a comparative assessment of methadone programs in the United States and Canada showed meaningful differences in adaptability, with Canadian services expanding take-home doses more rapidly. In contrast, many United States programs faced regulatory and structural barriers (Joudrey *et al*., 2021) [8]. This variation demonstrated how policy environments shaped treatment continuity during the crisis.

Early data documented increases in fatal overdoses across multiple regions. Modeling studies predicted that even short-term disruptions in care could elevate overdose mortality, especially where fentanyl dominated the drug supply (Linas *et al*., 2021) [10]. Isolation further intensified risk, as individuals were more likely to use substances without the presence of others who could intervene (Haley & Saitz, 2020) [7]. A prospective study from Ontario found rising opioid positivity among individuals in treatment, with stimulant co-use strongly associated with these trends (Rosic *et al*., 2021) [14].

These challenges were not evenly distributed. Structurally disadvantaged populations, including people with unstable housing, limited access to healthcare, or reduced employment opportunities, experienced disproportionate harm. Research from underserved urban communities reported that mental health strain, financial stress, and lack of supportive services contributed to increased substance use and related risks (Chacon *et al*., 2021; Abramson, 2021) [4] [3]. Qualitative analyses showed that reductions in harm reduction outreach and supervised consumption services made drug use more dangerous for people who continued using throughout the pandemic (Russell *et al*., 2021) [15].

This review brings together global evidence from epidemiological studies, qualitative research, policy analyses, and clinical observations to examine patterns of polysubstance use and overdose mortality during the COVID-19 pandemic. It explores how treatment disruptions, shifts in drug supply, mental health stressors, and longstanding socioeconomic inequities shaped outcomes across different populations and settings.

Methods

This narrative review synthesizes peer-reviewed full-text articles you provided, focusing on studies published between 2019 and 2021. Earlier works were included only when necessary to contextualize pre-pandemic trends. The reviewed literature includes epidemiological studies, modeling analyses, qualitative investigations, and policy-oriented commentaries from journals such as JAMA Network Open, Molecular Psychiatry, Journal of Substance Abuse Treatment, Journal of Addiction Medicine, Pain and Therapy, Addictive Behaviors Reports, and others.

Studies included if they examined opioid or polysubstance trends, overdose mortality, treatment accessibility, harm reduction service disruptions, or socioeconomic factors during the pandemic period. Commentary without empirical grounding and papers published after 2021 were excluded. Each article was evaluated for insights related to the interaction between COVID-19 and substance use behaviors, service availability, and risk patterns. Because the goal was to integrate complex and context-dependent information, a narrative synthesis approach was employed.

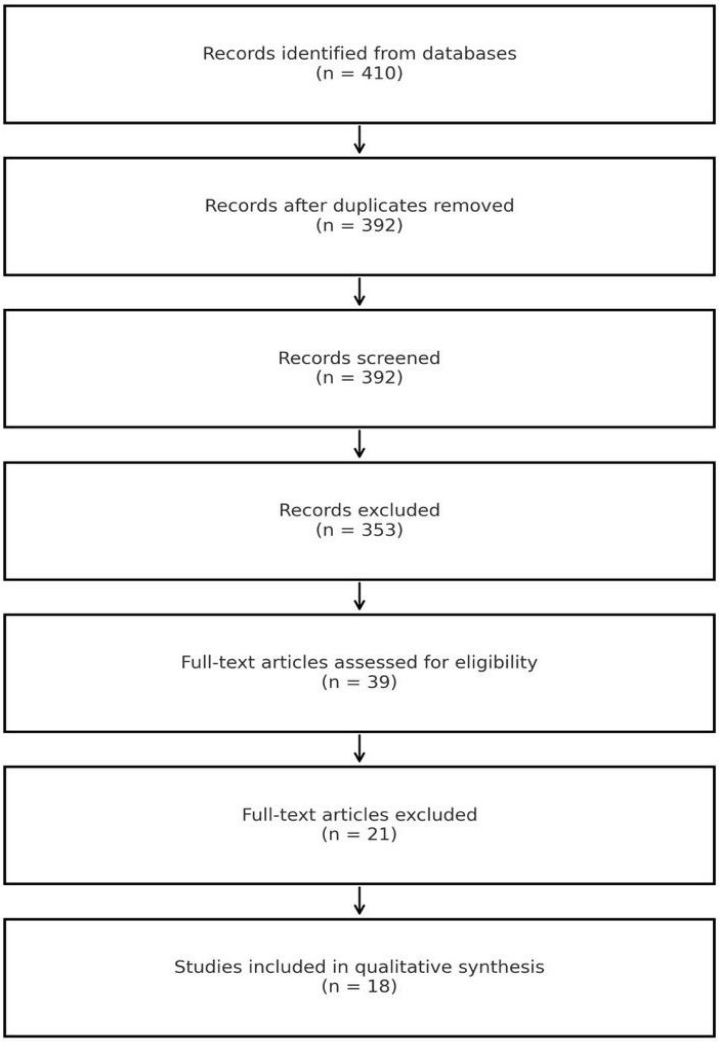

Fig 1: PRISMA 2020 flow diagram showing the identification, screening, eligibility assessment, and final inclusion of studies in the review.

Findings and Discussion

Increases in Overdose Mortality

Multiple sources documented increased overdose mortality during the pandemic. Modeling work suggested that treatment interruptions could lead to high-risk windows where mortality spikes occurred due to reduced treatment retention and heightened exposure to unpredictable drug supplies (Linas *et al*., 2021) [10]. Surveillance reports described increased involvement of synthetic opioids and polysubstance combinations (Niles *et al*., 2021) [12].

Commentary from Annals of Internal Medicine emphasized that the stress and isolation of the pandemic amplified existing opioid related risks (An Epidemic in the Midst of a Pandemic, 2020) [1]. Similar concerns were raised in early expert analyses, which described the pandemic as a crisis layered on top of an already severe opioid epidemic (Haley & Saitz, 2020) [7].

Treatment Disruptions and Service Limitations

Treatment systems experienced significant strain during lockdowns. Some clinics reduced hours, limited in-person visits, or experienced staffing shortages. The temporary closure of clinics and reductions in supervised dosing created challenges for people who relied on daily care (Khatri & Perrone, 2020) [9]. In contrast, some jurisdictions rapidly shifted toward telehealth or expanded the use of take-home doses. The work comparing Canada and the United States showed faster adoption of flexible methadone policies in Canada, which may have reduced treatment discontinuities (Joudrey *et al*., 2021) [8].

Harm reduction services, including outreach, naloxone distribution, and supervised consumption, also experienced interruptions. A qualitative analysis from Canada reported that reductions in these services left many individuals without lifesaving support (Russell *et al*., 2021) [15]. Similar patterns were reported globally as programs struggled to balance infection control with service delivery.

Changes in Drug Supply and Polysubstance Patterns

The pandemic altered drug supply chains due to border restrictions and shifts in distribution networks. These changes contributed to unstable purity, more contaminated products, and increased presence of synthetic opioids. In several countries, drug testing data showed higher positivity rates for fentanyl and greater involvement of multiple substances, including stimulants, benzodiazepines, and alcohol (Niles *et al*., 2021) [12]. A prospective cohort study found significant increases in stimulant co-use among people in opioid agonist treatment (Rosic *et al*., 2021) [14]. Research on polysubstance patterns highlights that combining stimulants and opioids can mask overdose symptoms and create unpredictable physiological effects (Compton *et al*., 2021) [5].

Mental Health Stressors and Population Vulnerability

Mental health effects of the pandemic played an essential role in substance use trends. Studies identified increased anxiety, depression, and general distress, which were linked to higher substance use across several populations (Dodge *et al*., 2021) [6]. Reports from psychologists noted that many individuals turned to substances as a coping mechanism for uncertainty and prolonged isolation (Abramson, 2021) [3]. Editorial reflections emphasized that individuals with chronic pain faced additional challenges, as many lost accesses to non-opioid pain care and became more reliant on medications during the pandemic (Manchikanti *et al*., 2021) [11].

Disproportionate Impacts on Underserved Groups

Individuals with socioeconomic disadvantage faced heightened risk during the pandemic. Studies have found that individuals with reduced employment, unstable housing, or limited access to healthcare encounter more barriers to treatment and support (Chacon *et al*., 2021) [4]. Pandemic restrictions forced many shelters and community programs to limit their capacity, leaving some individuals without access to basic services. Populations already marginalized experienced intensified harm during this period due to compounding stress and reduced access to lifesaving interventions (The COVID-19 Crisis Has Brought Substance Abuse to Light, 2021) [17].

Policy Lessons Learned

The early pandemic period highlighted the importance of flexible policies. Telehealth expansion and increase in access to take-home medications have offered critical support for many individuals and should be retained beyond emergency settings (Silva & Kelly, 2020) [16]. Maintaining continuity of harm reduction services is essential, as they play a central role in preventing fatal overdoses. Public health systems must also address underlying inequities by investing in housing stability, mental health care, and economic support.

Conclusion

The COVID-19 pandemic intensified vulnerabilities within global substance use and addiction treatment systems. Overdose mortality increased, treatment disruptions were widespread, and individuals encountered new emotional and socioeconomic pressures. Polysubstance involvement played a significant role in overdose risk, especially in settings where synthetic opioids were dominant. Although some policy innovations strengthened the response, longstanding inequities continued to shape outcomes. Future public health strategies must prioritize access to treatment, protect harm reduction services, and address the structural determinants that place specific populations at a higher risk of harm. These lessons guide building more resilient and equitable systems that are prepared to respond to future crises.

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