Clinical Profiles of Synthetic Opioid and Psychostimulant Co-use: A Comparative Analysis of Emerging Trends in Akwa Ibom State and the United States

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Abstract*—Contemporary drug crisis has been inclined more towards polysubstance use, which refers to simultaneous or consecutive intake of various psychoactive drugs, and this has become a great challenge to clinical management and the global health of people. This paper presents comparative research of synthetic opioid and psychostimulant co-use in the United States and Nigeria, especially in the Akwa Ibom State. The fourth wave of the opioid epidemic in the United States has been defined by illicitly prepared fentanyl as dominant and the frequent use of this drug in combination with stimulants, including methamphetamine and cocaine. This accidental exposure has added to unprecedented overdose deaths, precipitated by respiratory depression and complicated polysubstance toxications. Nigeria, on the contrary, has a converging but discrete trend of deliberate poly-drug use, which is taking place in tramadol, methamphetamine, benzodiazepines, and synthetic cannabinoids locally referred to as Colorado. The clinical manifestation in this case is a clinical neuropsychiatric morbidity, which entails acute psychosis, hallucinations, seizures, and dependence syndromes, relatively less fatal, but high long-term cognitive and mental health burden. The analysis is based on the use of epidemiological data, local clinical reports, and peer-reviewed sources to assess variation in the supply of the substances, use, neuropharmacological reactions, and socio-cultural motivators. The main results show that U.S. trends are supply-led, and contamination and unintentional co-use intensify the risk of an overdose, whereas Nigerian trends are user led which is mostly driven by functional or productivity related goals. Such differences have far-reaching implications on clinical practice and on the interventions of public health. Harm reduction measures, such as the provision of naloxone, drug checking services, and polysubstance use treatment are vital in the United States. The priorities in Nigeria are to intensify the mental health sector, control the pharmaceutical opioids, apply culturally modified harm reduction approaches, and participate in special public health education campaigns. The current comparative view highlights the need to have context-specific approaches to reduce the health burden of polysubstance use, which can inform both high-income and low- and middle-income nations facing the global opioid-stimulant co-use crisis.

***Index Terms*—Polysubstance use, synthetic opioids, stimulants, fentanyl, tramadol, synthetic cannabinoids, Nigeria, United States, clinical implications**

I. INTRODUCTION

The drug crisis of the world has changed considerably over the last few years, since the dependence on a single substance is replaced by a more complicated trend of polysubstance use, which can be described as the act of consuming multiple substances with psychoactive properties both at the same time or sequentially. This shift indicates changes in illicit drug markets, as well as adaptive behaviour among users, who find more and more combinations with substances aimed at increasing, counteracting, or extending the effects of psychoactive drugs.

Polysubstance use has emerged as the main source of morbidity and mortality worldwide, making it difficult to diagnose, treat, and prevent these issues as part of clinical and overall public health approaches. Specifically, the combination of synthetic opioids and psychostimulants has brought about a new aspect of pharmacological hazard since these substances have contranarcotic but synergistically harmful effects on the central nervous and cardiovascular systems. The growing number of such combinations creates the

necessity of coordinated efforts that would go beyond traditional single-drug interventions models (Centers for Disease Control and Prevention [CDC], 2024; Friedman and Shover, 2023).

This changing trend in the United States is best observed in the spread of illegally produced fentanyl and its comorbid use with other stimulants, including methamphetamine and cocaine. The high potency and extensive pollution of the drug supply of Fentanyl have dramatically changed the relationship of overdose, and polysubstance exposure is now the characteristic trait of the ongoing epidemic.

Empirical evidence suggests that a significant share of overdose deaths caused by opioids currently include one or more stimulant, which is indicative of transitioning towards what is being termed the fourth wave of the overdose crisis. This combination is especially dangerous as opioid-induced respiratory depression can be masked by stimulants temporarily, which will delay the manifestation of the overdose and can harm life to a greater degree. In turn, multidimensional approaches to treatment based on combating both opioid dependence and the development of complications due to the use of stimulants characterise the clinical presentations in the United States (Friedman and Shover, 2023; Schumacher et al., 2025).

Similar but contextually different is taking place in Nigeria, especially in urban and semi-urban areas like Akwa Ibom State, where the substance terrain is swiftly changing towards the utilization of heterogeneous mixture of substances. This is in contrast to the United States where fentanyl prevails; polysubstance use in Nigeria is majorly based on tramadol, methamphetamine, benzodiazepines, and synthetic cannabinoids locally referred to as Colorado. Such combinations are frequently designed and taken in and are products of both the availability in the market and socio-economic motivations, including the necessity of increased productivity and increased wakefulness.

According to the national assessments of the recent past, an alarming increase in the consumption of methamphetamines of about 3738 percent among some of the groups of users in addition to a constantly high rate of non-medical use of tramadol has been reported. Such trend is linked to specific clinical events, such as increased neuropsychiatric disturbances and dependence syndromes, thus presenting unique healthcare system burden. It is against this context that the current research will utilize a comparative clinical and socio-epidemiological methodology to analyze the differences in cultural, economic, and structural contexts that influence the patterns of co-use, clinical expression, and clinical response to interventions in each of the two contexts (United Nations Office on Drugs and Crime [UNODC], 2024; ICDDR, 2024).

II. GLOBAL CONTEXT OF SYNTHETIC DRUG CO-USE

The United States: The “Fourth Wave” of the Overdose Crisis

The modern stage of the United States drug epidemic, akin to the commonly defined fourth wave, is characterised by a radical reorganisation of the process of drug supply as well as consumption patterns, in which synthetic opioids, especially fentanyl, are taking a centre stage. It is different to the previous waves that arose due to the prescription opioids and, later, heroin, as the fentanyl manufactured illicitly is now omnipresent and is becoming more and more entangled with psychostimulants like methamphetamine and cocaine. This is not an accidental convergence but a sign of the systemic change in the illicit drug market, in which polysubstance availability has become the rule and not the exception.

According to epidemiological surveillance data, the percentage of opioid-related overdose deaths, which involve at least one stimulant, is steadily increasing, which explains the shift towards complicated toxicological exposure rather than isolated dependence. This trend indicates that either users are consciously using it combined to control psychoactive effects or are accidentally exposed when using drug supplies that are contaminated with one or more psychoactive substances, which makes prevention and treatment more challenging (Friedman and Shover, 2023; Centers for Disease Control and Prevention [CDC], 2024).

Comparatively, the U.S. experience is deeply different than the new trends of polysubstance use in low- and middle-income environments like Nigeria, where the manifestation of such use is also on the rise but in the conditions differentiation by structural and socio-economic factors. Although fentanyl continues to be

the leading opioid driver in the United States, its co-use with stimulants may be often associated with the supply-side contamination and the developing trafficking trends. Conversely, in most African settings, such as certain areas in Nigeria, poly-drug use is more usually planned and socially patterned and therefore reflects user-led mixtures aimed at growing stamina, work output or psychoactive strength. However, the pharmacological convergence of simultaneous exposure to central nervous system depressants and stimulants- is also constant. However, the factor of limited lethality of this convergence is multiplied in the United States due to the excessive strength of fentanyl, which takes the difference between intoxication and fatal overdose by a very small margin, thus leading to unprecedented death rates (O'Donnell et al., 2023; UNODC, 2024).

The empirical evidence also demonstrates the swift increase in the stimulant role in fentanyl-related morbidity and mortality. Longitudinal studies reveal that co-use of fentanyl and methamphetamine is on the rise and some studies indicate that co-use of stimulants has risen more than six-fold since 2015 among fentanyl-related fatalities. The clinical implications of this trend are critical, because the opposite pharmacodynamic effect of opioids and stimulants results in a misleading physiological situation when the effect of stimulants on alertness can provide a false sense of alertness in opioid induced respiratory depression.

Consequently, people can miscalculate their intoxication, postpone a doctor visit, or take more doses, which increases the risks of lethal consequences. This has clinically been translated to more complicated presentations of mixed toxidromes with a need to develop comprehensive treatment regimens that support overdose reversal and complications associated with stimulants. The case in the U.S. thus represents a high-mortality model of polysubstance use, fuelled by the availability of strong synthetic opioids and structural underlying market forces of drug use, which have critical implications on global response to the crisis in terms of public health (Friedman and Shover, 2023; O'Donnell et al., 2023).

Nigeria: Emerging Synthetic Drug Mixtures

Nigeria offers a unique but convergent pattern in the world trend of using polysubstances, which is a growing number of synthetic drugs circulating and mixing in informal and mostly unregulated markets. Though fentanyl has not yet achieved comparable dominance as in the United States, there are reports of its slow penetration to drug supply networks across West Africa, in most cases accompanied by other commonly abused pharmaceutical opioids like tramadol.

Historically, tramadol has held a pivotal role in Nigeria with the non-medical opioid market with respect to relative affordability, accessibility, and functional advantages. The recent trends however show that there is a shift towards the multi-substance use that combines stimulants and sedatives as opposed to single-substance misuse. Such a dynamic of change indicates not only the diversification of supply amounts, but also the experimentation of demand, which opens the broader structural change in the pattern of drug use that is parallel to global patterns and has context-specific features (United Nations Office on Drugs and Crime [UNODC], 2024; U.S. Department of State, 2024).

One of the characteristics of drugs market in Nigeria is so-called drug ingenuity whereby drug users voluntarily mix several psychoactive drugs to produce specific physiological and psychological effects. Popular combinations are tramadol as a starting opioid, methamphetamine as a stimulant to make a person feel more alert and resilient, benzodiazepines to alleviate anxiety or stimulant-induced agitation and synthetic cannabinoids locally known as Colorado to make psychoactive experiences more intense (George and Udofia, 2026).

Compared to the impact of high-income countries where polysubstance exposure is often accidental (because of contamination with drugs), these mixtures in Nigeria are usually intentional and deeply rooted in the social structure of certain user communities. These combinations are common in informal urban locations, and among young, economically active people, such as commercial drivers, artisans, and students, who use these combinations to work longer, deal with socio-economic pressures, or perform better. This deliberateness brings a new clinical and behavioural profile, where the use of drugs is strongly linked with functional and survival oriented motives instead of recreational use (International Consortium on Drug Demand Reduction [ICDDR], 2024; UNODC, 2024).

The growing popularity of synthetic cannabinoids, in particular, the use of Colorado, has made the clinical

picture even more complicated as it presents considerable risks to the neuropsychiatric level. Such substances which are usually prepared using variable and unregulated chemical compositions are linked with acute adverse effects like psychosis, hallucinations, severe agitation, and cognitive impairment. The pharmacological effects of mixing stimulants such as methamphetamine with the opioids such as tramadol, however, can result in unforeseen and usually dangerous effects, such as seizures, cardiovascular dysfunctions, and chronic mental illnesses. The situation in Nigeria is characterized by relatively low overdose mortality rates as compared to the United States, but considerable amounts of morbidity, especially in the psychiatric complications and chronic dependence syndromes. This deviation highlights the significance of placing the issue of polysubstance use in the local socio-economic and healthcare context, since the Nigerian situation exemplifies an icon of drug use based on accessibility, cultural acculturation, and functional need, and with profound clinical management and population health policy consequences (U.S. Department of State, 2024; ICDDR, 2024).

III. CLINICAL PROFILES OF CO-USE

Neuropharmacological Interactions

Complex and usually adverse neuropharmacological effects are observed when synthetic opioids and psychostimulants are used together because of their contrary but interactive mechanisms of action in the central nervous system. The main action of opioids including fentanyl and tramadol is to stimulate the μ-opioid receptors, resulting in the suppression of neuronal excitability, the suppression of neuron neurotransmitter release, and the general central nervous system depression, especially of brainstem respiratory centres (Volkow and Blanco, 2021; Ciccarone, 2021). Conversely, stimulants like methamphetamine can stimulate synaptic concentrations of monoamines, in particular, dopamine and norepinephrine, with an increased level of release and reuptake inhibition leading to increased arousal, euphoria, and sympathetic stimulation (Cruickshank and Dyer, 2009; Darke et al., 2021). The combination of these substances is what causes a pharmacodynamic interaction whereby the depressant and stimulant effects do not cancel but rather lead to a dysregulated physiological condition with serious clinical consequences (Volkow & Blanco, 2021).

Among the most dangerous effects of this interaction, there is the fact that the effects of opioid-induced sedation are masked by stimulant effects and, as a result, the life-threatening respiratory depression is delayed, which raises the risk of overdose (Ciccarone, 2021; Friedman and Shover, 2023). Moreover, the concurrent processes of opposing autonomous pathways promote the fact that the cardiovascular load is increased and mathematically characterised by high heart rate, hypertension, and increased risk of arrhythmia, especially in the presence of strong stimulants like methamphetamine (Darke et al., 2021). In addition to these acute effects, continuous co-use is linked to the increased neurotoxicity, which is caused by oxidative stress, excitotoxicity, and dysregulation of dopaminergic pathways, which can lead to long-term cognitive defect and neuropsychiatric disorders (Cruickshank & Dyer, 2009; Volkow and Blanco, 2021). These mechanisms are overlapping and this means that polysubstance toxicity is complex and difficult to manage clinically.

The clinical characteristics of these neuropharmacological interactions depend on different circumstances, as they depend on differences in drug composition and the use dynamics. Co-use of stimulants and opioids is most often manifested in the United States of America, where fentanyl is the primary cause of overdose, which is mostly caused by severe respiratory depression that is hard to detect at the initial stages (Centers for Disease Control and Prevention [CDC], 2024; O'Donnell et al., 2023). Conversely, agitation, acute psychosis, and seizures are more common clinical presentations in Nigeria where combinations often contain methamphetamine and synthetic cannabinoids like the so-called Colorado, which are strong neuropsychiatric stimulant drugs and may interact with other stimulants in their occurrence (United Nations Office on Drugs and Crime [UNODC], 2024; ICDDR, 2024). This confounding underscores the need to put neuropharmacological outcomes into context in terms of local drug ecologies since similar co-use patterns can result in very different clinical pictures as a function of the drugs involved and the socio-environment involved.

Clinical Presentation in the United States

In the United States, clinical manifestations of the use of synthetic opioids and psychostimulants in co-use are characteristic of severe and multifaceted actions, which are the impacts of the concomitant depressants and stimulants that act on the central nervous system. Respiratory depression is one of the most noticeable ones, and it is mostly caused by the fact that fentanyl is a μ-opioid receptor agonist making the risk of fatal overdose significant even in low dosages (Centers for Disease Control and Prevention [CDC], 2024; O'Donnell et al., 2023).

Along with respiratory compromise, the cardiac arrhythmias are also a common manifestation in affected people due to the stimulatory properties of drugs like methamphetamine and cocaine on the cardiovascular system, which increase heart rate, blood pressure, and myocardial oxygen demand (Darke et al., 2021). These compounding effects result in complicated clinical conditions that were referred to as polysubstance toxicity, as co-exposure to various drugs gives unpredictable and often synergistically damaging results and makes it challenging to diagnose and manage emergencies (Friedman and Shover, 2023). In turn, such a combination of toxicological profiles has been closely linked with high mortality rates, especially in the instances of fentanyl, which has become the main cause of an overdose death in the United States over recent years (CDC, 2024; O'Donnell et al., 2023).

One of the most significant aspects that increase the severity of such clinical outcomes is the rising presence of fentanyl in the supply of the stimulant drugs, not always known by the users. This accidental overdose has greatly increased the risk of overdose, especially in people not tolerant to opioids and thus more susceptible to fentanyl respiratory depressant influences (Friedman & Shover, 2023; Ciccarone, 2021).

The masking effect of stimulants may also delay the identification of opioid toxicity because the alertness and potential temporary blocking of the sedative effects of opioids by stimulants may postpone early intervention and raise the risk of fatal outcomes (Ciccarone, 2021). This changing trend indicates the intricacy of the clinical manifestation of the ongoing drug epidemic in the U.S. and the urgency of the combined surveillance, harm reduction measures, and clinical guidelines adapted to polysubstance exposure.

Clinical Presentation in Akwa Ibom State (Nigeria)

The clinical manifestations of polysubstance use in Akwa Ibom State and other such localities in Nigeria define a trend of neuropsychiatric morbidity being high due to the use of opioids coupled with stimulants, sedatives and synthetic cannabinoids. Acute psychosis, typically accompanied by hallucinations, paranoia, and severe behavioural disorders, is one of the most common reported characteristics, and has been closely associated with the use of synthetic cannabinoids like the so-called Colorado (United Nations Office on Drugs and Crime [UNODC], 2024; International Consortium on Drug Demand Reduction [ICDDR], 2024). They are unpredictable in chemical composition and highly reactive to the receptor and when used together with stimulants such as methamphetamine, they can cause dramatic changes to perception and cognition.

Besides psychiatric symptoms, the symptoms of seizures and other neurological disorders are common among the users, which is indicative of the excitotoxic and neurotoxic outcomes of stimulant-cannabinoid interactions, along with the possibility to reduce the seizure threshold related to high-dose tramadol abuse (UNODC, 2024; World Health Organization [WHO], 2018).

The occurrence of dependence syndromes with functional tolerance is also another characteristic clinical presentation here whereby people continue with habitual occupational or social activities despite the chronic use of drugs. The perceived usefulness of substances, including tramadol and methamphetamine, to increase physical endurance, alertness, and productivity is a trend that is commonly driven by the economically active groups of the population (ICDDR, 2024; Adebiyi et al., 2023). However, with time, there is physiological adaptation to the repeated exposure, escalating dose and being prone to psychological and physical complications. This type of dependence, as opposed to the classical one in the high-income environment, is often intertwined with the socio-economic stress and is, therefore, more complex to quit and more prone to relapse without providing structural support systems (UNODC, 2024).

Although such clinical manifestation is severe, the available mortality rates in Nigeria are relatively lower compared to the ones observed in the United States, which can be partially attributed to the lower potency

of such commonly used opioids as tramadol in comparison to fentanyl (CDC, 2024; UNODC, 2024). The seemingly positive side of this, however, is heavily counterbalanced by a huge burden of morbidity, especially in terms of chronic mental illnesses, cognitive disability, and frequent neurological complications.

The high rate of untreated or insufficiently treated psychiatric diseases in the user population reflects the anomalies in mental health services delivery, as well as the necessity of complex care models based on the combination of addressing substance use and the neuropsychiatric consequences thereof (George and Udofia, 2026). In such a way, although the Nigerian clinical picture might not be as acute with fatal overdose, it is a serious and chronic public health issue with complicated, non-fatal but disabling outcomes (WHO, 2018; ICDDR, 2024).

Comparative Analysis of Synthetic Opioid–Psychostimulant Co-use

Dimension	United States	Nigeria (Akwa Ibom State)
Dominant opioid	Illicitly manufactured fentanyl dominates the opioid market and is implicated in the majority of overdose deaths; it is highly potent (50–100× morphine), significantly increasing fatality risk.	Tramadol is the most commonly misused opioid, with pharmaceutical opioids accounting for ~4.7% prevalence nationally (≈4.6 million users); early reports indicate emerging fentanyl presence but not yet dominant.
Stimulant profile	Methamphetamine and cocaine are widely used; stimulant involvement in opioid deaths has increased sharply, with co-use rising more than sixfold in recent years.	Methamphetamine use has surged dramatically from ~0.6% (2017) to ~38% among people who use drugs (2024), indicating rapid expansion of stimulant markets.
Additional substances	Benzodiazepines and emerging agents such as xylazine (“tranq”) are frequently detected in toxicology reports, contributing to complex overdose profiles.	Benzodiazepine use has increased (3.4% → 19%), while synthetic cannabinoids (“Colorado”) have emerged rapidly (0% → 27%), reflecting evolving poly-drug experimentation.
Polysubstance exposure mechanism	Often unintentional, driven by contamination of stimulant supplies with fentanyl; approximately 1 in 10 stimulant samples tested positive for fentanyl in recent studies.	Largely intentional, with users deliberately combining opioids, stimulants, and cannabinoids to achieve specific psychoactive or functional effects.
Clinical risk profile	High rates of fatal overdose due to respiratory depression; polysubstance toxicity significantly increases mortality, with fentanyl as the primary driver.	Lower overdose mortality but high morbidity, including psychosis, seizures, and long-term mental health complications associated with stimulant–cannabinoid mixtures.
Neuropsychiatric burden	Increasing incidence of mixed toxidromes (opioid + stimulant), but mortality often precedes long-term psychiatric complications.	High prevalence of neuropsychiatric symptoms, including agitation, hallucinations, and cognitive impairment due to synthetic cannabinoids and methamphetamine use.
Prevalence and scale	Overdose epidemic driven by synthetic opioids; polysubstance involvement is now the dominant pattern in drug-related deaths nationwide.	National drug use prevalence is ~14.4% (≈14.3 million users), nearly three times the global average, with over 3 million people experiencing drug use disorders.

Dimension	United States	Nigeria (Akwa Ibom State)
Regional burden (Akwa Ibom)	Not applicable (U.S. national crisis with state-level variation).	Estimated drug use prevalence in Akwa Ibom is ~12.5%, reflecting significant regional burden within the South-South zone.
Use pattern	Combination use is often supply-driven (contaminated drugs), with both recreational and dependent use patterns.	Poly-drug use is user-driven, culturally embedded, and often linked to occupational or social demands.
Primary drivers	Recreational use, dependence, and evolving illicit drug markets; structural factors include drug adulteration and trafficking networks.	Functional and productivity-based use (e.g., enhancing endurance, coping with economic stress), alongside peer influence and accessibility.
Market structure	Highly industrialised illicit market with synthetic drug manufacturing and widespread distribution networks.	Fragmented and informal drug markets with local production (methamphetamine) and trafficking (tramadol, Colorado).
Public health implication	Acute mortality crisis requiring harm reduction (naloxone, drug checking, supervised use services).	Chronic public health burden with emphasis on mental health care, regulation of pharmaceuticals, and community-based interventions.

In the comparative analysis, it can be seen that, despite the fact that both the United States and Nigeria are witnessing a turning point in favor of polysubstance use, the dynamics and their health outcomes are highly different. The US has been marked by excessive mortality epidemic caused by illicit fentanyl and unintended co-exposure to stimulants though drug contamination leading to massive deaths due to overdose and rapid toxicological crises. Conversely, Nigeria (especially, Akwa Ibom State) shows the tendency of willful poly-drug mixing with tramadol, methamphetamine, benzodiazepines, and synthetic cannabinoids, with socio-economic and functional reasons (productivity increase) behind it. This causes relatively decreased mortality but greatly increased neuropsychiatric morbidity, psychosis and neuro-complications.

IV. IMPLICATIONS FOR CLINICAL PRACTICE

United States

Polysubstance use, especially the co-use of fentanyl with stimulants, is highly prevalent in the United States, and thus a complex clinical approach is required. The rapid diffusion of harm reduction measures, including mass naloxone distribution, is essential in overturning opioid-related respiratory depression and avoid fatalities related to an overdose (Centers for Disease Control and Prevention [CDC], 2024).

The introduction of drug-checking services so that users can detect fentanyl in stimulants and other substances and minimize unintentional exposure is also a complementary intervention (Ciccarone, 2021). Also, combined treatment programs to deal with opioid addiction as well as the stimulant-related complications are becoming increasingly significant because conventional single-substance treatments are not enough to solve complex toxicological and behavioural patterns of polysubstance users (Friedman & Shover, 2023). Together, these measures will decrease deaths, aid in recovery and reduce the overall population health burden of the overdose crisis in the fourth wave.

Nigeria

Clinical practice in Nigeria and the Akwa Ibom State specifically need to address a trend of purposeful poly-drug use with a high neuropsychiatric morbidity. Mental health services need to be reinforced to address psychosis caused by drugs, seizures, and cognitive impairment that can be long-term following synthetic cannabinoids and stimulants use (International Consortium on Drug Demand Reduction [ICDDR], 2024; United Nations Office on Drugs and Crime [UNODC], 2024).

Pharmaceutical opioids, in particular tramadol, should have regulatory controls to limit unregulated access to this type of opioid and lower the number of complications associated with dependence. Public health education campaigns ought to be focused on functional or productivity induced drug use by increasing awareness on the dangers of poly-drug use with the encouragement of less harmful alternatives to deal with socio-economic stressors. Lastly, gaps in care, improved adherence, and long-term behaviour change in local socio-cultural settings can be addressed by developing culturally appropriate harm reduction models such as community-based support and peer-led interventions (Adebiyi et al., 2023).

V. CONCLUSION

The comparative analysis of synthetic opioid and psychostimulant co-use highlights both convergent and divergent patterns across the United States and Nigeria. While the United States experiences a high-mortality, fentanyl-driven crisis primarily characterized by unintentional polysubstance exposure and fatal overdoses, Nigeria particularly Akwa Ibom State—exhibits intentional poly-drug use with lower mortality but substantial neuropsychiatric morbidity. These differences underscore the critical influence of socio-cultural, economic, and market factors on clinical presentations and public health outcomes. Effective interventions, therefore, must be context-specific: emphasizing harm reduction and integrated polysubstance treatment in the U.S., and strengthening mental health services, regulatory frameworks, and culturally adapted prevention strategies in Nigeria.

Suggestions

Based on the comparative analysis of synthetic opioid and psychostimulant co-use in the United States and Nigeria, the following suggestions are proposed for clinical practice, public health policy, and research:

1. Enhanced Harm Reduction Measures
   - United States: Expand access to naloxone, supervised consumption sites, and drug-checking services to mitigate unintentional fentanyl exposure and reduce overdose mortality.
   - Nigeria: Develop culturally appropriate harm reduction models, including peer-led education and community-based interventions, to address functional poly-drug use while respecting local socio-cultural norms.

2. Strengthening Mental Health and Clinical Services
   - Nigeria should prioritise the expansion of mental health infrastructure to manage drug-induced psychosis, seizures, and other neuropsychiatric complications associated with synthetic cannabinoids and stimulant use
   - In both contexts, integrated treatment programs addressing polysubstance use and co-occurring psychiatric disorders should be implemented to improve outcomes.

3. Regulation and Monitoring of Pharmaceutical Opioids
   - In Nigeria, stricter regulation of tramadol and other opioids is essential to prevent misuse, reduce functional dependence, and limit the emergence of high-potency synthetic opioids such as fentanyl.
   - Continuous surveillance of drug supply chains in the U.S. can identify contamination with synthetic opioids, enabling timely public health interventions.

4. Public Health Education and Awareness Campaigns
   - Nigeria: Promote awareness about the risks of intentional poly-drug use for functional purposes and provide alternatives for productivity enhancement that do not compromise health.
   - U.S.: Target education programs towards populations at risk of unintentional polysubstance exposure, emphasizing recognition of early overdose signs and the importance of timely intervention.

5. Research and Data-Driven Policy Development
   - Encourage longitudinal studies in both countries to monitor evolving patterns of polysubstance use, clinical outcomes, and intervention effectiveness.
   - Comparative research on socio-cultural and economic drivers can inform context-specific strategies and global best practices for managing co-use crises.

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Conflict of Interest

The author declares that there are no conflicts of interest regarding the publication of this paper. The research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

REFERENCES

[1] Adebiyi, A. O., Atilola, O., & Ola, B. A. (2023). Substance use and mental health outcomes among young people in Nigeria: Emerging trends and public health implications. *African Journal of Drug and Alcohol Studies, 22*(1), 45–60.

[2] Centers for Disease Control and Prevention. (2024). Polysubstance overdose. U.S. Department of Health and Human Services. https://www.cdc.gov/overdose/prevention/polysubstance-use.html

[3] Ciccarone, D. (2021). The rise of illicit fentanyls, stimulants, and the fourth wave of the opioid overdose crisis. Current Opinion in Psychiatry, 34(4), 344–350. https://doi.org/10.1097/YCO.0000000000000717

[4] Cruickshank, C. C., & Dyer, K. R. (2009). A review of the clinical pharmacology of methamphetamine. Addiction, 104(7), 1085–1099. https://doi.org/10.1111/j.1360-0443.2009.02564.x

[5] Darke, S., Kaye, S., & Duflou, J. (2021). Systemic disease among cases of fatal methamphetamine toxicity. Addiction, 116(5), 1234–1242. https://doi.org/10.1111/add.15264

[6] Friedman, J., & Shover, C. L. (2023). Charting the fourth wave of the overdose crisis: Geographic and demographic trends in polysubstance fentanyl overdose deaths in the United States. Addiction, 118(6), 1156–1166. https://doi.org/10.1111/add.16043

[7] International Consortium on Drug Demand Reduction (ICDDR). (2024). Rapid assessment of knowledge, attitudes and practices relating to synthetic drugs in Nigeria. https://icuddr.org

[8] George, I., & Udofia, N. (2026). Emotional reactivity and perceived social support as psychological correlates of internet addiction among Nigerian university students. Journal of Clinical Psychology and Neurology, 4(1), 1–8.

[9] O'Donnell, J. K., Gladden, R. M., & Seth, P. (2023). Trends in deaths involving heroin and synthetic opioids excluding methadone, and law enforcement drug product reports, by census region—United States. Morbidity and Mortality Weekly Report, 72(3), 1–8. https://doi.org/10.15585/mmwr.mm7203a1

[10] United Nations Office on Drugs and Crime. (2024). World drug report 2024. United Nations. https://www.unodc.org

[11] U.S. Department of State. (2024). International narcotics control strategy report (INCSR), Volume I: Drug and chemical control. https://www.state.gov

[12] Volkow, N. D., & Blanco, C. (2021). The changing opioid crisis: Development, challenges and opportunities. Molecular Psychiatry, 26(1), 218–233. https://doi.org/10.1038/s41380-020-0661-4

[13] World Health Organization. (2018). Critical review report: Tramadol. WHO Expert Committee on Drug Dependence. https://www.who.int