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## Continued Increases in Overdose Deaths Related to Synthetic Opioids:

### Implications for Clinical Practice

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**The current overdose epidemic** in the US that began in the late 1990s continues unabated. Since 2013, deaths involving synthetic opioids surged substantially, largely due to the rapid proliferation of illicitly manufactured fentanyl and fentanyl analogs (eg, acetylfentanyl, carfentanyl).<sup>1,2</sup> More recently, overdose deaths involving stimulants, such as methamphetamine and cocaine, have increased with and without opioid co-involvement.<sup>3,4</sup> As illicitly manufactured fentanyl became more ubiquitous, drug overdose death rates increased in all age groups, among both sexes, across most races and ethnicities, within all urbanization levels, and in the majority of US states.<sup>1</sup>

Importantly, the increases in overdose deaths are occurring against a backdrop of overall stable or declining rates of illicit drug use other than cannabis, underscoring that the illicit drug supply is a key driver of the current overdose crisis.<sup>5</sup> Illicitly manufactured fentanyl, which is easier and less costly to make, distribute, and sell, is observed in a steadily increasing percentage of overdose deaths and has displaced heroin in the illicit drug market in some communities.<sup>5</sup> The increasing availability, geographic dispersion, mixing or co-use of illicitly manufactured fentanyl with other drugs, and presence of illicitly manufactured fentanyl in counterfeit prescription pills resembling commonly misused prescription drugs underscores the urgency to evolve the approach to prevention.<sup>6</sup>

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A report released by the Centers for Disease Control and Prevention (CDC) on February 11, 2021, highlights the scope of the problem.<sup>7</sup> In 2019, 70 630 drug overdose deaths occurred in the US (21.6 per 100 000 persons), representing a 4.3% increase over the 2018 rate.<sup>7</sup> Among all these deaths, approximately 71% involved opioids and 52% specifically involved synthetic opioids excluding methadone.<sup>7</sup> No state had a significant decrease in synthetic opioid death rate between 2018 and 2019, and the West census region experienced the largest relative (68%) and absolute (1.9 per 100 000) increase.<sup>7</sup> Nine states (Connecticut, Delaware, Massachusetts, Maryland, Maine, New Hampshire, New Jersey, Ohio, and Vermont) reported that more than 70% of all their overdose deaths involved synthetic opioids in 2019.<sup>7</sup>

From 2018 to 2019, the death rate involving any psychostimulant with abuse potential (eg, methamphetamine), increased 28%, from 3.9 to 5.0 per 100 000, and 24 states had statistically significant increases in rates.<sup>7</sup> Between 2013 and 2019, the overdose death rates for synthetic opioid co-involvement increased for prescription opioids (from 0.3 to 1.8 per 100 000), heroin (from 0.1 to 2.7 per 100 000), cocaine (from 0.1 to 3.2 per 100 000), and psychostimulants with abuse potential (from 0.1 to 1.8 per 100 000).<sup>7</sup> The increase in synthetic opioid-involved deaths in the western states (eg, Colorado, California, Washington) and in psychostimulant-involved deaths in the northeastern states (eg, Maine, New Jersey, New York) indicates new geographic spread of these substances.<sup>7</sup>

The risk of overdose is elevated with any use of illicitly manufactured fentanyl, given its potency, lethality, and the variability in the illicit supply, but risk is particularly high among persons who are opioid naive or whose tolerance to opioids has decreased following periods of abstinence.<sup>5</sup> The coronavirus disease 2019 pandemic has exacerbated the overdose crisis as individuals struggled to maintain access to essential harm reduction, treatment, and recovery support services, initiated or increased substance use to cope with the stressors and social isolation created, and likely used illicit drugs while alone more frequently.<sup>6</sup> These changing dynamics demand innovative clinical, health system, and community solutions.

Clinicians can increase screening for substance use disorder using validated instruments, initiate counseling for patients after a positive urine drug screen or drug-related clinical visit, and expand overdose prevention education among their patients. They also could prescribe naloxone to persons who use drugs, including those who are not knowingly using opioids, their friends, and others likely to witness, experience, or respond to an overdose.<sup>6</sup> Health systems and community partners could expand locations where these services are offered and co-locate services whenever possible, including via primary care settings, retail pharmacies, support groups, outpatient substance use disorder treatment programs, syringe services programs, and mobile outreach.<sup>6</sup> This diversification of prevention strategies is especially important for rural areas.<sup>6</sup>

Treatment with US Food and Drug Administration-approved medications methadone, buprenorphine, and extended-release naltrexone remain standard care, but gaps persist, with only an estimated 20% of persons receiving medications for opioid use disorder (MOUD).<sup>8</sup> Additional efforts should be made to train clinicians about the evidence supporting MOUD treatment and to reduce stigma, encourage clinicians to become Drug Addiction Treatment

Act of 2000 waived, and prescribe MOUD up to their patient limit.<sup>8</sup> Further evaluation of regulatory barriers that impede wider utilization of MOUD are urgently needed.<sup>8</sup>

Opportunities to link individuals to MOUD and other risk reduction services should be pursued across health systems and in community settings, particularly for persons at highest risk, especially historically underserved persons such as those experiencing homelessness, those transitioning from institutional settings such as the criminal justice system, and those with a previous nonfatal overdose.<sup>8</sup> Linkage to care is an intentional strategy that works by connecting persons with a substance use disorder who are not currently accessing care with intensive support to initiate and sustain engagement with a treatment provider. A holistic approach would involve complementary services such as treating co-occurring mental disorders and assisting with access to housing, transportation, and employment.<sup>8</sup> Expanded use of peer recovery coaches and patient navigators should fit into broader efforts to adapt the cascade of care that has proven effective at retaining persons in HIV treatment.<sup>8</sup> Tracking linkage to and retention in care is also important for evaluating the effectiveness of programmatic efforts.

The role of clinicians and health systems fits into broader, coordinated, and time-sensitive response activities that connect clinical, public health, public safety, and other community partners to share data, monitor trends, and better respond to the unique issues facing their communities. Promising models already exist, such as the Public Health and Safety Team (PHAST).<sup>9</sup> PHAST partners collaborate to increase their understanding of the local overdose crisis, optimize jurisdictional capacity, and establish shared accountability for continuous improvement.<sup>9</sup> Other efforts capitalize on unique opportunities to link persons to treatment from public safety venues, such as prearrest diversion programs, fire or police stations, or drug courts.<sup>6</sup>

These partnerships are essential to address the US overdose epidemic and are supported in part by the CDC's Overdose Data to Action (OD2A) program. The OD2A program focuses on using more timely, comprehensive, localized, integrated, and actionable data to catalyze prevention activities in 66 funded state, territorial, and local jurisdictions across the US.<sup>10</sup> Additionally, through the Overdose Response Strategy, the CDC collaborates with 21 High Intensity Drug Trafficking Areas to coordinate data sharing and develop and support the implementation of evidence-based programs and collaborations between public health and public safety.

The actions outlined above should be taken in concert with longer-term primary prevention strategies that avert problematic substance use before it begins, including by addressing adverse childhood experiences and attending to structural and systemic factors that create and sustain health inequities.<sup>6</sup> Interdiction is also important, but experiences in other countries suggest that once illicitly manufactured fentanyl becomes entrenched, law enforcement action alone may not sufficiently curtail illicitly manufactured fentanyl availability.<sup>5</sup> Clinicians and health systems should be at the forefront of further reimagining how to address the crisis. The moment demands broader availability and access to services, increased and sustained coordination across sectors, and more intentional and integrated care and support for long-term recovery. Earnestly pursuing these interventions could enable a

more effective response to the current increases in deaths related to illicitly manufactured fentanyl while also building the capacity to address other emerging drug threats.

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