International Journal of Drug Policy 136 (2025) 104702

Contents lists available at ScienceDirect

International Journal of Drug Policy

journal homepage: www.elsevier.com/locate/drugpo

Stimulant-involved overdose deaths: Constructing dynamic hypotheses

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ARTICLE INFO

Keywords:
Stimulant overdose deaths
Polysubstance use
Dynamic hypothesis
Systems perspective
Community-based system dynamics

ABSTRACT

The overdose epidemic in the United States is evolving, with a rise in stimulant (cocaine and/or methamphetamine)-only and opioid and stimulant-involved overdose deaths for reasons that remain unclear. We conducted interviews and group model building workshops in Massachusetts and South Dakota. Building on these data and extant research, we identified six dynamic hypotheses, explaining changes in stimulant-involved overdose trends, visualized using causal loop diagrams. For stimulant- and opioid-involved overdose deaths, three dynamic hypotheses emerged: (1) accidental exposure to fentanyl from stimulants; (2) primary stimulant users increasingly using opioids, often with resignation; (3) primary opioid (especially fentanyl) users increasingly using stimulants to balance the sedating effect of fentanyl. For stimulant-only overdose deaths, three additional dynamic hypotheses emerged: (1) disbelief that death could occur from stimulants alone, and doubt in testing capabilities to detect fentanyl; (2) the stimulant supply has changed, leading to higher unpredictability and thus higher overdose risk; and (3) long-term stimulant use contributing to deteriorating health and increasing overdose risk. These hypotheses likely each explain a portion of the recent trends in stimulant-involved overdoses. However, confusion and uncertainty around the drug supply emerged as a central theme, underscoring the chaotic and unpredictable nature of the stimulant market. Our findings indicate the need for research to develop targeted public health interventions, including analyzing the extent of the effect of contamination on overdoses, reducing confusion about the stimulant supply, and examining historical stimulant use trends.

Introduction

The United States is experiencing an overdose epidemic that claimed 1.26 million lives from 1999 to 2024 (Ahmad et al., 2024; National Center for Health Statistics, 2021, 2022). Historically, the epidemic has progressed through waves driven by different substances, starting with prescription opioids, followed by heroin, and then (illicitly manufactured) fentanyl and other synthetic opioids (Ciccarone, 2019). More recently, overdose deaths have increasingly involved stimulants such as cocaine and methamphetamine (Hébert & Hill, 2024). Between 2010 and 2021, stimulant-only and stimulant-involved (stimulant-only as well as stimulants plus at least one other substance) overdose deaths increased 4- and 9-fold, respectively (Centers for Disease Control and Prevention, 2024).

The reasons behind these shifts in overdose trends and the evolving nature of the problem are not fully understood. Explanations for the increase in stimulant-involved overdose deaths most often cite the involvement of fentanyl (Cristiano, 2022; Friedman & Shover, 2023). However, the different processes driving purposeful versus unintentional use of fentanyl by people whose primary drugs are cocaine or methamphetamine (Bazazi et al., 2024; Fleming et al., 2020) need clear articulation to identify effective interventions. More broadly, an explication of why unintentional fentanyl use might be occurring in the first place is needed.

Crucially, fentanyl involvement cannot explain stimulant-*only* overdose deaths. From 2010–2021, fully 38% of psychostimulant (primarily methamphetamine) deaths and 21% of cocaine overdose deaths occurred without the involvement of benzodiazepines, alcohol, or *any* other substances (Centers for Disease Control and Prevention, 2024). There has not been any exploration in the literature of what could be causing these stimulant-only overdose deaths and, in particular, their recent rise. Without a clearer understanding, it is difficult to develop effective policies to prevent these deaths.

Often, questions about how and why phenomena occur are answered

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https://doi.org/10.1016/j.drugpo.2025.104702

Available online 26 January 2025

with qualitative data that describes processes. We have expanded upon this form of traditional data collection using the tools of system dynamics, a powerful method that examines processes as part of feedback loops that drive the evolution of public health problems (Jalali et al., 2020; Sterman, 2006). Feedback loops capture the complex interplay of variables within the system and provide deeper insights into systemic problems by identifying how the structure of the system contributes to its behavior. In other words, system dynamics emphasizes the importance of internal feedback mechanisms over external factors, enriching our understanding by illustrating how internal dynamics drive outcomes. System dynamics has been applied in substance use research (Herman et al., 2024; Thompson et al., 2024), among other complex health problems (Darabi & Hosseinichimeh, 2020).

A critical first step of any system dynamics assessment is to develop dynamic hypotheses, that is, propositions about how the different elements of a system could interact to create recent historical trends, hence the "dynamic" part of the hypothesis (Sterman, 2000). From a collection of interviews and group model building workshops, as well as supporting input from the literature, we developed dynamic hypotheses involving stimulant-involved overdose deaths. This report focuses on the critical task of (dynamic) hypothesis formulation as depicted in a series of causal loop diagrams – visual diagrams depicting interconnected feedback loops. Specification of dynamic hypotheses is an essential precondition to future research that can empirically examine the underlying drivers of stimulant-only and stimulant-involved overdose deaths and how these have changed over time.

Materials and methods

We used interviews, group model building workshops, and extant literature to develop dynamic hypotheses to explain increasing stimulant-involved overdose deaths as part of a larger CDC-funded project, OVERCOME (OVERdoses involving COcaine and MEthamphetamine). The goal of OVERCOME was to explore the interacting risk and protective factors that drive fatal stimulant-involved overdoses, including the disproportionately rising mortality rates among Black, Hispanic, and Indigenous communities (Friedman & Shover, 2023; Han et al., 2021; Kariisa et al., 2021; Townsend et al., 2022). To reach these populations, our research was conducted in South Dakota, a state that has disproportionately high methamphetamine use within its significant Indigenous population (Coughlin et al., 2021), and Massachusetts, which has a diverse population of people, including Black, Latino, and White, who use varying combinations of fentanyl, cocaine, and methamphetamine (Townsend et al., 2022). We also used peer-reviewed literature, results from national household surveys, and reports from the federal government to support and generalize our identified dynamic hypotheses. This multifaceted approach ensures our modeling considers both participant input and existing knowledge, a best practice that also mitigates potential literature gaps.

Study setting

Massachusetts and South Dakota have substantially different fatal stimulant-involved overdose trends, as shown in Fig. 1. Massachusetts had a similar rate of cocaine-only overdoses to the national average until 2020 when it began increasing more rapidly. South Dakota's methamphetamine-only fatal overdose rate was similar to or slightly higher than the national rate, but since 2020, it has been rising faster.

There are also racial disparities in both states when compared to Whites. In 2020, Indigenous people in South Dakota were 5.6 times more likely to die from a stimulant-involved overdose and 5.5 times more likely to die from a stimulant-only overdose. In Massachusetts,

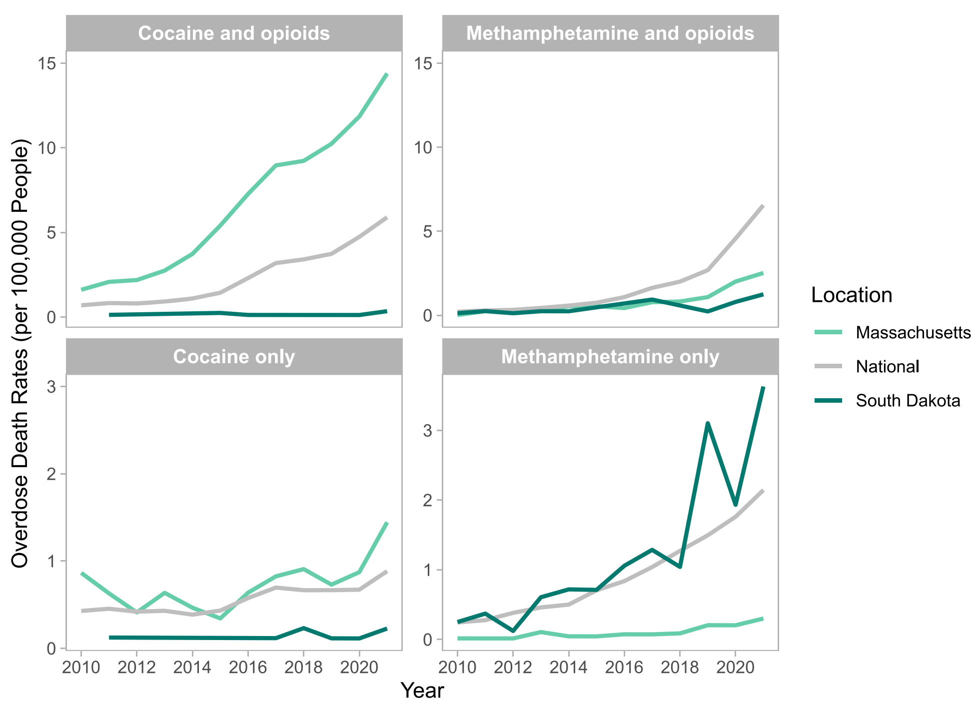

Fig. 1. Stimulant-involved overdose deaths in South Dakota and Massachusetts compared to the United States.
The figure is based on Mortality Multiple Cause Files from the CDC NCHS's National Vital Statistics System (Centers for Disease Control and Prevention, 2024). To define stimulant-only deaths, we included any deaths with an underlying cause of drug overdose that included the ICD-10 multiple cause-of-death codes T43.6 (psychostimulant toxicity) and/or T40.5 (cocaine toxicity), and that did not also include ICD-10 codes T36-T50.8 and T51.0 (alcohol toxicity) (Ahmad et al., 2024). We define opioid and stimulant-involved deaths as deaths with an underlying cause of drug overdose identified with at least one of the opioid-related ICD-10 multiple-cause-of-death codes present, including heroin (T40.1), prescription (Rx) opioids (T40.0, T40.2, T40.3), fentanyl and other synthetic opioids other than methadone (T40.4), or unspecified opioids (T40.6), and at least one psychostimulant or cocaine ICD-10 code present as well. The CDC categorizes methamphetamine and similar substances such as amphetamines, MDMA, and cathinone as psychostimulants, yet almost all deaths within this category are attributed to methamphetamine; hence, in this paper, we refer to them as methamphetamine overdose deaths.

Black people and Hispanic people were 1.4 and 1.2 times more likely to experience a stimulant-involved overdose death, and 1.8 and 1.2 times more likely to experience a stimulant-only overdose death (Centers for Disease Control and Prevention, 2024).

Qualitative data collection

Between 2022 and 2024, we engaged 44 individuals across Massachusetts and South Dakota through a combination of our professional substance use research networks, harm reduction programs, community partnerships, and snowball sampling. We employed a multifaceted approach to qualitative data collection that involved key informant interviews, individual qualitative interviews, and group model building workshops to enhance the richness and applicability of our findings and prioritize the safety and comfort of participants.

Differences in our team's relationships on the ground required a flexible approach. For instance, the lead researcher in South Dakota has multi-year relationships with key stakeholder groups, while in Massachusetts the team is still building these relationships. In South Dakota, these established connections, along with support from local non-profit community organizations, allowed us to organize and conduct group model building workshops. In contrast, in Massachusetts, each interview had to be individually coordinated through a third-party contact, creating logistical challenges. Thus, in South Dakota, we conducted workshops and interviews, while in Massachusetts we conducted interviews only.

In both states, the intersection of stimulant-involved overdoses and housing instability arose early in the project. Thus, we adapted our recruitment strategy to interview people experiencing housing instability and homelessness and those who provided services to this population.

Recruitment

We recruited people who use or have used cocaine or methamphetamine via flyers, one-on-one outreach in care-providing collaborating organizations (e.g., shelters, treatment groups), and referrals by healthcare providers. However, because unauthorized ingestion of a controlled drug or substance is a felony in South Dakota (South Dakota Legislature, n.d.), we only recruited people who were no longer using drugs for the GMB workshops there, while interviews were reserved for people who reported current stimulant use. This helped ensure that people would be able to discuss their current drug use privately without risk of legal repercussions.

Inclusion criteria for people who use stimulants included being age 18 years and older, self-reported methamphetamine or cocaine use, ideally in the past month, and residence in the given state. These individuals were compensated $50. The study's protocols and activities received approvals from the Massachusetts General Hospital and Avera Research Institute Institutional Review Boards. Verbal consent was obtained from all participants after they were informed of the study's purpose and their rights. Following consent, meetings were recorded, transcribed, and supplemented with notes.

We collected data from individuals and groups; interviews were conducted with key informants and research participants. Key informants were not formal research participants, so these interviews were not recorded; we recorded field notes during these interviews. They were engaged early in the process to help solidify the scope of the problem, but their early insights proved informative for developing dynamic hypotheses. Research participants were engaged later in the process; they formally consented to participation, and their interviews were recorded and transcribed. In total, we engaged 44 individuals through interviews with 13 key informants, qualitative interviews with 16 research participants, and two group model-building workshops with 15 research participants. Table 1 describes the activities, their objectives, and participant and setting details.

Qualitative interviews

Three researchers (hereafter, research team) trained in system dynamics and qualitative research conducted the interviews in private settings or online. The goal was to understand participants' perceptions of the factors affecting and affected by stimulant-involved overdoses. Thus, the interviews began with the question, *"What are the direct effects and consequences of stimulant-involved overdoses?"* The question is worded to identify factors that may exacerbate stimulant-involved overdoses by creating feedback loops. We used questions to encourage participants to reflect on patterns they observe within their communities, such as: *Do other people you know [experience or observe] the same?"*; and *"What about other people who [engage in specific behaviors or face certain circumstances]?"* However, participants were free to share personal experiences with drug use if they wished to, and most did.

Table 1
Summary of data collection activities.

Activity	Objective	Participant details and backgrounds	Setting details
Key informant interviews	To achieve a better understanding of recent trends in stimulant use to inform recruitment for semi-structured qualitative interviews.	• Researcher: 6 (1 in SD, 5 in MA) Focus on clinical addiction research, program evaluation, social work, public health policymaking, and epidemiology. • Public Sector: 2 (2 in SD) Staff from public medicolegal and behavioral health sectors. • Harm Reduction: 5 (5 in MA) Harm reduction coordinators and program directors, needle exchange and drug checking program staff, and overdose follow-up outreach professionals.	• Unstructured interviews • 1–1.5 h • 10 interviews in MA • 3 interviews in SD
Qualitative Interviews	To understand participants' perception of the factors affecting and affected by stimulant-involved overdoses.	• 13 people who use stimulants ○ 10 in SD, 3 in MA ○ 70% racial minorities (7 Indigenous individuals in SD, 2 Black individuals in MA) ○ 46% women or female-identifying (6 in SD, 1 in MA) • 3 providers (only in MA)	• Semi-structured interviews • 0.5–2.5 h • 6 interviews in MA • 10 interviews in SD
Group Model Building Workshops	To facilitate a collaborative setting for model development among participants with diverse perspectives.	• 15 participants in SD ○ 47% racial minorities (7 Indigenous individuals) ○ 73% women or female-identifying ○ Participants included people in recovery, addiction counselors, emergency services personnel, program managers for detoxification services or Indigenous healing organizations, community advocates for Indigenous health, homeless shelter coordinators, and family members of people who use drugs. Some people had multiple identities.	• 2 workshops in SD • 3 h each • Conducted by the research team with support from six individuals trained in group model building

Thus, we used their insights to query future participants by asking, for instance: *"We have heard other people mention this—what do you think?"* Additionally, we asked providers who engaged with cohorts of patients to think in terms of groups or populations they interacted with, encouraging insights from their outreach or clinical work with these communities. Finally, to explore changes over time, we incorporated questions such as, *"Is that changing?", "When did you first start seeing an increase in [*specific drug*] use?"* and *"Do you think there has been an increase or decrease?"*

Group model building workshops in South Dakota

For the OVERCOME project in South Dakota, we conducted group model building workshops, a structured event designed to facilitate a collaborative setting for model development among participants with diverse perspectives (Hovmand, 2014; Vennix, 1999). Group model building can help to overcome the limitations of individuals' mental models – their internal representations formed based on personal experiences, beliefs, and knowledge (Sterman, 2000) – by providing participants the opportunity to share and even change their perspectives (Hovmand et al., 2012). The workshops included several activities with the goal of creating a shared mental model of methamphetamine overdoses. We adapted scripts from established group model building guidelines (Hovmand et al., 2015). For a detailed agenda with scripts, please see Table S1 and Table S2.

Participant engagement

For all interactions with and language regarding people who use drugs, we conducted training for the research team and individuals involved in conducting workshops that emphasized the use of non-stigmatizing language and nonjudgemental reactions to people's experiences. For the workshops, we sought to overrepresent individuals with personal drug use experience and explicitly recognized lived experiences as a form of expertise, affirming participants' critical role in shaping the outcomes and direction of the workshops. To manage power dynamics, we did not conduct workshops in which people had pre-existing relationships involving a power imbalance (supervisor/supervisee, provider/client from the same organization). During the workshops, inclusive facilitation strategies were used, such as round-robin approaches to equalize participation opportunities.

For recruitment, interviews, and workshops involving Indigenous communities, the South Dakota team made efforts to adhere to culturally appropriate considerations (Deutsch et al., 2022). This included accommodating time for smudging, adjusting the role of timekeeper to signal the facilitator quietly rather than announcing time aloud to avoid interruption, keeping the agenda flexible to allow for delays in one activity and shortening the next rather than imposing time pressure, and assigning the convener role to an Indigenous team member to better reflect perspectives relevant to the participants' cultures. Our team collaborated with local community organizations and included members with lived substance use experience and Indigenous representation to ensure the work was both culturally sensitive and aligned with the needs of the communities involved.

Dynamic hypotheses and model building

The model building process is inherently iterative. Accordingly, our thematic analysis followed the constant comparative method from classic grounded theory (Glaser, 1965), which involves analyzing data as it is collected. This method enables researchers to refine their questions and focus areas based on emerging findings and results in hypothesis generation.

The first author compared each piece of data (i.e., segments of transcripts, meeting notes, and group model building artifacts) to identify patterns, similarities, and differences in participants' understanding of stimulant-involved overdose deaths. For instance, we examined descriptions involving stimulants and opioids, stimulants-only, or other combinations of substances and identified the characteristics of the individuals affected, noting both similarities and differences across contexts. Additionally, as the study aimed to understand changing trends, the data were compared across mentions of both past and present contexts to capture shifts over time.

In the initial thematic analysis, the first author began by assigning labels to pieces of data, which were subsequently grouped into categories based on shared characteristics. As new data were analyzed, the categories were continuously refined. Then, the identified themes were reviewed by two co-authors with expertise in substance use, who were also part of the interview team. Their involvement ensured alternative interpretations were considered, additional themes were not overlooked, and related themes were appropriately grouped into hypotheses based on shared similarities. Through this collaborative process, six overarching themes were finalized.

Following the initial thematic analysis, focused coding and data clustering were conducted. To support and manage the coding process, we used QDA Miner Lite. The first author systematically reviewed transcript quotes associated with each theme, grouping data into refined categories aligned with the emerging hypotheses (e.g., as shown in Table S3). The grounded theory approach allowed for the creation of new codes or the revision of existing ones. For example, an initial label such as "toxic street supply" was further specified after comparing data across contexts. This refinement reflected differences in how street supplies were considered "toxic," such as whether substances were contaminated, adulterated, or fillers. Through this process of constant comparison, the grouped data were used to identify key variables, feedback loops, stocks, and flows, which informed the development of six separate dynamic hypotheses.

The dynamic hypotheses were subsequently translated into causal loop diagrams to visualize the relationships between the identified factors. The causal loop diagrams visually depict interacting, reinforcing, and balancing feedback loops. Reinforcing loops amplify changes in one direction, leading to vicious and virtuous cycles, while balancing loops counteract these cycles (Sterman, 2000). The diagrams we developed feature stocks, representing people using different types of drugs, as well as flows, representing people initiating or quitting use or dying from a stimulant-involved overdose.

These visualizations were iteratively reviewed and refined by the same two substance use experts to ensure alignment with the data. For example, participants might mention that changes in the drug supply resulted in drugs not having similar effects as before. However, this observation also aligns with one of the diagnostic criteria for substance use disorder, where the same dose does not produce the same effect due to tolerance (American Psychiatric Association & American Psychiatric Association, 2013). Therefore, it was necessary to compare these reflections with the literature to determine whether these participant-reported changes reflected historical trends and broader experiences. To ensure accurate differentiation and contextualization of the data and to strengthen the thematic framework, a literature review was conducted. Using the themes and related terms that emerged from our data analysis as keywords (e.g., "fentanyl contamination," "potency of methamphetamine"), we searched PubMed and Google Scholar. Publications from the U.S. whose timing was relevant to the theme of interest (e.g., participants' discussion of the changing methamphetamine supply required reading research from earlier years than discussions of fentanyl) were reviewed to identify quantitative data, corroborate or expand on identified variables and connections, or provide alternative perspectives. This process allowed us to situate participant insights within the broader context of existing knowledge and evidence. Lastly, the final causal loop diagrams were reviewed by a co-author with expertise in system dynamics to ensure the clarity and validity of the representations.

This comprehensive and iterative process grounded the findings in both empirical data and the broader literature, enhancing the robustness and relevance of the study's conclusions. This process is represented in

Figure S1.

Separate causal loop diagrams for each dynamic hypothesis allowed us to represent multiple dynamic hypotheses transparently, following best practices in system dynamics that encourage consideration of different perspectives (Sterman, 2000). The study initially approached the issue with a broad focus on stimulant-involved overdoses. However, through research and iterative analysis, smaller constructs emerged as distinct dynamic hypotheses, each offering unique – though not necessarily correct – explanations of the overarching problem and highlighting areas for further investigation.

Results

We describe the dynamic hypotheses in two groups: stimulant and opioid-involved overdose deaths and stimulant-only overdose deaths.

Stimulant and opioid-involved overdose deaths

We identified three dynamic hypotheses regarding stimulant and opioid-involved overdose deaths. In all the following figures, stocks (shown as a rectangular box) and flows (shown with double lined arrow) related to stimulants are colored pink, those related to opioids are blue, and elements relevant to both are colored purple. The black arrows that connect variables show their relationship, and the arrows appear grey if they were introduced in earlier figures. A collection of arrows that form a circular relationship is called a feedback loop, and both black and grey arrows can appear as part of described loops.

Accidental exposure to fentanyl from stimulants

In Fig. 2, the stock represents people who primarily use stimulants such as cocaine and methamphetamine yet do not regularly use opioids; this can include but is not limited to "weekend warriors," people whose drug use is primarily at parties (O'Donnell et al., 2019). The purple flow represents the overdose deaths occurring among them because of accidental contamination from fentanyl.

The feedback loops in Fig. 2 demonstrate how, overall, the policy response to increasing overdose deaths could inadvertently lead to more overdose deaths. As overdose deaths have increased, supply-focused strategies have intensified, such as the scheduling of illicitly manufactured fentanyl followed by blanket scheduling of its analogues (U.S. Department of Justice, 2018, 2023). These strategies aim to reduce the availability of drugs on the street, which, if successful, can temporarily reduce overdose deaths (balancing loop, B1). However, in the long run, unintended consequences, represented by reinforcing loops (R1 and R2), have contributed to increased overdose risk.

Loop R1 shows how supply-side strategies create economic incentives to constantly adapt the supply chain, including the shift from heroin to fentanyl and its analogues (Mars et al., 2019), as well as changes in the sourcing of precursor chemicals and synthesis from China to Mexico (Greenwood & Fashola, 2021). This constant shifting of the drug supply not only affected the opioid street supply but also could have produced the side effect of fentanyl contamination of stimulants (loop R2) (Wagner et al., 2023). Participants reported that even those who sold cocaine or methamphetamine are rarely aware of the presence or extent of fentanyl in their supply as it is passed down through various hands (Loop R3). One individual in South Dakota described how they believed that contamination could escalate as products pass through different levels of distribution: *"This guy here, he [dealer] is doing that [lacing methamphetamine with fentanyl], and then this guy here [another dealer] can buy it off of him and lace it with fentanyl more, and all of a sudden, all you do is smoking fentanyl. So that is how people overdose… Mix it up, and they don't know that there's all this fentanyl."*

As a result, participants reported themselves or others experiencing accidental overdose, which they attributed to fentanyl in drugs they believed to be only stimulants. Some of these individuals might be ideal targets for harm reduction techniques that would help them identify fentanyl in their drugs. Indeed, in Massachusetts, where fentanyl test strips are regularly distributed, providers described a "subset of folks" who would avoid using stimulants if they knew their drugs were contaminated. On the other hand, providers believed there was a larger group of people who prefer to use stimulants and are likely to encounter fentanyl but are not likely to avoid use due to fentanyl-contaminated substances.

Primary stimulant users increasingly using opioids, often with resignation

In Fig. 3, the pink stock represents the same group as in Fig. 2, while the purple stock illustrates individuals who use both stimulants and opioids. The flow between the stocks indicates individuals who are primary stimulant users increasing their opioid (especially fentanyl) use. The flow on the right indicates overdose deaths where both stimulants and opioids are present.

Fig. 3 shows another way that the supply-side policy response to overdose deaths ultimately increases overdoses by normalizing the risk of fentanyl exposure among primary stimulant users. People who use

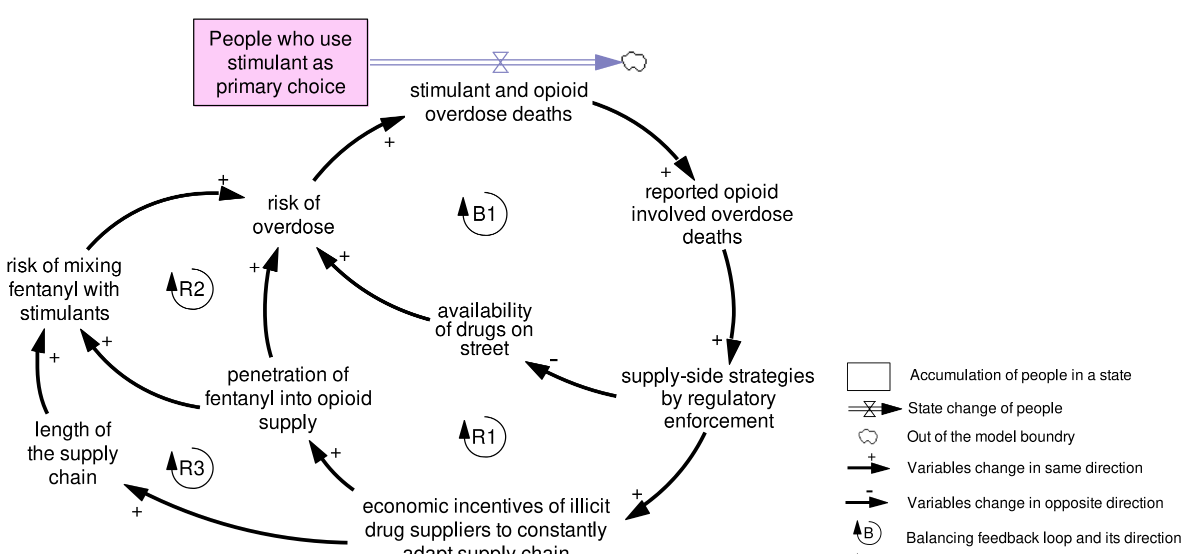

Fig. 2. Dynamics hypothesis regarding accidental exposure to fentanyl contamination from stimulants and increase in stimulant and opioid overdose deaths.

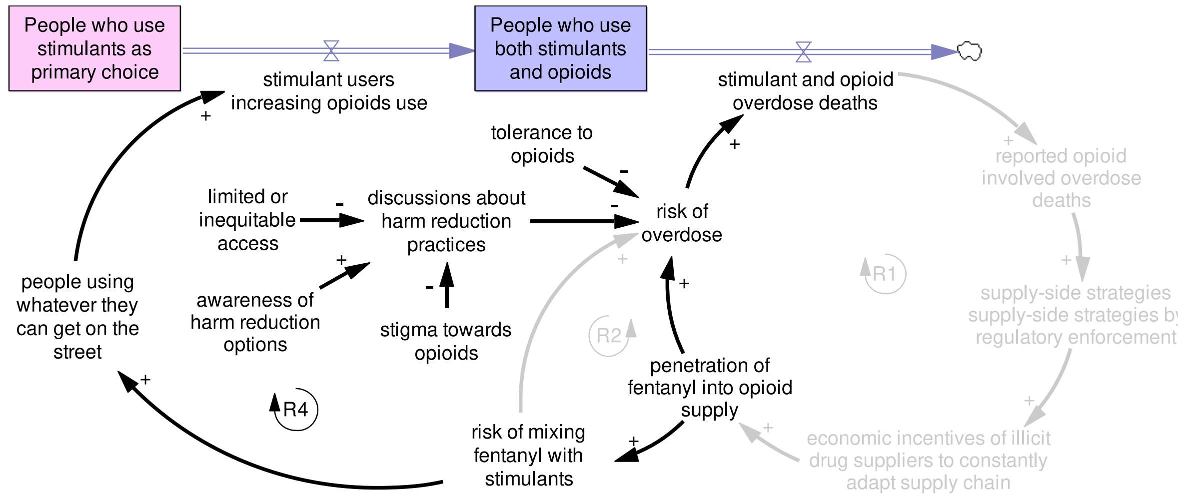

Fig. 3. Dynamic hypothesis regarding primary stimulant users increasing opioid use, often with resignation, and resulting in increased overdose death risk due to fentanyl presence in the supply.

stimulants continue using whatever drugs are available, knowing that their supply might be fentanyl-contaminated. One participant in South Dakota shared their experience: *"I had a friend that overdosed on fentanyl because that's what they put in it [methamphetamine]. But I don't know what I'm taking. I'm just starting to just get whatever."* The disregard for contamination reflects the desperation users feel, explained by a participant in Massachusetts: *"It's the difference about, well, do I care? Do I want [crack cocaine]? Do I care whether I live or die?... The next time you do that, it might just do you in, whether it was pure good or bad or whatever."*

This "normalization of risk" loop, R4, includes and expands beyond loop R1, which can lead to an increased number of people using both stimulants and opioids. A respondent described this shift: *"Back then, I was fiending for crack. I couldn't find it, whatever, whatever. So, I told this guy to get whatever [he] had. I saw someone shoot it [fentanyl] up. Then I tried it two times. I overdosed both times... I didn't ever try shooting up again... I've been sniffing [fentanyl], and that's how I started."*

Loops R1 and R4 interact with other factors noted by participants that are not part of feedback loops in the diagram but are ongoing factors driven by structural racism and inadequate investment in poor and rural communities. These include (as noted by participants) mutual stigma between people who primarily use opioids versus stimulants, low awareness of harm reduction options, limited or inequitable access to harm reduction, and low tolerance to opioids. These factors could prove particularly important in explaining the disproportionate rise in overdose deaths involving opioids and cocaine among Black people in the U.S. (Kariisa et al., 2021). First, harm reduction programs may be limited in certain areas. In Massachusetts (Nolen et al., 2022) and elsewhere in the U.S. (Khan et al., 2023), Black communities have inequitable access to naloxone. Second, Massachusetts providers raised concerns that primary stimulant users may be less aware of harm reduction practices because these efforts have historically focused on opioid users or people who inject. Third, providers reported stigma towards opioids within the Black community, who they said were more open about their crack cocaine use. If providers are unable to develop a trustworthy relationship with patients to overcome this stigma, harm reduction access is further limited in Black communities. Finally, there has always been a large group of cocaine users who use opioids (Malow et al., 1992) to "take the edge off" or provide "landing gear" for their stimulant high. Yet, to the extent that they are not regular users of opioids and are now exposed to fentanyl, the stakes have now been raised on their use.

However, fentanyl contamination is generally lower in crack cocaine compared to powdered cocaine (Wagner et al., 2023), and the Black community often uses the crack form (Liu et al., 2021). Thus, the disproportionate rise in overdose deaths involving opioids and cocaine among the Black community could potentially be attributed to increased overdose risk arising from fentanyl contamination of opioids that they occasionally use, in combination with lower access to harm reduction practices, rather than solely due to accidental contamination.

Primary opioid (especially fentanyl) users increasingly using stimulants to balance the sedating effect of fentanyl

In Fig. 4, the new blue stock represents individuals who primarily use opioids. The flow between these two stocks represents individuals who primarily use opioids but are increasingly using stimulants, especially methamphetamine (Strickland et al., 2019).

Fig. 4 introduces four new loops, two of which (R5 and R6) expand upon R1 to increase fentanyl- and stimulant-involved overdoses further via an overall increase in drug use frequency, especially injection frequency. As shown in R5, the penetration of fentanyl into the opioid supply has led to an increase in fentanyl and stimulant use frequency as users seek to counter fentanyl's sedating effects (which triggers a balancing loop, B2, that operates on a scale of hours compared to other loops which operate in weeks or even years). With more use episodes per day – participants reported a doubling or tripling in injection frequency – the greater the risk of an overdose occurring on any given day.

Loops R5 and R6 show how this increased frequency of use also threatens the stability of users; the need to inject as often as every two hours makes it difficult to work, retain housing, maintain relationships, or attend treatment. A provider described how these challenges affect adherence to treatment for opioid use disorder: *"It's harder for them [people who use opioids] if you're using meth. Very hard for you to stay in a clinic and be going to your methadone point. Also, very hard to come to Suboxone appointments and get on Suboxone."* Additionally, the barriers to housing stability were emphasized: *"More so than most other drugs, [it is] very hard for people who are using stimulants to adhere to our existing housing systems and requirements."* This lowered stability, including the homelessness experienced by several of the participants, is associated with a higher risk of overdose (Baggett et al., 2013, 2015).

Loop B2 is a short-term fix that ultimately fails, as stimulant use "eats up" the fentanyl, leading to increased frequency of use and more sedation, so more stimulant use (loop R7). This pattern exacerbates the overdose risks depicted in loops R5 and R6.

Stimulant-only overdose deaths

Here, we present three dynamic hypotheses regarding stimulant-only overdose deaths.

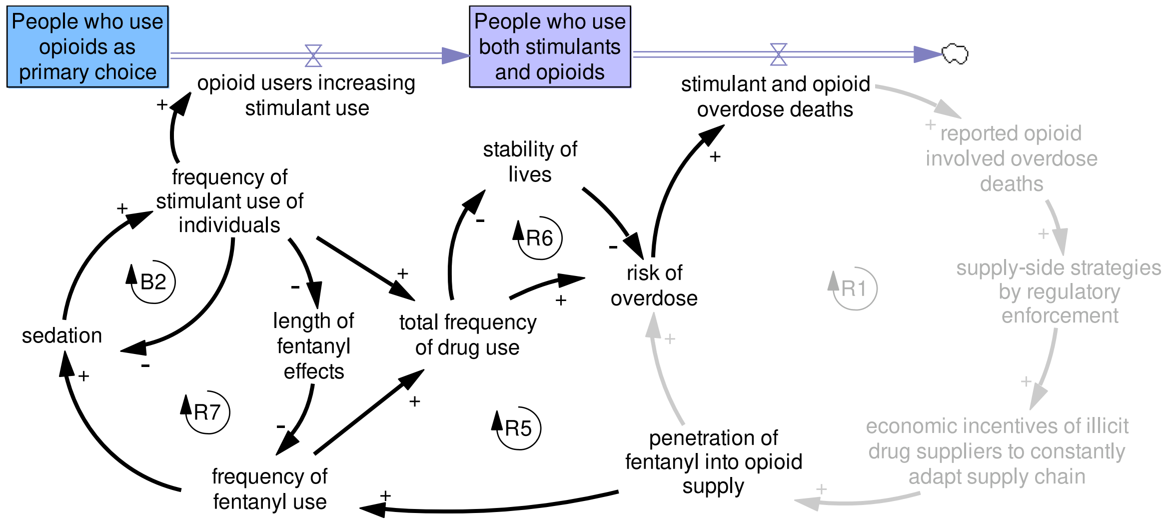

Fig. 4. Dynamics hypothesis regarding primary opioid (especially fentanyl) users increasingly using stimulants to balance the sedating effect of fentanyl and the increase in overdose death risk.

Disbelief that death could occur from stimulants alone and a subsequent doubt in testing capabilities to detect fentanyl

Figure 5′s stock includes people who primarily use stimulants, identical to Fig. 2. The outflow represents stimulant and opioid overdose deaths with an additional variable that shows some of these were reported as stimulant-only overdose deaths.

When asked about stimulant-only (often, methamphetamine) overdose deaths, most participants who used stimulants expressed skepticism about the possibility of such deaths: *"I've seen a person inject two one-milligram syringes in both arms at one time… of pure methamphetamine… and didn't overdose…I don't believe that you can overdose on pure meth. But mix it with fentanyl, it is a deadly killer."*

The emerging hypothesis, as reflected in participants' mental models, was that the deaths reported as stimulant-only were due to undetected fentanyl contamination (Fig. 5). Thus, this hypothesis represents a belief that there is a misattribution of deaths that should be part of one of the three hypotheses involving opioids and stimulants discussed above.

Some participants drew on their experience with urinalysis to explain their mental models, albeit with differing logic. This was especially the case in South Dakota, where methamphetamine-only deaths are a much higher proportion of overdose deaths than in Massachusetts. There, providers reported that urinalysis among living individuals almost always showed a mix of substances, so they would expect the same pattern post-mortem. Thus, for them, urinalyses results were the standard by which to compare autopsy data. However, people using methamphetamine reported inaccurate urinalysis results, such as failing to detect their recent use of substances besides methamphetamine, suggesting that toxicology tests should likewise be doubted: *"Her [daughter's] toxicology report only showed meth from all of the blood test and urine. Meth was the only thing in the system. And she smoked a blue pill [participant believed it contained fentanyl] that morning… But they can't test*

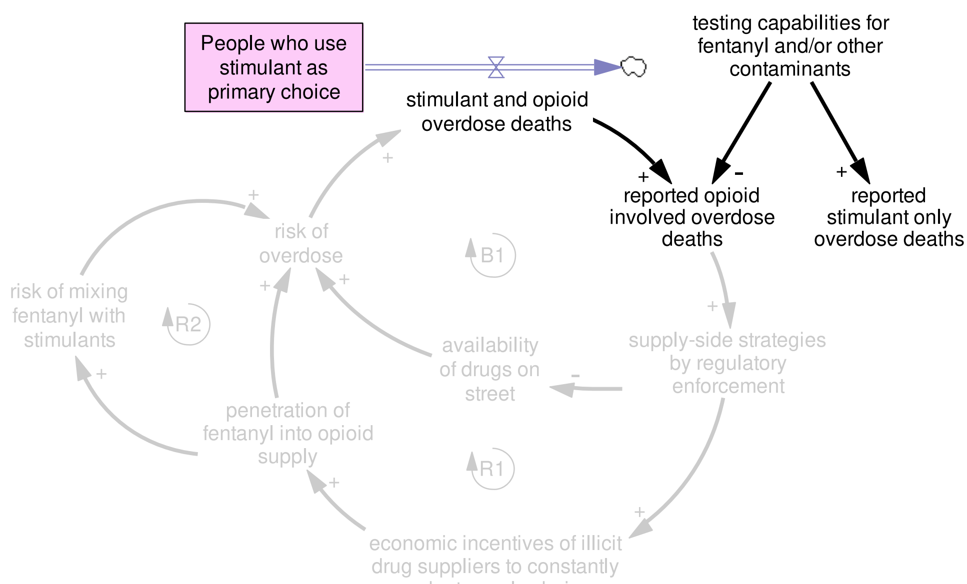

Fig. 5. Dynamic hypothesis regarding disbelief that death could occur from stimulants alone and a subsequent doubt in testing capabilities to detect fentanyl.

it [fentanyl]." Participants noted instances when authorities in South Dakota, such as police officers, also undermined participants' confidence in drug test results, with police saying they could not test the fentanyl because *"it's just not proper fentanyl."*

The stimulant supply has changed, leading to higher unpredictability and thus higher risk of overdose

The new flows in Fig. 6 represent two possible outcomes: stimulant-only overdose deaths or reducing stimulant use. Note that all loops present in this diagram are balancing loops that reduce the number of stimulant users, one of which does so via people quitting (B3) and three of which do so via more deaths (B4-B6).

Similar to loop B1 in Fig. 2, participants in South Dakota discussed the effects of supply-side strategies employed to reduce the availability of methamphetamine (loop B3): *"shipment[s] got interrupted"* or *"somebody got busted"* and as a result, that particular dealer's supply *"went dry."* The more this happens, the more economic incentives exist to constantly adapt, including switching dealers and thus distribution networks, resulting in variations in the impurities present due to different synthesis methods (Onoka et al., 2020) and different contaminants, reportedly ranging from baby formula and laxatives to vitamins and baking soda. Participants reported various and unpredictable forms of methamphetamine, including a syrupy liquid that was difficult to shoot up and crystals that too easily turned black and burned. These variable impurities increase the unpredictability of the supply and thus create difficulty gauging use, especially how much to use or what route of administration, which participants believed increases stimulant overdose risk (loop B4). These impurities and the inherent unpredictability of the drug supply are not new, but they are intersecting with larger changes in the methamphetamine supply overall.

Specifically, the supply-side strategy of arresting methamphetamine dealers is simply a continuation of decades of such strategies, with one notable policy in the last twenty years still reverberating today. The Combat Methamphetamine Epidemic Act of 2005 led to reductions in the availability of over-the-counter pseudoephedrine (USA PATRIOT Improvement and Reauthorization Act of 2005, 2006), which was used to synthesize methamphetamine in domestic laboratories, which were also aggressively targeted (Drug Enforcement Administration, 2024). The reduction in methamphetamine created an unmet demand and, thus, a vacuum to fill. As early as 2009 (Toske & McKibben, 2022), and driven by the same economic incentives that drove the rise of fentanyl, domestic production was replaced with imported methamphetamine from Mexico produced using the P2P (phenyl-2-propanone) synthesis method (US Department of Justice Drug Enforcement Association, 2024). P2P is also reportedly more potent (US Department of Justice Drug Enforcement Association, 2021), though notably, no participants spoke about a consistently more potent supply with a "better" or "stronger" high. Rather, as with the B5 loop, they reported unpredictable potency, making it difficult to gauge use:

> "Some people take big doses where [it would] wipe me out if I took [those]… And then they can run into a batch that, it's not weak… and then that'll wipe them out too. Everything you get from everybody ain't the same. You might get some here that are stronger than other different places, from different people."

Another change that arose with the shift to imported methamphetamine is an increase in the length of the supply chain, which starts with "super labs" in Mexico, requires conversion laboratories in the U.S., and finally, a distribution network (US Department of Justice Drug Enforcement Association, 2024) compared to domestic "shake and bake" methamphetamine that users themselves produced. This lengthening supply chain further increases the unpredictability of the supply, difficulty gauging use, and thus stimulant overdose risk (loop B6).

Stimulant users are using long-term, thus contributing to and/or exacerbating underlying health conditions and increasing the risk of fatal overdoses

The dynamic hypothesis in Fig. 7 is that overdose deaths could be a delayed effect of historical trends in stimulant use, wherein people who began using decades ago are still using and are now experiencing deteriorating health, which increases their risk of overdose. This creates three balancing loops that reduce the number of people using stimulants

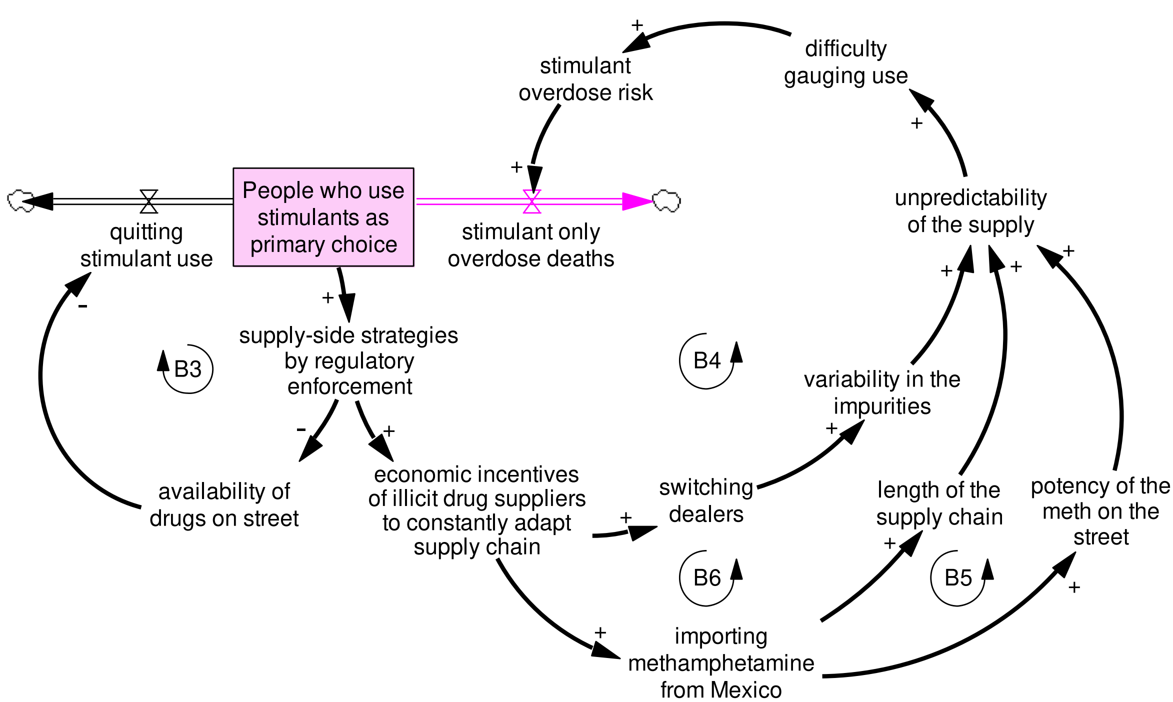

Fig. 6. Dynamics hypothesis regarding changes in the stimulant (primarily methamphetamine) supply leading to higher unpredictability and thus higher risk of overdose.

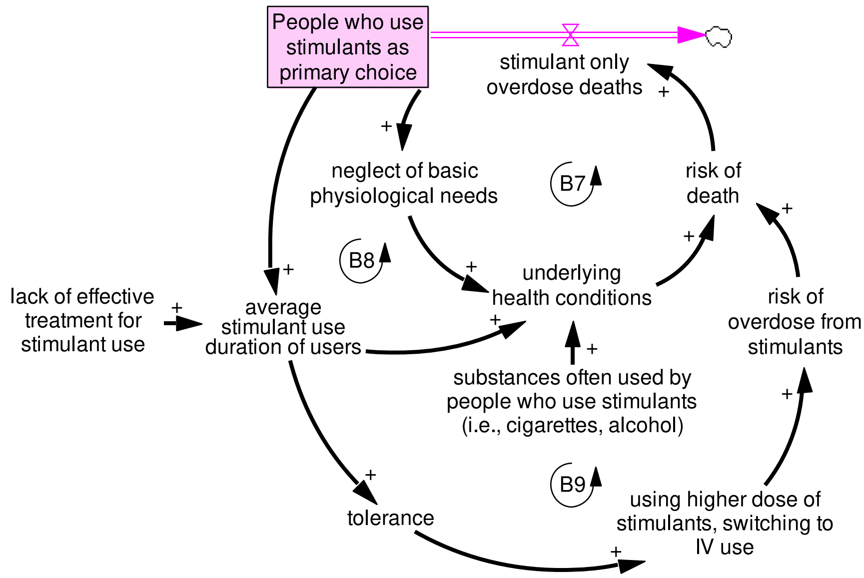

Fig. 7. Dynamic hypothesis on long-term stimulant use contributing to and/or exacerbating underlying health conditions.

via overdose deaths.

Loop B7 shows that as more people use stimulants, more people neglect their basic physiological needs, such as sleeping, eating, and hydrating during periods of active use (a "run"). When combined with underlying conditions such as diabetes, high blood pressure, and chronic obstructive pulmonary disease (examples mentioned by participants), this neglect could be contributing to stimulant-only overdose deaths: *"Well, if you don't eat, you won't feel it… So if you ain't got no nutrition, then it's going to start eating on your insides…then pretty soon there's no more you."*

Loop B8 shows other ways that underlying health conditions might contribute to risk of overdose as people age and continue to use stimulants. Their average duration of use continues to rise, increasing their risk of developing underlying conditions with the major concern being cardiovascular disease (Darke et al., 2017) and cardiovascular events even in young adults (Cheng et al., 2016; Darke et al., 2019), which participants recognized: *"And sometimes they can get a stone dose and then it'll exceed their heartbeat and take them out."* Moreover, people who use stimulants often use other substances, such as cigarettes (Weinberger & Sofuoglu, 2009) and alcohol (Higgins et al., 1995; Sharpe et al., 2022), thus increasing the likelihood of premature mortality regardless of cause (Hurt et al., 1996).

Loop B9 depicts how, in the long term, tolerance increases, leading people to take higher doses of stimulants and to switch to injection use. While injection use does not necessarily increase stimulant overdose risk, the higher doses and intensifying addiction can increase the number of people who succumb to stimulant-only overdoses when occurring simultaneously with deterioration of the body (loop B9). In both states, participants noted that many people who are using stimulants now have been using for years, if not decades, with risks that they were all too aware of: *"It [methamphetamine] does break down the system – can't keep hammering our heart." "I'm surprised it [crack cocaine] already didn't kill me."*

Finally, providers highlighted that due to the lack of effective treatment for stimulants, patients have even more difficulty stopping use compared to those with opioid use disorder, for whom effective medications are available. The result is continued use that might extend longer than it would if there were effective treatments.

Discussion

To address the rise in stimulant-involved and stimulant-only overdose fatalities with targeted public health interventions, it is essential to understand the underlying factors driving these trends. We used systems science tools, such as causal loop diagrams, to capture the complexity of the overdose crisis, influenced by numerous interrelated factors, feedback loops, and delays. We identified six dynamic hypotheses: three involving both stimulants and opioids and three for stimulant-only overdoses. While these hypotheses do not conflict in an oppositional sense, they represent different perspectives and potential contributing factors within this complex problem space. However, they are not necessarily equally strong or comprehensive explanations. Presenting them separately allowed us to capture these variations more explicitly, but these hypotheses should not be seen as interchangeable or collectively forming a 'complete' picture. Instead, they offer a multidimensional view that highlights gaps in understanding and points to areas where further empirical investigation is needed to validate or refine these hypotheses.

Our analysis revealed three key insights: First, many of the feedback loops described by participants ultimately depended on the presence of fentanyl in the drug supply, whether or not fentanyl is truly a contributing factor to increased stimulant-involved overdoses; second, and relatedly, the great deal of unpredictability across all drug supplies creates confusion among people as they try to make sense of what they are using; and third, delayed effects of historical trends in use could just now be making themselves apparent, vis a vis deteriorating health among aging users.

Regarding our first insight, four out of six dynamic hypotheses were driven by the very first reinforcing feedback loop introduced, R1, which formed when supply-side strategies were put in place as fentanyl overdoses began to increase. Illicitly manufactured fentanyl and its analogs were placed into Schedule I (U.S. Department of Justice, 2018), creating a cat-and-mouse game as suppliers continually changed their precursor chemicals, synthesis processes, and synthesis and distribution locations (shifting from China to Mexico) to stay ahead of the law (O'Connor, 2018). While these regulatory adaptations have slowed down over the years (Greenwood & Fashola, 2021) the U.S. has recently increased its efforts to pressure China to limit precursor chemicals (U.S. Department of Justice, 2023).

However, only one of these dynamic hypotheses has strong empirical backing: the increased risks that people who intentionally use both stimulants and opioids increasingly face (see Fig. 4). Because heroin is being supplanted by fentanyl in the U.S., anyone who uses street “dope” has a high chance of encountering fentanyl (Lim et al., 2024). People’s frequency of use, and thus of overdose, increases as stimulants and opioids chase each other in a constant “fixes that fail” balancing loop. The other three dynamic hypotheses that blame fentanyl for stimulant-involved deaths highlight unknown contamination, resignation toward contamination, or toxicology-missed contamination.

Thus far the contamination hypothesis has existed largely in anecdotal reports or isolated clusters (Bazazi et al., 2024; Daniulaityte et al., 2023). Contamination could explain a disproportionate share of deaths if the drugs that kill people are considerably more potent than the rest of the drug supply, but contamination cannot necessarily explain most or even many of the deaths. Emerging results from drug-checking research teams suggest that most – as much as 91% – of cocaine and methamphetamine samples are not contaminated with fentanyl or any other unexpected substance (Wagner et al., 2023). Thus, the mental model described by participants of widespread contamination of drugs with fentanyl – and echoed elsewhere – does not necessarily reflect reality. When asked about the disconnect between drug-checking results and reports of contamination, harm reduction providers noted that many people simply are unwilling – for good reasons – to be completely truthful with healthcare providers about their use. Stigma and criminalization prevent honesty. Regardless of the evidence for fentanyl contamination, the existence of a contamination narrative can normalize risk-taking, resulting in complacency and a reduced sense of urgency about harm reduction practices. Individuals with severe stimulant use disorders may accept a contaminated supply as their only option and not adjust their use behaviors to account for opioid (or any other unwanted substance) risks.

There is nuance to participants’ assumption that stimulant-only overdose deaths cannot happen. Deaths in which methamphetamine is the only drug present undoubtedly occur, even if some death investigations miss fentanyl. However, it is also the case that chronic cardiovascular disease could lead to death involving methamphetamine or cocaine, but not via acute toxicity, which is how ‘overdose’ is typically understood (Riley et al., 2022). Regarding the presence or absence of other drugs in methamphetamine-involved deaths, there is no county-level assessment of the nation’s toxicology capabilities to determine how often such deaths might be erroneously categorized. Although there have been historical limitations to toxicology comprehensiveness, standards across the nation have improved over time (Hedegaard et al., 2021). Hence, one would expect fentanyl detection to have improved and thus fentanyl-involved deaths would not be increasingly classified as stimulant-only overdoses. More research is needed to understand the extent to which death investigations are failing to detect fentanyl and misclassifying these deaths as stimulant-only.

Regarding stimulant-involved “overdose” deaths (which might in fact not be due to acute toxicity, as noted above), to the extent that data indicates thousands of stimulant-only deaths and a dramatic rise in some places like South Dakota, it is especially important to alert stimulant users to this possibility. However, the messaging might need to reference their long-term cardiovascular health rather than overdose. However, the widespread narrative of fentanyl contamination can be counterproductive if it leads people to misattribute their stimulant-related symptoms to a fentanyl overdose. Participants described their overdose experiences in various ways, such as feeling nauseous, vomiting, hallucinations, headaches, or having seizures. These symptoms, which they attributed to the presence of contaminants like fentanyl, are more likely to be typical symptoms of stimulant overdose (i.e., “overamping”) (Mansoor et al., 2022) or stimulant withdrawal (Li & Shoptaw, 2023). Thus, there is also a great need to more clearly define negative stimulant-only experiences, including those that can be fatal, and explain the symptoms to the public. Currently, only a few studies report symptoms to possibly look for that are distinct from opioid overdoses, including increased heart rate and body temperature, and/or cardiac arrest (Mansoor et al., 2022).

This brings us to our second takeaway: the great deal of unpredictability across all drug supplies creates confusion among people as they try to make sense of what they are using. Methamphetamine has reportedly become more potent since the early 2010s (Toske & McKibben, 2022), but analysis from seizure samples demonstrates a plateauing in potency in recent years, from 86% in 2015 to around 97% since 2017 (US Department of Justice Drug Enforcement Association, 2018, 2021). Yet fatal methamphetamine-only overdoses have continued to rise exponentially since 2017 (Han et al., 2021); it is unclear whether the increase in potency would be enough to explain this increase in deaths. Additionally, participants spoke more frequently about the unpredictability of impurities and potency rather than potency on its own. Their lack of knowledge about what was in their drugs was apparent; they were often unable to name specific substances they believed might be contaminating their supply—citing anything from fentanyl to horse tranquilizer, laxatives, baby formula, antifreeze, "ISO," or simply “fake meth,” but also reported they did not know what fentanyl was or how to identify it. Having more accurate information about the contents of the drugs people plan to use, beyond just the presence of fentanyl, would provide users with real data rather than hearsay.

Our third and final insight suggests that the current surge in stimulant-only overdose deaths may be a delayed consequence of historical stimulant use trends. Deteriorating health among aging users could be contributing to overdose deaths independent of supply-side changes. The older individuals who started using in the first wave of the stimulant epidemic, who are more likely to have age-related underlying health conditions, are at greater risk of dying with stimulants in their system. In-depth forensic research that examines multiple causes of death among stimulant-only overdose victims, as well as any known history of cardiovascular or other high-risk diseases, could greatly enlighten researchers and the public about the underlying causes of the rapid increase in fatal stimulants, especially methamphetamine, overdoses. Research on autopsy reports for overdose deaths classified as methamphetamine-only showed the presence of cardiovascular abnormalities, but due to variations in the involvement of other substances (Darke et al., 2018), further forensic analysis of true methamphetamine-only deaths is needed to rule out polysubstance interactions as the cause.

This study has several limitations. First, the sample size and geographic scope were confined to Massachusetts and South Dakota, potentially limiting the generalizability of the findings. Nonetheless, we believe the study’s overarching highlight on widespread confusion and the critical need for empirical research into underlying explanations has broader applicability. Second, the majority of the participants we engaged were either unstably housed or providers serving these populations. However, these populations are best thought of as the extreme end of a continuum of vulnerability to fluctuations in the illicit drug market (James & Maguire, 2024; Parkes et al., 2021) rather than a qualitatively different group of people, hence housed people might experience similar yet less intense forms of the loops described. A third limitation is that the models are constrained by bounded rationality (Meadows, 2008); i.e., people can only report on what they know, and none alone has all the relevant details. Even with multiple interviews and group model building workshops, it is impossible to surface all potential dynamic hypotheses. Additionally, even efforts to minimize power dynamics in group model building workshops can limit information sharing. A fourth limitation of our data collection approach was the use of group model building workshops only in South Dakota, while Massachusetts relied solely on individual and key informant interviews. This difference in methods may have affected the depth of insights obtained for Massachusetts, particularly in terms of participant engagement and group-derived perspectives. Finally, a limitation involves our decision not to conduct follow-up validation of causal loop diagrams with individual participants. Due to logistical challenges and the instability of some participants' circumstances, consistent re-contact was not feasible. Instead, we relied on expert validation by two co-authors, subject matter experts trained in substance use and system dynamics modeling. We also attempted to address these limitations by incorporating extant literature. While this approach ensured consistency, it has limited opportunities for additional participant feedback on the final diagrams.

Conclusions

Our study highlights the complexity and evolving nature of the overdose epidemic, emphasizing the need for targeted public health interventions. By employing causal loop diagrams, we identified factors contributing to both stimulant-involved and stimulant-only overdose deaths. The insights underscore the importance of addressing fentanyl's role, the unpredictability of drug supplies, and the health deterioration among aging users. Future research should empirically test our dynamic hypotheses to determine the most significant contributors to overdose trends and guide resource allocation toward the most impactful interventions.

Ethics approval

The authors declare that they have obtained ethics approval from an appropriately constituted ethics committee/institutional review board where the research entailed animal or human participation.

The study's protocols and activities received approval (protocol no. 2021P003355) from the Mass General Hospital and Avera Institutional Review Boards (IRB). Verbal consent was obtained from all participants after they were informed of the study's purpose and their rights.

Funding sources

This study was supported in part by grant number R01CE003358 from the U.S. Centers for Disease Control and Prevention. The funder did not have any role in the conduct of the research and preparation of the manuscript.

CRediT authorship contribution statement

Zeynep Hasgul: Writing – original draft, Visualization, Software, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Arielle R. Deutsch:** Writing – review & editing, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Mohammad S. Jalali:** Writing – review & editing, Supervision, Methodology, Funding acquisition. **Erin J. Stringfellow:** Writing – review & editing, Supervision, Methodology, Investigation, Formal analysis, Data curation, Conceptualization, Funding acquisition.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

We sincerely thank the participants for their time and trust in sharing their personal experiences with us. We also appreciate the community organizations for their assistance in providing space for the interviews. We thank Paul Forney, Catalina Puentes, Diane Smith, and the Avera Research Institute OVERCOME team for their efforts in participant engagement and recruitment and for organizing interview and group model-building sessions. We also would like to thank Hannah Lee for her assistance in quantitative data analysis and Jonathan Huang for his support in preparing transcripts. We also appreciate the feedback on earlier versions of this report provided by participants at the International System Dynamics Conference.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.drugpo.2025.104702.

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