Comment to the United States Sentencing Commission
Public Hearing on Methamphetamine
Submitted by Gavin Bart, MD PhD FACP DFASAM
Professor of Medicine
Hennepin Healthcare and University of Minnesota School of Medicine
August 5th, 2025

The opioid crisis and its approximately 800,000 overdose deaths since 2015 have understandably garnered public attention.[1] During this time, the significant rise in methamphetamine use and consequences have gone relatively unaddressed. Since 2015, the rate of methamphetamine-associated overdose deaths has increased nearly 8-fold.[1] There are parallel increases in methamphetamine-associated hospitalizations, emergency department encounters, and non-fatal overdoses.[2-4] Roughly 2.4 million people 12 and older in the United States used methamphetamine in the previous year, with two thirds of them meeting diagnostic criteria for a methamphetamine use disorder.[5]

In recent reports, overdose deaths due to combinations of opioids and stimulants such as methamphetamine have surpassed overdoses due to opioids alone.[6] While a number of methamphetamine overdose deaths are due to the unintentional co-ingestion of fentanyl (secondary to contamination or misidentification of the drug one intended to use), the intentional use of both methamphetamine and opioids has substantially increased. Some refer to this increase as the fourth wave of the opioid crisis.[7] Compared to those who use only opioids or only methamphetamine, those who use both drugs have higher rates of hospitalizations, emergency department visits, unstable housing, reliance on public assistance, and incarceration.[8] While the latter issues are more reflective of how our society chooses to respond to people who use drugs, the aforementioned medical consequences of methamphetamine such as psychosis, cardiomyopathy, lung disease, infections related to injection drug use and sexual encounters, trauma, and premature labor are resource intensive, expensive, and contribute to an unhealthy populace. In short, methamphetamine is a major public health issue.

Part of the rise in methamphetamine use is its increased accessibility and decreased cost due to the diversification of transnational criminal organization drug portfolios to include industrial level methamphetamine production. High quality precursor chemicals and refined synthetic techniques result in highly pure crystalline methamphetamine, with smaller scale production of less pure powder or tablet formulations. According to the most recent publicly available DEA Methamphetamine Profiling Program Report (CY 2022), purities average 96.6%. The MPP testing covers drug seizure throughout the United States and border regions and average seizure size is approximately 27 kilograms with the minimum seizure size sent for testing 6 grams.[9] Very recent data from street level testing by a harm reduction organization in Los Angeles reports the average purity of consumer level methamphetamine is 58%.[10] While it is unclear if these results generalize to other areas of the country, they likely reflect samples well below the MPP minimum 6 grams and thus more what a street level purchase may look like.

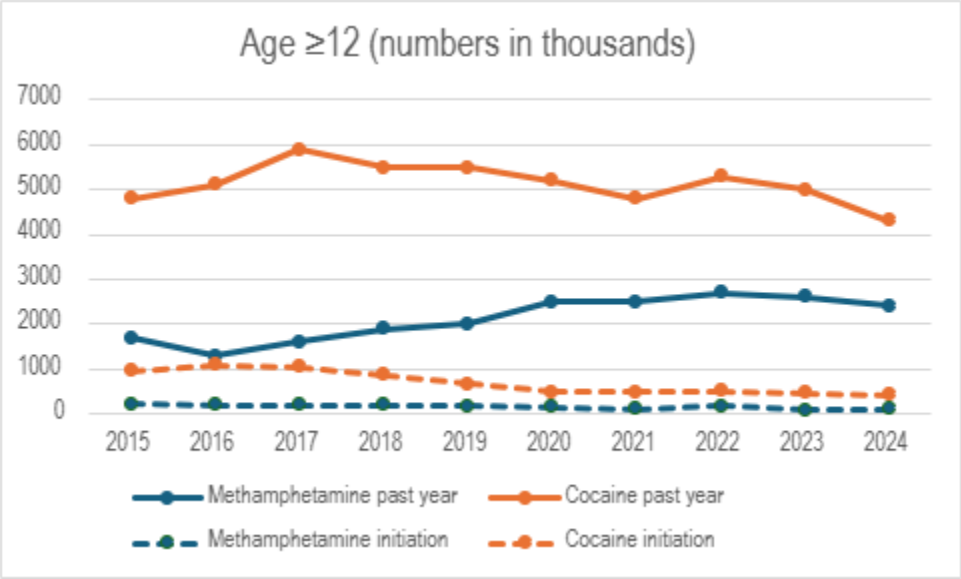
Traditionally, methamphetamine is a racemic mixture meaning the product comprises equal amounts of two different methamphetamine molecules that are mirror images of one another. The d- isomer, d-methamphetamine, is the principally reinforcing molecule with a 2-3-fold higher potency than the l-isomer, which has little abuse potential.[11] Thus, a gram of "pure" racemic methamphetamine is less potent than a gram of "pure" d-methamphetamine, yet both are considered synonymous under current US Sentencing Guidelines (methamphetamine "actual" and "ice", respectively). The DEA's MPP notes 95% of seized methamphetamine is the high potency d-methamphetamine isomer, however (by contrast this number was closer to 50% in 2010).[9] That being said, most testing used to inform sentencing standards does not discriminate based on potency. So, *if* there is to be a sentencing standard based on purity, it may be prudent to also account for differences in potency because methamphetamine actual is not necessarily the same as ice.

"If" here is a major operational word for two reasons. First, it is unclear from a pharmacological basis why methamphetamine is the only commonly used drug for which purity enters the sentencing

guidelines. Perhaps this is due to popular and fear-provoking reports of “supermeth” (that is, the rise of the pure d-methamphetamine product).[12] These reports are misinformed insofar as many people who use drugs have existing tolerance and titrate their use to the desired effect meaning that a person using a set amount of the racemic mixture will 1) not experience as heightened effect of d-methamphetamine compared to someone not already on methamphetamine and 2) they will simply use a smaller amount of the d- isomer only product that approximates the effect of the racemic product they may be used to. More scientifically, the nicotine literature informs us that when smokers are given cigarettes of differing levels of nicotine, smoking behavior is adjusted (deeper puffs, etc.) in “light” cigarettes so the smoker can maintain the nicotine levels they are used to.[13] Or using a cruder lay analogy, let’s say you went to a bar and wanted a gin and tonic but you did not know by taste or by measure how much gin was in the glass. The effect of a 16-ounce glass with 1.5 ounces versus 3 ounces of gin will be different. If you are drinking to effect, you may have two of one kind or one of the other. The challenge is that unlike in a bar or with smoking where the purity and potency of gin and nicotine, respectively, are standardized, the consumer of methamphetamine does not know *a priori* what they are using. This may be more relevant to other drugs where there is greater variation in purity levels such as fentanyl and a tendency towards the introduction of potentially dangerous additives such as xylazine and novel benzodiazepines (as last month’s string of non-fatal overdoses in Baltimore have shown); and for products where there is variation in potency such as heroin versus fentanyl versus nitizenes. It is the lack of consistency in product purity and potency and the frequent introduction of toxic undesired impurities that leads to many of the clinical complications we see.[14-16] This isn’t to say that well-regulated and consistent products such as cigarettes and alcohol don’t have public health impacts but at least here the consumer knows what they are getting and we don’t see things such as methanol poisoning as a result of an unpredictable alcohol supply or xylazine skin ulcers in those receiving fentanyl in the hospital. So, from a clinical and public health perspective, it may be desirable to have a purer and more predictable

product.[17] Whether sentencing guidelines can or should be aligned with public health interests is beyond the scope of this testimony but is worthy of consideration.

While cocaine has its own history of sentencing disparities that we do not wish to repeat, it may help to compare public health trends between methamphetamine and cocaine. For the period 2015-2024 (most recent available data), the number of people 12 and older in the United States initiating either drug each year has had only modest fluctuations.[18] The number of people who have used each drug in the past year shows a nearly 50% increase for methamphetamine but relatively stable cocaine use.



During the same period, cocaine-associated deaths increased 5-fold while methamphetamine-associated deaths increased approximately 8-fold.[19] After adjusting for age and US population size, these increases were 5.9- and 4.1-fold, respectively. For both drugs, the increase is mostly due to combinations with opioids such as fentanyl. The magnitude of increase in rates of methamphetamine- and cocaine-associated mortality across the population is not evenly distributed with the largest increases seen in American Indian populations.[20]

The rise in methamphetamine use has led to a subsequent increase in methamphetamine-related hospitalizations, with a nearly four-fold increase from 2005-2016.[2] These hospitalizations are commonly related to psychosis, infection, altered mental status, and mood disorders. During a similar timeframe, cocaine-related hospitalizations increased only 10%, with common reasons for admission being diagnoses related to depression with psychotic features, cocaine toxicity, schizoaffective disorder, and alcohol use disorder.[21] While there are twice the number of cocaine-related admissions as methamphetamine-related admissions and twice as many people use cocaine as methamphetamine, the economic burden of these hospitalizations is not proportionate between the two. The annual hospital expenses related to methamphetamine and cocaine are estimated to be $2.2 billion and $19 billion, respectively.[2,21] Length of hospitalization for methamphetamine may be approximately a half day longer than for cocaine so this is unlikely contributing to the cost difference. People hospitalized for cocaine tend to be older and thus are likely to have more comorbidities than those with methamphetamine-related hospitalizations. These factors along with methodological differences in the methamphetamine and cocaine literature are likely contributing to the cost disproportion.

Approximately half of people who used methamphetamine in the past year met DSM-criteria for a methamphetamine use disorder; yet in 2022 only 172,000 (fewer than one third of those in need) received any type of treatment.[5,22] There are no FDA-approved medications to treat methamphetamine use disorder and the US health system has yet to adopt contingency management, the behavioral treatment with the strongest treatment effect size.[23] Current methamphetamine treatments are often labor and time intensive (e.g., residential or intensive outpatient) and last only weeks to a few months. The outcomes are suboptimal with a 60% relapse rate in the year following treatment.[24,25] Opioid use disorder on the other hand has effective treatment medications (methadone and buprenorphine) that reduce the risk of death by more than half, decrease risk of HIV and viral hepatitis, and improve quality of life.[26-29] These treatments are offered in a longitudinal manner rather than episodic, and 50-60% of

patients remain engaged in treatment at one year.[30] While methadone is restricted to highly regulated opioid treatment programs, any provider with a DEA license can prescribe buprenorphine, including via telemedicine. As with methamphetamine, however, in 2022 only 354,000 people (fewer than one third of those in need) received treatment.[22] People with both methamphetamine use disorder and opioid use disorder are less likely to receive medications for opioid use disorder than those without a co-occurring methamphetamine use disorder.[31] As a result, this population remains at increased risk for poor outcomes and death.

Another aspect of methamphetamine relevant to the US Sentencing Guidelines is the public health impact of incarceration. Several studies have identified incarceration as a risk factor for early mortality.[32] Mortality rates during the first few weeks following release from prison are 14 times higher than the general population.[33] While all-cause mortality is increased following prison release, the main drivers of this are overdose, suicide, and trauma.[34] Length of incarceration also impacts post-release mortality, with one study showing parolees experiencing a two-year decrease in life expectancy for each year imprisoned.[35] Contributing factors may include comorbidities existing prior to incarceration that go undiagnosed and/or undertreated during incarceration, the loss of health benefits during incarceration, and the challenges of re-establishing healthcare (and healthcare benefits) upon release. There are no data that parse post-incarceration mortality by offense, so it is not possible to identify the impacts of methamphetamine-related incarceration or to compare them to other drug offenses.

While comparing one psychostimulant to another may make the most sense pharmacologically, it may also be helpful to contrast methamphetamine and cocaine to illicitly manufactured fentanyl. As mentioned previously, most methamphetamine-related deaths involve fentanyl, but 43% of the 75,000 fentanyl overdose deaths involve methamphetamine, and emergency departments see an additional 84,000 non-fatal fentanyl overdoses annually.[4,36] Fentanyl specific hospitalizations are not captured, but there are approximately 900,000 opioid-related hospitalizations annually.[37] From an economic

perspective, in 2017-2018 opioid-related emergency room visits and hospitalizations cost approximately $5 billion and $13 billion, respectively.[37,38] Since the number of people using fentanyl is a quarter that of those using methamphetamine, the proportionate public health impact of fentanyl is far greater than methamphetamine.

So, we circle back to the question of whether there is a pharmacological, medical, or public health rationale for methamphetamine sentencing guidelines to be adjusted based on purity. The answer is no. But, if purity is taken into consideration, it should also apply to other drugs. Here, then the real question is should higher purity be upward adjusting or downward adjusting to sentences recommendations? It is fentanyl's variability in purity with additives such as xylazine and medetomidine that enhance sedation and contribute to fentanyl's harms (e.g., xylazine-associate skin ulcerations). In this case, increased purity may have a public health benefit.

Ultimately, complications related to drugs are a combination of their direct medical effects and how our society chooses to respond to people who use drugs. The choices of this committee most directly relate to the latter, but the public health implications of these choices should not be underestimated.

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