Clinical Education Initiative
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ECHO: METHAMPHETAMINE USE AND HIV

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[video transcript]

00:07
I'm going to talk about methamphetamine use and HIV, and that's what I was asked to discuss. And this is a pretty focal presentation, given the time allowable, so this is really kind of shortened from a longer presentation on methamphetamine use and HIV. And we're going to go ahead and get started. So I do not have any relevant financial disclosures. I will be discussing off label use of medications for methamphetamine use disorder.

00:35
So just some learning objectives. Initially, I'm going to very, very briefly talk about the epidemiology of methamphetamine use disorder, discuss the link between methamphetamine use and increased HIV and STI risk, and discuss effects of methamphetamine on HIV outcomes. Discuss treatment options, including off label use of pharmacotherapy for methamphetamine use disorder. And discuss safety tips and overdose prevention for persons who use methamphetamine.

01:03
So first, some, very briefly, some data on methamphetamine use. So these come from the National Survey on Drug User Health from 2020. Just of note, they have not done their sub-analyses yet, so there's very limited information that's been released thus far from the National Survey on Drug User Health. So some of my epidemiological slides will be from the 2019 National Survey on Drug User Health. So this is looking at illicit use on the left, and you can see that marijuana is by far, again, depending on which state you are in whether it's illicit or not, it's by far the most commonly used illicit substance. And you can see that methamphetamine is actually far down on the list. So approximately 2.5 million users during 2020. And then on the right hand side are persons with diagnoses of SUD, and you can see that alcohol use disorder is the most common diagnosis. And then again, methamphetamine use disorder, 1.5 million persons with it.

02:05
So this data is from the 2019 National Survey on Drug User Health, on the left hand side it's showing methamphetamine use broken down into age groups. You can see that it's consistently a more significant issue in the age group of 18 to 25 year olds, that's not surprising. The other thing to note is that in persons 26 and older, use has been increasing over time. And that includes, we don't have data for 2020 yet, but we certainly have seen an increased number of overdose deaths due to methamphetamine use during the pandemic. On the right hand side is looking at methamphetamine use related to other substance use and a diagnosis of major depression, and/or serious mental illness. And again, you can see that poly substance use is common, particularly in persons who have serious mental illness. This is looking at a breakdown, this is from the 2020 National Survey on Drug User Health, this is looking at a breakdown of stimulant use. So it's looking at the confluence of cocaine use, methamphetamine

use, and then misuse of prescription stimulants. And so you can see that there is interplay between those three communities.

03:19
And then the other thing to just remind everyone is that despite the fact that we have high prevalence of both substance use disorder and mental health diagnoses, we have huge treatment gaps. So the gap is not as significant for persons with any mental illness. So with persons with any mental illness, 45% of them will at some point in their lives receive treatment for their mental illness. But with respect to substance use disorder, it's only about 11% of individuals with a diagnosis of substance use disorder will ever access any care for their substance use disorder. On the right hand side, this is data from 2020, this is looking at where people receive their help for substance use disorder. So the number one most common location is a self help group, such as AA or NA, and then that's equivalent with outpatient programs, and then going down in order you can see all the other options. But why that's significant and something to just be aware of, even though it's not part of the big book of AA or any of the sort of credos of AA or NA, often they're anti medication. So if individuals are on medication for their substance use disorder, that's often discouraged by members of those communities. So it's just, when you're making a referral or recommending something to someone, be sure you know what you're recommending them to and that you know the evidence behind what you're recommending them to. Which again, for 12 Step groups, people can find a sense of community in them. But with respect to efficacy and affecting outcomes for substance use disorder, there's only evidence for alcohol and not for other substances. So alcohol with AA and not any evidence for NA in improvement in outcomes.

05:16
So now we're going to very briefly look at the epidemiology of overdose deaths. So on the left hand side is reminding us that there were three waves of the opioid epidemic. We are now in the fourth wave. So the first wave was in prescription opioid overdose deaths. The second wave was the rise in heroin overdose deaths. The third wave was the rise in synthetic opioid overdose deaths, specifically referring to fentanyl and its analogs. On the right hand side though, you see the rise of the fourth wave. So this is overdose deaths related to stimulant use, either cocaine or methamphetamine, primarily because fentanyl and its analogs are added to the street illicit substance supply, whichever substance we're talking about, with the exception of marijuana.

05:59
This is looking also at pre COVID-19. On the left hand side is looking at stimulant and psychostimulant means, specifically methamphetamine. So this is looking at cocaine and methamphetamine deaths with opioids and not with opioids involved. And on the right hand side is looking at the percentage of overdose deaths involving psychostimulants with involvement of opioids. And you can see in the Northeast, our region, it's a very high percentage, so almost 80% of the stimulant related deaths have opioids involved. This is looking at specifically stimulant overdose deaths. What we've seen during the pandemic is that fentanyl has moved West and methamphetamine has moved East. So there used to be far more methamphetamine on the West Coast, far more fentanyl on the East Coast, and we've seen that convergence during the pandemic. On the right hand side is looking at suspected all stimulant overdose

deaths, those that are in orange show significant increase during the pandemic. And New York is one of those states with a significant increase in stimulant overdose deaths. This is looking at a period of time that crosses over between pre-pandemic and early part of the pandemic, so it covers the time period from September of 2019 to September of 2020. So fully six months before the pandemic started in the US, we started to see an increase in overdose deaths again. We had seen a decrease overall in overdose deaths during 2018, and saw a reversal of that before the pandemic even hit, with it also it being impacted by the pandemic. So what I want you to notice here is the increase, in the bottom row, an increase of 46% in methamphetamine related deaths, and an increase of 30% in cocaine related deaths, and then the increase in synthetic opioid or fentanyl and fentanyl related deaths of 55%. So the data on the left hand side is through January of 2021. And again, you can see a significant rise in stimulant related overdose deaths. I think we're all very well aware of the data that came out in April, showing overdose deaths between April 2020 and April 2021 of over 100,000, which is almost a 29% increase over the same period a year prior.

08:20
So let's switch over specifically to methamphetamine use and HIV. So what is the connection between methamphetamine use and HIV? So first of all, there's increased risk for HIV acquisition. So increased cytokine and inflammatory presence, in the rectum specifically. You can read which specific markers I'm talking about, but that's both in HIV negative and HIV positive men in the studies that they did. There are worse HIV outcomes. So epigenetic changes due to stimulant use that leads to further immune activation, in addition to the immune activation that HIV calls. And it's a question mark, does that lead to expansion of HIV reservoir? There's increased soluble CD14, again, another marker. This is of monocytes specifically, a type of white blood cell activation that predicts faster clinical progression, and faster progression of cardiovascular disease.

09:19
So this is a super busy slide, but there's a lot going on here. So when we think about methamphetamine use, and we think about MSM, and we think about sex, and we think about HIV, what are some of the factors that play into that? So there's a synergism between illicit substance use and unprotected sex. So I'm going to highlight the key points on this slide. So it's facilitated by environmental factors and norms. You can think of it as the role of sex in subgroup's lives. So this could be via social and sexual networking apps, and social venues. It's fueled by psychosocial burdens. So you have an intersectionality here between so many factors, including but not limited to racism, homophobia, trauma, stigma, discrimination, transphobia, minority stress effect, misogyny, intimate partner violence, comorbid mental health, and specifically I'm referring to depression, PTSD, generalized anxiety disorder and ADHD, psychological vulnerability. You have unstable or unsafe housing or homelessness, and victimization. It heightens the likelihood, so meth use heightens the likelihood of unprotected sex. So this is anal sex, oral sex, extreme sex, sexual compulsivity. So increased number of partnering, group sex, sex marathons, fisting, S&M, rectal trauma and bleeding, decreased sexual inhibitions, and also substances affect judgment about sexual partners and about sexual practices and about risk taking. Reduced condom use, development of erectile dysfunction or sexual performance anxiety in response to methamphetamine use, so maybe then the person

would choose to have increased receptive anal sexual intercourse, decreased desire for sober sex after having sex with substances, increased incidence of sexual assault, and over representation of HIV among MSM. Also, it enables the transmission of other pathogens. So other bacterial and viral pathogens, I've listed many there. There's also risk of seroconversion to HIV that's heightened by use of drug combinations. So if you're using stimulants only, the odds ratio is increased to 3 times. If you're using stimulants, amyl nitrite or poppers and erectile dysfunction drugs, for example like sildenafil or Viagra, that increases that odds ratio to almost 9, so 8.45. So the risk for sero conversion to HIV is similar between those who use via injection drug use and those who use psychostimulants via non injection drug use. And again, that increases with the number of drugs used. So if you use one drug, the OR or odds ratio is 3. If you use three drugs, regardless of the drugs used, that odds ratio jumps to 9 and is highly associated with psychostimulant use before sexual activity.

12:27
So what are some of the motivations when you use methamphetamine for drug use? There's a physical domain, so physical sensation that's non sexual, as well as sexual sensation and facilitation of sex. There's an emotional domain, emotional enhancement, emotional equivalence, and there's cognitive disengagement and emotional escape with substance use. And then there's a social domain, social interaction and overcoming social inhibitions. So there's also, very commonly with methamphetamine use, there's poly substance use. And I've listed many, many substances here, and all of these are commonly used in addition to methamphetamines in the context that we were discussing.

13:13
So just to look at some data, so this was looking at methamphetamine use and HIV risk in young MSM. So this was a cross sectional analysis in eight US cities, with approximately almost 600 adolescent boys and young MSM. And recent methamphetamine use was associated with a history of STIs, so over 50%, two or more sex partners in the last 90 days, that was almost 86%, and sex with someone who has HIV was almost 33%. And recent methamphetamine use was also associated with a history of homelessness commonly and less likelihood to be attending school. And poly substance use was common.

13:54
This is looking at methamphetamine use among MSM in New York City by race/ethnicity. So this was covering the time period of 2004 to 2017. What I want you to notice over time is the shift from primarily Caucasian or white MSM using methamphetamine, to the increased use among Latinx and Black. So what about methamphetamine use in people living with HIV? So it can lead to decreased ART adherence, decreased viral suppression, and actually increased mortality. So they have a three times elevated standardized mortality ratio, and this is more pronounced in people who are MSM, HIV positive, using methamphetamine, and tobacco or nicotine. So a 5 times increased risk. There's an increase in risky sex, especially with comorbid depression. And an increase in STI prevalence, particularly so in those living with HIV. So this is looking at methamphetamine use and cognitive function and other sort of markers of independent function and sort of what's the connection between that. So in this population, they looked at those who are HIV negative and not using methamphetamine, those that were HIV

negative using methamphetamine, those HIV positive using methamphetamine, and those HIV positive and not using methamphetamine. And the most impairment was seen in those that were both HIV positive and using methamphetamine, but you still see cognitive impairments in any individuals using methamphetamine. So I didn't have time to go into a lot of the effects of methamphetamine, particularly cognitive effects and psychological effects, but again it has a significant impact, particularly on those that are also HIV positive.

15:52
So what about treatment for methamphetamine use disorder? So as you may be aware, there are only FDA approved medications for the treatment of three substance use disorders. That includes opioid use disorder, alcohol use disorder, and tobacco use disorder. So when we're talking about treatment for other substance use disorders, including methamphetamine use disorder, you're talking about a combination of different forms and strategies for types of therapy, as well as the use of off label use of medications. So some of, and I don't have time to go into the detail of the behavioral interventions, but some of those behavioral interventions that have been successful in persons with methamphetamine use disorder include CBT, or Cognitive Behavioral Therapy, the Matrix Model, contingency management and community reinforcement, Motivational Enhancement Therapy, 12-Step facilitation, behavioral interventions combined with 12-Step support. And again, consider the level of care. Some individuals may need to have more focused care. So in other words, they may need intensive outpatient treatment or residential treatment in addition to the clinical supports you could offer them in an office based setting.

17:07
So this is a slide that basically just says I'm telling you about off label use of medications. I'm not condoning use of any particular medication, but just going over what data we have to discuss these medications. If you are prescribing medications for methamphetamine use disorder, particularly if you're doing off label use of stimulants for methamphetamine use disorder, then I do recommend doing toxicology testing to be assured that they are taking the medications you're prescribing. And again, if you're ordering toxicology testing, A) you should know how to interpret it and B) you should have a clinical reason why you're checking that toxicology. So what clinical decision making would you alter by those toxicology results?

17:54
So there is an OASAS map document, that's the Medical Advisory Panel document, that does go through off label pharmacotherapy use for both methamphetamine and cocaine use disorder. So I put the summary here. So some medications that do have efficacy in clinical trials are Naltrexone orally, Topiramate, Bupropion, Sertraline, and Mirtazapine, with the doses there. And then also a slightly more controversial is using stimulant medications, but particularly for persons who have a stimulant use disorder, either cocaine or methamphetamine, and also have comorbid ADHD, using stimulant medications often at much higher doses than would be used to treat ADHD alone have been an effective strategy for persons with methamphetamine use disorder.

18:47

So I'm going to focus on the medications that were positive in some clinical trials, there have been many negative clinical trials, those are listed on the right hand side. But some that do have evidence to support their use with methamphetamine use disorder are Bupropion, Mirtazapine, Naltrexone, Methylphenidate, D-amphetamine, Topiramate, Bupropion plus Naltrexone. So what are some of the problems with the literature, with respect to methamphetamine use disorder and the same would be true of cocaine use disorder? So they're often underpowered studies. So meaning there are not enough people who remain in the clinical trial so that they can actually show a difference in the treatment group versus the placebo group. There are often high attrition rates in specifically stimulant use disorder trials. And then just a couple of caveats here. So Bupropion may be more effective in individuals with a use disorder of less severity, and it may be better in individuals with depression and who are male. And there's low strength evidence that Methylphenidate and Topiramate may facilitate reduction in substance use. Topiramate is better if you have a negative drug screening at baseline.

20:02
So here are some of the clinical trial evidence for these medications specifically for methamphetamine use disorder. So this looked at Bupropion, and what was interesting and sort of the punchline here is it works reasonably well. It has a statistically significant result if people are adherent, but many of the people who are participating in the clinical trial were not adherent with the treatment. And so when they looked at the whole pool of individuals that were on the treatment, they did not get a clinically significant result. But when they actually checked Bupropion levels and they teased out who was adherent versus non adherent, they did have a clinically significant result.

20:48
The next one is looking at off label use of Mirtazapine. And again, I'm just going to summarize the data for you. So often these trials are very small, so this was 60 methamphetamine dependent MSM. This looked at methamphetamine positive urine test results, they were lower for those taking Mirtazapine versus placebo. They also noticed a decrease in HIV risk behaviors, were reduced in the group that was on Mirtazapine. So again, another possible strategy to use.

21:21
So this one was looking at Methylphenidate, and this was again relatively small, 90 persons seeking treatment for methamphetamine use disorder. They also used a CBT platform with motivational incentives. And so what they noticed was that the group that received Methylphenidate was associated with significantly fewer self reported days of methamphetamine use over the active treatment period, compared with placebos. So there was no difference actually in the urine toxicology results, but there was a difference in the reported days of methamphetamine use.

22:01
So this is looking at Bupropion and Naltrexone coupled together for methamphetamine use disorder. And again, just for the sake of time, I'm just going to summarize it. And they did show

that this was effective for individuals with moderate or severe methamphetamine use disorder in decreasing days of use.

22:25
And then this is a sort of summary. This was a meta analysis looking at agonist treatment, so this would be treating stimulant use disorder with stimulants. And so they combined studies and they looked at total of almost 3000 patients, 38 randomized, double blind, placebo controlled, parallel design studies of Modafinil name brand Provigil, Methylphenidate, and Amphetamines. And they did find that, again, reported days of use decreased, functionality increased, it did not show a change in toxicology results. But this is also just to remind you that toxicologies are just data points, we really need to look in our clinical trials at how optimally our patients do.

23:13
So just to summarize this dense data. So some strategies to think about are Bupropion 300 milligrams per day, Topiramate 300 milligrams per day divided BID, Naltrexone 50 to 100 milligrams, Mirtazapine 30 milligrams per day, Methylphenidate 54 milligrams per day, and extended release Naltrexone so that would be name brand Vivitrol injected every three weeks plus Bupropion ER 450 milligrams per day. Some caveats for safety considerations is that several of these medications decrease seizure threshold, so they would need to be tapered off and patients need to be warned not to stop medication, specifically that would be referring to Bupropion and Topiramate. Also, if a person has a history of a prescription stimulant use disorder, use caution when prescribing stimulants to them for their disorder. And then also consider their medical, psychiatric, and other substance use comorbidities when choosing treatment.

24:18
So the medications in red are the trials that had greater than 100 participants in them that showed promise. So again, just a summary of points I've already made. So you know, to wrap it up with the last couple slides here. So one thing to think about is applying syndemics theory here. So what I mean by that is that the complexities involved with methamphetamine use, particularly with potentially marginalized patient populations, so I'm referring to MSM, bisexual men, transgender persons, persons with HIV etc. requires very complex prevention and treatment agendas that recognize psychosocial components and vulnerabilities and stigma that are sex positive and address substance use in a harm reduction framework. The problem is that often our siloed worlds don't interact in that manner. So the HIV prevention world often focuses on sexual health for gay and bisexual men, while the substance use disorder treatment worlds ignore sexuality completely. And again, neither world may recognize the complex psychosocial vulnerabilities in these patient populations.

25:32
So very quickly, because I know I'm almost out of time, I want to go through some safety tips for methamphetamine users. So first the concept of overamping, so this is a negative reaction to using stimulants, it could be either cocaine or methamphetamine. So it is different from overdosing, but it can be life threatening. So symptoms can include chest pain, dyspnea, hypertension, tachycardia, hyperthermia, anxiety, paranoia, aggression. So tips to prevent

overamping include staying hydrated, replenishing electrolytes, seeking medical attention. About 30% of people who have chest pain while using stimulants will end up having a cardiac event. Finding a calm and quiet place, and protecting the head in case of seizure. With respect to overdose, persons will overdose if exposed to enough opioids, whether the opioid exposure is intentional, so for example, speed balling, mixing heroin or fentanyl with stimulants. Or unintentional, so fentanyl and its analogs added to the stimulant supply. So what are some tips to avoid overdose? So testing your drugs with fentanyl test strips, and just a reminder that federal funds can now be used to purchase fentanyl test strips. Avoid mixing drugs, use smaller amounts, so you know start low and go slow. Carry Naloxone at all times, regardless of the substance you're using. So providers should be dispensing or prescribing Naloxone to all persons who are actively using, regardless of the substance used. So again, the rare exceptions will be alcohol and marijuana. The idea of fentanyl in the street marijuana supply has been debunked many times, despite its continual reporting in the media. There's a Never Use Alone hotline. So if you intend to use alone or your patient intends to use alone, they can call this hotline which is staffed 24/7 and people will remain on the line with them to make sure that the person doesn't overdose, and they will activate EMS if they become unresponsive. And then advise people regarding mail order Naloxone and other harm reduction supplies that they can get sent to their home, that would be www.nextdistro.org. And if you have a patient who is intending to use stimulants, but has fentanyl or other opioids in their urine toxicology if you're checking it for a clinical reason, consider prescribing buprenorphine to them, again for harm reduction and decreasing the risk for overdose. So just a reminder, in case you're not familiar with it, there's the New York State Department of Health guidance called Build a Safety Plan, that's available for free online in English and Spanish.

28:12
So just a few conclusions. So methamphetamine use potentially confers high risk for patients, persons with methamphetamine use disorder have a complex milieu of psychosocial treatment needs. And there are medications that do show some efficacy with methamphetamine use disorder that can be used off label, utilizing other modalities of treatment with them in conjunction does increase their efficacy. And then just remember to do overdose prevention and dispense or prescribe Naloxone to all persons using methamphetamine. That's it. Happy to take any questions.

[End Transcript]