WEBINAR VIDEO TRANSCRIPT

Opioid Addiction Treatment ECHO

Addressing SUD-related comorbidities, such as hepatitis, HIV, depression, anxiety, and PTSD

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DR. THORNTON: So my goal today in this short amount of time I have is to describe the epidemiology of Hep C in the United States, and talk a little bit about how to interpret Hepatitis C testing. And you all may know this already, but I think its important to go over it 'cause there are some misconceptions about Hepatitis C testing, certainly in the community. And also recognize the importance of addressing Hep C in the primary care setting, and certainly in the setting that you all are practicing in. I think this is an extremely important slide that I show all the time now when I talk about Hepatitis C and some of you may have seen it before, but really what it shows you is that Hepatitis C causes more deaths nationally in the United States than all other infectious disease conditions combined that are reportable to the CDC.

So, at the bottom, you can see that includes TB, HIV, Hepatitis B and 57 other infectious conditions reportable to the CDC. So this is relatively new. In the past, HIV actually caused more deaths than Hepatitis C, but at this time, Hepatitis C is the big killer in the United States in terms of bloodborne viruses. So in terms of Hepatitis C prevalence, many of you have probably heard about the NHANES study. It's a study that's done every several years by the CDC. It's an amazing study called the National Health and Nutrition Examination Survey. And a lot of data that we have that we talk about national prevalence comes from that study. And so the numbers that you'll hear when people talk about Hepatitis C are the numbers that you see at the top, that we have about 3.6 million chronically-infected who've been exposed to Hepatitis C and about 2.7 million currently-infected, or 82% of those who are anti-HCV positive.

As you know, some people do clear Hep C virus on their own, but the majority of them go on to develop Chronic Hepatitis C. So the problem with the NHANES study, like I said, its an amazing study, but it leaves out a large segment of the population that has a high risk for Hepatitis C. So, as you can see here, on this slide on the left here, the NHANES study is really only done in people who have a home and have a phone. So they have to be contacted on the phone, you have to go see them in their home and draw their blood and interview them, really intensive study. And so everybody who's incarcerated or institutionalized, hospitalized, even people who are living on Indian reservations aren't included in the NHANES study. So there are a lot of people, probably close to a million people that probably didn't get counted in NHANES.

So people that think about Hepatitis C a lot or try to figure out how many people there really are in the United States. We think there are a lot more than 3 million, probably closer to 5 million people who

have Chronic Hepatitis C. So from the NHANES study, every year when they would evaluate this Hepatitis C antibody prevalence the people that were born between 1945 and '65 had a higher prevalence than the general population, and this prompted the CDC to make the recommendation for anybody who was born during this, we call it birth cohort testing, be tested for Hepatitis C at least once, and then if there are no ongoing risk factors to not be tested again.

The important thing that I like to tell people about this birth cohort testing, it's super-important that what we use to think about this group of people is that it was probably due to behavior because there was a lot of experimental injection drug use in the '60s, there was a lot of high-risk sexual behavior, there was the Vietnam War, there was all those things that were going on that people were doing, doing things that were putting them at risk for getting exposed to Hepatitis C. But what we found out from genetic studies of genotype 1A, which is the most common virus in the United States, is that the peak of transmission of that virus was in the '50s and so the thinking now is that a lot of people that got exposed in this birth cohort were actually exposed through the healthcare system in the United States. So it was before we were using disposable syringes, and it takes us sort of out of the realm of behavior and into the realm of you just got infected because you were at your doctor's office.

So when I talk to people about Hep C testing they don't wanna get it because they say they've never had a risk, you really need to let them know about that particular fact about the birth cohort. So there's been-- You know, the number of Hepatitis C cases went down dramatically after the virus was discovered in 1989 in the blood test. We had a blood test for Hepatitis C and the blood supply actually became clean in about 1992. The number of acute cases went down dramatically, but unfortunately, starting around 2010, the number of acute cases has been rising steadily over time and this is all due to the opiate epidemic and the epidemic of injection drug use. So the people that are now getting infected with Hepatitis C are a lot of young people, a lot of young people in rural areas, really all over the country who are starting to inject for the first time. So this doesn't have '16 and '17 on it, but it's continuing to rise. There's been absolutely no sign that this is going down.

So I just wanna talk briefly about what I think are the really important things that people can do in their own clinics in the primary care setting. Screening for Hepatitis C is super-important. I gave a talk that goes through all of this which I'm not gonna do today, obviously, but screening for Hepatitis C certainly in the settings that you're in is really, really, really important. Most of the people that have Hepatitis C in the country don't know they have it. At least 50% and maybe up to 75% of people who have Hepatitis C have never been tested, so that's one place where you guys could actually make a huge difference.

If you discover that someone has Hepatitis C you really need to counsel them on modifiable risk factors like alcohol use, which is probably the biggest one, to counsel people about the effect of alcohol on Hepatitis C. You really need to be able to evaluate how bad is their liver disease and a couple of other things that are really important when you diagnose somebody with Hepatitis C. And then, of course, getting them into treatment and I'll talk more about that.

So this is what I just mentioned that at least 50% of people who have Hepatitis C are not aware of their infection. So as I mentioned earlier, probably a lot of people know this, but I think it's important to understand about Hepatitis C testing and the most important take-away from this slide, and this is

available from the CDC, is that if you have a reactive antibody to Hepatitis C that you can't stop there. A lot of people get tested for Hep C, their antibody's reactive and they're told they have Hepatitis C and that's not true. You have to actually go on to do confirmation. So the way you confirm a Chronic Hepatitis C infection is by checking for the virus itself, the HCV RNA, and if they have the HCV RNA then they are considered to have Chronic or Current Hepatitis C infection and need to be linked to care and treated.

If they have a reactive antibody, but their RNA is negative, it could mean a couple of things. Most commonly it means that someone cleared the virus on their own. They're still at risk for getting Hep C again, but about 25% of people who get exposed to the virus can clear it on their own. And if they have no antibody then it means that they, the most common reason is that they've never been exposed to Hepatitis C.

So I just wanna talk briefly. This is a crazy slide, which now it keeps coming off the other end over here. So I started treating Hepatitis C back here, and over the last 10 to 15 years there's been a dramatic-- There's been a revolution basically in the treatment of Hepatitis C. This is 2011, there was the introduction of these two protease inhibitors, which were the first sort of-- What we'd call them in HIV were designer drugs, these drugs that were designed to basically stop the replication of the Hepatitis C virus. These weren't so easy to use, but over the next couple of years until 2014 we were using these protease inhibitors along with interferon, but in 2014 the release of this drug called ledipasvir/sofosbuvir or Harvoni came out, and at that point we were able to treat everybody with non-interferon containing regimens. So all oral, very easy to tolerate.

The usual duration of treatment now for Hepatitis C is about 12 weeks. It can be as short as eight and as long as 24, but 12 is the average. And the cure rates for these medications are way above 90%. So Hepatitis C is an incredibly treatable disease, and curable disease at this time. And another thing that I think you can talk to people about, even if you don't treat yourself, to really get them hooked up to treatment because they can get treated in three months, get cured, and they never have to worry about their Hepatitis C again, so really, really important time in Hepatitis C right now.

So what do we get when we treat somebody's Hep C? This was actually data from the interferon era, but we know that it's gonna be the same with treating somebody with non-interferon containing regimens. So this was in patients who were already cirrhotic when they got treated and this study looked at, over the next 10 years, there was a 70% reduction in liver cancer. A 50% reduction in all-cause mortality, which was not really expected but a very, very important thing because Hep C does impact people not only in their liver, but in all their health in general. And then a 90% reduction in liver failure. So we have a really great test, we can test people. We have amazing medications.

We have a ton of untreated patients and we have a ton of undiagnosed patients. So this was also from NHANES. This is considered the best information we have about the cascade of care. That there are a lot of people undiagnosed. So only, at least, half of them tested. Fewer referred to care, and as you go down this you can see that there-- This is old data, so this is from about 2012 so this is gonna be a lot higher now, but everybody truly believes that this cascade has really not changed that much even with the introduction of these medications, unfortunately.

So I just want to mention to you just really briefly that when we were using interferon that we would not treat people who were actively injecting drugs because it was too dangerous. Interferon was a very dangerous drug to use in general. But now that we have these new oral medications, there's a lot of push to try to treat people who are currently in treatment for drug use. Certainly, people who are on medication-resistant therapy, but also treating in people who actively inject.

And it's been still very limited because of a lot of reasons that you can imagine. That you talk a lot about on this network about stigma. Insurance companies can use drug use as a criteria for treatment exclusion. A lot of people are incarcerated in prisons where treatment is limited. The current guidelines for Hepatitis C treatment recommend that people who inject drugs be treated for Hepatitis C. And we know from a lot of studies now that you can successfully treat in this population and get very higher cure rates and good treatment completion rates.

So, that's my last side. I'm sorry I went very quickly through those

So I wanted to let you know that there are a lot of people that are working in settings where certainly in addiction treatment settings where they're also treating the patients Hepatitis C, which I think would be ideal. If we could do all of these things at once you can really make an impact. One of the things that we've found in treating people who are currently injecting is that actually gets them into the medical care system in ways that they had never had access before. And it's a real motivator, I think, for people to stay engaged in care and when they're treating the Hepatitis C they'll often get engaged in treatment of their addiction, as well. So it's a place where I think you can help people in many different ways in one setting. So I'm happy to answer any-- Can like I have--

MODERATOR: Yeah. Yeah, yeah, yeah.

DR. THORNTON: Yeah.

MODERATOR: Yeah, just go ahead and do a few minutes of questions. Dr. Thornton has to leave to go back over to the hospital so let's go ahead and have a little discussion now before we move on to Dr. Hager's talk.

DR. THORNTON: I'm gonna take off.

MODERATOR: Yeah.

DR. THORNTON: Okay. How about questions or comments for Dr. Thornton?

I have a question.

Yes, Casey.

Oh, sorry. Is that?

Hi.

Is it me or her?

Let's see, go ahead, Casey, and then whoever else is trying to talk will go next.

Okay, so we test people for Hepatitis C anytime they come in to our MAT program, but when we refer out we're having-- Refer to Hepatitis C treatment providers we're having a lot of pushback about, they want somebody to be off of Vivitrol or off of suboxone for six months before they'll start treatment. And I'm wondering if there's any way to advocate for these patients or provide some information to these providers to get them that treatment for Hepatitis C while they're on Vivitrol or something.

That's a great question. I mean, there's absolutely no evidence to support that-- To support people doing that. Sometimes it comes from the insurance companies. Sometimes it comes from the providers themselves, but there's a lot of evidence now that treating in that population, you do not need to wait. There's no reason to defer treatment. I have a talk that Ken Page, one of our colleagues, has been giving about the data behind treatment, in a drug-using population and I can send that to you if somebody connects me to you. That's one of the reasons I really think that the real way that these patients are gonna get treated is if people start doing it in their own setting. And you can learn how to do it. It's not that hard. It's hard up front, making the decision about what drug to use and things like that, but after that it's really straight-forward. These drugs have no side effects. You have to monitor people every month on them, but it's something that can be easily done in the setting, in the addiction treatment center.

Great, thanks, Casey. And then, Laurel, where you the other one who wanted to say something or ask a question?

Yeah, I just wanted to clarify. So when I do testing for HCV, we always do the antibody, of course, and then if it's positive then we do the RNA and look for both the number of virus, but also the genotype. And if the virus, if it says that it's not detectable then we kind of leave it at that point. We don't go back then later on and recheck. We just figure that they cleared the virus. Are we correct in that point?

That's basically the correct assumption. The only caveat is that if you're working in a population where people are becoming or exposed on a regular basis, people can clear the virus on their own and then get the virus again. And in that first sort of six-month period when people get exposed to the virus, sometimes the viral load can go way up and then way down and then way up, and it's very unpredictable. So I would say if you're working in a high-risk population that you should probably check six months later, as well. If it's negative, check them again in six months.

Okay. Thank you, appreciate it.

You're welcome.

Great, maybe one more question or comment? Josh.

Yeah, my question is, a lot of our patients have Medicaid and so they're able to receive the treatment, but we do have some patients who do not have Medicaid and I was wondering are there any programs that can assist in paying for the treatment because I know without the Medicaid it's very expensive.

Yeah, that's a great question. So if somebody has no insurance, which is pretty rare around here anymore, but if they absolutely have no insurance there's patient assistance programs that will get them the medications for free. So if you have insurance and it denies you it's more complicated, but if they absolutely do not have healthcare insurance then we could get them the medications for free.

Awesome, thank you.

Welcome.

So, Josh, is there a way we can help you with that? Do you wanna maybe email Crystal and we can send you more information about how to access the patient assistance?

Oh, that would be great.

Hi.

This is Brent with the psychiatry. Before you take off, I was just wondering what the estimates are for the rate of reinfection after treatment with one of these agents?

That's a great question. So it's being studied and there's more and more data coming out, but it looks like about 5%, which is-- You have to expect that people are gonna get reinfected if they're continuing to inject, but it's lower-- I mean, for me, then your curing 95% of the people and getting rid of it.

Right, right, yeah. The glass is 95% full.

Yeah, exactly.

5% over the next year?

5% per year, right?

Per year, okay, thank you.

Yeah.

Great, thank you so much, Karla.

You're welcome.

That was terrific.

Thanks, you guys, be Hepatitis C treaters!

All right.

Thank you, Karla.

Shameless plug.

Shameless!

Let's see, we've had a couple of other people join us. Let me just do introductions real quick before we go on to Dr. Hager's talk. Dr. Troxler, do you wanna introduce yourself? Let's see, you're muted.

Yeah. Okay, let me get the cursor in the right spot.

Okay. Joyce Troxler down in Silver City.

Great, thanks for joining us. And then Jillian from HIRSA, can you introduce yourself?

Hello?

Hi.

Hi, this is Jillian Harvey, public health analyst at HRSA.

Great, so nice to have you joining us, Jillian. Is there anyone else that I missed who hasn't had an opportunity to introduce themselves yet? Here we go, let's see. So somebody's just joining us. MHWFL1. Can you unmute and introduce yourself, the person who just joined us? Let's see, can you put your cursor over that microphone in the lower left corner of your screen and click on it and that'll unmute you I think. Okay, you're unmuted from our side, go ahead.

Okay, my name's Kelly Keyes, I'm a nurse practitioner. I'm in Queen Creek, Arizona, and I've just been working with the program for about three months. I think I have eight patients.

Great, wonderful, so glad to have you joining us. Thanks for signing on. Anybody else who I've missed? Okay, let's go ahead with Dr. Hager's presentation.

All righty, thank you. So while we're still on this Hepatitis C slide, I've got a perfect idea. I'll call it Harvoxone. Harvoni plus Suboxone.

MODERATOR: I think we should start manufacturing it.

DR. HAGER: Yeah, start manufacturing that one. That's a real winner.

JILLIAN: Oh.

DR. HAGER: Yeah, Harvoxone. All right, well, we've been talking about co-occurring psychiatric and substance use disorders in opioid use disorder. As you know from previous presentation, substance use disorders have a strong connection to adverse childhood events and trauma-related events, and many of these disorders will be trauma-related, as well. So when you're looking at somebody who's got a substance use disorder and they also have some psychiatric symptoms like depression or anxiety you really have to get a sense of whether or not it's being caused by the substance use disorder or being caused by an independent psychiatric disorder, or being caused by both.

So here's some basic questions that you can use in your history taking to understand this. Are the psychiatric symptoms present only during substance use disorder periods, then it's likely the psychiatric disorder due to substance use disorder. For example, somebody who has chronic alcoholism and who has depression symptoms, but before they got into alcohol they didn't have depression symptoms and when they're sober from alcohol they don't have depression symptoms. So that's probably alcohol-related depression.

Now, on the other hand, if the psychiatric symptoms are present before the substance use disorder and, or during extended periods of sobriety this is likely a co-occurring psychiatric disorder. So, for example, somebody has depression for five years and then in response to their depression they start using opiates, and then they are abstinent from opiates for three years while they're on suboxone and their depression returns, this is likely a co-occurring psychiatric disorder. And then there are instances in which there's both. There's a co-occurring psychiatric disorder plus or minus one due to substance use. So in this instance is when psychiatric symptoms are present before substance use, during extended period of sobriety, as well as during the substance use disorder.

So the example there would be somebody's who got depression at baseline, they start drinking and their depression gets worse, and then they stop drinking, their depression continues. So that is both they have. And this can be important because if you've got somebody who just has the psychiatric disorder due to the substance use then the treatment for that is treating the substance use disorder. If you've got somebody who has both, then the treatment, you'd treat both at the same time.

So psychiatric disorders are much more prevalent amongst people who have opiate use disorder than they are in the general population. And you can see here, in the blue, is the prevalence of psychiatric disorders in the general population and, in the red, is the prevalence of these psychiatric disorders in persons with opiate use disorder, and you can see marked increases in all of these disorders across depression disorders, bipolar disorder, anxiety disorders, PTSD, and personality disorders.

And then, as well, people who have opiate use disorder are also at much greater increased risk for having other substance use disorders relative to the general population. In blue, the general population, prevalence of alcohol, cannabis, cocaine, stimulant, sedative, inhalant, and hallucinogen use disorder. And then in red the prevalence of these disorders in people who also have opiate use disorder. So opiate use disorder has high, high, high comorbidity of both psychiatric and substance use disorders. Opioid use disorder increases the risk of a psychiatric disorder, and psychiatric disorders increase the risk of developing an opioid use disorder.

So if you've got somebody with a baseline psychiatric disorder then they are anywhere from five to 11 times greater at risk for developing opioid dependence. And if you have somebody with a preexisting opioid dependence then they are anywhere from four to nine times more likely to develop a psychiatric disorder so its a bi-directional relationship. So when you're treating psychiatric disorders you divide up the treatment into acute phase, continuation phase, and maintenance phase, and your treatment goal is to have durable remission of psychiatric symptoms.

Remission means the absence of symptoms for a specified period of time. So in the acute phase, which usually occurs over the course of a few months ideally, response is generally defined as a 50% or more reduction in symptoms. So, for example, a 50% or more reduction in anxiety, or 50% or more reduction in depression symptoms. Once you get a response, you should aim for remission. Remission means no symptoms over a period of, generally, it's like a month or two months. So remission from depression means no depression symptoms whatever over the course of a month or two. And then once you get somebody in remission or you get them in a fairly good response, your next job, in the continuation phase, is to prevent relapse.

So you're trying to keep them out of depression or keep them out of anxiety. And then as the years go on, the maintenance phase, the goal is very similar, prevent recurrence of the disorder. So we'll focus first on depressive disorders. And so co-occurring depressive disorders, when you treat co-occurring depressive disorders in the context of opioid use disorder, it's important to kind of look at the evidence base. And it's important to look at this because buprenorphine itself has empirical support as an antidepressant. And buprenorphine and methadone make a maintenance therapy, improve depression symptoms in opioid use disorder, whereas naltrexone maintenance therapy does not appear to worsen depressive symptoms, but doesn't really necessarily make them better.

And so when you look at the clinical trials, there's not many antidepressant medicines that actually have benefit in treating depression that comes in the context of maintenance therapy for an opioid use disorder. So imipramine and doxepin appear to be helpful for treating depression in people who are on methadone, but these same medicines plus Wellbutrin or Zoloft or Prozac did not appear to help people in Methadone maintenance in other studies. And there have been no randomized clinical trials looking at anti-depressant treatment for people with depression symptoms in buprenorphine maintenance therapy.

So one of the thoughts for treating people with co-occurring depression and opioid use disorder is to stabilize them on medication therapy for six weeks. So somebody with depression and heroin use disorder, get them on Methadone or buprenorphine and stabilize them over six weeks and see how their depression is doing at that point. And, oftentimes, the depressive disorder will remit just with opioid replacement therapy. That's what the evidence suggests. But if the depressive disorder persists then I would recommend just treating depression per established treatment guidelines. Measuring the depression at baseline, selecting an appropriate treatment, whether psychotherapy or medications and then being proactive about following up with the response to that medication treatment.

And your target is remission of depression. Here are some evidence-based treatments for depression. Psychotherapy is highly-effective for major depression and you can use cognitive behavioral therapy or interpersonal therapy or behavioral activation. You can use medications or you could add psychotherapy to medications and that appears to work better than either one alone. And the general treatment sequence is recommending psychotherapy first if you can access it and then moving on to a sequence of medications trying to maximize each one before you change to a different one.

So SSRIs are things like Paxil and Prozac and Zoloft. SNRIs are things like Effexor, Cymbalta. And if one of these medications at a maximum dose for a period of four to six weeks doesn't work you move on to the next step. And so this step-wise approach helps to improve response and remission rates. So co-occurring anxiety disorders treatment, most anxiety disorders respond quite well to psychotherapy. So psychotherapy is a treatment of choice for these things. They can also respond to medications. And the general treatment sequence for things like panic disorder is psychotherapy first and then moving on to SSRIs or SNRIs like-- SSRIs like Prozac. SNRIs like Effexor.

Same thing with social phobia. Moving from psychotherapy to the medications. Now, benzodiazepines are relatively contraindicated in medication treatment for opioid use disorder. There's about a two-times risk of all-cause mortality if you have somebody in buprenorphine treatment and they're also

being prescribed a benzodiazepine. Now, this risk is not the same with naltrexone necessarily, but we don't really have good long time date for people on maintenance naltrexone. Other antidepressants and benzodiazepines will increase their mortality. And avoid the monoamine oxidase inhibitors in medication treatment for opioid use disorder because there's a risk of serotonin syndrome. The monoamine oxidase inhibitors are used so rarely nowadays anyways so it may not be that much of an issue.

Generalized anxiety disorder is an anxiety disorder where people worry all the time. They're fretful, they're tense. They can be irritable. Psychotherapy, again, is the treatment of choice and then medication. All of these medications have come efficacy. And here's a general suggested treatment sequence for people with generalized anxiety disorder. Psychotherapy and then moving on to different medications in a stepwise spectrum. Hydroxyzine actually has pretty good evidence for treating generalized anxiety disorder. Again, avoid the benzodiazepines in medication treatment for opioid use disorder.

And there is some interesting evidence that came out that Lyrica or pregabalin was associated with a three-times increased risk of overdose death in people who were on medication therapy for opioid use disorder so that's something, to take with caution, so I'd only use Lyrica with caution on medication therapy for opioid use disorder. So co-occurring PTSD, psychotherapy, again, is the treatment of choice. There's various psychotherapies that can work for treating PTSD like cognitive behavioral therapy. PE is prolonged exposure. EMDR is eye movement desensitization reprocessing. And SS is seeking safety. There are positive trials for prolonged exposure for PTSD and methadone maintenance therapy and CBT for PTSD and buprenorphine maintenance therapy also reduces positive urines.

So there's some good evidence that treating PTSD with psychotherapy in the context of opioid replacement therapy can help both PTSD and help the opioid replacement therapy work better. Medication treatments for PTSD, prazosin can reduce nightmares and hyperarousal associated with PTSD, but it's only been studied as augmentation in other PTSD treatments. And the general treatment sequence for PTSD starts off with psychotherapy and then moves through the similar kinds of agents we were talking about before. SSRIs, SNRIs, and then ultimately TCAs if these other things don't do it.

Now, insomnia occurs quite frequently in opioid replacement therapy. About one out of five patients on buprenorphine maintenance therapy and up to 85% of patients on methadone maintenance therapy. Many people with buprenorphine maintenance can have central sleep apnea or nocturnal hypoxemia. And the same thing with methadone maintenance, many people can have central sleep apnea. And so there's no randomized clinical trials examining insomnia treatment in buprenorphine maintenance therapy. Keep in mind that medicines like Ambien and Lunesta and temazepam and so on probably will increase risk of accidental overdose death. There are some clinical trials looking at insomnia treatment in methadone maintenance.

So cognitive behavioral therapy for insomnia appears to be effective there. And there's some evidence for acupuncture and some evidence for a GABA-ergic Chinese herb. One of the strongest treatments for insomnia in general is just cognitive behavioral therapy for insomnia, and it certainly doesn't have a risk of accidental overdose death so it's a really nice thing to sort of choose first for insomnia in your

patients who are on buprenorphine or methadone maintenance. So when you're treating insomnia, the first thing to do when you're thinking about people who have un-refreshing sleep or they're really tired the next day and their on opioid replacement therapy, screen them for sleep disordered breathing and treat that.

So ask them if they snore, ask them if they stop breathing or wake up gasping for air, or if their bed partner notices them stopping breathing and waking up gasping for air. Assess them for excessive daytime sleepiness. And if these things are present then it's a good idea to refer them for a sleep study and to treat whatever apnea that they might have. CBT-I or cognitive behavioral therapy for insomnia involves these ingredients. Stimulus control means learning to associate the bed only with sleep or sex as opposed to associating the bed with, oh, let me go watch a movie, or I'm gonna go play video games in bed. Sleep restriction meaning only spending time in bed that's commensurate with the time that somebody sleeps. This can be difficult at first, but then it builds up a sleep drive and people get more sleepy so then they could end up sleeping longer. Sleep hygiene just means arranging your environment so that it's conducive to sleep as opposed to prohibitive of sleep.

So limiting noise, limiting light, keeping things relatively cool in the room where you're sleeping, not drinking too much water right before you go to sleep because that'll make you have to wake up and pee, not drinking caffeine after a certain period of time, usually like afternoon, not having bright light shining in your face like a television in the bedroom. And then training people in relaxation, how to calm their minds, how to calm their bodies. And then cognitive restructuring just means many people with insomnia catastrophize about the insomnia. I can't sleep tonight, oh my god, I'm gonna have a terrible day tomorrow. This is gonna be awful. And then the next night they're like I have to sleep.

Restructuring is like, well, you know, you're actually are gonna function all right tomorrow. And, yeah, you'll be tired, but you'll get through your day. And then don't try to force yourself to sleep. And these things work in clinical trials in patients with just insomnia. CBT-I appears to work better than Ambien so it's a really strong treatment effect. Medication treatments that have some evidence for treating insomnia, and then also don't have that increased risk of overdose death. Things like doxepin, low-dose doxepin. Ramelteon is Rozerem, it's a melatonin receptor agonist. Trazodone or hydroxyzine, which works by blocking serotonin type two receptors.

And then melatonin you can use as a pretty gentle thing. And then caution with the z-drugs because there's a 1.6 times risk of overdose death in people who are on these.

So just in summary, psychiatric disorders are highly common in people with opioid use disorder. Psychiatric disorders and opioid use disorder reciprocally increase the risk of each other. There's limited direct literature on psychiatric disorders treatment and opioid use disorder with or without medication therapy. So the general suggestion, stabilize the opioid use disorder using medication therapy. Select psychotherapy as a first-line treatment in things like major depression, anxiety disorders, PTSD and insomnia, if you have psychotherapy available to you. And then caution with the medications like pregabalin, the zolpidem, eszopiclone drugs. Avoid benzodiazepines, and then if psychotherapy is either not available or if it's something that the patient is unable to tolerate or unwilling to participate in, use

evidence-based treatment for that disorder, for the specific depressive disorder or the specific anxiety disorder for PTSD with your-- And that is that.