Key:

H = Hanna Ortiz

J = Dr. Jones

H: Dr. Jones, thank you for joining us for this interview. Your expertise and experience working with FDA, SAMHSA and now CDC is truly impeccable and beneficial to our topic. Let's begin with definitions. Judges might hear both the terms "MAT" and "MOUD." Can you explain these terms, and how they differ?

J: Well, Medication Assisted Treatment, or MAT, has been the term that's been used for about the last 10 years or so. And it's intended to encompass the use of medications – methadone, buprenorphine or naltrexone, in combination with psychosocial services, so things like treatment, cognitive behavioral therapy, non-medication treatments. More recently, the term Medications for Opioid Use Disorder Treatment, or MOUD, has taken preference in the field. And I think part of that is because individuals felt that the use of the term Medication Assisted Treatment de-emphasized the important role of medications, and that under use of the term MOUD, medications are really the central part of treatment along with ancillary psychosocial services, but really focusing in on the important role of medications.

H: You have mentioned methadone, naltrexone and buprenorphine. Can you explain how each of them works?

J: Methadone has been the primary medication used for opioid use disorder treatment for over 40 years. Methadone is what is called an opioid "agonist." So, it binds to opioid receptors in the brain in the same way that heroin or oxycodone or fentanyl bind to receptors in the brain. And when it binds, it essentially stops the craving or withdrawal symptoms, so that individuals feel normal. And methadone acts more slowly in the body than, say, something like heroin or fentanyl, where you get a rush from the drug very quickly, because the drug gets into the brain and has its effects, whereas methadone is slower to getting into the brain. So that's an agonist. It's a full agonist, meaning that it fully activates the opioid receptors in the brain.

Buprenorphine is a newer, synthetic opioid that was approved in 2002, and it is called a "partial agonist." So, it binds to opioid receptors like methadone does, but it does not fully activate the receptor. And the main difference – it still works in the same ways of

reducing craving and withdrawal symptoms, but the main difference is that if you continue to give higher doses of buprenorphine, you're not going to get any greater effect. So, it has a better safety profile, where symptoms like respiratory depression, which typically is what causes an overdose death, tend to just max out at some point of the dose, and you're not going to get a greater respiratory depressant effect.

Naltrexone works quite differently. Naltrexone is an antagonist, meaning that it binds to the opioid receptors, but it blocks other substances, like heroin or fentanyl or oxycodone, from activating the opioid receptors. So, it doesn't reduce craving or withdrawal symptoms in the same way that methadone or buprenorphine does, it simply blocks the effect of other opioids that might be taken.

H: So, these are the main treatment options. But when should the treatment itself start? And are there any risks associated with going for treatment?

J: Certainly, we know that the sooner we can start treatment, the better for individuals. And that can take many different forms. Medications are typically intended for people who have moderate to severe opioid use disorder, and that's based on a series of criteria that a clinician would go through with a patient, looking at their opioid use history and the consequences of their use. So that's typically when medications would be started. But the sooner you can identify an individual, get them into treatment, we certainly know that the chances of reducing overdose, reducing infectious disease transmission associated with opioid use, reducing recidivism, crime involved with that -- it certainly is much better.

H: Now let's talk about the effectiveness of medication assisted treatments.

J: MAT is the most effective treatment that we have for opioid use disorder. We have a series of very robust studies that indicate that when medications are given, outcomes are much better than any other treatment that's provided, any non-medication treatment, or abstinence-based treatment.

H: It sounds promising. But is there a general support for MAT within the healthcare and research communities? Also, what would you say to critics who believe MAT is just substituting use of one controlled substance with another?

J: The dosing for methadone and buprenorphine is done very carefully. The goal of treatment is to essentially have the person functioning as they normally would. They're not getting high from the drug, it's typically dosed just once a day, whereas someone's using heroin multiple times per day. And they have sort of the ups and downs of the effect of the medication, whereas with methadone and buprenorphine as agonist, you're essentially getting to the right dose where you don't have withdrawal symptoms, you don't have craving. And people are leading their lives as we would want them to do. And the evidence is just incredibly strong for the benefit of reducing overdose risk, reducing opioid use, reducing infectious disease transmission, reducing recidivism. And we don't have individuals who are getting high. That's not the goal. The goal is recovery and for people to just lead normal lives. And that's what's accomplished by the thoughtful and careful use of these medications.

H: One of the treatments you've mentioned, methadone, has been subject to extensive regulation. Can you explain some of the laws related to the use of controlled substances in treatment?

J: So, each of the medications have a different regulatory paradigm, or oversight, under the Controlled Substances Act. So, methadone has been the longest experience that we have with medications, and it can only be obtained through federally regulated opioid treatment programs, historically referred to as methadone programs, or methadone maintenance programs. And those are overseen and regulated by the Substance Abuse and Mental Health Services Administration, a sister agency of CDC. And methadone is typically, an individual would come to the clinic every day for the dose, and the dose is observed. As people progress and have more time under their belt in the program, they can get doses to take home, so they don't have to come every day. But that is the only way that you can get methadone. You can't go to your doctor's office, your primary care doctor, and get methadone for addiction treatment.

When the law changed under DATA 2000, that essentially created an opportunity for certain medications to be used in an office-based setting. So, you could get something not in an opioid treatment program. And that's really where buprenorphine comes into play. So, buprenorphine is the only product that's approved for addiction treatment that is a controlled substance that can be used in the office-based setting. It does have its own oversight; clinicians who have a waiver -- you have to get a special waiver to

prescribe buprenorphine -- clinicians who have that waiver can treat only a limited number of patients. So initially, you can treat 30 patients. After a year you can request to go to 100, and then there are certain requirements for certain physicians to be able to get up to 275 patients at a time. But that is still part of the oversight and managing the number of patients that can be prescribed buprenorphine at any one time.

Because naltrexone is not a drug of abuse, it's an antagonist, it blocks the opioid receptor, essentially any provider, within their scope of practice, can provide that medication for people with opioid use disorder, so long as it's clinically appropriate for that individual. So, there's no restrictions for use of naltrexone in an opioid treatment program or getting a special waiver like you have to for buprenorphine.

I think one thing that's important to note about opioid treatment programs is that they can provide all three medications. They're the only clinic or facility that can provide all three medications. And they can provide those medications, like buprenorphine, without the same patient limits that providers in the office-based, or outpatient-based setting, are constrained to.

H: You just mentioned that for some of the medical assisted treatments, people need to make daily visits to a special medical facility. This may be a good bridge to a conversation about guidance, or criteria, for opioid treatment programs.

J: So that applies specifically to the use of methadone and buprenorphine and opioid treatment programs. And there are guidelines under the federal regulations and guidance from SAMHSA around opioid treatment programs that lay out the criteria for when a patient doesn't have to come every day. But there is no specific stop point, as far as how long someone should be on treatment. That is typically if they're doing well and they want to stay on treatment, we should encourage them to stay on treatment. We know that when people discontinue treatment, especially in the short run, that's when people tend to have relapse or overdose -- those types of things.

H: It's been said that medication is best in a combination with counseling and behavioral therapies. Why is it so important?

J: One thing that's important to note is that medications, by far, are the most effective treatment. But we know that there are other issues that need to be addressed among individuals who have opioid use disorder. And providing clinically appropriate therapy or other services can help improve outcomes for individuals in combination with medications. It's also important to note that most individuals with an opioid use

disorder also use other substances, and we don't have medications for other substances, like cocaine or methamphetamine, that would benefit from cognitive behavioral therapy, or other psychosocial therapies. We also see high rates of co-occurring mental illness among individuals with opioid use disorder. Again, there are medications to treat serious mental illness or other mental illness, but also therapy-based approaches that can be beneficial to those individuals. So, bringing along those psychosocial services really helps to address the holistic needs of those patients.

H: As you mentioned earlier, medication assisted treatment has existed for more than 40 years. How has its use changed over time?

J: Well, for many years, methadone was the only game in town. If you wanted to have a medication to treat opioid addiction or opioid use disorder, you had to go to an opioid treatment program, and those were typically located in urban areas. So, if you were in a rural area, or a suburban area, you didn't have medication options for many years. Or you had to drive a really long distance to get to an opioid treatment program. Under DATA 2000, which is the law that allowed physicians initially -- now nurse practitioners and physician assistants -- to obtain a special waiver to prescribe drugs like buprenorphine in the office-based setting, that really changed the paradigm of how people could access addiction treatment. And Suboxone, or the brand name of buprenorphine, that was first approved in late 2002 is the drug that is applicable to that particular waiver at this point in time. So that opened up federally qualified health centers, that opened up primary care doctors, opened up emergency departments to be places where medications could be offered.

Most recently, extended release naltrexone was approved in 2010 by FDA for the treatment of opioid dependence. So that provided another option for individuals who maybe were not interested in something like methadone or buprenorphine, or agonist-based treatment; it provided another option for those individuals. And what we've seen for all three medications is that the number of individuals who are receiving those medications has been going up over time. And we see that even in opioid treatment programs, they are not only offering just methadone, they also offer -- in some cases, not all cases -- buprenorphine, and to a lesser extent, naltrexone, recognizing that we really need to meet individuals where they are. They may have a particular preference, or they may have had prior experience with one particular drug or another, and they may not be interested in that. And we want them, if they're making that important step forward to getting treatment, we want to be able to meet their needs as best we can.

H: Now let's talk about very specific demographics: pregnant women. Numerous CDC and SAMHSA reports show that the number of pregnant women with opioid use disorder exponentially increased within the last 20 years. And if in 1999 we were talking 350 women, in 2014 that number already went up to almost 6100 women. What are some concerns regarding treatment for pregnant women with opioid use disorder?

J: Well, we know that unaddressed opioid use disorder among pregnancy can have severe consequences for mom and baby. So, treatment is, by far, better than not getting treatment. And methadone and buprenorphine are the primary drugs that would be used among pregnant women. Naltrexone, because of certain issues around antagonist in the particular drug itself, is not typically used. I would say more recently, one of the concerns that has come up is neonates who are born physically dependent on opioids, you know, abstinence syndrome, or, you know, opioid withdrawal syndrome is what it's commonly termed. And there is certainly a large group of pediatricians and obstetricians, gynecologists, and others in the field who are concerned about the effects on the developing fetus, and on the neonate. But we know, by far, that treatment during pregnancy is much better than unaddressed addiction treatment.

H: How do you feel about alternative treatment options available for opioid use disorder?

J: Medications are really considered the standard of care, but there are other non-medication-based treatments. Typically, we would want to see those in conjunction with medications. But there are things like 12-step programs, abstinence-based programs that have been around for many, many years. We don't see the same success rates that we see, with non-medication treatments that we see for medications like methadone, buprenorphine or naltrexone. But those are available, and people do take advantage of those. I think where we're trying to move the field is to make medications a central component of treatment.

H: Now please walk me through the opioid treatment programs, and the steps the opioid treatment program sponsors must take to become certified.

J: Opioid treatment programs are regulated by the Substance Abuse and Mental Health Services Administration. There are specific criteria that have to be met at the federal level, and then often states, or even some local jurisdictions have their own licensing and credentialing for opioid treatment programs. But they are heavily regulated. They

provide tremendous amount of structure for individuals who are coming into treatment. They have requirements for certain types of patients to see, and what timeframe they have to see them. They can use methadone, buprenorphine, naltrexone -- they really are the only place that can provide all three medications that are approved. But they are limited in number, in geography around the country. Historically they have been mostly in urban areas, although in more recent years, we have seen opioid treatment programs opening up in more rural and suburban areas to address the unmet need that exists there.

H: What are the some of the challenges in implementing MAT programs in criminal justice settings?

J: One of the biggest challenges is the theoretical concerns about substituting one drug for another; sort of stigma that exists. You know, there's sort of a fundamental belief that it should be abstinence or antagonist-only treatment. And I think there has been some inroads in getting extended release naltrexone, naltrexone products into the criminal justice setting, more hesitancy with agonist-based treatments like methadone and buprenorphine. I think there is the real concern of diversion within the criminal justice system. But we do have models that have shown great success in reducing outcomes among incarcerated populations, that can be done in a thoughtful way that reduces diversion. I think Rhode Island is a very good experience, where they were able to offer all three medications, so patient had choice in the Rhode Island criminal justice system. But what they found is that among recently-incarcerated individuals, the expansion of medication assisted treatment among that population resulted in a 61 percent decline in overdose deaths, which actually translated to a 12 percent decline in overdose deaths at the state level -- so really remarkable changes in our primary outcome of interest, reducing overdose deaths, by expansion in criminal justice.

I think it's really important to understand that the criminal justice population is one of the highest-risk populations. And so, we have to address these issues within the walls, as well as at that critical point in time where people are re-entering into their community. We know that within the first couple of weeks of release, individuals are at astronomical risk for overdose death. Giving medications prior to release, and having people connected, intentionally linked and connected, to services at re-entry can substantially reduce that overdose risk.

H: Is there anything else judges need to know about MAT and related treatment options?

J: I think a key thing to know is that medication treatment works. We have decades of experience demonstrating the effectiveness of medication treatment for opioid use disorder. So not only do the medications work, but recovery is possible. I think we all have been so overloaded with opioid overdose deaths increasing in all the people who have addiction, that we lose sight of sort of the power of recovery. So, I think that judges have such an important role in setting the tone of what's the social norm. Medications are the social norm, or should be the social norm, and judges have an important role in advancing that and improving the lives of individuals with opioid use disorder.