# NAMI Ask the Expert:
## A Research Update on Psychedelic Mental Health Treatments
July 25, 2024

Featuring: Dimitri Perivoliotis, Ph.D.

**Katie Harris** (00:00:00):

That, I'm going to hand it over to NAMI's Chief Medical Officer, Ken Duckworth.

**Ken Duckworth, MD** (00:00:06):

Thanks Katie. And thanks for all you do. We're going to have an interesting conversation today with a friend of NAMI. Dmitri has presented a couple times at NAMI conventions in-person in Denver, extremely well-received and oversubscribed and online.

(00:00:28):

Dimitri has an interesting Greek name and he's going to tell you a little bit about the connection between being Greek and the field of psychedelics. He is a clinical professor of the University of California San Diego Healthcare System. He works primarily with veterans, with a particular interest on veterans with trauma, and he has a lot of clinical experience in this area.

(00:00:54):

He has a lot of slides and a lot of information. Stay with it. We're going to get to your questions at the end of his presentation. This is a complicated area and obviously there's a lot of need for new treatments in the mental health space. So, Dr. P. is our link to some of the best thinking in this field. So, thank you everyone, and I'll see you back at the Q&A. Thank you, Dmitri.

**Dimitri Perivoliotis, Ph.D.** (00:01:27):

You're so welcome. Thank you, Ken. Apologies. I accidentally unshared my slides. I'm going to bring them back up and hopefully they will show up. Let's see here. Okay. Great. Can everybody see my slides?

**Ken Duckworth, MD** (00:01:45):

There's a handsome lad on the right and today's expert. That's the slide I'm seeing.

**Dimitri Perivoliotis, Ph.D.** (00:01:51):

Oh, okay. Great, great, great. Okay. Good, good. Let me try one more thing. There we go. Okay. Now, it's working on my end, too. Well, thank you for having me. It's an honor to be here. I really appreciate the invitation to talk about something that's extremely interesting and an important topic, I think, which is psychedelics for the treatment of mental illness.

(00:02:10):

But before we get into all the information, so much of it today, I want to start off with some stories from people who've actually participated in these treatments. So, this first one is from a participant in an MDMA-assisted therapy for PTSD study. He said, "I keep getting the message from the medicine. Trust me, when I try to think it doesn't work out. But when I just let the waves of fear and anxiety come up, it feels like the medicine is going in and getting them, bringing them up and then they dissipate."

**Dimitri Perivoliotis, Ph.D.** (00:02:43):

This next one from a veteran that I've been working with at our ketamine clinic here at the VA in San Diego, who kindly allowed me to share this quote of hers, she's somebody with treatment-resistant chronic depression and PTSD in ketamine treatment. She said, "I felt my ancestors' presence saying, you're not alone. You're protected and loved."

(00:03:05):

And to counterbalance that a little bit, this is a quote from an attendee at the NAMI Con in 2021 where I presented also on psychedelics. "I experienced terrible out of body experiences with ketamine despite being told I would totally be in control of my mind and body, not so and no decrease in depression, $2,700 later."

(00:03:28):

So, I think these quotes are good because they give you a sense of the range of experiences that are possible with psychedelics ranging from the transformative and therapeutic to the heroin, and that gives you a feel for a little bit of the potential and the power of these medicines.

(00:03:47):

So, before we get into them though, some basic facts. As we all know, I think unfortunately, mental illnesses rising around the world. Suicide is currently the 11th leading cause of death in the United States. A use of antidepressants has quadrupled between the '90s and early 2000s. But unfortunately, they've not really noticeably reduced the prevalence of depression in this country.

(00:04:12):

And although they work for many people, the larger view studies suggests that the effects are not really overall that strong and about over a third of people have an inadequate response to them. It's probably safe to say there hasn't been a major breakthrough in psychiatry for decades. The last medication to be approved for PTSD, for example, was about 25 years ago.

(00:04:35):

And we have some effective psychotherapies that are evidence-based for conditions like depression and PTSD. But there's challenges there too. For example, we have a high dropout rate in those therapies for PTSD, and even though people's symptoms might reduce, there isn't always a translation to improve functioning quality of life.

(00:04:55):

So, I think it's a sobering state of affairs and it's time for us to think outside the box perhaps, and I think we're past due for a breakthrough. And the question on everyone's minds is, could psychedelics be part of that?

(00:05:11):

So, what are psychedelics, first of all? So, they have been defined in many ways. The word comes from a Greek word, as Ken hint it, meaning mind manifesting. They've been defined as powerful psychoactive substances that alter perception and mood and affect numerous cognitive processes.

**Dimitri Perivoliotis, Ph.D.** (00:05:32):

And there is a range of psychedelics. On the left here, we have what we call classical psychedelics. These are grouped into this category because they all primarily act on a specific type of serotonin receptor. And on the right, and these are things like psilocybin, LSD, mescaline, DMT. And on the right, we have the non-classical ones that act in a somewhat different fashion like MDMA and ketamine.

(00:05:58):

But for the purposes of this talk and a lot of the research that you see out there, we're going to be grouping these all together as psychedelics. MDMA specifically to put it to completely oversimplify, is I would say a serotonin releaser, but it also works on hormones and other things. And ketamine is a dissociative anesthetic drug that acts on the NMDA system primarily, but a lot more complicated than that.

(00:06:25):

So, what do we know about psychedelic use? So, we know that in terms of the ... most of our data are on classic psychedelics like LSD and psilocybin. According to population studies, 13% of people report lifetime use of these psychedelics. The survey suggests that they're generally safe and have a low addiction potential.

(00:06:46):

You could see on this slide here, the relative harm caused by different drugs with the dark portion of the line being harm to others and the light being the harm to the user. So, usually, classic psychedelics like LSD, mushrooms tend to fall near the lower end of the risk scale. And some of our other psychedelics are a little bit higher, as you could see, ecstasy is a street name for MDMA, and we see ketamine on there as well.

(00:07:14):

Interestingly, in terms of recreational use of classic psychedelics specifically, there's been a couple of large-scale surveys looking asking over 100,000 people about their mental health history. And they found that use of those classic psychedelics wasn't linked to long-term development of serious problems like manias and psychosis or mental health treatment. That's not to say that they don't have any harm or any risk of course, but just to put things into context a bit, I'll be getting more into the risks of the specific treatments in a minute.

(00:07:47):

So, what are psychedelic experiences? These are a little bit hard to define and there's no one agreed upon way to define them. But the way I like to educate the veterans in our clinic here in San Diego, I show them a diagram much like this, and I tell them the psychedelic experience can show up in many ways. It could show up in your body, your senses, your thoughts, your emotions in how you relate to people in the room, and also in a spiritual way, too.

(00:08:18):

Some of the common phenomena that we see across the board are the intensification of perception and emotions. If you have something you haven't been fully processing like grief or trauma or anxiety or whatnot, it could bring that to the surface. Imagery, people will see textures, shapes, sometimes picture somebody in their life, various kinds of imagery. They pretty reliably change your perception, how you're experiencing things.

**Dimitri Perivoliotis, Ph.D.** (00:08:49):

They create what we call a non-ordinary state of consciousness or an altered state of consciousness. And that could be how you perceive yourself, your body, the environment around you. They may slow your sense of time. In some cases, they could induce the sense of unity with your surroundings, with nature or the universe, and might even lead to what we call mystical experiences. And these are things like having a sense of unity with all things, transcending time and space, having these deep profound insights into reality, a sense of awe, maybe even touching the divine, that kind of thing.

(00:09:28):

And interestingly, mystical experiences have gotten a lot of attention in the research because at least in the psilocybin research, they've been linked to better outcome. In other words, when people have those, they tend to get a better response of the treatment. Somewhat specific aspects of the other to the non-classical ones like MDMA, for example, can induce a sense of empathy. It's called an empathogen for that reason.

(00:09:54):

It can promote a feeling of connectedness to the people around you wanting to be with people, wanting to share with them, share your emotions, especially MDMA is also particularly known for being able to dampen the fear response, although some of the other psychedelics have as well. But because of that especially good effect of MDMA on that, it lends itself to trauma work as I'm going to explain in a minute.

(00:10:20):

And ketamine, as I mentioned, is a dissociative anesthetic drug. And dissociation essentially means disconnection from your environment and your body. So, it leads to things like a sense of floating, an out of body experience, a dream-like state. You might feel like your body is heavy or you might not feel it at all in larger effects, and that's a somewhat unique property of ketamine.

(00:10:44):

So, how does psychedelics work? This could be an entire webinar on its own, probably the hardest slide I had to put together, because the answer is it's pretty complicated. So, I'm going to try to my best to summarize it here. And we're still learning about them. So, they seem to work on different levels. One is the neurobiological. So, they affect neurotransmitters. Some of them affect hormones as well in the brain.

(00:11:06):

Most of them are known to stimulate neuroplasticity, which means increasing the growth and density of the cells of our nervous system in our brain, creating new neural pathways that we believe have been damaged by things like chronic depression and PTSD. They also alter the way the brain communicates within itself.

(00:11:27):

And more recent research is suggesting they seem to, some of them anyway, seem to reopen critical learning periods, which basically means putting the brain in this temporary state where it's more open to change and learning and it's more flexible like we are when we're younger and we're taking everything in and shaping how we think about the world. And there's also an anti-inflammatory effect too.

**Dimitri Perivoliotis, Ph.D.** (00:11:52):

Psychologically, which is my domain as a clinical psychologist, I think this is really fascinating. They tend to do various things. One is they can loosen rigid thinking patterns and get people out of ruts in their thinking. Part of that is in creating some insights. A lot of times with the veterans I work with, they talk about this phenomenon of almost zooming out from their problem. They come in really focused on the depression and everything that's wrong in one aspect of their experience, like the trauma for example.

(00:12:25):

But then with the psychedelic work, they start to expand their view and start to see the whole context and also see the people who've been around them all along, like, "I now appreciate my wife. I realize I've disconnected from my son and I need to spend more time with him." So, there's this beautiful zooming out that happens.

(00:12:42):

One thing they seem to do really reliably is bring unresolved traumas to the surface. And you have to be really prepared for that. There's a great potential there, but also, it's important to be prepared if you're somebody going into this therapy that that might happen. We talked about the fear dampening response that MDMA is particularly known for, but others can do that as well.

(00:13:03):

And there's this interesting effect that some of them have, what I would say changing the response to trauma memories. We call this memory reconsolidation, where the trauma memory can come up and be laid back down in the brain in a different way, in a way that doesn't have so much pain and emotion associated with it. And they can also, in some cases in the right context, trigger positive emotions like gratitude, contentment, peace, love, and that some of our folks in these therapies so desperately need and haven't felt in a long time.

(00:13:36):

I like to think that they can also, especially for some of them, like MDMA in particular because of its social element work on a relational level to the work that we do in the room with people in psychedelic therapy is very deep and can be quite intense. So, I think there's a beautiful opportunity there for corrective healing to take place. And if it's a group therapy, which some people are looking into, you have a powerful opportunity for people to connect with each other and during their experience. And that can be a particularly useful thing we think for veterans because of their natural comradery and support of each other.

(00:14:14):

So, one of my colleagues, for example, Chris Stauffer in Oregon is doing an interesting MDMA-assisted study for PTSD in veterans in a group format, which I am really excited to see what comes out of that. And finally, as I touched on earlier, they can also work on the spiritual or existential level, especially if people have these mystical experiences that I talked about.

(00:14:36):

One veteran that I work with, for example, talked about how when is at ketamine was put to the highest dose, he had these near-death experiences that were terrifying, but he would come out and say, "I realize I was alive and I realized how lucky I am to be alive and how lucky I am to have my wife and my son." So, it is a good example of the duality of psychedelics. They could be harrowing, but also transformative at the same time. And that's where I think the importance of the therapy and having support becomes really critical.

**Dimitri Perivoliotis, Ph.D.** (00:15:10):

So, just to put a little bit of a metaphor to it, if you think about if you've ever lived in snow, I grew up in Chicago, you know that when you go over snow repeatedly driving or skiing or biking or whatever it is, hopefully you're not biking on snow, you create these ruts and it's really hard to get out of the ruts. And we get this way with our thinking too, especially when we're looking at chronic depression, PTSD.

(00:15:31):

So, if you imagine this snowy path inside of a snow globe, this is Michael Pollan's metaphor with the snow globe. You shake the snow globe, there's temporary chaos, but then the snow falls and clears the path and you get this even layering of snow. And the translation of that here is it gives the mind the ability to get out of those ruts if you so choose to take advantage of that ability. So, that's a really critical thing that I'm going to be touching on in a bit in a minute. How do we actually take advantage of this increased of this opportunity and this window of opportunity for the brain to be able to change?

(00:16:15):

So, psychedelic therapies in general have three phases. The preparation phase involves getting the person prepared so that they have fully informed consent, they know what they're getting into, they feel as safe as possible. You start a connection with the person too, so they feel safe with you. We talk about various things like setting an intention for what you'd like to get out of the experience.

(00:16:40):

We coach them on things that we think will make for an optimal response to the therapy. And then in the medicine session, we administer the psychedelic. And integration sessions happen after and between the medicine sessions and those are really important. Those are regular therapy sessions where the opportunity is to translate what came up in the psychedelic session into changes in day-to-day living and lifestyle changes, and also to make sense of what could be a really big experience that just happened.

(00:17:14):

Some basic concepts, and these are things that we want to educate people about in the preparation and throughout is that are tend to be common across psychedelic therapies are the following. One is that we have an innate drive toward healing. So, just like the metaphor we use is just like if we have a cut, if we clean the cut and create the right conditions for healing, it's going to want to naturally go in that direction. The same for our psyche and our heart. And psychedelics are thought to be able to create that condition. And also, the clinical supportive setting with a therapist, or facilitator too.

(00:17:51):

I love that because I'm a recovery-oriented psychologist, so that's implicitly recovery-oriented. And so, that really resonates with me. We talk about the importance of your mindset and the setting. What are you bringing into the room? Are you shoehorning this in between in a busy workday? Hopefully not because that might shape your experience. Are you mentally prepared to do this? Are you taking some time to settle, to ground yourself beforehand? And then what is your setting? Do you feel comfortable in the environment? Is there anything you can bring?

**Dimitri Perivoliotis, Ph.D.** (00:18:22):

What's your music going to be like? Music is a very important part of this process. Will you maybe wear eye shades? We talked about intention setting. Inner direction, we really tend to encourage people to go inward. This is different than traditional therapies, at least the ones I've been trained in where I have an agenda of things I'm going to teach you and things I'm going to ask you to do. A lot of that is the reverse. We trusting what's coming up from within you.

(00:18:50):

And part of that is leaning in to anything that comes up, including very difficult things that might come up. So, there's a lot of mindfulness and presence and surrender and being open, and that's very, very hard. It's a tall ask, especially with our folks with trauma to surrender to something like this in a vulnerable state.

(00:19:10):

I love this quote that one of my veterans said when I was explaining this to him. "The mind is like a parachute. It works best when it's open." I think it's perfect. And of course, we really want to emphasize the importance of the integration and the work that's done between the sessions. It's so, so critical.

(00:19:28):

So, as you may be guessing already, this is very recovery-oriented, I think. Psychedelic-assisted therapy is very consistent with the recovery movement. We see it's person-driven, inner healer, inner direction, trusting what's coming from inside. It's holistic. They're complicated medicines. They work on different levels. And part of that, I think, is you can incorporate different disciplines into the process.

(00:19:52):

For example, we have a collaboration with rec therapy. Incredibly helpful to us. We have an art therapist coming to work with our veterans in their ketamine sessions. We're working to get chaplaincy involved as well. Peer support can have a critical role in this too. My colleague that I mentioned in Oregon is involving peer support specialists as part of the therapeutic process for the veterans.

(00:20:18):

Obviously, it's relational as I mentioned. Culture is so important. We have to be respectful of cultural factors that the relationship and the energy in the room between the therapists and the participant tend to be amplified in these states. So, anything, they have to feel really safe. And if there's a difference here in a power differential or difference in culture or ethnicity that can come to the surface. There's just so many issues about culture you have to be mindful, the music that you use, the decor of the room and so on.

(00:20:51):

So, obviously, trauma-informed and strengths-based, I believe. We really tap into the ... I've seen many times we're tapping into the person's best self. So, sure, a lot of pain and difficult material can come out of these sessions, but sometimes really lightness comes out, too. I have a veteran who's been doing really hard work in ketamine treatment for his PTSD and depression and suicidal thinking and he's made a lot of progress.

**Dimitri Perivoliotis, Ph.D.** (00:21:20):

And the other day, because he's shedding all that, he started talking about his interests. His interests are in fashion and he'd like to start a YouTube show. And we talked about last few minutes of the session was, "What would that be like and how fun that would be?" And I saw his best self come out. You see the potential of people come out. It's a pretty great thing to witness and that's very recovery-oriented care, I think.

(00:21:46):

So, we're going to go into some of the specific therapies next starting with MDMA-assisted therapy for PTSD. I'm covering just the three that are at the top of the line in terms of the closeness to potential approval or furthest along in the research, I would say. So, I'm not going to cover all psychedelic therapies today, there's just too many. But these will give you a good feeling, I think. I hope.

(00:22:09):

So, MDMA-assisted therapy for PTSD was developed by the Multidisciplinary Association for Psychedelic Studies or MAPS and research by its Public Benefit Corporation, which is now called Lykos Therapeutics. I actually worked as a contractor for this organization for about five years. It's one of the things that really pivot, changed, helped me to pivot my career from psychosis where I worked primarily for much of my career into psychedelic therapy.

(00:22:42):

And basically, what we did as part of that endeavor is myself and a team of others would view video recordings of sessions of these MDMA-assisted therapy for PTSD sessions from their phase three clinical trial studies, hot off the presses and would rate the therapist on how well they adhered to the protocol to the therapy manual as a sort of a consistencies measure and quality control. And that feedback would go to the supervisors. So, I'm really grateful for that experience. I learned a lot about this.

(00:23:16):

And now, full circle, I'm serving as one of the therapists on our MDMA-assisted CBCT study here at the VA, which is a Cognitive-Behavioral Conjoint Therapy, which is an established evidence-based couples intervention for people with PTSD and their partners. And we're testing to see if MDMA can combine well with that and what happens when you combine those two based on some really promising pilot data from Anne Wagner's group in Canada. But we're trying it in veterans. And we have an MDMA-assisted prolonged exposure therapy study coming soon after that.

(00:23:53):

So, what do we know about this research? Promising findings, I'm sure you've read about them many times in the press that led the FDA to grant this therapy, breakthrough therapy designation, which basically means that the FDA is fast-tracking the development and the review. This typically happens for new treatments. For serious conditions, it seem potentially better than existing treatments. And this means that the FDA collaborates with the organization on the design of the study closely collaborates in order to fast-track its potential or its review with potential outcome of approval. It's not guaranteed, of course.

**Dimitri Perivoliotis, Ph.D.** (00:24:31):

What we have found in this research where they have compared MDMA with a psychotherapy that was specifically developed for the MDMA for PTSD compared to placebo or sugar pill in the same therapy is in the MDMA group, a significant and clinically significant reduction in PTSD symptoms, higher rates of remission and improved or reduced functional impairment. Just to put some numbers on it, they've done two phase three clinical trials.

(00:25:06):

And the last one showed a 71% of people in the MDMA group lost the PTSD diagnosis at the end of the treatment versus 46% in placebo and 48% were in remission versus ... in the MDMA group versus 21% in placebo. So, losing the diagnosis means you no longer meet the criteria, DSM criteria. But a lot of people, and we see this in the VA sometimes when people go through our standard therapies, they might lose the diagnosis, but there's still quite a bit of symptoms going on and they might still be struggling.

(00:25:39):

So, remission is a higher bar. Remission usually means that they've lost the diagnosis and they're very low on the PTSD symptoms. So, that's why you see I think lower percentages there. Some of the previous studies, the phase two studies showed some interesting things, too. They tracked people about a year out and found that the effect persisted.

(00:26:06):

In fact, 11% more had lost their diagnosis at the one-year mark. This I found super interesting. The MDMA group had increased post-traumatic growth after in quality of life compared to the group that just got the therapy. And post-traumatic growth I think is a really fascinating phenomenon. That basically means, as I like to explain it to veterans, your new chapter emerging from the darkness with new growth and new wisdom and having a new direction and tapping into all the positive things that can come as a result of growth, helping others and more self-compassion and so on.

(00:26:47):

One major caveat for this and other psychedelic studies though, is the blinding problem. It's very hard to have a good placebo group in psychedelic studies because it's very obvious whether or not you've taken a psychedelic. So, in these studies, for example, I think this was from the phase three, if I'm not mistaken, about 90% of people correctly guessed that they had MDMA or not. This is a controversial topic.

(00:27:11):

Could that mean that people were influenced by that to self-report greater benefits? One thing to point out about that is the placebo effect tends to be strongest at the end of treatment and fades out over time. So, the organizations pointed out that the fact that people are doing better at follow-up suggests against that. They have some not yet released data from phase three showing that those studies maintain the effect at least six months. So, we'll see. But it's a major caveat.

**Dimitri Perivoliotis, Ph.D.** (00:27:44):

Some risks for these that come out of this work. The first bullet here are the most common adverse events or side effects in the treatment. A lot of these are things you might expect from a stimulant drug. Thankfully they tended to be temporary and mild. However, it is a stimulant drug and it tends to increase heart rate and blood pressure during the session. And the FDA has stated that they're concerned about that. So, they will probably want to look at that data more carefully or get more data on that. I'm assuming.

(00:28:18):

It's trauma therapy, so obviously, there's probably ... It's going to be some kind of distress during the session. And some people experience temporary anxiety after the sessions. Tends to be mild to moderate and tends to decrease over the course of one week after the session. So, you've probably also seen in the press that recently the FDA appointed an advisory committee to advise them on this treatment.

(00:28:46):

So, these advisory committees are periodically appointed. They're panels of experts to provide outside expertise on key decisions to provide guidance to the FDA on things like potential drug approvals. So, the committee had an all-day meeting recently and they had two questions they were tasked with. One was, do the data currently support the effectiveness of this treatment? And second, do the data suggest that the benefits outweigh the risks? And they voted 9 to 2 against the effectiveness question, and 10 to 1 against the benefits outweighing the risks.

(00:29:22):

They were careful to point out. They didn't mean that there's no promise. They said that it has potential and it looks promising, but they cited some problems with the data collection and design that made them skeptical. So, the VA doesn't have to necessarily abide by this. They're going to decide by August 11th, 67% of time they do abide by the committee's recommendations not to approve, but we will soon find out.

(00:29:48):

The concerns of the committee are summarized in this table on the left. And on the right, are Lykos Therapeutics responses, which are detailed on their website if you'd like to read a bit more. But we've talked about the potential unblinding problem. There have been allegations made by a nonprofit about research misconducts, like concealing reports of certain adverse events influencing participants to report in certain ways, that kind of thing.

(00:30:19):

They cited the fact that some people had used MDMA before, something like 20% to 25% of the sample had used in the past 10 years. So, they might be more favorable toward MDMA. There was a lot of talk about the therapy. Now, FDA doesn't usually regulate therapy, so this is an unusual situation. They criticize the therapy for not being standardized enough, at least relative to our traditional psychotherapies.

(00:30:48):

Who's going to regulate the therapy? The concern about therapists acting unethically with people who are in these vulnerable states during the sessions, which unfortunately did happen once and triggered a podcast that you may have seen. And finally, they were concerned that there wasn't enough data looking at potential addiction related phenomena like how euphoric people got when they took the MDMA and also cardiovascular and liver function data.

**Dimitri Perivoliotis, Ph.D.** (00:31:18):

So, Lykos has to summarize, has pointed out the fact that, yes, they acknowledged unblinding can be an issue, but they had independent blinded raters. The effects don't seem too strong and too durable to be explained just by unblinding. They denied the allegations, said the FDA can inspect their data. They pointed out that the FDA has been working with them on the study design for a long time. So, it was a little surprising to get critiques about the study design.

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Also, that people who had used MDMA before did not show significantly different response to those who had. And they pointed to the process I was referring to earlier about the adherence rating as being one of the methods to standardize the treatment and the fact that the outcomes were equivalent across the different sites suggesting that people were delivering the therapy in a standardized consistent fashion.

(00:32:14):

Finally, they acknowledged that therapists, of course, unfortunately, could act unethically. The onus there is on us as therapists, we have an ethical code that we have to follow, but also on licensing board professional societies. But also, that this is a potential risk and if it is approved, a REMS process will be implemented, which is a drug safety program the FDA uses to monitor safety concerns for treatments to measure, do the benefits outweigh the risks? So, therapist misconduct can be tracked there as can potential biological problems like cardiovascular, liver function tests and the collection of those data like the euphoria that I mentioned too.

(00:33:01):

So, moving on to psilocybin therapy for depressions. My picture might look very similar here. What do we know about this? So, this also has been granted breakthrough therapy designation for treatment-resistant depression where it's in phase three trials right now and also for regular or major depressive disorder where it's in phase two.

(00:33:22):

This is Compass Pathways is the main company behind this. And the studies have found basically large rapid effects on depression including treatment-resistant depression better than placebo or controlled groups. And usually, in a one or two psilocybin administration protocol, which is pretty remarkable. The effects in the study so far seem to persist.

(00:33:51):

The follow-up periods range. I've seen three weeks to a year is where the effects have been monitored. You could see on the graph on the bottom, this is the results of the treatment-resistant depression trial, which I'm particularly interested in because that's what we do here at our VA in San Diego and the ketamine clinic. You see that big drop in depression right after the psilocybin session and then the lines track the person over all the way out to 12 weeks.

(00:34:21):

Gray line is the lowest dose, green line is mid-dose, and blue line is the heaviest dose of psilocybin. So, you see a greater effect for the larger doses. One other interesting study in this area was looking at psilocybin versus escitalopram, which is the generic of Lexapro in people with moderate to severe depression. Not a lot of psychedelic studies pit the psychedelic against the traditional antidepressant.

**Dimitri Perivoliotis, Ph.D.** (00:34:48):

So, what they found in essence here was equivalent effects on depression. But the psilocybin group seemed to be better in other things, including ability to cry and feel compassion, intense emotion and pleasure, less drowsiness, possibly better functioning. But the study didn't have enough power, statistical power to determine if these were statistically significant differences. But all the numbers, if you look at the numbers tilted in the direction of psilocybin looking better.

(00:35:22):

These aren't perfect studies either. There's a lot of variability in the design. How many psilocybin sessions happen? What the dosage is? What depression measures are used? How long people are followed up? How much training that their facilitators have had? I should say though, I forgot to mention this, that there is a little bit of a different approach in the psilocybin therapy sessions where in the MDMA sessions, there's a lot of encouragement to go in and out of the experience, go inward with the eye shades and music come out and talk to the therapist, process.

(00:35:52):

In the psilocybin, it's a lot more of an inward experience. Both of them are pretty long six to eight sessions. But there's a lot more emphasis on doing your own work with the facilitator in the room. In fact, a lot of the studies don't even call them therapists. They call them facilitators. So, this is an important distinction there.

(00:36:11):

Risks to psilocybin therapy, the adverse or side effects are common. But mostly, thankfully, are non-serious. You see them on the screen here. However, the treatment-resistant depression study, which was a phase two study, did find a small incidence of serious adverse events. 1% to 5% of people had these suicidal ideation behavior, self-harm, and specifically 3%, something like 3 out of 91 participants had suicidal behavior. Thankfully, no completed attempts.

(00:36:48):

But interesting when you really drill down, those people had not responded to psilocybin. It didn't look like it was helping them and they had previous histories because it was a treatment-resistant depression group. But it's important to monitor suicidality, obviously. And a review a couple of years ago that happened of the psilocybin studies so far as you could see the quote on the screen here came out with a pretty strong endorsement of what seems to be a good safety data on these studies. Generally, well-tolerated when administered in a controlled setting.

(00:37:21):

I can't emphasize that enough that this is very different than recreational use. We're talking about controlled settings that have been very thoughtfully designed with trained facilitators or therapists in a carefully controlled environment and with very limited dosing of a pharmaceutical grade product. That's quite different than recreational use. So, we have to be really careful about that distinction in our minds.

(00:37:50):

Next up, ketamine treatment for treatment-resistant depression. That is something we do here in our clinic in San Diego. That's me and our very kind nursing assistant who is kind enough to take this photo for me. This is an actual kind of what it will often look like in the room when we're doing therapy with folks during their ketamine session.

**Dimitri Perivoliotis, Ph.D.** (00:38:10):

Ketamine is a little bit of an interesting psychedelic for various reasons. In the research, it's one of the things that makes it interesting is that a lot of the early research of it, and still to this day, was done using it by itself as a biological treatment. Unlike psilocybin and MDMA, which is part and parcel with psychotherapy, it's just by itself.

(00:38:35):

So, most of our research is ketamine alone, and that research shows that it leads to rapid, robust, strong antidepressant effects. Anti-suicide effects are pretty strong, too. Not quite as consistent, but they're pretty impressive. Large effects or potency. And people with treatment-resistant depression, about 45% of them, the estimates vary depending on multiple factors like dosing and things respond and about 30% achieve remission during the treatment.

(00:39:09):

However, unfortunately, there's a high rate of relapse once you pull the medicine. So, something like a 55 to 70-ish percent will have relapsed about a month out. So, clearly, it's not a one and out done treatment. And the billion-dollar question in the field is, can we extend the effects of ketamine short of administering it indefinitely? That is one model. You could do maintenance treatment. But that has its risks. I'll talk about in a second.

(00:39:44):

So, one potential there is what about adding psychotherapy makes sense? You have a window of neuroplasticity and all those positive changes that I talked about. You have people with chronic conditions that could really benefit from lifestyle changes and skills training, learning how to regulate their emotions, and they're in a more open amenable space. So, why don't we add psychotherapy?

(00:40:05):

So, ketamine-assisted psychotherapy or KAP has been conducted for many years and has a lot of promising findings, a lot of anecdotal findings, open-label studies, case studies, really rich data suggesting that it's very promising to maximize the effect of ketamine and synergize it. But unfortunately, we don't have much randomized controlled trials. We really need a lot more rigorous research in this area.

(00:40:32):

I could tell you. Here in our VA, we've did some internal program evaluation and we found that ... My colleague, Andrew Bismark, actually did this. That when veterans are in ketamine and we added psychotherapy, they had a bump in benefit. And interestingly, those that also joined our group therapies bumped up even higher. So, we're hopefully soon going to be ... Now, that we're doing a lot more ketamine-assisted therapy. We're going to be re-analyzing and seeing if there was really a signal there and to learn more about it.

(00:41:08):

One promising finding research study that came out recently was looking at people who finished ketamine therapy, adding cognitive behavioral therapy, which is what I was trained in. What happens when you do that? And they found that those folks who responded to ketamine and got the CBT had stayed better longer compared to those that didn't get the CBT. So, that's an interesting signal that confirms our hunch about the potential power of adding therapy that's really inspired our approach here in San Diego.

**Dimitri Perivoliotis, Ph.D.** (00:41:44):

So, the risks of ketamine treatment, it's a pretty safe drug. So, thankfully, in clinical settings, it's pretty safe and the risks are usually limited to the session itself. Obviously, dissociation is going to happen. I don't personally consider it a risk. It's a dissociative drug. Of course, you're going to have dissociation. There's an elevation of blood pressure and pulse for a lot of folks. Changes in heart rate or rhythm could happen. We do a medical screening to rule out people who might be too risky with cardiac issues or hypertension, for example, confusion, agitation, drowsiness.

(00:42:17):

Sometimes people get nauseous or vomit. There could be some dizziness, blurred vision. And the long-term risk is of a dependence, including psychological and probably more so in terms of clinical settings, psychological dependence, potentially bladder and liver damage for long-term chronic use that usually comes out of the recreational use literature. It's not so clear how much that translates to clinical use. And there are some models that give ketamine maintenance treatment fairly indefinitely. So, it'll be interesting to track that, see what happens.

(00:42:55):

So, I get a lot of questions from NAMI participants, which I love because I'm an SMI guy. What about SMI? I mean, you can argue treatment-resistant depression, PTSD are SMI too, but I'm talking more like bipolar disorder and psychosis. So, we have much less research here. So, with bipolar disorder, there is a concern here about psychedelics triggering mania. So, it's been avoided.

(00:43:27):

But some of the signal that we have seen in the research suggests that maybe we don't need to be quite so cautious about it. People who use psychedelics recreationally ... psilocybin, I should say, specifically do report that they have an increase about a third, say that they have new or worsened symptoms when they use psilocybin, mania, insomnia and anxiety, for example.

(00:43:50):

But a tiny, tiny proportion of them said it got so bad where they had to get help for it. And they say that the benefits outweigh the risks. So, there is a risk there, but people are reporting that it's helpful. There is this belief that in a clinical context with very limited dosing, under close monitoring that might mitigate the risk. And also, in studies looking at psilocybin use by itself, mania appears to be uncommon.

(00:44:19):

So, the first of its kind that I'm aware of came a study looking at this was a psilocybin for bipolar II pilot study that was done by Compass, the folks that are doing their depression work with psilocybin. Again, this is a pilot non-randomized controlled study. But they found 80% ... They were targeting depression, I should say, 80% remission of depression at three months after the treatment ended. So, that's very exciting and we will see. There's going to be more research done, I think.

(00:44:54):

I haven't seen a bipolar I study yet. But maybe it could be that I've missed it. But I looked, I couldn't find one yet. Oh, by the way, regarding the bipolar II study, interestingly, they found no elevation or mania or suicidality, and they found that people who had more of an intense psychedelic effect or trip had a better outcome.

**Dimitri Perivoliotis, Ph.D.** (00:45:21):

Ketamine seems to be quite safe. It can elevate the risk of mania, but it's considered generally speaking safer and people are a little bit more comfortable using ketamine in folks with bipolar disorder with the right monitoring, of course. And one study that I found using ketamine in people with bipolar disorder, for example, found 71% responded to it versus just 7% in the placebo group. Again, it was targeting the depression, not the mania.

(00:45:53):

Psychosis, so, this is something very near and dear to my heart given my work in psychosis. For years, I was scared to ever bring this up at conferences because it was such a taboo question, because everyone automatically ... Well, I shouldn't say everybody. But researchers typically automatically get very nervous about the idea of using psychedelics for psychosis because there is this belief that psychedelics create a psychotic state, they're psychotomimetic.

(00:46:22):

So, giving them to people with psychosis could make them worse. And there's all these anecdotal reports about that happening. But when you really look at the data, it's not really that clear at all. At least the data that I've looked at. Some of the very early research back in the '40s to '60s looking at psychedelics for psychosis had mixed results. And people have started to, there's a little bump in the last couple of years, which I'm very happy about of papers looking at this question.

(00:46:50):

And some of the things that have been talked about are that state of psychedelic experience is different than a true psychosis. It has different features. People who have been surveyed who use classic psychedelics have not shown an elevated ... have not reported more ... adults, I should say, have not reported more of a psychosis after their use. And those are for classic psychedelics, I should say.

(00:47:22):

In terms of actual studies, the only thing I was really able to find was ketamine. So, there's about 10 or so studied looking at ketamine for people with treatment-resistant depression who also have psychosis with psychotic features. And they were very promising. They essentially found that it was safe, it helped ... it was very effective in reducing the depression. Psychosis blipped up a little bit during the treatment session, but then went back down before the person left the clinic.

(00:47:53):

And that in some cases, the psychosis improved and even remitted, which is really, really interesting. So, ketamine, I think, is a particularly good candidate, I think. So, you're starting to see a little bit of a movement in this area. UCLA, our colleagues, Anya Bershad and Dr. Stephen Marder, who's a legend in the field of schizophrenia, are planning a MDMA for negative symptoms study.

(00:48:23):

So, last time I talked to them a couple months ago, they were planning this, getting it going, and they're going to start off by administering MDMA to people with schizophrenia who have negative symptoms to see how they tolerate it and slowly work up the dose. And if it's working, well eventually develop and test a psychotherapy alongside it.

**Dimitri Perivoliotis, Ph.D.** (00:48:45):

I did a lot of work earlier in my career on developing recovery-oriented cognitive therapy for people with severe negative symptoms, which is a very unmet need. So, this is really exciting. And there's been some talk about how to mitigate the risks of using psychedelics in people with psychosis and to brainstorm about how that can be done.

(00:49:10):

And I'll read you this 2023 expert opinion piece that was published for using psychedelics for people with psychosis. They said psychedelic agents may be less likely to provoke symptom exacerbation than has been thought. It would seem possible to consider cautious use of these agents in schizophrenia if steps are taken to mitigate potential exacerbation of positive symptoms. So, we will see.

(00:49:37):

And then moving on to some other conditions, there is a really promising pilot study that has been done on MDMA-assisted therapy for social anxiety and autistic adults that found really good findings that stayed, and they really emphasized training the people on social skills outside of the psychedelic session in the surrounding therapy sessions. Just a pilot study, we will see yet to be studied further, but I suspect, I'm assuming more is coming.

(00:50:09):

And OCD, some survey findings of people who use classic psychedelics anyway are promising for people with OCD saying that they benefit them. And Yale finally has launched, and I think it's currently running two trials, looking at psilocybin-assisted therapy and they have some promising early results. One quote that I read in a paper recently, subjects describe sustained improvement in the ability to sit with present feelings and tolerate negative affect with a reduced sense of self-judgment. So, TBD on that one too.

(00:50:45):

In terms of legal status, where can you get these treatments? This is a great website, Psychedelic Alpha that has a map showing the different status of policy and laws across the country and where each state is at. And the red states here are the ones that are legalized or have some kind of regulation in place to permit people to access some of these treatments. So, there's three right now. We have Oregon, Colorado, and Utah.

(00:51:14):

So, Oregon was the first. They have what's called Psilocybin Services. They've been doing this for about a year now. And it's a super interesting website, actually a really well-designed website. If you're interested, you can poke around and really get to know this really well. They dictate that this is a non-directive approach like we talked about with psychedelic treatments that facilitators have to offer one prep session, the psilocybin session, and optionally, an integration session.

(00:51:47):

And they're very careful to call them facilitators, not therapists. There's been a lot of confusion about this. This is not psilocybin therapy. This is technically adult supervised psilocybin administration. In fact, this is find really interesting. If you're a mental health professional or have somebody with a license, you're not allowed to use that license when you're acting as a facilitator. So, I'm not sure how I would do that as a psychologist, how I would not be a psychologist in the room.

**Dimitri Perivoliotis, Ph.D.** (00:52:16):

But there is training you have to go through. There's requirements. It's 120 hours of training, a practicum, so I'm assuming they cover it in there. Colorado is next in forming Healing Centers. First, with psilocybin, but by 2026, they're going to expand it to DBT, ibogaine and mescaline. And they, too, are calling them facilitators. They're going to start accepting applications in December of this year. So, we don't know all the details yet.

(00:52:46):

And Utah is the most recent. So, Utah is probably the most restrictive. They're allowing only psychedelics that are in phase three studies. So, right now, MDMA and psilocybin, and you can only administer them in medical settings in two healthcare organizations by licensed healthcare providers. It's a three-year pilot program.

(00:53:08):

The VA, which is my institution, there has been a lot of movement and talk in the VA in the last couple of years here. We have, last I checked, it might be more now, approximately 40 ketamine clinics in the country. About 12 or so of them have some form of psychotherapy, including ours in San Diego, built into the clinic.

(00:53:29):

We have at least nine current or planned PTSD studies, seven of them with MDMA-assisted therapy. I mentioned the two here in San Diego. And the VA announced recently that it's accepting applications for research proposals to study these drugs specifically for now MDMA and psilocybin, which has generated a lot of flurry of interest in meetings with researchers and clinicians here at the VA and excitement.

(00:53:57):

And they've recently launched a group to develop an implementation plan in case MDMA-assisted therapy for PTSD gets FDA-approved next month. This is a huge challenge. How are we going to make this work in a regular healthcare system? So, it's a huge responsibility. I think we're poised is an only nationalized healthcare system in the US to hopefully set the stage and be leaders in this effort. But we'll see.

(00:54:24):

So, there's a lot going on. A lot of really interested clinicians meeting regularly. We have a psychedelic medicine group, for example, where a lot of like-minded clinicians are talking and networking. So, starting to wind down here, if you are somebody who is going to wants to explore these treatments, what are some guidelines?

(00:54:44):

These are just my own personal guidelines based on my experience working with veterans. I think it goes without saying you have to seek out a well-trained, experienced, ethical provider. This is a really, can be a very powerful treatment. You're going to be in a vulnerable, susceptible state. You really want to make sure you're in good hands. And that the setting in which you're going to be doing the treatment feels right and feels safe to you.

**Dimitri Perivoliotis, Ph.D.** (00:55:08):

Making space for the process, too. One of the challenges we have in our study is we've had a lot of veterans we haven't been able to see in our study because it wasn't really the right time or their schedule didn't permit it. And you have to make sure you have the time and you're in the right mindset to be able to really go all in and know that it's not just what happens in the session. You might be opened up and that integration process could take weeks, months, potentially even a lifetime if you think about it, of what unfolds. So, making sure you have the space for it mentally and energetically, physically.

(00:55:47):

Managing expectations is huge. And this has been a big thing that we've learned with our veterans in our MDMA study. These are not magic pills. You might feel like it when you read these media reports. They're tools, they're catalysts like anything else. I like to think of them as presenting an opportunity for healing and how much you use that is up to you. You have to put in the work, I think. You have to, especially if you're somebody who's dealt with chronic, chronic depression, for example, lifestyle changes, taking some courage to go and try new things.

(00:56:24):

Not expecting thunderbolts. You might get a thunderbolt, but it might be a slower process. I have one veteran that said, "I don't have major things happen in ketamine, but sometimes when I'm washing the dishes a couple days later, I start to think to myself, I realize now why my dad treated me that way." And she reflects on that and she has a little bit of a bump in her insight and her healing. And that's the thing that I encourage my veterans to look for.

(00:56:48):

Not just thunder balls and know that it can be challenging, say as we talked about earlier, being prepared to handle that with your breath work or mindfulness or yoga or therapy, whatever you're doing. And of course, committing to that self-work and the integration.

(00:57:06):

So, there's a lot of challenges here, limitations and cautions. A lot of the studies have small sample sizes, really variable in their design. We have the blinding problem. Diversity has been lacking. We want to make sure that we have representation of people of color in our studies and also that people of color and people in low SES can access the treatments. They're going to be very expensive. In fact, they already are very expensive. So, there's ethics there that we have to consider.

(00:57:37):

We talked about making sure the hype doesn't overtake the science. Access considerations and all the cultural considerations, too. It's so, so important anytime in psychotherapy, any treatment, but especially in the psychedelic space where these dynamics can be amplified. And there's also the concern about cultural appropriation, too, of some of these plant medicines that have been used for centuries with cultural practices around them.

(00:58:03):

We're taking them up, and in some cases, even tweaking the molecule and removing the therapy even. Is it going to be as effective? Is that ethical? We need a lot more research into many things including replicating the studies independently, testing alternative models like we're doing here in San Diego, combining it with traditional therapies. So many things we can research.

**Dimitri Perivoliotis, Ph.D.** (00:58:30):

Training is going to be a huge thing if these therapies are approved. We have a lot of training to do. Figuring out how we're going to make them work in normal, busy, low-resourced healthcare settings, and then hopefully, extending them to neglected conditions, which we saw a glimmer is starting to happen there already.

(00:58:50):

And finally, if you want some more information, these are some nice website I would recommend you look into that have things like therapist directories, education, policy trackers, finding research studies and so on. And a plug for the psychedelic support line of the Fireside Project as well. Thank you so much.

**Ken Duckworth, MD** (00:59:12):

Well, thank you. That was an incredibly comprehensive talk on a fast-moving field. So, I'd like to you back in a year or two because this is moving.

**Dimitri Perivoliotis, Ph.D.** (00:59:24):

It is.

**Ken Duckworth, MD** (00:59:25):

But to review, there's no FDA approvals of any psychedelic indications for any mental health condition today. Several are in a pipeline or a process. So, to answer a couple of questions real quick, your insurance will not pay for this, because at a minimum it has to be FDA-approved. Where could a person in the VA system and outside of the VA system find a study if they wanted to participate in this emerging area? Is it clinicaltrials.gov or should they contact their VA system?

**Dimitri Perivoliotis, Ph.D.** (01:00:05):

Yeah. Great question. The one caveat to what you said, Ken, I guess technically is we do have Spravato, which is the nasal form of ketamine, which is technically the only FDA-approved psychedelic right now for depression. But yeah, everything else, exactly right.

(01:00:22):

And yeah, in terms of the studies, I would suggest ... I actually just discovered this recently, psychedelic.support is an incredible website led by a psychedelic neuroscientist, if I remember correctly, where there's a nice directory of studies. So, you can drill down by condition, by psychedelic. So, that's one site. clinicaltrials.gov is another site, too, to look at federally-funded studies.

(01:00:50):

And then if you want to be really sure you've left no stone unturned, if you go to the psychedelic.support site, they have links to some of the pharma companies and some of the companies like Compass and Lykos and all the others that are cropping up that are testing existing psychedelics or tweaks of psychedelics or new novel compounds, you can always go to their websites and look for research opportunities. And I think between all that, you probably got it covered.

**Ken Duckworth, MD** (01:01:20):

So, you do a lot of work in this space and we saw a picture of you doing a ketamine session with someone. Is the work you're doing in the VA system part of a trial or you simply helping people?

**Dimitri Perivoliotis, Ph.D.** (01:01:37):

No.

**Ken Duckworth, MD** (01:01:38):

Search question.

**Dimitri Perivoliotis, Ph.D.** (01:01:39):

No. This is a clinic. It's a specialty mental health clinic called the Neuromodulation Program where veterans who have not responded well to antidepressants will get sent to us from their prescriber for a different treatment. So, we do ketamine as part of that clinical practice is one option, TMS or ECT. Yep.

**Ken Duckworth, MD** (01:02:06):

A lot of questions ... Go ahead.

**Dimitri Perivoliotis, Ph.D.** (01:02:08):

We're also collecting data as part of our clinical practice that we're looking at to see how are things moving and what happens when you add psychotherapy. So many questions that we're looking at. And big thanks to the veterans who are completing these measures every single week to help us not only track how they're doing, but also how we're doing as a program.

**Ken Duckworth, MD** (01:02:28):

Great. And that website can tell somebody if you're in the VA system where you could go to find a service, specialty service or a clinical trial?

**Dimitri Perivoliotis, Ph.D.** (01:02:39):

Yeah. Good question. I'm not sure if they cover VA ketamine clinics, but that is something if anybody's not finding that you can always reach out to me, because I have a directory and I can send you in the right direction.

**Ken Duckworth, MD** (01:02:51):

Oh, fantastic. Let's talk a little bit about the complexity of the indigenous nature of this. So, these interventions that have been around for thousands of years, how are people thinking about intellectual property, sharing these ideas? As western medicine tries to do randomized controlled trials, that's the western medicine way. The one question I think that's obvious is what is lost when you take the cultural context out? And the second question is, what is owed to people whose communities have developed these treatments over many years?

**Dimitri Perivoliotis, Ph.D.** (01:03:33):

Right. These are such important questions and I am afraid, I'm not sure if I have a great answer because it's a major challenge and it's a source of criticism, I think, for these treatments. And it depends, I think, on how you look at it. One way to look at it is, especially for the plant medicines like psilocybin or especially things like ayahuasca or ibogaine. One way to look at it is we have no business to go and take these treatments and they should stay there.

(01:04:07):

The other approach is to see these are tools for healing, so everybody should have access to them. A lot of what you'll see in the field is kind of an in-between, recognizing that we really need that, but also trying to honor the tradition. So, for example, there are ... I've talked mostly about academic, clinical research type settings, but there are organizations like Vets, Heroic Heart Projects.

(01:04:33):

The mission within that, partly because of legal restrictions, will have people go to these. We'll fund veterans to go to Mexico and South America, for example, to get the treatment partly because they can't get it here, but also so they can have the context of the cultural practices in place. Even that has been criticized. So, it really depends on your perspective. And yeah, it's a big active ...

**Ken Duckworth, MD** (01:05:04):

It's a tough question.

**Dimitri Perivoliotis, Ph.D.** (01:05:05):

For sure.

**Ken Duckworth, MD** (01:05:06):

I'm really interested in better treatments. So, we want to continue to have you back in the future. We know how early this field is and I just want to thank you for really digging into some of these questions that your part of studies does not mean they're FDA-approved, does not mean your insurance will pay for it, but you're asking really good questions because some people find the current treatments really lacking what they're wanting. So, we like that you're doing this work and that you're asking these questions.

(01:05:39):

I wanted to ask about the psychotherapy. Why if having a license to practice psychotherapy safely, you're not eligible to be the guided psychotherapist, did I hear this correctly? I'm interested in who becomes a guide for some of these interventions?

**Dimitri Perivoliotis, Ph.D.** (01:06:02):

Yes. This is another active area of discussion too.

**Ken Duckworth, MD** (01:06:05):

Yes.

**Dimitri Perivoliotis, Ph.D.** (01:06:06):

Well, there's different ... Actually, another thing before I get into that, it's a little bit piggybacking your last question. One of the questions that's being talked about in the field is do we even need the psychotherapy at all or even the trip? And there are some companies trying to adjust the molecule. So, there is no psychoactive effect. That's going to be very interesting to see. I'm very biased because I'm a psychotherapist, so I have my opinion on that.

(01:06:35):

But in terms of the person in the room, so, I think that having some kind of training is so important to know what it's like to be with somebody who's in an altered state of consciousness. Now what that training should be, people have different opinions on that. There is a perspective, which I think is a valid perspective that there's different healing modalities and disciplines that bring a lot to the table. And they may not be licensed mental health providers and a peer support, for example.

(01:07:11):

Or you could think of many other things. So, one model that's been talked about is maybe pairing a licensed mental health provider, like a therapist with another discipline like that. But there are models out there if you go into the underground, if you will, or even in some of these states where you don't have to be a therapist. The Oregon requirements I think are high school diploma, Oregon resident, complete the training, do a little bit of a practicum.

**Ken Duckworth, MD** (01:07:40):

I just want to say NAMI doesn't have a policy position on that, given how vulnerable people are. I'm just going to say when I'm asked, I like licensed people who are trained to do no harm. I just think that's the case.

**Dimitri Perivoliotis, Ph.D.** (01:07:56):

I know.

**Ken Duckworth, MD** (01:07:57):

All right. This last question is a vibes question. Do you think the research is expanding quickly, slowly? Do you feel the regulatory environment is becoming more favorable to this research? This is just your opinion on these questions. There's a lot of specific questions in the Q&A and we're just not there on most any of them. What do you think about where we're going in terms of the culture of supporting asking these hard questions?

**Dimitri Perivoliotis, Ph.D.** (01:08:35):

My impression is that ... I mean, even in just the few years that I've been in this work, I used to be what they called in the psychedelic closet, where just a few years ago I was ... and a lot of my colleagues, too, who hadn't been doing this work, were nervous about sharing with our colleagues that we were interested in this and, wow, have things changed.

**Dimitri Perivoliotis, Ph.D.** (01:08:57):

So, there's definitely a culture shift that's happening in the field of psychiatry and psychology and mental health. And then in the regulatory environment, it looks to me, I believe, that that's been moving a lot too. Just the fact that the FDA's granted breakthrough therapy designation to MDMA-assisted therapy for PTSD. Also, recently, I didn't touch on LSD today, an LSD treatment for generalized anxiety disorder, psilocybin for depression. And there's another one I'm forgetting too, really says a lot.

(01:09:31):

But we will see. The issue with the advisory committee and all that was a little bit surprising for me with the Lykos Therapeutics. So, I think a lot of people are waiting to see what happens with this decision. But I think good things can come out of it either way. Obviously, a lot of people are hoping that it gets approved so we can get this treatment out there to people who need it.

(01:09:52):

But even if it doesn't get approved, already, I know that companies are monitoring it closely to learn from it. The companies who are a little further behind in the development, how can we learn from this so that we can be more ready when we get there, too?

**Ken Duckworth, MD** (01:10:08):

And you mentioned that people can contact you if they have questions. Would you put your email in the chat? Or everybody's going to get the slides who signed up for this? The 600 people who attended today have learned a lot about a field that is really still growing. So, I hope we can have you back in a year or two because this is fast moving and as you've said, there's more openness. So, I just want to thank you for everything. A lot of positive comments about you doing work that is challenging.

**Dimitri Perivoliotis, Ph.D.** (01:10:43):

Thank you. I appreciate that.

**Ken Duckworth, MD** (01:10:45):

And it's not mainstream. A lot of the comments were very laudatory and we of course consider you a great friend of NAMI because you're asking a question that we really need. Are there better ways to approach some of these vulnerabilities that people develop? So, with that, let's move ahead to the next couple slides before we call it a day.

**Dimitri Perivoliotis, Ph.D.** (01:11:06):

And the feeling's mutual, by the way, with the friendship with NAMI.

**Ken Duckworth, MD** (01:11:09):

Friend of the family. We all need friends.

**Dimitri Perivoliotis, Ph.D.** (01:11:12):

That's right.

**Ken Duckworth, MD** (01:11:13):

So, I'm sorry I didn't get to all your questions. It's 600 people. We're taking a month of August for vacation. So, imagine, Ask the Expert with a chair on a beach and a book, perhaps NAMI's book, You Are Not Alone. All the royalties go to NAMI, a USA today bestseller and the good Dr. P. does discuss psychedelics in his essay.

(01:11:41):

We will see you in September. That's the book that the Ask the Expert will be finishing. And I'm going to show you the next slide. That's the book they'll be starting. On September 10th, our new book written by our associate medical director, Dr. Christine Crawford, You Are Not Alone for Parents and Caregivers. This is interviews with teachers, parents, aunts, teenagers, and kids. So, this is devoted to kids, younger people who are developing behavioral and emotional concerns.

(01:12:13):

It includes NAMI programming, like NAMI Basics, but also interviews with experts. And so, that's what the Ask the Expert we'll be doing on vacation this August. We'll be back in September. We have sponsors. The sponsors have no input into our content of any kind. But they give us resources so that we can produce these. And Delta, Johnson & Johnson, Neurocrine, The Hartford, and Teva, happen to be the sponsors today.

(01:12:46):

We appreciate support so that we can provide things like this to you for free, from great researchers who are asking good questions. You Are Not Alone, and this is not medical advice. A lot of the questions today we're pretty devoted to, would this help me with my, we can't answer those questions in general, but particularly on this topic where the research is so early.

(01:13:14):

And next slide. I want to thank you. You can always email me. My name is Ken. I don't let NAMI hire anyone else named Ken as an agreement I have with Human Resources. So, my email incredibly is ken@nami.org. Even I can remember it. asktheexpert@nami.org, if you have an idea for a topic or researcher or something that you are seeing that you want other people to learn about, send an email and we'll see what we can do.

(01:13:48):

So, I want to thank you, Dimitri, for all your great work. I look forward ...

**Dimitri Perivoliotis, Ph.D.** (01:13:52):

Thank you.

**Ken Duckworth, MD** (01:13:53):

... to having you come back in the future as this field emerge. You'll see a brief survey at the end of this. Please give us feedback. We do read it.