Considerations for Buprenorphine Initiation and Maintenance Care – Day Two

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Meeting Transcript

Opening Remarks and Recap of Day One

Susan Winckler, RPh, Esq., CEO, Reagan-Udall Foundation for the FDA

Susan Winckler (00:00:25):

Hello and welcome day two of our two-day virtual public meeting where we've gathered a number of speakers to discuss best practices in buprenorphine initiation and maintenance care, strategies for increasing patient access and priorities for research and product development. I'm Susan Winckler and I have the honor of serving as the Chief Executive Officer for the Reagan-Udall Foundation for the FDA, and we are pleased to be working with the US Food and Drug Administration to host this virtual event. Before we begin, I have a little bit of housekeeping issues. Because of the size of the meeting, attendee cameras and microphones will remain off throughout the event. Slides from yesterday and today are posted on the foundation website and we will probably have a few moments in each session, rather, to address audience questions. Please submit your questions and comments through the Q&A function. Also, we are recording the meeting and plan to post the recording along with the transcript on the foundation website next week.

(00:01:28):

So let's talk about what we're going to do today. If we remember yesterday's conversations, if you had the opportunity to join us, our experts discussed clinical strategies for initiating and maintaining buprenorphine care in both the hospital and community care settings and identified potential products to help meet patient needs. Today we're going to hear from research, public health and policy experts about strategies to promote access to buprenorphine. We'll have a session to talk more about research priorities and product development efforts. And finally, we will wrap up with a panel discussion with leaders from federal health agencies and clinicians on future directions.

(00:02:08):

Now, you may recall that yesterday, I talked about the various ways that buprenorphine is available, both its indications, the product formulations, and the dosage. That chart is still available on the foundation website and we'll drop a link in the chat to that. But as a reminder, we will use buprenorphine to refer to both buprenorphine, solo products and buprenorphine combination products. We're using buprenorphine, writ large, in its treatment for opioid use disorder. So with that, I am going to introduce our first speaker. I will step away and we will get started with the content. So our first session for day two is about promoting access to buprenorphine in the real world setting. Dr. Barbara, or Basha, Andraka-Christou is our presenter and she is an associate professor in the School of Global Health Management and Informatics with a joint secondary appointment in the Department of Internal

Medicine at the University of Central Florida. Dr. Andraka-Christou, thank you so much for joining us. Take it away.

Session 5: Promoting Access to Buprenorphine in the Real-World Setting

Presenter: Barbara Andraka-Christou, PhD, JD, University of Central Florida

Panelists: Dwayne Dean, RCPF, CPRS, RPS, Peer Recovery Training and Support Services

Tom Menighan, MBA, ScD, FAPhA, Catizone, Luce & Menighan

Matthew Strait, MS, Drug Enforcement Administration

Robert Bailleu, MD, MPH, FAAFP, Substance Abuse and Mental Health Services Administration

Barbara Andraka-Christou (00:03:19):

Thank you so much for having me. I'm going to present a concept that will hopefully make it very clear the number of barriers that people face when they're accessing buprenorphine. I'm going to walk you through the journey of someone with an opioid use disorder and the various barriers and facilitators that they may encounter, and I'll give you some policy suggestions or ideas that could help address these barriers.

(00:03:56):

All right, so here's the concept. We have a patient who has realized that they have opioid use disorder and potentially buprenorphine could help them, but that's just step number one. They're going to need to go through steps 2, 3, 4, 5, and 6, and at each step, they're going to encounter some barriers and potential policy solutions. So let's go ahead and dive into step number one. So first, the patient or the person has to realize they have opioid use disorder and that buprenorphine could actually help them. Now, that may sound very simple in theory, but in practice this could be actually quite difficult and here are the reasons why. First of all, as I'm sure everyone is aware, opioid use disorder or OUD is very stigmatized, and there are also many misconceptions about buprenorphine, such as the misconception that it's just another drug, that it should only be used in the short term and not the long term. That use of buprenorphine is just another addiction.

(00:04:57):

And so in theory, it may sound easy for someone to go ahead and start using buprenorphine, but in practice, they may never even get to the point of feeling comfortable using buprenorphine, until they address these barriers. Now, we as a society have unfortunately, through our culture and our stigmas, perpetuated some of these barriers, but we also have potential ways that we could address them. So some ideas from the literature. One would be public service announcements, whether it's on billboards or on television, framing opioid use disorder as a health condition. And we know from various studies that when you use narratives of individuals, their true stories, presenting them as real individuals, which they are, this can help the general public see that opioid use disorder is a health condition, a chronic health condition, that is not too dissimilar from other chronic and relapsing health conditions, like hypertension and diabetes that need medical treatment. We could also use public service announcements about the benefits of buprenorphine. So both what is buprenorphine, but also how can it help people? How can it prevent overdose deaths? How can it stabilize individuals and their families, and help them return to a happy, productive life? And we know from instances around the world, such as decriminalization of drug possession in Portugal, that when you decriminalize drugs in public policy, not necessarily legalize but decriminalize, you can sometimes help address the stigma that's associated

with the substance use disorder by helping people again realize that it's a medical health condition and not a criminal or moral condition.

(00:06:53):

So step number two, on the journey of our individual or patient with opioid use disorder, now they've realized they have the opioid use disorder. They've heard that buprenorphine could help them, but now they actually have to find a buprenorphine provider. And as most of you are likely aware, the great news for 2023 is that we no longer have the waiver requirement. There are no patient limits anymore for providers. However, we know that even when people had the waiver before, very few were accepting new patients or prescribing buprenorphine. So chances are that despite this wonderful elimination of the waiver that people are still going to have difficulty finding providers willing to prescribe buprenorphine.

(00:07:38):

So let me just summarize briefly some of those related barriers, even the public provider list from when the waiver existed on the SAMHSA website, we know were in accurate, that as many as 60% of the names on the contact list were actually not contactable. Buprenorphine providers, again, may not actually be accepting new patients or may only be prescribing to a few patients or may prescribe for a few months and then just stop prescribing to new patients altogether. We know that there's few buprenorphine providers in general, but particularly in rural areas and communities of color. We know that there's limited MOUD provision, including buprenorphine provision, in emergency departments, substance use disorder facilities, that includes residential treatment facilities, and within the justice system. So for example, there was a study that came out a few years ago that only approximately 5% of people with opioid use disorder in the justice system are referred for either buprenorphine or methadone. There are also some states that have restrictions on advanced practice clinician prescribing. For example, they may have prohibitions on clinical pharmacists from prescribing. They may prohibit nurse practitioners or physician assistants from prescribing independently and require collaboration or supervision.

(00:09:03):

And then there might also be additional state imposed buprenorphine prescribing barriers, such as mandatory counseling requirements or a mandatory frequency of visits. And all of these could prevent providers from beginning the process of providing buprenorphine. Fortunately, there are various potential policy solutions here as well. So one is of course to educate providers, the full range of providers including the advanced practice clinicians, and in fact having their schools educate about buprenorphine prescribing as a condition of receiving federal or state funding. We can have states and the federal government expand student loan forgiveness and stipends for people who are willing to prescribe buprenorphine in underserved areas, including again, rural areas and communities of color. We can clarify the legal standard of care for opioid use disorder. And what I mean by that is making it very clear that if a prescriber is seeing patients with opioid use disorder and never actually even mentions or offers buprenorphine as an effective treatment, that this is a potential liability issue. This would be a negligence issue.

(00:10:21):

We can have states continue to expand the independence of advanced practice clinicians, such as nurse practitioners and physician assistants, so that they can prescribe buprenorphine without having to first find a physician to collaborate with. And we can also further facilitate the prescribing by clinical pharmacist practitioners and collaboration with physicians and other clinicians. And then finally, we can also have states mandate emergency department initiation of buprenorphine or warm handoffs to

community-based providers, of course, with the voluntary consent of patients, require licensed substance use facilities in the states to either provide, have the capacity to provide buprenorphine or connect patients to buprenorphine. And we can also mandate justice institutions, whether that's drug courts, prisons or jails to allow buprenorphine. There is some evidence that this is beginning to be effective in the very few states that actually have initiated these requirements in their state laws. So more states should consider having, as actual regulations or statutes, these requirements.

(00:11:45):

Now, if the patient who has the opioid use disorder has acknowledged that buprenorphine is effective, has found a provider, now needs to get to the provider, they may then again encounter some specific barriers that have been made clear over and over again in the literature. And one of those big barriers is transportation. Again, particularly in rural areas. They may also, depending on the state they live in, have a mandated frequency of visits, meaning that they may have to go once a week, once every two weeks, once a month to see their provider, even if they have difficulties accessing the provider for reasons like lack of transportation. And then when telehealth is an option, it unfortunately may be difficult for the person to have reliable internet or a computer that would allow them to actually take full advantage of the telehealth options.

(00:12:42):

Policy approaches to address these barriers include continuing to maintain the pandemic era telehealth flexibilities, which currently have been extended to the end of this year, but probably should be made permanent beyond that, especially given that we see that telehealth helped expand buprenorphine prescribing, and indeed retention, in certain areas of the US, including rural areas. We need to, as a nation, improve WiFi access everywhere, make internet access equitable, consider internet access to be a social determinant of health. And then in the few states that currently have frequency visits mandates, whether it's weekly or biweekly or monthly, they should really carefully consider whether these timestamps of needing to attend weekly or biweekly are actually evidence-based, whether there is really good evidence to suggest that patients should indeed be seeing a provider that frequently, again, in an ideal world that may make sense, but when transportation is a barrier or internet access is a barrier, this can be a real problem.

(00:13:57):

So now the patient has found their provider, they've gotten to their provider, whether that's through public transportation, a car, or even using telehealth. They have to of course, pay for the treatment. And as we know, this may also be another form of a barrier. So we have good evidence that providers often will only accept cash, that they might not accept Medicaid, which is the predominant insurance coverage for people with opioid use disorder in the United States. They might be accepting Medicaid, but the patient might live in a non-expansion state. And then of course, we know from numerous studies, that unfortunately there have been prior authorization barriers for buprenorphine and in some insurance formularies, low coverage or lack of coverage of buprenorphine. Now the good news is that this is becoming less common of a barrier for the oral and sublingual formulations of buprenorphine. I just had a paper come out, a few days ago actually, that unfortunately showed it's a substantial barrier for the extended release formulation of buprenorphine. And so advocates and policymakers need to start shifting their attention towards the extended release formulations and the insurance barriers that exist for those.

(00:15:18):

What are some potential policy approaches to addressing these barriers? Well, first of all, state laws could mandate coverage of buprenorphine, including extended release formulations, and similarly state

laws could prohibit prior authorization for buprenorphine. In fact, we do know that some states already do this, but this should be a much more common mandate across all US states. All states should expand Medicaid. We have numerous studies showing that Medicaid expansion leads to greater ability to pay for buprenorphine treatment and indeed higher rates of buprenorphine access. And then in order to incentivize clinicians to accept Medicaid, we need to further increase the reimbursement within Medicaid for buprenorphine treatment and other behavioral health condition treatments.

(00:16:17):

Next, the patient is going to actually need to pick up their buprenorphine treatment, assuming it's the oral or sublingual formulation. Unfortunately, we know that in especially some areas of the nation, pharmacies have low stocks or even refuse to stock buprenorphine. And we also know that hospitals often lack buprenorphine on their site. So that of course would prevent adequate induction of people onto buprenorphine in the emergency department. We also know that patients frequently experience stigmatization when they go to the pharmacy to get buprenorphine. And all of these are just one additional barrier, one additional layer, in a long chain of barriers, as hopefully you've seen in the real world to accessing this life-saving medication.

(00:17:04):

Potential policy solutions include the following; mandatory buprenorphine education in pharmacy schools, again, potentially is a condition of federal or state funding. Clarifying that the standard of care for pharmacies is to have buprenorphine on stock, especially as the overdose rates continue to rise nationally. And then we should have policies for expanding access to extended release formulations. As I mentioned on the previous slide, these could be prohibitions of prior authorization or requirements for insurers to cover the extended release formulation. As obviously if someone is provided the extended release formulation once a month in the clinician's office, then they don't need to deal with the barriers of picking up the buprenorphine at the pharmacy. And then lastly, now we've had our patient get onto buprenorphine, they've found the provider, they've paid for the medication, they've picked it up from the pharmacy, now they need to actually continue the buprenorphine treatment. And we know from study after study that longer term buprenorphine is more effective than short-term buprenorphine. So this is really critical. Unfortunately, to continue buprenorphine, the patient will likely need to face all of the barriers that I described on the previous slides over and over again. We also know that there's additional barriers just to retention on buprenorphine, and those include housing and stability. The misconceptions or stigma that buprenorphine is better in the short term versus the long term, high threshold treatments, those would be things like clinicians forcing patients out of the practice if they're found to be testing positive for cocaine or miss an appointment here or there. Basically holding patients to a very high standard that we frankly don't often see in other health conditions.

(00:19:07):

And then sober living homes which are utilized, for example, when people leave incarceration, those might require cessation. So finally here, we could of course have some of the same types of policies I mentioned earlier for addressing stigma. We can increase housing access and we can also have some state laws mandating sober living homes to accept people who are using buprenorphine. I'd like to finalize my presentation with this slide here. Imagine for a moment that these same barriers I mentioned, the same long tedious process of getting on and staying on the medication, existed for other deadly health conditions such as diabetes or hypertension or asthma. What an absolute outcry there would be in the US. And I think it's behooves us as advocates and policy makers to think of this health condition, a deadly health condition, as being one that should have policies being addressed, addressing the same barriers that I mentioned on the previous slides, just like we would do for any other health condition out there. Thank you so much for your time.

Susan Winckler (00:20:20):

Thank you so much, Dr. Andraka-Christou and you raised something that came up in our discussions yesterday about the idea of better understanding opioid use disorder as a chronic condition, like other chronic conditions and using the language to refer to it like that. So thank you for that stage setting presentation. And now we're going to bring our panelists on screen. So I want to invite some new faces to our discussion. I'll introduce them in alphabetical order. First, we have Dr. Rob Baillieu who serves as a physician and senior advisor at SAMHSA in their center for substance abuse treatment. Next is Dwayne Dean, a recovery coach professional and a recovery coach professional facilitator through the International Association for Recovery Coach Professionals. Dwayne is a certified peer recovery specialist and a registered peer supervisor through the Maryland Addictions and Behavioral Health Professional Certification Board. Dr. Tom Menighan is founding partner of the consulting practice, Catizone, Luce & Menighan. He is also the CEO emeritus of the American Pharmacist Association. And rounding out our panel today is Matthew Strait, Deputy Assistant Administrator for the Office of Diversion Control at the Drug Enforcement Administration. So we're all on camera here. Let's jump into the conversation. I'm going to fire some questions to individuals and then we'll do some questions that will just be open for response. Let me start with Deputy Administrator Straight, and I'm going to call you Matt from now on.

Matthew Strait (00:21:59):

Please do.

Susan Winckler (00:22:01):

All right. Well, Matt, tell us what DEA is doing about access to buprenorphine while also mitigating misuse and diversion, and just what should people think about or need to know about DEA's role in ensuring appropriate access to Buprenorphine?

Matthew Strait (00:22:20):

Yes. Well, thank you so much for that question. And actually thanks for the awesome presentation, Barbara. I thought that was really well laid out, because I actually wanted to try to frame DEA's role within some of the very barriers that Barbara laid out. We have a very important role in the step two, the step three and the step five of that process. And in many ways, I think folks tend to think about DEA as a law enforcement organization, a public safety organization. And I think sometimes that overshadows the very important public health role that we have. Within the diversion control division, which represents about 20% of our organization, we have this very important responsibility to ensure an adequate and uninterrupted supply of controlled substances, in this case buprenorphine, but we could also be talking about methadone or any other controlled substance for that matter.

(00:23:29):

That is a very necessary function that we are compelled to work towards. So when we do hear about a lot of access issues, that should be, at least for the audience here, it should be really important to know that while we traditionally think of our public safety folks at the Department of Health and Human Services, DEA is very much in that space. And we have been doing a bunch of things over the last two years, generally locking arms with our HHS colleagues, like Rob over at SAMHSA, who we've been working a ton with in the last couple years. But I will just kind of frame up two of them, if I have a moment.

(00:24:16):

First and foremost, the celebrated repeal of the data waiver requirements, just for the folks in the audience, that is something that was baked into the Controlled Substances Act, something that DEA is responsible for enforcing, and DEA was one of the federal agencies at the table representing the administration, talking to Congress about the importance that it had for improving and perhaps expanding access to buprenorphine. And then of course a whole bunch of flexibilities that we put into place during the COVID public health emergency, which as Barbara laid out, now we're going to be expanding some of those effective today actually. And then some of them seeking to make permanent, which I can go into all sorts of detail on, but specifically in that telehealth space and the idea of being able to induce new patients using audio only forms of induction, I think are really important areas that we've been helpful.

Susan Winckler (00:25:30):

Matt, that's a great framing, underscoring the public health responsibility in assuring supply, because I'm confident that I'm not the only person who's worked with DEA for many years, who probably wouldn't have put that in the description of the agency until you just put it right in front of us there. So thank you for that and for the update, it's a really helpful grounding. So we are putting DEA in the right structure, particularly as it relates to buprenorphine.

(00:26:03):

I then want to turn to, came up maybe on steps four and five, if I got those right, and that's to talk a little bit about the pharmacy side. So that we turn to you, Tom. What are some of the challenges and opportunities you have encountered from the pharmacy side as it relates to stocking and dispensing buprenorphine?

Tom Menighan (00:26:27):

Thank you, Susan. And thank you to FDA, Reagan-Udall participants and attendees for your work in this area, and just a high five to Barbara and Matt for your kicking us off. My observations are not criticisms and are instead opportunities as we all strive to do the best we can for our patients and the public. My simple message is let's take the bullseye off buprenorphine. I'm a former CEO of APHA, as Susan mentioned. I'm also a consultant and I maintain ownership in a practice that I founded many years ago, that focuses now today on helping patients in recovery. In my years in community practice, I was held up at gunpoint three times by men who wanted my percodan and Dilaudid. This is pre-Oxycontin days. In 2018, I lost my great niece to a heroin overdose. This promising student athlete suffered a broken leg, was treated and became addicted to opioids. Despite best efforts to get MAT, while trying to keep a job and find a pharmacy that would dispense it, she faced too many challenges when street drugs were easier and cheaper. I think we can do better.

(00:27:44):

And contrary, perhaps to what Susan mentioned earlier in our nomenclature, when I say buprenorphine, I mean specifically monotherapy. When I say Suboxone, I'm referring to combination of buprenorphine and naloxone. Much of the literature that we read refers to buprenorphine when in fact the research was done with Suboxone and that was the medication being used. And I think we need to be precise in our nomenclature and say what we mean. I applaud the elimination of the X waiver program for prescribers. Unfortunately, this action has done nothing, absolutely nothing, to improve access to MAT meds in pharmacies. Many, if not most pharmacies are still reluctant to stock MAT meds. Last year, over half of US pharmacies reported they don't stock it.

(00:28:32):

We community pharmacies, in general, and my pharmacy in particular, continue to be stigmatized as suspicious by distributors whose focus is solely on the ratio of controlled and non-control, and monotherapy with buprenorphine versus combination therapy with Suboxone and the dispensing patterns. This focus on these two ratios makes access by pharmacies, especially those who specialize in stigma free treatment of this patient population of these life- saving meds, very difficult. Distributors won't sell to a pharmacy that dispenses higher than average quantities of these meds. Averages are calculated from ranges, both higher and lower. There needs to be room in the distribution calculation for pharmacies that specialize in serving this patient population and may fall on the high side of average. I believe distributors are being held to settlement agreements that require them to treat buprenorphine as suspicious, on the face, despite an agreement to analyze pharmacy use.

(00:29:32):

This could be modified and distributors could be allowed, under their settlement agreements, to look more closely at the patient population being treated by pharmacies and do actual analysis, beyond just the ratios. We need a process. Everyone knows red flags, the red flags that are quantified as part of PDMP programs. MAT meds raise the NarxCare score. This could be modified. NarxCare scores could be a force for even greater good than they are now. We could supplement red flags with green flags. Is the patient compliant with therapy and on schedule not early? Is the patient getting behavioral healthcare in an active recovery, if indicated? Distributors could actually know their customers as they're supposed to do, rather than making decisions based solely on two ratios. Compliance officers of distributors should have conversations with pharmacy teams to understand who and how pharmacies manage their patients.

(00:30:31):

Green flags could include low NarxCare scores. These can be documented in patient profiles. Excursions can be documented with additional information on a patient with a potentially high score. I know there are provisions in state law related to how PDMP programs can work, yet in our practice, we document every time we dispense a buprenorphine or Suboxone prescription, we go to the PDMP and we document, in their patient record, what their NarxCare score was on that day and we can report out on that as needed to anyone who wants to know. So that could be become a green flag. Documented vetting of prescribers. Is there good communication? Is the patient seeing the provider or is the provider just automatically reauthorizing prescriptions? Prescribers should be encouraged to provide their treatment plans to the pharmacy. Currently, we often face resistance from prescriber to provide that plan or for results from toxicology screens if warranted.

(00:31:35):

Who the pharmacy is serving should matter and telemedicine needs encouraged, as this population does not like to be seen going in and out of treatment facilities and suffer further stigmatization. Regarding need and dosage forms, we need flavor free Suboxone and generics. The flavoring is known to cause buccal irritation and worse for some patients, more options here could enhance acceptability of the combination therapy, many professionals and regulators prefer. Pharmacies and distributors should not fear DEA taking paper off their walls, as one distributor explained to me. There could be clear guidance that encourages rather than discourages effective MAT meds for patients with solid documentation. Currently, it's my suspicion, that distributors are held to settlement terms that are fixed in time and that do not change when DEA makes policy changes to enhance access. I encourage continued dialogue among stakeholders with a clear purpose to enhance access to lifesaving MAT. Reduce or eliminate the control status of buprenorphine and Suboxone and limits on purchases.

(00:32:43):

It's okay to hold pharmacies to standards of care, but include care in that calculation and include that in the analysis of purchase patterns. There's little evidence of buprenorphine causing harm to patients, despite it being subject to diversion and priced high on the street, patients and people with addictions who cannot get buprenorphine turn to fentanyl and other street drugs. Rarely does someone die from a buprenorphine overdose. Treatment guidelines are broad in both dosing and length of care, yet regulators and payer expect patients to be cured in weeks rather than acknowledging recovery is a lifelong journey. Finally, pharmacy boards and enforcement agencies have to become more comfortable with the fact that pharmacies need to work with challenging populations. Despite our best efforts, diversion may be a consequence of this and pharmacies do work to avoid that as much as possible. But the alternative path of continued limited access to buprenorphine is pharmacies turning challenging populations away and that's the current state of affairs. The result of that denial to access to buprenorphine is often death.

Susan Winckler (00:33:54):

So Tom, you packed a lot in there, but helping us on the pharmacy side of... I think you even described a bit of a vicious cycle of there's a lot of...

Susan Winckler (00:34:03):

I think you even described a bit of a vicious cycle of, there's a lot of pharmacies who don't stock and then those who do are held to norms which are going to be artificially low because you have pharmacies who don't stock. So there's that dynamic in a categorizing buprenorphine with a number of other products. And you started us on what dosage forms do we need. So now we've got to get some other voices in here because we've got this discussion started. Dwayne, I want to turn to you and as you think about this, what else can we do within hospitals and clinics to increase buprenorphine access? Tom just took us through a lot of things we could do on the pharmacy side. Let's think about the hospital and clinic side.

PART 1 OF 6 ENDS [00:34:04]

Dwayne Dean (00:34:49):

Okay. So in answering that, I just want to really talk about the importance of peer recovery coaches. Asbury has a wonderful model that we've been using mostly in most emergency departments in the state of Maryland where we have peer recovery coaches or peer recovery specialists in the emergency department. Also in a couple other units such as inpatient OBGGYN, shock trauma. And I had a chance to actually supervise peer recovery specialists in the larger hospital, level one hospitals. That was some of the first to even start buprenorphine initiation or induction in the emergency department. When participants or recoveries come to the emergency department and report substance use disorder or particularly opioid use disorder, peer recovery coaches and specialists, they go in and do the intervention and consult, then talk to a nurse or a doctor about concerning opioid withdrawal scale and seeing if a person is appropriate and willing and desire medicated assisted recovery by way of Suboxone or even the mono form buprenorphine.

(00:36:09):

So in the emergency department, I think just educating, continuing to educate peer recovery coaches because a lot of times they're on the frontline, they're their first point of contact, especially if they're using an expert model, they're their first point of contact. So to educate them on the initiation and induction, but just on interventions and educating the recoveries or the patients at that time on the

effectiveness of buprenorphine when it comes to supporting or addressing overuse disorder and also just eliminating overdose. When we're talking about Suboxone, where I think Tom mentioned that, rarely do you see a person overdose on Suboxone because of the blocker that's in there. We do educate and I serve several roles. One is I do peer [inaudible 00:37:11] research and we do have a MTU mobile treatment unit that does telehealth in the eastern shore that we're doing some studies on adherence and retention, but also just educating peers on being able to support recoveries when it comes to stigma, when it comes to the misconception, because there's a lot of stigmatization, there's a lot of misconceptions.

(00:37:32):

I've heard so many different stories, oh, I can't take buprenorphine because it makes me sick. Yeah, but you took it while you still had opiate in your system. So just addressing the misconceptions, educating them on the different forms of buprenorphine or just educating them on medicated assisted recovery. So I think from my perspective, I think it's just it's education is advocacy. I can remember when I first started working as a peer recovery coach in the emergency department, and I believe it was a few years ago in the X waiver where doctors was able to administer buprenorphine. You had doctors that traditionally just felt as though it wasn't emergency medicine and they were against it. And because of peer recovery coaching and they starting to see how effective peer recovery coaching was in emergency department and how instrumental the tool of that waiver was with getting people a continuum of care with the induction in the emergency department, which led to a warm handoff to a treatment facility because the intake is two to three hours.

(00:38:42):

A person that's in opioid withdrawal did not want to sit for intake, they would leave. But because of induction in the emergency department, our numbers, you could see it just in the data itself that people stayed for intake. And just in the peer recovery coaches being a resource broker had to, because I've seen Dr [inaudible 00:39:05] Crystal in one of her steps, she was talking about what buprenorphine or when it comes to the... I'm sorry, the providers and things of that nature, the list that we had. And she's so correct. I would call dozens of people, dozens of providers, and they're like, "We don't do it." Or, "We're not taking new patients." As a resource broker, one of the roles of peer recovery coaches, I update my contacts, find out who's doing it, who's not, who's willing to support, who's willing to accept new patients, what programs have provides that are going to be able to prescribe buprenorphine on a maintenance level.

(00:39:48):

But again, it's about advocacy. I'm a strong believer that when we encounter barriers, especially when we are addressing addiction, which has evolved, recovery has evolved, peer recovery coaching has evolved, and instead of running into the same barriers, we have to advocate to create some liberation. Instead of keep moving the barrier, let's remove the barrier and create liberation. And in doing so, we as a resource broker, we find out who can I send someone to when my participant is willing, ready and wants medicated assisted recovery by way of buprenorphine or any other medicated assisted recovery. The peer recovery coach themselves has to be armed and geared with the providers who will accept them. And again, it's a thing of education advocacy and just liberating these barriers instead of keep stubbing our toe and bumping our knees on the same barriers over and over and over. Let's get them out the way, we got to get away from the traditions.

Susan Winckler (00:40:56):

Yeah, Dwayne, that's so articulate and I'm putting down resource broker as a great phrase in what it is that you and your colleagues do in addition to the de-stigmatization, which Bacha pointed out to us is so

important. And that's a de-stigmatization from peer, from provider, from the pharmacist providing the product. So important throughout. So thank you Dwayne. Just great grounding for us to think through those. We've got to get Dr. [inaudible 00:41:31] to unmute and then I'm going to do a rapid fire question to everybody. But Rob, you've been in some of the planning conversations here and I know that you at SAMHSA, you are doing a lot to support buprenorphine access, but help everyone understand, talk to us a bit about the grants, the resources for patients, trainings for healthcare professionals. How can SAMHSA the help in this situation?

Robert Baillieu (00:42:00):

Well, thank you so much Susan, and thank you for including SAMHSA in this discussion and to all of your participants here, thank you for the work you're doing and certainly just the conversation we've just had has really raised some essential points. The first is stigma and how pervasive that can be in just at the patient level, the healthcare level, community level, policy level as well, and how that really impacts access and how in turn access is also impacted by disharmony between federal and state law. And then the big takeaway I found here is the need for all of us, all the attendees here and beyond, to keep talking, to keep listening, to keep sharing. And that never stopped sort of doing this work. So this is really exciting. And Tom, I really love the idea of green flags. I think that positive spin is so important because there are too many red flags, as you said.

(00:42:57):

And so at SAMHSA, our privilege is to really work in that space to try and expand access through grants to provide education to communities and those who might benefit from buprenorphine to provide education and to work in the policy space as well. So certainly our grants, which is our primary purpose at SAMHSA, are really exciting. Particularly our state opioid response grant and our prescription drug monitoring and opioid access grant. So the Matt [inaudible 00:43:27] grant, which uses all the words we shouldn't be using in terms of addiction and drug, and unfortunate but combined, those grants provide over a billion dollars to the states to expand access. And in the last several years, they've expanded access to almost 2 million people for buprenorphine. Matt [inaudible 00:43:49] in particular works in the education space by providing education to communities to individuals. And then saw the state opioid response grant works in the harm reduction space as well.

(00:44:02):

So making sure naloxone is available across the states as well. The other big sort of piece of those grants is the collection of data as well. Data is so important for us to understand what we're doing right, what needs to be done, where things need to be up-regulated. And that informs another important aspect of our work at SAMHSA, which is evidence-based practice. And so we are very proud of our evidence-based practice guidebook series, our treatment improvement protocols, our tips and taps, all the other acronyms that are out there in the SAMHSA store. And they're really founded on evidence. They help our grantees provide evidence-based treatment and they also are a resource for individual patients as well. We hope that many of our resources help patients understand the importance of their decision. We hope that practitioners will print out our resources and help patients understand the benefits of buprenorphine and how it can be delivered.

(00:45:05):

Certainly we also engage in education because we recognize that that's a key piece in overcoming stigma. And so our PCSS grants focus on providing education across universities. More recently we've had the profound privilege of working with Matt and his team to work on the MATE Act and that that's been a really interesting piece in terms of looking at how education is provided across the board through state agencies, through different sort of professional societies and things like that. And that

brings me to the last of my SAMHSA related points, which is working within the policy space. And certainly the implementation of the buprenorphine waiver has been very rapid, but very interesting and very important at the same time.

(00:45:53):

Working on education through the MATE Act has been fascinating, but also we're incredibly proud at SAMHSA to be working on what is our space, OTPs, and that's through revisions to 42 CFFR part eight. And at the heart of that is what we consider to be the most important thing, which is patient centered care. And we hope that through 42 CFR part eight, we've really promulgated that. We hope that we have created a more accepting de-stigmatized environment and we're incredibly proud of all the work we've done. And working through the public comments has been a privilege and an opportunity to really strengthen the regulations there. So again, I'm really grateful to everyone here and to all the work that's been done across the board too.

Susan Winckler (00:46:43):

Well, and Rob, what a great fabric of programs and projects to try and strengthen and improve buprenorphine access, access and use. So thank you for that overview. I'm going to the panelists. I want to make sure that we get through two questions in our time that remains. One that has to do with adequate insurance coverage. Because Bacha raised it, but it usually comes up a lot in these conversations. And so I want us to talk about some solutions there. And then the second one, to really think through this idea of what incentive might we have for clinicians and pharmacies to prescribe stock and dispense buprenorphine. And Matt, I'm going to say in particular, I'm going to come to you for that second one because we rarely think about DEA in the incentive space. So you can be thinking about less disincentive if that's easier. But Bacha, I'm going to turn to you first. You mentioned insurance coverage. What are some policy levers we should be thinking about in that space?

Barbara Andraka-Christou (00:47:59):

Well, I think it's critical to think about the role of state laws. I did a systematic review of state laws in the last year related to prior authorization and insurance coverage of buprenorphine. And there's a minority of states that actually have in their state statutes or regulations mandates to cover buprenorphine or prohibitions on prior authorization and quantitative limits. And really it's such an obvious policy tool that it's surprising more states haven't adopted. And like I also mentioned, the prior authorization requirements are actually becoming less common, thank God, with respect to the oral and sublingual formulations. But they still are very common when it comes to the extended release formulation, which can address barriers for retention and other issues for many people.

(00:48:52):

And a lot of my work is in the justice system and including in problem solving courts, and there's always this concern of misused diversion. Well, when you have that extended release formulation, at least for justice institutions, it can help address that concern. But when you think of someone with low income, maybe lack of housing in the justice institution, and now they suddenly need to get onto an extended release formulation with no insurance coverage or prior authorization, that can unfortunately create a barrier. So my short answer would be, let's better utilize state laws, let's have regulations and statutes mandate and coverage and prohibiting prior authorization.

Susan Winckler (00:49:37):

Really helpful. Particularly we heard yesterday some of the situations were extended release just makes more sense if it's adolescents or if it's the housing insecure. Can we reduce the burden or even lifelong

use, which it is part of managing a chronic illness. Are there ways to think more about the adoption there? Other thoughts on what else we should do in what are some insurance barriers that we need to overcome?

Tom Menighan (00:50:15):

Well, this is Tom. I could comment that reimbursement is awful for MAT meds in general, not unique to buprenorphine and suboxone and pharmacy [inaudible 00:50:27], all reimbursement as being inadequate, but it's particularly acute with buprenorphine and its various dosage forms. I think the other thing we could do is expand the latitude of wholesalers. My pharmacy alone has been turned down by five wholesalers, totally based on the ratios of controlled and non-control in buprenorphine to suboxone. Our data gets swept. It's reviewed by the same vendor for all the wholesalers. They in turn go back to the compliance folks at the wholesalers, give them the ratios and the compliance folks come back to us and say, "No, thanks. We don't want your business." And there's absolutely no interest in looking under the covers at how we take care of patients, how we document their care, how we vet the prescribers, et cetera. Absolutely no interest. There needs to be a bigger story as part of the analysis that wholesalers are required to conduct.

Susan Winckler (00:51:29):

Right, So to allow more context in that discussion.

Tom Menighan (00:51:31):

Yes.

Susan Winckler (00:51:31):

Rob, I saw you unmute.

Robert Baillieu (00:51:33):

Yeah, no, thank you Susan. And as a primary care physician, I can just reinforce what Tom said. Reimbursement rates are terrible. Certainly when it comes to in the primary care setting, we're expected to see 20 patients a day. And it is so important if you are inducing someone on buprenorphine to spend some time with them, obviously you've got to sort of check on them, make sure they're doing well. And billing codes don't recognize that work. Resource value units as well are not recognized through that either. So on one side, there's the reimbursement issue, and I think if that's fixed, then there'll be a whole lot of physicians and practitioners advocating for decreased barriers for patient access as well. The other thing is with insurance, as Dr [inaudible 00:52:24] mentioned, the disheartening between state law and federal intent is striking here. And certainly there are expansion states, non-expansion states, and that further inhibits access as well.

Susan Winckler (00:52:39):

Yeah, really, really helpful. Matt, did you want to jump in on this or, we turned a bit to incentives anyway. Do you want to jump in?

Matthew Strait (00:52:47):

Well, for the sake of piling on, I think I probably will just, we've been involved in these conversations for the better part of two years now, and whenever we're gathering stakeholders, it always seems like the

reimbursement question is just set off to the side and that we never have the stakeholders that represent those who control reimbursement, that are actually there to effectuate it. And from the federal side, that makes some of us feel a little inadequate because we really can't address that issue in a responsible way because we're not really the ones controlling some of those levers, unfortunately.

Susan Winckler (00:53:29):

Yes. Well, and I know that's a piece that's come up in some of the other... A lot of the work that's being done on substance use disorder broadly is helping the insurance community, health insurance community better understand the investment and the necessary, really to treat opioid use disorder and substance use disorder as a chronic illness that can be managed well. But not if the individuals with coverage have to play games or fail on one to get to another. So definitely hear you, and we know that's a part of broader conversation that we have facilitated and that continue to drive. Let's talk then about incentives. And maybe this is a question, Robin, Matt to you is you're looking about the change and no longer having the waiver and the changing dynamics of who can prescribe buprenorphine. How should we think about that in removing, to Dwayne's language that removed a barrier, but we've still got to get the prescribers to pick up that opportunity. Are there things you've been thinking about in that space, thoughts on incentives to help the prescribing community see now there's no barrier or that barrier has been changed. What else can we do to incentivize it?

Matthew Strait (00:55:05):

Well, I will jump off on this point because from DEA's perspective, while the prescriber community perhaps needs incentivization, they still have to wait for states to catch up. So I know that there's a lot of state laws that really need to catch up before I think we'll see that full group of prescribers coming in and being able to do this work. But from DEA's perspective, and I want to piggyback off a lot of things that Tom was saying, that there's a lot that we can do with our distributor community in terms of some of their obligations under these settlement agreements that, I think first of all, they can do that. They can make decisions now that will help the throughput going to the retail pharmacies, but they might need a little assistance from DEA, maybe some assurances that while there could be an increase in purchasing coming from the retail pharmacies that might otherwise be considered a suspicious order under federal laws, that we fully expect those increase in orders and that we actually welcome those orders. So I think that's the conversation that we're having right now within DEA is how can we provide some very public messaging to our distributors and to our retail pharmacies that will give them the assurance that they don't have to fear the overregulation by DEA.

Susan Winckler (00:56:42):

That is a great point because I'm going to guess that the prescribing community paid attention to the changes but doesn't, I'm not sure that's something that would be discussed at the Healthcare Distributor Alliance meeting, right? Because it was a change at prescribing end versus it really is about socializing. That change in law really creates an expectation that there would be more buprenorphine flowing through the system.

Matthew Strait (00:57:14):

Yes.

Susan Winckler (00:57:15):

Yeah. Bacha, you unmuted.

Barbara Andraka-Christou (00:57:17):

Yeah. I just was struck by some of the conversation here about the risk scores and ratios, and it made me think of in the PDMP world, there's similar conversations occurring right now about are these formulas used for risk scores? Are they validated? Are they transparent? Are they evidence-based? And I just think it's so critical for that same conversation to be occurring when it comes to buprenorphine stalking and dispensing and pharmacies.

Susan Winckler (00:57:51):

That it's about thinking through it. Well, recognizing that buprenorphine is different and that in fact part of our path out of the opioid crisis is more use of buprenorphine, which...

Dr. Barbara Andraka-Christou (00:58:10):

Absolutely.

Susan Winckler (00:58:11):

Right. I think we'd have head nods here as logical, but for a lot of folks, we would've to connect those dots to bring that logic. Yeah.

Tom Menighan (00:58:22):

Can I get an amen?

Susan Winckler (00:58:27):

You may, Tom. I hear one. I hear one. So that I think really is an important, and Matt and Rob, I applaud that idea of really communicating that the inherent expansion of prescribers of buprenorphine and then if the intent is to have more users of buprenorphine, then we need more access and more use of buprenorphine. Are there other things we should be thinking about in the incentive space? Rob, you unmuted. Fire away.

Robert Baillieu (00:59:05):

Thank you. And I just wanted to mention the [inaudible 00:59:08] SAMHSA report that was done last year, and this was alluded to in one of your discussions yesterday. We looked at the impact of the accepted waiver, the 30 E waiver, and really found that while there was an increase in applications for the waiver, there was no sort of commensurate change in prescribing. And it was really interesting. And most of the individuals who got the accepted waiver were actually physicians who previously only required eight hours of training as opposed to 24 hours of training. And it was mostly people working in emergency departments who got the accepted waiver. So it was a really interesting finding. And when we talk about evidence, what does the evidence tell us? So tells us that in a world where education in medical and professional schools around buprenorphine and substance misuse is heterogeneous and in many cases substandard at best, the prescribing that there is minimal incentive to describe or understand how to case find as well.

(01:00:14):

The evidence tells us that if we improve education, have really good didactic education with concurrent exposure to patients, then that is going to improve understanding of substance misuse. It's going to improve acceptance of buprenorphine prescribing and moving forward, it will create a far less stigmatized environment. So the evidence, I think falls into DEA SAMHSA's lane here in terms of the

provision and ensuring the provision of education. It's a long-term game, unfortunately, it's not something we can turn on overnight. And certainly it's something that we at SAMHSA are passionate about and been working on. But it's a decades to several decades strategy.

Susan Winckler (01:01:01):

And I was struck in the conversation yesterday with the emergency services physician who said he didn't plan to be in addiction care and hadn't imagined that that would be part of his role. And it very much so was but only on the initiation side, right? That's the place for the EMS engagement, which then requires that you have someone to hand off to. So that when Dwayne's doing his resource brokering, who can he help that patient access post initiation? So yay on the uptake in EMS. And then we need the uptake on the other side.

Tom Menighan (01:01:50):

Just a quick comment.

Susan Winckler (01:01:51):

Yep. Go ahead, Tom.

Tom Menighan (01:01:51):

Just a quick comment on the limitations and length of therapy covered by many health plans and insurance companies is just shortsighted. If you look at the treatment guidelines, there really aren't limits. For many this is a lifelong treatment, just like a diabetes drug. For others, they can be in and out in six to eight weeks and never think about it again. But everybody's different. And the insurance companies oftentimes look at, well, they should be cured at the end, number of weeks, and it doesn't work like that.

Susan Winckler (01:02:34):

Yeah, yeah. It's back to that kind of both stigmatization and lack of understanding. We've learned more.

Tom Menighan (01:02:40):

I would quickly say, I think most pharmacists are pretty well-trained about not to stigmatize patients because of their addictions, but the stigma is more about what happens in a pharmacy that goes down the path of supporting patients in recovery only to find themselves cut off by their wholesaler. And then all of a sudden they can't take care of all their other patients either. And that's real stigma when you shut down a business, that's stigma. So I think it's more an economic stigma than it is a social stigma that pharmacists may face with patients in recovery.

Susan Winckler (01:03:22):

Yeah. Yeah. Dwayne, I want to give you a chance. I've got 74 seconds left. Dwayne, I want to give you the chance. What do you want to make sure that we all take with us in thinking through the incentives and the opportunities? Your job as a resource broker, you've got the microphone.

Dwayne Dean (01:03:43):

I believe buprenorphine is an awesome tool, but it's also other supports that helps the effectiveness when it comes to adherence and retention, especially on the maintenance of the substance

reimbursement with peer recovery coaches. June, we start reimbursement only level one and level two. So level one and level two ends in 90 days. How about the person that needs long-term support on the medication, IOP, intensive outpatient programs? Let's extend those six months. Six months, I'm just getting my birds together. I haven't found housing, I haven't reunited with my family, reunited with employment. I just believe that if we're [inaudible 01:04:23] going to be on maintenance for longer, let's get the other supports, peer recovery coaching to be supportive. IOP, intensive outpatient treatment and therapy that goes along with the medicate assisted recovery. We need to extend those and make sure we have reimbursement and longer support for the people that are going to be on maintenance for a longer time.

Susan Winckler (01:04:45):

Brilliant summary. Thank you, Dwayne. We needed that reminder of the things that we need beyond the tablet or the strip or the ejection in longer term. With that, thank you to each of you for sharing your insight and your expertise. I've got to move to the next meeting room because we've got another panel lined up ready to share their insight. But thank you so much for joining us. I know that our audience appreciated it. If you all stay here, I'm going to move to the next meeting room and we will kick off the next panel.

(01:05:25):

Here we are going to begin with a presentation from Dr. Kelly Dunn about opportunities to address treatment needs through product development. Dr. Dunn is a professor in the behavioral pharmacology research unit within the Department of Psychiatry in behavioral sciences at Johns Hopkins University School of Medicine. Dr. Dunn, we heard yesterday, I think there is a laundry list. I stopped counting at 12 different ideas for product development. And so we'd love to hear your presentation and then we will move to the panel discussion. I'm going to turn it over to you.

Session 6: Opportunities to Address Treatment Needs through Product Development

Presenter: Kelly Dunn, PhD, MBA, MS, Johns Hopkins University

Speakers/Panelists: Pouya Azar, MD, Vancouver General Hospital

Bartholt Bloomfield-Clagett, MD, U.S. Food and Drug Administration

Jody Green, PhD, FAACT, Uprise Health

Iván Montoya, MD, MPH, National Institute on Drug Abuse

Michelle Winberg, Harm Reduction Michigan

Kelly Dunn (01:06:00):

Thank you for the opportunity to talk and for convening this panel. As I go through this presentation, I'm struck by the consistency and some of the statements that were made in the last panel and then also in reviewing the presentations that were completed yesterday. And what's nice about that is I think that there's a lot of consensus, growing consensus in our field as to where the gaps are for our patients and where we could use help in some innovation. So for today, I wanted to address opportunities to address treatment needs through product development. I'll start by just providing a little bit of a context.

(01:06:43):

You're probably familiar, and I know that this was reviewed at length yesterday, but we are faced with unprecedented rates of drug poisonings. This is a graph showing rates of drug overdose deaths beginning around 1999 up until the past few years. You could see across the bottom that they are

conceptualized as occurring in four different waves. The first being prescription opioid related overdose deaths, the second in blue being the increase in heroin. Third, the most prominent is the rise in synthetic opioid related deaths, most often attributed to fentanyl exposure, illicit fentanyl exposure. And then finally, this most recent wave is actually characterized by a co-occurrence of synthetic opioids like fentanyl as well as stimulants like methamphetamine and cocaine. Importantly, one of the big challenges that we're facing, and I know that this was a main topic of conversation yesterday, is that buprenorphine is likely interacting with illicit fentanyl and causing precipitated withdrawal. So we recognize that buprenorphine can cause precipitated withdrawal, and we previously had standardized induction procedures to be able to transition patients from full opioid agonists onto buprenorphine in a comfortable manner. There's features of fentanyl that seem to be interacting with buprenorphine and are disrupting our ability to use that...

Kelly Dunn (01:08:03):

All that seem to be interacting with buprenorphine and are disrupting our ability to use that comfortable induction strategy. We don't have a lot of data on this, from an empirical perspective, but we have a lot of anecdotal experience with it. And we certainly know that this is presenting as a barrier to both providers and patients in their willingness to accept buprenorphine as a treatment strategy.

(01:08:22):

These data here are data that we collected from across 49 treatment clinics throughout the United States, more than a thousand patients, and they were just self-reporting to us their experience with precipitated withdrawal. The figure on the left hand side, we asked them, "Have you taken buprenorphine or methadone in proximity to using illicit fentanyl, either 24 hours, 48 hours, 72 hours, and so on? And if you did, what was the likelihood that you experienced any form of precipitated withdrawal?" And you could see that, statistically, the participants were significantly more likely to report that they had experienced that when they used buprenorphine within 24 to 48 hours of their last fentanyl exposure. At 72 hours, we no longer saw a difference.

(01:09:06):

And when we asked patients who had used both buprenorphine and methadone, were both of these drugs equally likely to precipitate withdrawal or to cause an adverse reaction, or was one more likely, they were significantly more likely to state that buprenorphine was itself causing the precipitated withdrawal response.

(01:09:24):

So this is a context. This is kind of the big challenge that the field is facing, right? We have increasing rates of overdose death. We have a need to expand treatment access for patients, and we have the predominant drug opioid that people are using is interacting with one of our most commonly administered medications for opioid use disorder.

(01:09:44):

The good news is that we have this very robust continuum of care and existing medications for opioid use disorder. This is the ASAM Continuum of Care model. You can see that it stretches from early intervention and outpatient services, all the way through different levels of intensity, up to medically managed intensive inpatient. So this suggested, if we have innovation in this area, that we could plug it in to this continuum of care, right? We're lucky in that we have this very robust treatment infrastructure. We just need to find ways to optimize it to get access to our patients.

(01:10:17):

Some of the ways that we could optimize it are things like creating good outcome assessments from these various forms of care, methods to match patients to treatment intensity, to better match them to treatment intensity, and the ability to predict relapse and success from various forms of treatment. We're not, at the moment, very good, I think, at identifying which of these forms of treatment a patient may best benefit from. And that's important when you consider that some of the treatments are scarce. And so we would like to be able to match people appropriately the first time they go to treatment so that we could maximize our ability to treat them effectively and to retain treatment access for other patients as well.

(01:10:57):

So where might innovation help most? As I mentioned, a lot of the things that I'll raise were discussed by the prior speakers, and I appreciate them raising those concerns and the conversation that was generated. I'll try to focus on kind of concrete, actionable items that might be something that you could contribute, if you are in the position where you could identify medications or devices or various innovations to the field to help us, I guess, best address these issues with our patients. So again, for context, buprenorphine of the medications for opioid use disorder is our most scalable treatment model. It's the medication that we can currently give from primary care offices. It has the best potential for us to be able to optimize and to expand access. As you see, however, on the right hand side, this is a study that was recently just published that estimated the number of people that are receiving medications for opioid use disorder, which is predominantly buprenorphine, and the number of people who need it. So across the top here, these are the individuals that were estimated based on national epidemiological surveys to be affected with opioid use disorder and to have some potential benefit in receiving access to medications for opioid use disorder.

(01:12:14):

And then across the bottom here, this is the treatment gap. So they estimated, more than 7 million people annually would benefit from having access to these treatments, yet only around 1 million people on a regular basis are receiving them, which represents an 86% gap in the treatment care for these patients.

(01:12:32):

When you ask providers what the barriers are, right? So we know that buprenorphine is available, why is it not being dispensed? They will tell us, in part, that they don't have time to take on new patients. They have concerns about precipitating withdrawal, and they have concerns about diversion. So these are three actionable areas that there could be either medications, protocols, or devices that might be able to help alleviate some of these concerns or burdens for providers, and increase their willingness to prescribe buprenorphine.

(01:13:03):

We do know that on average, the average buprenorphine provider is treating five patients or fewer. And those data were collected at the beginning of around 2010, and then again, repeated several years later, and they didn't change. And that's, I think, notable because a lot happened in the public area between that period of time to increase willingness to provide, and this was all before the waiver was removed, but still, we didn't see, despite all of the public health efforts, we did not see a change in the number of patient, the number of providers who were, or the patients that were being treated per provider. And I think that that speaks to the concerns that providers have in expanding their practice.

(01:13:44):

And so, again, where is this unmet need and where might innovation help most? So we need novel strategies to support comfortable induction onto buprenorphine, particularly among people who were

recently exposed to fentanyl. I know that this was discussed at length yesterday, and if you haven't seen those talks, I encourage you to go back and review them. But from a product development perspective, the field has split somewhat into a low dose and a high dose strategy. Neither has strong empirical support, but again, both have strong anecdotal support and both are being utilized by different groups throughout the country. So empirical validation of either of these approaches would be very helpful.

(01:14:21):

Also, if you prefer a low dose strategy, it would be useful to have doses that start or that begin below two milligrams. So the lowest dose of Suboxone at the moment, or the combination product, the sublingual product, is two milligrams. And we know often that, actually, many cases, providers will cut the dose strips into smaller dose increments. However, that's not something that can be prescribed in that manner. And so it's a bit of a challenge. There's also a need to explore transdermal or buccal dosing, things that might be able to deliver even smaller doses of buprenorphine to help with that low dose strategy. In contrast, individuals who are interested in pursuing the high dose strategy, maybe we look at more mono-products. Many of our patients report in aversion to the naloxone, and we've actually seen in our clinic that if we do shift people from the combination to the model product, that we do see a reduction in the withdrawal severity that they have on those first few days. It might also be the case that we just need higher doses, that we could go straight to higher denominations than eight milligrams, to be able to hit people really hard with this high dose and surmount the fentanyl withdrawal.

(01:15:36):

We also need help with precipitated withdrawal management. So we know, many patients are experiencing precipitated withdrawal. Also, it's beginning to be reported by patients as a concern for starting or initiating buprenorphine treatment. And that's a major concern to me because that's our most scalable treatment model. So if our patients are not willing to use our most scalable treatment, I think that we're going to have significant problems.

(01:16:02):

So what might this look like to help with precipitated withdrawal? One thing that we could consider is investigating short-acting opioids as a bridge. Our clinic has been able to use hydromorphone in a research setting, to be able to bridge patients for a few days to wash out the illicit fentanyl, and then initiate buprenorphine inductions. We've found some success with this. It's not well studied yet, but that might be one actionable target that we could investigate. Another would be to look at opioid medications that might have lower potency like tramadol or kratom. These are medications that potentially could be used to bridge participants over that would have their lower scheduled medications. And so maybe there would be fewer legal restrictions on being able to do so. We also would benefit from non-opioid adjunctive or supportive medications. For instance, ketamine is something that I've heard reported as used in hospital settings to treat precipitated withdrawal. That's certainly an off-label use of that medication, but perhaps it could be investigated for that purpose and actually clear so that hospitals could use it in a more straightforward manner.

(01:17:11):

In addition to that, we would value induction protocols, actual clinical guidance or clinical guidelines as to how to induct patients from illicit fentanyl to buprenorphine. And then also to kind of address some of the concerns that providers have regarding their confidence in doing this. We could look at structured provider training and mentoring programs like ECHO programs or hub-and-spoke models.

(01:17:34):

We also need to increase treatment access in rural settings, and this includes supporting remote medication management. As was stated in the last panel, opioid problems are exacerbated in rural

areas. There's lots of comorbid mental illness and chronic pain in these patients are complex. And we also know from the literature that women are less likely to enter treatment than men. Often, they report structural barriers, things like childcare, restrictions that prevent them from getting access to the clinic.

(01:18:00):

In addition, we know that in many rural counties, there's no providers. There's few or no providers of Suboxone. This is even more scarce in tribal communities. These data here were recently published, showing the driving distance to a provider, to a physician, in West Virginia. And you can see that the majority of counties had significant driving distances that they had to go to be able to get access to providers. That's a common trend, something that we've seen for years, and there were several reports actually that came out last year showing the same relationship. If this is a barrier that patients have, if they can't afford to drive these distances or to spend that amount of time, or they don't have reliable transportation, we need to find other ways to get access to their treatment.

(01:18:44):

This could entail extending the extended release formulations or expanding access to them. We know that we have these extended release formulations of buprenorphine available in weekly and monthly formulations. We had hoped that they would help with the compliance issues, or that they would maybe address some of the compliance concerns and increase the likelihood that patients, particularly in these lower resource areas, would have access to these efficacious medications.

(01:19:11):

However, as you just heard in the last panel, there's many structural barriers preventing that may be preventing that from happening. And that includes challenges with the induction or the eligibility for the medications, the fact that they're often required to be distributed through specialty pharmacies, which could be scarce in rural settings. There's complex payer structures that could be prohibitive. And then the physician and patient adoption are currently low. And our experience has been that providers often are unaware of these medications or unfamiliar with how to use them.

(01:19:44):

We can increase provider confidence by reducing diversion risk. Novel packaging or monitoring could provide secure and remote medication management. These are examples in the market currently of products that could be used for this purpose. One is Emocha, which is observed treatment. MedMinder and Pippa Tipper Dispenser are two forms of commercially available products that are used for remote management of polypharmacy and maybe could be pivoted or leveraged for investigation in the area of opioid use.

(01:20:12):

And then finally, we also want to treat complex clinical conditions. So we know, many of our patients at the moment, there's high rates of polysubstance use, particularly stimulants. We need novel medications, perhaps things that treat both opioid and stimulant use, or treat craving in general. We need access to behavioral strategies such as contingency management. The medications for opioid use disorder are important, but they need to be complemented with counseling. If we could extend digital therapeutics to support that or telemedicine expansion or methods to expand other platforms to support telemedicine for our patients, that would be useful. We need ways to manage comorbid chronic pain, things to manage cravings.

(01:20:53):

So what examples of innovation are currently being studied? We know that there are biosensors being developed to investigate craving, to investigate withdrawal and overdose. There's a product called the naloxone parachute, which can administer naloxone automatically in response to dropping oxygenation levels. There are people pivoting devices from analgesia to opioid use, such as percutaneous nerve field stimulators, or the bridge device, for instance, to treat opioid withdrawal and pain.

(01:21:21):

There's investigation of psychedelic treatment of opioid use disorder, predictive algorithms to match patients to treatment intensity, digital therapeutics, chat-bot based counseling, virtual reality-based interventions. So there's lots of things that are being developed, that could be shifted into the substance use field, to be able to meet some of these gaps that we are seeing. Because again, the medications, we have the medications, we just need to optimize patients getting access to them.

(01:21:49):

So to conclude, I don't believe that we can adequately solve our current substance use crisis by employing the same existing strategies. We need new ideas and big thinkers who can introduce new approaches and ways of thinking to be able to solve this. Thank you.

PART 2 OF 6 ENDS [01:08:04]

Susan Winckler (01:22:06):

Dr. Dunn, I'm not sure you could have summed it up any better than saying we need some big ideas and bigger thinking, and that's what we're aspiring to do. And so, not to put our panelists on the spot, but we're going to challenge them to be thinking big ideas and big thinking. But thank you for pulling together so much of the content that we've heard and grounding us in those opportunities.

(01:22:31):

I want to have our other new faces for this panel come on screen, and I'll introduce you all in alphabetical order as well. Dr. Pouya Azar is head of the Complex Pain and Addiction Service within the Department of Psychiatry at Vancouver Coastal Health in British Columbia, Canada. Welcome, Dr. Azar.

(01:22:52):

Dr. Bartholt Bloomfield-Clagett is a medical officer in the Division of Anesthesiology, Addiction Medicine and Pain Medicine in the Office of New Drugs at the FDA's Center for Drug Evaluation and Research. Then we have Dr. Jody Green, who is Chief Scientific Officer for Uprise Health Inflexxion. And then Dr. Ivan Montoya, who's acting director of the Division of Therapeutics and Medical Consequences at NIDA, and chair of the NIH HEAL Initiative in Medications Development for Opioid Use Disorders Program. And then rounding out our conversation is Michelle Winberg, who is medical clinic lead and a phlebotomist with Harm Reduction Michigan.

(01:23:36):

So, panelists, thank you for joining us, and I'm going to ask each of you a question to get things started, and then we'll continue our conversation. Dr. Azar, I am going to start with you. So as you heard the conversation about potential additional formulations of buprenorphine, which formulations do you think have the potential to make the most difference for patients? Different dose, root of administration, duration of effect, where would you target effort?

Pouya Azar, MD (01:24:12):

Well, thank you for that introduction, and it's a real honor and pleasure to be here amongst this panel.

(01:24:18):

So I've also been asked to provide some context with regards to pain patients who may benefit from buprenorphine. So I think I'll start by changing the context a little bit, in the sense that, when I treat my patients, whether they're using illicit unregulated fentanyl, or if it's the elderly patient who's been on oxycodone for fibromyalgia for the last 15 years, they can both obviously benefit from buprenorphine.

(01:24:44):

But as we know, and as has been mentioned already, the expectation right now, as far as on-label use, is for the patient to go into withdrawal before receiving this medication. For our pain patient, this means not only opioid withdrawal, but also rebound pain. And for our addiction patient, this means severe withdrawal, and we know that many of our patients will use solely to avoid withdrawal. So it's a large ask. And to ask patients to go into withdrawal first, most will refuse. Many will try and fail.

(01:25:20):

So the solution to this initially has been low dose inductions or microdosing as is been described in the past. The first paper was by my friend, Dr. Hamming and Dr. Vogel out of Switzerland. So this circumvents the need for the patient to go into withdrawal before receiving buprenorphine, whether they're a chronic pain patient or they're an addiction patient.

(01:25:47):

Now, the problem with these protocols, often, the way they're used, particularly in an outpatient setting, is that they're started at unusually and unreasonably low doses, and they take many days to complete. And during this time, the patient's still expressing cravings and withdrawal, and has a high risk of relapse during the induction process. So our solution, from our institution, starting about six years ago, was to initiate rapid microdosing protocols, so being able to get people to a full dose of buprenorphine within one to two days, without the need for them to go into withdrawal. In fact, I can't remember the last time I did a cow score or expected a patient to go into withdrawal. And we've done hundreds of these.

(01:26:34):

Now, this is where the product innovation comes in, because the way these protocols have been set out, and they're published, and you're welcome to look at them, is that the patient will require dosing every one to three hours. This works okay in hospital, but it is a barrier to outpatient inductions. So our solution to this was to compute a model, this expected serum levels that a patient will experience during our sublingual rapid low dose inductions, and then to convert that to transdermal delivery of buprenorphine, so using the patch. So we've been able to come up with a protocol, where a patient can go from no buprenorphine to a full dose of buprenorphine, in one to two days, by using the transdermal patch only.

(01:27:28):

Now this can be once a day application. So this overcomes the need to dose a patient every three hours. So you can imagine, in an outpatient setting, whether you have a patient with addiction or with pain, they can put on patches on day one, put on more patches on day two, and then by the end of day two, they're ready to receive a full dose of buprenorphine.

(01:27:52):

The difficulty there is that the patches are expensive, and in the past presentations, it has been mentioned that people are looking for patches because they want to start with much lower doses than the sublingual formulations. We're doing the exact opposite, in fact. And the patches that we use, the maximum dose we're able to have in Canada are 20 micrograms per hour. So we're needing to use 12

patches to get people to the adequate serum levels for them to receive a full dose of buprenorphine. So what our need would be is to have patches that are much higher doses, to avoid the need to put 12 patches on a patient, and to remove the restrictions that the patches currently have because they're only on label for pain. And to reduce the expense associated with the patches. In Canada, the full induction costs about $900 in an outpatient setting. It's free in an inpatient setting because we have socialized healthcare.

(01:28:57):

And I think the last, and I'm sorry I'm going over time, but the last point I do want to make is that, regardless how easily you get somebody onto buprenorphine, we know that the majority of patients will relapse within a year. And we know that a significant barrier is compliance to medications. And we have an excellent solution to this. And one of those solutions is the extended release default preparation buprenorphine. As mentioned previously, the barrier to this is that, again, patients have to go into withdrawal. They have to be dosed onto eight milligrams of buprenorphine, and then you have to wait seven days for them to get the injection.

(01:29:34):

So we've combined all of our protocols, and what we're doing now is going from day zero patient using fentanyl, putting them on the patch, and then going directly from the patches to a sublingual injection within 24 to 48 hours, without even any need for the sublingual formulation. Now, for this to be more widely used, would have to remove the limitations of the injection, which are that a patient has to be stabilized on eight milligrams of sublingual buprenorphine for a minimum of seven days, because we know, first of all, it can be difficult to get a patient onto that eight milligrams, and then we have to wait another seven days before they get the injection. So, there's plenty of opportunity for failure during that type of induction.

(01:30:24):

The last thing I want to mention, and I do apologize for going overtime, is that I know there's been a lot of discussion around the interplay between fentanyl and buprenorphine, and how that impacts inductions. But we do know that during the low dose induction phase, so the first 24 to 48 hours, the patient's opioid requirements are not met. And we do need to meet those opioid requirements by giving a full agonist. So we've been doing that in hospital, using hydromorphone for about the past five, seven years. More recently, we have a fentanyl protocol where we're giving patients IV fentanyl during the induction phase to avoid withdrawal because opioid tolerances are exceedingly high in the age fentanyl use, and sometimes, hydromorphone is not enough.

(01:31:11):

Now I mentioned this because we're going from round the clock IV fentanyl to buprenorphine without any difficulties. So that's sort of, it may speak against this interplay between fentanyl and buprenorphine, but I think what the problem that many providers are running into is the difficulty to meet patient's opioid requirements while they're being low dose induced on to buprenorphine, and the patient going into withdrawal. And that may seem like precipitous withdrawal, but it's likely as a result of the patients not having their opioid requirements met.

(01:31:44):

So just to summarize, we need lower doses of buprenorphine, no lower than 0.5 milligrams. There's never a need to start any lower than 0.5 milligrams. We need larger doses of the transdermal patch, and to remove the restrictions associated with the patch. And we also need to remove the restrictions associated with the default preparation buprenorphine injections.

(01:32:08):

I'll just leave it there for now. Thank you.

Susan Winckler (01:32:10):

Yep. Excellent list, Dr. Azar. Thank you for walking us through that.

(01:32:16):

Michelle, I want to turn to you next. We've got Dr. Azar's really constructive, right kind of thinking through what we need on the microdosing part, the inventive, in a good way, use of the transdermal patches, and the extended release, from the clinician initiating and working with patients. Bring us to the patient perspective. What do you see as a helpful additional formulations that would help make the most difference for patients? Whether that's a different dose, a root of administration, how long it lasts, what should we internalize from the patient perspective?

Michelle Winberg (01:33:08):

Myself. Yeah. I'm both a patient and a clinician. I work in an office that does suboxone treatment, but then I'm also a patient of another office and have been for around 13 years. So I've been around since it was just suboxone tablets to choose from, and they cost a fortune.

(01:33:33):

But nowadays, there are other options available. And Medicaid lifting that prior authorization requirement was huge for us. But there is a definite need for a different dosing regimen and also different formulations and different ways for a person to take it. One of the other speakers was talking about these different options that might become available to people, which I was unaware of. So that's pretty exciting to think about, that there's research and studying going on around that.

(01:34:18):

But one of the biggest challenges with the dosing is that it's kind of been the same for a really long time. There's two milligrams, four milligrams, eight milligrams, and local pharmacies tend to really only stock the eight milligrams. So we've got lots of people that are on a lower dose, but they're having to split these tablets or film down into tiny little pieces. And so I think, by reaching out to the different drug companies and seeing how do we go about producing different formulations and strengths dosing at a wider scale so that pharmacies are more willing to stock it, I guess.

(01:35:11):

But from my experiences, I have been on two milligrams and four milligrams, and when you go to the pharmacy, they don't actually have that medication in stock, but you do need it that day. And so it's really important that it's there. And so we'd have to really get the buy-in from pharmacies and stocking. So yeah, I've been splitting eight milligram tablets into six pieces at some points just to take a daily dose.

Susan Winckler (01:35:43):

Which requires some visual acuity that you can see it, and then some dexterity, which is-

Michelle Winberg (01:35:52):

And pill cutters that you can buy. They're the best. So.

Susan Winckler (01:35:56):

Yeah. Sometimes they're tablet crushers.

Michelle Winberg (01:35:59):

Yeah, yeah.

Susan Winckler (01:36:01):

Instead of the splitting. Michelle, that's really helpful in helping us think about how it's actually used, and the ability of thinking about how to split and shrink that down.

(01:36:15):

I want to turn. Dr. Green, you've done some work on packaging and the impact that packaging can have on buprenorphine safety. Would you introduce us to that?

Jody Green (01:36:30):

Sure. I think that was a great lead in, Michelle, in terms of having to take a product that is packaged specifically to keep it safe both for the therapeutic and integrity, but also out of the hands of kids who could potentially get into the medication. And so the requirements you're talking about will force the patient to have medications outside the original packaging and present additional risk in the home.

(01:37:04):

One thing, we've talked a lot yesterday and today about the clinical applications, and I think the work I do comes a little bit more from a safety perspective, for both the pediatric unintentional exposures, which is actually part of the buprenorphine rems. For those of you not aware, that is one of the requirements that the physicians are supposed to be counseling patients on safe storage of these medications, specifically asking about children in the home and such.

(01:37:34):

So the good news is, and promising news, is that the study that Susan alluded to were intended to evaluate the impact of unit dose packaging, specifically for buprenorphine products, and both the CDC data, I work with the group at CDC, the National Electronic Injuries Surveillance System published a paper showing a reduction of 66% of emergency department visits in kids, once the market reached 80% using unit dose packaging. So that is a significant impact, when you think about the safety of these children in these homes.

(01:38:26):

So we repeated the study using Poison Center data and found the same thing. Actually, it was even higher. It was a 80% reduction in reports of pediatric exposures following that, the 80% mark for the unit dose packaging. So that has, I think, made a significant improvement and hopefully also the confidence in the prescribers and encouraging that news that these products out in the real world can be kept safe from people that they're not intended for, while allowing appropriate treatment for the people who do need these medications.

Susan Winckler (01:39:09):

And of course, Jody, that is heartening that we know we can get them focused for the folks who do need them. Of course, then it starts with the inherent, is it the right dose? And then, it could although contribute perhaps to greater stocking in the pharmacy, if there's just better understanding of the availability and then the protections in the unit dose. All right.

Jody Green (01:39:39):

Yeah. I just wanted to add one thing about the patches as well. That conversation is fascinating, and yes, we all know that they're appropriate or currently labeled for pain. We actually did a study, it's been a handful of years, but looking at abuse and diversion of the patches compared to the other buprenorphine formulations, and also compared to, say, like a fentanyl patch. And the transdermal buprenorphine patches had absolutely the lowest rates of abuse and diversion, significantly lower than any of those other product types.

(01:40:16):

So I think that's other encouraging news as we consider putting these other products out into the intended patient population, but then also thinking about the other risk factors that come in those populations with different products. And that stays a little outdated and maybe we need to update the information, but I think that should also be encouraging news when we think about incorporating these patches into treatment regimens.

Susan Winckler (01:40:43):

Yeah. Yeah. Great. Thanks for that update, Jody, and reminding us of that.

(01:40:47):

Let's turn a bit to the regulatory side. That means I'm turning to you, Dr. Bloomfield-Clagett. Are you ready? Let's talk about the potential regulatory pathways and the programs that facilitate development of additional formulations of buprenorphine, because we know we can have the work done and then it needs to come to the agency. So what are some ways that the agency can facilitate that or is thinking about this space?

Bartholt Bloomfield-Clagett (01:41:16):

Right, Susan. So first off, I just want to say thank you to Dr. Dunn for excellent presentation, as she mentioned some themes that we've been hearing throughout the meeting over the past two days, but she also presented some interesting new ideas to add to the list and it's been a very fruitful discussion. And so thank you for moderating that so well as well.

(01:41:41):

But to answer your question, just to note that all of the available pathways for drug development are available to sponsors who wish to make buprenorphine products. And so you might hear regulatory terms like 505(b)(1), 505(b)(2) efficacy supplements. I won't go into the details of all of that, but just to mention that there...

Bartholt Bloomfield-Clagett (01:42:03):

I won't go into the details of all of that, but just to mention that there are multiple pathways and they differ in terms of the type or the source of the information that the sponsor is using to support their application. In some cases, the information may be coming from another source and that could even be a previous agency finding. And so in those contexts, the process of drug development and regulatory review has the potential to move more swiftly and more rapidly. But, as you mentioned, I also wanted to note some of the other programs that are intended to also help speed the process of development and regulatory review for drugs. And these are for drugs that treat serious diseases, and of course opioid use disorder would be considered one of those.

(01:42:54):

I just wanted to highlight both the fast track designation and priority review. There are others, but those are perhaps the programs that might be most relevant to this particular product area. And what those programs allow for is increased interaction with the agency in terms of getting feedback about study design, answering questions. It also provides, in some cases, rolling review. That means that a sponsor can submit components of the application as they're completed and become available and we can review them. And then it can also mean that the actual timeline of the review for the new drug can be shortened from the standard regulatory clock. Regardless of the type of regulatory pathway or a program that a sponsor might pursue, we always encourage sponsors to come to us early in the development process to discuss any questions about study design or any other questions they need answers to. And what that does is it helps to ensure that when we get to the point of the new drug application, of the marketing application, that we have all of the information that we need in order to make that regulatory decision.

(01:44:26):

I'll just note in reaction, in response to some of the comments from some of the other panelists in terms of products that we've heard quite a bit about or product ideas we've heard quite a bit about throughout the meeting, transdermal products have been coming up a lot, low dose transdermals, low dose buckle products, lower doses of sublingual formulations that people might want to see. And because of some of the things that I've mentioned in the regulatory pathways, it's possible that those are kind of the low hanging fruit. That said, we've heard about a lot of great and innovative ideas and certainly lots of different types of approaches are going to be needed. Not every approach fits every patient.

PART 3 OF 6 ENDS [01:42:04]

Susan Winckler (01:45:19):

Really helpful. If I heard you right, there are many ways to navigate the FDA process and it's really helpful to talk to the agency in that navigation process. So you can have some agreement on what it takes to move forward.

Bartholt Bloomfield-Clagett (01:45:45):

Exactly.

Susan Winckler (01:45:47):

Okay. Which will likely involve some research, which means, Doctor Montoya, it's time to turn to you. What are the NIDA research priorities related to buprenorphine initiation and maintenance care?

(01:46:06):

Unmute for me. There you go.

Iván Montoya (01:46:11):

Thank you Susan. And thank you Kelly for the great presentation, it really set the stage. And thank you to the panelists because it give me a great ideas. I think one of the things that we are very interested at NIDA is to think about not just the medication. The medication in diabetes, we know that insulin or metformin are very good medications, but we always need a diet and we always need something else. There's a lot great of interest in the support of psychosocial interventions to improve the initiation and adherence, and staying and adherence to the buprenorphine treatment. So that is something that is of

great importance and we think is something that sometimes is neglected and some treatment programs focus a lot so much on the medication and then tend to forget that those patients have [inaudible 01:47:14] needs that may help to improve their treatment outcomes.

(01:47:21):

Kelly outlined some of the areas that NIDA is already supporting, I think we are supporting right now research and I would say almost all the areas that Kelly presented. But I just want to summarize some of the topics that some of the compounds and areas that we are very interested right now. One of them we know is that adherence to buprenorphine is pretty low. And especially now in the time of fentanyl when, based on the data that Kelly presented, it is very difficult to induce and keep people addicted to fentanyl on buprenorphine. We are looking at ways to improve the adherence. And one of the products that is being supported by NIDA, the development is called LYN-O13. LYN-013, this is an oral formulation of buprenorphine that lasts for one week so the patient only needs to make a good decision once a week. That product is already being tested in humans. And it's really a game changer, in my opinion, because it's going to allow patients to take only one dose per week. And the mechanism of this compound is quite unique and it has been tested for other indications and we think that has a lot of promise or adherence.

(01:48:50):

And this is kind of a long story, but we also have, and I don't know if it was discussed yesterday, I looked at the slides, but I didn't see a description of the six-month implantable buprenorphine that was approved by the FDA. So we shouldn't forget that there was at some point an implant that worked for six months. It was approved, it was marketed in the US but, unfortunately, I think the company took it off the market. My understanding was that the REMS program, all the protections and the transition from oral buprenorphine to this implant was very difficult. And the visit require a small surgery and then removal of the implant. But still, the company decided that it was not feasible to continue in the market and it was withdrawn.

(01:49:47):

Now the early important area in this is the, as has been mentioned during this meeting, the opioid withdrawal associated with buprenorphine initiation. And that's something that we have supporting multiple projects, looking at how to improve the treatment of opioid withdrawal. We know we have lofexidine, which is approved by the FDA for treatment of opioid withdrawal, but we also know that it's not sufficient. That sometimes we need more than just this alpha-2 agonist lofexidine to treat opioid withdrawal. So we are looking at our approaches that can be not alone or in combination or with lofexidine, including approaches. Like there's a compound that is being developed in Australia is called KNX-100 by a company called Kinoxis that has a very unique mechanism and we are very interested in that type of compound, and many others. I can spend the whole afternoon talking about the whole portfolio of compounds that we have.

(01:50:56):

The other important area that is a big deterrent for treatment with buprenorphine is insomnia. I don't know the clinicians, if they hear the patients complaining that they can't sleep. And it's more unique to buprenorphine than to methadone. In general, patients on methadone are more sedated, but patients with buprenorphine, they complain about insomnia. And we have a large program right now, research looking at different medications to treat insomnia in patients with substance-use disorders. And actually, Kelly, is being supported by one of those projects. And one of the areas that is of great interest is the study of orexin receptor antagonists is a group of medications including one that is approved, or several that are approved by the FDA. The one that Kelly is testing is suvorexant. So that's another area

that we think that by improving sleep in patients treated with buprenorphine, we can improve also the buprenorphine outcomes.

(01:52:06):

Another complain that we have heard from patients is that they can't sit still when they are on buprenorphine. It's part of their withdrawal syndrome, but they have to be moving all the time. It's sort of like a restless leg syndrome sort of like, but it's not quite. And so then we are supporting the study looking at pramipexole for treatment to improve. At least the patients can sit still and not have to be moving all the time. And many are joint medications so I can spend the whole afternoon.

(01:52:42):

But we also, in addition to improving the treatment of buprenorphine, we think that buprenorphine is great but there are other options. There may be other options that may have less problems than buprenorphine, that have less abuse potential, that is easier to induce. I cannot go in detail with all the projects that we are supporting right now in that area, as well as methods to discontinue buprenorphine then transfer people to opioid-free, which is I think the dream of many of people who are on opioids, who are dependent on opioids, or to the opioid antagonist naltrexone. And we have a long-acting formulation of Naltrexone. So there are several projects looking to transition and help people who are not happy on buprenorphine help them to transition to other treatment approaches.

(01:53:43):

Something that was mentioned before that also caught my attention and I think is something that we are keeping in mind at NIDA is the issue of polysubstance abuse. And as you may know, the HEAL initiative help to end addiction long term was initially developed to support tools to improve the outcome of opioid use disorders and pain. But because of the comorbidity of opioids, and especially with stimulants, the scope of the HEAL initiative was expanded to include stimulants. And right now several projects are being developed in that area.

(01:54:26):

And I think something that really needs to be investigated further is the role of buprenorphine in the treatment of dual opioid and stimulant use disorders. Because there's a lot of data, preclinical data supporting that, and also a couple of pivotal studies with significant results showing that buprenorphine can help people who are dependent on opioids and on stimulants. This is just a very brief description. I'll be happy to go in more detail about any of the projects or any of the areas that NIDA is supporting. Again, thank you to the Congress passing the helping to end addiction long-term initiative because, thanks to those funds, we are now in the process of being able to offer many, many more opportunities to patients with opioid use disorders and also stimulant use disorders.

Susan Winckler (01:55:30):

It's just so heartening to hear of all of that research activity, Doctor Montoya. Thank you for that. I want to ask a question then on the research and in what I'm going to call patient centricity. And Michelle, I'm going to turn to you with a specific question and then I'd like Doctor Green and Doctor Azar and Doctor Dunn to noodle while I ask Michelle the question, think about, I was struck by the visual and manual dexterity required for splitting the tablets or cutting the strips. I'd love for you to be ready to talk about what are the research needs there in thinking about the errors that might occur from that tablet splitting or the film splitting. I'm going to come to you for that.

(01:56:23):

But first up, and Michelle, I want to ask a question I was struck in the discussion of the long term and the maintenance use. I think I know the answer to this question, but would love for you to give voice to it. Are there problems getting refills, in a way you said that already, but I want you to talk a little bit more about accessing refills. And then is this a medication that you forget to take or is it from a patient experience pretty disciplined and you remember, or you put in a structure to help you remember? Talk to us a little bit about the patient dynamic of accessing refills. And then day-to-day, is it relatively easy to remember or not?

Michelle Winberg (01:57:17):

Thanks. The filling at the pharmacy as of late, it seems like there's more challenges and they just are able to keep enough in stock. Some pharmacists have said they're limited. And I can't remember if it was how much they can order or keep on their shelf, but that seems counterproductive to say the least. We do have challenges I have had as a patient, but also as the support staff for our physician. When a patient leaves the office and they go to pick up their medication in a rural community, there's only a handful of pharmacies. And so that can be challenging and take time to figure out what we're going to do.

(01:58:09):

And then on a personal note, I've had to go a couple days without having my medication. Very quickly you'll start to feel withdrawal. And so that's usually our indicator, either A, you forgot to take your medication, or B, you're still waiting for the pharmacy to have it in stock. Those are real challenges.

Susan Winckler (01:58:34):

Then that tells me that you know you take it daily or whatever your regimen is.

Michelle Winberg (01:58:45):

Yeah. In the beginning, the first several years, when you're just getting clean, you're kind of used to a process anyways. For me, it was IV drug use. The whole process of doing all that, I had to replace with something. And so that was kind of my thing with buprenorphine in the beginning years. Now it's been several years of being clean so I'm not as addicted to the process of having to do something. And I do forget to take my medication some days. But usually the first indicator for me and a lot of people is they'll start sneezing or start feeling the restless legs at night. And so they're like, "Oh crap, I got to take my meds."

Susan Winckler (01:59:27):

Okay. That's really helpful. Really, really helpful. So Doctor Green and Doctor Azar, Doctor Dunn, anybody want to jump on what do we need to do to help Michelle and everyone in splitting those tablets? What are our research needs there? All right, Doctor Azar, you started talking first. Fire away.

Pouya Azar (01:59:49):

I can speak to what's worked here in Canada for us. Really the only time a patient would need to split the tablets is when they're in the low dose induction process. They're starting at small doses and gradually building up the dose. So what we've done in the outpatient setting is first of all, our pharmacies split the doses and we've asked the pharmacies to package the doses in blister packs or bubble packs, so it's all laid out for the patient. Day one, dose one, day one, dose two, et cetera, et cetera. And then day two. And then once they're at their full dose, then it's just the same dose everyday and there's no longer the need to split the tablets. But this expectation to have patients split tablets and

create specific doses, I think it's a lot to ask, particularly given that the lowest dose is a two milligram tablet, it's very difficult to split it to any lower dose increment in 0.5 milligrams.

Susan Winckler (02:00:48):

Really helpful. Tablet splitting, even for those of us who are trained as a pharmacist is not for the faint of heart if you're trying to do it accurately. Jodi, do you want to add anything there?

Jody Green (02:01:02):

I think when you think about other compliance tools, you can look at things like birth control pills and having the actual doses as Doctor Azar was talking about, the specific doses for the specific days. Even z-paks we become accustomed to that. We know that the design and the concept is certainly there.

(02:01:26):

I'm glad you brought up the splitting at the pharmacy because that was also going to be my question is how do you engage the professionals in making sure that the doses are appropriate? Because if the pills are not splitting equally, if the amount of active ingredient is not well dispersed in the product, then that variation in dosing could also have some negative clinical impacts as well in these individuals.

(02:01:58):

The other thing that we had heard in some of my other research in looking at root cause is there's still a kind of stigma with having your bottle of pills or your film. And so a little bit more disguised packaging, if you will. We had heard reports of patients would take a pill out of the packaging, wrap it in a Kleenex and put it in their pocket for the day because they didn't want anyone to see what medication they were on. And so that is kind of a unique concept that maybe we don't think about when we're asking people if they're not always taking it at home, if they need to take it with them. And then the pills wrapped up in the Kleenex, we learned about that when we studied the pediatric exposures because then that presented the risk to the other younger population as well as to the patient either losing it or forgetting where they put it or falling out of their pocket. But some of those other, I think, packaging ideas should really be explored with the actual users. Having user groups of patients telling us about their day, telling us how they maintain their regimen, what are their challenges, and if they miss a dose, why do they miss a dose, if they're not feeling well then... And have those conversations, more conversations with the patients that are doing it every day.

Susan Winckler (02:03:40):

The patient centricity is really just essential in any drug or product development, but certainly in this space. Doctor Dunn, you're unmuted.

Kelly Dunn (02:03:51):

Just to add to that, I think those are really great ideas. And I agree that probably it's not the best long-term strategy to have a situation where patients are having to split their doses. It would be more ideal, I think, for them for those doses to be produced in those denominations. However, because that might take a bit of time to do, one thing that seems like it could be more immediate would be even just to print on the doses, the points. The filmstrip, for instance, for buprenorphine doesn't indicate easily. There's no lines to tell you where to cut. Something like that could be a relatively quick solution that would just facilitate a little bit more and be a more immediate solution in the interim, while we're waiting for products to be able to packaging, which I agree with completely, or these lower dose dominations to be available for people.

Susan Winckler (02:04:41):

Even notches, right? Either a printed-

Jody Green (02:04:46):

The scoring.

Susan Winckler (02:04:47):

... or a notch. Yeah, a scoring of the strip. It's really intriguing. But Doctor Dunn, you mentioned kind of digital interventions, other non- pharmacological, non-drug support tools. I want to open it up to everyone on the panel. Where do you see opportunities for some of those I was going to say non-product, but I mean non-active pharmaceutical ingredient interventions, whether it's digital or some other support tool. What are some opportunities that we should be thinking about in that space?

Pouya Azar (02:05:32):

I can mention about a couple of things we're doing in a research setting now. We know that there are very sophisticated digital algorithms that are designed to induce dopamine release in specific settings. Gambling apps are a very good example of such and such an algorithm. We're working on developing algorithms to induce open release that can be used in specific settings. So maybe counter open release that you may receive chemically or through another behavior. And these specific algorithms would be targeted for the patient behavior, but would also have a tapering algorithm built in. Essentially it would be a way of replacing another behavior or chemical that induces open release with a tapering algorithm to get them off. That's sort of an area of digital research that we're involved with now.

Susan Winckler (02:06:29):

Exciting and an interesting piece. Doctor Dunn, you want to go? And then Doctor Montoya, I'll turn to you.

Kelly Dunn (02:06:35):

I'll just add, when we talk with providers about what some of the barriers are to adopting buprenorphine or to increasing their patient limits, often it's that they don't feel equipped to be able to direct people to counseling, and they feel that that's necessary for them to have. That's not what they're trained in. They don't know how to access counseling or where to reliably send people. And so often they report reluctance and taking on too many patients and taking on new patients essentially. They're really treating the patients that were already in their practice that acquired opioid use rather than taking on new patients. So I think products that expand that access, that could allow the providers to treat the medical side and someone else to treat the psychosocial side, I hope would be something that could kind of expand the treatment capacity. And I think the use of artificial intelligence, especially as being rolled out in other areas of mental health, like these chatbot- based counselors, or these virtual reality programs that help with craving mitigation, or you can do virtual meetings to do kind of virtual self-help guided groups. I think we're seeing them be employed and be developed in other areas of medicine. And I think those are things that could be pivoted over into the substance use field somewhat quickly, and they could qualify as devices or cleared devices to be able to support reimbursement.

Susan Winckler (02:07:57):

Even broadening where those might be applied. But I like the idea of being able to expand your pool of prescribers with those additional resources. Doctor Montoya?

Iván Montoya (02:08:12):

I think that also expanding the pool of alternatives to patients, not everyone needs the same. Some patients may benefit more from individual interventions, some may benefit more for group therapy, some may benefit from digital interventions, some may benefit from chatbots. So the idea will be to individualize the treatment and match the patients to the best treatment possible.

(02:08:46):

And in the non-pharmacological or non-molecule area that Susan mentioned, I think there's also a place for neuromodulatory devices. Devices like transcranial magnetic simulation. There's very interesting data with deep brain stimulation and even more interesting very recent data with low intensity focal ultrasound, or LIFU is the acronym. With ultrasound, you can reach the nucleus accumbens without having to do any intervention. And then it just stimulate the capsule of the nucleus accumbens and reduce craving. Those are things that seem to be like science fiction, but they are right now being investigated and that may help the patients, too.

Susan Winckler (02:09:47):

You've then challenged us to think even more forward in the opportunity and think ultrasound and another intervention.

Iván Montoya (02:09:57):

And that can be complimentary to the pharmacological or maybe standalone treatments or combination. Who knows?

Susan Winckler (02:10:08):

Yeah. Doctor Bloomfield-Clagett?

Bartholt Bloomfield-Clagett (02:10:11):

I just wanted to mention in the same vein of come speak to us early in the center for drugs if you're developing a drug, we encourage individuals and companies that are developing devices or digital technologies that are indicated for treatment of opioid use disorder to speak with our colleagues and CDRH, the Center for Devices and Radiological Health. And then there are also these combination products where the drug and device are working together and we have a office of combination products that people can reach out to and they can help decipher what center will review the product and what the best pathways are.

Susan Winckler (02:10:59):

That's great. Yeah, go ahead Doctor Azar.

Pouya Azar (02:11:01):

If I may, since we're discussing technologies, I think something exciting that we're working on is, really one of the major difficulties, whether it's buprenorphine or any other form of opioid agonist therapy, is not having an objective measure of an individual's opioid tolerance if we don't have a test that we can do. One of the technologies we're working on is essentially like a desktop electrochemical device that

quantifies analyzer molecules in a solution or in powder form rapidly inexpensively. Essentially the goal there is to develop a product that can rapidly quantify various molecules in the physiologic setting or in a powder setting and use that as a calculation based on patient's opioid tolerance, and then start their agonist therapy catered specifically to their calculated tolerance. That's something we're working on. We have a prototype actually that we're testing so it's exciting.

Susan Winckler (02:12:07):

Yeah, really intriguing. You have a better sense of how to start that induction in the path forward. I am looking at the time and we have just over six minutes left together. And there are six panelists here on my screen. I'm going to give you each up to a minute to share if there was something that you wanted to share that you didn't get a chance to, or if there's something that you want to highlight that you thought was really powerful and you want to make sure that we remember and take as a, "Yes, we want to move that forward." I am going to go in the order of Jodi, [inaudible 02:12:52] Yvonne [inaudible 02:12:54], Kelly, Michelle. Michelle, you're going to get the last word. So everybody else leave a minute for Michelle. All right? Jodi.

Jody Green (02:13:03):

Thanks Susan. I think because maybe it's my world, but just remember that we have great access through our surveillance networks to be gathering data from the patients, specifically through our treatment center programs and the use of our clinical tools at Upright Health. And it really just gives us great access to support other research endeavors to get to that other aspect of the behavioral pieces of people that are in it right then and there at that time, and accessible and really expanding to those psychosocial domains as well to understand the comprehensive approaches to the opioid use disorder treatments, the medication-assisted therapy and beyond.

Susan Winckler (02:13:58):

So reminding us to talk to patients and there's a way to do it.

Jody Green (02:14:02):

Absolutely.

Susan Winckler (02:14:03):

Great. Doctor Bloomfield-Clagett.

Bartholt Bloomfield-Clagett (02:14:06):

Sure. The focus of this meeting is not necessarily hearing from us, but from hearing all of the patients, providers, researchers, and all stakeholders that are involved in buprenorphine products and initiating buprenorphine. And so that's why this has been such, as I mentioned, a fruitful conversation and the continuation of the conversation is so important. We look forward to hearing more. We always want to hear more about the research areas that are needed, hearing from patients and providers about what products they need, and that's been very powerful so thank you.

Susan Winckler (02:14:47):

Excellent. Doctor Montoya, what do you want to underline or highlight?

Iván Montoya (02:14:55):

I think the point just made about listening to patients, we need to listen to patients what is needed for research. So that's a message that I want to highlight and please communicate to us, to NIDA if you have some suggestions or areas that you think need to be investigated when improve their approaches and treatments. The other thought that I have is that buprenorphine is great. It's a wonderful medication game changer. It has improved the lives of many, many people, but we have to think a little bit outside the box and think also about potentially other types of medications that will not have the problems that buprenorphine can have in any other area in medicine, that we have multiple options for multiple patients. Be open to the possibility of having also other medications and embrace them if they're going to improve the lives of patients.

Iván Montoya (02:16:03):

I mean, they're going to improve the lives of a patient,

PART 4 OF 6 ENDS [02:16:04]

Susan Winckler (02:16:04):

Right. To have an array of options. Excellent. Dr. Azar, Dr. Dunn, and then Michelle.

Pouya Azar (02:16:11):

Thank you. I think the only thing I want to mention is that in these types of discussions, we run the risk of oversimplifying opioid use disorder and addiction in general to a pharmacological exercise. And we know that many of our patients are using because of underlying driving factors, psychosocial factors, underlying mental illness. And really we can be as sophisticated as we want to be in terms of induction strategies, getting people onto buprenorphine. But we know even with the deep opioid buprenorphine retention is extremely low. And I feel like there are many other underlying driving factors that we need to address, including underlying mental illness if we're going to have any long-term success with the opioid use disorder. So I'll just end with that.

Susan Winckler (02:17:01):

Yeah, great reminder that as on our last panel, we needed a resource broker. It was not just about the resources of accessing the medication, it was about all of the other resources that we need in this space. Dr. Dunn?

Kelly Dunn (02:17:18):

Yeah, I just hope that this conversation helped encourage people to consider investigating some of their innovations or their ideas in this field, because I know that there's lots of scientists and clinicians that have really good ideas and don't know how to develop them. And I know there's lots of people working in other fields that are working on things that would have direct applicability to our field. And I just want you to know that we welcome that because I think we need people that are bringing fresh ideas and perspectives to help us. And I also want to mention that NIDA has funded several grants in the past year looking at helping people train in entrepreneurial skills to be able to do this. And that would help develop ideas in a pathway that would be accessible or that you could submit to the FDA. And so I encourage people to look for those programs because I think there's a lot of interest and value in being able to develop new approaches and we just need people to provide their ideas to do so.

Susan Winckler (02:18:13):

Absolutely. So there's interested hearing those and in helping them be developed. Great. All right, Michelle, you get the last word. What do you want to underscore or highlight for us or make sure we remember?

Michelle Winberg (02:18:29):

Yeah, I think taking advantage of the opportunity to engage with the patients that we serve. They have a lot of information and suggestions. And I'll tell you, I work with them every day, all day and they'd be more than happy to help with anything. So getting more of those folks in on calls like this could really help streamline where we need to go. All these people have lived through it. A lot of people have been on Suboxone for multiple years and think of it as a lifesaving, life-changing medication and they plan to be on it forever. So yeah, just engaging more with the population.

Susan Winckler (02:19:15):

That is an excellent way to end, Michelle. Thank you so much. So to all of our panelists, really appreciate you investing your time in and challenging us to think differently in this space and to think about the possibilities and the opportunities of what we might do. We're at the point in the meeting where we're going to take a 10-minute break and so we are going to go offline and we will return at the bottom of the hour. So it's technically nine minutes, but we will be back. Go check your email, stretch your legs, and we will see you for our final session at the bottom of the hour. Thank you. Welcome back. You have arrived at the final session of our two-day meeting where we are going to discuss the future directions of research, product development and public health interventions for using buprenorphine. I want to welcome and introduce our final set of panelists. Joining us today Dr. Brian Clear is Chief Medical Officer at Bicycle Health. Dr. Nora Volkow is the director of NIH's, National Institute on Drug Abuse. And we have three individuals who are coming back to our virtual stage. They are Dr. Michelle Lofwall from the University of Kentucky, Dr. Yngvild K. Olsen from SAMSA, and Dr. Marta Sokolowska from FDA.

Session 7: Future Directions

Speakers: Brian Clear, MD, Bicycle Health

Michelle Lofwall, MD, DFAPA, DFASAM, University of Kentucky

Yngvild K. Olsen, MD, MPH, Substance Abuse and Mental Health Services Administration

Marta Sokolowska, PhD, U.S. Food and Drug Administration

Nora Volkow, MD, National Institute on Drug Abuse

(02:20:46):

So we have introductions out of the way. I want to turn straight to conversation and I'm going to turn Dr. Lofwall to you first. You mentioned yesterday, and we've heard it again today, that there are often differences in policies and regulations at the state and local level versus the federal level and even at the health system level. How should we think about navigating those differences and what can we do to have better alignment when we have a major, for example, federal policy change that then requires change downstream at state and local level?

Michelle Lofwall (02:21:24):

So it's so complicated, but there's so many opportunities and I think that all of us are going to have a different piece and we have to be really creative. So a lot of advocacy I think from physicians and remembering our Hippocratic oath that we have the four medical ethics that are also the four research ethics but first do no harm, trump's all, but also beneficence, providing benefit, justice, our treatments get to everyone, not race-based and autonomy. So I always try and think of that and I think everyone agrees that this is a medical illness, it's legitimate, it's real, and then I try to bring that model to it. So I think everyone's going to have a different answer from the medical perspective. I'll say what we're doing that's really novel in Kentucky, we're the heart of the opioid epidemic. It started in Kentucky and Appalachia.

(02:22:23):

We're seeing the really severe cases of it and we're dealing with a federal policy, the federal inmate exclusion policy of 1965, where when people are incarcerated in jails that their Medicaid gets turned off. But frequently we've lots of runs from our detention center to our hospital and it gets turned back on if they're hospitalized for 24 hours for bacteremia, sepsis, from an untreated opiate use disorder. So we're treating really complicated infections. We're spending a lot of money on heart valve repairs, osteomyelitis, and then we're treating the underlying cause because that's what good medicine does. We get at the underlying pathology causing it, which frequently is an untreated opiate use disorder. We offer the three FDA approved medications. Lots of times they want buprenorphine. And then when we try to make it very clear to the jail because they have to go back there, they're incarcerated while they're in the hospital, that this is a legitimate treatment.

(02:23:19):

It's part of a chronic chronic illness and they need to provide it. It's a disability covered under the Americans with Disabilities Act. And in the past we would have lots of residents and our learners get very frustrated because it wouldn't get continued and we would later hear from loved ones that that person had passed away. So what we have done is we have educated ourselves as physicians on the Americans with Disabilities Act. We're starting to learn case law and we're learning how to advocate for our patients this way. So that is one thing that's novel and that has helped us for the first time. Now I will say I was in clinic this morning, I had patients with orange jumpsuits come in after several years from our detention center that are now getting treatment, but that took a Department of Justice settlement.

(02:24:07):

So I think it's really getting creative. I hope that we could look, do all of our jails in prisons have buprenorphine and methadone? Do all of our state psychiatric hospitals have buprenorphine and methadone? If we consider this a chronic illness for which medicine should be available if the person wants it, do we have it where our patients go? Do we have the continuum of care? How do we make sure that it's there? How can FDA make sure that it's always at each of these critical junctures where we know this patient population touches?

Susan Winckler (02:24:37):

So Michelle not only challenging us to make sure that we flow through those changes, but then thank you for the story of a difference made and those individuals having access. It struck me, it aligns a bit with in an earlier panel when we talked with the DEA, they were recognizing that they spoke to their responsibility that if we're going to have more prescribers of buprenorphine, then we should expect that there would be more buprenorphine needed in the country. But it might seem obvious in the conversation, but really isn't when you're thinking about what policy lever was pulled, then we have to look through and say, what is that flow through and have those conversations. So you've reminded us

that the changes can be made. We have to keep at them. Dr. Clear, I want to turn to you next. Talk to us about some of the innovative methods for reaching patients who might benefit from buprenorphine care. How do you navigate that patchwork of state and local regulations that might not align with the federal policies? What thoughts do you have to add to Michelle's opening there?

Brian Clear (02:25:59):

Yeah, absolutely. Thank you Susan. I'll start with just a little quick context on my program. So we're a medical provider group that focuses on patients with opioid use disorder. Since the COVID waivers went into place, we've implemented a fully telemedicine model of care and now we're serving patients across 32 states, which I think gives me a pretty unique perspective on this path for regulations that we have to navigate. We're serving just over 10,000 patients now and we've got 80 full-time employed addiction medicine specialists in our program. I think one of the major successes we've achieved has been reaching patients who don't and probably never would engage with more traditional in person OBOTs and OTPs. So over 30% of our new patients have never previously been diagnosed with opioid use disorder or attended care for opioid use disorder before. Half of those patients have primary care homes but won't disclose their opioid use disorder to their PCP or just haven't tried to talk about it with their PCP.

(02:27:03):

The other half don't have any connection to the healthcare system and we end up being their entry point. And so relying on typical referral and outreach services to try and reach this population of patients who don't engage with the healthcare system or won't disclose their opioid use to the healthcare system, it just wouldn't work. And we know that that makes up 85% or more of everyone in the U.S. Who has opioid use disorder. So our innovation to reach this population, I think it's been a pretty obvious one, but it's one that's not always employed in the healthcare system. We use the internet, we put opioid use disorder related content on the internet and we advertise. We use paid search, we use social media to get ourselves out there and people call us when the content resonates with them and they understand through it, but there is a potential solution to a problem that they're experiencing.

(02:27:57):

We also do a lot of work to ensure that our team treats patients with respect and we work to discard arbitrary barriers to treatment that don't meaningfully improve outcomes. And we've been extraordinarily successful. We really have. We'd be in all 50 states by now if doing this weren't still illegal in 18 states. And that kind of brings us to regulatory barriers and arbitrary barriers to providing OUD care. Of these 18 states it's still explicitly illegal to prescribe buprenorphine via telemedicine in some, but in others there are special hoops that have to be jumped through. I actually, there's an 11th hour update on this one, but I was going to mention in Pennsylvania there's specifically a requirement that a stethoscope exam of the heart and lungs and blood pressure be done before you can prescribe buprenorphine to a patient, which not a big deal in an in-person setting, but that's a huge barrier to the telemedicine setting.

(02:28:58):

Glad to announce as of about three hours ago, the Pennsylvania Medical Board waived that in conjunction with the DEA extension of telemedicine flexibility. So we now have another six months to continue serving Pennsylvania patients, whereas we had planned to close in Pennsylvania because we were unable to meet this reg that was going back into place. Another example, many states mandate very specific counseling in case management services like Massachusetts, Tennessee and Indiana, which of course are a great idea to offer and we do offer these services, but when you mandate them for an

entire population of patients and you hold treatment hostage and say that you cannot treat OUD unless a patient engages in this counseling service, we know that to be unhelpful and we know that to be a barrier to treatment. Similarly, some states, Kentucky being one of them, mandates specific lab work and I'm from Kentucky, but we can't operate in Kentucky because we're unable to make sure that all patients get a CBCCMP and infectious disease screening before starting treatment. Again, these are good things to do for a patient who's engaged in treatment for OUD when you can't, but to have to withhold treatment until that requirement's met, makes no sense. And I'll go ahead and wrap up, but there are lots more examples to potentially name. Overall though, states tend to be moving in the right direction toward eliminating some of these arbitrary barriers, although it's taking a tremendous amount of time. I think the DEA kind of changes of their plans for proposed telemedicine rulemaking. I think is a big step in the right direction. I think that sets an example for state legislatures and state medical boards of where we need to be going. So that's been reassuring.

Susan Winckler (02:30:41):

So kind of you're seeing states continue some of that momentum that they're seeing from the federal. So there's still friction, but you're seeing some opening?

Brian Clear (02:30:53):

We are.

Susan Winckler (02:30:53):

Yeah.

Brian Clear (02:30:54):

Yeah.

Susan Winckler (02:30:54):

Okay.

Brian Clear (02:30:54):

We are. The only state that's really moved in the wrong direction in the past two years has been Alabama, which implemented a new law effectively abandoning telemedicine based OUD care about a year ago. But aside from that, most states are moving in the direction toward more enablement of expanding on UD care.

Susan Winckler (02:31:12):

Yeah, okay. So you mentioned some of the DEA changes Dr. Lofwall did as well, so Dr. Olsen, let's talk about a SAMSA angle here. So with the elimination of the X waiver, how does that change what SAMSA does? What do you do to continue to support and expand buprenorphine care and access?

Yngvild Olsen (02:31:37):

Yeah, great. Thank you for that question and really so appreciate just having the opportunity to be here with such amazing thinkers and doers in this space. So I think SAMSA's perspective has always been that really expanding access to training, in particular training and supports for practitioners who are prescribing buprenorphine, treating opiate use disorder. I think one of the big funding buckets that are

portfolios is technical assistance and training. So through the provider clinical support system for example, that really is a platform through which provider prescribers can get mentoring and other training in how to prescribe buprenorphine as well as just kind of the overall general treatment of opiate use disorder with medications including buprenorphine, Methadone, and naltrexone. The opioid response network is a very large program that is really based in implementation science. And so there are specialists within each state that really can serve as implementing consultants for whether it's practices, primary care practices, emergency departments, jails, court systems, et cetera, to really look at how do we take the science and how do we take what we know is effective and really get it into practice.

(02:33:15):

I think the other piece to this is because of the removal of the X waiver requirement, we have really been messaging broadly. We will continue to message broadly that this is now something that prescribers of all disciplines of wherever in multiple different settings that really the availability and the ability of prescribers to now treat opioid use disorder has tremendously expanded. At the end of 2022, there were 130,000 wavered practitioners that now that universe has now expanded to 1.8 million DEA registrants. So you know, can imagine that really just the universe of where people can access and the workforce that is really there. Now we need to make sure that the workforce also is trained and feels supported. And so those technical assistance and training opportunities that I mentioned are really a big piece of that.

Susan Winckler (02:34:26):

And I'm really intrigued by the implementation support that is, I would think that really helps with some of the stigma and helping prescribers understand just to have a better baseline understanding of what we know about buprenorphine today versus what we might have said about it or has been said about it for a while.

Yngvild Olsen (02:34:58):

And I think that both what Dr. Lofwall and Dr. Clear are talking about is that really being able to raise awareness. And I think having been in this field for 20 years, just making sure that, and focusing on the fact that this is not a mystery, this is not a mystery disease. These are not kind of mystery tools that need to be complicated. I think one of the things that Dr. Sokolowska mentioned yesterday morning was that SAMSA and FDA just released a letter yesterday morning really highlighting what Dr. Clear I think was speaking to a little bit, which is that when you look at the mortality benefit of buprenorphine, methadone, that is so significant. Over 50% that really being able to initiate people on buprenorphine is incredibly important.

(02:36:02):

And then being able to offer and wrap around those services in an individualized way as people also then their treatment trajectory changes, their recovery progresses. But that really having that medication as an initial component is so incredibly important and that being able now to have a broad swath of prescribers that are then being able to address this chronic condition also does remove some of that stigma and being able to kind of we're slowly just chipping away at it. So I really so appreciate all the work that everyone's doing in this space.

Susan Winckler (02:36:46):

I think we're seeing progress being made and I hope that's not just happy talk, but that we're actually seeing some things change. As we think about changing things, Dr. Volkow, I'm going to turn to you, we

heard from Dr. Eva Montoya on your team about the clinical research and the things that we're learning about molecules, but how should we think about NIDA and making sure that the research and the research grounding that we have from NIDA informs the policies and the policy makers so that we can continue to drive some of this change?

Nora Volkow (02:37:29):

Yeah, no thanks Susan for that question and thanks for having me. And unfortunately I had counsel, so I haven't been able to attend to the buprenorphine session, but I actually look forward to hearing the deliberations. So there are many ways, and to start with in a meeting like this one, and just by listening to the points that Michelle and Brian were saying and also Yngvild, it just comes up with specifically why science becomes so very important. So in terms of what we hear from Michelle is that we don't really know at this point what is the reality of treatment access in justice settings in hospitals and that for example, in terms of where the research can come to investigate and provide information that can help us identify where there are gap areas. So that's one of the aspects that we have of science.

(02:38:26):

Then we have the presentation of Dr. Clear was saying, okay, we have telemedicine has enabled us to show how basically if I heard him correctly, they are helping 10,000 patients across multiple states with a staff of 80. Which actually highlights to me first of all the ability of generating a network that can provide support in ways that we couldn't do it before. And therefore, again, from the perspective of research, how do we evaluate this in terms of not just how many people that we are able to give them buprenorphine, but what are the outcomes? And in listening to Dr. Olsen, I mean I think that she mentioned two things that are very consequential. One of them is of course that now we have 1.8 million people that physicians that in principal could prescribe or providers that could prescribe buprenorphine. What are going to be the consequences of expanding the group of people that are ready to do it?

(02:39:27):

And I think that that is a very, very important issue that requires investigations. Is certainly from what we have seen during the COVID pandemic, we have learned those emergency measures that had to be done to ensure that people that had an opioid use disorder had access to treatment showed that they actually significantly improved the outcomes. And I shiver to think what would have happened if these things would have not actually occurred. And I'm glad that we don't have those numbers in front of us. But we had now also the advantage now of knowing that it was safe. We didn't see an increase in people dying from methadone nor from buprenorphine. And we saw access to people that as was mentioning before that otherwise had not, it was the first time through telemedicine that they're getting medications for opioid use disorder. But it does behooves us two things.

(02:40:23):

And actually in terms of the comments that were made by Dr. Olsen, we need to initiate, but we still have a serious problem. And I think again, from the perspective of implementation research and strategies and model development services, retaining people in treatment because we still have extremely high rates of relapse. And these medications are very useful in preventing overdose deaths if you are on them. But when you stop taking them, your risk go up. And I think it behooves us therefore to develop strategies and in partnership, because you said to me, where do we stand? And I says, we don't stand in isolation. Our scientific questions should be driven by what the agencies and what the data is showing us. And I'd like to see how we can improve that retention. And the other thing that I do want to comment because it's something that is central in my brain in again by listening to providers and

organizations, when we had the X waiver, there were many people that were X wave and were not prescribing buprenorphine.

(02:41:32):

So I think that we cannot become overconfident that because now you don't need an X waiver, people are going to prescribe. So we were trying to understand like many others why people are not that an X waiver are not prescribing buprenorphine. And one of the things that we've heard again and again and again, is the notion that the physicians or providers feel that the level of reimbursement given to treat someone with buprenorphine is not sufficient to actually incentivize them to go and engage in treatment. And I think that we have to keep our eyes wide open and not close them to realities that maybe barriers of implementation of an intervention that we know has a very large effect size in preventing overdoses and improving outcomes.

(02:42:19):

We still need to do better on retention. But that element is one that I think that two from the perspective of research is one that we need to evaluate. So I'm sorry to divert some of the question that you asked me from the perspective of medication, but I was just so fascinated by the comments that were being thrown at all of us and how the science agency can work and partner to help address some of these questions.

Susan Winckler (02:42:48):

Dr. Volkow, you helped weave together a number of things we've heard, including the important one about reimbursement for the services and being able to do that. So it took us in exactly the right direction, which then Dr. Sokolowska, what do you want researchers and sponsors to take away from this meeting? What should they right now be writing down?

Marta Sokolowska (02:43:14):

First of all, thank you very much Susan and thank you for including us all in this discussion. I think it's been such a bridge discussion over the last two days regarding what are the barriers and opportunities for buprenorphine treatment. So we've heard so many different opportunities. I like to frame it as opportunities that I'm hoping that the sponsors are really hearing as opportunities from their perspective maybe for improving their business value. But from clinicians perspective and healthcare professionals is opportunities to really better address the needs of patients. And there are so many great suggestions, not only from buprenorphine perspective, different formulations, transmucosal, transdermal, different flavorings of bugle films and different dosage forms, higher forms, lower forms, extended release forms, but also comments regarding different treatments other outside of buprenorphine I found very exciting the discussion regarding potential device contribution to helping to address this issue.

(02:44:27):

So we really have to think broadly. And FDA is a regulatory agency. So our main role is to review, approve, or authorize not only pharmaceutical treatment but also the devices. So I'm thinking about it more as a treatment options for the patient. And I think this meeting hopefully provided a lot of great guidance for the industry as well as for researchers more broadly, what are the areas of interest? What are the data gaps that are still needed? Because if we have high quality data to address some of those issues, some of the questions that were being raised regarding easier methods for induction or the maintenance components, if we need some additional safety information, if data is published, we can definitely utilize, we need high quality data. So we can't just make changes to our labels without having

strong scientific data and support. That's FDA mandate to make sure that we have strong data to support it.

(02:45:31):

But that's why the call is not only to sponsors both potentially new and the current ones that are within this space, but also to researchers and our partners both within the federal government like NIDA and other academic institution to really provide the quality data that is needed to really move it forward. And as we are working on that, we also find it so exciting to work with our other federal partners such as SAMSA for instance, and other HHS agencies to help to push the policy forward to make it easier to access those medications. So even though our primary focus is regulatory as a regulatory agencies is to review approve of authorized new treatments, we do see the value and we try to contribute and we hope that our message to other sponsors and researchers is to provide us with the information that will help us to lead to the better policies on new products approved.

Susan Winckler (02:46:37):

So the sponsors and researchers had a lot of rich content provided in potential options both within buprenorphine and beyond and should have an opportunity to think. And you mentioned this as well, the patient centricity, right? That some of this is driven by Michelle, who we just heard from, who at 13 years of use is still splitting tablets because that's all that her pharmacy is carrying. We could do better. So Michelle from the prior panel, sorry, Dr. Lofwall.

Marta Sokolowska (02:47:20):

Absolutely. And that's why we strongly believe in having those meetings. This is not our first meeting regarding substance use disorder. So again, thank you very much to RUF for really holding these meetings and really help us to move forward with discussion not only on opioid disorder and buprenorphine, but on stimulant use disorders and other treatments because we do understand that this is an area of great need. And yeah, as I stated earlier, if FDA stands ready, we publish guidances to help to move this area forward. We recognize that it's an area of great needs. There are your regulatory approval, accelerator approval frameworks that we can also utilize. But in order for us to use it, we need to have applications and we need the research to be conducted. So we stand ready and we are looking forward to see the outcomes of this meeting turning into applications.

Susan Winckler (02:48:15):

Excellent, excellent. So let's take maybe a step back and take a broader look here. So each one of you has spoken about the need to improve the public understanding to decrease the stigma around opioid use disorder, about opioid use disorder treatment, about buprenorphine generally. What else can we do? What are anything intriguing or just things that we need to put into our thoughts and our quiver of potential things to do to help improve that public understanding of benefits, risk and evidence for buprenorphine, both with policy makers and the broader public. If there was one myth you could dispel or one step you could take, what would it be? I need somebody to unmute and jump on in.

Marta Sokolowska (02:49:15):

I can jump in. I think that we can learn from lessons learned. I think that I was delighted when the FDA approve a formulation of naloxone over the counter because one of the things that they are actually doing by basically making it over the counter, is sending very clear message. This is a very safe draw for use because otherwise it would not be over the counter. So you can go and get it in your drugstore alongside your toothbrush. So that is an incredible message that's happening with the over-the-counter

naloxone. From the perspective about what is it that changes stigma and changes a culture, I mean certainly the more people, I mean the information is given to a public and starting with-

Nora Volkow (02:50:03):

I mean, the more the information is given to the public and starting with healthcare providers and starting with people that aren't involved in treatment systems of the efficacy of buprenorphine in terms of its outcomes and when compared with known, I think that the data will carry an enormous impact and open it up in forums of discussion.

(02:50:24):

I think that one of the challenges has always been people don't really understand and dismiss buprenorphine, like they dismiss methadone by the notion that you're changing one drug for the other. So, being able to articulate what are the differences between buprenorphine or methadone versus taking something else as a drug in ways that are salient and basically they can incorporate, actually can do an enormous amount of good, including for clinicians or for treatment programs that actually have traditionally be abstinence-based and that they have rejected the use of medications.

(02:51:03):

So, bring forward this dialogue and openness and the data that speaks eloquently about the differences in outcomes and risk for mortality and doing it consistently in different forums with different narratives that touches the diverse audiences. I think it's a key issue. Starting with this meeting that you're currently conducting.

PART 5 OF 6 ENDS [02:50:04]

Susan Winckler (02:51:27):

We need to keep talking, yes. Doctor Olson and then Doctor Lofwall.

Yngvild Olsen (02:51:31):

I might add, because I think Dr. Volkow is absolutely right, that really being able to raise that awareness, be talking about it, and that includes people with lived experience. I know that that was such a great piece of this meeting as well, that it really included people who have that lived experience and kind of have benefited from the medications. Because I do think that the more and more we can, to some extent, kind of normalize and really say this is a medication. This is a medication for a health condition that has benefits. It also has some side effects, so people need to understand what those are, but, really, it's not this mystery thing.

(02:52:24):

When people can put a face and a name and a story to that, it really does change the perception and those misunderstandings that people might have, that includes with clinicians, it includes with other policy makers, it includes with just healthcare professionals in general, includes with the public. And I think part of what [inaudible 02:52:53] has also really been focused on increasingly is that lived experience, that peers, really incorporating also kind of the peers into multidisciplinary teams, multidisciplinary, whether it's also in the community, in healthcare settings, in jails, in other places, so that it demystifies kind of what this thing is. I think that the more and more we can continue to support that, we'll keep chipping away at some of that stigma as well.

Susan Winckler (02:53:29):

Dr. Lofwall and then the Dr. Sokolowska.

Michelle Lofwall (02:53:32):

I agree with both, but combine it, right? Have public health campaigns for healthcare providers. We love data bar graphs. Show me what happens with placebo? What happens on medication? What's the change? What's the outcome? What's the treatment effect size? That's what we're used to training healthcare providers. So, you say what the disease space is, you compare it to another disease space. You ask them are they prescribing blood pressure medication for hypertensive patients? So are they prescribing buprenorphine, methadone, whatever, Vivitrol for OUD. And if not, why not? Here, go to PCSS. Here, go to the ORN.

(02:54:08):

For the normal lay population, that has a whole bunch of stigma, we need to hear from the people with the disorder who are now in remission and recovery. We can't forget that word remission because it reminds us that it is a medical disorder worthy of treatment if the person wants it. We've got to put the medical terminology in there. We've got to get the people who are willing like were willing to come here and talk about it, to share that just like Dr. Olsen was saying, but that's for the general public and that's what we see with other disease spaces. We need to do what we do with other kinds of illnesses that are often chronic, relapsing. Sometimes they're not, where what's happening that we want to see, isn't.

Susan Winckler (02:54:53):

Really helpful and particularly that idea of I can see you and I've put that face and the experience with it, and can see that you didn't become a statistic that we don't want to see. Dr. Sokolowska.

Marta Sokolowska (02:55:12):

I just wanted to add that the recent removal of the X waiver actually is such a critical component because now it's not any different than treating pain with buprenorphine, the same molecule we required, until recently, very different set of qualifications, and trainings, and pads in order to make sure that we can prescribe for this medication. Now, it's the same. I think it's really critical component as well as in combination with the [inaudible 02:55:47] that actually makes everybody to learn regarding substance use disorder. It's not scary. It's not something different, it's just one of many disorders. If we can get more prescribers or more medical students being introduced to this concept when they are learning about hypertension, also to learn about substance use, just like any other treatment early on, I think that it really de-stigmatizes the disease, especially for the medical professionals.

(02:56:17):

Also, we need to hear, as it was mentioned many times, the success stories of people next to us who might be having substance use disorder or have had and now they are in successful recovery. Hearing those success stories are so important because that will give help for people who might be hiding it right now, hiding these struggles to actually see hope and see the help that might be coming. I think that talking more about it, I think that's what happened with HIV/AIDS. We started talking about it. We started normalizing it. Breast cancer, how many people are not walking around with pink ribbons? Now, it's something that everybody is proud of to support. Until recently, it was something that was hidden. If we can figure it out how to break this barrier and bring it up to the mainstream, I think that's going to really help. And we have examples when it was helpful and successful before, so we should just try to figure out to follow that example.

Susan Winckler (02:57:20):

Yeah, we know that it's possible. Dr. [inaudible 02:57:24], I was struck by your observation about advertising and some of that component, but what voice do you want to add to this question?

Brian Clear (02:57:35):

Oh, absolutely. First, just a brief comment on the prior question. I agree with everything that's been said. The key is around normalization. Eliminating the X waiver system is a huge step in that right direction. We need to continue breaking down this sequestering of treatment of opioid use disorder as if it's something very different from the rest of medicine. Let's stop calling it [inaudible 02:58:02], please. It's just treatment for opioid use disorder like treatment for heart disease, or hypertension, or diabetes.

(02:58:10):

In addition to regulatory barriers, we have these extensive guideline barriers where medical boards, which typically do not issue specific guidelines for how to treat hypertension or how to treat obesity, will have a 90-page document that is telling providers exactly how they're supposed to treat opioid use disorder, which is unnecessary. It is considerably less complex than managing something than fully understanding the treatment of something like diabetes, which takes a semester of training in medical school. UD is not as complex. The most complex part is understanding all of the kind of artificial complexity and regulation we've built around it. So, breaking through that is key.

(02:58:56):

In terms of advertising, I think there are a lot of rules and laws that have gone into place to prevent dissemination of false or misleading advertising in healthcare, and that has to be there. That's real. We can't have exploitative organizations putting messages out there that are misleading around medications or forms of medical treatment. So, it's a difficult balance to strike. How do you permit healthcare organizations that are operating in good faith to get their message out freely and build awareness around the services that they're offering while also keeping controls in place that prevent unscrupulous organizations from taking advantage of that to pull to patients into their care who otherwise would be getting help elsewhere.

(02:59:54):

That's challenging. I don't know that I have an answer for that. I think the answer is not like blanket restrictions on advertising in healthcare, like in Massachusetts and New York specifically. As soon as a provider puts a sign up or puts on their website that they treat opioid use disorder or some other substance use disorder, this obligates them to obtain special licensure to do so, which is an extremely onerous process that smaller practices simply cannot do. So, it effectively prohibits smaller practices from doing any form of advertising whatsoever. Again, I don't have an answer, but cutting through some of that red tape is probably part of it.

Susan Winckler (03:00:41):

Yeah, [inaudible 03:00:45] in seeking different healthcare services, sometimes the only way you provide it is when someone has said, "Yes, we provide these services," but also recognize, we also don't need the introduction or the perpetuation of advertising things that don't work, but service availability. So, the intriguing thing there. Dr. Volkow, you have your hand raised. Go ahead.

Nora Volkow (03:01:10):

Yeah, no, I had a thought as Brian as speaking because it's something that we have tried to figure out. When people come to us and asks for help with a loved one, where should we be sending them? Actually people that are experts themselves in the field of addiction and they basically are craving for a

source of information that enables them to choose a particular program for which actually has outcomes that indicate high quality. So, we've been trying to build up a report card that will become open access, that will incentivize then the public to look at it and determine and identify those programs that have the best outcomes. You're going to have cardiac surgery, you want to see the survival rates and you make those decisions based, of course, on your insurance, but on the maximizing your benefits.

(03:02:02):

So, we've been working on this. There are organizations that also have been building on this to try to engage quality metrics from the one hand to reimbursement parameters. And this would be an extraordinary variable if we can demand quality care and that determines the reimbursement, but also at the same time have this method for citizens to contribute to the information of their experiences. And so for example, Bicycle, if the people that are basically receiving the services report actually how it was helpful or they have negatives, someone else can go and look at it without having to actively engage with advertisements. There would be a centralized place where people can get that information. I think that this is one potential aspect of trying to get that information out about which are the programs that lead to the best outcomes.

Susan Winckler (03:03:01):

Really helpful. I was also thinking as we asked the question that the more we also normalize and perpetuate treatment for opioid use disorder, it should become easier to find without having to do so much seeking. Dr. Olson.

Yngvild Olsen (03:03:17):

Yeah, so piggybacking off Dr. Volkow's comments. I might want to just highlight that SAMSA just within the last two days or so, released a new update out of findtreatment.gov, which is the SAMSA treatment locator that also has incorporated pieces of what to expect. There's some stories, kind of journey maps there, learning about finding quality treatment. I think that there's much more to that that needs to be done in this space as Dr. Volkow is mentioning, but also pieces around understanding addiction, understanding mental health, paying for treatment. I might encourage folks to also check out the findtreatment.gov as an updated new resource in the space.

Susan Winckler (03:04:10):

That's great. We saw at least two different kind of journey maps in the presentations over the last two days. And there were a lot of steps in that journey. And so just having an understanding of what's involved I think would make that journey easier. So, great resource.

(03:04:34):

I've heard from each of you and throughout these two days distinctly there's hope. I want us to articulate those areas for hope in buprenorphine care and access. Dr. Sokolowska, you could do, there are these opportunities that we're going to pursue, but I want to open it up to whoever un-mutes first. I'd welcome each of you to flag what you see as the areas for hope in buprenorphine care and access. And Dr. Lofwall, you are quickest off the unmute button.

Michelle Lofwall (03:05:13):

Well, so I'm so hopeful just because I think it's just incredible that FDA has put this all together with so many different organizations and has included patients in it. I haven't seen that before during the opiate epidemic. To me, just the fact that this is happening and people have spoken freely and provided so

many different ideas, that is incredibly hopeful because clearly people are listening and have really creative ideas. So, my hope is that there'll be really a lot of thought about the REMS distribution for extended release buprenorphine products because I think it's been clear that it's been really hard to get that to patients with the current REMS.

Susan Winckler (03:06:02):

Thank you. The patient experience is just so powerful. I have the privilege of getting to listen to it on each of these panels and it's one of my favorite parts. Who wants to unmute and offer next a thought about an area for hope in buprenorphine care and access?

Nora Volkow (03:06:25):

I can jump in an actually I'm at a tremendous disadvantage because I didn't hear the patient's reports, which I also had carried them from the naloxone. And it was the other FDA meeting that I was able to attend at least, and it was incredibly valuable. But what I'm very, very excited just about by looking at the data that is emerging is how effective the extended release formulations for buprenorphine are. I'm specifically thinking in terms of the data where we have information, in terms of people that are being released from justice settings and compare with immediate release buprenorphine. You don't need statistics to see the difference on the extended release buprenorphine.

(03:07:09):

Particularly because right now with the fentanyl crisis, your physical dependence is much greater than that that you have with heroin. And so when you're taking it once a day, you're going to have coverage levels, plasma levels that are maybe sufficient at the beginning of the 24 hours, but towards the end it's going to go down and that may generate craving and lead people to actually go and seek drugs. With extended release formulations, you don't come down, but they're not being used. So, it's actually, again, one of the challenges that it behooves us, and that's why I brought up the notion before that we cannot be complacent. Having more providers will provide more buprenorphine, but they need to be reimbursed properly. Similarly, we need to figure out a way of reimbursing for extended release buprenorphine, even though it may be slightly more expensive than methadone or buprenorphine sublingual in consideration ultimately of ultimate outcomes.

(03:08:09):

I think that this is... Martha was saying, "Well, we are the regulatory agency. We cannot determine the accessibility." And that's exactly the same thing with us. We can help develop these products, but if then the products are not going to survive because no one is prescribing them, it's sort of running on a treadmill and not going anywhere. I'm excited about the products very much. I think that they can help enormously, but I do realize that we need to shift the paradigm and remove the stigmatization of addictions overall as of lower importance as diseases than Alzheimer's or cancer where you're willing to pay. I think we need to change that framework.

Susan Winckler (03:08:51):

That will we know that that changes provider behavior. We had a primary care doctor earlier today said, "If you're supposed to see 20 patients a day, but two of them take up eight of your slots, you've got to be able to keep your practice moving." Dr. Sokolowska, I saw you unmute.

Marta Sokolowska (03:09:16):

I just wanted to add the one area that I find quite exciting is that we've been hearing about some additional data regarding buprenorphine and other treatments that have been collected and is just about to be published or have been published already, regarding the long-term impact of buprenorphine treatment for UD and the other methadone as well, treatment for all opioid use disorder, the long-term impact. The additional data that we have that potentially has impact on incarcerations, data that we've heard about mortality, the more data we have on that topic about the long-term consequences, hopefully we'll speak to the payers and to others to really show that the value proposition is actually saving money, not only saving lives and the value of the life to the person who is suffering from the disorder, but actually saving money for the payers, and hopefully that is going to speak volumes.

(03:10:20):

But just wanted to take a step back and you ask about things that get me excited maybe a little bit outside of buprenorphine. I think that it's important to highlight that as we are thinking about the overdose framework from the HHS and FDA, there have been quite a few movements in this space recently, and the FDA has recently updated labels for opioids and treatment with analgesics for both immediate release and extended release, making quite significant changes, such as an indication statement for extended release opioids, or making recommendations regarding the duration of treatment for acute injuries with immediate release formulations.

(03:11:13):

We have issued or released updated REMS including disposal options. Again, trying to get the unnecessary medication out of the houses and medicine cabinets when they are no longer needed. As Dr. Volkow mentioned, we have approved the non-prescription naloxone. Again, another piece of a puzzle, and we have just updated scheduled stimulants labels to really emphasize, and streamline, and harmonize language regarding misuse, and abuse, and addiction that might be associated with utilization of such products. So, it's a really full front approach and multi-prong approach to address the issue of overdose from on, not only from treatment from substance use disorder and opioid use disorder, but also from prevention. People do not get into these issues in the first place.

Susan Winckler (03:12:18):

Really important to have a movement on all of those fronts. I'm struck, too, that the information about long-term use and long-term effect also helps normalize that long-term is for many individuals their reality, that it is a maintenance medication that you would expect to use for a chronic condition. Dr. [inaudible 03:12:45], areas of hope you want to identify.

Brian Clear (03:12:48):

Yeah, absolutely. Everything that we've all said so far, and that itself is an area of hope, just the general evolution of conversations around OUD care that I've noticed over the past three, even eight years. I do a lot of conversations with CMOs of the HMOs and health plans and payers and regulators and even boards. It used to be about establishing buprenorphine is actually safe. Establishing this is something that you can actually prescribe in a primary care office or via telehealth without doing a directly observed eight hour long induction process with an anesthesiologist on hand. Or it's something that, yes, long-term treatment is actually indicated and helpful and safe.

(03:13:39):

It was just the basics of going back to these Cochrane reviews and regurgitating these facts to try and build basic awareness. But we've moved on from that. Looking at the takeaways from earlier sessions.

They're all about expanding access. They're all about improving the way that formulations of buprenorphine are developed to consider patient needs and to consider modern practice techniques that may utilize microdosing, that may utilize telemedicine, and less kind of intensive observed processes. It's like we have moved on from the basic safety efficacy conversation and we're now at next steps, which is very hopeful progress. These conversations are fun.

Susan Winckler (03:14:27):

Yeah, very well said. Dr. Olsen.

Yngvild Olsen (03:14:30):

Yeah, I think the other thing I would add is that I'm really hopeful about all the collaboration and the partnerships in this space because I do think at the federal level between FDA, and NADA, and SAMHSA, and CDC, and DEA, and all of the HRSA, there's a long list, and I think being on the same page around what the end goal is, which is kind of expanding access to MIUD, is really pretty exciting. Then having the partnerships and the collaborations with researchers and providers and people with lived experience and all the state level entities. That's really what it's going to take. We can see those, we feel those partnerships and collaborations that really are going to be so critical in moving all of this forward. That's what really gives me hope.

Susan Winckler (03:15:39):

Yes. So well said. Particularly earlier today, I was struck with deputy administrator straight from the DEA who gave voice to DEA having a public health responsibility in making sure that there is an availability of controlled substances, and particularly in buprenorphine. I'm confident I wasn't the only one who put DEA in a new light with that discussion that they want buprenorphine to be used and to be considered differently from other controlled substances. And so that partnership was particularly evident in the conversation between the HHS operating divisions that you all are significant parts of, and the collaboration to Department of Justice. Really impressive.

(03:16:44):

We are at nearly the end of our time and I don't believe in extending things just for the chance to extend things, but I'll allow if anyone wants to unmute and say, what do you want to make sure that we take from this? We know now that we have hope. We have an articulation of areas where we need research and development that I will say one piece that did not come up on this panel but was said quite loudly yesterday that I have to give voice to, which is it's doing more for adolescents and understanding how to... What is it that we know about buprenorphine and use in adolescents and then in disenfranchised populations, making sure we reach those. But you've helped articulate hope. Is there anything that anybody wants to unmute and say, "Let's make sure we see." Dr. Volkow, I knew you were going to be right there with it, so go for it.

Nora Volkow (03:17:40):

There are many things that I think that are very crucial, but when you spoke about adolescence that says, yes, we need more research because there's no clinical research or study that actually has evaluated methadone and it's so in adolescent surprising and buprenorphine is 16 or older. But there's another population, and this way I wanted to jump in, and that's women that are pregnant that have an opioid use disorder, where the studies have shown significantly better outcomes when you treat them during their pregnancy then when you don't, and studies have also show better outcomes when you

give them buprenorphine than methadone as it relates to the neonates having to have lower time spent in the hospital, less severe withdrawal symptoms.

(03:18:20):

I think that identifying the unique barriers that women that are pregnant and that have an OUD is something that we need to address and it brings forward that, I think it was basically Brian who brought up the differences between the states where there are certain states that will penalize a woman that is pregnant and taking opioids. They can end up in jail or they can have their children removed to children administrative support systems into foster care. So, this is an area that we need to work for. I mean, buprenorphine works during pregnancy and the longer you retain someone on buprenorphine, the lower the risk for them overdosing and dying. And I do want to highlight it because one of the main causes of maternal death in the United States, which has the highest rates among the first country developed countries is overdose deaths. Yes, this is a population that is dying because of overdosing during pregnancy and the 12 months that follow up. I do want to just highlight that area of need.

Susan Winckler (03:19:25):

Absolutely, and as we had someone articulate, it's also a great window of opportunity where you may have an individual who is motivated to pursue it. So, let's take that open window and help an individual, help save a life and perhaps more than one.

(03:19:43):

With that, I am going to close us out. Thank you so much for to each of you for joining us for this panel. Really helpful in crystallizing what we need to think about and the opportunities that we can change the future of treatment for opioid use disorder and particularly the use of buprenorphine.

(03:20:05):

With that, I want to thank everyone who has joined us for the last two days. I'll note we are going to post the recording and other materials for this event on the Foundation's website by next week. With that, we're going to let you go back to the rest of your day. Thank you so very much for joining us.

PART 6 OF 6 ENDS [03:20:27]