Considerations for Buprenorphine Initiation and Maintenance Care – Day One

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Meeting Transcript

Welcome

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

Susan Winckler (00:00:25):

Hello and welcome to day one 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. We're so pleased to be working with the U.S. Food and Drug Administration to host this virtual event both today and tomorrow, and I hope you'll join us for both days. Before we begin, I have a few housekeeping issues we need to run through. Because of the size of the meeting, attendee cameras and microphones will remain off throughout the event. We have a fantastic lineup of speakers and panels, I hope that you will agree with that, and we have used the questions that you submitted during registration to inform the discussion that we'll have with those panelists.

(00:01:22):

We also have a few moments in each session to address audience questions. We invite you to submit your questions and your comments through the question and answer function. I'll note we are recording the meeting and we will post the recording along with the slide deck and the transcript on the FDA foundation website next week. To orient you to our time together, I quickly want to have you run through our agenda. In just a moment I'll be turning the podium over to Dr. Marta Sokolowska from the FDA and Dr. Yngvild Olsen from SAMHSA to offer opening remarks. Then we will move through a series of sessions where we will hear about clinical best practices for buprenorphine care, additional forms for support beyond the medication and what else is needed in terms of formulations of buprenorphine to meet patients' needs. The full agenda is available on the FDA Foundation website and the link is posted in the chat.

(00:02:21):

Now to help set the stage, I want to invest just a moment to ground our conversation. So over the next two days, we're discussing buprenorphine, which is available for different indications, so how it's used, in different combinations, what other drugs it can be packaged with, and in different formulations; so how it actually gets into a patient's body. I want to quickly walk through these and note that the chart here is on the foundation website on the event page.

(00:02:52):

So buprenorphine formulations have been approved by the FDA for two quite different indications; to treat opioid use disorder or separately to treat pain. Buprenorphine is available as both a mono product,

so straight buprenorphine, and a combination product with naloxone. On the screen now, this is showing you a list of currently available formulations of the just buprenorphine product. You'll see there it can be taken as a tablet or a film that dissolves in the mouth or be given as an injection, can be a patch worn on the skin or a short-acting injection. So we have a number of different ways that it can get into the patient's body.

(00:03:43):

Buprenorphine is also available as a combination product with naloxone. So we have a next display of that. Many people know the naloxone by one of the branded names, Suboxone. The combination product was designed to reduce the chances of misuse or diversion, so it's often the preferred formulation if using the tablet or the film. Now, I'll note that in our conversations speakers will refer to buprenorphine rather generally and for its use in treating opioid use disorder. I apologize upfront for that lack of precision, but our discussions are exploring the various dimensions of using the active pharmaceutical ingredient buprenorphine in one of its currently available formulations to treat opioid use disorder. And if you want to refer back to this table during the meeting, it is on the FDA foundation website and there is a link in the chat now or will be shortly now.

(00:04:45):

One more minute. I want to do just a quick snapshot of a potential patient journey to access buprenorphine and to illustrate what we're going to discuss over the next two days. So the next slide has a number of steps that patients navigate to begin and maintain using buprenorphine. So patients might become aware of or have the opportunity to begin buprenorphine treatment in a number of different ways; after experiencing an overdose, through an outpatient clinic and inpatient stay, through harm reduction programs or other peer recovery services. So there's an assessment by a prescriber and then the patient and that prescriber work together to decide whether to start buprenorphine and work out a strategy for starting it. Throughout today's sessions, we are going to hear more about specific initiation strategies and the many factors that are considered when choosing how to start buprenorphine.

(00:05:43):

After you make the decision to start, then there's a prescription for ongoing care and accessing the medication through a pharmacy. What you see on this slide and what we're going to talk about over the next two days is there are many dynamics and some barriers that can emerge as we're going through that journey. So we wanted to give you a quick snapshot of what we're going to talk about over the next two days. And with that, let's dive into today's program and I'm going to move to the virtual room that has our keynote speakers, introduce them and we will be on our way.

(00:06:15):

[inaudible 00:06:39]... Substance use and behavioral health in FDA Center for Drug Evaluation and Research. And Dr. Yngvild Olsen who served as the director of the Center for Substance Abuse Treatment at SAMHSA. Dr. Sokolowska, you are first up, so please take it away.

Opening Remarks on Current Regulatory Landscape

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

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

Dr. Marta Sokolowska (00:06:55):

Thank you very much, Susan, and good afternoon. It is with great pleasure that I welcome you all to this public workshop on buprenorphine initiation and maintenance care for opiate use disorder. I would like to express my gratitude to all speakers, our panelists and attendees for joining us today and directing us to a deeper understanding and impactful opportunities in expanding access to medication for the treatment of OUD. We are here to learn from clinicians, pharmacists, people who want this treatment and the community supporting them such as peer recovery specialists. Impactful changes cannot happen without you, so thank you for taking the time and joining us today. I would like to take the opportunity to recognize Reagan-Udall Foundation for organizing this workshop and working with SAMHSA and FDA staff to develop a robust agenda that gives a voice to both challenges and opportunities in improving buprenorphine treatment and quality of care. We could not do this work without them or without you all.

(00:08:02):

The overdose crisis remains one of the country most pressing public health concerns and the top priority for the FDA. In 2021, more people age 15 to 54 died in the United States due to opiate involved overdose than due to COVID. Medication for opiate use disorders are safe, effective, and regrettably underused, treatment options. According to National Survey of Drug Use of Health in 2021 data report, only about 22% of 2.5 million people with pasture opiate use disorder received medication for the disease. The question is how do we provide more treatment to those who need it? This workshop is a small but an important effort we are undertaking to implement comprehensive approach we've named the FDA Overdose Prevention Framework. This framework was established last August to undertake impactful creative actions to prevent drug overdoses and reduce deaths.

(00:09:14):

This workshop is part of a collection of actions under one of the FDA framework's priorities, which focuses on advancing evidence-based treatment for substance use disorder. More specifically, we are here today to focus on expanding access to medication for OUD, which is a lasting area of focus for FDA. I want to highlight a few actions we have taken to support buprenorphine treatment to encourage innovation and development of new treatments for opiate use disorder. In the past few years, FDA published several guidances for industry including on clinical endpoints for demonstrating effectiveness for OUD and drug development for modified release products for injection and implantation. Additionally, FDA has approved new dosages of both branded and generic buprenorphine products in the past few years. I would like to briefly highlight the importance of two pieces of recent legislation that are quite impactful for treatment of people of opiate use disorder.

(00:10:20):

The first one is the Mainstreaming Addiction Treatment Act, or the MAT Act, which removed the federal requirement for practitioners to have an X waiver to prescribe buprenorphine for treatment of opiate use disorder. This will permit all healthcare providers with current DA registration the ability to prescribe buprenorphine for OUD, just like they prescribe other controlled substances medications. Second, the Medication Access and Training Expansion Act, or the MATE Act, requires healthcare providers to complete an eight-hour one-time training of managing patients with substance use disorder. This is a condition of receiving or renewing DEA registration to prescribe controlled substances. FDA remains committed to work with our federal partners to ensure that prescriber education is comprehensive and appropriate regarding conditions such as pain and substance use disorder. We expect to hear a little bit more about that from our SAMHSA colleagues today. On note of working with federal partners, I have one more buprenorphine related activity to tell you about that took place just this morning.

(00:11:36):

In collaboration with SAMHSA, we issued a joint letter to healthcare providers. This letter elevates person center prescribing and clarifies that counseling, while recommended it beneficial, is not a prerequisite for initiating on continuing buprenorphine treatment for opiate use disorder. And today, thanks to our collaboration with SAMHSA and the Reagan- Udall Foundation, we have brought together one wide range of experts who will be sharing they knowledge and insights which we'll carefully consider in developing actionable outcomes and FDA authorities. But let's talk why we are here today; about improving access and uptake of buprenorphine treatment for opiate use disorder remains a key challenge and opportunity as the drug overdose crisis evolves. Buprenorphine is a safe and effective medication for OUD. However, we have heard that there are barriers to buprenorphine initiation and long-term care we hope to bring to forefront today. I see these barriers as opportunities we can all work together to address.

(00:12:47):

I also see them as call to action for regulators, researchers and sponsors to work together and meet the needs of the people on the ground, the treatment providers and those wanting the treatment. We are going to hear about barriers to buprenorphine initiation. We recognize that the need to be in mild to moderate withdrawal is a challenge to initiation and the difficulties posed by this level of withdrawal are increased due to fentanyl, another synthetic opiate in the illicit drug supply today. In the context of this unmet need, various buprenorphine initiation strategies, including low and high dose initiations, are being used in clinical practice. Some are working better than others in different settings and in different populations. We are hoping to hear from researchers as well as those in the trenches about best practices, lessons learned, and where support is needed. Beyond initiation, there are challenges to continuation of care.

(00:13:51):

We hope to learn about the successes and pain points in optimizing buprenorphine dosing and management in the transition to stabilization and maintenance. Initiation is happening at various settings; emergency medical services and emergency departments and outpatient facilities through telehealth. How do we optimize outcomes after initiation? What do different patients need to succeed and how do we define success? We also can't ignore that for some patients there may be a need or, in some cases want, to discontinue buprenorphine. This may be due to health condition, an access issue or desire by a patient. In cases where it's indicated, how and when should patients safely taper? In covering these topics, I expect to hear about product needs from those who use, dispense and prescribe buprenorphine for OUD. We are available for discussions with sponsors when appropriate about the data needed to change or update product labels, the potential for expedited review of product applications when appropriate, and other ways we can support areas of unmet need.

(00:15:13):

I also want to hear about specific research needs to support product developments, improve patient care and changes to policy. Several of our federal partners are here today and your input will help inform our understanding of gaps in research and data and plans to address those gaps. In conclusion, impact of overdose crisis and opiate use disorder touches us all. Once again, I'm grateful that people who use drugs, families, friends, harm reduction organization, first responders, pharmacists, clinicians, researchers, and federal partners are taking the time for joining us today for this important conversation. This diverse set of voices and experiences is key to advance our collective understanding of what is and isn't working in buprenorphine treatment for opiate use disorder. We need to come to a better understanding of how buprenorphine is being used to start and keep patients in treatment when they are ready to seek it.

(00:16:15):

We often hear that the perfect medicine isn't perfect if no one wants to use it. So I cannot overemphasize the need to listen to those on the ground. Their real world experiences must inform, and in many cases, drive innovation and we must be agile in meeting their needs if we want to make a difference. I hope this workshop can serve as a catalyst for improved treatment approaches, research, collaboration, product development, and policy change. Thank you again for joining us today and we look forward to a productive and informative discussion. With that, I would like to introduce Dr. Olson from SAMHSA.

Dr. Yngvild Olsen (00:16:54):

Great, thank you so much, Dr. Sokolowska. Thank you so much to the Reagan-Udall Foundation for convening this important, important workshop. And thank you all for being here. SAMHSA is incredibly excited to be part of this and with our partners at the FDA, our partners that you're going to hear from also from DEA tomorrow, our partners with NIDA. This really is about a partnership because as you know, Dr. Sokolowska mentioned, that when there are over 107,000 people who died of an overdose, primarily driven by illicitly manufactured fentanyl in 2021 alone, and we have effective tools like buprenorphine, we really need to do absolutely what we can to make sure that people actually can have and benefit from the access and benefit from those medications. Much of what SAMHSA does is really to try and promote access to an uptake of buprenorphine in various different settings. Overdose prevention is one of the key strategic priorities for SAMHSA and it is one of the pillars.

(00:18:13):

The evident access to evidence-based treatments is one of the pillars for the HHS overdose prevention strategy as well. And the actions that have the policy changes that Dr. Sokolowska mentioned, in terms of the Mainstreaming Addiction Treatment Act, that removed the requirement for a special waiver to prescribe buprenorphine is an incredibly huge step in the right direction to really be able to advance access to buprenorphine. The MAID Act, Medication Access and Training Expansion Act, likewise is a significant partnership between various different federal agencies to really make sure that practitioners have the training in substance use disorders, including opiate use disorder, to really be able to take advantage of these other policy changes that Dr. Sokolowska mentioned. And finally, the fact that we now have medications like buprenorphine and expansions and different proposals related to methadone access as well, I think puts us in a historic place and time to really have advances in how we are addressing and treating opiate use disorder.

(00:19:34):

As an addiction medicine specialist, I have watched over the past 20 years how this situation on the ground, with respect to opioids and opiate use disorder, have evolved from prescription opioids to heroin and now to illicitly manufactured fentanyl. And that situation really has created a need for looking at how we are prescribing buprenorphine, how we are initiating buprenorphine, how we are helping people stay on buprenorphine, as well as how we're really learning from the flexibilities that we have all, as practitioners, been living under for the past several years under COVID.

(00:20:17):

And so I think today's and tomorrow's workshop and hearing from the number of different experts, the multidisciplinary voices and the multiple voices across research providers, peers, people with lived experience in various different settings is going to provide additional information, and really, a significant amount of learning for us as we really continue to look at how to advance these therapies. So I just want to say thank you all for what you do every day and thank you for being here and being part of this incredibly important work. And so appreciate the opportunity for SAMHSA to be partners with FDA

and with the Reagan-Udall Foundation in really learning from all of you. And with that, I'll pass it back to Susan.

Susan Winckler (00:21:14):

Great, thank you so much, Dr. Sokolowska and Olsen. I heard you clearly talk about cross-agency collaboration, the multidisciplinary approach and the efforts that we want to pursue to do a better job in treating opiate patients with opioid use disorder and preventing those overdose deaths. So thank you for kicking off our meeting and for helping make this meeting happen so that we can advance care for these important individuals.

(00:21:47):

With that, we're going to turn to our first session where we're going to hear an overview of the current clinical guidelines. So I want to introduce Dr. Melissa Weimer, who is associate professor of medicine and public health at the Yale School of Medicine and medical director of the Yale Addiction Medicine Consult Service. Dr. Weimer is also the chair of the American Society of Addiction Medicine Clinical Practice Guideline Methodology and Oversight Committee. We are going to turn to the virtual room with Dr. Weimer and dig into our first content presentation. Thank you.

Session 1: Overview of Clinical Guidelines

Speaker: Melissa Weimer, DO, MCR, Yale University, American Society of Addiction Medicine

Dr. Melissa Weimer (00:22:30):

Hi everyone. Thank you for inviting me. Very happy to be here with you all today. I'm Dr. Melissa Weimer. I'm here to discuss buprenorphine clinical considerations and clinical practice guidelines that have been established by the American Society of Addiction Medicine. So I wanted to spend a minute to talk about the American Society of Addiction Medicine and the clinical practice guidelines that we produce. The scope of our clinical practice guidelines typically involve areas within the scope of addiction medicine that address prevention of addiction, screening for addiction, diagnosis of addiction, and then treatment. Sorry. I need to go back and it's not letting me. Nope. Going forward. Not back.

(00:23:44):

All right, keep going. All right, thank you. So the ASAM, starting in 2021, started to update our clinical practice guideline methodology. So we have had produced clinical practice guidelines for a very long time. However, in 2021, a committee was established that I chair that is working to establish a new methodology. And the reason for the update is so that we can be within the standards of the IOM for clinical practice guidelines that we trust and to do many of the things that are listed here on this slide. Essentially to establish transparency, better manage conflicts of interest if they occur, balance our guideline group composition so we are clearly representing many different perspectives and expertise around the country, utilizing a systematic review and all of our clinical practice guidelines with all of our recommendations, establishing a strength of evidence that supports them, and then a strength of the recommendation.

(00:25:09):

We want to be able to articulate our recommendations clearly and succinctly, engaging stakeholder review in all of our clinical practice guidelines, promoting health equity throughout the clinical practice guidelines, and then establishing a clear process for any of our updates to our clinical practice guidelines. So I state that just to level set so you have an idea of the hard work that ASAM's doing to

ensure that our clinical practice guideline methodology is the best that it can be and the most transparent and the most able to address many of the complexities that we're seeing. At the same time, making sure that we are establishing what the evidence is for some of the clinical practice guidelines. And unfortunately within the management of addiction, sometimes our evidence is not as robust as we would like it to be.

(00:26:06):

I think I'm going to have to have someone else take my slides for me. I'm sorry. Thank you. So I'll just let you know when I need to go forward. So in the updates of the methodology that we have established, we also recognize that there are times when, as I just stated, evidence does not necessarily support a full clinical practice guideline. However, we continue to want to be responsive to the needs of our patients and of our profession and make sure that we are able to provide consensus statements guidance when it is needed. So you can see here that within the last two years we've established some different types of clinical documents. And I'm going to present two of them to you today. But one of them specifically a new type of document called a clinical consideration.

(00:26:59):

So I discussed what a clinical practice guideline is. It's based on very rigorous scientific evidence, very time intensive. There are other types of statements that we can provide, such as a clinical consensus statement, which is still informed by evidence, but may have a broader scope, maybe based more on case studies or reviews and a scoping type of literature review. And then finally, for areas such as say, the initiation of buprenorphine in the setting of high potency synthetic opioids, we needed to create something such as a clinical consideration. And this is a document that is a clinical document meant to address issues that are immediately clinically relevant, though we may have limited evidence. And these clinical considerations are typically informed by narrative literature review and really based on expert clinical consensus. And so I will present that to you today. Next slide. Before presenting that, I do want to bring your attention to an existing ASAM clinical practice guideline for opioid use disorder. The original clinical practice guideline was written in 2015, it was then updated in a focus update in 2020. The focus update had 35 revised recommendations, 13 of which were new, and then there were 14 that were specific to buprenorphine, then which I'll quickly go over. And this is freely available. You can find this on the ASAM website. Next slide. So the 2020 opioid use disorder focused update that was part of it specific to buprenorphine, I've listed some of the key recommendations that related to buprenorphine initiation and treatment. So within this 2020 opioid use disorder focused update, there was the recommendation that you should initiate buprenorphine once opioid withdrawal begins. The starting dose for buprenorphine was a dose of two to four milligrams with a recommendation to increase by two to eight milligrams at a time.

(00:29:12):

The recommend, the clinical practice guideline discussed that office-based and home initiation are both safe and effective. There was information about following initiation of dose, and so the recommendation there was to titrate the dose of buprenorphine to alleviate symptoms. In the clinical practice guidelines, 16 milligrams or more was generally recommended and they stated that there was limited evidence on doses greater than 24 milligrams per day. The clinical practice guideline recommended not to delay or withhold treatment if patients did not want to engage in psychosocial treatments. And they recommended monitoring and supported patients with medication management. There was no time limit placed on how long someone should be treated with buprenorphine and the authors recognize that buprenorphine taper could be a very challenging time and should be a slow process that needs careful monitoring. Next slide.

(00:30:14):

This was written in the clinical practice guideline. Focus update was written in 2019, published in 2020. And yes, we had high potency synthetic opioids within our drug supply at that time, but really, after 2020 is when the complexity of buprenorphine initiation, and some of the issues that are going to be discussed today, really became a bit more apparent. So some of the clinical complexity that we have recognized and know that we need to be responsive to are the presence of high potency synthetic opioids in our drug supply. 2019 has been the use of low dose initiation, which I know is going to be a topic of discussion today. There's been the-

Dr. Melissa Weimer (00:31:02):

... Going to be a topic of discussion today. There's been the use of high dose initiation. We've had more reported incidents of precipitated opioid withdrawal. However, I know there's some recent research that's that's really sort of countered the extent to that we're seeing that we've also seen Xylazine and other novel components within the drug supply and then of course, extended release buprenorphine became more available. So these are some of the things that have really changed since 2020 that we need and want to be responsive to. So that led to the development of some of the recommendations I'm going to provide for you today. Sorry, go back, back, back, back, back. Okay, now go forward. All right. So again, we have created, and this will be coming out hopefully in the next couple months. A clinical consideration document specifically for some of these complexities. Again meant to be highly clinically relevant to address some of these real world complexities.

(00:32:16):

It is based on expert consensus mostly, even though we have to the extent possible included all the evidence we have for this topic, there is limited evidence for this at this time, and of course it's less rigorous than a clinical practice guideline or consensus statement. Next slide. So these are the authors of the Buprenorphine Clinical Considerations Writing Committee. There were five authors listed here and then they had an extensive peer review as well as by the ASAM, quality Improvement Council and the as ASAM board of directors and it has been approved by all of those entities. Next slide. This are the key questions and the key components. So we're really discussing individuals with severe opioid use disorder who are chronically exposed to high potency synthetic opioids. We include pregnant individuals and we're discussing initiation stabilization, long-term treatment comparing to our current existing clinical practice guideline and really addressing this in any setting. Next slide. So I don't have time to go through all of the considerations that we've listed, so I'm going to only discuss two of the key questions that we asked and I'm going to quickly go through some of the clinical considerations that we have created. Next slide.

(00:33:45):

So one of our key questions was what specific clinical situations favor use of low or high dose buprenorphine initiation strategies? And you can see the clinical considerations here. Basically showing that observational data suggests that buprenorphine initiation is best individualized by setting and patient preference. Low dose buprenorphine with opioid continuation, which we have defined within the clinical consideration document in hospital settings, appears to be well tolerated based on observational data. We need more evidence to determine the optimal strategy for low-dose initiation in ambulatory settings for patients who are ineligible for medically prescribed full agonist opioids under our current regulations within the United States. And in patients with chronic exposure to high potency synthetic opioids who are initiating buprenorphine after abstinence and development of withdrawal, rapid dose escalation has been observed to be safe primarily in the emergency department setting. Next slide. So we've summarized that here. This is going to be a quick summary as you can see. And again, this should be coming out in the next month hopefully in the Journal of Addiction Medicine. Next slide.

(00:35:07):

Key question three. After buprenorphine initiation, what range of buprenorphine dosing and or dosing strategies can be considered during stabilization and long-term treatment? And so we have acknowledged that some patients with high opioid tolerance may require buprenorphine doses greater than 24 milligrams per day, particularly during the stabilization phase of treatment. We discussed that there are physiologic changes during pregnancy that alter metabolism, necessitating an adjustment of dose and dosing intervals. We recommend that you consider dose and frequency adjustments, psychosocial supports, and a higher level of care if individuals are unable to stabilize on buprenorphine. And then consider a reassessment of the higher dose greater than 24 milligrams of long-term doses once patients really enter that long-term form of treatment if they do not have any ongoing use of opioids. Next line.

(00:36:11):

What are some of the indications for injectable extended-release Buprenorphine compared to the sublingual formulations will be discussed. Considering extended-release buprenorphine formulations for individuals who are unable to stabilize on the sublingual formulation, particularly for individuals who've had extensive high potency synthetic opioid exposure, they have unsafe living environments or multiple overdoses. Considering the administration of extended-release buprenorphine soon after successful buprenorphine initiation to achieve a durable overdose prevention. And then while extend-release buprenorphine is reaching that steady state, we need to consider the risks and benefits of additional sublingual buprenorphine, particularly for pregnant individuals. Next slide. So I'm happy to take any questions. I know that was a very quick overview, but I hope that we were able to quickly present some of the salient features from our new clinical consideration for buprenorphine.

PART 1 OF 7 ENDS [00:31:04]

Susan Winckler (00:37:16):

Dr. Weimer, that was great. So appreciate you walking us through a bit on the process and how you got there as well as then the results and what in fact those clinical guidelines are. So we appreciate that you've set us a good grounding so that we're ready to go to our next session where we will talk about buprenorphine initiation in the inpatient setting. So with that, I'm going to leave this virtual meeting room and go to the next virtual meeting room. But thank you so much Dr. Weimer. I have found my way into the virtual meeting room that has our next panel. So our next session we want to talk about buprenorphine initiation in the inpatient setting. So here we're exploring starting buprenorphine in that inpatient hospital setting. Care that takes place in the hospital and the pre-hospital setting. We'll talk about care in outpatient or the community setting in the following session. So for this discussion, we are going to begin with a presentation from Dr. Amer Raheemullah, who is clinical associate professor at Stanford University in the Psychiatry and Behavioral Sciences Department. He specializes in the treatment of addiction and is the director of the Addiction Medicine Consult Service at Stanford Hospital. Dr. Raheemullah, the microphone is yours. We are anxious to hear your presentation.

Session 2: Buprenorphine Initiation in the Inpatient Setting

Presenter: Amer Raheemullah, MD, Stanford University

Panelists: Dionna Berkholder, North Colorado Health Alliance

Gerard Carroll, MD, FAAEM, EMT-P, Cooper University Health Care

Gail D'Onofrio, MD, MS, Yale University

Amer Raheemullah (00:39:15):

Okay, great. Thanks so much for having me. Before we talk about inductions in the inpatient setting, I wanted to talk about the goals of induction regardless of the setting, the induction is not the goal in itself, but it's a means to stable buprenorphine maintenance. And through buprenorphine maintenance, not using it once or twice. Through buprenorphine maintenance, we get all the great outcomes like decreased mortality, improved outcomes, improved patient retention, decrease illicit drug use. The second goal of induction is to minimize withdrawal, to increase our chances to get to buprenorphine maintenance. So on one end we don't want to give buprenorphine too soon and precipitate withdrawal, but on the other end, we don't want to wait so long that we unnecessarily prolong withdrawal. Withdrawal increases dropout, and if we can avoid withdrawal altogether, that's great. The third goal is keeping people on buprenorphine and illicit opioids is not the goal in people with opioid use disorder.

(00:40:24):

The ideal goal is buprenorphine maintenance without illicit opioid use, the goal is to increase the buprenorphine as quickly as possible to achieve an adequate dose that treats withdrawal and cravings and to stop illicit opioids as soon as possible if they're continued. So understanding these goals of induction, then we have a menu of buprenorphine inductions available in order to achieve those goals. There's a great paper reference at the bottom that discusses macro dose induction, microdose induction standard inductions. It summarizes the evidence clinical scenarios that highlight which method to use, especially in the area of fentanyl. Feel free to read it. I'm going to attempt to give us a helicopter view of these. The first induction style, standard induction. So guidelines suggest clinicians typically wait for opioid withdrawal to manifest, then administer an initial buprenorphine dose of two to four milligrams, wait one to two hours if well tolerated, administered additional doses in a step-wise fashion up to 60 milligrams in day one.

(00:41:34):

Some guidelines recommend up to eight milligrams in day one. High dose inductions differ in that they typically start with eight milligrams or more. For example, American College of Emergency Physicians suggest starting at eight milligrams. There's also rapid high dose or macro dose inductions that start at 16 milligrams or more as seen in the reference at the bottom and you can administer up to 32 milligrams of sublingual buprenorphine within the first few hours. Low dose inductions are different in that they don't wait for withdrawal to develop, and in fact, if withdrawal develops, it sort of defeats the purpose of it. So with low dose induction, we start with small doses of buprenorphine, small enough that they don't precipitate withdrawal, and these overlap their current opioid use. So we're going to go into low dose inductions in more depth, but the point I want to make here is that you want to pick the best option for the setting and the patient.

(00:42:36):

So when we talk about inductions in the inpatient setting on the next slide, the emergency department will most often be the first point of contact prior to patients being admitted to the hospital. The ED will have its own set of considerations. Higher dose induction are used here for many reasons, including the increased potency of illicit opioids, commonly encountered delays in access to follow-up care and other reasons as well. It's important to recognize the ED as a low barrier setting to get people on buprenorphine easy and fast. If I want to go to the clinic to get buprenorphine, you have to schedule appointments, wait for them, so on and so forth. But the ED is a low barrier setting to get buprenorphine easy and fast. It also needs to be simple and fast for ED providers to get trained on and implement buprenorphine inductions.

(00:43:34):

Complicated slow protocols for ED physicians are not high yield and may not be practical for wide adoption. Most ED clinicians should continue buprenorphine inductions using established guidelines such as those disseminated by the American College of Emergency Physicians, which recommend eight milligrams, starting with eight milligrams. This is likely going to be discussed more by our panelists, but the point I'd like to make here is that low dose inductions generally become a consideration when we're talking about the inpatient setting. Generally become a consideration after patients are admitted. On the next slide, if buprenorphine is started in the emergency department, great. After they're admitted, you maintain that buprenorphine, if not started yet and their admission does not require opioids, then you have another opportunity to just start the buprenorphine directly while they're admitted if withdrawal is anticipated. However, if withdrawal is not anticipated, if their hospital admission requires opioids like full agonist opioids such as morphine and oxycodone, which many hospital admissions do, then a standard induction or directly starting buprenorphine is not an option. Because oftentimes patients will stay on opioids, full agonist, opioids throughout hospitalization and perhaps afterwards. And we don't want to miss that opportunity to start buprenorphine in them.

(00:44:56):

On the next slide, when people are admitted to the hospital, it's because they're ill enough to be admitted to the hospital. So regardless if people need opioids are not in the hospital, patients are requiring hospitalization are often fragile and cannot risk opioid withdrawal worsening their conditions. Opioid withdrawal is an unnecessary layer of complexity that affects multiple organ systems and it can be avoided with low-dose inductions and one of the largest studies examining low-dose initiation and the hospital setting referenced at the bottom, researchers documented the reasons for using low dose buprenorphine. Most common reasons were acute pain followed by patients already having a high level of distress while they're in the hospital or medical fragility. Other reasons were previous failures with a traditional induction. Examples of patients that can't tolerate opioid withdrawal include patients with opioid use disorder who are post-op and require opioids for acute pain needs or patients who have sustained a trauma possibly due to being intoxicated, which fits the archetype of somebody with opioid use disorder.

(00:46:10):

Also, patients with opioid use disorder and co-occurring acute psychiatric conditions. With patients with co-occurring acute psychiatric conditions we have to treat their opioid use disorder to treat their psychiatric conditions and they can't often tolerate the dysphoria and anxiety of going into opioid withdrawal before starting buprenorphine. Then there's people that just don't want to tolerate opioid withdrawal on the next blow point. So there's people that are ambivalent about opioid use disorder medications, patients that are on methadone who want to switch to buprenorphine because of some new development in their hospitalization, which doesn't allow them to be on methadone. Or patients in the outpatient setting stable on methadone want switch to buprenorphine and don't want to go into the days of withdrawal that it requires to start buprenorphine and also patients with the history of precipitated withdrawal. On the next slide the point I want to make here briefly is that patients with opioid use disorder are increasingly being hospitalized.

(00:47:17):

We can't afford to miss opportunities to start buprenorphine due to the hospital factors that I mentioned before. Many of these hospital factors are a downstream consequence of their opioid use disorder. As you see in the slide, opioid use disorder in hospitalized patients could has quadrupled from 93 to 2016. The opioid epidemic has only gotten exponentially worse since that time. Also, opioid use disorder in hospitalized patients has been increasing 8% annually. So point being low dose

buprenorphine deductions are an option for many patients in the hospital who would other not otherwise not be able to start medications for opioid use disorder. On the next slide, sometimes with low dose buprenorphine inductions, there can be confusion about the names of them. The Bernese method was first described the low dose initiation method, and the authors use the term microdose inductions or micro doses. The term micro doses is still used in the literature but slowly falling out of favor because micro doses has come to be associated with psychedelics.

(00:48:28):

The term low dose induction are being used more frequently. It sounds simpler, which reflects the simplicity of the principle behind the method. And the principle is that low doses of buprenorphine don't precipitate withdrawal. So the study reference at the bottom looked at opioid dependent subjects who were receiving 30 to 40 milligrams of methadone. They were opioid dependent and they measured the vital signs and withdrawal scales in these patients and compared this with giving them placebo on another day. The point is they found that low doses of buprenorphine did not cause withdrawal and there was no significant differences from placebo. So what this means is precipitated withdrawal is not is caused by buprenorphine, it's caused by the starting dose of buprenorphine. Withdrawal is not an inevitable consequence of buprenorphine's partial agonism and high binding affinity. It is due to the starting dose of buprenorphine.

(00:49:28):

On the next slide, just to talk a little bit about how low dose buprenorphine initiation works. Small doses, you start with small doses which are considered 0.5 milligrams of sublingual buprenorphine or their buccal film equivalent, which is about 225 micrograms, or you use 20 micrograms per hour transdermal patches or less. Those are considered small doses. The second main point, and perhaps the most important point is to continue opioids to prevent withdrawal, opioids need to be at an adequate dose to prevent withdrawal. So the transdermal protocol that we've been using for the last six years, we rarely see opioid withdrawal and it only occurs when their full agonist opioid use is clearly too low to meet their opioid debt, their opioid need. And oftentimes if you're unable to find an indication for opioids, then you can use methadone for opioid use disorder while you titrate up buprenorphine.

(00:50:25):

And there's many protocols that have been used to switch from methadone to buprenorphine. Your third point is you want to titrate up the buprenorphine. Ideally, you are on an adequate dose of buprenorphine in a matter of days because hospitalizations can be unpredictable. There's several protocols that can get you on an eight milligram dose of buprenorphine within 48 hours and 16 milligrams within 72 hours. If you know your patients will be there longer, then you can consider a longer up titration. But you want to avoid keeping your patients hospitalized unnecessarily if a faster protocol can be used safely. So the recent review at the bottom discusses different starting doses and durations that have been reported in the literature. So I'm going to attempt to simplify that with Transmucosal formulations, sublingual doses are commonly 0.5 milligram doses or below. The problem with that is the lowest commercially available sublingual dose is two milligrams.

(00:51:29):

So patients have to cut their dose or inpatient pharmacies have to cut their dose, so a half a milligram as a quarter film or tablet. And then the up and 0.25 milligrams, which is also used in the studies is one eighth of a tablet. And the duration to reach 12 milligrams and some of the reports have been by day three but typically these protocols, the sublingual protocols are four to seven days. And the buccal formulation, the largest study using buccal film started at 225 micrograms. The transdermal protocols start at 20 microgram patches or below, and eight milligram doses can be reached by 48 to 72 hours. I'm

going to start to talk about the barriers to transdermal inductions. And if we don't get to this or finish this in my time, what we can do is discuss the rest of it in our panel discussion.

(00:52:28):

In general, transdermal protocols published tend to be faster reaching an eight milligram dose by day two and 60 milligram dose by day three or four. Low dose inductions use patches. Using patches were first described in 2015, patients were on eight milligrams by day two or three. This protocol was used at other institutions and shown to be safe and demonstrated the same timeline over the years. And another study that just came out a few months back, the reference at the bottom shows that this faster transdermal option is still well tolerated with no incidence of precipitated withdrawal. And in their study, they had 54% of them as fentanyl users. The problem with the transdermal induction on the next slide, the problem is that patches are currently only FDA approved for pain and they are expensive as an outpatient. So films are a few dollars, patches are a few hundred dollars and they're not consistently covered by insurances. And the transdermal route can be better facilitated with FDA approval for opioid use disorder. Inexpensive transdermal formulations or better insurance coverage. And on the next slide, I can talk a little bit about the barriers to sublingual buprenorphine. I believe I have a few minutes left. For the sublingual preparation, many of the protocols take longer to get on an eight milligram dose, typically four to seven days. But there are protocols that have been done in fewer days. For opioid use disorder patients the goal is to reduce their time on illicit opioids or hospital administered opioids that are short-acting and highly reinforcing as fast as possible. So shorter protocols are generally preferred, whether that be sublingual, transdermal buckle. Also, the most common low doses are 0.5 milligrams to 0.25 milligrams on the next point. However, cutting the pills and films lacks precision and can generate uncertainty, confusion, they're difficult to explain, they're complicated to explain.

(00:54:38):

High performance liquid chromatography analysis only showed a content uniformity in films cut in half. Inpatient pharmacies may not approve films cut in a quarter because of this, because of this lack of established content uniformity in films. But buccal film preparations are still available and still an option. And sublingual and buckle films are a great option especially if patients are going to be hospitalized for days and will be around for that protocol. Some solutions to these barriers include manufacturing smaller doses of sublingual buprenorphine. If patients can just start on sublingual buprenorphine and continue on it, that's obviously preferred. Other solutions are pre-formulated medication packaging or blister packs to make dosing simpler and more research to develop clinicians' confidence in sublingual buprenorphine's ability to do faster protocols. Thanks so much. We can skip this part. I know I don't have much time left. That's fine. I can't do this justice, so I'm happy... Yeah.

Susan Winckler (00:55:49):

That's okay. Well, so we know we want to do this and I'll ask our panel to come on camera while you finish that last slide.

Amer Raheemullah (00:55:57):

Okay, great. Sounds good. So the evidence for low dose initiation is limited and based on retrospective studies, case series and case reports. For opioid use disorder, we want to learn how to use low dose inductions to get people on therapeutic doses of buprenorphine of 8 to 16 milligrams or higher as fast as possible. So this means what is the highest dose we can start with? How fast can we up titrate buprenorphine and how fast can we get them off their other opioids? We also want to know what formulations and protocols lead to the most adherence. There are better quality studies underway. One randomized controlled trial is in progress with an anticipated completion date of 2026. Until then, we

have enough information to start using low dose inductions for people that would otherwise not start buprenorphine for opioid use disorder.

Susan Winckler (00:56:54):

Excellent. So Dr. Raheemullah, thank you for... I'm struck by your underscoring the different ways that individuals present and therefore the different approaches that have to be considered. I want to invite our panelists to the conversation here. We are bringing four additional folks into the conversation and so I'm so glad to see all of you joining us on the screen. So joining us, we have Deanna Burke-holder, who is a peer care coordinator with the North Carolina Health Alliance. Welcome Deanna. We also have Dr. Jerry Carroll, who's program director for the EMS fellowship at Cooper University Hospital, Dr. Gail D'Onofrio, who is the Albert E. Kent professor of emergency medicine and of medicine and public health at the Yale School of Medicine. And rounding us out, Dr. Michael A. Smith, a clinical associate professor in the Department of Clinical Pharmacy at the University of Michigan College of Pharmacy, and also a clinical pharmacist in pain and palliative care at Michigan Medicine.

(00:58:01):

So we are going to have a conversation among the five of you. I want to turn first, Dr. D'Onofrio, would you tell us more about your experience initiating buprenorphine in the emergency department and just a little bit of illustration how that might be different from other hospital experiences?

Gail D'onofrio (00:58:21):

Sure. So my experience is that through a NIDA and NIH Heal ED initiative, we are looking at sublingual versus the CAM 2038, which is Brooksville seven day injectable. And we have now, as of today, enrolled over 1500 patients and we have had 10 cases of precipitated withdrawal in 28 sites all across the country. So we are not seeing, I shouldn't say we're not seeing, we're seeing the same patients affect our patients are probably a lot more seriously ill and having different types of co-occurring illnesses, et cetera. But we are quite capable of initiating buprenorphine with very few side effects. The things that I think that we do well is that if patients are not feeling better or they're feeling a little worse, we give them even more buprenorphine. And so we can easily get people up to 24 milligrams during their period of time with us, or we could use some ancillary medications if we need to.

(00:59:38):

In the unlikely event, the less than 1% that developed precipitated withdrawal, we can treat them very effectively. And we've shown how to do that. In our last one I unfortunately had in my institution by me, I could treat in a couple of hours and they were doing fine. So we do know how to treat that and get them out, but clearly it was precipitated withdrawal. So I would say that really we can just treat it very quickly and if there is any comment, it's more [inaudible 01:00:10] better than less [inaudible 01:00:10]. And I'm just going to go right out there and say that we cannot, as an outpatient providers ever give what's considered low dosing because that requires individuals to use illicit drugs. So I would be saying, go out and use another dose fentanyl, in which case I could kill you. So we will never do that.

(01:00:30):

One thing we could do if that was ever allowed by the FDA is give a pharmaceutical dose of morphine, for example, over periods of time along with a patch. Again, the patch would be the best. And so if we could get the patch approved for OUD and get it in a reasonable amount of money, then we could do that. And that could be very a great option for people. And when patients are being admitted to the hospital, there's whole kinds of things that could be done. The only thing that's really serious is that patients who are going into the hospital are, have co-occurring substance use disorder or other

problems. And they generally don't stay long in the hospital. So these long protocols will never work. They're all going out and then I'm seeing them back in a day.

(01:01:14):

So it's important we straighten this out and we could, it's very different for different people, but clinicians and patients should not be worried about a [inaudible 01:01:28] induction because we can do it very well in our setting and we should not be fearful of that. And if should the unlikely case that we do precipitate withdrawal, we can treat it. But quite truthfully, it's not any different than what we were doing 10 years ago without fentanyl. We did put people in precipitated withdrawal there in a small amount, and we will continue to do it, but we'll learn how to treat it. And I would just say that because our population is so much more vulnerable than it's ever been before, 50...

Gail D'Onofrio (01:02:03):

More vulnerable than it's ever been before. 50% of our patients have unstable housing, only 20% of them are employed. Very few of them have educations that can get jobs so that it's just we have to deal with all of this, as well as their addiction. And so, it's a complicated route.

PART 2 OF 7 ENDS [01:02:04]

Susan Winckler (01:02:26):

Right. There are many considerations in that approach. I want to turn to Dr. Carroll. Tell us about your experience initiating buprenorphine within emergency medical services. How is it different from what we heard from Dr. Raheemullah and Dr. D'Onofrio?

Gerard Carroll (01:02:49):

So really dovetailing off of Gayle's kind of work there, we kind of built a similar ED bridge program here at Cooper and emulated a lot of that. And again, like she said, micro induction is great for the outpatient arena. There is that huge challenge of what we're telling people to do while they're still using opiates. And then, if you translate the ED experience into the pre-hospital experience, all of that gets more challenging.

(01:03:14):

And there's really two models in the pre-hospital world. And I want to talk about the latter. And the first is kind of this mobile integrated healthcare, or community paramedicine where you're really moving outside of the 911 system, and having paramedics visiting and doing almost like community health worker activities, and visiting nurse activities. And then, the second where you're actually repurposing, or increasing the purpose of 911 units on overdose calls and other opiate complications. And the kind of critical thing there, you had to teach both that engagement piece, which all healthcare providers really need to learn in this space. And then, just the actual much more easily taught pharmacology of medication for opioid use disorder.

(01:03:52):

And things we found again is you needed to be rapid. This is, there's 911 calls holding everywhere. You can't tell an EMS service that they're going to spend hours on scene with this patient population. So we opted for a high-dose induction. Typically, we... Not typically we induce with 16 milligrams and within 10 minutes we'll go to 24 milligrams. So very high-doses based on traditional.

(01:04:16):

Interestingly for the 200 cases we've had, plus another about 150 I'm aware of around the country, some of that data published, some of it not, we have had really no precipitated withdrawal. We think that may be linked that all of these patients have had naloxone first. And there's some, really interesting pharmacologic reasons for that, but none of them proven. So it's not worth getting into with my few minutes. But I think that's pretty safe and it's been pretty exciting stuff.

(01:04:41):

The other big thing which is hard pre-hospitally, and hard for the emergency department is that you need somewhere for these patients to go. Us operating in a vacuum is just not useful. When we started this program, we had a six points crazy diagram to get people to follow up. Now, Monday through Friday you can walk into the same place, which has been hard to reproduce as we spread this around the country.

(01:05:03):

On the FDA side and what we need as far as medications, the hardest thing is that we're doing high-doses, and high-doses don't exist. I have to put two sublingual films. Or worse, two tablets under your tongue right after I woke you up from an overdose, had this very difficult conversation while you're still looking for whether you got robbed, or what else happened before we got there. And hopefully, you will not throw up from your withdrawal that we induced while I try to get this absorbed.

(01:05:29):

So a one film and 16 milligrams could be super useful for us. An IV formulation, which I have a lot of experience with, is also very interesting to me. But those are, I think, avenues where we can kind of expand this and actually really get... 'Cause again like Dr. D'Onofrio said, this is the sickest population. This patient has no resources, chronically homeless, no support system. By the time you end up in some of these inner city areas overdosing, you've kind of hit that end stage opiate use disorder. And so, we need to be a little bit more aggressive, in my opinion. So that's kind of a good, hopefully, three minutes.

Susan Winckler (01:06:05):

It was perfect, and helpful in context about when the products are being used, and what might be helpful in additional product.

(01:06:16):

I want to turn then... Let's turn to the pharmacist perspective. Dr. Smith, what can you tell us about hospital-based buprenorphine initiation from the pharmacist perspective?

Michael A. Smith (01:06:30):

Yeah, so can you hear me with this microphone or no?

Susan Winckler (01:06:33):

Yeah, you're good.

Michael A. Smith (01:06:36):

Okay, good.

(01:06:36):

So I think the first thing from a pharmacist perspective, one is can we-

Susan Winckler (01:06:41):

Actually, get a tiny bit closer.

Michael A. Smith (01:06:43):

Sure. I think from the pharmacist perspective, the first thing is it safe? What's the safest way to do this for the patient? And then, the next is how do we get the drug that we're choosing to the patient in terms of delivery? I think Dr. Raheemullah has brought up some good points about the low- dose initiation problems. You really can't cut Subutex more than in half 'cause it just disintegrates. And so, that's one issue. So we really actually shy away from that.

(01:07:11):

The other is how do we get patients to the doses as fast as we can that we are looking for? And we're here actually moving away from the transdermal product because we've looked at our data versus another institution's, and found that there was really no difference. The only reason we got to higher doses faster is because we were just using higher doses of Suboxone faster. And so, I think really for us, it's a matter of somewhat using the gray area to our advantages.

(01:07:42):

As an example, we recently had a case of a patient with head and neck cancer, who we really needed to use buprenorphine in, but the concern was there wasn't sublingual space. Well we used it anyway, because although they didn't have a tongue, they had the vasculature there in order to absorb the drug. So I think it's trying to be creative in ways with the drugs that are available in current form. And thinking about how you can skirt around some of those issues.

(01:08:07):

And one of the other ones that was brought up was the expense of a Bupe trans patch. It's $150 at a minimum for a box of four, and no pharmacy's going to cut that box just to give somebody one patch when they can't give somebody else the other three. And so, really having flexibility in the formulations to give the doses that we need, the very high-dose in a single formulation, or very low-dose in a single formulation I think that spectrum is important. And those are the things that really, from my perspective is what we're trying to think through is because, and I think Gail said this best, is more buprenorphine is better, but any buprenorphine is better than zero. And so get it on, get it started and understand the cons to your approach so you can anticipate them and manage around them.

Susan Winckler (01:08:54):

Yeah. So, helpful reminder that in the interim there are things we can do with the existing dosage form, but recognizing that there's, certainly, an opportunity for additional ones. I'm going to come back to that idea of whether the currently available formulations are enough to meet the needs of patients. But you've already started to answer that. So, keep thinking on that.

(01:09:22):

Dionna, we want to bring your voice to the conversation here. As a peer care coordinator in an inpatient setting, what strategies for buprenorphine initiation have you seen work well?

Dionna Berkholder (01:09:37):

So what's worked best for our patients members is initially having them partnered up with a peer support specialist. So somebody who has lived experience, who's in recovery from not necessarily opioid use disorder, but substance use disorder who can say, "I've been to a clinic, I've been kind of where

you've been." And this helps the patient be able to have a voice to help them advocate for themselves. Whether that's communicating with the provider, maybe the patient isn't sure what kind of questions to ask, or how to say, "This is what I want." Or, "This is what I feel like I need," because a lot of these folks, like the other people are talking about, are underserved, vulnerable populations that don't have a lot of confidence in advocacy for themselves. So, initially, having a peer we think has worked really, really well.

(01:10:33):

Another aspect to it is that after having options, I think, the more clinics the better. So here in Northern Colorado we have 8 clinics that have 11 locations and they also do pop-up clinics, mobile clinics. You can get initiated on this life-changing medication same, or next day every day of the week. That is so important to what we do here. And we feel like it's been able to reach patients that we just wouldn't have even known where to start with.

(01:11:07):

For example, I had a 15-year-old client who she was in the emergency department, and couldn't get dosed for their protocols because she wasn't in withdrawal. Again, I'm not the expert on the emergency department side. But she didn't get initiated. But we have so many community supports, so she was able to get referred to a peer at the North Colorado Health Alliance that set her up with an addiction treatment services appointment the very next day. Met her there, she got induced. And is now actually doing the Sublocade shot, which just breaking down those barriers for patients.

(01:11:48):

She's a high school student and so taking strips in the middle of the day might be a barrier for her. And so, we don't want that. We definitely just want to break down as many of those barriers as possible. And so, definitely just having access to the clinics, access to peers and support in and outside of clinics once they're started on buprenorphine. And once they continue that with the clinic is really what we've seen work well.

Susan Winckler (01:12:15):

That's great Dionna. And well, always good to hear the "Yes, we've found a solution there."

(01:12:26):

I want to turn this question to everybody. You've, actually, all already said we could use some additional formulations to meet the need of patients. So who wants to jump in and say what other formulations would be most helpful in terms of whether it's dosage, route of administration, duration of effect. Who's going to fire off and unmute first for me? Gail, you're unmuted. Then, I'm going to Michael.

Gail D'Onofrio (01:12:54):

Okay, fine. So there are a lot. I'll just say that just as other speakers have demonstrated, we need them at low-doses. So we need small dosing so we don't have to cut up the film, so that's great. We need the patches available and the FDA approval of those and a single dose patch at a time. We also need the 7 day injectable. And I don't want to say with the company or anything but it's not under FDA approval quite yet because of exclusivity, and some other reasons. We need that approved because we can initiate that. We've been doing it easily with CAL scores of four and we know that we can do it even with people without withdrawal, but in certain circumstances.

(01:13:48):

So that would be a great thing for an ED to be able to administer. Patients seem to like it. It's a very small injection. They're not making commitment for 30 days. And the way the phar way that the

pharmacokinetics of it are is that it takes a while for it to reach to really 2 nanograms per milli about 4 hours later than a sublingual. So it's great. It's not like Sublocade that's immediate, which is hard to use right away in low levels of withdrawal. So it's a great thing to start with, and then to transition people to the Sublocade at another time. There are people we could use Sublocade with in the ED, but those are for unusual circumstances. So I would say we need all of that.

(01:14:35):

The other thing though, I just want to say quickly is because Dionna, you said this, the FDA packaging is still that buprenorphine cannot be used under the age of 16, although we do outside it. And so, I would also suggest that we work on that. That we should be able to under an addiction specialist, we can start it in an ED, but under an addiction specialist, it should be able to be used in all teenagers. It should not be regardless of age.

Susan Winckler (01:15:06):

All right, we've got our list-

Gail D'Onofrio (01:15:09):

We have to do it under IND and we would really not to be able to do that.

Susan Winckler (01:15:14):

Yeah. All right, we've got our list started. Michael, what are you going to add to the list?

Michael A. Smith (01:15:18):

I think we have the routes right. I think that's fine. Sublingual, IV, we have the implant. I think we have the routes. I think it's a matter of dosage form and packaging as part of it, which we've already kind of discussed. And the way that a patient is going to use it.

(01:15:33):

I think the other kind of limiting factors are regulatory-related. The package inserts and the number of concerns, and side effects, and warnings, and precautions I think need to be reexamined, like QT prolongation as one example. I think age is another, as Gail pointed out. We actually used Suboxone in an 11-year-old. It was for pain, but it was still safe. I think the safety aspect, we've kind of touched on it, but it's wildly safe relative to everything else. It's an incredibly safe drug to use. And I don't think we're touting that enough. I think we're being held back by it.

(01:16:21):

And so, I think some of those things really need to be addressed because there are limitations around insurance coverage. And some of that definitely is driven through the package insert, and what is available there. And with these new approaches, we're seeing less and less side effects from that. But like I said, I think we have the routes. I think it's about getting better dosage within those routes that we can give to patients.

Susan Winckler (01:16:48):

And Dr. Carroll, 'cause I think I heard in your presentation a higher dose, is that right?

Gerard Carroll (01:16:55):

Yeah, definitely. I mean, a challenge of all the sublingual formulations is the time of absorption. This is both clear in the outpatient arena. Patients often take it incorrectly, they're not patient about it. And then, the more films you're asking people to take, I mean it's a bad taste, there's all kinds of different psychosocial challenges with that. So a 16 milligram film would be huge.

(01:17:17):

I think the other big thing is the challenge. The 7 day injection is super exciting. I think every time I consult with people about doing a rural EMS program or ET program. They don't have that follow up piece, and they're never going to have it, not in 24 hours, maybe in 7 days, maybe in 30 days. But both the approval of that and then also just the cost.

(01:17:40):

We give Sublocade in our emergency department to a select group. We have a reallocation program with one of the local Medicaids, but it's a small population. But it's great for some of our most unstable patients, who we have not otherwise been able to induce successfully due to a lot of different reasons. But at $2,000 or more that's not attainable. No one's going to carry that on an ambulance and hope that we can give it out. It's just not going to work. So those are the other challenges. But I don't disagree with the idea that we have the routes down, but I think absorption rates, and the amount in those doses could definitely make a big difference for what we can do. And then, it's always cost, which I is hard, I know.

Susan Winckler (01:18:19):

Yeah.

Michael A. Smith (01:18:19):

One thing to piggyback really quick that you just brought up is taste. We've had to switch patients between products because of taste. Or we've actually, whether or not we should have, co-administered with hard candy. And so, I think dealing with that taste in some form, whether there's studies on what you can co-administer it with, or that won't affect absorption, or changing the taste of it would be really important because those are low barriers, but they're still barriers that people don't enjoy. And if there's a way around it, we should work around it.

Susan Winckler (01:18:52):

The co-administration with hard candy, it's a fascinating idea component there.

(01:18:58):

Dr. Raheemullah, I want to invite you, anything you want to highlight here, put on our list?

Amer Raheemullah (01:19:04):

Yeah, absolutely. Taste is a big one. If we can change that, that'd be great.

(01:19:09):

And with transdermal patches, like we mentioned, patches being FDA approved for pain and opioid use disorder, coming up with patches that are inexpensive, figuring out ways to get these covered by insurance.

(01:19:22):

And then, sublingual buprenorphine preparations 0.5 milligrams is what is used most commonly in the case reports and the case series. And the lowest available dose that we have commercially is 2 milligrams. 0.4, 0.2 milligrams formulations exist in other countries. So 0.5 milligrams requires us to cut the 2 milligram forms into a quarter. 0.25 milligrams requires us to do it, cut it in 1/8. So, again, just reinforcing that smaller formulations would really facilitate this.

(01:20:04):

And then, I agree with what everybody said, and I want to reinforce that low-dose inductions are not used in only specific, and special circumstances. Oftentimes, when standard induction, and high-dose inductions can't be used, and low-dose inductions shouldn't be used in any in sort of cookie cutter manner. And it's really almost like a last resort when other inductions can't be used.

Susan Winckler (01:20:32):

Okay so, thinking about the paradigm is when you can do a higher, do the higher. It's only when you need to do the lower. Okay.

Amer Raheemullah (01:20:40):

Yeah, absolutely. Patients in withdrawal, let's go directly into induction. Patients who are going to develop withdrawal soon, let's wait and go directly into an induction. And not prolong. And, of course, not asking patients to use illicit opioids, illicit fentanyl along with a low-dose induction, and putting them at risk of an overdose.

Susan Winckler (01:21:03):

Yeah.

(01:21:04):

I want to ask one follow up question on the packaging. And so, this is going to come to you, Dr. Smith. You mentioned that the patches are in a box of four. And so then, do you ever split those boxes? Or it's generally you wouldn't?

Michael A. Smith (01:21:22):

No. So yeah, so that if it's split, they come in a pack of four because that's a 1-month supply for a pain indication. So if it is split, that pharmacy is then left with 3 patches out of box that's not a month supply. And so, they either have to continue splitting, and they may not have that. Or they lose out on hundreds of dollars a drug on their end as well. And this isn't the only product that's like that. This is just within the scope, but it's already pre-packaged for a month supply, and we're not using that month supply in these settings. That's only for the pain indication. So I think with an additional indication of opioid use disorder would also need to come in additional packaging, so that it could be delivered in the same way that we would want to be using it, which would be one patch.

Susan Winckler (01:22:11):

Right, 'cause you'd need that for the information, the package labeling that would need to come with it.

Michael A. Smith (01:22:18):

Correct.

Susan Winckler (01:22:19):

Okay.

(01:22:21):

Anything else on formulations? 'Cause then I'm going to turn Dionna. How about safe storage of buprenorphine? What do you hear from patients about the storage considerations?

Dionna Berkholder (01:22:36):

So we have a lot of members that we work with that use the locking pill bottles, the plastic container that has the locking mechanism on the cap, so to keep it safe from children, pets, whatever. But, honestly, there hasn't been a lot of concern from people that I know using the medication, cutting strips, storing them afterwards about the efficacy of the medication. There doesn't seem to be any kind of argument that my cut strip isn't as effective as a whole strip. It's just, obviously, the amount of medication that they're taking at one time. But overall, I don't have too much from the people taking the medication that I work with. I haven't heard a whole lot about safe storage concerns, honestly.

Susan Winckler (01:23:28):

Okay. Well, if you haven't heard then that's part of the answer too, right?

Dionna Berkholder (01:23:33):

Yes.

Susan Winckler (01:23:33):

Great.

(01:23:34):

So then let's talk a bit, and I want to say this is this back to everybody and would love to start with you, Dr. Raheemullah, and then turn to you Dionna. If we're thinking about the use of buprenorphine, in addition to that, what other forms of support do you offer patients? Is that adjunct medication, social support? You've all mentioned that it's more than just getting an active pharmaceutical ingredient into an individual. It's a broader question. So Dr. Raheemullah, would you take a shot at that first?

Amer Raheemullah (01:24:13):

Yeah, absolutely. Keeping in with the spirit of getting people on buprenorphine maintenance, and going through induction processes buprenorphine is used directly in the induction process, but also other adjunctive medications can be used in order to relieve any excess withdrawal that's occurring that's not being treated immediately by that induction process. So we shouldn't be shy away from using supportive medications in order to serve that greater good of getting people onto buprenorphine, and buprenorphine maintenance.

(01:24:53):

And in terms of other support, absolutely, when patients are going through withdrawal, having a peer support specialist, or having our substance use navigator come in and talk with patients, and provide them support to keep them motivated and encourage them to keep moving forward is incredibly important in the hospital and then, following up with them after the hospital, and then linking them to ongoing care.

Susan Winckler (01:25:20):

And are there situations where you have folks who have the anticipatory anxiety of starting buprenorphine, how does that factor in, and how do you think through that? And Gayle's going to jump in. Go ahead.

Amer Raheemullah (01:25:38):

Yeah, Gail is the best to answer this question. But what I'll say is that not all anxiety, or sometimes withdrawal symptoms can be confounded just by anticipatory anxiety. And just requiring the patient to wait until the buprenorphine gets kicked in, until it kicks in. It's not necessarily precipitated withdrawal. So all withdrawal is not precipitated withdrawal. And oftentimes, there's solutions to that as well, just continuing to give higher doses of buprenorphine in order to manage it. But I'll let Gail and others discuss that.

Gail D'Onofrio (01:26:19):

Yeah, so I was just going to mention two things. Thank you for saying that because there is so much anxiety in patients who are using lots of fentanyl, they use it repetitively during the day. They're very anxious if they can't get a hold of it. And so sometimes people misinterpret withdrawal signs from their generalized anxiety. So sometimes off the top of my head, I often say, "Maybe they need a little bit of Ativan first." Say, "Chill out. When you're ready, we'll be ready to provide it for you." So I think that's why sometimes people misinterpret the withdrawal signs from generalized anxiety.

(01:26:56):

On the other hand, there is also really a lot of anxiety about Bupe because people keep saying this constantly, "Oh, in the [inaudible 01:27:06] fentanyl, we can't give out Bupe." That is wrong. And I wish we were not saying that. We do need to be careful and understand everything, but that is not true, that Bupe does not work in the [inaudible 01:27:18]. It does work very well. So one of the things we do in the ED, or at least I try to tell people is this is what we know. It rarely happens, it does happen, but we will tell you that we will not leave you. If this happens, we know how to treat it, and we're not going to let you go until you feel better.

(01:27:37):

And in the ED, that often requires, since people are homeless, keeping them overnight. You're not going to let them go out in the street feeling badly. So we do and this [inaudible 01:27:46] that happened to me just in the last few weeks. It happened pretty quickly in the evening, but by 11 o'clock it was fine, but the person stayed overnight. I saw them first thing in the morning, they were ready to go, they got their morning dose. So it's a matter of just saying, "I'm not gonna let you go. I'm going to be here. I know how to treat this. And we're going to do this together. And I can't promise you, but it's a small percentage, but I'll be here." And that's what we say to people to try to allay their fears of initiating Bupe.

(01:28:21):

But you're right, you have to be very careful that people are not using that anxiety, and those subjective symptoms as withdrawal. I think that's what happens. And then, people start Bupe much too early.

Susan Winckler (01:28:34):

Yeah, okay.

(01:28:36):

Dionna, you unmuted.

Dionna Berkholder (01:28:38):

I just wanted to add to that. I have talked to many members who are hesitant in getting started on the medication because they are facing, like Dr. Gail just said, the misinformation of, "It's not gonna work for me. I only do fentanyl." And so, really talking to those members, and just the community as a whole to get it out there kind of the same idea. We know Naloxone works. It might not be as immediate on somebody who's struggling with fentanyl, but kind of the same with that it will work. Some is better than none.

(01:29:14):

And getting that concept out to our members, as well as assuring them, working with the unhoused population, working with the unemployed, working with a lot of folks who don't have phones, who don't have... "I know I live in New York, but I couldn't tell you what block. It depends on the day. And so how am I going to get to my clinic?" 'Cause this is a medication, once you start, you have to continue, and make those appointments, and continue with those community services. So we like to offer assistance with transportation, assistance with Medicaid copays for these unhoused and unsheltered folks, and people that are hugely benefiting from it.

(01:29:53):

So pretty much anything that could be a barrier we try to put to rest right away so that they're willing to initiate and even just go meet with somebody at a clinic and talk to somebody and get kind of the facts on how life changing it could be for them. And like I said, whether that's transportation, gift cards to help pay for copays, or somebody to go with you, whatever those barriers are, so that way they aren't afraid to start something. And they feel like they're supported in their ability to continue to stay on the medication.

Susan Winckler (01:30:26):

So thinking there's the initiation, and then it's the start of a journey, and continuing through.

(01:30:36):

Dr. Smith, do you want to jump in? 'Cause I've got a specific question I run want to run to Dr. Carroll as well.

Michael A. Smith (01:30:41):

Yeah well, I also think it's just rehashing how safe it is. I think that Gail pointed out in her other data, very few withdrawal, her paper in JAMA was very few precipitated withdrawal cases. There's ways around withdrawal, and there's ways to treat it. And it's just an extremely safe medication to use. And I think highlighting that it's safe first is really important.

(01:31:06):

And then, it's effective. We know it's effective. There's lots and lots of data that says it's effective, whether it's retrospective or randomized control trials, in all settings it's effective. But it's also wildly safe for patients. They should have very little concerns from a safety perspective of taking the drug because we know how to manage those things, and manage them well.

Susan Winckler (01:31:29):

I can hear wildly safe resonating with a number of the folks who are watching today.

(01:31:37):

Dr. Carroll, I'm struck that in your environment it may be Naloxone, and then buprenorphine, and then you're kind of in and out. And so, talk to us a little bit about the adjunct in medication or social support or the realities that it's a little different in the emergency... Not a little, it's different in the emergency medicine and EMS space,

Gerard Carroll (01:32:03):

Yeah, both in the emergency department and especially in EMS those resources are hard to come by.

(01:32:07):

In the emergency department there's more and more resources though it's not standardized across ERs. It's very variable, if I have chest pain what will happen to me in one ER versus another is pretty similar. If I come in with withdrawal very, very different. Not even just if you get care, or where you'll be sent, will there actually be medication for opioid use disorder in those rehabs? Will they actually link you or just release you back onto the street after? All of that is kind of a big mess.

(01:32:35):

In the field, really the only option is the emergency department. And what really built our EMS program, and what is kind of going nationwide is that this patient population has been marginalized in healthcare for a lot of reasons, and has no interest. I mean, going to the emergency department isn't fun for anyone. And it's especially not fun for this population. And so, over a 5-year period here in the city, we saw our refusal rate after an overdose go from 3 to 5% to over 50%. And that's kind of being near to...

Gerard Carroll (01:33:03):

... 5% to over 50% and that's being mirrored across the country, which means EMS is the only healthcare provider for these patients in extremes. So as far as the adjunctive medications, EMS has a much more limited toolbox for pharmacy. I think rightly so. We do provide Ondansetron or Zofran for nausea, but that's really the only thing besides the Suboxone, and then just restoring dignity and comfort and engagement, which is one of the reasons, like I said, we talked about formulations. We need some way to get people beyond that. Even on the weekend, we still have that challenge. If you don't want to go to the ED, I don't have a whole lot to offer you.

(01:33:40):

I guess on the FDA side of things, and also just on DEA issues, there's no dispensing. It would be great on a Friday to dispense for strips so they could follow up on Monday. We're already there. You're in direct communication with the physician or can be, so there's huge options there that regulations don't allow us to do. I always say for each one of these lectures, I put up a strange call behind me because I'm an EMS guy, but this is a call with an accident. We induced the patient who overdosed, crashed, caused a six car pile up and then started Suboxone, so it's one of my favorite pictures, but anyway, just my thoughts there.

PART 3 OF 7 ENDS [01:33:04]

Susan Winckler (01:34:22):

The power of visual. Thank you, and helpful on what's available and the ability to dispense and thinking through that. You triggered me then to think... So what else do we need to research? What are our remaining knowledge gaps to inform guideline development and product development? What are the priority areas where we need to do some additional research? So maybe I should say Dr. D'Onofrio, what do you have in the queue or what do you wish you had in the queue for research in this space?

Gail D'Onofrio (01:35:00):

Well, we have a bunch in the queue. First of all, we are hoping that we will be funded very shortly for a high dose protocol as in comparison with our standard and our standard dosing is at least 8 milligrams, 8 to 12 during the day. Our high dose would be 24 milligrams, just initiating people right off the bat. I think Dr. Herring and I did publish something. It was a retrospective report out of Highland of all the individuals in the past year that he had and really inducted with high dose because there had been nothing else previously. We considered high dose 12 and over since that's what we've been doing, and we found it very safe and it happened very quickly and we were able to do it.

(01:35:47):

That was a retrospective study in one place, so we're going to do a multi-centered study looking at high dose versus standard dose. That's one thing. We're hoping to work with Dr. Carol on an EMS protocol that we've applied for in the basic sense of that into looking for a Delphi consensus because there are only a couple places doing it. Everybody does something different. So what should we do in the field and then how would we evaluate that? That would be really important to get everybody else on board. The other thing we're looking at is adolescents really and treatment of adolescents. That's a hard lift with everyone because one, we have to get rid of the insert that says that you can't do it, so we have to go under IND. While there are few in each institution, as you've seen, the adolescents are the ones who are dying, many because of overdose that have opioid disorder and many who don't even really know they're taken an opioid, that is an inadvertent ingestion that they're taking something else.

(01:36:54):

So there needs to be work in that space with adolescents and that's a difficult space to get into and that's why people avoid it because it's so difficult, but we need to get into that space, so I'll stop there and let everybody... But I also want to say telemedicine. We now have a reprieve only until November, but we need to continue telemedicine because imagine all those rural areas. Imagine people that just don't have cars. Are you going to take three buses and whatever? Imagine new mothers. You want to keep them with their children and they have to go somewhere, which is why you work so much better, by the way, if you can use bupe but not methadone because we can give you 30 days and 60 days, and then again, we have to make sure that the pharmacists are not reporting these people as questionable, which is also what's happening to individuals who are going to try to fill their prescripts. So we need that more telemedicine, if we have to research it more, whatever, to get people to realize how important that is for our communities.

Susan Winckler (01:38:00):

Lots of research to tick off there from the high dose to the adolescent to understanding and how we diffuse things in the EMS space. Other thoughts about research priorities? Anybody else want to jump on there with... Yep, go ahead, Dr. Smith.

Michael A. Smith (01:38:16):

Yeah, I think just highlighting two of the things is we know that pediatrics have different pharmacokinetic properties from buprenorphine. They clear the drug faster, so we don't know would high dose work for them or would they need BID dosing for it because of the differences there. We need more research in that area for sure to better understand. We know that when it's been used, it's been safe, but we don't know the right dosing for those patient populations. I think that's big.

(01:38:44):

Dr. Carroll brought this up too, but I think it's important to highlight is we talked about right sizing the package formulation for individuals taking a smaller dose of a film or a higher dose of a film or a single patch, but like Dr. Caroll said like, what about a 72- hour dispensation thing that could be given to somebody to get them through a weekend or whatever it is. I think that those transitions are where we lose a lot of people, so are there ways to study how to improve our transitions, whether it's packaging or supportive services or even billing availability for peer support or whatever it is. There's lots of ways that we need to research supporting patients during those transitions because that's where they're the most vulnerable.

Susan Winckler (01:39:31):

I am hearing you on the components and the connection and I'm struck, Dr. Raheemullah. Your first slide was about, let's remember the goal of induction is maintenance and keeping folks on it, and so that idea of connecting the initiation to the longer term piece, is there a way to help with that? I'm struck, Dr. Smith, on the adolescent difference in clearing. Do we have any issues on the other end with older adults or we know more there? Do we have any gaps in research on the other end of the age spectrum?

Michael A. Smith (01:40:23):

We certainly have gaps in the geriatric spectrum for sure. I don't think it's as glaring for several reasons. One, they're more well studied. Two, they're less of the population that are suffering from opioid use disorder. I think the pediatric population is more of a focus, but in the older adults, buprenorphine is so safe in that space that even patients that require dialysis, it's stable. Those are the things that we would face in older adults, so we know more about in that space than we do relative to pediatric patients.

Susan Winckler (01:40:57):

Okay. Okay. Really helpful. Thank you. So we are to our last five minutes of this panel where I'm going to give you all an opportunity to say, is there something that you wanted to say that you didn't get a chance to? You'll have that opportunity, and then what do you want to highlight or underscore and say... What do you want people to take home from this discussion as most important, either in a need or a consideration or what would you want to highlight from what we talked about here? Deanna, I'm going to start with you. I'm going to go you, Dr. Caroll, Dr. Raheemullah. Deanna.

Dionna Berkholder (01:41:41):

The one thing that I didn't get a chance to bring up that I wanted to talk about was the availability of the current formulations in pharmacies. So that same adolescent that I was working with, she had gotten an appointment on a Friday, went to pick up her prescription at a pharmacy and they didn't have it, so they sent it to another pharmacy and that pharmacy wouldn't release it to her because they didn't have her doctor authorization. This is in the evening, and so this young person had to get dosed at an ED over the weekend and then that's when we came back the next weekend, decided Sublocade was the way to go because it is easiest for her lifestyle, and so the barriers, so that was something I wanted to say.

(01:42:21):

I'm not quite sure exactly where that fits into the conversation, but I've heard that twice now of a pharmacy not having a certain prescription and actually had a provider talk with a member of mine about... that it's very common that the pharmacy is out of this and so are you willing to try this? Obviously, that's not what we like to hear. We want to hear person-centered and that person is getting what they feel they need and the provider's able to prescribe what they feel the person needs versus what's available. I know there are workarounds for both of those things, and then the biggest takeaway I

would just like folks to get out of this is exactly what Doctor... I'm going to butcher it. Rama... I'm not even try.

Susan Winckler (01:43:13):

Raheemullah. That's all right.

Dionna Berkholder (01:43:17):

In the slides of initiation is we do initiation for ongoing care. We initiate these folks not just to get them past their overdose or to get them past their withdrawal that they're in the emergency department for. Ultimately, the goal is to get these folks into long-term recovery or at least connected with services that they're not going to return to heavy opioid use disorder and that initiation is the first step of that.

Susan Winckler (01:43:43):

Great. Thank you, Deanna. Dr. Carroll?

Gerard Carroll (01:43:46):

Yeah. Two things. I think on the research side and the FDA focus of medication, I think on the emergency side of things, the focus on rapid induction, whether it's IV or sublingual forms and the size of the dose is going to be critical, and then that second piece, researching how we bridge people to long-term care when we don't have availability. I think more globally in this crisis, you get on these kinds of panels and I'm like, "We've solved this. The opioid crisis is done," but when you realize it and you think about this group, the majority of the country has no access to what we're talking about. I think especially on the emergency side of things, emergency department care, I think the data is in, and just like chest pain, you should walk into any ED and this should be available to you and that needs to start being pushed out. I think EMS will be there shortly and I think it needs to be like... It can't be that I just moved one town to another and suddenly my care is completely different. I think that's the theme. I think all of different healthcare, including non-traditional places where you didn't expect this, EMS and emergency department being two places. I never thought I would be doing addiction care while us be board certified in due emergencies, but as we've leveraged the healthcare system in different ways, we now need to standardize that kind of problem solving longitudinally across the country, so that's my thoughts.

Susan Winckler (01:45:01):

Yep. Normalize it. Got to have it-

Gerard Carroll (01:45:05):

Great word.

Susan Winckler (01:45:05):

... consistent. All right. Dr. Raheemullah, Dr. D'Onofrio, Dr. Smith, we'll let you have the last word. Dr. Raheemullah.

Amer Raheemullah (01:45:11):

Yeah. So takeaway from my presentation would be that for low dose inductions, having FDA approval for patches for pain and opioid use disorder, creating patches that are inexpensive would facilitate these

low dose inductions and also sublingual buprenorphine forms that would be low enough to facilitate these inductions, and then also having clarity around when it's okay to do these inductions and when it's not okay to do these inductions when a high dose and standard induction is more appropriate. The other thing I'd say is just piggybacking on... Of course, more research in adolescents, that's wonderful, and then also the telemedicine thing.

(01:45:55):

We have a lot of telemedicine companies and telemedicine protocols that are in works to improve follow up for buprenorphine on discharge and then just access to buprenorphine in general and repealing that or not really having certainty of that being a stable option in the future is going to really prohibit growth in that. We're just getting started with that and it's really going to be a big step back if we don't have a stable future to allow those things to continue to grow. Yes, we have a treatment gap. We have a huge treatment gap, so we need to continue to have options and clarity around which options make the most sense in which scenarios.

Susan Winckler (01:46:43):

Excellent. So more options and then understanding how to use them. All right, Dr. D'Onofrio, Dr. Smith, and then we're going to go to our break.

Gail D'Onofrio (01:46:53):

Sure. I don't have much else to add. I think it's been a great discussion and everybody has focused on a lot of different things. I wish that there would be some quality measures put forth. I know we do that a lot from CMS in that and the older populations, but I wish we could have some really federal quality measurements so that we could push this forward. It isn't an option for people to want to treat. It should be like everything else. It is evidence based. Every ED should do it, every hospital should do it. Every community should have these resources and I wish we could put some more teeth into those and therefore, we could do better, and the regulatory issues around EMS are enormous, because when you've seen one system, you've seen one system and they're state regulated, sometimes county regulated in my state. So the more we could do to standardize certain things throughout the US, the better that would be.

Susan Winckler (01:47:52):

Awesome. All right. Dr. Smith, last word and then we'll run to break.

Michael A. Smith (01:47:57):

Sure, and I'll be real quick. I think highlighting safety, remembering that, and I think piggybacking Deanna's point, reducing barriers. There's a group from Texas looking at pharmacy-related barriers and I think a lot of it has to do with misunderstanding of the drugs and misunderstanding of the patient population.

Susan Winckler (01:48:14):

Yes, yes. All right. We'll remember wildly safe. All right, everyone. Thank you so much for joining us today for sharing your insight. We're going to go to a quick break and we will return in eight minutes at the top of the hour, but thank you so much for joining us for the conversation and for what you do every day. Welcome back everyone. I hope you took the opportunity to refresh and recharge before we settle into our next session. We're now going to turn to Dr. Michelle Lofwall, who is going to kick off session

three. She is board certified in psychiatry and addiction medicine and serves as professor in the departments of behavioral science and psychiatry in the Bell Alcohol and Addictions endowed chair at the University of Kentucky. We are now talking about buprenorphine initiation and maintenance in the community setting. Dr. Lofwall, I'm going to step away from the stage and let you step right up.

Session 3: Buprenorphine Initiation and Maintenance in the Community Setting

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

Panelists: Jeffrey Bratberg, PharmD, FAPhA, University of Rhode Island

Jeremy Dubin, DO, FASAM, Front Range Clinic

Eliza Hutchinson, MD, Packard Health

Jade Waits, Boulder Care

Michelle Lofwall (01:49:23):

[inaudible 01:49:23] here with you and to be talking to you today about buprenorphine in the communities and we'll talk about dosing and beyond. Our outline for today's talk, as you'll see on the next slide, is going to cover multiple phases. Next slide. From what we've initially have always talked about, initiation, maintenance, stabilization, discontinuation, tapering, and of course, lots of other strategies to help people get and stay into treatment. We're going to talk about some pharmacological factors as we go through, but also lots of non-pharmacological factors that you won't be surprised to hear about if you heard the previous two talks and discussion, and then we'll conclude. Next. Factors to consider when initiating. Really important factors because we know initiation, in the first 30 days, lots of dropout.

(01:50:17):

So be thinking about what are the patient's preferences, what are the basic needs of the patient? Do they have food, housing, transportation? These are all things that we think of as social determinants of health, Maslow's hierarchy of needs that will impact whether they can get to you and whether they can come back. The healthcare system of course, we're interested in who can pay for the medication. Is it on the formulary and will the pharmacy have it? We know that there's some pharmacies that just will not stock sublingual buprenorphine. This is published.

(01:50:44):

Of course, pharmacy access is more challenging with the injectable because of the complicated REMS distribution. Housing status and their rules. Where is your outpatient living? Interestingly, we're seeing some jails actually bring their inmates to us in the context of having some settlements for violations of the ADA for not allowing patients to continue on the medication, so this is a really incredible opportunity to try and get treatment into our criminal justice settings that have been very difficult in the past. What about outpatient recovery houses? What are their policies? Are they going to allow the patients to be on sublingual? Injectable? These are all things to be thinking about.

(01:51:29):

Of course, state regulations. We're talking about what dose. Well, maybe there's state regulations that are going to say what dose you can give or whether or not you can go macro. You have to think about those things. Provider and clinic level factors for the injectable is that clinic. Do they have a locked refrigerator that can hold the DEA schedule three? Do they have the administrative support for the required record keeping? Next slide. Other factors to consider when initiating. Next slide. We heard

home is very well accepted but so important to think about how are you teaching that patient about observed objective withdrawal?

(01:52:15):

We've heard anxiety. There can be misinterpretation of what withdrawal is, so make sure we're teaching our patients. Look at their pupils. Is their belly rumbling? Make them start thinking about what are some more objective signs of withdrawal that can help them have a good response to that home induction. Of course, encourage them to do it on a day your clinic's open so that way, there can be some office support that they can call or potentially even come in if there's a problem, so still having the potential to have some in-office observation is certainly helpful.

(01:52:47):

What's that first dose going to be? We've heard a lot about the sublingual doses that we have available. Two and four I have highlighted because that's what's in the FDA labeling. We frequently are trying to cut in all that to try to figure out if we need to go lower or try and go higher with the injectable. The labeling says there's a seven-day lead in. Can we do it earlier? People are doing it earlier but sometimes, how early can we do it? There have been really few outpatient RCTs. We have Dr. D'Onofrio's wonderful JAMA with the ED showing yes, we can do it. It's very low overall rate of precipitated withdrawal. Very reassuring. That included people on fentanyl.

(01:53:34):

Some people also are going to be testing positive for heroin, might still have methadone, xylazine, methamphetamine, still also very complicated picture and what's their previous experience? Are they already freaked out and thinking it's not going to work? Really, really important to acknowledge what the patient's anxiety level is and what their expectations are because we need to try and shift that. Our whole thing is to try and exude hope and success. This is really important. Remember the placebo effect, the role of conditioning and expectations.

(01:54:08):

So we as the healthcare provider really want to have that positive expectation there. This is an older study I just bring up because I think it's still really interesting to think about from a scientific perspective. This was done over a decade ago, thinking about... We knew that buprenorphine could have antagonistic properties under certain circumstances. That was well known when we rolled out waiver training when buprenorphine was approved initially and it was thought that it was due to level of tolerance of physical dependence, and so this was a study that looked for what is the dose that's going to precipitate withdrawal among people with a very high level of physical dependence.

(01:54:48):

It's a human laboratory study. People were maintained on 100 milligrams of methadone, so high level of physical dependence. This is a within subject triple dummy study. Really complicated. Beautiful scientifically... found the dose that precipitated withdrawal, gave up to 32 milligrams of the combination product sublingually. That was the first phase of the study, and then the second phase, they gave that same dose but under divided doses just to see if you could eliminate that precipitated withdrawal experience. On our next slide, we'll show you 10 subjects. Three we're able to get to 32 milligrams and never had any withdrawal. Incredible.

(01:55:36):

So there's something else going on here. Different alleles, SNPs, things that I think are really interesting but we don't know much about so we could do some more science there, but seven did experience that precipitated withdrawal and at a variety of different doses, 4, 8, 16, and when you split, you had less

precipitated withdrawal. So I think this is where the whole idea of giving the smaller dose came from. So I just wanted to remind us about this because I think there's scientific factors that could be further explored. Next slide.

(01:56:12):

Other things we want to consider. We heard from Dr. Weimer our practice standards. There's dosing guidelines but we're supposed to individualize treatment and continue it as long as the patients are benefiting. We're talking about how the population's getting sicker, experiencing more medical complications. I think we need to start really inserting a framework of other complex illnesses that are affected by social determinants of health, have environmental factors, everything. Think about major depressive disorder and diabetes to help guide our thinking here. Are we happy with these definitions of stable, maintaining and talking about who and why to taper?

(01:56:48):

Why aren't we talking more about remission? We talk about remission of major depression. Clinicians focus on outcomes like function, quality of life, trying to prevent the complications of untreated or undertreated disease. This parallels the medical management of other complex disorders is what we're seeing with the previous talk with EMS managing people in the field and seeing what happens with untreated disease. You end up with a motor vehicle accident we just saw, not just overdose. This is a study that was undertaken as part of a dissertation with Feitong Lei and her supervisor Dr. Svetla Slavova that is under review. Took Kentucky's KASPER data, our state prescription monitoring program, and these are all Kentucky residents, adults, that were initiating transmucosal buprenorphine and they had no previous transmucosal buprenorphine, put them into three buckets of their first average daily dose over 30 days. You see these three buckets of less than 8 milligrams a day or greater than 8 to 16 or greater than 16. The cohort, which was just under 50,000 patients, was then followed for 365 days and we were able to connect KASPER and our death certificate records and what we find is that opioid-involved overdose deaths are much reduced if you're on a higher dose compared to that less than eight milligram dose and deaths from other causes also were lower.

(01:58:26):

So nice dose effect and complete contrast to what happens with prescription opioid analgesics for pain. Next slide. If we adjust for other things like gender, urban-rural residency, what they've gotten in the last 30 days, like benzos, other controlled non-opioid substances, these results are holding steady with the higher dose having less risk of death. Next slide. Wraparound service is so important and can help people stay in treatment. It's really important to have well-trained others besides the healthcare system if the person drops out or can't get in. So part of the HEALing Communities study in Kentucky, we partnered with a recovery community organization to develop a training for peer supports where they work in the field at places likely to encounter people with opiate use disorder, like a syringe support program.

(01:59:21):

We train them. The training curriculum is 150 hours. We make sure they have good health literacy themselves about MOUD so that they can explain risks, benefits, the basics of the medicine. They have a competency check before they're deployed. We've trained about over a hundred now recovery coaches and their supervisors and this can just be really, really helpful. They bust barriers along the way. Our next slide is going to show one of our most effective barrier busting programs, which is a transportation program where this was the major barrier to getting and staying in treatment with buprenorphine and methadone and we've had so much transportation.

(01:59:58):

The total miles in the first wave of the study has been eight times around the world and the beauty of having the recovery coaches that are trained being the drivers is that they can share their stories of hope and learn maybe about other barriers and assist while you're driving. Very helpful for our rural counties. Next slide. So other things that we should be thinking about. Mobile treatment I think holds much promise, especially for rural areas. The potential for injectables including injectables within mobile vans. Other pharmacy models. Australia has supervised dosing within pharmacies for sublingual buprenorphine.

(02:00:36):

The injectable certainly decreases risk, I think, for diversion or in the eyes of people that this is their focus, everything is about diversion, like our criminal legal system, they like this idea. Definitely helps solve some adherence and provides that steady level so that we don't have to worry if the pharmacy is going to have it or they can't get to the next clinic appointment, but it has a really complex distribution in REMS that actually, if the patient no-shows and you've had it shipped to you from one of the specialty pharmacies, you may have to waste the medicine. You can't automatically just give it to a different patient.

(02:01:11):

Some patients feel more of a sense of agency over this. They get the medicine, they know they have it, but some feel the opposite. Tapering, we want to keep our end goal in mind. Some patients can taper slowly over time and stay in remission. There's the luxury, I call it, of some of us who have patients who are on two milligrams now, where it's really hard to get down from that dose. It's notable. Previous speakers have mentioned Europe has lower milligram formulations. The 0.2 and the 0.4 milligram temgesic. The US has micrograms but they're for pain and not for OUD.

(02:01:42):

Can we taper with injections by either increasing the duration, spacing out those injections, decrease the dose? Those are other, I think, opportunities and adding on ancillary meds to help I think is also another opportunity. Next. This is a complicated slide. The point here I was just trying to make is this with our sublingual subutex, current sublocade that's here in the US, two other, the weekly and monthly product available in Europe and Australia that FDA will be reviewing later this month. We have potential new products coming down the line that are going to offer lower doses, higher doses, and potentially be an opportunity to help patients get to and stay in care. Next.

(02:02:29):

But this is a really big issue, is all these regulations, so much change that's really positive. The letter that you shared to try and make it clear that we shouldn't be withholding doses if someone's not going to counseling. The providers, the clinicians, the pharmacists, the direct doctors, nurse practitioners, we all have licensing boards that we have to follow. One of the questions we had in the HEALing Communities policy work group was whether or not, with the HHS, April 2021, allowance for the 30-E was whether the licensing boards were going to allow their licensees to get the 30-E, because we already knew that some state regulatory boards had educational requirements and extra things besides the federal regulations.

(02:03:17):

We called all 50 state licensing boards and also single state agencies to try to mimic what it would be like as a provider if they were going to go and try and get their 30-E to see if they would be allowed to do it. We also asked if they were going to be discussing the new HHS regulations and we searched Westlaw. What we found were 15 states were not aligned. So if you're following your state's regulations, you wouldn't be really in accordance with being able to prescribe. We found a lot of

different reasons for that. The next slide is going to show you some of the things that we heard. So medical boards, some just said they couldn't provide us with any other information. Some told us they didn't know. Nursing boards, some referred us to private legal counsel.

Michelle Lofwall (02:04:03):

... words. Some referred us to private legal council. In single state agencies, we sometimes heard one of the agency's major advocates is very old school, so they've decided we just basically don't know yet. So lots of different things, but really good to hear this because it tells us of how can we address this. And the next slide I think has just has me thinking more about all of this policy change. And since there's so many, when you make policy change at the federal level, it travels through so many different agencies and boards and then to healthcare systems and their CMOs and then down to the providers themselves to get to the patients. And of course, the pharmacies is that how do we prevent communication breakdown in such a rapidly evolving area of both science and policy and what are you allowed to do too? Our doctoral student pointed out that HHS has a great social media platform with more than 2.5 million people following through Twitter, YouTube, Facebook, Instagram and LinkedIn.

(02:05:10):

And our licensing boards and pharmacies, we're not trying to throw anyone underneath the bus. We recognize these are made up of volunteers a lot of times and lots of times they don't have expertise. And we have to remember that a lot of the licensing boards kind of got in trouble with the prescription opioid epidemic by some of their legislatures that regulate the licensing boards for not doing enough with the prescription opiate epidemic. Like why weren't you pleasing your doctors and your licensees then? And this gross misunderstanding about buprenorphine and methadone affect these agencies. I'll hear things like how could another opioid really be the answer, really? When people are being really honest with me. And how does the board, even when they do have members that really get it, how do they spread the information so that they can do it and not get backlash? Are we allowed to have public health communication campaigns?

(02:06:19):

So with that, I know I'm out of time, but whirlwind tour, not just dose, lots of things other than dose. But for my point of view, I'm trying to go at it to think about four things. Medical ethics, which are also research ethics, do not harm, beneficence, justice and autonomy and trying just to find a positive way forward wherever we can. So I feel like I'm on a rapid diplomacy 101 class and trying to do that with everyone. Stay calm, don't jump to conclusions, ask questions. I'll stop there, thank you. Oh no, I can't stop there. I have to do my acknowledgements and gratitude because all of this wouldn't be available if we didn't have FDA, NIDA, SAMHSA, KORE/ SORE funding in our own Department of Behavioral Health, which funds a lot of our clinical services for medication for opiate use disorder. And our great Kentucky Heal team that's led by Dr. Sharon Walsh. We have over a 100 faculty and staff and so many state and community agencies that have supported us. So thank you.

PART 4 OF 7 ENDS [02:04:04]

Susan Winckler (02:07:18):

That's great. Thanks, Dr. Lofwall, and for helping us pivot to what we need to think about when we're looking at buprenorphine initiation and maintenance in the community setting. So we're going to bring our panel up to have a discussion here for about the next 40 minutes or so. So I want to welcome to the stage Dr. Jeff Bratberg, who is a Clinical Professor of Pharmacy Practice at the University of Rhode Island. Also, Dr. Jeremy Dubin, who is Chief Medical Officer of Front Range Clinic in Colorado. Dr. Eliza

Hutchinson, the Medical Director of MAT Services at Packard Health, and an Assistant Professor of Family Medicine at the University of Michigan. And Jade Waits, who is a Peer Recovery Specialist with Boulder Care.

(02:08:04):

So thank you all for joining us. We want to pivot from the panel we had before that was talking about what we do in emergency services and initiating in the hospital environment and turn to another common place for initiation and that being the community setting. And so, Dr. Hutchinson, I'm going to turn to you first. Illustrate for us some initiation strategies that you've seen work well in the outpatient setting.

Eliza Hutchinson (02:08:38):

Absolutely. Thanks so much, Susan. Really glad to be here and just wanted to say I'm so grateful for this conversation. Part of my role and passion is expanding buprenorphine and prescribing in the primary care workforce and the waiver elimination provided this amazing opportunity to train up lots of new folks. But at the same time, the challenges of initiation have prevented a lot of folks from wanting to walk through that door of opportunity. And so, the conversation, I think the guidelines and the innovations that will stem from this conversation will really help in that effort. For context, I'm working sort of mostly in the community health center and previously in a syringe service-based clinic. So my patients are very much low resourced, a lot of housing instability, social chaos, lots of morbidity and mortality from OUD. And so, really, our initiation strategy is anything we can do to get that patient started and I'll talk the kind of things that I'm considering when I think about that.

(02:09:32):

Most of our folks at this point... This is really, I guess, to boil it down, it's shared decision making really with a patient and trying to lend our medical knowledge but really find out what's the patient willing to do and able to do. So things that we always talk about, at this point almost everyone has had experience with buprenorphine. So really talking through with people what has been their experience previously. Some people have a way that they already know they get started and they want to just do that same thing even if it doesn't fit our protocols. So we go with that. Other people have felt like they've experienced precipitated withdrawal, so they're very nervous about that and they want to try a new way. So a lot of conversation about prior experience, thinking a lot about people's living situation, whether they have social support, phone access, whether they can go through withdrawal symptoms if they're living in a tent outdoors, may or may not be safe for them to be incapacitated by withdrawal when they're living outdoors.

(02:10:26):

Also, as it was mentioned, thinking about what is local insurance coverage for different dosing limits? What's their housing situation? Can they be on buprenorphine? Those are a lot of the things that we're trying to think about all in that first visit. That being said, we are trying sort of all three types of initiations that have already been discussed. Sort of what has been used in the inpatient and the ER setting. I'd say the majority, we're still using more of a traditional or standard start, sometimes doing the higher dose or macro starts. That's a little bit newer for us. And patients feel because of prior experience and everything they've heard about buprenorphine, a lot of folks are very nervous about the thought of sort of a macro dose or a higher start. But we've had some good success with folks doing that. We are doing low dose initiations in some settings, and this was referenced in the inpatient conversation, and something we struggle with a lot is can you ask a patient to continue using their illicit opioid for a week while they start their low dose initiation?

(02:11:27):

So if we have someone do this, it's really oftentimes someone who first of all, isn't quite ready to stop using anyways. So this is sort of a nice on-ramp for them to try buprenorphine out, but maybe they're not fully on board to stop. So that can be one good situation. And then if they are going to continue using for that week, then we do a lot of really careful counseling about safer use strategies if they're going to continue doing that. But again, if that sort of is the only way they're going to get started from a harm reduction standpoint, we use that. And then lastly, we just do a lot of counseling with folks. What's their withdrawal symptom cascade? How do they call us? What's precipitated withdrawal versus your existing anxiety? What do you do if you think you've precipitated, how do you contact us? And we really use our multidisciplinary team in following up with folks by phone during this process and particularly helpful as our peer support folks. So I'll leave it at that and pass to the next person.

Susan Winckler (02:12:23):

Thanks, Dr. Hutchinson. Really, I'm struck by the prior experience and the importance of having that conversation. Dr. Dubin, what would you kind of confirm or contrast with your experience in initiation setting with what Dr. Hutchinson chaired?

Jeremy Dubin (02:12:42):

Great. Thanks, Susan, for having me and couldn't second more when Dr. Hutchinson was saying, give a little context. What we do in Colorado, we have a large network of outpatient clinics that are motto is low barrier, high access, and we treat mostly underserved folks. So we're embedded in all sorts of different flavors of environments from homeless shelters to strange access centers to hospitals, to brick and mortar clinics, to mobile units that go to the frontier in rural sites. So we get to see a lot of different folks out there in ways that we can get folks induced quickly. And I would really second, almost everything Dr. Hutchinson said. We go from regular induction very quickly now to low dose initiation with fentanyl, that's happened quicker. We are a large harm reduction site. So the idea that access is more important than continuity for us, so to get you in is really important.

(02:13:33):

That's always been what we've thought, but it's become more important than ever. I'm going to throw out something that I don't think has been said yet, but going to... I think it's been spoken to, but I couldn't second more ever what everyone is saying. But the idea of extended release buprenorphine, so the sublocade's out there, we are experimenting with lower doses with folks. So as we're going to talk more about that at the end of these different recommendations that have been thrown out there. We have been doing that because what we've been noticing is that as everyone has said, this low dose initiation, although is a great harm reduction process or a sign of progress, we all hold our breath.

(02:14:13):

And we all hold our breath when we say to our folks, "Hey, we can't condone this, but be careful this week. We'll see you tomorrow. We'll see you in two days. We'll see you next week. Here's some bupre in your back pocket, please start to take this even if you're using out there." And we all hold our breath when that happens. And we have some preliminary data on using some lower doses of some extended release. So in other words, a 100 milligrams is what they're using right now, 50s, even less than that. We need some more research on that. But in other words, get a depo on there at day three, maybe day two even. The idea that we have to wait seven days, that has been an obstacle for a lot of folks. Because with fentanyl, getting the depo in there is always going to be helpful. So we can challenge the behavioral, the habituation with films and things like that. I would also say piggyback what Dr. Hutchinson was saying about alternative inductions sites, if that makes sense.

(02:15:05):

So what I mean by that is we have kind of our standard emergency room, and like we said earlier, that there's different receptivity to what happens when you go to different ERs. Not knocking our ER colleagues, just, it is what it is, stigma, philosophy, training, that kind of thing. And then you have folks that are in the brick and mortar clinics, we're doing either low dose initiation or the regular in inductions. We're doing something kind of in the middle, which we all, I think can collaborate that or agree happens already. So some of these more social detoxes is 3.2s out there where someone goes in there, they know they need medicine, they're not meeting criteria for an emergency room. So they either contract with a provider or they send them to an urgent care to hopefully get some Phenergan or some buprenorphine if you're lucky. And then they go back to the detox or quasi detox so that it gets administered by kind of a nonmedical person.

(02:16:02):

There's a lot of different in-betweens, and that's where there's a of gaps. So the idea of, we all walked away from in-house inductions at the beginning, which I think many of us that are out there in the trenches know we do about 99%. We send people home to do inductions. That's changing. We're bringing people in now and letting them sit in a room for 5, 6, 7 hours. It's not an official detox, but it's us getting the medications, us actually initiating induction and in that time hooking up all these wraparound services if they're feeling okay with case management, counseling, things along those lines. We also have just to add to that, what we call [inaudible 02:16:39] ambulatory medically supervised withdrawal, not the best there.

(02:16:42):

But the idea is when someone induces, we actually have a medical assistant calling them that evening with their information on their protocol and their confirmation of their appointment usually the next day or the day after. And then some recommendations for ER triage if they need to. So what's been spoken here before and what Dr. Lofwall was saying earlier was how important that is that in that initial 24, 48, 72 hours, and then some of our colleagues earlier from the ER, we're here, we're not going anywhere. We're going to keep trying at this. So I think that would maybe piggyback on what Dr. Hutchinson was saying. And I mean, I have some more, but I'll let some other folks go.

Susan Winckler (02:17:23):

Yeah, really helpful. I'm particularly thinking about the dosing, but then the wraparound services. So Dr. Bratberg, tell us about how are there initiation of buprenorphine in a pharmacy based setting? Is there a role for pharmacy to play here?

Jeffrey Bratberg (02:17:42):

Well, I absolutely think so. We have 60,000 pharmacies that are all in different states with different state laws. In Rhode Island, we successfully inducted over a 100 folks and had a massive difference in a randomized controlled trial where they went from induction in the pharmacy to be randomized to usual care or to continued pharmacy care and 89% at 30 day state in the pharmacy. We can't do this study again. It's essentially unethical to not offer induction buprenorphine in the pharmacy. I think we'd all agree there, all the pharmacists for trained, this is our New England Journal of Medicine paper that we published with Dr. Joseph Green and reaching our folks, and we have a great supplement that explains our collaborative practice agreement. So this was enabled because of the DEA telehealth regulations, which are on pause, I think many of us would agree, should be permanently on pause to allow what we call physician delegated induction.

(02:18:43):

Now with the waiver gone, because pharmacists were never part of the waiver, and so, people live within five miles of the pharmacy. We talk about mobile clinics. I think that's fantastic, you know where they go? To the pharmacy parking lot. When we need people to be able to go into the pharmacy, we recruited from outreach. A third of our participants were actually recruited from word of mouth. Which meant that the pharmacy was the experience that they had. I totally agree, I've researched pharmacists and community pharmacies. There are limitations to stocking, there are limitations and stigma and discrimination. But nothing really any different than any other healthcare provider. So I just want to make sure we're not making that distinction. So we need to have pharmacies, we need all these dosage forms, we need withdrawal treatment. Talk about Phenergan, we can do that right now without buprenorphine, and we need everyone to be an advocate to say, "Let's offer this."

(02:19:35):

And I think it'll become more popular if we pass federal law that allows methadone to be dispensed, prescribed by primary care and dispensed from pharmacies. Now we can offer complete medications for opioid uses, order treatment in the pharmacy where there's already methadone, where most pharmacists can administer naltrexone, where pharmacists can stock buprenorphine. But now, initiate therapy for people. In our study, 80% of people were either in know or mild withdrawal. And so, it's very important. A 100% of our participants were unobserved induction, safe, effective, and a larger percentage of people were stabilized and came back than even some of the most effective ED settings. So this is a setting that needs to be used, it doesn't need to be studied anymore, and will have more data coming out on the outcomes at three months.

Susan Winckler (02:20:27):

So we're thinking more of a continuum where you have individuals who may be able to initiate in the pharmacy versus those who would be better in the setting where they're kind of quasi supervised. That's the label I'm going to give what you described Dr. Dubin or have availability of those services versus those who might even be in the prior panel and in hospital and EMS.

Jeffrey Bratberg (02:20:50):

Well, they're the connector. I mean, our program is called Pharmacy Bridge. We're in Rhode Island, we've got lots of the ocean state. We have lots of bridges, but everything we talk about is bridge to care. We can ask our colleagues what happens when a provider of 250 patients on buprenorphine retires or dies? Where do those patients go? Pharmacies need to be there to bridge therapy. They need to be there to initiate therapy. They need to maintain therapy from ED programs, from mobile pharmacies, from inpatient discharges. And I'll emphasize what my colleagues have said. We have a huge problem with the ERMs that unnecessarily excludes community pharmacies and community pharmacists from administering that, which would be a huge advantage for upcoming forms that can be used for induction and the current form FBA approved forms that are used for maintenance.

Susan Winckler (02:21:37):

Okay. So when we're going to come to that, I want Jade to unmute because we need to hear her voice and thought, and then I'm going to come to everyone to say what other formulations would be helpful. So be ready with that rapid fire response of what other formulations we need. But Jade, you work with individuals who are using buprenorphine in a different way. Tell us about that and what's essentially in the work that you do.

Jade Waits (02:22:10):

Yeah, absolutely. Well, first of all, thank you for inviting me here. This has been really informative and exhilarating. So I work for a telehealth recovery service, and we see a variety of patients in diverse forms of recovery, diverse times in their lives. We're seeing folks that are houseless. We're seeing folks that are in long-term remission that may just want a maintenance or to look into tapering off of buprenorphine. We're seeing folks that maybe are in active crisis that have come to us after immediate overdose or the overdose of a loved one and just initially considering induction. And so, we're definitely getting a variety of patients and patient interests in terms of how they want their care model to look. And one thing that's super important to all of us at Boulder is making sure that the patient autonomy is the priority and that we center the care around that.

(02:23:11):

I think the biggest difference, especially from what I've heard a lot of today, is that ERs urgent cares, even an EMS vehicle are all equipped with different supports that someone coming to us through in an outpatient program does not have access to or may not have access to. So even in an EMS vehicle, you're seeing fluids, you're seeing other stabilization medications, you have people interactively there to support a crisis. There's Narcan in the vehicle. There's so many other opportunities for support. And so, oftentimes in our work, we're seeing folks that maybe don't even have access to clean drinking water to take their medication or a ride to the pharmacy to pick up what is prescribed to them at the end of a visit if they're prescribed medication. So we definitely try to identify different needs and as well as goals of a patient.

(02:24:08):

I think that with outpatient and telehealth, there is are still stigmas that exist that kind of affect the providers and prescribers. Obviously, nobody wants to feel that they're either over-prescribing a higher dose when it's not needed. And I think there's a little bit of a difficulty in being able to say what is right for a patient through a screen. Because in person, I think people are able to triage situations differently. Even as a peer with lived recovery experiences, we're able to pick up on body language and tone of voice. And if we see someone coming with five kids, then we kind of know more of those barriers. But I think through telehealth, it can be more challenging. And so, really focusing on the patient in the initial interaction and engagement and making sure that we're asking the questions, what are your goals? What are the barriers that brought you here?

(02:25:03):

Some folks are kicked out of an inpatient facility, or they leave an ER after being there for five hours with their children and they say, "Well, I returned to use and now I'm going to focus on trying to navigate this app and get into care here because I can't do it any other way." And so, I think that maintaining that focus on the autonomy of the folks involved is huge. And that kind of transcends into what type of dose or what type of induction method might be right for someone. We are doing a lot of research with quickstart method, which is the word I feel is spreading to a lot of other folks in recovery services that are promoting different forms of induction. So basically inducing with Naloxone or Narcan, inducing withdrawal and then following up with buprenorphine and a variety of doses in a safe manner to make sure that some folks that are having a hard time with that induction are kind of able to have a shorter time span of their withdrawal effects alleged what we could hope for.

(02:26:12):

It's different for everybody, but that has offered a lot of hope. And another option to folks that are houseless, maybe only have a motel for a few days to go through the more severe withdrawal effects that they might be experiencing. And so, we're kind of working through a lot of that research right now

and just finding what works for people and what might not and what other supports might be needed to be added to the care that we can provide. And we're also working with folks that might be having childcare limitations, recently released from incarceration, things like that.

Susan Winckler (02:26:49):

Yeah, so reminding us that there are stops and starts as well, and thinking through those services. Well, we know that FDA asked for this meeting, so they have a very kind of this question, what is it that product developers should be thinking about? What are the needs in this space? So what might you want to see in terms of different dosage forms change to the REMS, but what else would you like to see? I'm going to say whoever unmutes first, Dr. Dubin wins, and then Dr. Hutchinson. And so, start unmuting if you want to jump in. Dr. Dubin, what do we need on the dosage? What do we need in alternatives?

Jeremy Dubin (02:27:37):

Yeah, I think you can start to see a trend going on here. I think let's start with sublingual dosages. I think that we need the lower dosages, the point fives, the films, the one milligrams, even the 0.2 fives. We do this a lot, I think that that would be very useful. Going into the transdermal second, when our colleagues were saying having indication for transdermal for opioid use disorder would be great, especially as the folks that are using some of these medicines, they can learn more about the speed of delivery and things like that. Because you got to know that all these addiction providers don't have a lot of experience with the transdermals on the outpatient. So we need a little bit of research there, but that would be really great to be able to use those, have an indication and make it cost-effective, especially for our underserved folks. And I mean, I can't speak enough about the transdermal, what a colleague said earlier in the hospital setting. But the idea that you can take it on and off. I mean, this is a really good medicine route there. And then the last one I would say is the extended release buprenorphine piece. I think that it is worth us doing a little research into giving those doses a little earlier than that seven-day window as well as potentially even a lower dose to just get the depo in there and what that barrier can do. I know that the data's kind of based on from the pharmaceutical company. But we're doing this in practice and colleagues here have said they're already doing this anyway, and we're doing this in the peds population. So just to throw a big umbrella over the whole thing on those formulations. Peds indications, we are doing this with 12, 13 year olds and younger. We are already doing this, and we'd much rather be giving them depos and have them having films and doing harm reduction with an adolescent. So yes, those are my preliminary ones.

Susan Winckler (02:29:23):

So only lower dose sublingual break the boxes of the patches, extended release depo and pediatric indications. Those are all great lists and echoes a bit of what we heard earlier. Dr. Hutchinson, what do you want to add?

Eliza Hutchinson (02:29:38):

Yeah, mostly strongly sucked everything Dr. Dubin said that I would also just add different starter packs for different types of start. So starter pack for a high dose, a starter pack, especially for the low dose. It's tricky for folks. So starter packs would be huge. Different flavors I think was mentioned before, but flavor is often... I've definitely seen folks discontinue just because they get nauseous whenever they taste the flavor. Films that could dissolve more quickly, that's another barrier. And then I think if I were to go to huge dream world, co-formulation with PrEP or co-formulation with various forms of

contraception, I think would be amazing. There's a lot of unintended pregnancy in our population. So lofty goals would also be though those co formulations.

Susan Winckler (02:30:26):

Co-formulation, or even just co-packing all in one there, yep. Go ahead, Dr. Bratberg.

Jeffrey Bratberg (02:30:32):

And I would extend that to say that we have data that pharmacists are unlikely to, again, we're not treating 90% of the population that wants OUD treatment. And even though we've removed the waiver, prescribers aren't stepping up and that's not unexpected. So if we have pharmacists who are prescribing or if we do actually do see that pickup, pharmacies are not going to stock something that they don't sell. And so, it's important that not only, I agree with all the other dosing forms that we really need flexibility in the package sizes. So maybe not necessarily a starter pack. And I think other folks mentioned this, but something that's, again, not set, but just allow you to say, we're going to buy seven days worth, or things that come in film packages or things like that.

(02:31:18):

Because otherwise, you take one film out, you take one patch out that was mentioned we do that. I think the other thing is that we, instead of asking someone to use a extraordinarily unsafe, unpredictable supply as they ramp up on their buprenorphine, why not approve controlled release morphine or have morphine patches, these things that already exist? Fentanyl, we need safe supply as well. We need those kinds of approvals so that prescribers or prescribing clinicians can use multiple forms of buprenorphine to assure patient safety. Everything we're hearing today is all about what the patient wants. Let's give them what they want.

Susan Winckler (02:31:56):

Really helpful. And thinking about other ways to address. Dr. Lofwall, did you want to add anything to the formulations that might be needed?

Michelle Lofwall (02:32:11):

I think it's so hard. I mean, I think that I appreciate that FDA has an incredible number of regulations that it has to follow that are largely based on safety and efficacy. It's incredibly complicated for them. At the same time, the opiate epidemic has become so much more severe. So 10 years ago, it would be very hard for me to have found. Most of the people were just snorting or insufflating. And now, it's really hard to find someone that's not injecting. And 10 years ago, our hospital was not full of people with bacteremia, seeding, valves, bones, mycotic, aneurysms due to untreated or inadequately treated opiate use disorder that was very severe and all injection related. So Dr. Donofrio or someone in the last session just talked about endstage addiction. There is a lot of end stage kind of addiction that we're seeing now.

(02:33:13):

There's also a population that we see that's been in treatment, long-term remission. They need to get off. They want to be off, they would like to try to go down gently and be comfortable and not... So we need the lower doses for them. But if there was a way... So when they're considering REMS and all of this, how do you make it just and respect autonomy, provide the most benefit and do no harm? The medical ethic of do no harm is also FDAs, I think with their principle of safety. But there's all these other things. And so, I'm just trying to think about creatively and how hard this all is. Pharmacies are

ubiquitous. The criminal justice connection is complicating everything. Jails are not excited about giving anything that is sublingual. They are very interested in something that's quick and fast. Because even if you do telemedicine, they don't have jail staff to bring the person into the telemedicine room. They've had a really hard time having normal standard of care for other medical illnesses. So this is complicated.

Susan Winckler (02:34:30):

So let's come back. I want to come back to the incarcerated in a bit, but you mentioned something we should talk about and that's tapering or discontinuation. And we know that that's not recommended or the goal according to kind of clinical guidelines. But we also know that some patients might want to discontinue buprenorphine treatment. So how do you help patients manage that process if they want to decrease? Dr. Dubin, you want to jump on that?

Susan Winckler (02:35:00):

Jump on that.

PART 5 OF 7 ENDS [02:35:04]

Jeremy Dubin (02:35:04):

Providers collaborate about it's not philosophically whether you should be on this medicine or not. It's the idea of if you want to taper off buprenorphine, if there's not a medical reason to do it, the question comes up is, "Okay, what is your abstinence-based strategy?" And so let's work that out and let's really let that be sound. And often we find that we might not get there. We might still end up on two milligrams and that's okay too. So it's an opportunity for education, opportunity for goal setting. It's not in a manipulative way to say to somebody, "Hey, you shouldn't be on buprenorphine." It's more of a time, an opportunity to reinforce to somebody what this tool is often doing for them. I would challenge that. A lot of the time folks will walk out of a good educational setting like that and say, "Well, things are going pretty good."

(02:35:50):

My first 15 years are pretty awful and these last five years have been pretty good. What am I pushing this for? The folks that really want to taper off, the idea is let's get that program in place. Is it naltrexone? Is it Lexapro? Is it a good counselor? Is it divorce? Is it marital counseling? Is it quitting your job? Is it treating the co-occurring issue? And is there enough of a threshold that you can meet that we can taper off this slowly and with the understanding that you might have some biochemical vulnerability to this kind of diabetes and maybe you do end up staying on two milligrams, and that's okay too. So if anything, when the tapering conversations come up, we always look at those as great opportunities to discuss the big picture.

(02:36:36):

I could get into dosing and stuff like that with you'll, but I think that's one of the biggest things we like to say is let's set this up successfully so that when we do say, "Okay, let's go down by two milligrams," if you're at 16 or something, and that's not for most people. But we are really clear about that. Before we do that, let's set the stage. Let's really set the table well so they feel confident about that taper process. And leveling out whenever, even if you level out at eight milligrams for a year and a half and you're still in a trajectory like goals.

Susan Winckler (02:37:12):

Yeah. Dr. Hutchinson.

Eliza Hutchinson (02:37:13):

Oh yeah. I would just add similar conversations we have with patients, but I think this really points to, I think something we haven't discussed a lot, which is stigma against buprenorphine. And I think I certainly experienced a lot of folks coming to me wanting to taper because someone in NA told them they shouldn't be on it or because they're housing, their recovery housing doesn't allow it or because they think they're going to be incarcerated and they're not going to be on it. So I think as we work to eliminate some of the social stigma hopefully against Feds for OUD, I think some of those tapering conversations will taper off. I think it will always be relevant and it will always be important for some folks to be able to do that. But I do think a lot of it is driven by community stigma.

Susan Winckler (02:37:56):

And [inaudible 02:37:57]-

Jeffrey Bratberg (02:37:56):

I would just say... Oh, go ahead.

Susan Winckler (02:37:57):

Go ahead.

Jeffrey Bratberg (02:37:58):

I was just going to say normalizing bup is the thing. We've got a generation to overcome prescribers, reluctance to prescribe opioids. And as long as bup is an opioid, which we can't change, and as long as it's a scheduled medicine which DEA is in charge of, we need to take efforts to say we're not getting rid of long-term chronic pain but implement guidelines like the VA just did, which says their go-to chronic opioid is buprenorphine so that pharmacists see it, so the prescribers prescribing clinicians see it. And so it becomes a normal thing to stock. And guess what? Other dosage forms help. It helps all of those folks too. So there's two groups of people to think about.

Susan Winckler (02:38:38):

So not just in the opioid use disorder. Yep, go ahead Jade.

Jade Waits (02:38:41):

I would also mention from the patient standpoint in regards to tapering that along with the stigmas in general that can exist that kind of prevent folks from wanting to stay on maybe preemptively before they're ready to taper, there also exists a reluctance to taper because oftentimes there's been such a barrier in getting medication in the first place, whether that's because access issues or because of stigma that exists or just recent relapse. And so when you finally retrieve medication and you find a provider that feels inclusive and that is providing what you need, sometimes feeling like, "Okay, well am I ready to taper? I want to have this conversation, but what happens if it's preemptive and now I'm left without meds or now I am preemptively tapering and then they don't want to prescribe the dosage that was initially working for me in the first place."

(02:39:33):

And so sometimes we're seeing folks that are tapering and then having the conversations after the fact and saying, "Oh, well I've actually been taking a quarter of a strip now, but I didn't want to say anything because I was scared that I wasn't ready to say much." And obviously those conversations are more helpful to providers when they are had because it allows folks to know what's working and what's not, what's needed. So I think remaining open as a provider in any position is helpful for patients and encouraging the conversation that whatever medication or dosage works in a safe manner for that patient can still be reconsidered even if tapering is something that's happening.

Susan Winckler (02:40:15):

So really helpful in using that as a conversation to continue the conversation about why tapering and then opportunities to do so if they so choose, but keeping that conversation open. I'm struck, and it's come up a bit in the telemedicine angle, but what are the other strategies for those who are in rural settings what do we do do differently when it's not three buses to get somewhere. It's a long car ride without a car available.

Jeffrey Bratberg (02:40:54):

Pharmacy. That's my answer.

Susan Winckler (02:40:58):

Definitely an option. Yep. Go ahead Dr. Dubin.

Jeremy Dubin (02:41:00):

We see this in a lot in Colorado. We serve a lot of the rural and frontier areas. And to second with my colleague Jeff Bratberg is saying the importance of collaboration with community facilities. So the ER and pharmacy as well as just community health is really, really vital when it comes to these places because not to challenge what my colleagues are saying, but the idea that you don't know which pharmacy you're getting into and you don't know which ER you're going to. And so you go into these rural communities and you kind of make that assumption. And often that can make someone that never want to use bup again and never look at that as an option because they've just been burned by that. So that's really important.

(02:41:42):

Now I'd second it just from a provider standpoint, the treatment place, our mobile units have been very successful in this estate funded grant. We have four mobile units and we cruise around and we tour a lot of the different rural areas and we partner with different community facilities. So this could be a counseling center, this could be a hardware store. So the idea that we would be in their parking lot and find kindred spirits in the community to, you kind of have to secure your pharmacy and you have to secure your either urgent care or/ER higher levels of care. And just speaking to something that Jade was saying earlier, speaking to the idea, this importance of continuum of care with the essence. And so when you're talking about telemedicine, there's two flavors of that, I guess there's the phone consult, which is allowed, and then there's the virtual assessment where you could have someone in there maybe getting vitals for you and things along those lines, maybe even a urine drug screen. And then seeing that person virtually.

(02:42:41):

And then there's the regular brick and mortar actually putting your hands on somebody. And so not to challenge any of my colleagues that are doing purely telemedicine, but there is a challenge there. So

when you're rural centers where we have our patient in a world situation that needs to climb that ladder, we did a phone consult, we're going to do a virtual consult with you. All right, let's go back to phone. You know what, things have gotten a little severe for you. We'd like to be able to touch you. And so having the access to a actual human being that's going to be important versus going to a facility that might not really have the education or the experience or the seasoning with this. So things can go south very quickly if you do a phone virtual into a rural area and then say, "Well, if things go south you just go to the ER." That could go south very quickly.

(02:43:34):

So having that, and that speaks back to this whole idea of a community induction site where people can count on the capacity of that site. So whether it's the ER, primary care, even in an addiction clinic, orthopedist pharmacy from the public that you know that, these folks 89% don't need to be in an emergency room and they can pull this off in a place, but that you know what to expect in something like that. And I've been reading more about that and I know things are headed that way.

Susan Winckler (02:44:06):

So more on that continuum and providing what you can virtually and then where it might be needed.

Jeremy Dubin (02:44:16):

Being able to climb the ladder, being able to bring them up to a higher level of care if you need to. And that's collaborating with colleagues that might do something different than you, that might be a detox, but it's finding those kindred spirits because that's stigma, where we're all speaking to it, that stigma is so powerful that this is the major obstacle, to do all of this because if we didn't have this, this would be like insulin. And we would say, "Yeah, all our goal is no heart attack and stroke and we'll go down your insulin." As long as that's not [inaudible 02:44:44], it'd be a whole other conversation.

Susan Winckler (02:44:46):

But that's a kind of, I think Dr. Lofwall mentioned this a bit in her slides. You didn't say it quite this way, Dr. Lofwall, but have we medicalized it enough to understand that they're much like treating major depressive disorder or something else, that we are in remission and it's a lifelong illness. And so you may be on a maintenance medication for the duration.

Jeremy Dubin (02:45:13):

Yeah, and Samson does a great job doing it. We're continuously educating and just to kind of regroup really fast, people were saying that buprenorphine is a very, very safe drug. I agree. It's a very safe drug. But we do have a couple decades of some of experienced buprenorphine users that have been told differently. So the education is important. Although we all on this call can say, we know it's safe and, "Hey guys, don't worry, I'm going to give you some medicine now." And I told you few years ago this would precipitate withdrawal for you and you'd be growing up in the bathroom. But now I'm telling you that's not true. So we have some work to do also with that education piece at the public. I'm just saying it, we all know it's safe, but I'm just throwing that out. That's been our experience.

Michelle Lofwall (02:45:50):

I think it's like a thing though. It's like Stevens Johnson syndrome. Very rare event, but you focus on it, you teach everyone about it when it's associated with the medication. That's what we've done with Buprenorphine. But what we haven't done with buprenorphine is we haven't made the framework

similar to other chronic, often chronic relapsing remitting illnesses, that have a variety of different severities, a lot of different components in the behavioral, the bio psychosocial that influence it. We've missed that. We have not applied that kind of framework to it. And I think that we have to do that because we have a mortality reducing medication by more than 50%. We have an ongoing opioid epidemic and we have people that frankly can't access it and have completely misinformation about it from the patients themselves to all the different agencies that impact how the patients actually get it.

Susan Winckler (02:46:42):

Which is a piece that we have to, as we think about extending the services and then understanding and making better use of the product. And I'm struck Dr. Dubin, it's also science where we learn a lot and adapt our thinking part of the scientific test. So we thought it did that and now we have a better understanding and experience in it.

(02:47:07):

We are quickly approaching our time. And so I'm going to take the privilege of the moderator and say, Dr. Hutchinson and Jade, do you each get 30 more seconds and then we're going to close out this panel. Because then we're going to talk about special populations, which Dr. Lofwall, I know they're going to talk about incarcerated populations on the next one, but Dr. Hutchinson 30 seconds then Jade, 30 seconds. Fire.

Eliza Hutchinson (02:47:30):

Great. I think the last thing I was going to add with rural, I think just increasing the primary care workforce is really key in getting everyone to prescribe. And I think that would really help with what Dr. Lofwall saying of making this a chronic disease just like any other. You get it treated in the exact same place in the exact same way. And then really glad they're going to talk about incarcerated populations because I think that is a huge point of this conversation. So thank you.

Susan Winckler (02:47:55):

Right. Excellent. All right, Jade, your 30 seconds.

Jade Waits (02:47:59):

I was just going to add in terms of having safe induction sites, I think that a good place to start along with what Jeff was saying about pharmacies is huge because folks are already going to those spaces. And I think even more innovative would be needle exchanges where folks are already going to find harm reduction supplies, naloxone distribution spaces, things like that where there are community efforts already happening and they feel like safe spaces to folks.

Susan Winckler (02:48:26):

Excellent. So great point to close out on. Thank you all for bringing us to think about the community setting and how we initiate and maintain buprenorphine use. So I've got our list of things we need including starter packs and the ability to break boxes and an extended release form and co-formulation and a whole bunch of other things. Thank you all so much. With that, I'm going to walk out of this virtual meeting room and I'm going to walk into the next virtual meeting room and we're going to talk about special populations. Thank you. Take care. I'm going to jump to the next session.

(02:49:19):

All right. I'm in the last session of the day meeting room where we're going to talk about initiation and maintenance care in special populations. If you've been with us, we talked about inpatient, we talked about community, and now we're going to turn to a panel discussion to talk about special populations. Let me do some introductions. First. Dr. Andrea Bonny is chief of the division of Adolescent Medicine at Nationwide Children's Hospital and is a professor of clinical pediatrics at the Ohio State University School of Medicine. Dr. Caitlin Martin is the director of OB-GYN Addiction Services at Virginia Commonwealth University. Dr. Amesika Nyaku is assistant professor in the division of infectious diseases at Rutgers New Jersey Medical School. And Chad Sabora is a senior advisor for Faces and Voices of Recovery.

(02:50:12):

So we're to the four of you to talk about now what we've called special populations, unique populations. Let's talk about adolescents. It's come up at least seven times. I was keeping track on my tally. Dr. Bonny, how do you manage buprenorphine initiation among adolescents, particularly when you are thinking about dosage and choice of formulation?

Session 4: Buprenorphine Initiation and Maintenance in Special Populations

Panelists: Andrea Bonny, MD, Nationwide Children's

Caitlin Martin, MD, MPH, Virginia Commonwealth University

Amesika Nyaku, MD, MS, Rutgers University

Chad Sabora, MS, JD, Faces & Voices of Recovery

Andrea Bonny (02:50:44):

Well first of all, I want to thank you for letting me be here and I have thoroughly enjoyed the conversation this afternoon and a lot of the comments regarding adolescent and the need for more work in that area. And I'll just add that, last year it looks like less than 4% of adolescents with an opioid use disorder will get any type of opioid substitution therapy or medication therapy. And for younger adolescents or underrepresented minorities, it's like even less than 1%. So happy to be here. I will say that our technique is very similar to what's been talked about already this afternoon. Because of our population, we have very limited support of programs that will take care of our patients. So our ER does not do induction. We have limited ability to do supervised induction. So we've been doing this for about 15 years now and we've been doing home induction the entire time.

(02:51:38):

We do pretty much standard dosing where we tell people to wait till they're feeling experiencing withdrawal. As was mentioned in the last section, we do a lot of talking with our patients, kind of meeting them where they're at, we discuss dosing and what they're comfortable. Most of them have actually tried buprenorphine. Most of them have bought it to try to treat themselves. Many know what the experience of opioid withdrawal. I think we don't give adolescents the credit for how much they actually do know. And so I think we've induced over 500 adolescents since the start of our program. And I can tell you we've had no safety issues. It has been very safe, very well tolerated. Initially we were getting to doses of about 16 milligrams a day for maintenance with the onset of fentanyl. Now we're really going up to 24 a lot more often and we're needing to prescribe additional meds, Zofran, clonidine, etc, to support them.

(02:52:38):

Two issues that I wanted to bring up though within providing this to adolescents and getting them started is one, the issue of consent. Many states require consent. My hospital actually requires that I have the family sign an opioid consent, which that they know that this is an opioid and that this is potentially addictive, which I find really counterproductive when I have a child who already has opioid use disorder and I'm trying to prescribe her safer medication and I have to tell the family to sign this paper. It really does nothing to prevent stigma and it certainly doesn't make this feel like a safer option. We get through it.

(02:53:14):

And then the other issue is around who is going to manage the medicine or hold the medicine initially. And it really is a case by case scenario. We have some instances where maybe in the younger adolescent, the parents really are going to be holding it and they're going to be administrating it. But then I have patients who their family is many family members with substance use disorder, lack of family support. I had one individual who he told his family he'd been given this med and they drove him to his dealer where they beat him up, stole his Suboxone and left him without any. And so it is really case by case who manages it and we need to have a long conversation around how is that going to work for you and who's going to oversee it, etc.

(02:53:59):

And then we have 24/ 7 call for patients to call with any concerns. I will tell you, my colleagues were worried these patients do not call very often. Everybody thinks they will, but they really do not. It's rare that they would call the on-call doctor.

Susan Winckler (02:54:16):

So that really instructive for us as we think about, yet you really have most in the home setting because we don't have the availability in inpatient and yet it has worked. But with these unique things, I'm struck to the opioid piece. Talk about creating mixed messages and trying to understand what you're navigating in that space. So that's adolescent side.

(02:54:56):

Let's turn to a second special population. We're going to run through our special populations and then come back and think through things. So I'm going to turn to Dr. Martin and let's talk about initiation and maintenance strategies for pregnant individuals and the postpartum period, what needs to happen in there with any dosage adjustments, when to initiate. I would imagine you get a lot of safety questions. Talk to us about the pregnant individual and postpartum dynamics.

Caitlin Martin (02:55:37):

Yes, and thank you for having me. And also for the emphasis on both pregnancy and the postpartum period, which I define and most of us also define as a year after delivery or a year after the end of a pregnancy, even if it was a miscarriage, abortion, etc. There's a lot of things I could cover. Just to piggyback on what was just talked about for the adolescence, for pregnant individuals, we start them on buprenorphine, which is a safe medication in pregnancy and we have lots of data to show that. And that includes both the combination product, buprenorphine naloxone, as well as the mono product buprenorphine. There was a meta-analysis or a cystic review, I'm sorry, that was published last year, the year before, looking at the combination product and essentially pooling a lot of observational data together showing that it is safe in pregnancy.

(02:56:25):

And we actually recommend that now as the standard of care. People I know are working on updating the SAMSA guidelines regarding the combination product. And so the reason why people generally used to think that we could only give the mono product or plain buprenorphine, in other words, during pregnancy is solely just because the first randomized control trial of methadone versus buprenorphine for the treatment of opioid use disorder in pregnancy was done using the mono product. And like everything else in obstetrics, we do one randomized control trial and then we can't do it again because of all the ethical things that revolve around clinical trials in pregnant people. And so we keep doing the same thing over and over again. So that is the first thing I will bring up.

(02:57:05):

And it's kind of the newer thing I hear a lot, people ask me questions about is the combination product and that it is safe. That is the only thing that we prescribed unless someone has a documented allergy to Naloxone for all of our pregnant individuals in our clinic here at VCU and we continue them on that during the postpartum period.

(02:57:24):

How do we start buprenorphine for pregnant individuals? It's the same as anyone else, but because this is a special population, highly vulnerable population and also "window of opportunity" where a lot of people, this might be the time during their life course where they may be more able to initiate treatment and access treatment because there are increased services for pregnant individuals. We offer an inpatient, outpatient and home inductions along with the program that I manage and the team that we have here at VCU. So for example, I collaborate with my OB colleagues and the residents here at our hospital. And what we do is any pregnant individual who comes in to the labor and delivery triage just as they would go in to see if they're in labor for example, and they say, well, they want to start buprenorphine for opioid use disorder, they're given that option to stay in the hospital and do that.

(02:58:16):

And we make sure that the residents and my OB colleagues are all trained in how to do that. We have order sets for that. And it's not that hard. So people are willing to do that and collaborate. Obviously we do the normal outpatient inductions like any other opioid use disorder or substance use disorder treatment clinic, and as well as home inductions. There has been published literature on home inductions during the COVID 19 pandemic among pregnant people showing that it's feasible and safe. And we've recently looked at data from our own program looking at inpatient versus outpatient buprenorphine initiations in our pregnant individuals and found that their outcomes, in particular the outcome of continuing buprenorphine till the time of delivery are pretty similar according to observational data. So we do all three. When we start people on buprenorphine? How I counsel all of my patients is my recommendation to continue that medication through at least the baby's first birthday or 12 months postpartum. And that is for many reasons, the most notable reason is that mental health conditions in particular overdose have now become the leading cause of pregnancy associated deaths in this country, the leading cause. Above and beyond all the "traditional" medical causes that I was trained as as an obstetrician, postpartum hemorrhage, hypertension, all those things. And most of those overdose related deaths that are occurring in the pregnancy and postpartum periods are happening in the six to 12 month postpartum period. A long after they've come in for their birth control or whatever other postpartum needs that they may need from a general OB GYN or women's health clinic. Though I counsel all my patients on my recommendation to continue their buprenorphine until their baby's first birthday.

(02:59:53):

Buprenorphine dosing changes are very, very, very common in pregnancy and postpartum, just like with any other medication. Pregnancy leads to a lot of specialness. When you're dosing medications, you're talking about things, levothyroxine, insulin, buprenorphine, they're all kind of the same. So how we manage that is that we very carefully and repeatedly monitor our patient's symptoms, craving, withdrawal, etc. And we see patients very repeatedly during the pregnancy and postpartum period to monitor them for those symptoms. In general, but everyone is different and we publish the paper on this. Essentially the take home point is you have to individualize it to the individual patient. However, if you're looking for a rule of thumb, generally patients as they progress through the pregnancy period, they will generally need increases in their dosing. And they would also need split dosing too. And that's the same as we do for methadone also.

(03:00:51):

So if a patient was taking 16 milligrams once a day before they were pregnant, it's very likely that that patient may gain some benefit from splitting that into eight twice a day and maybe increasing up to 24 or so. Postpartum, it's a really big [inaudible 03:01:11]. When we looked at data from our health system, we found about a third of patients increase their dose, a third of patients stay at their dose and a third of patients decrease their dose. Again, every patient is different how the postpartum period manages out. And we really have a severe lack of data to guide buprenorphine changes through the pregnancy and postpartum period. And that's an area I feel very passionate about because again, that postpartum period is when women are dying and their children are being separated from their mothers. And so there's ways that we can improve the treatment quality. And so optimizing buprenorphine dosing based on clinical and other factors and seeing how well we can preemptively help patients tweak their dosing rather than waiting till maybe they're unstable would be a really big benefit to the research world.

Susan Winckler (03:01:59):

Yeah, really I'm struck in the dosing changes and all the dynamics there, but then I will say when you started out, it just is still not common enough that we understand medication use in pregnant individuals. So at least we have some of that information here.

(03:02:22):

Dr. Nyaku, I want to turn to you, Dr. Martin mentioned that kind of window of an opportunity. Sometimes I think we see that in infectious disease and where that might be a window of opportunity. Would love for you to talk about infectious disease as a potential entry point for initiating buprenorphine. And then also tell us more about the work you do with incarcerated population.

Amesika Nyaku (03:02:50):

Thank you. And like others have said, I really appreciate being able to be on this panel. I probably will start with the context first so that you can understand where I'm coming from. So I'm an infectious disease physician that focuses on addiction treatment, particularly for individuals with HIV or at risk for HIV that have a substance use disorder, and so that's my clinical hat. And then I also wear a hat as a physician scientist really looking at clinical trials. And these clinical trials are testing the efficacy or effectiveness of novel therapeutics either for HIV treatment or prevention as well as for opioid use disorder so that we can really think about how do we best deploy these advances we're having in our therapeutics so that we can be able to address and provide differentiated care to be better matched to the needs of our patients.

(03:03:50):

And then my third hat is as the co-director of the Northern New Jersey Medication Assisted Treatment Center of Excellence. So our governor, in response to the rising overdose deaths that were occurring in New Jersey made these two centers of excellence. And so we have the northern that's situated here in Rutgers New Jersey Medical School in which we're focused on providing technical assistance, education and support at the elbow support to providers across New Jersey, so that are particularly focused on providing care to individuals that are insured through Medicaid. And so with these kind of three hats is where I'll answer these two questions.

(03:04:37):

And so for the first part about thinking about infectious disease is an entry point for initiating buprenorphine, what I'll actually say is to have you all understand the framework that we're currently using around HIV and ending the HIV epidemic as a part of a national strategy.

(03:04:55):

And in this framework we think about a continuum and we characterize this as a status neutral continuum. So when we think about providing comprehensive services for somebody that's living with HIV, in many ways we can look at that mirror of those type of comprehensive services for somebody that may be at risk for HIV. And so all of the things that we're doing to prevent somebody's HIV is also a good practice for helping to treat someone's HIV. And so this is where we can see that initiating buprenorphine as it's related to today's conversation, and as for opioid use disorder, but really addressing any substance use disorder can work both ways. It is very effective. And so I know we are talking about some of the data for that is the foundation for the work that we do.

(03:05:46):

So for instance, we know that with buprenorphine that it is incredibly effective. So buprenorphine and methadone will use in this scenario that the data supports how effective it is to promote someone staying on their...

Amesika Nyaku (03:06:03):

... active it is to promote someone staying on their HIV treatment and achieving virologic suppression. And so out of all of the different evidence-based interventions that we have in my world for HIV treatment, how powerful buprenorphine is as one tool to improve somebody's virologic suppression is it's actually quite amazing. Similarly, when we think about this on the other side of our continuum, so we think about it on the HIV prevention side and then I'm going to throw in hepatitis C prevention as well, that we see that somebody who has an opioid use disorder that's on a medication like buprenorphine will have at least a 50% reduction in the risk of contracting HIV or hepatitis C. And so this is the way in which buprenorphine and other... in similar agonist, partial agonists type medications become very powerful tools as we think about the rising number of HIV infections that we have, rising number of hepatitis C infections, and then we can talk about what do we understand about someone who ends up with serious bacterial infections and is hospitalized.

(03:07:19):

And so we're talking about heart valve infections, cell endocarditis, osteo vertebral or vertebral osteomyelitis, septic arthritis. We've seen precipitous increases in these diagnoses and they have the potential for significant morbidity and mortality. And so when someone is hospitalized and being treated for these infections, this represents an opportunity to have comprehensive addiction medicine services. And a part of those comprehensive addiction medicine services is the initiation of buprenorphine or potentially other medications for their opioid use disorder. And it's really important both in terms of helping them to complete the antibacterial treatment that is required for that serious infection, but

then also reducing the risk of readmission, overdose related presentations and those things. And so I will make the thread of why I'm also working with individuals that have criminal legal involvement. And that is because there is a kind of very strong connection between, or I should say that there is a high prevalence of incidence of HIV infections and hepatitis C infections in individuals that have criminal legal involvement.

(03:08:39):

And so this became a very natural extension of my HIV treatment and prevention work to really think about what is the needs for someone that has criminal legal involvement. And so with that, it really comes back down to these principles that we talk about around harm reduction. And with these harm reduction principles, again, it's where do medications sit? Where does buprenorphine sit in this conversation? And so that really is what brings us to, again, because of not only the infectious disease risk that we see in someone that has criminal legal involvement, but also the incredible overdose risk.

(03:09:17):

And so there are studies showing that within the first two weeks of somebody being released from incarceration, that during that time of reentry into the community, their overdose risk some studies have it as high as 49... 40 times as high as the general population, as high as 129 times that of the general population in the first two weeks. And so this represents... So someone that has criminal legal involvement is incredibly and has an opioid use disorder, is incredibly vulnerable to overdose, overdosing and dying in this period of time. And so really having buprenorphine and other medications available while that person is incarcerated is incredibly important in that time in which they're in a correctional facility represents, again, another critical intervention point for that individual. And so with that, I can pause there.

PART 6 OF 7 ENDS [03:06:04]

Susan Winckler (03:10:15):

Yeah. Fascinating and particularly the connection right in the viral load and the use of buprenorphine as well as recognizing the risk when we're thinking about incarcerated populations. So everybody get ready, I'm going to come back to you and say adolescent pregnant postpartum and infectious disease incarcerated, what other dosage forms do you need? But we're first going to hear from Chad. So Chad, a theme-

Chad Sabora (03:10:48):

That was amazing information and thank you so much for having me. I'm coming from a completely different perspective.

Susan Winckler (03:10:55):

Yes.

Chad Sabora (03:10:56):

So, I am a policy advisor and content expert at Harm reduction for ONDCP and SAMSA, person in long-term recovery from poly substance use disorder and also an former attorney. So, my little experience I have is much different. So my take on this is because I do a lot of implementation of outreach programs for disfranchised communities. I'm not going to call them special populations because they're disenfranchised. So, we specifically work with people from LGTQI plus communities and people from

bipod communities. So that population is extremely difficult to reach for numerous reasons. Many have treatment trauma. There's individuals that are not going to access a brick and mortar building because of fear of safety.

(03:11:50):

Individuals don't access good Samaritan immunity, overdose laws out of fears of physical harm being cause to them by police. So we have to make sure that when we're delivering services especially bup induction to populations that we have proper diversity amongst peers. So this removes... I mean obviously we need a physician, but that would be the only clinical person in that situation because we want to have a feeling of comfort and vulnerability and we have to make sure that we have proper diversity. One of the benefits of diversion of buprenorphine is we know that 80% of people that I've diverted bup used it to treat their own OUD.

(03:12:37):

And I'll speak a little off here from... I'm not sure what other people said, but if it's easier to get fentanyl on the illicit market in your neighborhood than suboxone, you're doing something wrong. Both should be readily available and there should be active outreach programs that are targeting communities that we know have been systemically disenfranchised by our war on drugs and are not going to access treatment in a traditional fashion. So our methods today in response to what we've done for the past 140 years have to be untraditional. We have to create routes of access for individuals that we know are not going to accept those traditional routes. And that comes with a lot of creativity, ingenuity and partnering with other community organizations, partnering with people who sell drugs at the same time and getting community buy-in and involvement. So that whole area is very complex, much longer than 10 minutes.

(03:13:43):

But when we talk about that, when I talk about special populations, I'm in a whole other world of people that are dying and their deaths are being ignored completely. Also, they're dying from cross-contamination on a few medications. And a lot of the times it's assumed because of a post-war on toxicology that cannot identify time of consumption that a person intentionally purchased and ingested fentanyl when that is not what happened. We have issues with the lean supply right now, which is contaminated and issues with the ecstasy supply. Now, it's very difficult to engage populations that... when you understand their cultural competency that some don't identify what they're using as a drug. And not only that, to tell them they're a drug user would be offensive and culturally inappropriate. They also don't identify that they're a risk for overdose. So we have a very unique population we are trying to reach with some of these drugs that have been contaminated by fedi. Sorry, fentanyl. I use my street words. So, that's the services that I work on from a street outreach program and from a public policy standpoint.

Susan Winckler (03:14:59):

Yeah. So Chad, in that space, if you think about the currently available dosage formulation for buprenorphine, whether it's the singular product or buprenorphine with Naloxone, we've heard earlier in the day that higher dose, lower dose, the ability to get more access to the transdermal patches. Are there dosing needs there? You're obviously-

Chad Sabora (03:15:32):

No. I mean, there's an educational-

Susan Winckler (03:15:33):

... dealing with much broader ones. Yep, go ahead.

Chad Sabora (03:15:36):

There's so many needs. There's an educational piece there because we know that some of the fedi analogs do have a second metabolite period. So people are going to precipitate withdrawals without being properly educated Bernice method or micro-dosing. We have the ability to use full agonists to alleviate withdrawal symptoms until the street fentanyls out of their system. We are not allowed to use those full agonists. We have issues with traditional recovery communities bashing medication, and if you listen very closely, they're never attacking the medication. They think they are, but what they're presenting is a logical fallacy or they're attacking their doctor who didn't understand how to do a proper taper. So, the education piece is huge. The inconsistency of the street product right now is the biggest barrier because we'll do testing of live samples that I'll purchase off the black market. And on an average we have four different fentanyl analogs. Diphenhydramine on a bunch of different cuts.

(03:16:42):

There's no consistency. So one person could actually have a successful induction at two or four milligrams, another person is going to be on the floor very, very sick. So that's why we get to discussions that are this country or not is not ready for, we're talking about access to a safe supply and things of that nature, but we do have access to full agonists that could stave off withdrawals until the fentanyl is out of their system. And the fact that we're not using prescription heroin, prescription fentanyl or Dilaudid at this point is a mystery to me.

Susan Winckler (03:17:18):

We're actually going to to hear a little bit about that tomorrow as well from an outside the US use there. But I want to turn to Drs. Bonny, Martin and Nyaku, thoughts on different formulations that you might need. Actually, Dr. Bonney, we heard earlier about adolescent needs that having to do anything during school, not ideal, but what do you see for needs in the adolescent space? What might be helpful?

Andrea Bonny (03:17:55):

I'm going to break it up into three different categories of I think issues that could be addressed. So what is just broader age indications for treatment options? We had a family come in with their 14-year-old and they wanted Sublocade and we had to get ethics board, pharmacy board approval. Then Sublocade you have to order through a central pharmacy, get prior authorization. It's a really delayed process. So I think making the process easier and really getting broader edge age indications would really help because when they're not approved for younger kids, it sounds like well then they're not safe for this population. The second is that we now have a population of say about 50 to 60 individuals who've been with us 10 to 12 years who are on maintenance buprenorphine. They're really into three... I would say that we have three populations. We have the population who was maintained for three, four or five years and then slowly weaned and some who've come off. Those people, you finally start ripping their film into corners and pieces and whatnot while they're trying to wean off.

(03:18:59):

So again, that's where those lower doses or ween packets would be really helpful. But slow pros... packets. Then I have a group who's weaned down to a lower dose, maybe eight milligrams. And when you start the ween, you really only want to drop by one or two milligrams because you don't want them to be uncomfortable and the current doses don't allow for that. So sometimes we're having them cut

them in order to just do a small drop so there would be more room for formulations. And then that brings me to my last population, which is I have a group now who's been on 16 to 24 for years and may never wean down, but are doing great. They're parenting, they're working. And I would love to see a single rob like the Nexplanon contraceptive, very easy to put in, can last for several years, doesn't require anything daily so that these people don't need to have a daily reminder for the rest of their lives.

(03:19:56):

And these are people, I mean 28, 32, what is the long term lookout for them? So it'd be really nice to have something that can last years for them and they can go on and live their lives. And then the last comment I want to make is about containers, because we were talking about safety and the safety is both keeping children out, but as I mentioned, the biggest safety we have is family stealing it. That's the biggest issue. It'd be great if we could make containers that are like fingerprint locks so that the only person who can open it is the actual person for whom it was prescribed. I'm sure that technology exists, it's probably expensive, but if there's a way to do that, that would solve a lot of safety issues, I think on both ends of the safety spectrum.

Susan Winckler (03:20:40):

Yeah. Yeah, really in intriguing ideas. I'll go to Dr. Nyaku and then Dr. Martin. Any dosage you want to see? And Chad, I am going to come back to you. I know you want education, but I'm going to come back and see if there's a dose-

Chad Sabora (03:20:54):

I've got the dose part, too.

Susan Winckler (03:20:55):

All right.

Amesika Nyaku (03:20:57):

And so I think that I'll piggyback off of what Dr. Bonny said that before we even start to talk about formulations, we really have to think about accessibility. And so, I think that it is very critical to put out there and continue to push for more widespread action is the fact that people are unable to fill their current prescriptions for buprenorphine from a pharmacy in their communities and people have to go to such extreme lengths to be able to get these medications. And so this needs to be addressed by the continued perception of the DEA coming, auditing, shutting down pharmacies because they're dispensing too much buprenorphine. This really needs to be addressed and tackled head on so that we can alleviate one of the bottlenecks that we're currently seeing in accessibility. Then I think that the other part of accessibility is around cost because we do have other formulations that we've talked about.

(03:22:16):

And then here, so if we're talking about extended release buprenorphine that you have to do for your prior authorization, some plans it's not covered under your pharmacy benefits, instead it's under a medical benefit and being able to go through the logistics that then on the clinical side it's got to be a buy-in bill and that's not what these clinics are set up to do instead of it being directly charged and processed through someone's insurance. So these types of barriers reduce the accessibility. And so again, we don't even need to talk about formulations. Dr. Bonney mentioned about having an implant. We did have an implant for buprenorphine, but there was such low uptake of that because cost and

then accessibility because of the cost. When people are then trying to get that paid for that ultimately it has no use.

(03:23:13):

And then some specific things around formulations I think are again about understanding what are the needs for how people take medications. We see this very much in the HIV world about single tablet formulations to make things much more convenient for what people need. And so again, instead of having to cut the films and do these things or if they're going to either do an induction where it's going to be slow, when they're going to need to have a gradually increase, having those pill packet or pill or film packaging to make it easy for people to be able to follow along because that often is impeding the out, this being feasible in the outpatient setting. And similarly, if someone is needing to do a higher dose kind of administration, again, formulations or packaging that then helps so that someone is able to do this is very, very much necessary.

(03:24:09):

I would say that some of the things around extended release buprenorphine is relate to tolerability of receiving the injection. There's incredible burning sensation with the depo placement. It's a subcutaneous abdominal injection and so that often can cause people to discontinue treatment. They also end up with subcutaneous nodules that persist for months and months. And that too is something that is deterring people for wanting to uptake this even though it's really nice to not have to think about their medications a month at a time because they come to their clinical visit, check in and then receive their medications. And so, definitely much more development in this regard is needed so that we can be able to use these or make sure that there's a full array of formulations available for individuals to be able to match their preferences.

Susan Winckler (03:25:19):

And I wanted to flag for you, Dr. Nyaku, the end of our prior panel, they also suggested a co-packing of buprenorphine with prep and contraceptive. So, Dr. Martin, you want to add anything that we're missing on the formulation and absolutely hear you on the accessibility and it speaks to kind of the great need for those who will go to the healthcare system that the healthcare system serve and have product available. But Dr. Martin.

Caitlin Martin (03:25:56):

Yeah, I have three more things to add on. I agree with everything that's been said, for extended release options, those are excellent. And we've looked at patients in the postpartum period who elect to transition to post... to extended release options. And there's a lot of additional benefits for our patients, especially the ones who started buprenorphine in pregnancy. Now we're nine months later and they're parenting and they have a lot of things going on and trying to take your medication still every day can be quite hard when you have a newborn infant home. And so, extended release options are exceptionally important, especially for the postpartum people. However, as I mentioned earlier, the physiologic changes that are inherent to pregnancy in the postpartum period make its extended release options for any medication quite challenging sometimes. And what makes it the most challenging is that pregnant and people who are breastfeeding are almost always excluded from clinical trials and that is a huge problem.

(03:26:53):

I don't need to emphasize that more, everyone knows what happened in the COVID-19 pandemic with the vaccines and the same similar situation occurred. And so my push is more research on extended

release options that incorporate pregnant and postpartum individuals, do get pharmacokinetic data, do get physi that correlate with clinical symptomatology so we can get the data from clinical trials as they're working on these extended release options to inform the next phase of research to see how can we tailor these extended release dosing options for the pregnancy and for the postpartum period. Because right now these things come out and then we have no idea what to do with my patient population. And that's... Have a lot of issues that I can go on a whole soapbox about. The second thing is dosing. Like I mentioned earlier, because of the physiologic changes of pregnancy, just patients a lot of times will need increased doses of their buprenorphine in order to maintain the same level of symptomatology.

(03:27:50):

You have a higher blood volume, the medication gets diluted, your pH of your saliva even changes when you're pregnant, which changes the absorption. There's a whole host of things that are occurring. And what happens in my state is that I can't prescribe above 24 milligrams without a whole bunch of paperwork. And there has been data to show that pregnant individuals especially may need higher than 24 milligrams. I know that varies by state by state, but that is a huge problem that we deal with. I very commonly need to go above 24 milligrams, especially as I'm splitting the dose for my pregnant and postpartum people. I say pregnant and postpartum, pregnancy is obvious with the physiologic change of the pregnancy, but that postpartum period, people are dealing with comorbid perinatal mood disorders. They're dealing with increased depression, increased anxiety, all the things that are putting them at a higher risk of those overdose related deaths, which are the number one cause of pregnancy associated death through the postpartum period.

(03:28:46):

And then the third thing I would call for, which might sound kind of silly, but it's a big deal in my world, is the taste of the film and the tabs. If you've ever been pregnant, you might have experienced that you're just a little extra nauseous and you might just be a little bit extra. You have a little more sensitivity to certain tastes or smells. And so if you take the film, which doesn't really have a great taste to start with when you're not pregnant, it's a big bear. I'm not kidding, it's a big... I've had patients have to stop their buprenorphine because the taste is so just aggravating to them during the pregnancy period and that's putting them at overdose risk because they can't tolerate the taste. It's become that extreme. So we do all the things to try to get around it, but if someone can make a buprenorphine tab or film that tasted good, that would be a big deal in my life.

Susan Winckler (03:29:39):

I know we're going to hear that again, as well as some that would dissolve faster. But Chad, I hear you on the different approach to... Rethinking the overall approach generally and the education need. Any thoughts on dosage or-

Chad Sabora (03:30:03):

Definitely.

Susan Winckler (03:30:03):

I want to give you the stage to say more.

Chad Sabora (03:30:06):

Yeah, we only have a few minutes. It's been 12 years. I can still taste what it tastes like and that's that bad. So lots of issues. First off, we're still... We're babysitting individuals by adding naloxone for no reason except we don't want you to possibly abuse a partial agonist, which is much safer than the fentanyl that will kill you. So, we would get more people induced if it was just Subutex, which would help with the cost issue, induction issue, so many issues. But we have to nanny people in this country, which is absurd at this point. Next issue... Any doctor. I have not met a single person that has been on Sublocade for six months, stop and had any withdrawal symptoms. The problem is the jump from one milligram off is very difficult for people, as the doctors know. And if we take it back up to eight and put them on Subloclade, it will be easier for some people.

(03:31:04):

Doctors won't do that and that has to be something that has to be discussed. And then for, I don't have my glasses on for Dr. Bonney, you can make a tincture with vinegar. When you have to get below one milligrams, you have to use vinegar... In order to make a tincture, you have to use alcohol or vinegar. Obviously, I can use alcohol, but if you dissolve the strip into vinegar, you can make a homemade tincture and then you can dose out those little micro doses and apple cider vinegar might help with the taste problem. I don't know how that would taste, but it might be better. But lots of issues there.

(03:31:41):

But especially the biggest issue is the unnecessary cost addition to prevent the possible misuse by adding the [inaudible 03:31:53] to the formulation. At this point, it's just... I'm scratch scratching my head. And then with the implant as I believe you can only get two because of the location from that first one that went out. So I think that would be a great option if they had a different way to administer it. But the Sublocade reports I've heard back from hundreds of people that have been on it have been very positive as far as mild withdrawals there's almost none. So take your patience from one back to eight.

Susan Winckler (03:32:25):

Chad-

Chad Sabora (03:32:25):

That's all I got.

Susan Winckler (03:32:26):

I think that is just spot on. If my colleagues agree, we're going to let you have the final words because that was a powerful reminder of how we should think about things and thinking through and moving forward. So, thank you to the four of you for the work that you do during the day and for joining us today to share your thoughts about how we might do better in buprenorphine initiation and management in marginalized populations. Right, Chad? That's my phrase.

Chad Sabora (03:33:07):

Either one works. I say disenfranchised-

Susan Winckler (03:33:07):

There we go.

Chad Sabora (03:33:07):

Marginalized works.

Susan Winckler (03:33:07):

All right.

Chad Sabora (03:33:07):

But we know who we're talking about.

Susan Winckler (03:33:08):

All right.

Chad Sabora (03:33:09):

The group on our war on drugs.

Susan Winckler (03:33:11):

Absolutely. All right. So thank you all very much. I will say to everyone who is listening to our session today, thank you so much. We're going to end today and we will be back tomorrow. We will be posting our recording for this event by next week. But we hope to see you back tomorrow to continue the conversation. Thanks so much and have a great afternoon.

PART 7 OF 7 ENDS [03:33:41]