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Session: Opioid Dose Reduction in Patients Prescribed Long-Term Therapy for Chronic Pain

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CIDER Staff: And since we are just past the top of the hour here, we’re going to get things started. Just want to introduce our presenter for today’s session. Our presenter for today is Dr. Travis Lovejoy. He is a core investigator with the Center to Improve Veteran Involvement in Care at the VA Portland health care system, and he is joined by Dr. William Becker who is a core investigator with the Pain Research, Informatics, Comorbidities and Education, or PRIME, Center of Innovation at the VA Connecticut health care system. Travis, can I turn things over to you?

Dr. Travis Lovejoy: Yes, let me just verify. Heidi, are you seeing my opening slide here?

Heidi: I am, yes.

Dr. Travis Lovejoy: Perfect. Alright, we’ll go ahead and get going. So thanks so much for the introduction. I won’t go over one myself, then. I just want to let everyone know that I have no disclosures or conflicts of interest associated with this presentation. And to give you a brief overview of what Dr. Becker and I will be talking about, first, I will be providing a little bit of a background on opioid tapering and discontinuation, and then my portion of the talk will focus on some on-going research that I and my team have been conducting that is looking at care processes and patient outcomes after VA patients discontinue opioid therapy. And then Dr. Becker, in his portion of the talk, will be talking about clinical approaches to opioid taper and discontinuation, as well as identifying who may be appropriate for taper.

So this particular figure may not be entirely unfamiliar to many of you on the call. This shows opioid prescribing in the U.S., not just in VA but across the entire U.S. from 1992 through 2016. And as you can see, opioid prescribing was increasing from the early 90s all the way up to 2012 where it plateaued. And then since that time, over the last four years, we’ve seen a year-over-year decline, a slight decline in opioid prescribing overall. And these figures very much mirror what we’re seeing in VA as well, where within VA, opioid prescribing hit its peak around 2012 and has been declining slightly since that time.

So why might this be? Why are we seeing slight reductions in opioid prescribing over the last few years? Well certainly there have been a number of clinical practice guidelines that have been released, most recently the VA and Department of Defense guidelines around opioid prescribing that were released earlier this year, the CDCs guidelines last year, and prior to that, there’ve been a number of other guidelines such as those released by the American Pain Society and the American Academy of Pain Medicine, all of which have been discouraging use of long-term opioid therapy for patients with chronic, non-cancer pain. There’s also been a considerable amount of information that’s been disseminated through the popular press. It’s probably not uncommon that you’re seeing articles in the paper and in other magazines and publications that have been talking about this opioid epidemic. So the consciousness around this issue is raising, not just in the medical community, but in the general population as well. A number of recent systematic reviews have also shown that there’s limited evidence for the long-term efficacy of opioid therapy for chronic, non-cancer pain, and that this type of therapy is often associated with risk of adverse harms, including overdose and death. We’ve also seen an increase in the availability of various types of monitoring procedures to determine if patients on long-term opioid therapy may be engaging in aberrant behaviors. So urine drug testing is a common approach, but we also have the state prescription drug monitoring programs, where clinicians can query these databases to determine if a patient is being prescribed controlled substances from more than one prescriber within that state. And then we’re also seeing a variety of initiatives that are taking place at the local, state, and national levels to increase safer opioid prescribing. So an example nationally, certainly within VA, is the Opioid Safety Initiative that launched in 2013.

So one of the questions that comes up periodically is what happens to patients in terms of patient outcomes when they discontinue from opioid therapy? One of our colleagues, Dr. Joe Frank, recently led a systematic review that was published just this month in *Annals of Internal Medicine* that was examining the effectiveness of various interventions that targeted opioid dose reduction. And some of these studies also reported on patient outcomes such as pain intensity, functioning, and quality of life following opioid dose reduction. Now, all of these studies that examine patient outcome for observational studies, the vast majority of which were rated as poor quality, but several of them were rated as fair quality. And among those fair quality studies, opioid dose reduction was associated with reduced pain intensity and improved functioning and quality of life. And I will provide the one caveat that many of the patients received interdisciplinary pain treatment; that was the intervention that was targeting opioid dose reduction. So in addition to reducing opioids, they were also receiving a number of pain treatments along with it. So this might not necessarily be indicative of, you know, the patients that I think are commonly seen in primary care, those who are engaging in aberrant behaviors, and who are discontinued by clinicians and not been volitionally by the patients.

Something that our group has been interested in is looking at other outcomes associated with opioid discontinuation, and specifically some of the potentially unintended negative consequences of opioid taper and discontinuation. So there’s been a growing conversation around what other types of substances may patients be using once they’re no longer prescribed opioids. So heroin is a primary one that has been looked at recently under literature, and then there have been some that have suggested that as we see decreases in opioid prescribing, we’re seeing uptake in heroin-related overdoses and deaths. Our group has also been looking at the onset of new, or exacerbation of existing mental health symptoms, and specifically we’ve been looking at suicidal ideation and suicide attempts following discontinuation, and I’ll be presenting some of those data later in the talk. And then, something that I think is very, that clinicians are very aware of is the negative impact that discontinuation, depending on how it’s done and other circumstances, the impact that that may have on the relationship patients have with members of their care team, and specifically the Patient Aligned Care Teams within the primary care setting. And we’ve also shown that some patients completely discontinue care. So we don’t see them in the VA anymore after they discontinue opioid therapy.

So I have a poll question, and Heidi, I think you’re going to pull this one up here before I proceed?

Heidi: Yep, I’m opening it up right now.

Dr. Travis Lovejoy: Perfect. I just wanted to get a sense from the audience of who we have on the call, and what roles you have here within VA or external to VA. And I apologize, I didn’t put a 5th ‘other’ option, so you may not fit into any of these four categories that you’re seeing in the poll.

Heidi: If you fit into another option, please feel free to use the ‘questions’ box and you can type that in, and I’m happy to read you what those results are.

Dr. Travis Lovejoy: Great.

Heidi: What if I open the question box back up so people actually have access to it. So our poll here is: What is your primary role? And the options on the screen here are: clinician/prescriber; clinician/non-prescriber, for example PT, OT, or psychologist; researcher; or administrator. And we’ve got a good number of results in here. I’ll give everyone just a couple more seconds and I’m going to close it out, and we’ll go through the results that we’re seeing. I’ll close this out, and what we are seeing is: 19% saying clinician/prescriber; 40% clinician/non-prescriber; 33% researcher; 9% administrator. And then the people who wrote in, we have a pharmacist and a clinical educator. Thank you, everyone.

Dr. Travis Lovejoy: Great. Thank you very much. So I’m going to talk a little bit about a study that we’ve been conducting that is examining opioid discontinuation in Veteran patients with and without substance use disorders. And we were targeting this particular group because we were interested in looking at care processes and patient outcomes following discontinuation in individuals who are at high-risk of discontinuation due to aberrant behaviors. So this particular study was a retrospective electronic health record review, as well as administrative data abstraction. So we identified all VA patients who were prescribed continuous opioid therapy in all of 2011. So 12 continuous months of opioid therapy, and these individuals subsequently discontinued opioid therapy some time in 2012. And we defined that as being off opioids for at least a year. Then from that overall cohort of about almost 8,000 patients, we randomly sampled 300 patients with a substance use disorder diagnosis in the year prior to discontinuation, and we assessed statistical technique called propensity scores to match 300 patients who did not have a substance use disorder diagnosis in that year prior to discontinuation. So we had a sample of 600 patients altogether.

Now, patients could discontinue for a variety of reasons. Some of them could be volitionally, so the patient decides that she or he no longer wants to be on opioid therapy. Perhaps they are starting a job operating heavy machinery and they can’t be using opioids. Or perhaps they’re finding that they’re developing, they’re feeling somewhat addicted and then they don’t want to take the medications anymore. There could be a variety of reasons that patients would initiate that. We actually found in the sample that a minority of patients, only 15%, discontinued of their own volition. The vast majority, 85%, were discontinued by the opioids-prescribing clinician, and the primary reason was aberrant behaviors. So you can see in this table, we have here the proportion of patients with substance use disorder or without substance use disorder who discontinued for a variety of aberrant behaviors: A known or suspected substance abuse; aberrant urine drug test; opioid misuse, which might be something like continually presenting for early refills; other nonadherence to pain plan of care, and this may be something like not coming into the clinic when requested by the care team to provide urine drug tests; and known or suspected opioid diversion. And you can see on the top two rows as you head over to the right, these are odds ratios, so values greater than one are indicating that patients with substance use disorder have a higher likelihood of discontinuing opioid therapy, generally due to aberrant behavior, then also perhaps not surprisingly, due to known or suspected substance abuse. But I highlighted in red some proportions here because these are statistically non-significant proportions. So, individuals with and without substance use disorders are statistically comparable in terms of being discontinued due to an aberrant urine drug test, opioid misuse, nonadherence to the pain plan of care, and known or suspected opioid diversion. And I think that this is an important finding, given that recent guidelines are suggesting that patients with substance use disorder are probably inappropriate with active substance use disorder, and who are not in treatment are probably inappropriate for long-term opioid therapy. I think that these data indicate that it’s not always just patients with substance use disorder. There may be others, as well, without these diagnoses who have similar risk profiles.

We also looked at pain intensity, and this is a spaghetti plot for those of you who haven’t seen this, this is a spaghetti plot. Essentially what we were doing here is we were looking at pain, and you can see down on the x-axis, there’s a time of zero in days, and so this time zero is the time of discontinuation, and as you go backwards in time, that’s the year prior to discontinuation. As you move forward, that’s the year following discontinuation. And each of these lines represents a different patient of these 600. And this is just a garbled mess. We have, you know, all 600 patients here, and their pain scores are going all over the place, both before and after discontinuation. So what we did is we randomly selected 50 to try to make more sense of this schematic, and it really doesn’t look that much better. It’s still going all over the place. And I think this points to the fact, and many clinicians would attest to this, is that people’s pain, an individual’s pain, varies considerably. Anyone whose every administered a brief pain inventory or a similar measure where patients are asked to rate their pain, on average, over the past week, what was their high in the past week, what was the low pain in the past week, there’s considerable variability. So we know that within patients, their pain varies quite a bit. Not just across a week, or a month, or a year, but even within a single day. So we have a lot of within-patient variability in this particular sample, both before and after discontinuation. So one of the questions that we asked ourselves was, well maybe the variability actually widens after someone discontinues. So we see people experiencing more extremes, and specifically, more extreme highs in pain intensity after discontinuation. And the data didn’t really bear that out.

So this particular figure here shows the average minimum, maximum, and mean denoted by the circle there, in pain across the sample prior to discontinuation and following discontinuation. And you can see here that the bar is a little bit wider in the pre-discontinuation period, and actually narrows, suggesting that there’s a little bit less variability within patient variability in pain scores after discontinuation. Now what did the pain scores that, on average, across patients and within patients, look like in the post-discontinuation period? Essentially a flat line. There’s a slight negative trend, but I would argue it’s clinically insignificant. It’s less than half a point. It’s actually closer to a quarter of a point, as you can see in this next slide here. So we [inaudible 14:08 to 14:11] also looked at correlates of post-discontinuation pain trajectories, knowing that we essentially have a flat line that, on average, patient’s pain doesn’t change much at all in the post-discontinuation period. Now, there are certain variables that are associated with what their pain looks like immediately at the time of discontinuation, as well as their 12-month trajectory of pain post-discontinuation. And that perhaps not surprisingly, their average pre-discontinuation pain, so the higher their pain is, the higher their pain is going to start at in the post-discontinuation period, and that’s represented by that .61 beta value there. And then as you move over in that first row, you see the -.02 beta, and that indicates that there’s a slight negative statistically significant, but probably clinically insignificant negative trend to a person’s pain over the year following discontinuation. So people who start with higher pain, when they discontinue, their pain is higher, and we see their pain go down ever so slightly, but probably not in any clinically meaningful way.

We also looked at patient reasons for discontinuation, and clinician reasons for discontinuation as potential correlates of post-discontinuation pain. And we found that when patients discontinued of their own volition versus being discontinued by a clinician, they actually, those individual’s pain was lower. So people who were being discontinued by clinicians have higher pain than people who are discontinued of their own volition. But their pain trajectory in the 12 months following really doesn’t differ, and it’s essentially flat across both of those individuals.

Down at the bottom of this slide, you can see that the pain rating at the time of discontinuation was about 4.7 on a scale of zero to 10, so this is, on average, where patients started at the time of discontinuation. And their pain decreased by about a quarter of a point over the year following discontinuation. Now, once we control for a variety of different clinical and demographic variables, this is statistically not different from zero, meaning that no change in pain at all. And these findings actually haven’t been published. We’re in the process of publishing these right now.

We also looked, in this particular sample, we looked at the individuals who were discontinued by clinicians. That 85% that I had mentioned, and that represents 509 people in the sample. And we looked at the onset of suicidal ideation and suicidal self-directed violence, abbreviated as SSV here, and we found that about 12% of the sample of patients who were discontinued by clinicians had some documentation in the electronic health record, the VA electronic health record, of having suicidal ideation or suicidal self-directed violence in the year following discontinuation. That was about 9% who had suicidal ideation only, and about 2½% had suicidal self-directed violence, which is a suicide attempt. And the majority of those attempts were due to overdose, not by opioids as one may expect, but actually the most common substance that was attributed to that overdose attempt was benzodiazepine. We looked at correlates of whether someone would have suicidal ideation in that post-discontinuation period versus not, and you can see a couple bolded items in this table here. I’m realizing that my, was my slide not advancing here? I realize here’s the pie chart that I was describing. I think I might have been advancing the wrong slide. So the 12% with SI and SSV, and the breakdown there. And then here’s the table that shows the association between various correlates; mental health diagnoses, substance use disorder diagnoses, and so forth, that are associated with whether or not someone has suicidal ideation or an attempt in the year following discontinuation. And as you can see here in the table in the bolded figures, PTSD and the psychotic-spectrum disorders such as schizophrenia were, having those diagnoses were associated with a greater likelihood of having suicidal ideation, documented with a medical record, or some attempt. Now, other variables that one might think would be associated with these things, substance use disorder diagnosis, being prescribed benzodiazepine, as well as the dose of opioids prior to discontinuation. None of those variables were associated with having suicidal ideation or suicidal self-directed violence.

We also looked at various substances for which patients may be discontinued in the likelihood that these patients would be referred to specialty substance use disorder treatment. So, these are individuals here, this pie chart represents individuals who were discontinued due to testing positive on the urine drug tests for these particular substances. So 96 patients were discontinued due to testing positive for cannabis, 44 for cocaine, and so on. And we wanted to see if the type of substance for which one tested positive and was subsequently discontinued was associated with referrals to specialty substance use disorder treatment.

And you can see in this table here within the first row for cannabis, these are associations with substance use disorder treatment referral by the opioid-prescribing clinician, that patients who were discontinued for cannabis were less likely, so the odds ratio less than one, were less likely to be referred for specialty substance use disorder treatment, as well as less likely to actually show up and engage in treatment. However, those who were discontinued due to cocaine were more likely to be referred for specialty substance use disorder treatment and more likely to actually engage in that treatment. And this is an inside joke between Dr. Becker and myself, but I’m going to let you, if anyone has questions about the cannabis findings, you can direct those to Dr. Becker at the very end of this presentation.

I wanted to talk about a few limitations in this particular study that I think are really important to note. So first, we obtained data exclusively from the electronic medical record. So in some circumstances, this may result in under estimation of the prevalence of certain events. So for example, suicidal ideation, or a substance use disorder diagnosis. Patients may be experiencing suicidal ideation and may even have an attempt that never gets documented in the medical records. So our findings are likely an under estimate of the actual prevalence of these phenomenon in this sample. We also focused on patients who were at high-risk of discontinuing due to aberrant behaviors, namely patients with substance use disorders and matched controls. So it certainly wouldn’t be generalizable, or may not be generalizable to a general population of patients who are prescribed long-term opioid therapy and discontinue this treatment. However, I think that these patients are also some of the more, can potentially be some of the more challenging patients to work with in a clinical setting, and so this is part of the reason we targeted this particular population. We used some pretty conservative definitions to define long-term opioid therapy, as well as discontinuation. So patients had to be on opioid therapy for a full year, and the discontinuation had to happen for at least a year. I mean, part of the reason that we wanted people on for such a long period of time is that many patients may discontinue due to side-effects that they experience in the first several months. And while others have used 90-day periods of time to define long-term opioid therapy, we really wanted to make sure that these were the individuals who had been prescribed opioid therapy for a considerable amount of time. I also note that the discontinuation in this particular sample occurred in 2012, and as you may recall from the very first figure that I showed, this was the peak of opioid prescribing, both within and external to the VA and the United States. And since then, we’ve seen a growing number of discontinuations, and there may be other reasons for discontinuation that were not necessarily captured in the data that I presented here.

So a few conclusions that our team has drawn from these data. It’s really unclear if there is a specific risk profile for patients who ultimately engage in opioid-related aberrant behaviors. I think our data indicate that certainly patients with substance use disorders are at heightened risk for discontinuing due to aberrant behaviors in general, but there’re specific aberrant behaviors for which these patients are not necessarily any more likely to discontinue opioid therapy, and namely, urine drug testing for example. So I think that this is an important finding. It’s something to consider as clinicians moving forward as you think about whom should be tested for illicit or non-prescribed controlled substances. We also saw little change in pain following long-term opioid therapy discontinuation. And we’re doing some additional follow-up analyses to try to understand the nuances of this a little bit more. But our data, and a number of different analyses that we’ve done really point to, on average, within and across patients, a flat line, meaning that pain is really not changing much in the post-discontinuation period. We’ve also noted that there’ve been other adverse events that haven’t really been talked about that much in the scientific literature. Certainly in some clinical publications, but not necessarily in the scientific literature. And we’ve been looking at the exacerbation, or nuance, set of mental health symptoms. And so that’s an area that we intend to explore further in the future. There’s also differential approaches to specialty substance use disorder treatment based on the type of substance use that leads to discontinuation. So as we noted previously, those who were discontinued due to cannabis were less likely to be referred for specialty substance use disorder treatment, and those with cocaine were more likely. And I think this is a very important area, as we’re seeing more and more states pass legislation to allow medicinal cannabis, as well as recreational cannabis. And so I think that this is going to be a very important clinical phenomenon that we’re, if we’re not already seeing it, that we’re certainly going to be seeing it in the coming years.

I wanted to acknowledge my collaborators with this work, as well as the funders. Health Services Research and Development through VA, as well as the former substance use disorder Quality Enhancement Research Initiative. And here are references that I presented in my talk today that I believe you’re able to pull up on your own slides. So at that point, Heidi, I think we can do the switch-over to Will.

Heidi: And Will you just need to put that, yep, perfect, right there.

Dr. William Becker: Alright. Thanks, Heidi. Thanks, Dr. Lovejoy. Really interesting work. So as Travis mentioned, I’m going to discuss the clinical aspects of tapering/discontinuing long-term opioid therapy for chronic pain. The whys, the whens and hows. We’re going to cover a lot of territory, so I’m going to be moving pretty quickly, but hopefully not too quickly. So I also have no conflicts of interest related to the content of this presentation. And I’ll start out with a poll question, which I believe Heidi will take control of. Just one second. And the question is: Complex chronic pain and related opioid issues are A) the most challenging thing I treat clinically; B) among the most challenging things I treat; C) sometimes challenging, sometimes not; D) not particularly challenging. Oh, wait. I changed the response items. D is downright easy; and E is n/a, I’m not a clinician.

Heidi: And responses are coming in. I’ll give everyone a few more moments to answer, and we’ll close this out and go through the results. And it looks like we’re slowing down, so I’m going to close that, and we’re seeing: 13% of the audience saying the most challenging thing I treat clinically; 36% saying among the most challenging things I treat; 9% sometimes challenging, sometimes not; zero saying downright easy; and 41% saying n/a, I’m not a clinician. Thank you, everyone.

Dr. William Becker: Thanks everybody, and do I have control back again, Heidi?

Heidi: You do, yes.

Dr. William Becker: Okay. Alright, so let’s start out with when to taper. And I’m starting with the guidance that was from the AAPM/APS, our last, most substantive guideline in 2009. Clinicians should taper or wean patients off chronic opioid therapy who engage in repeated aberrant drug-related behaviors or drug abuse/diversion, experience no progress towards meeting therapeutic goals, or experience intolerable adverse effects. So then fast-forward to the CDC guideline from last year: If benefits do not outweigh harms of continued opioid therapy, clinicians should optimize other therapies and work with patients to taper opioids to lower dosages or to taper and discontinue opioids. So I really like that this element of balance was brought in. It really helps me conceptually move forward with some of the complex scenarios that I deal with clinically. Furthermore, I’d like to highlight that, note that benefits should outweigh harm to continue long-term opioid therapy. It’s not that they cancel each other out. You really ought to be getting some benefits, and we’ll talk about that as we move forward.

So again, this notion of weighing benefit versus harm, and this evaluation of the balance, is fundamental to every pharmacotherapy, and every therapy, indeed, that we provide as clinicians. And I would take it another step further, which is acting on the results of this evaluation in a patient-centered, yet decisive way, is our duty. And I think that sometimes we get a complacent phase where we’re letting a therapy that clearly isn’t benefitting a patient, sort of, ticket down the road if you will. And I think that’s where we’re running into a lot of problems. So how do we weigh benefit and harm? Well first, we’ve got to assess. How do we assess benefit? So the goal of long-term opioid therapy for chronic pain is to maintain or improve function, and to reduce pain-related functional interference. Things pain is keeping patients from doing. And to assess benefit, my recommendations are to establish specific, measurable, action-oriented realistic and time-bound goals with the patient, and frequently monitor progress toward these goals over time. And to use a validated measure of pain-related functional interference. Erin Krebs’ PEG scale is a great example, and follow that over time. Also, we need to observe and listen to the patient. We need to observe and listen to the patient’s companions.

So we talk about assessing harm and safety. I want to highlight some of the harms that are typically observed early in therapy, or with dose escalation: Constipation, nausea/vomiting, sedation/drowsiness, mental clouding, itching, euphoria or dysphoria. These are things that, you know, if we’re thinking only about the patients’ potential for misusing the medication, we may ignore some of these other adverse effects that are quite important. So I encourage folks to ask explicit questions related to these symptoms. Then when we get to potential longer-term harm: Hypogonadism, osteoporosis, hyperalgesia, worsened sleep apnea, declining function, anhedonia or frank Major Depressive Disorder, and opioid use disorder. That’s going to require careful chart review and detailed assessment of the patient. When it comes to concerning behaviors or aberrant medication behaviors, or use inconsistent with the treatment agreement, we want to use urine drug testing, and we want to query the prescription drug monitoring program. And then, when we’re talking about the kinds of harms that are always highly relevant, whether early in therapy or longer-term: falls, motor vehicle accidents, and overdose always, again, asking explicit questions and performing a thorough chart review. And we’re talking about in follow-up of the patient, you’re seeing a patient, say, every three months, you’d be looking in the chart to make sure you are sure of what happens in that 90-day interval.

So we’re going to spend, I’m going to mention morphine equivalent dose a number of times, so I wanted to establish a definition. So, it’s the method of standardizing potency across various opioid compounds. It’s based on equianalgesic tables from dose ranging studies. It shouldn’t be taken as gospel because there is high inter-patient variability, but they, in fact, are the best measure we have. So I do refer to these charts with every patient I treat. So an example would be 20 milligrams of oxycodone, three times a day. As you can see in the chart on the bottom right, oxycodone is one-and-a-half times as potent as morphine, so that’d be a 90-milligram morphine equivalent daily dose. There’s a website there that you can access. It’s got a nice calculator and it has a smart phone app that you could use.

So dose is becoming increasingly salient, as I’m sure we’re all probably aware. Some seminal studies, observational studies from the early 2010s from Dunn, Gomes, and Bohnert really establish that the odds of overdose increase in a dose-dependent fashion as morphine equivalent daily dose increases on the left-hand column.

Another term I used already that I want to carefully define is opioid use disorder. This is DSM 5’s terminology that collapsed the former abuse and dependence. There are 11 criteria that comprise the diagnosis, and I, to help me remember them, I break them down into physiologic sequelae that you can see there, loss of control, and then adverse consequences. This is where the pattern of compulsive use is impacting the patients’ social, occupational, or recreational activities.

So the box is around tolerance and withdrawal because, per the DSM 5, those two criteria cannot count towards the diagnosis of opioid use disorder because tolerance, especially, is a typical finding and this means higher doses required to achieve the same effect. And in pain treatment, that’s a fairly normal finding, so that can’t count toward opioid use disorder. Withdrawal I have a bit of a quibble with, and I'm going to depart from the DSM-5 here. If I'm prescribing opioids to a patient for chronic pain, and they’re taking them in higher frequency than I'm prescribing, and they run out a week early, and they go through withdrawal, I'm going to count that toward the diagnosis of opioid use disorder. I want to highlight the fact that, you know, for many years, and still on-going, you know, there’s been a bit of a tension between the DSM-5 criteria and then the pain literature-guided criteria for what people consider opioid use disorder. You see the DSM-5 on the left that we just reviewed, and then the pain literature findings on the right. And I want to recognize that, you know, in clinical care when we’re monitoring patients, we’re not always going to have this neat checklist of behaviors that the DSM-5presents. We’re monitoring them using the tools that we have, and we may, in fact, be evidencing the things that are on the right-hand side. You know, you can spend a lot of time trying to force the things that you’re seeing on the right-hand side into the boxes on the left, but I wouldn’t get tied up in knots about that. I would say, if you’re observing things, going on on the right, and those have common multiples, there’s a pattern emerging, then you should make the diagnosis of opioid use disorder. And so to further elaborate, your role, prescribers’ role, in identifying opioid use disorder is actually to partner with the patient when you’re prescribing long-term opioid therapy. Be transparent, forthright, and non-judgmental. I'm going to give you an example of that next. And that is to say, in the treatment agreement, or in signature informed consent process, I say: I want to ensure your safety as we embark on a therapy; I will be monitoring that in these ways, urine drug testing, prescription drug monitoring; specifically, I’m looking for your safe use behavior, which I described; and then simply if you demonstrate lack of safety, it’s my duty to stop the therapy and transition you to safer therapy. So in a sense, you’re partnering with the patient. This is a potentially dangerous medication, and I'm upholding my duty to make sure you’re safe. And again, reiterating what I already said, the patient evidences recurrent problematic behavior. So you’ve laid out what you think is safe behavior, and they evidences recurrently problematic behavior. That suggests that there is loss of control, and the diagnosis of opioid use disorder needs to be strongly considered.

So we talked about assessing benefit and harm, some of what those harms are. Now, let’s talk about the weighing benefit versus harm. So, sort of the, first what I’ll talk about is prohibitive harm, and this is when harm is so great that it doesn’t matter what the benefit is, the therapy needs to be stopped, and that includes life-threatening harm. If there’s non-fatal overdose, serious or recurrent falls, serious or recurrent motor vehicle accident, opioids must be tapered markedly and/or discontinued. If there is incident opioid use disorder, opioids must be discontinued and pharmacotherapy for opioid use disorder should be offered and initiated. And then finally, hazardous drug or alcohol use that the patient cannot discontinue and/or will not accept treatment for, opioids should be discontinued. We’ll get into the details of this a little bit more.

So when it comes to prohibitive harm, and this is, you know, clear and imminent danger, the taper should be fast. For example, 25% per week, or even per day. If you’ve recently prescribed the patient a supply of medications, you could consider advising a taper of that supply if the patient already has on-hand, meaning you don’t write another prescription. Critically important in opioid use disorder, if that’s what’s driving the discontinuation, there needs to be a feasible, accessible linkage to evidence-based pharmacotherapy. We as a system have to be able to deliver that to patients to be providing evidence-based care. And I’ll, my editorial comments is, we need to get better at seizing opportunities to transition patients to buprenorphine. I’ll give you an example. A study done by Gail D’Onofrio and David Fiellin here at Yale, patients presented to the emergency department with overdose. They initiated buprenorphine in their clinical trial in the emergency department and compared that to just giving a regular old referral, hope you can find an outside treater, and not surprisingly but still a big breakthrough finding, the patients who got initiated buprenorphine were three times as likely to be engaged in addiction treatment at the study conclusion.

Another interventional moment that I think we need to capitalize on is patients who are admitted to the hospital with major adverse events. A nice study by Marc LaRochelle showed that patients who came in with non-fatal overdose, admitted to the hospital, 90% were discharged on opioids. We need to have interventions where those folks are getting started on evidence-based treatment for opioid use disorder in the hospital.

So the next scenario when we’re weighing benefit and harm is when benefit is absent or negligible. And this figure is the cycle of pain leading to loss of function, leading to insomnia, stress that can sometimes precipitate substance use and mood disorder, which cycles back on the pain. And, you know, though we’ve all had patients with this complicated cycle, I still want to say it’s, perhaps, 10% of patients. But this is a scenario where benefit is absent and patients who are on opioids need to be discontinued. So again, if per the guidelines, benefit needs to outweigh harm to continue LTOT and benefit is absent, then the recommendation is to taper. And here’s the statement that may be a little controversial, but if the patient disagrees with the assessment of absent benefit, our role is to try to educate them and try to express to them our observations of their declining function. But they may not end up agreeing with that, and a unilateral taper decision may still be necessary. You know, I think there’s sometimes a feeling, as a prescriber, that I know this patient isn’t doing well, but opioids are all they have. Or the patient may say this is the only thing that’s working for me. But what we’ve learned is that, you know, it’s not that the opioids are helping them be even more miserable. It’s that the opioids might be making them miserable. And so if they’re really having no benefit, we need to taper them off.

Category that we encounter a lot in our referral clinic, and that is patient who is doing reasonably well who is on high-to-ultrahigh dose of opioids. This is a patient who has decent, non-declining function, who’s on a high dose, no apparent harm at this very minute, but risk is accumulating by the day because there are harms that are accruing over time, like osteoporosis and hypogonadism, and as patient ages, their risk of overdose increases as well. At the present time, my recommendation here is to bring to bear all the resources at your disposal to help the patient to choose to initiate a taper. In other words, an involuntary taper in this scenario is not recommended. However, you should have increased vigilance for opportunities to lower the dose, especially for a patient who is newly entering the system. You know, they come in on 200 milligram morphine equivalent. You can do a patient-centered biopsychosocial evaluation and agree to take over their opioid prescribing, but you can say with that first prescription I’m going to write for you is going to be at 25% less, and we’re going to see how you do with me supporting you. And then, if you also increased vigilance for evident harm that is tipping the balance towards a necessary taper. Meaning, there’s something that’s evolved in the patient’s medical care that means that harm is now prohibitive. And this would be say, for example, a patient who gets a sleep study and they have newly diagnosis severe sleep apnea, that would be an indication to lower the dose. So it’s important to frame the low-benefit conversation in a patient-centered way. An empathic tone, expressing concern. I recommend talking about the shared responsibility, but also bringing in optimism. So an example: we know more about safety problems related to opioids and we’re concerned about your health and safety. We recognize that we or the system prescribed you these medications, so now we want to help you be safer while still managing your pain. The good news is, many patients feel better once they’re on lower doses.

So as Travis had already mentioned, when it comes to tapering or discontinuing in low benefit, there’s fairly limited evidence to guide us. Joe Frank’s systematic review, and his prior work, his qualitative work, showed that patients report increased willingness when offered empathy, support, reassurance, and a team-based approach. Other recommendations and my own clinical observations: if you are to offer choice and flexibility when possible, for example, which medication would you like to decrease first? Which dose of the day could you most easily lower? And in the case of low benefit as the reason for taper, there’s almost no such thing as too slow of a taper, meaning if the patient’s willing to drop down even, you know, 4%, even, you know, 15 milligrams of MS Contin when they’re on 400 milligrams, that’s still an important step, and that’s fine. Because what I’ve found is success in each step-down breeds success. Come back and say that wasn’t as bad as I thought, and the next month we do another 15 milligrams. And offering the patients the option to pause, if needed. Meaning, you know, they’re, they’ve taken a couple steps toward their tapering successfully, and they come to you and say I’m okay with the long-term plan. I’m just having a bad month, or a bad two weeks. It’s okay to pause in this low-benefit situation. So Travis already mentioned Joe et al.’s finding, or I should say Dr. Frank et al.’s finding, that in the fair or good quality studies, patients’ post-tapering outcomes were improved in terms of pain severity, function, and quality of life. And critically important is that Travis also eluded to is that in the studies where successful tapering was evident, there was also evidence-based high value chronic pain care that was delivered. Patients were getting what we consider the gold standard. They were getting a multimodal care plan. Putting behavioral therapies, physical activation, and rational pharmacotherapy, all the while promoting self-management and self-efficacy, all typically in an integrated health system such as the ones we have in the VA.

And what were the evidence-based non-pharmacologic treatments that were employed? A variety, and I can say with excitement that there’s the evidence-base for these modalities is already fairly well established for the underlined therapies, and growing for the rest. And really becoming evident that, you know, combining treatments, empathizing with non-pharmacologic is the way forward.

There are non-opioid pharmacologic options: NSAIDs, acetaminophen, the gabapentanoids, the SNRIs, topical therapy. It’s important to note that while we may be pursuing some of these therapies to avoid opioids, still have to recognize that many of these medications have neurocognitive side-effects and we need to observe best practices in med management of these medications as well, including starting low, going slow, and monitoring patients for side-effects.

Optimizing co-occurring conditions is also part of pain, high value pain treatments. Major depressing, anxiety, other mental health conditions, diabetes, obstructive sleep apnea and other chronic medical conditions, and of course substance use disorders.

Now, I know the primary care providers on the line are thinking about how difficult it is to do a taper when you’re, sort of, a one person show. And it’s really coming out in the literature that having team-based care and collaborative care may be exactly what’s needed. In our qualitative work, we’ve heard from PCPs that they strongly endorse a need for support and tapering. And there is this emerging model of the integrated pain team model, that’s one of the emerging models, multidisciplinary in nature. There’s time and space for more in-depth assessment and closer follow-up. There’s the biopsychosocial orientation. And these teams tend to assume pain care responsibilities on a time-limited basis. There is some early evidence that these teams are not only effective in managing chronic pain, but they’re also good at dose-lowering (San Francisco VA and here at VA Connecticut). Another model that is similar to IPT, collaborative care. This is where a pharmacist or an RN care manager collaborates with a single or group of PCPs, perhaps a bit of a narrower model than IPT; similar biopsychosocial orientation. And because all the multimodal care isn’t in one group, there is more reliance on referrals for multimodal care.

One example of a study we’re undertaking that is a collaborative care model is the primary care integrated pain support program. It’s part of our improved query. I’ll sort of, in the interest of time, move through this quickly, but basically pharmacists collaborate. We send letters to patients who are identified on high-risk regimens. Ideally Veteran receives the letter, brings it to primary care, primary care places the consult, and pharmacists receive the consult, engages the Veteran in treatment of helping them achieve dose-lowering goals and helping them engage with non-pharmacologic pain treatment. We’ve got some nice preliminary qualitative findings on how facilities have found this program helpful.

Just wanted to quickly mention, we’ve got the IPT model, we’ve got the telecare collaborative management model. We do have a study that’s underway, Erin Krebs overall TI, to test these two models against each other on the primary outcome of improvement in pain-related functional interference, but secondary outcome of opioid dose reduction. And then among patients on high dose therapy, we’re also going to test optional rotation to buprenorphine to help patients get on lower opioid doses.

So in summary of my remarks, opioids should be tapered and discontinued when benefit does not outweigh harm. We need to carefully and frequently assess benefit and harm. When to taper: if there’s prohibitive harm; if there’s absent benefit; when there’s decent function but at a very high dose. I think scenarios one and two can be involuntary if necessary. Three should only be voluntary. How to taper: the speed of taper should be guided by the degree of current harm; it should offer options when available; should always be patient-centered; collaborative; and bolster other multimodal treatment. And given the amount of work that this is, the emergence of models of care that support primary care are shown to improve tapering rates.

And so thank you. I’d be happy to take any non-marijuana related questions. That’s actually a joke. Happy to talk about marijuana, and there’re my references. And lastly, some resources. The dose calculator, the VA opioid guidelines, CDC has some great tools out there that are worth looking at. And then our own VA PBM also has some really good tools from the academic detailing service. And I think I’m done.

Heidi: I love how you tell them you’ll take marijuana questions when they have literally four minutes left. You know I’m just going to get slammed with marijuana questions now. So I’m just going to start at the top with what I have. They’re non-marijuana questions, then we’ll work our way down. Our first question for Dr. Lovejoy: Can you comment on problems with trying to use problem list of OID or SUD for research? How often is OUD diagnosis appropriately documented in chart. Perhaps because of not screening for false negative, or misuse of diagnosis, false positive, physical dependence and not OUD?

Dr. Travis Lovejoy: Yeah, that’s a great question and I think that Will commented on that a bit in terms of, you know, what clinicians see in terms of patient behaviors, and what the Diagnostic and Statistical Manual, the DSM, has listed as criteria for opioid use disorder. So a lot of times the behaviors we see in patients aren’t necessarily mapping perfectly onto the DSM. However, opioid use disorder may be a very appropriate diagnosis. So my suspicion is that it is, in fact, underdiagnosed and thus not listed in the problem lists or medical record to the extent that it probably should be. So I agree completely. That’s a bit of a concern in terms of trying to identify individuals with opioid use disorder.

Heidi: Thank you. Regarding likelihood of discontinuation for UDT, urine drug testing, what about missing prescribed opioids?

Dr. Travis Lovejoy: Yeah, we were, that’s exactly right. So we also coded for failure to show opioids in the system. That should be there. However, that wasn’t one of the criteria that we examined in that particular study because we were interested in referrals to substance use disorder treatment, and we found that in our work, that it’s less common that clinicians would make referrals, or that it may not even be appropriate to make referrals because opioids are absent in the system. A lot of times what we were finding is that there was suspicion of diversion, or in more commonly diversion rather than overuse, for opioid use disorder.

Heidi: Thank you. If mean pain scores did not differ before and after discontinuation, what did LTOT treat exactly?

Dr. Travis Lovejoy: There’s a risk/benefit. What was Will’s, the number one in terms of, or I guess that was potentially number three, right? Individuals, or no, whether there was not improved functioning. So that was, I think, one of the issues. Are we seeing continuance of long-term opioid therapy, even in the absence of improvements?

Heidi: Thank you. Can you provide guidance on how reliable urine drug screens are for evaluating medication adherence? I have several patients that I have initiated de-escalation of therapy due to negative drug screen. Meds I’m expecting to be there, not showing up, but I’m concerned about the limitations of these tests.

Dr. William Becker: I can take that one. So if your screening assay’s going to be an enzyme-mediated immunosorbent test or EMIT, if you get a negative on the EMIT test, your screening test, of something you’re prescribing the patient, I would run a confirmatory test because you want to be sure if you are going to potentially discontinue therapy that there really is no evidence of that substance in their urine. The other part I would say is, you want to make sure you’ve asked the patient when the last time it was they took the medication. If they say, well it was 10 o’clock this morning, you’re doing the test at 1pm, and there’s no evidence of that substance in screening or confirmatory test, then that is, that’s our evidence that there is potentially diversion going on.

Heidi: Great. Thank you. We are at the top of the hour here. Right now I have 6 pending questions. I’m not sure if you two have time to stay on and answer a couple more, or if you want to handle these off-line, or what you would prefer to do.

Dr. Travis Lovejoy: I’m happy to stay on for 10 or 15 minutes.

Dr. William Becker: Yeah, as am I. I have time.

Heidi: Okay, perfect. So for in the audience, if you have a pending question, I’m going to try to get to what we have here. We are recording the session, and so this will be available in our recording. So if you do need to leave, please come back and listen to the recording. We will have the information for you there. The next question here for Dr. Becker: Please comment on use of STORM report in assessing risk. STORM gives one and three-year predictions of accidental overdose or suicidal-related events. Could these odds help in making case for starting small, gradual taper sooner rather than later, for those who think they are doing well on high-dose opioids.

Dr. William Becker: Yes, the STORM, for those of you who aren’t aware, you know, it’s a informatics tool that calculates risk. Well, I guess the question already included that, but I think it is, you know, I’m just trying to see how it might impact based on the recommendations that I gave. I mean, the STORM’s going to see someone on high-dose greater than 90 milligrams morphine equivalent as at high overdose risk. I think it may be useful in bringing some objective, sort of, data to the discussion. And I think some patients, that resonates with some patients. So in that way, yes. And I will, on the flip side of that, raise the caveat that many patients are not very concerned about their overdose risk. And that’s why I mention quickly tailoring potential benefit to the patient of a taper to their particular life goals. If they say they want to play more with their grandkids, and you say, you know what, I actually think on a lower dose, you may find yourself more alert, and more willing, and more able to do that. So while on the one hand, the overdose risk calculation will be meaningful and important for some patients, certainly not all.

Heidi: Great, thank you. The next question, also for Dr. Becker: For the PIPS pharmacist, assisted taper of opioids, please discuss some factors as to why there’re so few letters of offer of pharmacist taper or acted upon by Veterans. What might improve PIPS usefulness?

Dr. William Becker: Yeah, that’s a great question, and our team was having that very conversation just this week. You know, we had this vision that the letter would arrive, the patient would think, hum. The letter’s actually quite, it’s not meant to be provocative at all. It’s meant to say we’re concerned about the medication regimen. We’ve got a program that can help you and it’s going to support you. So we wanted to invite them to at least raise the subject with their primary care provider, and that would fuel the placing of a consult. And, you know, early days it’s looking like it’s not working. So, you know, we’re going to explore some other options. We’re considering making the letter a little more, I’m looking for the right word, a little more provocative. We’re considering really just promoting primary care providers access to just placing the consult, whether or not the Veteran has received a letter. But I agree, that low yield is concerning, and we’re looking into it.

Heidi. Great, thank you. The next question here: In the study looking at TCM versus IPT, if TCM is reaching out to other disciplines for assistance, how are these groups different?

Dr. William Becker: How are they different? I think that questioner is saying, well, it’s more or less, if it’s a pharmacist making referrals to specialty care rather than a team that’s all there together. That isn’t particularly enough of a difference to be worth studying. Not to cast it in too negative a light. That actually is quite a substantive difference because most of the management, if almost all of the management done in the TCM arm is over the phone, and then IPT is almost, well, a much larger proportion, it’s going to be in-person. And IPT is much higher resourced. So it’s really asking the question, how well resourced a team is necessary to manage pain effectively, and also lower opioid dose?

Heidi: Thank you. The next question here. The questioner is wondering if either of you know of any peer-reviewed resources that talk about the role of non-prescribing clinicians, especially psychologists, in treating SUD opioid use disorder?

Dr. Travis Lovejoy: You know, if the caller’s online, I think that if, I think that there’s copious literature on some of these, as Will indicated, some of these nonpharmacologic approaches to treating opioid use disorder. I think that if the caller’s on the line, they can email me directly at travis.lovejoy@va.gov and I’d be happy to share some of those. Will, I don’t know if you have any off the top of your head you could point this person to?

Dr. William Becker: I just, gosh, I mean I know studies where psychologists and other non-prescribers for major interventionists, but not a sort of review of roles. So no, not off the top of my head.

Dr. Travis Lovejoy: Yeah, that’s my though as well. I would be sending the audience member some citations for studies that are showing various psychotherapeutic approaches for patients with substance use disorder and chronic pain, or opioid use disorder more specifically.

Dr. William Becker: Yeah.

Heidi: Okay. Thank you. Next question here: Have you used survey questionnaires post [inaudible 1:05:46 to 1:05:48] perception of patients on the effectiveness of nonpharmacologic treatment options?

Dr. Travis Lovejoy: Heidi, you cut out. Could you repeat the question one more time please?

Heidi: Sure. Have you used survey questionnaires post-discharge to evaluate the perception of patients on the effectiveness of nonpharmacologic treatment options?

Dr. Travis Lovejoy: I have not yet done that work, no. And by post-discharge, I’m not sure if the person is meaning post-discontinuation, or maybe post-discharge from some type of multidisciplinary program that sends there, but no, I have not done any work on either of those looking at the effectiveness of non, or patient perspectives on the effectiveness of nonpharmacologic approaches.

Heidi: Okay, thank you. And the last question that I have here: Were PTSD and psychotic spectrum disorders statistically significant predictors of increased risk for SI post [unintelligible 1:06:52]?

Dr. Travis Lovejoy: Yes, they were, yeah. Those were the two mental health diagnoses; depression, bipolar disorder. Other anxiety disorders were not, but PTSD and psychotic spectrum disorders were the ones that stood out and were statistically significant.

Heidi: Okay, fantastic. That wraps-up all of our questions. Travis, Will, do either of you have any final remarks you’d like to make quick before we wrap things up here?

Dr. Travis Lovejoy: Thanks everyone for joining.

Dr. William Becker: Yeah, thank you.

Dr. Travis Lovejoy: Hope it was helpful.

Heidi: And I want to thank both of you for taking the time to prepare and present today. We really, really do appreciate it.

[ END OF AUDIO ]