Pain and Addiction - Salsitz

Fri, Jul 21, 2023 10:36AM 34:41

SUMMARY KEYWORDS

opioids, patients, opioid use disorder, pain, prescribed, people, addiction, chronic pain, years, problem, prescription opioids, chronic opioid therapy, cdc guidelines, buprenorphine, tapering, asam, guidelines, sickle cell disease, medications, taper

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00:01

This presentation is entitled Pain and Addiction: Trends and Treatments. I will now turn it over to Dr. Edwin Salsitz to begin our presentation.

00:09

Good morning, everyone. The topic I'm going to speak about today is Pain and Addiction: Trends and Treatments. I'm Dr. Salsitz. I'm an addiction medicine specialist. I work in New York City at Mount Sinai, Beth Israel. Should you have questions during the presentation, please enter them into the chat. And I will answer them during the presentation.

00:33

The topic of pain and addiction has evolved over the years. I have no financial disclosures by the way. And the evolution has to do with moving from prescription opioids on to heroin and fentanyl. And so the topic has been presented differently over the years. And I'll try to give you some feeling for that as we go along. But all healthcare providers have been struggling with trying to provide adequate pain relief yet avoiding problems with opioids such as addiction or misuse. And it has not been a simple task over the last 30 years or so.

01:14

And we'll start with the epidemic of untreated pain. So now we're going back to 2011 or 2012, when an important article was published in the New England Journal of Medicine, from the Institute of Medicine, and it reported that many Americans, even 1/3 of Americans have chronic pain that lasts for weeks, months to years, and that this was a very expensive proposition, and that some physicians or other health care providers were over-prescribing opioids, while others refuse to prescribe any opioids. And there was a recognition that there was a lack of education on both the providers and the patients. And that the type of pain that we were talking about was chronic noncancer pain, which included headache, low back pain, neck pain, joint pain, and fibromyalgia.

02:03

And this slide really depicts what this prescription opioid epidemic was all about. This is only one decade 1999 to 2010. And there was a quadrupling of sales of prescription opioid medications, a quadrupling of opioid overdose deaths, and a quadrupling of patients admitted into treatment with opioid use disorder. So this epidemic really began about 10 years before- before 1999 and has morphed and continued up to the present time.

02:35

And I'm sure in the previous lecture on opioids, you were- you were shown this slide, but I thought I would just emphasize a couple of points: that the the opioid epidemic began with prescription opioids, and then it segued into heroin, in approximately 2010. But at that time, when people started using heroin, about 80% said they had started with prescription opioids, that was the first opioids they were exposed to. And then we had the change from heroin to fentanyl in 2013, which is an ongoing problem. And the fourth wave is sometimes called the increase in cocaine and methamphetamine use.

03:19

The- the opioid problem was different in America than other places. This is a look at the amount of opioids prescribed for inhabitants of a country. USA is over here on the left side, a real outlier in terms of the number of opioid prescriptions prescribed compared to other countries. And this has a number of different meanings. These other countries that have well established healthcare systems... in western Europe, they don't prescribe as many opioids and yet they have people who are satisfied with their health care. On the other hand, way over on the left-hand side, we have countries that have very little opioids to be prescribed. And one of the reasons they say for that, is that they don't want to happen in their country, what happened in America with the prescription opioids. Unfortunately, the negative unintended consequences there is- that there are people in these countries who really require opioid analgesia, let's say for end-of-life care, and they're unable to access that medication because of the restrictions in those countries.

04:27

So how did all of this happen? How did we get to where we are? And many people point to this letter in the New England Journal of Medicine, which was published in 20, in in 19, in 1980. Long, long time- 1980- a long time ago. And this is simply a five-sentence letter, pointing out that these researchers had looked at something like 40,000 patients who were admitted to Boston hospitals, about 12,000 received some limited dose of- of- of an opioid or narcotic as they called it back then. And yet they were only able to find four cases of the development of addiction out of these 12,000 exposed patients. And so the conclusion was that widespread use of narcotic drugs in hospitals, the development of addiction is rare in medical patients with no history of addiction.

05:23

So what happened was that somebody published this article in the New England Journal of Medicine in 2017 looking at the number of times this one letter was cited in the literature, and was it cited as

2017 looking at the number of times this one letter was cited in the literature, and was it cited as affirmational? In other words, reinforcing the idea that chronic opioids do not lead to chronic- to addiction problems, or was it was cited in a negative way, saying that there could be problems? And you can see this is 1981 to 2017. That over the years, it was mostly affirmational, the number of citings saying that, yeah, opioids don't cause a problem. And then as the years went by, and we saw the problem that did develop, there was some increasing negative citations.

06:10

So from 201- from 1980, to 2017, there were 688 citations of this one letter. 75% used that as evidence that addiction is rare in chronic opioid therapy. When they looked at other letters published in 1980, they were cited an average of 11 times. So this really was an outlier situation with this one letter. And that was part of a perfect storm.

06:39

Included in the perfect storm was the introduction of oxycontin, and I'm sure you've all followed the Purdue pharma case and the Sackler family, etc. Pain became a fifth vital sign. So now if patients said, "My pain is an eight or nine," it had to be addressed somehow. And there were many publications indicating that chronic opioid therapy for chronic non-cancer pain had a very low risk of addiction. The numbers cited many of these excellent that time papers, something like three or 4% of patients might have a problem. Many of the thought leaders at the time had significant financial and pharma conflicts with the companies making the opioid products. The patient satisfaction surveys came along at that time, and there were at least four questions relating to how was your pain managed. And there were articles at that time that suggested that healthcare providers- their salaries were sometimes tied into the satisfaction survey scores they got. So that that would lead them to want to prescribe opioids so that they would get a better satisfaction score.

07:48

Physicians was successfully sued back then for not treating pain. And while all this was going on, there was no really good evidence for long term effectiveness of chronic opioid therapy for chronic non-cancer pain. And what people said, and I certainly believed back then, was that if you took chronic opioids, you would become physically dependent, but you would not become addicted if you didn't have any risk factors. And if you wanted to stop, it would be a simple matter of tapering.

08:19

And that did not turn out to be correct. So here's 2001, a long time ago, a physician in California was successfully sued for $1.5 million for not treating pain adequately. And then we skip 20 years in the future. And we have a physician sent to prison for 40 years, prescribing tremendous amounts of opioids, including the death of one of his patients.

08:47

And one of the very significant problems depicted in this article is that the 16% of Americans who

have mental health disorders receive over half of all opioids prescribed in the United States. And it became well known that if you had psychiatric problems, you were more likely to misuse opioids or that was a significant risk factor for misusing it. And this phenomenon was termed "adverse selection," that it was particularly the people or the patients who would have the highest risk of misuse, of developing an opioid use disorder, who were being prescribed the most opioids in the development of this opioid use disorder epidemic.

09:29

Two slides on benzodiazepines, and that is from the FDA. This advisory from the FDA came out in 2016. And they pointed out that the combination of benzodiazepines and opioid analgesics pose a problem in terms of increased respiratory depression, and that providers should try not to use them in combination, and if they do to be very, very careful and diligent on how they use it. And I think that both the benzos and the opioids received Black box warnings about this combination.

10:04

On the other hand when it came to treating opioid use disorder, this is a announcement that came out a year later in 2017. It's got a lot of text on it. But the point of this one was to say that in patients with an established opioid use disorder, who are also using benzodiazepines, do not- do not withhold methadone or buprenorphine treatment, because of the benzos. And they pointed out that the risk of death from the ongoing opioid use disorder was more significant than the combination drug interaction.

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So there were- there was a large reaction as this opioid epidemic kept going on. And what were the intended and unintended consequences to this prescription opioid epidemic? Well, the PDMPs were established. They've only been around for about 10 or 15 years. Now it would be hard to visualize practicing without a PDMP. But back then, nobody thought it was needed or useful. Now, there were limits placed on the quantity and dosage of opioids prescribed for acute pain. This was done by by states, putting different dosage limits on how much could be prescribed initially. And urine drug testing became the standard of care. Not so much in addiction medicine, where it always had been, but in pain clinics. Prior to that, urine drug tests were not commonly done on patients receiving opioids for chronic pain.

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There was a massive attempt at education of prescribers. The FDA established these REMS courses on safe and effective opioid management. CDC guidelines came out, we'll talk about that too. Got two- two sets of guidelines have come out so far. And then there was an emphasis on tamper resistant/abuse deterrent formulations, which sounded like an answer to the problem. Except it wasn't. And it wasn't because most of the overdose deaths that occurred with prescription opioids occurred in people who just took too much of what was prescribed, rather than crushing them and injecting the the opioid medications.

12:18

The other unintended consequence was that patients who were physically dependent on opioids, had been on them for a while for chronic pain... Suddenly, their prescribers decided they couldn't prescribe any longer; they were worried about being on the PDMP. They were looking at the CDC guidelines and taking the wrong conclusions from them. So now many people were left in the lurch. They were physically dependent, they were in withdrawal, they couldn't get a prescription opioid. Heroin was available at that time, this is in 2010, it was cheaper and easier to get than an oxycodone prescription. And then, of course, heroin segued into the current ongoing fentanyl epidemic.

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So the efforts at education and getting people to de-prescribe were very successful. There was a dramatic decrease in prescribing of opioid prescriptions for pain. There was much, much increased use of the PDMP, so you could see if people were doctor-shopping. And there was massive efforts at education, and many 100s of 1000s of providers were educated.

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However, there have always been a group of people who thought that there was a miss- misguided view of this whole problem. And they published papers over the years. And this is representative of their point of view. And the point of view was that prescription opioids- prescriptions for opioids have gone down dramatically as represented on this line. Heroin and prescription opioid overdose deaths have remained relatively stable. And yet, total overdose deaths have gone up dramatically, primarily due to fentanyl. And so the argument is that it's no longer a prescription opioid problem, and people should be able to get adequate prescription opioids for analgesia. It's really become a fentanyl problem that's driving the overdose death deaths in America.

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So the CDC guidelines, the first set of guidelines came out in 2016, long time ago, and the second set came out last year in 2022. They overlap significantly. There are some differences which you should know about. There are similar recommendations on opioids: should be the last option for chronic pain, and in many cases for acute pain. So even for acute pain. The new guidelines make the point that sometimes NSAIDs and Tylenol can provide adequate treatment, for example, dental pain. And they say to always start with immediate-release opioids, not extended-release opioids and do it for the shortest amount of time and the lowest effective dose.

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What has changed is the tone of the guidelines- saying that "these are guidelines- just guidelines. Use your clinical judgment, do individualized patient-centered care, as to duration, dose, risk, benefit of chronic opioid therapy to treat chronic non-cancer pain and the need for tapering." In other words, you don't have to taper everyone who are on high doses of opioids. And these guidelines are not to be used by health systems, pharmacies, insurance companies, medical boards of governments to

determine standard of care. Because what was happening with the 2016 guidelines is that many insurance companies and medical boards were using that as a standard of care. And any provider who deviated would come under some sort of investigation. And that was not the purpose of the guidelines. So- so there were some significant changes from 2016 to 2022.

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In both guidelines, they recommend starting with non-pharmacologic therapy. Here you have a list of some of the evidence-based non-pharmacologic therapy. The problem with these treatments is that they're hard to access. Insurance sometimes doesn't cover them. And so they're easy to talk about in a lecture, but often not easy for patients to be able to access.

16:16

If non-pharmacologic therapy is not working, then they say non-opioid pharmacotherapy. And there's a whole list here, I won't go through all of it. The NSAIDs however, the NSAIDs come with significant adverse effects, particularly in elderly people, people with more medical comorbidities. Some of the antidepressants can be used for neuropathic pain. There are drugs that are approved for fibromyalgia. anti-depressant drugs and anticonvulsant drugs...very often pain and depression go together. So some of these drugs can treat both.

16:51

Topicals... lidocaine patches... there's an NSAID topical now: capsaicin. Muscle relaxants are a blurry kind of category. Exactly the what- their mechanism of action is is not clear, but certainly for some patients baclofen and cyclobenzaprine can help. Avoid benzodiazepines as muscle relaxants because of their misuse potential. And the same thing with this medication called carisoprodol.

17:18

Ketamine, ketamine is being used now by pain physicians for acute pain, particularly from what I've seen in the emergency department. So that's an option to keep in mind. And interventional procedures. Some of them have evidence, some of them the evidence is very mixed. There's increasing evidence for neuro- neuro- neuromodulation or spinal cord stimulation. So certainly that's an emerging topic.

17:46

One slide on gabapentanoids, because they're being used more and more. Most of the use of gabapentanoids, and we're talking about gabapentin and pregabalin, are used off-label for any variety of different medical ailments. And we use them a lot in addiction medicine in trying to avoid opioids and benzodiazepines. However, they have significant misuse of gabapentanoids, particularly among people on either methadone or buprenorphine. And there's a reasonable literature supporting that. But even at therapeutic doses, there can be significant adverse effects from gabapentanoids.

They're renally excreted so renal function has to be accounted for. Generally, death is uncommon, but it's increased in combination with opioids. And again, there have been a number of papers substantiating that issue as well.

18:38

Gabapentin is not scheduled federally, so it's not on most PDMPs. Pregabalin is a schedule five. So it's listed and some healthcare facilities are now testing for gabapentin on the urine drug screens.

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So if all of that fails, you get to opioid pharmacotherapy. Generally, that's indicated for acute pain, like post-operative pain, maybe in- in burn patients with severe trauma. But again, limited duration. In New York state, seven days is the max you can write for the first prescription for- for an opioid. Sickle cell disease was added this year... on the guidelines and 2022 to the exceptions to opioid prescribing. So sickle cell disease, cancer pain, palliative care, hospice, end-of-life care are not included in the CDC guidelines in terms of the opioid restriction information. And I'm very pleased that sickle cell disease was added. Those of you who treat sickle cell disease know that it is a very complicated disease and pain is a severe pain, a feature of sickle cell disease, and certainly opioids are required, and there is no evidence does this increase addiction problems or misuse in patients with sickle cell disease.

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Then we get to the most vexing category and that's chronic opioid therapy for chronic non-cancer pain. And this is where really the opioid epidemic began, and then segued into the heroin, fentanyl.

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And the question is "how effective is chronic opioid therapy for chronic non-cancer pain? How safe is it? What are the adverse effects? And what about immediate release versus extended release?" So the NIH commissioned a panel to look at the effectiveness of chronic opioid therapy for chronic non-cancer pain. This was way back in 2015. And the conclusion was, evidence is insufficient to determine the effectiveness of long term opioid therapy for improving chronic pain and function. Evidence supports a dose-dependent risk for serious harms.

20:43

But let's say you are going to initiate opioid therapy. So this comes from a paper by Dr. Chou and also is an agreement with the CDC guidelines. And I'm not going to read all the material on the slides, except to say, if you're initiating opioid treatment, think of it as a therapeutic trial. It may not have to last very long if it doesn't work out. And look for functional improvement. I think we all recognize that the visual analogue scale of saying "my pain went from a nine to a seven" is so subjective, what does it really mean? So we're looking for functional improvement, back to work, back to school, school,

back to family activities, etc. And we want to keep our eyes open for problematic behavior. So we're going to monitor patients, going to look at the PDMP, going to check urine, drug toxicology, and all of those things are recommended in the CDC guidelines.

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If you're going to start opioids and continue opioids on patients, you have to know how to taper them, and that that is represented here by "can you land the opioid plane", and obviously this student could not land the plane.

21:54

So opioid tapering, it depends. Does the patient request or agree to the opioid tapering or is the patient resistant? If they're resistant, it's going- not going to be very easy. And what are you going to do about pain? If the pain is still present, after you taper the opioids, you can use the alpha 2 adrenegic agonists clonidine, lofexidine to help during the taper with some of the withdrawal signs and symptoms.

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Maybe if you're- if you're- feel comfortable with methadone, you can switch to methadone and taper with that or switch to buprenorphine and taper with buprenorphine. You always have these comfort medications that can help people over some of the bumps and the tapering. But patients who do tape,r not even completely off but reduce their dose significantly- Most report favorable outcomes after tapering, including decreased pain.

22:42

And this gets into a topic that we don't have time to get into, which is opioid-induced hyperalgesia. A counterintuitive concept that, as you increase opioid doses, the body now becomes more sensitive to pain, and pain increases rather than decreases, and decrease the opioids, pain may decrease.

23:03

So again, going back to that evolution of the opioid epidemic, many patients were left in the lurch because now they went to their provider. And their provider says "No, I can't prescribe because of the guidelines." And these are the folks who unfortunately had some of them very bad outcomes.

23:20

And so the FDA came out in 2019. And they said, "Hey, we didn't say that you should taper everybody off opioids." And there can be serious adverse effects of doing that. These include withdrawal symptoms, uncontrolled pain, psychological distress, suicide, and there have been at least 12 papers now, going over this topic.

23:41

This is one representative paper showing overdoses, opioid overdoses of people have been tapered either off or too quickly. And these are mental health crises or mental health admissions, including suicides, which go up dose-dependent with how quickly they were tapered. The faster they were tapered, the more likely they will have to have problems. So tapering events were significantly associated with increased risk of overdose, and mental health crisis.

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And then Health and Human Services came out with a directive in 2019, and said, "Hey, the guidelines never said that you should discontinue opioids if the benefits are outweighing the risks. Don't worry about the morphine milligram equivalents as long as patients are doing well. And whatever you do, don't dismiss the patient from your care." And these concepts were reinforced and incorporated into the 2022 guidelines.

24:36

One slide on cannabis cannabinoids. You're going to have a talk on cannabis and I'm anxious to see what the speaker says in terms of cannabis and pain. This was the national national... the National Academy of Medicine came out with this monograph in 2017, I think, and they acknowledged that there are FDA-approved cannabinoid products like, like marinol, which are which are approved for chemotherapy-induced nausea and vomiting, some forms of cachexia. There is a multiple sclerosis medication not not approved in America but in Canada, which is sublingual. And that helps people with spasms for muscular- for multiple sclerosis. But here's a conclusion: For these conditions, the effects of cannabinoids are modest. For all of the conditions evaluated, there is inadequate information to assess their effects.

25:29

Just one para- one sentence here on... many states have have approved medicinal marijuana or medical cannabis for opioid use disorder. There are no trials that confirm that it's effective for that. And so that's very controversial. And also there's conflicting data over the years now, whether in states that have either medical, medicinal cannabis or have recreational cannabis, that opioid overdose deaths have gone down. There was an initial report in 2013 that did say that. But that has been brought into question now. And further data and analyzing of the data has shown that no, if anything, the opioid overdose deaths have increased in states with more liberal cannabis policies.

26:18

Another issue with opioids, particularly prescription opioids, is that people don't use as much as used to be prescribed. I mean, it was very, very common. You go to the dentist for a dental extraction, you walk out with 30 percocets, which you didn't need. So this looks at all these different types of surgery, and about 70 to 80% of the opioids given to people on discharge were never used.

26:41

And so that gets into the issue of how to get rid of the opioids, which used to be a problem because especially teenagers will go through medicine cabinets, and find opioids and other medications that they would overdose on. So the DEA has take-back programs- Just bring back the medications, no questions asked. There was some other pharmacies, police stations take it back. You can mix it with cat litter and throw it out in the trash. You can flush it down the toilet. Fentanyl patches have to be flushed down the toilets. What you're not supposed to do is throw it away in the trash with the label on them.

27:16

And naloxone. I also included nalmefene, which was just approved- a longer acting opioid antagonist, which is coming out in a nasal spray. Whenever opioids are prescribed, a patient should be given access to naloxone and taught how to use it to reverse a potential overdose.

27:35

In finishing up I want to talk about this intersection between chronic opioids, chronic non-cancer pain, and the development of opioid use disorder or opioid addiction. And I call it the ASAM niche because I think that ASAM providers are uniquely qualified to determine "Am I dealing with a case of opioid use disorder, or a pain case kind of gone bad or not treated appropriately."

27:58

And pain and addiction overlap to a large extent. Here's a definition of pain: multi-dimensional kind of problems, sensory, emotional, cognitive, developmental, spiritual, etc. And a similar definition in this is the ASAM addiction definition that again, it's multi dimensional; in people it's not just one thing, but involves many components of their life.

28:21

And if you look at people with chronic non-cancer pain, like fibromyalgia, or addiction, they have many of the same comorbidities, some of the psychiatric comorbidities, and other comorbidities. Both in pain and addiction, we don't have very objective biomarkers like we do for hypertension or for diabetes.

28:42

I'm just including this slide to show that I keep up with the current literature. This was published only a couple of weeks ago. And there's increasing imaging studies now that are able to detect when people have chronic pain, the level of their chronic pain. So hopefully in a year or two, we will have

more in the way of objective biomarker evidence. When people say that I have my pain as a seven, we'll have a way to understand what that means by looking at their brains.

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Sagittal section of the brain, lots of different areas with opioid receptors. We're hoping that when we take an opioid analgesic, the periaqueductal gray, mu opioid receptors are activated to provide analgesia. However, we have the reward system, which you've heard about from Dr. Levounis. It has a lot of mu receptors. It's going to be activated and we have the locus coeruleus where physical dependence and withdrawal are subserved. So when somebody takes an oxycodone pill, the- the opioid is going to go to all these different receptors, and people who were vulnerable to becoming opioid addicted. This is some of the reactions that they might have.

29:55

And I always ask new patients with opioid addiction "What did it feel like the first few times you used an opioid, doesn't matter whether it was heroin or an oxycodone pill." And these are verbatim responses from people. Now, I haven't embellished them, haven't changed them. But imagine if you took an oxycodone pill. And you said that "I felt relaxed for the first time where I feel like I forgot about all the sexual abuse." "Everybody always says I was energized," which is counterintuitive for an opioid. So if you like an opioid, you probably have some vulnerability to becoming to be developing a problem with opioids.

30:32

This is another problem that you know, is an ASAM kind of situation. Treating pain in the addicted patient- that's complicated, particularly if the addiction is to opioids. But we have to find the solution to it. And the reason is what's highlighted in the- in the orange text: that untreated pain is a trigger for relapse. So patients are going to find an opioid if you don't provide them with one, if they need an opioid for their pain. So address both pain and addiction. And the bupe formulations approved for opioid use disorder, the sublingual tablets and films and now the subcutaneous depo can work for that.

31:07

And there's evidence that they- that the those these formulations can be effective for both pain and addiction. Usually, when it's used that way, it would be given q.i.d. or t.i.d. rather than just once a day. And if there are significant others, that can be very helpful in terms of securing and dispensing the medications. So you don't have to worry so much about by not taking the medication properly.

31:32

In terms of people with pain, who have gotten to needing an opioid. I think the buprenorphine formulations that are FDA-approved for pain but not for opioid use disorder are a very reasonable first choice, particularly something like the transdermal patch, or the buccal film which is taken twice a

day. These are not approved for the treatment of opioid use disorder, and they cannot be used off label to treat opioid use disorder. Whereas the medications, the buprenorphine formulations approved for opioid use disorder, can be used off label to treat pain.

32:08

A lot of text on the slide making a simple- simple point. This was looking at people who are on schedule two opioids for chronic pain, who rotated to buprenorphine, and most patients found that their pain was improved on buprenorphine. They felt better on the buprenorphine. So this is a very reasonable thing to think about as well, to go from a full agonist to a partial agonist, if you're treating chronic pain that does require opioids.

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So physical dependence does not necessarily equal addiction. And there are some people who have been placed on chronic opioids who have physical dependence, have no no further pain, don't want to be on the opioids, don't like them. But every time they try to taper off, they develop withdrawal problems and they can't get past it.

32:59

And Dr. Ballantyne, a noted researcher, has called this complex persistent prescription opioid dependence. And many of these patients may have to be maintained on something like buprenorphine, even though they no longer have pain,

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Aberrant or problematic behavior does not necessarily equal addiction. There may be good reasons why a patient ran out early or took more than was prescribed.

33:23

And chronic pain does not necessarily equal suffering. I think it's the people who suffer with their chronic pain, who are most likely to run into problems with opioids. Because the magic of opioids really is the relief of suffering, I think, more than the relief of physical pain itself.

33:40

So there's been this evolution on opioid prescribing. A long time ago when I was in medical school opioids were hardly ever prescribed except in the hospital. People call it opioid phobia. Then we went into this massive opioid philia, which has been going on for about 30 years now. And now I think we're at opioid cautious where we're going to prescribe opioids sometimes, but we're going to be very diligent about doing it and very, very determined about monitoring it closely.

34:08

"To have great pain is to have certainty to hear that another person has pain is to have doubt." It's shameful, but I think that that is such a true statement. "Physical pain does not simply resist language but actively destroys it." "Morphine is God's own medicine. We can't live without opioids. We have to learn to live with them." And good luck on the exam. I'm willing on ASAM here's my license plate- ASAM MD. I hope this was interesting and enjoyable. Thank you for your attention.