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ECHO: CLINICAL APPROACHES TO MEDICAL CANNABIS

Deepika Slawek, MD, MS, MPH

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[video transcript]

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Dr. Deepika Slawek is an assistant professor in the division of general internal medicine at the Montefiore Medical Center, and is board certified in infectious diseases and internal medicine. She provides HIV AIDS care Hepatitis C treatment and general internal medicine care at the Montefiore Medical Center, where she also helped lead the Montefiore Medical Cannabis program. Dr. solid research focuses on improving outcomes and people living with HIV. And she is currently studying how medical cannabis affects pain in this population. He is the recipient of a K 23 award from the National Institute on Drug Abuse to test how different formulations of medical cannabis affect pain and inflammation, and people living with HIV in an innovative quasi experimental study, Dr. Slawek, I will hand things over to you from here.

00:58
Well, thank you for that introduction. And I'm really happy to be here and to be talking about medical cannabis with everybody. I don't have any financial relationships to disclose. And in terms of the learning objectives for today, by the end of today's session, you should be able to discuss some of the historical and cultural context of cannabis regulation in the US that has impacted current policy and practice patterns. And this is really going to focus actually on New York state policy for this talk. demonstrate an understanding of the risks and benefits of using medical cannabis and describe harm reduction principles to patients who use cannabis in clinical practice. As an outline for my talk, today, I'm going to start off with discussing medical cannabis in New York State. Then move on to a brief description of cannabis pharmacology and the endocannabinoid system and therapeutic use of cannabis and cannabis for pain. We'll really focus on that part. And then I'll run through practical integration of medical cannabis into clinical practice. So to start medical cannabis in New York State, it's been a journey. Medical Cannabis initially started to gain traction in the US in the mid 90s. So that was really in California. spurn created by and pushed forward by AIDS activists and people who had other chronic illnesses like cancer and hemophilia. And these individuals really pushed to make medical cannabis available in the state of California. And once that happened, it really just took off. So we have now over the past 25, close to 30 years seen actually 38 not 37 states with legalized medical cannabis laws and 22 states with legalized adult use, also known as recreational cannabis laws. This is old data. But this kind of shows us exactly which state regulated programs exist in the US this is probably pretty up to date, it really changes like every month, it seems. So you can see that this light green kind of sage color our states with both adult use and medical use programs for medical for cannabis. So that's recreational and medical. Those states with this yellow color are states that have a comprehensive medical cannabis program only without the recreational or adult use program. The orange states are states that have only high CBD, low THC cannabis available. And then finally, the white states are states with no cannabis policies in place that are state based. And you'll see that one of the US territories has an adult use program and no medical regulated program. And this really works out to as of 2021, and estimated 5.5 million medical cannabis patients across the country. So this is all just to say that

this is a growing movement. It's rapidly changing, as you can tell, and there are many patients who are seeking it out and interested in it and are likely to ask questions about it. In New York State, this this whole process of changing cannabis laws and legalization has really been started off in 1973, when we had some of the most severe punishments for possession of drugs, including cannabis, and those were with the Rockefeller laws in the early 1970s. And then by the time we got to 2014, we really saw that public opinion and the general data showed that that just wasn't working. So in 2014, the mayor of New York announced the decriminalization of cannabis so that just meant that people who were found with cannabis on them were not actually sent to jail or prison or arrested or they should not have been. But they were actually given a ticket. And around that same time in New York State, we saw that the state legislature passed a medical cannabis law. And that was implemented two years later in 2016. So that was I believe, called the compassionate care program. And once that was implemented, it meant that there were medical cannabis dispensaries where cannabis could be distributed to patients after they had been seen by a clinician who deemed them someone who would might benefit from medical cannabis. Five years after that the marijuana regulation and taxation Act was passed. And that not only maintained some of the Compassionate Care Act components with the medical cannabis legalization but added on recreational or adult use legalization and intended to create a plan for total legalization of cannabis. And so this was passed in 2021. It's been a bit of a difficult time trying to transition from the medical cannabis program that was put in place in 2016. To this dual program, a program of medical cannabis and recreational or adult use dispensaries and programs available. And but what we see now is that at the end of 2022, recreational dispensaries were finally opened in the state of New York and the number of recreational dispensaries that are regulated by the state are rapidly expanding by the day and the week. So let's briefly discuss cannabis pharmacology and the endocannabinoid system. This won't be comprehensive, but it's mostly just to help with understanding cannabis. So starting with the basics, what is cannabis? It's really not one thing. So I almost feel like it's a misnomer to call it medical cannabis in general because it's contains greater than 100 biologically active chemicals. And the most common ones and most well known ones are delta nine tetrahydrocannabinol, which I'll refer to as THC from here on out, and cannabidiol, which I will refer to as CBD. From here on out. These two chemicals are cannabinoids and they're responsible for the therapeutic and euphoric effects of the plant. Also included within the cannabis plant or other cannabinoids that we're still learning about as well as terpenes, which are chemicals which contribute to the smell, taste and appearance of the plant. So it's important to really understand the difference between THC and CBD. THC is, was the first discovered cannabinoid, it was discovered in the 1960s. It is responsible for many of the CNS effects that we're aware of of cannabis. I contributes to the intoxicating sedating anti nausea, components and effects of cannabis as well as some of the appetite stimulation of it. peripherally it can lead to analgesia, and in terms of plants that tend to have a higher concentration of THC. Generally speaking, traditionally, botanically we think of plants that are called Cannabis sativa, as being high in THC. And I tend to remember this with a mnemonic that sativa has a T in the middle of it, and so it tends to represent THC. And these plants tend to be bred to be higher in context of THC and use for recreational purposes. And I'll get to the standardized dose after I talk about CBD, which in terms of its CNS effects tends to have anti oolitic effects, and it has proven CNS effects. peripherally it's known to be an anti inflammatory and cannabis plants that have a higher proportion of CBD in them or tend to have a higher CBD content, or often excuse me,

referred to as Cannabis indica, again, indica has that CNS so that's how I remember that. And these plants tend to be bred for purposes of making fiber or hemp. Traditionally, kind of in the before times before we had this massive increase in in use of cannabinoids for therapeutic purposes. It's important to know that while there are these therapeutic, differing effects of THC and CBD, while THC causes attacks, occation and sedation, etc, and CBD causes NCR lysis and anti convulsant prop components. When they're used together, they tend to have very different effects. So for example, THC can be very toxic Eating when used alone, and I'll get more into some of the data around this later in my talk, but when it's used together with CBD, that intoxicating effect is kind of muted compared to when it's used by itself. And one kind of tidbit that I find very helpful in clinical practice is that NIDA or the National Institute on Drug Abuse, announced a couple of years ago that for research purposes, not necessarily for therapeutic purposes, but for research purposes, they consider one standardized dose of THC to be five milligrams of THC. So this is something that I just kind of keep in my back pocket when I'm thinking about dosing and talking to patients.

10:44
So how do these cannabinoids work within our own bodies, we all have an endocannabinoid system that is actively working whether we are administering exogenous cannabinoids or not, we have our own endogenous cannabinoids and they work within the system. So there are two known cannabinoid receptors this is something that is we're growing in knowledge about and we're still learning about the two that we are aware of are CP one and CP two CP one is represented on this diagram with the green areas. And it's primarily displayed in the brain or the central nervous system, the GI tract, lungs, fat liver skeletal muscles, and CB two which is represented with the brown areas on this diagram is expressed in the brain macrophages and microglia, bone and liver. So I tend to think of the CB two receptors being very highly predominant in immune areas areas with white blood cells and other immune cells. So we know for sure that THC binds mainly to CB one receptors, they do bind somewhat to CB two receptors, but for simplicity's sake, I tend to think of it really binding primarily to those CB one receptors. CBD on the other hand, seems to bind many different locations that we are very unaware of. And I have read in some places that people say that a binds primarily to CB two receptors. But on further digging and investigation, I've really found that we're just unsure of where it binds. And I think it might bind on multiple different receptors. So how can we kind of synthesize this and how is this used therapeutically. So the evidence in terms of using cannabis therapeutically, is not in the same place where we are with many other substances and treatments. So there is this could be an entire talk talking about all of the various barriers that exist to conducting research on cannabis, a lot of it is based in barriers created by the Controlled Substances Act, the 1970s, which make it very difficult to actually conduct this research. One must have a schedule one license and get approval not only at the federal level, but the state level and the institutional level. And so what this has caused is kind of a chilling effect in terms of research on cannabis and how it might be used therapeutically. And so for many of the things that our patients are already using cannabis for, we don't have the scientific data for it yet. And that I think is a big problem. But it really contributes to where we are in terms of being in a very unique position with cannabis and our knowledge around it. So we do know, though, that patients across the country who are using cannabis seem to be using it primarily for pain. So this is a survey of patients who visited a clinic within the CB two insights Clinical

Network, and these are clinics across 12 states where they have medical cannabis certification or evaluation. And they surveyed 61,000 charts and found that over 50% of these patients were seeking out medical cannabis for pain. And then about 13%. Were using it for anxiety, a smaller proportion for PTSD and then some for insomnia, depression and other things. And so this is to say that this is consistent with a lot of other surveys. It's consistent with my clinical experience. And so when I talk about cannabis in the setting where I don't have many hours to talk about it, I tend to focus primarily on the to use for pain, because it's where we have the most data and it's what our patients are using it for. So what's the evidence for using cannabis for pain? I like to focus on some key studies that were done kind of early on. This was a study that was conducted by Donald Abrams out in California among individuals living with HIV, who had HIV associated painful neuropathy, and so these 55 individuals were prospectively blinded and assigned to either smoked cannabis cigarettes that were used three times a day. And you'll notice were only 4% thc versus placebo cigarettes that were used also three times a day. And they were observed over the course of 12 days during the study period, and eight days preceding that. So what they did in this study was they observed they had these individuals complete pain journals and visual analogue scales for a week. And in the then they had a two day inpatient lead in phase. So they admitted these individuals to a research hospital for a full week. And for two days, let them kind of washed out of whatever they were using out in the community, and then washed watch them for five days where they use one of their products that they were randomized to. So during this intervention phase, they found that individuals who were using the smoked cannabis had a 34% reduction in pain, and those who were using placebo only had a 17% reduction in pain. And this was a therapy, this was a statistically significant difference between these two groups. These two groups were then discharged from their research hospital. And they continue to report their their pain with the visual analog scale. And it looks as though both of the groups kind of started to return back to their baseline from the pre intervention phase. So this study in itself, I find to be very instructive for two reasons, we see that the individuals who use cannabis had definitely had a reduction in pain, which is very interesting, even though it was a short study period and a small group. But this also shows us how difficult it is to do cannabis research. So these participants were required to be observed in a research hospital because of all of the regulatory barriers to doing cannabis research. And this remains to be the case. So if you want to do the type of randomized studies where you're using National Institute of Drug Abuse cannabis products, and you're studying it, you must admit these individuals to a research hospital and literally watch them using the products and watch them in the after effects. And so I find this to be a very important study not only for its results, but also for what it teaches us about policy. There are many other studies that I could talk about in detail, but I think it's important to kind of look at summary data. This is just a chart of seven meta analyses of randomized control trials that looked at whether cannabis and cannabinoids treat pain, and they are not all looking at the same types of pain. And some of them may have been focused more on acute pain versus chronic pain. But each of them looked at between seven and 43 studies. They looked at both plant based and synthetic cannabinoids. And ultimately all of them found that cannabis and cannabinoids reduced pain for all of these for all of these meta analyses. And so I think that that is really the bottom line. There are nuances involved in this. So most of the evidence showing that cannabis and cannabinoids reduce pain have been looking at products that had high THC content, or at least equal parts THC and CBD. And we probably need many more studies to be done for us to fully understand whether CBD

helps with pain and what doses actually help with those symptoms. Another way of thinking about this is looking at whether people change the way that they use their other pain medications when they use cannabis. So this is a really interesting study that was published earlier this year, collaborating with the state of New York and looking at prescription monitoring program data of both opioids that were prescribed and report and the prescription monitoring program as well as medical cannabis products. So medical cannabis products when they are dispensed in the dispensaries, that is reported in the PMP. And so they looked at individuals in a pre intervention period to see what their opioid dosing was, and looked at their mean morphine milli equivalents, and then they watched them after they received certification for medical cannabis. And they kind of looked at it in three different groups depending on how much how many opioids are the dose of opioids that were prescribed to them in the pre intervention period. So for those who had a lower pre intervention period, you can see that those who did not receive certification Should may have had a little bit of a dip in their opioid dose over time.

20:05
And this may have just been because people are kind of D prescribing opioids right now. But in those who received certification for cannabis, it looks like they did have a pretty substantial reduction in opioid dose over time. And this was not only for people who were on low doses of opioids to start, but also those in kind of a medium dose range, and in those in a high dose range. So this is very interesting. It doesn't tell us anything about the details of what type of cannabis that they are using, and how this relationship works. You know, is it just that these people want to be getting off of opioids, and so they're particularly motivated to do so. But it is really encouraging data. So how do we integrate some of this knowledge into practice, and I'm very lucky to be working at Montefiore. We where we have a comprehensive primary care based medical cannabis program that we've had in place since 2016, soon after the implementation of New York's medical cannabis program. When I first joined Monty in 2017, I was able to join about three other clinicians who were certifying patients for medical cannabis. And we have now grown to about 13 clinicians who are certified patients for medical cannabis across our medical system in the Bronx, in six clinics who all see Medicaid patients, two of which are FQHCs. And we integrate this into primary care. So I became the co director of this program in the past three or four years. And so I spent a lot of time thinking about how we integrate this into care, and what the implications are. And we published our our findings on how we kind of got this started in New England Journal of Medicine catalyst recently. And so you can see that many of our patients who were seeing in the Bronx are accessing medical cannabis for the purposes purpose of managing chronic pain, it's over 75% of our patients. There are other indications that people are using cannabis for and this is really looking at the primary reasons. So individuals might be using cannabis for two indications possibly. But this is what was documented in their initial note. So we kind of codified our way of using medical cannabis and integrating it into our practices, with clinical guidelines that we wrote with the New York State Department of Health AIDS Institute, and were published back in January of 2022. We're very proud of these. And they really do go into more detail than I'm going to go into this afternoon. So I really encourage you to look them up and look at some of the more detailed recommendations that we put in there. But I'm going to try to kind of give go over some of the most salient points here. So from from my time, and from my colleagues time of working in the Montefiore Medical

Cannabis program, we've really learned important lessons. And I think some of the most important lessons are that our patients are using cannabis and really want to do so safely, that they're motivated to use cannabis in a safe way in which they know exactly what they're using. And they know that they cannot be harmed or harm other people by using it. And we really have the power to communicate reliable and evidence based information to our patients on benefits and harms and to communicate to them. Whether there's evidence, why there are gaps in the evidence, and whether they should understand where that gap is. We can also promote harm reduction and provide relief to our patients with intractable symptoms, especially for pain. So on each of our visits, we try to get pretty detailed with our patients and talk to them about their motivations for us. We talk about the risks and benefits of them using cannabis and integrate that into understanding their full medical history and the other medications that they're taking to talk to them about formulations and dosing, adverse effects. And then we try to contextualize this within state and federal regulations to make sure that they're not doing things to put them at risk in terms of legal risk. It's important to understand what the modes of delivery are for cannabis. I'm not going to go into detail on this, this whole chart and many more details on it are in the therapeutic guidelines. I think the most important thing to understand from this chart are that combusted flour is what most of my patients come to me saying that they use before they see me. If they're already using cannabis, they're most likely using combusted flour combusted flour is usually used in joints, or pipes, or bombs. And when it's inhaled, they're inhaling very hot smoke. That onset of action is within seconds. And they're able to really easily titrate. Their dose when they're using combusted flour like they can use it, the effects of it were off within a couple of hours. And so they know if they need to administer an extra dose or not to impact their symptoms or the level of intoxication. The downsides are that it can really lead to chronic bronchitis. And so this is something and we also don't know what the long term health effects are to the lungs. So this is something that we talk to our patients a lot about about the risks and the benefits of using combusted flour. And oftentimes, if people switch from combusted flour, they are advised to switch to ingested or edibles. And the key difference between those two products is that ingested products take up to two hours to take effect. And so that's a really important difference for our patients to understand. In other states, like in Colorado, they saw that when ingested products were put on the market, they started to see a lot of emergency room visits from patients who may have stacked their doses. So they took a gummy. They felt like nothing happened after 30 minutes, and they took another and then 30 minutes later another and they felt far more intoxicated than they intended four hours later. So this is something that I definitely communicate to my patients about and talk to them about in detail. I would love to another time when I have a longer talk or maybe a 2.0 talk talk about dads or waxes because this is an important thing to talk to our patients about that's not usually available in our regulated system either. So within that context, understanding the difference between unregulated and regulated cannabis is really important. We have a lot of unregulated dispensaries in the New York City area, and I believe outside of New York City in New York state as well. So this is an unregulated dispensary, that's probably about a block away from my apartment, I can probably throw a stone and hit about 20 more of them in Queens right now. And this is literally another one that was right next to the testing center where I took my addiction medicine boards last year. So these are everywhere, they're they're all over the city, they're proliferating, there's a lot of talk about the city doing things to try to address them and shut them down. Because we have no idea what it is that they're selling. We know that they're

selling cannabis, we don't know whether it is safe cannabis, we don't know whether it is cannabis that contains contaminants or other drugs in it. And on the flip side of that is the actual medical cannabis dispensaries that we visited, which don't necessarily feature cartoon characters outside of them or have flashy signs or have things that try to draw in young people, right, they are much more clinical, they kind of look like my clinic honestly, or like a pharmacy that I would go to. And they're just have regulated products from the state of New York where we know what the cannabinoid dosing is, we know exactly whether or not they have pesticides or other drugs mixed into them. And they have other forms rather than just smoke forms in them. So this is just a chart kind of laying out the differences between unregulated and regulated cannabis. Unregulated when I refer to that here is not just those products that are sold and sold in those unregulated dispensaries, but it also includes products that are sold, you know, from the traditional avenues so acquaintances, friends, people who live in your neighborhood. And you know, we do know that these that unregulated cannabis in the past has been kidnapped contaminated with drugs like K to spice cocaine and probably not recently but in the past with PCP as well. And so we are really providing an harm reduction option to our patients by offering them something that we know the exact dose of cannabinoids have, we know does not have pesticides, we know doesn't have these drugs and has safer delivery modes and dosing available.

29:30

I also talk to my patients about the way that they use their smoked cannabis if they really feel like they're not going to change the fact that they're inhaling their cannabis. Many of my patients either use cigar papers which is a tobacco leaf, and they refer to this usually as blunts. Or they mix loose leaf tobacco into their joints and sometimes that's referred to as a spliff. So when I talk to my patients, I explicitly ask them what type of papers they use, and I explicitly ask them if they ask add other things like loose leaf tobacco or other drugs to their joints. And when I do this, I tried to be very specific about canceling them on trying to change the rolling papers to something that's not tobacco or nicotine containing, and to try to leave out their loose leaf tobacco in order to reduce the risk of other tobacco related lung adverse effects, and cancer related effects with the tobacco excuse me, sorry. And while I do this, we also and this is put in great detail in the in the therapeutic guidelines with the AIDS Institute, but we try to quantify the exact amount that patients are using with their unregulated cannabis when they come to us. So if there's someone who is already using cannabis to begin with, we try to get a sense for how much cannabis they're using per week, per, per day per month. And then we try to calculate out exactly based off of grams, the amount of THC that they're consuming. So if they tell me they're using an ounce per month, then we know that there are about 28 grams, that's that equals about 28 grams of cannabis. And we are guessing that that's about 10 to 20% of THC. So we multiply that all out when we come up with an exact dose of THC. And I find that a very useful method for talking to my patients about, you know, you might be using about 100 milligrams of THC per day, going back to that NIDA definition of a single dose of THC. That's 20 NIDA doses of THC that you're consuming. And so that's a nice way to really talk to your patients about, you know, the implications of what they're using. So when I initiate cannabis for my patients, for those who come to us who are cannabis naive, these are typically individuals who have failed multiple other treatments for their symptoms. So, you know, most often pain like I've mentioned, so the way that we recommend that they use this is to use a non inhaled form of cannabis and

start with the lowest possible dose of THC, usually equal parts THC and CBD. And we encourage them to not increase their dose unless they have tried this two to three times. And then after that very slowly titrate their dose over the course of about two weeks. And so the goal is to get them to a to a dose at which they have pain relief, or symptom relief. And as little side effect or intoxication as possible. And people who are cannabis experience. And like I mentioned in the prior slide, we try to estimate their current THC intake. And what I really do, I probably need to change this in this slide. But what I really do is like cut that amount that they use in half. So if someone is using 100 milligrams of THC, I say, Okay, so let's start off at 50 milligrams of THC. And then we're going to re titrate you up to a dose that helps your symptoms. So the goal there is to try to limit the amount of potential withdrawal symptoms from cutting out THC or reducing their dose and then finding a dose that actually helps their symptoms. And then beyond that, we also give them a lot of counseling on using their cannabis in a safe place, trying to be in a familiar location and trying to maintain your safety like not driving, keeping their cannabis in a safe place or in a medication safe, and other things so that they are safe while they're using their cannabis. We discuss adverse effects with our patients, I would say these are all important adverse effects, but the ones that I talk to my patients the most about are drowsiness and fatigue, especially with my patients who have polypharmacy and dizziness. Those are things with patients who have other medications that could cause the same symptoms we really need to talk to them about. high doses of of THC can lead to anxiety rather than improve anxiety and can also lead to cognitive effects. And nausea. In terms of other things that we take very seriously and try to discuss with our patients is the intoxication piece, especially when people are driving as well as cannabis use disorder are we screened for cannabis use disorder at all of our appointments with our patients? And then we also talk to them about psychosis and paranoia, especially in our younger patients who are more more vulnerable to developing new symptoms of psychosis and in patients with pre existing psychological disorder, as well as these other things like cannabis hyperemesis, diarrhea, tachycardia, these are all important and just something to keep in the back of your mind when you're seeing patients who are using cannabis, whether it's medical or not. And to mitigate some of the has adverse effects, especially in patients who are naive to cannabis. Some of the ways to do that are to titrate up slowly, which I've already mentioned once before. So we found that in other studies that had been done with THC containing products, when individuals were given THC at high doses to start, they had really severe dizziness, somnolence dry mouth and vertigo. But if they were started at a low dose of THC, and then slowly titrated up, the number of individuals with these symptoms was much lower. Similarly, if patients are given a combination of THC and CBD rather than THC alone, so individuals tend to have fewer of these adverse effects. So this is representative of two different studies. So one of them is one of them is a study that looked at Marinol, which is synthetic THC alone without CBD. And the other one is sad effects which is THC and CBD combined one to one. And they found that individuals who received Marinol needed a much lower dose before individuals started to have toxic psychosis symptoms. And individuals who use the combination Sativex could tolerate much higher doses before they develop those symptoms. Now, I mentioned traffic accidents before already, but it's just important. So this is a study that looked specifically at inhaled cannabis. And they looked at inhaled cannabis that was everywhere from placebo, to to CBD alone, THC alone and THC and CBD combined. They found that those products that people inhaled that had any THC in it led to more ln weaving in this in this specific type of driving course. And that persisted for at least 100

minutes and may have persist, persist persisted excuse me, for up to 240 minutes. So 240 minutes, they saw that things kind of evened out and people weren't Lane weaving as much. So this is something that it's important to communicate to our patients on and counseled them on safety. If they're planning on driving at all. I find myself to be very lucky that most of my patients don't drive because I live in New York City. But you still have to be careful about things like crossing the street and operating motor vehicles and, you know, just maintaining your full executive function when individual individuals might be intoxicated. So that was really rapid fire. But just to summarize, patients are using cannabis and manage their symptoms with it. And they really need evidence based advice from clinicians. There is evidence that cannabis is effective for the management of pain. And we are able to promote harm reduction by giving patients advice on their source of their cannabis, their modes of use and their dosage and titration. And a lot of this information is in great detail in those in those guidelines.

38:12
Thank you so much.

[End Transcript]