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TRANSCRIPT - GR 02 04 22 ""Therapeutic Uses of Cannabis: Where We Are and How We Got Here" ***Deepika Slawek, MD, MS*** **from** Montefiore Medical Center

- 00:16:36Alright, everyone have a good go ahead and get started now.
- 00:16:39So I'm Jamie one of the chiefs for those that don't know me, I had the pleasure of introducing our speaker so joining us today for the Department of medicine grand rounds, we have Dr. Deepika Slawek counselor from the Department of medicine at the Montefiore medical Center and Albert Einstein college of medicine.
- 00:16:55 Deepika completed her internal medicine residency at the stony brook University Hospital and then, subsequently completed infectious disease and general internal medicine fellowships.
- 00:17:04at New York University in Montpelier medical Center and addition to our work as a staffing into the atmosphere.
- 00:17:11She was also funded through and I K 23 award to study the impact of medical cannabis, on pain and inflammation and people living with HIV.
- 00:17:20Dr Sarah has published extensively in the field of addiction medicine and chronic pain, with a focus on the role of cannabis in opioid use disorder and chronic opioid use.
- 00:17:30And, as outlined in her day 23 the novel application of cannabis in chronic pain issues for patients with HIV.
- 00:17:37She also peer reviews for press one general internal medicine and a slew of other journals that address, not as a general medicine addiction medicine, medicine and the intersection of these two fields.
- 00:17:48Given her expertise in the area of medical cannabis and Virginia's recent changes regarding recreational cannabis and the evolving literature surrounding medical cannabis we're.
- 00:17:56very excited that our practice our give us this timeline update on a paraplegic uses of cannabis so with that I will turn it.
- 00:18:03Over to Ashley.

Deepika Slawek

00:18:05Thank you for having me, and thank you for that great introduction you dug up a lot on me.

- 00:18:12So I'm really excited to talk to you guys this afternoon about therapeutic uses of cannabis I don't have any disclosures but I will be discussing the therapeutic use of cannabis, which is not FDA approved.
- 00:18:25And so objectives for my talk today by the end of this activity, you should be able to take away have an illustration of how the historical and culture.
- 00:18:42I'm sorry I didn't realize, I was muted.

Deepika Slawek

00:18:48So I'm hoping that you all, should be able to illustrate how the historical and cultural context of cannabis regulation in the US has impacted current policy and practice patterns.

- 00:18:57demonstrate and understanding of the risks and benefits of using medical cannabis and apply harm reduction principles to patients who use cannabis and clinical practice.
- 00:19:07So this is just an outline of my talk today we'll be starting off with why this topic is important.
- 00:19:13followed by canvas and the endocannabinoid system cannabis history and policy in the US and then therapeutic uses a cannabis formulations and administration methods.
- 00:19:23And cannabis and clinical settings and finally we have time I'd like to talk about some of our canvas studies at Monte and Einstein.
- 00:19:30So why is this topic, important.
- 00:19:34As it was just alluded to the number of states that have been legalizing medical cannabis over the past 25 years it's just exploded.
- 00:19:42It started around 1996 when California legalized medical cannabis really in the setting of the AIDS epidemic and since then there's been a gradual increase in states that have.
- 00:19:54passed legislation to eight to legalize medical cannabis, as well as adult use also those recreational cannabis, there are now 37 states that have legalized medical cannabis, the most recent of which was Mississippi and now 18 states that have legalized adult use cannabis.
- 00:20:12There are an estimated 5.5 million medical cannabis patients in the United States based off of public record data put together by the marijuana.
- 00:20:20Policy project as of May of 2021, so this is not a small number of patients who are seeking this out and obtaining certification for medical cannabis and our patients are really.
- 00:20:32interested in it and there's a favorable.
- 00:20:35feelings about medical cannabis and cannabis, in general, by the public, there are now over 90% of the public based off of Pew research Center datum.
- 00:20:45That say that cannabis should be legal either for medical purposes or for medical and recreational purposes as well.
- 00:20:51And as you can see here, this has changed over time since the 16th we've gone from.
- 00:20:57Not very many people thinking that it should be legalized most people thinking, it should be illegal to a total reversal of that.
- 00:21:06And now, most people really feel like it should be legalized, and this is represented in all of our coffee popular culture.
- 00:21:13So you name it every single publication out there has published something on.
- 00:21:19Medical cannabis or cannabis and the use of it in our popular culture so patients are being bombarded by these messages and as clinicians we are all hearing it right we're all hearing about our patients.
- 00:21:32Wanting to use it having questions about medical cannabis and wanting to know how that could fit into their lives.
- 00:21:40So let's talk a bit about cannabis and the endocannabinoid system, so what is cannabis it's really not one thing.

- 00:21:48Cannabis is a term and it's also been cultivated and use recreational and medicinal purposes, for centuries, now by many different cultures.
- 00:21:56Cannabis is a term that has been used to broadly defined products derived from the cannabis plant and there are three subspecies of the cannabis plant.
- 00:22:05Cannabis lativa cannabis Indica and cannabis reader Ellis fear pictured here, and the most commonly seen or cannabis city, but in canvas Linda.
- 00:22:16can have a city tends to be a plant that's taller skinnier the leaves tend to be thinner and they're known for having a higher concentrations of delta nine thc.
- 00:22:27And cannabis Indica is a shorter can shrub your plant that has leaves that are wider and are known for having a higher concentration of connect the dial, also known as CBD.
- 00:22:40While you know, in the literature, we people tend to think about cannabis city, but in canvas into separate things in reality.
- 00:22:48What we see on the ground and in real life is that most of what's out there right now is a hybrid of these two substances in order to achieve specific ratios of thc and CBD.
- 00:23:01Within cannabis, there are greater than 100 biologically active COMP chemicals, including cannabinoids which the most well known, of which are thc and CBD.
- 00:23:12And cannabinoids contribute to the therapeutic and euphoric effects of cannabis also included in those biologically active chemicals or Europeans which contribute to the smell taste and appearance of the plants.
- 00:23:26So more specifically about thc and CBD thc is really the most well known and best studied at the cannabinoids it was identified in 1964.
- 00:23:36And is known for being psychoactive and intoxicating there's evidence that effects pain muscle spasms nausea appetite stimulation.
- 00:23:45And plants, particularly those that are used for recreational purposes are often bred to have high thc content to maximize maximize on that psychoactive effect.
- 00:23:57CBD was discovered around the same time as thc in 1963 it has been found to serve anti-inflammatory purposes, as well as anti-convulsants.
- 00:24:08And it's psychoactive but not intoxicating so it has angelic and facts and effects on impulsivity and there's also evidence that it's an antioxidant and that might act as an Anti-tumor this is based off of animal studies.
- 00:24:23plants that are bred to be high in CBD are often used for fiber, also known as him.
- 00:24:28And an interesting thing about each of these cannabinoids is that while thc and CBD might have their own individual effects.
- 00:24:37When they're used together they act differently so, for example when thc and CBD are used together they may be more effective in treating pain than when either is given alone.
- 00:24:50So these cannabinoids work in the human body within the endocannabinoid system, so the endocannabinoid system interest cannabinoids derived from plants just thc and CBD which I just discussed, as well as endogenous cannabinoids.
- 00:25:03There are two known receptors in the endocannabinoid system that has been studied the most extensively.
- 00:25:12there's the CB one receptor and cvt receptor so looking to our right, this diagram is.
- 00:25:20shows us the location of these different cannabinoid receptors and so CB one receptors are primarily located in the CNS like in the brain and spinal cord, and the peripheral nerves.

- 00:25:32And it's the most abundant and G coupled receptor and the CNS and it has impact on the experience of pain stress and anxiety.
- 00:25:41CV to receptors are highly concentrated in the immune system, and they do have some CNS expression but they're primarily involved in inflammation.
- 00:25:52So thc when an interactive and cannabinoid system finds primarily to see be one receptors, and this is responsible for its psychoactive effects, an analgesic properties.
- 00:26:04CB to it also finds the CB to not as strongly as it doesn't CP one and that might account for some of the anti-inflammatory properties of thc.
- 00:26:16CBD binds primarily the cpt receptors and that accounts for its anti-inflammatory effects, and it has some binding in a cms system on those CV one receptors, which is why it has that angelic an effect and effects on impulsivity.
- 00:26:35There are endogenous cannabinoids as well, they interact with CB CB to they are not well understood and we don't really.
- 00:26:43know exactly what they do at this time, most of our research has been done in animal studies, but two examples of them are amanda mind and to record an oil glycerol, also known as to ag for short.
- 00:26:57So, putting all of this into context of our history and policy in the US, I think is very, very important.
- 00:27:05And I could go back centuries to to the beginning of when cannabis was first used, but I think I'm going to start with more modern history, at the end of the 19th century, when cannabis was really widely used by the population.
- 00:27:19It was broadly available people could purchase it and pharmacies and dispensary's it was recommended by physicians and people were using it for things like pain.
- 00:27:29For najah insomnia, and all sorts of other ailments and there were providers their physicians and other healthcare providers who used it regularly in their clinical care.
- 00:27:42between the end of the 19th century in the 1930s, a lot of things changed in the US.
- 00:27:47There was a big drive toward prohibition, we saw you know alcohol was outlawed in the 1910s and teams, we saw many ramifications from that.
- 00:27:57Additionally, science, was advancing we had more pharmaceuticals that were available for the treatment of all of those things that people were using cannabis, for, in the past.
- 00:28:06And at the same time, we ran into quite a bit of economic instability of the 1930s, with the Great Depression.
- 00:28:13People were experiencing enormous economic hardship and much like we've seen and other times in our history.
- 00:28:21When that happens, we tend to want to blame it on somebody and about in around 1910 is when the Mexican American revolution occurred and after that there started to be a big influx of Mexican American immigrants into the US.
- 00:28:36What this really for this perfect storm created was that.
- 00:28:40All of the societal ills and problems and economic issues of our country were largely blamed on Mexican American immigrants and we saw that.
- 00:28:51Cannabis was transition from being spoken about, as this scientific botanical thing that was called cannabis to being called marijuana.

- 00:29:00And that term was actually very intentional that that people started calling it marijuana was a distinct rebranding and it was in order to make it.
- 00:29:12To talk about something that sounded more foreign and something that could be easily associated with these Mexican American immigrants.
- 00:29:20This is the real the birth of reefer madness, this is the time when we were starting to blame cannabis on everything from psychosis to murders to.
- 00:29:31orgies to a drug crazed abandon as you could see on this poster and this persisted in our culture for years after that in 1937 the marijuana tax Act was passed that was a law that was opposed by the American Medical Association and it taxed the.
- 00:29:53Attacks physicians for recommending cannabis for any type of medical ailment or symptom.
- 00:30:00Despite the fact that the AMA was against its passage it did pass and soon after that and 1942 canvas fell out of the pharmacopeia physicians really just use other things to manage whatever symptoms people were using at that point.
- 00:30:17Soon after that, in the 1950s and 60s, we saw a multitude of subcultures really adopt cannabis, as part of their subculture.
- 00:30:25That beat next in the 50s including Allen Ginsberg the hippies in the 60s, as well as the antiwar movements really adopted it felt like it was a big part of their culture and use it as a way.
- 00:30:37What they felt what to as they felt to expand their minds and their perceptions of the world, this was met in 1970 by President Nixon signing the controlled substances Act, which created a scheduling system for all substances that did not exist before this time and so.
- 00:30:58The controlled substances act created this I think it's something that we're familiar with in the clinical setting.
- 00:31:05And it was really an attempt to try to classify substances as having any type of medical use, as well as whether or not they have a serious.
- 00:31:16risk of abuse or other risk so in 1970.
- 00:31:23It wasn't really decided upon whether canvas should be included in the scheduling system in fact there are quite a few people who said, you know we don't really know that much about cannabis, I mean thc and CBD were just discovered seven years ago, or six years ago.
- 00:31:38And so, a bipartisan Commission was created to try to determine whether or not cannabis should be scheduled.
- 00:31:46They gathered experts in the field of pharmacology who then went and researched what we know about it and came back to Congress and said listen, we think that cannabis should be kept unscheduled.
- 00:31:58We don't know enough about it, we should do more research on it to try to understand what the real risks and benefits are of this substance.
- 00:32:06Despite that President Nixon felt strongly that it should be scheduled and ultimately schedule it as a schedule one drug.
- 00:32:13in the company of LSD mdma and heroin and define to something with a high potential for abuse was no accepted medical use in treatment and the lack of accepted safety for us under medical supervision.

- 00:32:28This was really a crackdown on the counterculture and communities of color all those cultures all those sub.
- 00:32:35Sub groups that I was talking about earlier, who really adopted cannabis and john ehrlichman who is.
- 00:32:41President Nixon's chief of staff at that time was later quoted in a biography saying.
- 00:32:46That we knew we couldn't make it illegal to be either against the war or black, but by getting the public to associate the hippies with marijuana and blacks with heroin and then criminalizing both heavily we could disrupt those communities.
- 00:32:59And that's really what was accomplished, we saw that starting in 1970 which is around here, you know it's a small graph, but this is 1970 on this graph that we had this huge increase in the US Federal and State prison population based off of national data and even as recently as.
- 00:33:20A restaurants for black people were 3.6 times higher than for white people nationally, as is despite the fact that there are nearly identical rates of cannabis use among black and white people in that same year and national polling data.
- 00:33:33So what we really saw it in the 21st century in the 20th century and bleeding into the 21st was that cannabis was.
- 00:33:44turned into something that was decidedly thought it was a very big thing affecting every aspect of our life and in the end, racist policies and systemic racism.
- 00:33:57have really impacted disproportionately communities of color, despite the fact that we don't really know that we haven't really know that much about it and legislation was created to make it difficult for us to know anything about it.
- 00:34:12So what are the clinical implications of cannabis is scheduled one classification.
- 00:34:18So what this has meant for our patients and for us as providers is that even in states where you have legalized medical cannabis.
- 00:34:26providers cannot prescribe cannabis, they can only certify it it's technically the technicality it's just a term, but we cannot use the term prescribe and we're talking about cannabis.
- 00:34:37Further in many states, patients have autonomy with the content, like the cannabinoid content of the products that they're purchasing, as well as the dose amount and route that they're using.
- 00:34:49On top of all of this there's no insurance coverage, because, as we know, insurance coverage is deeply linked to federal policy.
- 00:34:56And patients are required to pay for their cannabis products with cash and sometimes some digital payments patients are not allowed to use baking or credit cards and what this has really created is a huge disparity in who's able to access this legalized cannabis products.
- 00:35:15Additionally, patients are not able to travel across state lines with these products so even in our modern day and age, where people really live, not necessarily all in one place, we really have to counsel strongly to patients, not to take it across state lines.
- 00:35:31implications on research and on the evidence that we have for the therapeutic use.
- 00:35:35of cannabis has been huge so this scheduling of cannabis has created many, many barriers on the federal side.

- 00:35:42for implementing research on medical cannabis, and this includes high quality research like randomized control trials in order to do those randomized control trials.
- 00:35:51Research require multiple approvals, including investigational new drug approvals from the FDA promises from nine that you'll be able to use their night of cannabis products.
- 00:36:03So what that means is that when you're doing this research, you can only use cannabis grown by the National Institute on drug abuse in Mississippi.
- 00:36:11That is delivered as whole flower has absolutely no resemblance with products that our patients are using in state regulated symptoms systems.
- 00:36:22and on top of that provider or researchers have to obtain a DEA licenses that are pricey and difficult to get.
- 00:36:30You also often have to get federal funding for all of us, so you must meet neither priorities if they're not interested in studying cannabis, which they had not been for quite a long time you're really not going to get funded to do this work.
- 00:36:43In addition to all of this when you're doing randomized control trials with cannabis federal regulations, make it so that you must directly observe administration of the cannabis.
- 00:36:52So for patients who have chronic symptoms, such as chronic pain researchers are required to often admit these patients into Inpatient research facilities and literally observed them watch them using those products.
- 00:37:06And then observe their response to the products after that this makes for an incredibly difficult onerous and expensive experience for researchers and it's difficult to do on top of that people require.
- 00:37:21Often States require their own approvals and licenses that might conflict with federal policy.
- 00:37:26And then, this is all just really lands on the institutions and the investigators.
- 00:37:31who find themselves in a bind you know they want to do the right thing they want to research, things that their patients are using and try to find evidence for the things that they see on the ground.
- 00:37:40But they're often met with increase IRB scrutiny increase federal scrutiny, and they have to pay a lot of money down, you know they have to have appropriate storage and security for these products in order to do so and it's expensive and difficult.
- 00:37:56So, within that context little review some of the therapeutic uses a cannabis.
- 00:38:02In 2017 the National Academy of Sciences engineering and medicine published this huge report called a comprehensive review of the evidence.
- 00:38:11Of by experts in the field that has been peer reviewed it's a large documents about 400 pages long they really go into the nitty gritty of everything and try to evaluate what the evidence is for all of the indications that people are using cannabis for at this time.
- 00:38:28They did conclude that adults with chronic pain treated with cannabis were more likely to experience a clinically significant reduction in pain symptoms when they were using cannabinoids.
- 00:38:37And they found conclusive or substantial evidence that cannabis is effective for the treatment of chronic pain and adults, they also found substantial evidence for chemotherapy induced nausea and vomiting and for specificity associated with multiple sclerosis.
- 00:38:52So.

- 00:38:54What do people use cannabis, for, and you know when I first came into this world, I thought it was going to be for all sorts of things you know.
- 00:39:01But this is data from my home state New York State after a little over two years of our program being in existence, and this is publicly available data.
- 00:39:11They looked at the indications for cannabis that were listed for medical cannabis certification that were listed on the certification documents.
- 00:39:18And what they found was that 73% of patients who received certifications and those first two years.
- 00:39:26did so for severe chronic pain so patients were really, really looking for their cannabis products to manage severe and chronic pain and this actually plays out in a national landscape as well, my heavier and colleagues.
- 00:39:41Looked at electronic medical record data from a network of clinics that exists in 12 States across the country, so they ultimately looked at 61,000 patients who received medical cannabis and found that greater than 50%.
- 00:39:55Of those patients were seeking out medical cannabis certification for the management of their pain, so this is all to say that much of my talk on the therapeutic uses of cannabis are really going to Center around pain and chronic pain and whether cannabis works for that indication.
- 00:40:15So there have been six Meta analyses of randomized control trials on this question of whether cannabis and cannabinoids work for pain.
- 00:40:26And so, these six Meta analyses have looked at really different types of pain.
- 00:40:32ranging from multiple sclerosis neuropathic pain to many different pain ideologies to chronic pain and they looked at various different forms of cannabinoids whether it was synthetic cannabinoids like journal.
- 00:40:44or plant based medications that may have been inhaled or smoked versus administered in other ways, like tinctures or pills.
- 00:40:52Ultimately, what these six Meta analyses found were that consistently they all found a reduction in pain when they did Meta analyses of the various studies that they looked at.
- 00:41:04And i'm going to look at one Meta analysis that was published in 2015 in JAMA more closely.
- 00:41:10So penny waiting and colleagues in 2015 published a systematic review of the benefits and adverse events of cannabinoids so they looked at 79.
- 00:41:21randomized control trials and it looked at many different indications, but the lion's share of these studies were looking at cannabis and cannabinoids for chronic pain.
- 00:41:31Most of these studies tested products cannabinoids that are not available.
- 00:41:36In medical cannabis programs and state regulated medical cannabis programs, they were often either synthetic thc neither supply cannabis or sprays and tinctures that are available, not in the US, but might be available in other countries, like in Europe.
- 00:41:53So what they found in the Meta analysis of data specific to chronic pain was that the odds indicated 30% or greater improvement and pain was cannabinoids compared with placebo.
- 00:42:06And what they were looking really looking for was improvement in a numeric rating scale, so this is an example of a numeric rating scale, and I think most of us in clinical practice are pretty.

- 00:42:17familiar with them, so what they were looking for was a clinically significant reduction in pain and that's typically thought of by pain researchers.
- 00:42:25As at least a 30% reduction in pain so somebody lives at around 10 days have the worst possible pain every single day on average they're looking to at least get down to a seven on a scale like this.
- 00:42:41And they were able to see that with cannabinoids but not with placebo.
- 00:42:46Looking at some specific randomized control trials, I am biased I look a lot at the HIV data, because I am an infectious disease doctor, but this is one.
- 00:42:54landmark study that was published in 2007 by Abrams and colleagues and they conducted a prospective blinded placebo randomized control trial on 55 people living with HIV.
- 00:43:07With painful sensory neuropathy, and so what they did was that they observed these patients for seven days in the outpatient collected data on their pain.
- 00:43:16And then admitted them into one of these Inpatient research facilities for two days, and this is a lead in phase, so they didn't receive any study pop product at that time and they continue to collect pain date on these patients, then.
- 00:43:28Then during the five day in patient intervention phase that they were randomized to receive either smoked cannabis with 4% thc or placebo, and each of these were used at least three times per day.
- 00:43:42And then they were observed in the outpatient setting for an additional seven days, so what they found was that the cannabis group.
- 00:43:51had about a 34% reduction in pain verses 17% reduction in pain and this is a clinic uses a statistically significant.
- 00:44:01difference in another study published by Ellison 2009, this is a prospective blinded crossover trial, so they enroll 28 people living with HIV, who had again refractory painful sensory neuropathy and what they did was they actually did crossover so.
- 00:44:23Participants had a wash in phase where they were not to use any type of cannabinoids or other pain products, then they had a five day study period where they used either smoked cannabis or smoke placebo.
- 00:44:36And then, a washout period for two weeks, where they didn't use anything and then again they switched so they would switch to if they use placebo, in the first period, they would use cannabis, in the second period.
- 00:44:47or they use cannabis, in the first year they use placebo in a second.
- 00:44:51They were interested in pain severity scores, and what they found was that pain reduction was greater with cannabis compared to placebo, and this was a statistically significant difference.
- 00:45:01So while these are pretty small sample sizes 28 and 55 these are strong findings that were statistically significant.
- 00:45:10Another way of thinking about this is on a population basis whether people change their other medications when we start using cannabis.
- 00:45:19So this is a study that was published by binky and colleagues out of Michigan and they conducted self-reported online questionnaires with patients who were visiting dispensary's in Michigan between November of 2013 and February of 2015.

- 00:45:35They enrolled 185 patients and ask them questions such as how was your opiate prescription drug use changed since you started using cannabis and they repeated the same questions question for other medications as well.
- 00:45:49So what they found was that for patients who answered the survey before starting medical cannabis.
- 00:45:58Most most participants or respondents reported using about 65% of their prescribed opioids after starting medical cannabis this amount dropped to around 18% of their opioid.
- 00:46:13There were similar there were similar patterns, with the anti inflammatories and sets as well as with antidepressants for whatever that is worth.
- 00:46:21And you know there's lots of confounders here, but this is very interesting that people really reduced their other pain medications when they started the medical cannabis.
- 00:46:33Another study looked at people who were visiting a pain management clinic in New Mexico.
- 00:46:40So what they did was they follow patients for 21 months and followed patients or patients who are on opioids and so a 37 of those patients decided to start medical cannabis treatment.
- 00:46:52And another 29 event decided to continue on their chronic opioids without additional medical cannabis.
- 00:46:59So what they found so what you can see here on this grant on this graph is the green line is going to be those who started medical cannabis and the orange or yellow line is those who did not start medical cannabis.
- 00:47:12So those patients who start a medical cannabis in 41% of them ceased opioid prescription versus 3% of the comparison group so that comparison group is those who did not start medical Canada.
- 00:47:24And 84% of those instrumental cannabis reduce their opioid use versus 45% of the comparison group, so this is another ecological study that.
- 00:47:36Admittedly, has a lot of confounders kind of supporting the idea that people are reducing their other pain medication use when they start medical cannabis and seemingly are getting some pain reduction when they're using medical cannabis.
- 00:47:56So what about non pain conditions so for severe and persistent muscle spasms this is mainly been studied and multiple sclerosis with thc and CBD combined when that has been used, compared with placebo there's been seen and improve patient reported specificity.
- 00:48:14For ptsd is not well studied but it's primarily been studied in combat veterans in small sample sizes and those small sample size studies, they have seen an improvement and sleep quality and reduced intensity of nightmares.
- 00:48:28For severe nausea we've seen that synthetic thc like your national compared with placebos effective and chemotherapy and use nasza and an animal studies we've seen some improvement in nasza with CBD alone.
- 00:48:42For caixa and wasting there's some evidence that an AIDS wasting syndrome and cancer, since you have your weight loss.
- 00:48:50There is some improvements in Poughkeepsie and wasting However, these studies had high risk of bias and very, very small sample sizes.
- 00:48:59Finally, for seizures CBD is the only FDA approved plant based cannabinoid that's been FDA approved.

- 00:49:07And this is called EPA dialects and has been approved for the management of severe intractable seizures and children who have Dr a syndrome and Linux gusto syndrome, which are really rare childhood seizures syndromes.
- 00:49:22there's a lot of advocacy in the seizure community and people with seizure disorders.
- 00:49:28To continue to study this and there's been some small sample size studies that have looked at high doses of CBD in adult populations refractory symptoms and in those few studies, there have been there has been seen a reduction in seizures when using high doses of CBD.
- 00:49:49So let's talk about formulations and administration methods So how are these patients using medical cannabis and doesn't resemble what we prescribe to patients when it's not cannabis.
- 00:49:58In all honesty, it does not really resemble that much or other pharmaceutical based medications but I like to think about cannabis as unregulated versus regulated first so unregulated is also called street cannabis or.
- 00:50:13elicit some people might call it that it's generally bred to have high thc content remember Is this something that's usually used for the purpose of having that euphoric psychoactive effect.
- 00:50:24Typically, unregulated cannabis has totally unknown untested doses of cannabis cannabinoids people are not testing to know exactly the doses of thc and CBD and if they are who knows what methods they're using.
- 00:50:37there's also unknown content pesticides tars heavy metals other drugs such as synthetic cannabinoids like a to and spice and even potentially cocaine.
- 00:50:48And the availability of different routes of administration, other than smoked or combusted cannabinoids is really variable and inconsistent and dependent upon the person from whom you're purchasing your unregulated cannabis.
- 00:51:02Regulated cannabis, on the other hand, is typically regulated by the state, usually in most states there's available either high thc equal parts thc and CBD or high CBD products.
- 00:51:15In most states exact cannabinoid dosing is confirmed by the state or entity, who has been told to do so by the state.
- 00:51:24Where they could tell you the exact dosing of thc and CBD and these products are typically tested for pesticides and if they have them removed from the market and test for contamination with other drugs and removing the market if they are contaminated.
- 00:51:39In most states there's a variety of different routes of administration available, including tinctures and edibles and other non-smoked options.
- 00:51:50So in Virginia state where you guys are now your patients are able to pick up who those who have a medical cannabis certification are able to pick up a 90 day supply.
- 00:51:59of products that have at least five milligrams of CBD and no more than 10 milligrams of thc and produce.
- 00:52:05As of September of 2021 your patients are able to pick up whole flower products, as well as even before that they were able to pick up tinctures joints or combustible smoked cannabis vapor products.
- 00:52:23And edibles that can come in all sorts of forms like gummies candies pills capsules and other edible pitch goods.

- 00:52:32And finally, in Virginia state patients are able to pick up highly concentrated cannabis products called concentrate is a million different words for this product and people call it dabbing other people call it.
- 00:52:45wax because sometimes it comes in a waxy type of a product, and this typically has very, very, very high concentrations of thc you'll see here this 63% thc contained in this little.
- 00:52:59This little container So how do patients use all of these different forms of cannabis, this is a busy table I'm going to walk us through it.
- 00:53:08So dabbing which I was just talking about this product, right here is a very high concentration of thc that's usually administered by inhaling it after it's been placed in a hot platform.
- 00:53:23It makes the cannabinoids make their way into your bloodstream through the upper Airways and it's almost an immediate effect people feel a whatever if they're going to feel almost immediately and that lasts about two to three hours.
- 00:53:38Patients often like that quick onset of action, especially if they have acute symptoms, however, this form of cannabis has many, many disadvantages, the way it's.
- 00:53:48The way you get that product involves the use of lots of solvents and it's really unclear what exposures those solvents means for people's lungs Airways.
- 00:53:58If there's a potential for lung injury, especially for unregulated dabbing products, and it has really, really high thc doses, which could potentially cause psychosis and hallucinations, particularly in people who are predisposed to that.
- 00:54:13smoked flower very different right is smoke through either joints or pipes it's dried flower, that is.
- 00:54:22An ember is created by lighting it and then smoke is generated that's inhaled that cannabinoids make their way into the bloodstream.
- 00:54:29Through the lower Airways and onset of action is around three minutes and can last a bit less than two hours people tend to like that there's a quick onset of action and not too long the duration so they're able to tie treat their dose.
- 00:54:44But the downsides are that when you're inhaling that hot smoke, you can have a risk of chronic bronchitis there's also intoxication with consumption of thc.
- 00:54:53And then I find this to be one of the most biggest downsides of smoked or or vaporize cannabis is that the dosing very in precise.
- 00:55:02So people lose a lot of their dose or sites dream, so the smoke might not all make its way down into your lower airway it's lost by going behind the head or through whatever gravity does to smoke and vaporized products.
- 00:55:17So you lose a lot of your cannabinoids through that site stream loss, and so you don't actually really know exactly what you're using and it's hard to get a precise dose for what helps your symptoms.
- 00:55:31The main difference between smoke flower and vaporized flower oil is that, instead of heating it through an ember it's heated through a battery operated device.
- 00:55:41And he generates a vapor that's a lower temperature than smoke products and so that can actually be a little safer for patients and that there's not as hot a temperature.
- 00:55:51Product making its way down your airway and potentially causing bronchitis, we don't actually know.

- 00:55:58Long term yet what that will mean for patients in terms of risk of chronic bronchitis, but hopefully we will in the future for unregulated products these vaporize oils could have other additives and then like vitamin E acetate which could cause VP lung injury.
- 00:56:14there's also tinctures and sprays, which are oil concentrates, these are oils that are administered under the tongue or sprayed in the mouth and cannabinoids or are.
- 00:56:23absorbed directly into the mucous membrane at the mouth onset of actions around 10 minutes and can last a little less than 10 hours, so it last quite a long time.
- 00:56:33it's a relatively quick onset of action, however, people tend to not really like the taste of it, it has variable flavors and there is a potential for user error in that people might accidentally swallow it and then it's effectively and ingested product rather than a sublingual products.
- 00:56:50suppositories are not used very frequently there's not very much from a kinetic data on it.
- 00:56:56When cannabinoids are administered as a depository they do avoid a first pass effect, so the onset of actions relatively quick around 30 minutes.
- 00:57:06And it can last around eight hours, while it is an undesirable dosing method and might be appropriate in some patients, such as those who are in end of life care or who cannot do these other things, for various reasons.
- 00:57:19Finally, ingested cannabis comes in capsules dummies edibles and it must be metabolized by the liver through a cyp for 50 system.
- 00:57:29And so the onset of action is actually pretty long, it could be like one to two hours before someone feels and effect.
- 00:57:35It does not last a long time, so it can last up to 25 hours, so, while that slow onset of action can be seen as a disadvantage by some patients.
- 00:57:45It that long duration of action for people with chronic symptoms, could be a good thing.
- 00:57:51Because of that slow onset of action there's a high index of error, with it, so people might think that it's not working for them and then add on another dose On top of that.
- 00:58:01That puts you at risk, for having to higher dose of thc or unforeseen dose of thc and then side effects after that.
- 00:58:12So how do we use these products in clinical settings so I'm going to try to go through this relatively quickly, but not too quickly, so in Virginia state where you guys are.
- 00:58:23MDS videos pH and MPs who are licensed to practice medicine and Virginia, are able to certify patients for medical cannabis, if they are registered with the board of pharmacy to issue certifications.
- 00:58:37Each practitioner is able to certify up to 600 patients per year each of those certifications only last one year, though, so it's different in every state I'm always interested to learn what each state is doing.
- 00:58:51The way that I manage medical cannabis in my clinic and with my colleagues, is that.
- 00:58:57We really approached this much like primary care and integrated into our primary care clinics, so we assess patients motivation for cannabis use their prior experiences with cannabis and we get a really good history of their medical and psychiatric history.

- 00:59:13Then through patient interviews talking to them about all the other medications and their other medical issues and psychiatric issues and talk about the relative benefits and risks of.
- 00:59:22Using cannabis and the potential for the therapeutic benefits for that specific patient, we also review the New York state prescription monitoring program just like you would with any other controlled substance.
- 00:59:35We then talk to them about recommendations for how to use their cannabis, including dosing and route of administration.
- 00:59:42We often recommend not smoking, so that people can have a more precise dosage and less risk of damage their airways, so we might we usually recommend tinctures or or ingested cannabis products and we tell people to start with, as low a thc dose as possible and to type straight up slowly.
- 01:00:03In New York state patients are required to register with the state I couldn't really get a clear sense in Virginia, if this is something a step that patients have to do, but I think that it is.
- 01:00:13We also discussed with patients location of dispensaries risk of using cannabis and another big thing we talked to them about cost of medical cannabis, because it is not covered by their insurance.
- 01:00:25Finally, we complete a treatment agreement with patients, just like we would with other controlled substances like opioids.
- 01:00:32When dosing cannabis patients, we tend to take a bit of a different approach and cannabis naive versus cannabis experienced patients.
- 01:00:40For naive patients, we start them at the lowest possible dose of thc and we very, very slowly, increasing every two to three days we tell patients.
- 01:00:47To increase the dose in as low as small increments as possible, we also tell patients to start your cannabis at night before bed and a safe place where you don't feel like you were threatened or other things will go wrong.
- 01:01:02And do not mix it with other sedating substance substances or other things that might be psychoactive or intoxicating such as alcohol or other medications like.
- 01:01:12That benzodiazepines or sedatives and cannabis experience patients, we often try to estimate patients current thc into intake by asking them about you know what.
- 01:01:24What are you using how much of it, are you using and we actually try to calculate the amount of thc they're using and then we usually start patients at around 50% of that dose and follow a similar pattern of increasing every two to three days.
- 01:01:40In patients who are not using cannabis all that regularly, we should start them at around five to 10 milligrams of thc in those cannabis experience patients.
- 01:01:48So this is the real take home point for initiating cannabis start low and go slow to limit risk of side effects.
- 01:01:56The side effects can range from feeling high or euphoric to having dizziness to being able to concentrate and then drug interactions are a big thing and a big part of our evaluation, where we.
- 01:02:08Try to look for others tip for 50 inhibitors and medications that might need to either not be given, or maybe contraindications to use and cannabis is someone.

- 01:02:18Someone is on those medications a big potential for adverse events is driving impairment.
- 01:02:25We counsel people extensively on not driving under the influence.
- 01:02:30And then other adverse events or anxiety paranoia panic attacks and psychosis, particularly those who are predisposed to psychosis and in very, very high thc doses, as well as low birth weight in patients of childbearing potential.
- 01:02:47Rare adverse events are nausea vomiting and abdominal pain and tachycardia with high doses of thc.
- 01:02:54Aside from this, we counsel patients on keeping their cannabis products in a safe place away from children and pets and not across state lines with cannabis products and I cover these other things already.
- 01:03:06So I just wanted to talk really briefly about traffic accidents and our clinic and then i'll leave it open to questions, so this is a big concern by a lot of people about the.
- 01:03:17legalization of cannabis what's going to happen with traffic accidents are we going to see traffic accidents from cannabis, just like we do from driving under the influence of alcohol.
- 01:03:26So San Tele Tenorio and colleagues in 2017 published in the American Journal of public health, this very interesting analysis of federally available data.
- 01:03:38On traffic fatality rates, and so what they did was they compared states without any medical cannabis laws as of 2015 with states that had passed, medical cannabis laws either before.
- 01:03:50or after 2001 so before 2000 once the dotted line and after is a dashed line and what they found this graph is for patients, for people aged 1524 and this graph is people aged 25 to 5244.
- 01:04:04They actually found that there were statistically fewer traffic fatality accidents.
- 01:04:10In those states that have legalized medical cannabis than those that had not so that concern about an increase in traffic traffic fatalities has not really played out yet.
- 01:04:21I think that there's still a lot of data that needs to be acquired from this and more analysis, need to be done to look at it further, however it's really important for us as providers to counsel patients on this risk, and to make sure the patients know not to drive are the influence.
- 01:04:38We monitor patients around two weeks after certifying them to make sure that their dosing is going okay and.
- 01:04:46This can be done either by us, or by a pharmacist at the dispensary and then we follow up with patients every three to six months to.
- 01:04:53evaluate for side effects, as well as evaluate for any sign of cannabis use disorder we use acute are for that and make modifications to our recommendations if any of these things are coming up.
- 01:05:05So why do I certify patients for medical cannabis, I have a lot of reasons, but the bottom line is harm reduction, were able to protect patients against arrest parole violations and employment discrimination.
- 01:05:17prevent exposure to contaminants such as pesticides and other substances and promote safer delivery modes than smoking, as well as specific dosing of thc and CBD.
- 01:05:27And we're really able to help patients who have refractory symptoms, who are running out of options and communicate reliable evidence for evidence based information.

- 01:05:35i'm able to practice in this network of cannabis clinics in the bronx that has four clinics across the Bronx was established in 2016.
- 01:05:45By my division chief Dr Julia Aaronson It started off as three providers and has grown to 13 providers and we integrate this into a primary care setting that accepts Medicaid.
- 01:05:57As of April 2021 we've seen at least 1600 patients, this is based, this is data that we published recently in New England Journal of medicine catalyst and we did go and speak with patients who were in our clinic to try to get a sense of.
- 01:06:16Of who, who was coming to us and what their experience was like, and so we were able to survey about 182 of these patients.
- 01:06:24And I think the most interesting thing on this on this table it's really that about half of these patients report is that they're still using unregulated cannabis.
- 01:06:34Three quarters of them, though had at least purchase or medical cannabis once.
- 01:06:38And, half of them 48% did not purchase more than once, so we asked these patients, you know why is it that you did not purchase more than once.
- 01:06:47And what they really told us was that it was price that they could not afford it unrelated to cannabis was significantly cheaper for that.
- 01:06:54and on top of that convenience, you know there's only one cannabis dispensary in the Bronx there are like six in Manhattan and so.
- 01:07:02You know, getting to the cannabis dispensaries is very difficult for them, and so this is very unfortunate, you know it really highlights that there is a disparity in New York City when it comes to our medical cannabis programs and we're hoping that with time that this will improve.
- 01:07:17So I'm actually going to leave it at this I'm happy to take questions later about our cannabis studies.
- 01:07:24You know, but I did just want to summarize, to say that the historical of cannabis.
- 01:07:30historical context of cannabis in the US includes a long history systemic racism has shaped the way we do it now.
- 01:07:37Patients are using cannabis to manage symptoms and need evidence it but bass advice from our clinicians and there are a citizen conditions that may benefit from the management with medical cannabis.
- 01:07:47We can promote harm reduction by informing patients that regulated cannabis is safer try to avoid smoking cannabis, if possible and be aware of how various groups differ from each other and start low and go slow.
- 01:08:01Right, so I can take questions now I'm sorry that that went a little long.

IM Chiefs

01:08:08perfect, thank you for a wonderful talk, anyone who has questions, and some have already started Please submit them in the chat and I can read them out or, if you prefer to be unmuted just asked to be unmuted and I can unmute you to ask in person, but first question we have.

- 01:08:24How much of the pain relief from cannabis is felt to be doing to the thc versus the CBD content.

Deepika Slawek

01:08:30So that's a really great question, thank you for asking it because I can actually sit in some stuff about our research studies now so we don't actually know, so I think a lot of our.

- 01:08:38A lot of people's experience of pain is secondary to inflammation so it's thought that perhaps some of the impact of CBD on inflammation might account for some of the pain relief from cannabis we're doing three studies at Monte right now we're looking at.
- 01:08:54People who are receiving varying concentrations of cannabis so whether it's high thc or equal parts thc and CBD or high CBD and we're hoping that we'll get more of a sense from these studies of whether or not.
- 01:09:08Cannabis you know TC versus CBD is really what's impacting pain people have worked in this field, for a long time tend to say you know, like people think it's all the thc but CBD is so important and we for a lot of people, they need to increase their CBD and that's all anecdotal evidence.

IM Chiefs

01:09:28I guess a follow up question to that view Council any differently for patients only undergoing like CBD therapy, as opposed to thc combined with CBD.

Deepika Slawek

01:09:38So I do only because the laws around CBD are very different so CBD is legally available through a farm bill that was.

- 01:09:45passed in 2018 so people can purchase it like everywhere, like on Amazon in their district like CVs everywhere, and they get just like random.
- 01:09:56doses of CBD that way I generally speaking, try to tell people not to use some of those products that are not well regulated, we have no idea what's in them.
- 01:10:07And so, sometimes i'll try to point people toward kind of trusted brands that we know of that have been in existence now for like 20 years in California, or something like that so that's usually how that counseling goes.

IM Chiefs

01:10:22Thank you another question from the chat clearly research in the US has been significantly limited by policy decisions, is there any good international research to support us.

Deepika Slawek

01:10:32So there is some good in international research, interestingly, a lot of the policies that overseas are very similar to ours, even in England, I mean they're stricter than we are, if you can believe it.

- 01:10:44And a lot of the research has been done on this product and the pixels which is thc and CBD oral spray.
- 01:10:51has been done in Europe and a lot of our data around cannabis is from that those studies in Europe, and you know those were included in that study I talked about the Meta analysis I talked about published by waiting and L.
- 01:11:06So, yes and no.

IM Chiefs

01:11:10To the next one comes back to a little bit of kind of the different modalities I guess you can administer and the question why is that cannabis available and fill or capsule form seems like it would be a lot easier to hydrate.

Deepika Slawek

01:11:21yeah so in our research studies we use capsule form I'm in New York state it is available as a capsule.

- 01:11:28It really varies depending on the state what they have available, and my suspicion is that in Virginia, it is available, but I wasn't able to find it on any of your dispensary websites, when I was looking.

IM Chiefs

01:11:42For one of our current ID fellows better get.

- 01:11:46That they get a great talk, but have you found a difference in cannabinoid use and effect and people living with HIV compared to that of the general population.

Deepika Slawek

01:11:55So this is a difficult question, I mean like the reason the reason for why this has been studied so much in the HIV population I think it's mostly historic you know, like people living with HIV had this horrible pain caused by uncontrolled HIV, we didn't have a reviews at the time.

- 01:12:12Now I think a lot of our patients with chronic pain, you have HIV have a neuropathic source of their pain and we think that cannabis is effective for managing neuropathic pain.
- 01:12:24Now, in my clinical setting i've seen that people living without HIV, also have a lot of pain effect.
- 01:12:31But we don't have any scientific data kind of explaining to us why certain types of pain conditions might do better than others, and I think that that's a to be determined thing it's a very interesting question, though.

IM Chiefs

01:12:46The one coming in from another resident team um any thoughts or concerns about the increased use of delta eight products.

Deepika Slawek

01:12:54yeah I mean delta eight it's like totally unregulated and we don't know anything about it so yes it's concerning.

- 01:13:01I counseling patients, not to use it, I kind of tell them, you know, like try to use them it's trusted it's not regulated, just like that message of regulated a safer, I really tried to stick with that.

IM Chiefs

01:13:16makes perfect sense and just a couple more here quickly, I want to be respectful of your time as well, but I have there been any studies comparing CBD and thc versus synthetic cannabinoids like Dr and all directly.

Deepika Slawek

01:13:30There have not been direct studies on this, so a lot of our studies have been really.

- 01:13:35specific to the synthetic cannabinoids because people you know, research and were able to get around a lot of these FDA approval issues and DEA issues.
- 01:13:45So unfortunately there's not been a lot of studies that have done the legwork to get all of those federal approvals, in order to look at.
- 01:13:53Plant based cannabinoids versus synthetic.
- 01:13:58I will say as a add on to that is that most of my patients cannot tolerate synthetic cannabinoids it's usually teach see by itself without any opposing CBD and people just feel excessively high they just cannot tolerate it.

IM Chiefs

01:14:16And then last one here any evidence supporting the use of cannabinoids for anxiety and depression and I had shown some data for kind of pain and spasticity but any specifically for anxiety and depression.

Deepika Slawek

01:14:29So not very much for depression, people do seem to reduce their antidepressant doses after starting medical cannabis for anxiety there's decent evidence that is effective in specific immediate anxiety situations like.

- 01:14:43So for people who are fearful of giving public grand rounds at uva there's been evidence that I've looked at have looked at that you know so people who have likes speech fears or whatever panic.
- 01:14:58CBD and Lotus of the thc have been found to be effective in that situation.

IM Chiefs

01:15:07Just just one more question just thinking about Marin all do you have any kind of pearls about its use or anytime that you prescribe it or recommended even over a medical cannabis.

Deepika Slawek

01:15:17So I rarely do primarily because I have personally went into a lot of insurance barriers to using marinol it's often not approved by insurance companies but best of my experience here in New York state.

- 01:15:30You know, there are times, where someone might really, really, you know not be in as being a State where they don't have availability of medical cannabis and maybe marinol will be good at those situations.
- 01:15:43I think that there's definitely been.
- 01:15:46A resource I've shown that it's effective and people who have chemotherapy induced nausea and vomiting.
- 01:15:53So you know I think in those situations it's been used the most out of anything else um and it might be worthwhile to try in those situations, does it.

IM Chiefs

01:16:02Does it appear to have the same kind of impact on reducing those.

- 01:16:08Patients are just not enough data to support.

Deepika Slawek

01:16:10It not a lot of data, but you know, primarily the issue is that it makes people feel high as a kite cannot they cannot tolerate it so people will be like, why would I take this i'll just take my opioids you know.

IM Chiefs

01:16:27awesome well Thank you so much for a wonderful talk for everyone, thank you for joining with that will wrap it up here.

Deepika Slawek

01:16:33Absolutely, and people have other questions they are can feel free to email me I'm happy to answer by email.

IM Chiefs

01:16:40Thank you, thank you.

Unknown Speaker

01:16:41Thank you.