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ECHO: PAIN MANAGEMENT FOR PEOPLE WITH OPIOID USE DISORDER

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[video transcript]

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Dr. may help alar who specializes in the treatment of addiction and pain medicine. Dr. Pillai has served as a senior instructor at the wellmont Cancer Centers integrated cancer pain clinic and their Department of Anesthesiology and perioperative services. She is also a senior instructor for the University of Rochester Medical Center of Department of addiction psychiatry. Dr. Barr, I will hand it over to you here.

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Thank you so much, Lauren. So I have no financial disclosures. And so, the learning objectives from today's webinar basically involved involves the opioid pharmacology talking about dependence and tolerance, recognizing the impact of opioid tolerance and achieving adequate analgesia, discussing the strategies for pain management and using both opioid and non opioid medications. So, why are we here today, we are here because people who use drugs should have access to adequate pain management. But when they go to a primary care physician or a pain clinic, they are labeled as drug seekers and they require an MD receive suboptimal care. We're here to talk about it so that we can fix that or at least work start working on this aspect. So, I will start with discussing the basic opioid pharmacology. There are three main receptors mu delta and kappa. So mu receptor functions are super spinal and spinal analgesia it works for sedation respiratory depression, it slows the gastrointestinal transit time produces euphoria and is responsible for physical dependence. The next is delta. It also produces the super spinal and spinal energy analgesia. It was It is responsible for modulation of hormone and neurotransmitter rates. The other one kappa receptors in Super spinal and spinal analgesia it it produces the psycho mimetic effects also slows the gastrointestinal or transit time. This figure here it shows the potential receptor mechanism for analgesic drugs. The primary efferent neuron the cell body is not shown here. It originates in the periphery and carries pain signals to the dorsal horn of the spinal cord. It's synapses there with the glutamate and neuropeptide transmitters with the second neuron. The pain stimuli here can be attenuated in the, in the periphery by opioids by acting at the mu opioid receptors, or blocked by afferent axons by the local anesthetic which also is not shown in this diagram. Action potentials reaching the dorsal horn can be attenuated by the presynaptic endings by opioids, or the calcium channel blockers like cyclotide by alpha agonists, like clonidine, and possibly by drugs at increased synaptic concentration, or norepinephrine blocking drugs like dependent on opioids also inhibit the the postsynaptic neurons as to certain neuropeptide antagonists acting on tacky keinen, or NK one or other neuropeptide receptors. The opioid agonist produce analgesia by binding to the specific G protein coupled receptors located in the brain, as well as in the spinal cord region involved in the transmission in Europe and the neuromodulation of brain. I know it's a lot of information. It's intense, but it just is too so that we have an idea how opioid works and how they produce pain relief. So the next part I want to discuss is the opioid therapeutic agate, therapeutics, which is what agonist versus antagonists so agonist, the strong agonist involve fentanyl, heroin, hydromorphone, methadone and morphine. The mild agonist involve codeine hydrocodone and oxycodone. Partial is a buprenorphine and antagonist Naloxone and naltrexone. I will discuss in

detail in other slides where where they fit. The other thing which is important as we use these opiates and opioids interchangeably, but opiates are extracted or refined from natural plant matter. Opioids are synthesized in laboratory or factory settings. The other part where we come which is important is opioid dependence and pain tolerance. So evidence shows less pain tolerance than controls in siblings without addiction history on agonist maintenance, we also see that increased pain and up to 70% more oxycodone requirements and women on methadone maintenance following C section. So that's what the the slides is basically saying. Now the types of pain and other variables, acute pain versus chronic pain, I want to take a minute and emphasize why it is so important to identify acute versus chronic pain. The most important thing here is something called a centralization. Centralization leads to chronic pain. Anything which is less than three months is acute pain, when it goes or is has extended the period of three months and becomes chronic. It is critical to understand the chronic pain are the intractable pain because we commonly see the degenerative disc diseases like the low back pain herniated disc arthritis, or prolonged healing from an injury like surgery or fracture leads to prolonged signaling of pain. The nervous system is continuously reminded over and over again that there is something wrong, it's like the nervous system is constantly being displayed flashcards over time to recall becomes quicker and more vivid. The underlying physical condition may not necessarily worsen but the pain intensity grows, because the nervous system reorganizes itself, the body essentially learns how to feel pain. So that is why it is absolutely critical to identify when the pain is becoming chronic collaboration with the pain management doctors collaborating with collaboration with a primary care physician collaboration with the substance abuse doctors or the addiction doctors is important because this in future not treated will will will make the patient more prone to dependence or use disorders. Pain versus suffering. Patients are most at risk for suffering with pain. This is pretty evident patient with substance use disorders, history of violent injury abuse both physical or emotional, any kind of trauma, interpersonal violence, dysfunctional family. Alcoholism has shown alcoholism is also a pertinent factor. attitudes and beliefs of pain, lack of effective coping skills dependent traits. They all lead to lead to putting the patient at risk for centralization of pain. Here we have the WHO analgesic ladder for adults. They have divided into step one, step two and step three, mild pain, moderate pain severity. Now what is mild pain? Anything between zero to four is considered as a mild pain. What they recommend is non opioids, first adjuncts to treat that kind of pain not non opioids like we all know, ibuprofen and said Tylenol, aspirin, adjunct variety of drugs, antidepressants, anticonvulsants muscle relaxants corticosteroids, which are mostly used, then we come to the step two, which is moderate pain. Anything between four to seven would be moderate. They recommend a weak opioid what they consider is like coding Tramadol, low dose morphine. Addition offer adjunct non opioid along with a weak opioid might help to take care of this pain. They escalate it to the step three, which is severe pain. Anything between six to 10 is considered severe pain. They recommend strong opioids, which is morphine, fentanyl, oxycodone, hydromorphone, buprenorphine, adjuncts, and unknown opioids. Like I discussed ibuprofen NSAIDs, these kinds of medications. So, to appropriately treat pain, we have to continue to treat dependence. Symptoms like opioid craving withdrawal dependence might make us pain presentations. So it goes both ways, so treating pain and dependence. To appropriately treat pain it is important to appropriately treat use disorders and dependence. The ASA national practice guideline for treatment of opioid use Sauder the 2020 focused update intends to inform and empower clinicians, Health System Administrators, the

criminal justice system administrators and policymakers who are interested in implementing evidence based practices to improve the outcomes for individuals with opioid use disorder.

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Now we come to the non pharmacological treatments for pain. Cognitive Therapy is involves monitoring thoughts and feelings, attention diversion, distraction, Mejuri, and highpass. hypnosis. See CBT cognitive behavioral therapy I need to I want to take a minute and impress upon its importance. It's a psychological goal directed prong approach in which patients learn how to modify physical, behavioral and emotional triggers or thoughts of pain and stress. Another therapy which is called as pain reprocessing therapy is a system of psychological techniques. That retrains the brain to interpret and respond to signals from the body properly, subsequently breaking the cycle of chronic pain. It has five steps, which involves the gathering and reinforcing personalized evidence or brain origins and reversibility of pain, attending to the appraising pain sensations to a sense through a lens of safety, addressing other emotional threats, gravitating to positive feelings and sensations. So, pain reprocessing therapy in my personal experience, I've seen significant improvements in patients dealing with chronic pain. So something which is new, but pretty good. The other aspect is behavioral therapy, activity monitoring, stress monitoring, relaxation, biofeedback, assertiveness and training. So goal setting and monitoring. These do make a huge difference in patients with chronic pain, exercise, yoga, aqua therapy, which is swimming, PT, OT, stretching, diet, weight reductions. So just like goal setting, if a patient is overweight, making sure that they have realistic expectations that these are the goals which will help in decreasing the pain as well as feeling of overall well being. mindfulness and meditation. Some of the apps calm and headspace patients rave about them and they make a huge difference. Other treatments like acupuncture, pressure therapy, massage therapy 10s unit, orthotics braces, which appear to be simple but when used appropriately and consistently, do make a huge difference. regional anesthesia injections steroids nerve blocks neuro modulation, like spinal cord stimulators. When identified when used in correctly identified patients, they significantly reduce both opioid and non opioid medication burden. So what are the non opioid treatments for pain? I'll quickly go over go over these. So anti inflammatory medications like the NSAIDs Aspirin, Tylenol, corticosteroids, anticonvulsants, like the gabapentin, pregabalin, Topamax, carbamazepine, and Lamotrigine. These are the medications which help with the chronicity of the pain and aesthetics like lidocaine antidepressants, tri cyclic antidepressants, SNRIs old I also want to mention SSRIs and this because sometimes the cycle the vicious cycle of pain and mental health system symptoms like depression, if given the if SSRIs are given, improve the overall well being and also decrease the perception of pain. So muscle relaxants like baclofen tizanidine, Cyclobenzaprine, Cyclobenzaprine, muscle relaxants like Pagla baclofen also has an additional benefit of decreasing the cocaine cravings, just like Topamax also helps when helps with certain cocaine cravings. So dual benefits, disease topicals like lidocaine and sets salon patches Voltaren gel capsaicin or the qutenza patch, disease specific medications like a triptans which helps for migraines, migraines, ketamine, huge benefit in in properly identified patients, low dose Naltrexone in patients with inflammatory diseases or pain coming from inflammatory processes. So This is what I this is this. There are two pictures on this slide which I wanted to talk about and they are part of regional anesthesia. First one shows about shows genicular nerve block which is for very common problem knee osteoarthritis. Most of the patients are on opioids, be it

older or younger, multiple injuries, traumas to the knee. They take opioids for a long period of time and take them for many years can lead to substance use disorder. Patients on substance use disorder, they are not sometimes appropriately sent to the primary or to the pain clinic or pain providers. So that they can have this simple blocklists genicular nerve block. What we do is a little bit of steroid, a little bit of numbing medication. You give this block with the goal to do RFP, which is radiofrequency ablation, burning of the nerves if the burning of the nerves which lead to the knee pain coming from osteo arthritis or multiple other problems, if this works, gives a relief of three to six months significant reduction in opioid medications or the non opioid medications. So that's one of the things like I said collaboration of multiple, multiple multiple disciplines is very important for our patient population suffering from various use disorders. The second slide, this is very common problem again, low back pain, leading to radicular symptoms patient comes to your office B is an addiction clinic, be it a primary care physician clinic, saying that our low back pain and it really eats into my legs, collaboration with a pain management physician, simple procedure college transforaminal epidural steroid injection, little bit of a steroid numbing medication provides relief both for the low back pain as well as the radicular symptoms, if works gives reliefs for gives relief for three to six months. This can be repeated every three months also. So that was the transforaminal. Here I'm talking about the celiac Plexus block, which is a treatment for pancreatitis we all know for treating pancreatitis patients are on opioids for a long period of time. Doesn't matter if the pancreatitis is coming from alcohol use disorder or if it's coming from anatomical problems or other liver related issues. This block involves putting numbing medication in the patient like 30 CC's huge amount of numbing medication, gives relief on pancreatitis significantly reduces opioid medication burden. This like I said, if properly identified patients collaborated with a primary care physician pain physician and addiction provider can significantly reduce the opioid as well as non opioid pain burden, medication burden and also gives significantly more relief. For example, the patient is clock watching the opioid like six hours, this will give relief for six months. And the other thing to this is that we can add a little bit of alcohol in this procedure, patient might have an burn, the nurse patient might have relief for one year also. So something to think about I feel that this regional anesthesia is not is a very important tool which is not being used as frequently as it should. So other firstline non opioid pain medications, we discuss Tylenol, it has been discussed multiple times like Tylenol, we think the benefit is small. But all these medications, if they are appropriately dose, for example, Tylenol, to be dosed 1000 milligrams three times a day might produce good relief. The only problem is like patient don't use it as recommended can and can lead to hepatic toxicity.

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So that's something which has to be monitored. Tylenol harms could be the gastric ulcers renal problems, cardiac issues should be used carefully in patients with all these issues. It is also a first line analgesic Cox to selectivity prevents the GI issues, but still has to be monitored appropriately. Gabapentin and pregabalin so I just want to take a minute these are. This has been FDA approved for post herpetic neuralgia and has been used as an adjunct therapy for partial seizures. but it is becoming an opportunistic drug of use to do low cost classification as a non controlled substance and the struck being a structural analog of GABA. So, the and it as we see, there are increasing rates of a being used inappropriately. And it is also one thing which is very frequently used in the pain clinic because of a lack of an alternative or for opioids for pain

management. So that's also fueling this increased use of Gabapentin and Lyrica. The good thing about Lyrica is that it's a controlled substance, it can still be managed, monitored to up to a certain limit through eye stop, but Gabapentin as we see how it's misused has increased significantly. The other classes try cyclic antidepressants and SSRIs. T TCAS have to be used carefully because they have anticholinergic and cardiac toxicities. SNRIs are safer to use firstline agents for the neuropathic pain for example, trigeminal, for example, the fibromyalgia, post herpetic neuralgia and TCS are used for migraines and headaches, topical agents, alpha two adrenergic agents very important, even though we consider them trivial. That's what I I get the sense of but if they are used in a multimodal way they are they do add and patients do have benefit from them. Capsaicin like the qutenza patch clonidine For Complex Regional Pain Syndrome, very helpful, but used minimally. So they are considered firstline are considered alternative to firstline and they are considered safer to the systemic medications. Now, we come to the buprenorphine for pain management. We know buprenorphine has strong affinity for mu opioid receptors and slow dissociation may provide sustained analgesia at relatively low days low doses, the low doses which are considered transdermal and buckling or moderate to high which are the the tablets FDA indication does not always match the clinical use. When co formulated with Naloxone, there is minimal sublingual absorption until unless it is injected. The next slide we talk about, first we talk about full agonists. So, what are full agonist, full agonist they produce maximum response even when only a fraction of the receptors are occupied, what is a partial agonist which cannot produce a maximum response even when all receptors are occupied, they become they act as a competitive antagonist in the presence of the full agonist and reduce the response of full agonist what is an antagonist a drug or a substance which does not which does not activate the receptors and leads to the blockade. So here we are talking about the buprenorphine pharmacology. So it's a very high returns very high affinity for opioid receptors, partial agonism partial activism of the opioid receptors, and risk of precipitated withdrawal. So the risk of precipitated withdrawal occurs if taken prematurely, which means before the other opioids have dissociated from your receptor, and the patient is in mild to moderate control. Buprenorphine will displace other opioids and partially activated receptor which is experienced by the symptoms of withdrawal. The other thing I want to mention here is ceiling effect, which is makes buprenorphine so desirable. And something which I see more and more people using now for pain management. So see what the ceiling effect means. So, there is a limit to respiratory depression, which makes it safer than full agonist because after a certain limit, the buprenorphine stops addition stops adding up and and is more safer as compared to methadone or oxy codons. So it will. Yeah, so that's the ceiling effect. Why is more desirable? So moving on to the next slide. To LOTOS buprenorphine FDA approved for pain. So the low dose buprenorphine considered is considered transdermal or buccal formulations. The beauty trends is a transdermal it starts at five micrograms and goes up to 20 micrograms. And the buccal is the Bellevue car which you see Here, these are the two formulations. They can be used in opioid naive individuals. There's no risk of precipitating withdrawal. If already on a full agonist. In terms of nutrients patch, what we recommend is if the person is already on full agonist, you put the nutrients patch about start decreasing the doses of the opioid, full agonist the patient is on because this takes at least 24 hours to work. So that's something to be careful about with the nutrients patch, the moment you put on it will not give relief within that timeframe. is similar to other opioid rotation rotations. chock full agonist start buprenorphine is the bell puka low dose used off label for buprenorphine initiation, moderate to high dose off label for chronic

pain, often an individual's originally on full agonist. So this is also important in patients who are very sick cannot take oral medications or have problems with like PEG tube TPN. So this is an excellent pain management tool for them when they when we don't know how they are going to react with fentanyl. So I use these for patients in those conditions. I'm in this study where we talk about the conversion from high dose opioid agonist to sublingual buprenorphine reduces pain score or an improved quality of life for chronic pain patients. So in this study, they had 35 chronic pain patients between 24 to 60 years of age, they converted them from high dose opioids. The morphine equivalents were like 550 milligrams to sublingual, buprenorphine, so they continued buprenorphine for two months, the pain scores decreased from 7.5 to 3.5, which is a big deal. And the quality of life scores improved from six from 6.7 to 8.1. Another journal in the American Journal on addictions they they talk about an observational study of buprenorphine treatment for prescription opioid dependent pain patient. For the three chronic chronic pain patients with opioid dependence were treated for with buprenorphine for three years. And the ranges were from 45 to 60 years, all dependent on prescribed pain medication, they were split into two groups, those with a history of alcohol and substance use and those without the treatment with buprenorphine was affected effective. Most patients had improved pain treatment. With the treatment of opioid dependence, there were no differences noted between those with or without history of alcohol or substance abuse. Overall, patients had much less preoccupation with pain and greater satisfaction than buprenorphine. Major guideline revisions, so the 2020 focus update says that when an opiate when full opioid agonist is needed for pain management, discontinuation of buprenorphine is not required. The addition of short acting full agonist opioid to the patient regular dose of buprenorphine can be effective for management of severe acute pain in supervised sent settings, such as hospitalization, for I'm seeing in my practice that the surgeons are calling and they are making sure that the how they should make sure that the buprenorphine is continuing if the patient needs regional anesthesia, or if the patient needs additional doses of oops, more short acting opioids, what should be the game plan of a patient with opioid use disorder getting a major or a minor surgery. So these I'm seeing these changes in my setting in my location. For patient taking methadone or buprenorphine for treatments of opioid use disorder, temporarily increasing the dose or those frequency which basically means the dosing during a TRD helps in managing the pain and a very effective

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now coming to methadone. So methadone is mudstone pharmacology. It occurs in two forms the RNN, chimeric and s&m chimeric forms, the activity comes through the RNN chimeric forms. It acts by binding and activating the activating the mu opioid receptors centrally and peripherally. It leads to analgesia euphoria, constipation, sudden sedation, respiratory depression, nausea and miosis. The NMDA receptors increase the activity of methadone, antagonizing the NMDA receptors, increases its effectiveness in treating the neuropathic pain as compared to the other opioids The interesting thing about methadone is it's biphasic elimination, which basically means that an alpha phase of two to three hours and a beta phase that is extremely variable. The beta phase has been reported as ranging from 1987 hours in post operative patients 8.75 to 75 hours in opioid dependent patients and up to 120 hours in cancer pain patients. Okay, so this is a dosing risk with methadone accumulation. So because the metabolic ism is so variable, we have to be careful how we chose not methadone, and the unique five pharmacokinetics of

methadone and long and variable Half Life, large volume of distribution. If those inappropriately or those too quickly it leads to accumulation, which leads to sedation and risk of respiratory depression and death. And it is fatal. So the most important thing is making sure that the concomitant competent use of sedatives alcohol anti-psychotics is considered. And it's looked at carefully, collaboration with the outpatient provider for those adjustment and making sure that it's a safe discharge, some will will monitor what's happening with the patient and things like this, the respiratory depression shouldn't happen when they're discharged from the inpatient setting. In this article that European management for patients receiving maintenance methadone or buprenorphine therapy, first I'll talk about the methadone. The most important thing is not stopping the methadone, continue the methadone. Consider splitting the doors into ti d dosing, if you have to convert the methadone from oral to IV. The if the this is I mean, it's an easy, it's relatively easy. The parent rule 50% of the oral dose will be equivalent to the IV of methadone, using short acting opioid analgesics on top of methadone if the pain is not controlled by the Ti d dosing of methadone. In terms of buprenorphine, of course, making sure that they haven't the Miss. They haven't missed any dose of buprenorphine. That's splitting or dividing the buprenorphine doses. Adding supplemental tools of buprenorphine considering IV buprenorphine for acute pain or procedure. I'm aware that most some hospitals do not have like our we don't use IV buprenorphine that often. So if that's the case, if that's the case, then the other steps we can follow, we can add full agonists on top of the buprenorphine. The only thing is this we have to increase the dosing of the opioids maximize non opioid agents consider regional anesthesia nerve blocks. So like I discussed in the past patient has chest pain fractures, consider bringing on the pain medicine physician serratus nerve block, pectoral nerve blocks intercostal nerve blocks, they are they are the modalities which provide long term relief. If the patient they can even put catheters for seven, seven days. So it brings down the opioid use the other medication use and save the patient from side effects, and at the same time provides excellent analgesia. In any case, if we have to discontinue buprenorphine, we discontinue buprenorphine and use full agonist analgesics. convert back to buprenorphine when the pain is a result reduction needed. But what happens is make sure that the long acting full agonist for example, Oxycontin, the patient is off of it for 48 hours to prevent the precipitated withdrawal. If the buprenorphine is discontinued and patient has transitioned to methadone, so make sure that you start the dose remains between 20 to 40 milligrams and use short acting opioid analgesics to treat treat pain in during this timeframe. The 2020 focused update according to the ASAM national practice guidelines for patients taking methadone for treatment of opioid use disorder who have acute pain, refractory to other treatments and required opioid based analgesia, considering short acting full agonist opioids to the regular dose of methadone can be considered to manage a moderate or severe acute pain. So continue methadone but keep an add short acting opioids in between discontinuation of methadone or buprenorphine before a surgery is not required. high potency intravenous full agonist can be used for separately for analgesia which we see very often like Dilaudid. The hydromorphone has been added for a short period of time for two or three days. To get them over the hump after a surgery to get over the acute phase, and then continuation off methadone or buprenorphine. Research shows that additional full opioid agonist can be effective for treatment of pain in these patients. Pain Treatment should be coordinated with opioid use disorder treating clinician to optimize pain care, and reduce potential for relapse. If it is decided that buprenorphine or methadone should be discontinued before a planned surgery, this may occur the day before or the day after surgery, methadone or

buprenorphine can be resumed post operatively. In general presurgery daily doses of these medications can be resumed if they are withheld for less than two or three days. So the next is the naltrexone or the long acting, naltrexone. Very interesting that naltrexone, you can we can overcome an antagonist with a full agonist. naltrexone varies by time of day and month. The only thing which is very important is if a patient is on vivid shawl and if they need pain management which I'm going to address in my next slide. So, naltrexone and emergency pain management, so we are trauma with multiple fractures. We use high dose parenteral full agonist to clinical effect. For example, two milligram for milligram, eight milligram hydromorphone. The most important thing in this setting is we know if we give hide they will require high doses of opioids if they're on long acting. naltrexone it has to be done in a setting where cardiopulmonary resuscitation can be done. Because patient may have deeper respiratory depression, longer respiratory depression, so that has to be considered. nerve blocks regional anesthesia, again a major deal for patient is taking long acting naltrexone, ketamine underused but excellent in terms of pain management. If oral naltrexone giving given at the end of the day or prior to those, it's easier to overcome because you can give higher doses of full agonist if a patient has abscess they're coming to the IDI using local anesthetics and sets, common presentations fractures, dislocations and alcohol intoxicated patients, ketamine or propofol short acting anesthetics, back pain in patient maintain on naltrexone seen in IDI it's easier said than done if a patient will have relief from lidocaine patch notes shouldn't shouldn't be done should be given to the opportunity to the patient that it is a multimodal way to treat pain. So NSAIDs lidocaine patch ketamine, Tylenol, all these medications together. So if planning for surgery, switch to oral naltrexone and stop 24 hours prior to the procedure, have in skilled hospital consultation for reinstatement of naltrexone, if possible can consider switching to buprenorphine after surgery. So it depends upon the provider the need of the patient at that point of time. The new recommendations, naltrexone blockade of the immune sectors can be overcome when necessary with high potency full opioid agonist. In these instances, patients should be closely monitored in emergency department or hospital settings, especially because of the respiratory depression and concerns about that patient. Why should we do that and patients are naltrexone may not respond to opioid analgesics in the usual manner. high doses are typically needed to override opioid receptor blocking.

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Other part of this is since we're talking about Naltrexone is low dose Naltrexone. So no no dose Naltrexone has demonstrated to reduce symptom severity in conditions which are mostly inflammatory for example, fibromyalgia, Crohn's disease, multiple sclerosis Complex Regional Pain Syndrome. LDN may operate as a normal anti inflammatory agent and central nervous system action on the microG microglial cells. These effects care maybe you need to lower doses of Valtryek zone and may appear to be entirely independent from the actual zones, better known activity and opioid receptors. As a daily OPA oral therapy LDN is inexpensive and very well tolerated. Despite initial promise of efficacy, the use of LDN for chronic disorders is still highly experimental. But in my personal experience when I've used this patients have definitely experienced relief and they have been consistent with it. So that's the end of presentation. If you guys have any questions.

39:57

Thank you so much, Dr. probar. That was at Samsung.

[End Transcript]