Dr. Hunt: Good afternoon. My name is Dr. Hunt. And Dr. Olatoye and I are excited to be able to share with you information about chronic pain and polycystic kidney disease this afternoon. I hope that everybody's been enjoying a great time at the virtual conference for PKD Connect. So, Dr. Olatoye and I both work for Mayo Clinic. We've known each other for several years, but I just still happen to be at Mayo Clinic in Jacksonville, Florida. And he's at Mayo Clinic in Rochester, Minnesota. So, he and I will be doing the presentation together today. So let me go ahead and share my screen. And Dr. Olatoye, let me know if you can see it. Can you see my screen?

Dr. Olatoye: Yes, I can.

Dr. Hunt: Perfect. All right. So, I serve on the polycystic kidney disease Education Advisory Panel and Dr. Olatoye has no disclosures to share. And I like to just start out with understanding what is chronic pain fundamentally. What do we mean by chronic pain? And the International Association for the Study of pain defines chronic pain as an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage described specifically by the person experiencing chronic pain. We have a lot of different ways to measure pain. But really, they're subjective they rely on I'm sure many of you guys have seen these pain scales that can sometimes it can be very difficult to rate pain accurately and one person's two maybe someone else's 10. So, pain is inherently subjective.

We have the brief pain inventory questionnaires, lots of different questionnaires that folks might fill out at doctor's offices to try to communicate their pain experience. We don't have a temperature measurement to get an objective measure of what pain is and it's really different from everybody not like taking a temperature or taking a blood pressure. And so really, I wanted to just focus on that this is a sensory and emotional experience. It's not necessarily simple. When patients are experiencing chronic pain that by some definition may just be four to six weeks, this can be considered chronic pain. And we know that up to 60% of patients with polycystic kidney disease may experience chronic pain, which is why the foundation wanted to have this as part of the talks for this

conference. And it's just very important to understand that everybody's pain experience may be different. And how that's communicated is not just limited to tissue damage that may have occurred, but inherently implies the emotional experience, suffering and an overall symptom burden. And when we're talking about pain, it can become very complex. And we'll try to highlight some of that today. So again, chronic pain is really a sensory and emotional experience.

And this is a humility slide here, and this is a favorite one that I like to share with patients. Whenever patients visiting their doctor, especially if they have a rare disease like polycystic kidney disease, they may feel like they're the ones who have to educate their physician about what they're going through and the doctor may have questions herself about some of the nuances of the disease and what may be a pain generator in patients like polycystic kidney disease, for example.

So, what can be sources of pain in kidney disease? So, patients can have chronic renal pain and that can be sort of pain that's felt in the flank area, for example, sometimes in the back. Patients can actually have mechanical back pain, kind of the classic low back pain experience. They can have a sensation of abdominal fullness, early satiety, bloating, nausea, those types of symptoms and they can also have chronic liver pain. And that pain that's typically experienced in the upper quadrant. And so, some of it may be epigastric or upper quadrant area.

And then I didn't want to get too much into the weeds here, but I just wanted to highlight how complex the anatomy is when it comes to pain structures and polycystic kidney disease or the kidneys in general. And there are various different ganglia that reside here and can provide intervention to some of these structures that can be painful. So, a little bit later in the talk, I'm going to share information about different nerve blocks that can be tried and sometimes it's not necessarily straightforward. Whether a nerve block will help and which nerve block is the correct one to do. Sometimes it's a little bit of trial and error because there are several different nerve block bundles if you will, that provide intervention to different parts of the kidneys. And so,

it can be a challenge sometimes to identify if any of these nerve blocks will be helpful and if so which one.

So, I put this kind of slide up here, I want to talk about how we evaluate patients with chronic kidney disease-related pain. This is an algorithm proposed by these authors here by a group of urologists and really it comes down to evaluating, is it acute, is it chronic? What structure is it coming from? And what might be some of the solutions that we think of? So that's really the first decision point, is it acute pain or chronic pain. And that's really important to understand because acute pain can be associated, or acute pain should drive the provider to ask additional questions about potential risk of infection and potential hematuria or blood in the urine and it takes you down a different pathway. I'm evaluating acute pain versus chronic pain, acute pain may require immediate or urgent, disease directed interventions.

The scope of this talk is focused on the chronic pain question, but that's the first early decision point when it comes to evaluating pain and chronic kidney disease or a polycystic kidney disease. If it's chronic, do we think that it's renal origin, hepatic or liver origin? Is it more mechanical back pain type of pain. Either way, we always want to start out with more conservative treatments, medications like Tylenol, adjuvant analgesics that we can get to a little bit later. And we'll talk also a little bit about you know, is there a role for opioid, when do we consider opioid.

And then we think through the kind of the breadth of options. Really in pain management, like I said, we always want to start with conservative treatment and really progress from there. And if patients aren't doing well, with conservative treatment, we might need to think about nerve blocks, spinal cord stimulation. We might need to think about is the patient a surgical candidate. If so, what's the right type of surgery to consider. And then there are also some kinds of advanced interventional therapies that may be appropriate in some but not all patients with polycystic kidney disease-related pain.

So, think about conservative pain management and polycystic kidney disease. Typically, patients are urged to avoid medications like Ibuprofen or

Motrin, really non-steroidal anti-inflammatory medications, because those aren't good for the kidneys. But Tylenol is typically recommended, you know, recommendations like trying to heat, ice, whirlpool, those types of treatments can be helpful in some patients. The Alexander Technique comes up a lot in the literature. And the Alexander Technique is really focused on, you know, kind of teaching patients different body positions and things like that in order to try to kind of help with pain. And that can be helpful when we think about kind of, it's actually first studied by musicians, but it's different ways of kind of studying posture and movement and being aware of one's positions. And it's been described for use in patients with polycystic kidney disease.

I do have a question here. Jeanette asks, is there ever a time that NSAIDs would be used to help control pain for a short duration? Maybe, if patients don't have really much in the way of impaired renal function that could be considered in the short term, but generally, it's recommended to be avoided in patients with polycystic kidney disease, even in the short term, if they have any type of impaired renal function that could just accelerate that. So typically, no. From my standpoint, I'm really deferring to the nephrologists, and I've never had a nephrologist who approves of NSAIDs, both in patients with and without polycystic kidney disease. Then the kidney doctors and the GI doctors, the gastroenterologist really don't like nonsteroidal nor do internists, for that matter. Good question.

And please, guys, feel free to have the chat open. Let's make this interactive. If you have questions as we go through the slides, we'll have time for Q&A later. But please speak up as we're going through if you have questions.

Cognitive behavioral techniques can be really helpful in pain management. Dr. Olatoye will talk about that a little bit. Nutrition is super important. I know you guys have nutrition lectures, there's so much incredible data about the role of nutrition and reducing the body's inflammatory response and how foods can actually trigger inflammatory responses in the body worsening chronic pain. And we're learning more and more about that. So, nutrition is incredibly important in managing chronic pain. These are adjuvant pain

medications things like gabapentin, pregabalin, amitriptyline, nortriptyline, duloxetine, these may or may not be helpful in some patients, and then sometimes there might be a role for opioid medications. Many of the patients that I treat with polycystic kidney disease, do take opioid medications and we'll talk about some of the issues with those for any chronic kidney disease. And then sometimes there can be treatment directed at the cause, I would like to say I will have a talk about a little bit to think short of surgery.

And as we transition into Dr. Oludare's portion of the talk, I just wanted to briefly introduce, there's the World Health Organization that developed the analgesic ladder in the 1980s. And it was really designed for cancer pain patients, and it was designed to explain, here's when a provider, you know, here's when the doctor and the patient should think about introducing opioids how to treat pain. But since then, it's kind of really been adapted for non-cancer-related pain and we ran into some problems when we applied that to the non-cancer-associated chronic pain patients. Briefly, it just kind of summarizes thinking about, you know, avoiding opioid medications, trying other things. If that's not helpful, I'm accelerating that to opioids. Kind of the milder gentler opioids on. Some people might have been exposed to Tramadol, for example, while also using some of these other agents and stepping it up to maybe more potent opioid medications.

And then finally, considering some of these more invasive treatments or nerve blocks, that sort of thing. I personally recommend considering if a patient's candidate for a nerve block or something like that before considering the opioid medications. I would probably put step four more so in between step two and three to be quite frank, but it's really a case-by-case basis. So, it's important to talk with your doctor about what is the right choice for you. And with that, I'll hand it over to Dr. Olatoye.

Dr. Olatoye: Yes. Thank you so much, Dr. Hunt, for the introduction, as well as going through the first portion of your slides here. So yes, as Dr. Hunt mentioned, there are several options to manage pain in patients with PKD. And you can think of medication as certainly one of those options. And when we think of medications, one can think of medications in different categories. One can

think of them as what exactly it's targeted in the body. So, some medications are designed to help with nerve pain. Some are designed to help with musculoskeletal or what we call kind of diffuse body pain. And there are some medications that are designed to help with visceral pain, pain coming from internal organs, one of those being the kidneys. But unfortunately, or perhaps maybe more in a more complex manner patients with PKD or patients with chronic pain typically would have a combination of all these symptoms. So, it ends up being we're utilizing multiple medications, in an attempt to cover these types of pain.

One could also think about pain both in an acute or chronic form. There are patients I mean, most patients with PKD typically are dealing with chronic pain, but there might be times when they're admitted to the hospital for acute pain. And certainly, the fact that they've had chronic pain for you know, for a while can influence how we manage the acute presentation. And so, one has to be safe with these medications and ultimately, we want the medications to be effective. So, there's always a balance here. So, one of the medications we typically utilize in patients with PKD are opioids. And this also obviously can be used in chronic pain in general.

Opioids unfortunately, even though again, they have their use, I'm sure you guys are all aware, the opioid crisis is still an ongoing issue. I think we've made some headway over the last few years. But the last couple of years, unfortunately, and I'm sure the pandemic did not help. The numbers were seen as far as opioid-induced adverse effects has only risen over the last couple of years. And these are just some data here available through different government organizations on the trend with the opioid crisis. And unfortunately, these numbers like I said, over the last couple of years have only gotten worse.

Here is one of my colleagues here at the Mayo Clinic, Rochester, Dr. Halena Gazelka. She is a national voice on the topic of opioid crisis and opioid-induced deaths. And here she is testifying in Congress on ways to help curb that issue, as well as finding alternatives to opioids for the management of pain.

So opioid medications, like I said, certainly have a use. I think it's recommended that if we can utilize non-opioid options first, that's ideal. But there might be times when a patient might require opioids such as in acute pain or frankly uncontrolled chronic pain. But when opioids are utilized, there are a few things to consider, and this is just in general. One is the issue of tolerance again because as time goes along, the patient's need or requirement tends to go up and so patients, unfortunately, may require higher and higher doses of this medication to help control their pain. There's also the issue of dependence where, again, where if a patient is not able to get this medication, they might potentially have physiological signs that would imply they're a bit dependent on this medication.

And last but not least, and certainly, something that is very important is the whole concept of addiction. I think one needs to be very careful. And I am also very careful about utilizing this term because addiction is not something that is as commonly diagnosed as we do. It is actually on the reverse side, but something that we have to be very mindful of in patients who are taking opioids chronically. I think another way to think about addiction or maybe a better term will be pseudo addiction, which is patients are not getting adequate pain control, and as such, are potentially showing signs of what might be interpreted as addiction. So, addiction is one thing that I'm always very mindful about labeling patients with. It is definitely an issue, but not something that we need to take too lightly, or something that we need to label all patients with.

So, these are some of the issues that we have to deal with when patients are utilizing opioids for chronic pain more so though, in patients with PKD. And other issue with opioids, in general, is they tend to be cleared by the kidneys. And so, if a patient has relatively, poor kidney function, one needs to be very mindful of utilizing opioids in this patient population because this metabolized could hang around and as a result can cause side effects. Again, some of these are listed here, but other side effects might include respiratory depression, these opioids can certainly induce itchiness and a variety of other side effects. So, being very mindful of the dose, the frequency in patients with PKD went on opioid is very, very important.

There are other non-opioid analgesics that we can certainly utilize in patients with PKD and frankly, chronic pain in general. Dr. Hunt mentioned anti-inflammatory medications, but certainly, analgesics for example we need to be very mindful of the dose we're taking. Just because it again, that could be damaging to patients with kidney dysfunction at baseline. It's recommended if a patient has some baseline kidney dysfunction, Tylenol might be a better option for those patients. But again, one has to be mindful of the maximum daily dose because that is cleared by the liver and can affect liver function.

Other non-opioid analgesics that people sometimes utilize for chronic pain are, for example, Serotonin Norepinephrine Reuptake Inhibitors. An example of that is Cymbalta or Duloxetine. That helps a lot both with nerve pain, it helps with mood, it also helps with diffuse musculoskeletal pain. So that's a very good option for patients who might have pain that perhaps has all these qualities. And we also have neuropathic pain agents specifically, including things like gabapentin, pregabalin, but the issue with those medication again, just like with opioids, they're cleared by the kidneys. I'm going to pause here for a bit before I get into my last medication. Yeah, it looks like there are a few questions here. So okay, so I think some of these questions perhaps will, we might answer towards the end here because they're very general. And so, I would like Dr. Hunt to also contribute as well.

So, medical cannabis, someone I believe asked the question about medical cannabis. I think medical cannabis is a great option. I think before we go into that, we need to talk about the Endocannabinoid System. So, this is actually a group of receptors present as you can see, in various portions of the body. And so, what we found out over time, is that by challenging the system, we can actually help control pain. So, as I mentioned, endocannabinoids are present in a variety of body structures and utilization of cannabis can help with pain control. Certainly, cannabis in general perhaps has some stigma associated with it, but what we're finding out is that it is actually very useful for patients with chronic pain, especially those that are not well managed by first or second-line medication such as, again, Tylenol, NSAIDS, even SNRIs. I think medical cannabis is a good option.

The issue with medical cannabis, unfortunately, is that it is federally illegal. So, it is hard for us to properly regulate what's in this medication. Certainly, you can get CBD over the counter, which is the less psychoactive portion, or one could think of CBD as more or less the anti-inflammatory portion of Medical Cannabis, but THC has sometimes been shown to help with pain as well. However, the THC component tends to be psychoactive. And that's typically what will result in a high or even potentially hallucinations and not the desirable side effects that we want. So, THC unfortunately, is one that we're very, very mindful of in patients taking Medical Cannabis.

So, in the United States, Medical Cannabis, in general, is still a controlled substance, it's a DEA Schedule I drug. When we certify patients for Medical Cannabis, if I feel like a patient is a good candidate a clinician may certify of no certification is state-based. And so, a provider cannot certify another patient who is now within the same state. And so that's something that patients' needs to be mindful of and providers as well. Now, if a patient is certified, then they would need to go to the pharmacists that actually dispenses this cannabis. And based on you know, different factors, they might have to prescribe different doses and different combination of CBD and THC for these patients. And as mentioned here could vary by state.

So again, depending on the state, some states may allow Medical Cannabis, some might not. And like I mentioned, a variety of conditions might be eligible. I think, ultimately, I think it's worth a try, at least for my patients, if especially if I'm struggling with first and second-line medication. This is something I certainly speak to my patients about. There are some health risk associated with Medical Cannabis. And a couple of those include hallucinations and certainly suicide risk if taken at very high doses, which is why I think going to a pharmacist to have a more controlled dose, is a key.

So, I think we've talked about opioids, we talked about non-opioid analgesics, but one also has to consider the biopsychosocial model for chronic pain. And what we're thinking about essentially, is how one's biology, one's psychology and one's social environment can affect pain. And this is unfortunately, there's a focus heavily on biology. But we cannot ignore the contributions of

the patient's psychological background, as well as a social background on pain. And so, as you can see the different components of each major category here that one needs to consider and if we only focus on one aspect, unfortunately, especially in chronic pain, if the other aspects are not well addressed, pain never improves. And that's just that's actually well studied and that's well established. And so, you know, one needs to consider things like coping behaviors, we also need to consider relationships with either social support groups or patients' family members, these are things that we need to be factoring in when trying to manage chronic pain in these patients and peer support as well. Again, as I mentioned, these all would impact a patient's pain experience.

A key to that, especially a modality that can be used to manage this model is something called Cognitive Behavioral Therapy. Here at the Mayo Clinic, Rochester, we have a Pain Rehab Center, that actually helps patients, as far as, coping strategies, developing ways to deal with the pain because we know over time pain involves more than just the patient's biology. And so, again, as a patient, it's important to put yourself in the shoes, like what exactly are some of the factors that might potentially affect my pain beyond just a biological or physiological aspect of pain. So again, one is to consider this in all patients with chronic pain. And for reference or resources, these are some of the examples that you can maybe take a picture of the screen that could help with the bio-psychosocial aspect of pain control. So, I'm going to pass this back to Dr. Hunt, to finish up the talk on procedural aspects of pain control in our patients with PKD.

Dr. Hunt: Hopefully everybody can see my screen. Perfect. And David, let me know if you can't see my screen. So, as we move on from kind of the medication management, I'm just going to take a moment here to address some of the questions that have come through. So, when we think about Medical Cannabis for PKD symptoms, again, because this Medical Cannabis has not been well studied because of the laws in the United States, you're not going to have NIH funding really to study this for really any disease indication and it might all end in kind of anecdotal experience. What I would say is that there are some patients I've had both with and without polycystic kidney

disease who have benefited from Medical Cannabis. I would say most patients, in my experience, I don't certify for this, but I've just treated patients who take it tell me that they don't tolerate it or that it's too expensive. So, I've seen mostly limitations with it. But certainly, some patients do report benefit, but we don't have any dedicated studies to tell us about how effective this is for PKD symptoms in general.

And then Jacqueline has a great question about how do you identify back pain, mechanical back pain versus can you relate a pain? I'll talk about that in just a moment. And then I'll just briefly answer the question about bulging discs. Cystic kidneys would not cause bulging discs. So, I can say no to that, certainly, a person could have both problems. But bulging discs wouldn't be caused by large kidneys. And then the opinions of using a Tens unit for managing chronic pain, especially back pain? Absolutely, I would definitely recommend trying that. That's kind of in that area of conservative treatment. And I think a Tens unit is a great thing to try for chronic pain management and see if it's helpful.

So, in procedural pain management, one question that comes up really in every consult I have for polycystic kidney disease and chronic pain is the use of some of these nerve blocks. So, I'm going to list several here. At the end of the day, what I would like to share is that we don't know these some of these procedures, particularly the Celiac Plexus Blocks are not without risk. Celiac Plexus block, Splanchnic nerve blocks are not without risk. And so, I don't offer them casually to any patient, but they may be reasonable to consider because I shared with you the anatomy is so complex that there's no way for us to know ahead of time really is a patient likely to benefit from this or not, but maybe worth a try, my bias.

Some providers recommend neuroleptic blocks so that is using alcohol with these blocks to kind of really sort of destroy those nerves. That is a particularly risky procedure that I really reserve for cancer-related pain. I don't recommend doing that routinely in non-cancer-related pain. And so, it's possible that a person might have a Celiac Plexus block or Splanchnic nerve block without alcohol, and they only get temporary relief for a few hours.

And so, it's probably not a whole lot of patients who respond really robustly to some of these procedures. But again, I would talk with your doctor about is it a good treatment for your specific situation. There have been case reports described in the uses of spinal cord stimulation for polycystic kidney disease, but no definitive large studies just case reports.

And then also cyst aspiration or ablation when done with ultrasound can be an effective technique if only one or two cysts are thought to be causing the problem. But if it's many different cysts, then just not feasible to get at those with ultrasound. So, these are some of the procedural pain management approaches that folks will take. From surgical standpoint, I'm not a surgeon, but I'll just speak about it briefly. But fair warning, I really won't be able to answer many questions about this other than to kind of just tell you very general information.

Cyst decortication has been the most well studied, there are 15 different studies out there all showing positive results with cyst decortication. It's kind of the most commonly employed if a person's a surgical candidate for that procedure. Renal denervation is more experimental and involves a lot of mobilization of the kidneys. And it's a very large procedure where it's basically kind of destroying the nerves going to the kidneys. Again, it's more experimental and so not all places will offer that. Nephrectomy can be offered for patients with end-stage renal disease could be the candidate for that procedure anyway and in some of those patients that may bring pain relief. And then transcatheter arterial embolization is really reserved for patients who are in stage renal disease status, but for other medical reasons are poor candidates for surgery. And then kind of hepatic cyst fenestration or transplant fenestration can be used kind of along as part of the TAE therapy in some patients, if there are many different cysts and that you can't get at them just with an ultrasound technique I talked about earlier.

Again, I'm going to try to get through this a little bit quickly just so we have some good time for Q&A. But there's a group out of the Netherlands that's published a lot of different studies on this. And I always take this with a grain of salt because when you have one group publishing a lot, it means that they

have a lot of experience with this, which is great. But it's not necessarily something that's been reproduced at many other centers. So just because people propose a way to do this doesn't mean that this is definitely what should be taken as definitive. But what they propose is, again, to kind of evaluate what the possible causes like we talked about earlier, starting with non-invasive treatments first, like some of the behavioral modification, ice and heat, physiotherapy, I would put Tens unit in that category for sure.

Medication choices that we've already talked about. And then some of these procedural therapies or minimally invasive therapies, we talked about really many of these, I think all of these targeting either the kidneys or the liver kind of depending on which one is felt to be the cause. And then the more invasive therapies that I talked about earlier. And really, with every one of these choices, it's all a risk-benefit discussion between the patient and their doctor about what the right choice is for that specific patient. Just because you've heard about a procedure that might have worked well for somebody else doesn't mean it applies to your specific situation. So, these are really thoughtful conversations that have to be had with a multidisciplinary team. As a pain management physician, I'm never making these choices in isolation, I'm always talking with the patient's nephrologist, maybe their hepatologist. I mean, we're really making decisions kind of as a group, the surgical team, that sort of thing.

I'll mention here the back pain. So, when it comes to mechanical back pain and deciding is this referred from the kidneys or even liver, or is this mechanical back pain and there are specific back procedures that we do very commonly. And essentially, if a person responds well to some of those back pain interventions, that tells us that probably the low back and it's not occurred from the kidneys. So that's again, something that we can definitely identify and then treat, which one is causing the problem. And so, with that, we have some time for questions and discussions.

This is our beautiful Florida Campus. They'd have all different base lights that they'll kind of light up at different times. And then also just want to kind of give a plug for the ADPKD registry here as well. I don't know what the

TED Talk slides are, that might be referring to somebody else's slides. I see that from Peggy's daughter. I don't know what she's talking about there. But we have time I think for any questions if people have questions. And Dr. Olatoye, please feel free to unmute yourself and chime in as well, of course. We think about back pain assessments. Oh, Dr. Olatoye's resource slide. Okay, let me see. I can go back to that, doctor. Oh, yeah, I know what he's talking about. Yep, right here. Here we go. I'll leave those up. Great.

So, when it comes to back pain assessments or intervention, so, again, it's kind of outside the scope of this talk to talk about that in a lot of detail. But that's the bread-and-butter stuff that Dr. Olatoye and I do every day. You know, it always starts with a physical exam and then using any imaging that's available, at a very basic minimum using X-rays and doing a good spine exam that involves a musculoskeletal exam and a neurologic exam. And then, from an interventional standpoint, when it comes to you know, one of my big things I think about is the pain just in the back, is it going down the leg and then thinking about different procedures, including facet joint injections, facet joint ablation, like kind of nerve ablation that goes with the side joints and epidural injections if the problem was more related to a pinched nerve like a radiculopathy problem.

All right, and then I see I'll go through the questions here. Amanda says I use red light therapy twice a week to assist in pain management. Do I recommend red light therapy? I'm actually not familiar with that. That's a great question. So, I don't recommend it. But that doesn't mean that it doesn't work. It just means that I'm not familiar with it. I don't recommend that in my practice.

Alice asks, what is one of the most important questions you'd recommend someone ask their doctor if they have chronic pain? Oh, that's a great question. A question that they would ask their doctor. I guess really one of my questions would be, you know, how comfortable do you feel managing a patient with polycystic kidney disease? And I don't think that it's necessarily important that they be an expert in managing chronic kidney disease, I think what's more important is that they feel comfortable reaching out to team members regarding questions that they might have. So, Polycystic Kidney

Disease is a rare enough condition and there are many doctors who may not have treated that before or at least who may not have a really broad experience with treating a lot of different patients who have this. But if they feel comfortable reaching out to you know, a nephrologist reaching out to other resources that they might have at their disposal to get some of their questions answered.

I think that's what's very important is that you have a doctor who displays humility, who displays curiosity in you and your condition. And who really takes the time to try to understand your specific problem. And he feels comfortable reaching out for other resources in order to understand what a good treatment plan is for the patient as opposed to somebody who kind of doesn't feel comfortable asking questions and finding out more. I wouldn't be entirely comfortable working with my doctor not feeling like she knew all the answers. But, who at the same time felt comfortable, people who I can reach out to or I'll look to find out.

Dr. Olatoye And to that point as well. One could also think about, I mean, certainly, I think it's important to utilize a provider who is perhaps comprehensive and multimodal in nature, right. And so, there are some providers, all they do is give opioids or medications, there are some providers, all they want to do is just stick a needle in someone just to treat the pain, but one has to at least be on the lookout for providers who are comprehensive in their approach to pain control. And that typically is more successful than just one approach in general.

Dr. Hunt: That's such a good one. I think, probably the question I would ask the doctor is who do you refer for cognitive behavioral treatment related to pain? And if they say, what is that? That probably tells you that they're not comprehensive. A great point Dr. Oludare. I think that kind of addresses Christian's question hopefully. Doctor, may I ask what's the safest long-term pain meds that you use clinically for PKD management? So, I think the safest, Dr. Oludare, do want to take that?

Dr. Olatoye: I'm sorry, which question was that, again?

Dr. Hunt: Doctor, may I ask what's the safest long-term pain medication you use clinically and for PKD management, but it would be you know, kind of basically in terms of the adjuvants versus opioid.

Dr. Olatoye: Right. I think there's no one medication that is safe to be used chronically, I think. Each medication needs to be evaluated on a scheduled interval. Obviously the less potent, especially as it relates to the kidneys, the better. But certainly, every medication, no matter how benign might seem, would have a footnote. There are possible side effects associated with it. So, it's not necessarily what type but just making sure that you know you are communicating with your provider and vice versa, about any possible side effects and just constantly adjusting and thinking about all the means of controlling pain. So, unfortunately, there is no one good drug that can be used chronically because every single drug has its side effect and benefit. But certainly, one needs to consider that.

Dr. Hunt: Yeah, I would totally agree. And I would just say that anytime you can avoid using opioid in the long term, not just do the safety profile due to the fact that opioid use chronically worsens pain in the long term, we know that. So anytime you can avoid using opioid and use some of the adjuvant medications, that's better. That's where I tend to pick adjuvants plus maybe interventional therapies, even while trying to avoid the opioid as much as you can that can be helpful. And like Dr. Olatoye pointed out earlier, when a patient's taking a lot of opioid medications when it does come time for that surgery, that can be really difficult to manage surgery-related pain, and that becomes a problem too.

And then there's a question about aspiration sclerotherapy is fairly successful or not? So, I don't do these procedures myself, but I'll tell you what I know about it. So, these are the cyst aspiration and Sclerotherapy is considered very effective in patients who are the right candidate and that's why you really have to kind of talk with your doctor about it. However, it's not necessarily long-lasting. In one study, at least two-thirds of patients had pain return in 18 months. So, this might be a good procedure to think about if a patient's not quite in stage renal disease yet, but they're kind of approaching that maybe

and this can kind of be a temporizing measure, kind of to get through until they can have that nephrectomy surgery.

Oh, yeah. *[unclear] [01:13:29]* so I talked about adjuvant medication. So, this is kind of what Dr. Olatoye was talking about earlier. These are basically non-opioid pain medications. So, things like you might have heard about Gabapentin medications, for example. Those are the anticonvulsant class, gabapentin, pregabalin or Lyrica is the brand name for that. Amitriptyline or nortriptyline, those are tricyclic antidepressants. Duloxetine, venlafaxine those are serotonin, norepinephrine reuptake inhibitors. There are a variety of medication classes that can be looked at to help with chronic pain that aren't opioids. You're welcome. You know, David's going to try to keep us on track here. Anything else you'd add to that Dr. Olatoye?

Dr. Olatoye: I think those are all, you know, again, basically, non-opioid medications are typically referred to as adjuvant medication. So, they can come in, you know, various types as far as mechanism of actions and where they act. So yeah, I think that's a comprehensive list you mentioned.

Dr. Hunt: Perfect, yeah, are SNRI safe in ADPKD? So, I'll tell you what I do. So, whenever there's any medication that we're talking about adding to some of these patients' regimens, if we're really worried about hypertension, I'll just work with a nephrologist, like I told you earlier, I'm never making these decisions in isolation. One thing about Mayo Clinic is that, for better or for worse, we really do work in an interdisciplinary fashion. So, patients with complex diseases, you know, you might have five different doctors in five different specialties or more, who are managing different elements of your disease. And so, we're really making team-based decisions. So, I might, for example, suggest the use of an SNRI and that may or may not be appropriate for that individual patient due to hypertension risk. So, it just kind of depends on patients that may be appropriate or not. So that's why I talk about these different medication classes. But it really depends on the patient and what's safest for them.

You know, there are many patients I have, who kind of opioid is kind of all that's left and you know, we've tried everything else and it doesn't work and

they're waiting on surgery. And then that becomes really challenging. And I'll just share this *[unclear] [01:15:36]* you know, medications, like, you know, this is what I think about medications like buprenorphine, maybe methadone in some patients. Some of these medications are a little bit safer in the long term but do require more careful management. And it really have to be considered when a patient's approaching surgery, things like that. So again, none of this, as you guys all know, I'm not getting medical, none of us are giving medical advice for each individual people, but more so things that you can maybe talk with your doctor about for more information.

So, I think that our time is coming to an end here. So, we'll just say thank you to everybody for your time. Thank you so much, Dr. Olatoye for joining me in giving this very important talk to such a very important special group of patients near and dear to our hearts. So, we thank you for your time and hope you have a wonderful rest of your conference. Thank you.

David: Thank you, Dr. Oludare and Dr. Hunt. We appreciate your time as well.

[Audio Ends] [00:41:54]