MIGRAINE WORLD SUMMIT

TRANSCRIPT

INTERVIEWS WITH WORLD-LEADING EXPERTS

MENOPAUSE, PERIMENOPAUSE & MIGRAINE

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Introduction (00:05): And along with other changes in the perimenopausal years, women begin to have those vasomotor symptoms. They have hot flashes, rushes of heat. Women will talk about feeling like somebody turned the heat up and then suddenly they're quite cold. And they also have difficulty sleeping —may be related to the hot flashes — but sometimes just challenges with sleep in and of themselves. So as the sleep begins to change, then we're more vulnerable to migraine attacks being more frequent and more burdensome. So it's a real sort of chaos; it's just an avalanche that hits these women in those years. But with the right sort of education around it and the understanding of what's going on, and looking at different tools or using the same tools in different ways, we can generally help women pass through this time effectively managing their migraine.

Lisa Horwitz (00:50): Hormone fluctuations during a menstrual cycle trigger migraine attacks for many people with migraine. What happens during the phase of life when menstrual cycles begin to wane? Dr. Christine Lay is here to help us explore the often overlooked intersection of migraine, perimenopause, and menopause. Here we'll gain valuable insights in navigating the sometimes tumultuous seas of migraine during this transformative phase of life. Dr. Lay, welcome back to the Migraine World Summit.

Dr. Lay (01:22): Thank you so much for having me. It's a pleasure to be here, Lisa.

Lisa Horwitz (01:25): So, for people who are not aware, what is the difference between perimenopause and menopause?

Dr. Lay (01:34): So, it can be confusing, but if we look at the word, and the root of the word "peri" is around menopause, and "menopause" is actual menopause, but this can be a very prolonged phase. So for some women, perimenopause could begin in the late 30s even, a time when the menstrual cycle might become a bit irregular. She might begin to notice difficulty sleeping. There may be issues with hot flashes, and menopause itself can go all the way into the 60s. It's really officially one year after the last menstrual period or the final menstrual period. But hormonal fluctuations can go on for a few years after that. So, perimenopause we look at as a time when women are still having a menstrual cycle, although it might begin to be irregular, and menopause is really once the menstrual cycle has ceased. For women with migraine, the change in migraine can begin even a couple of years before a woman enters perimenopause. It may be one of the first signs that perimenopause is on its way.

Lisa Horwitz (02:32): Are you kidding me? You just kind of blew my mind a little bit. I was not expecting to hear that. What kind of changes can people see in their migraine that might indicate perimenopause is on its way?

Dr. Lay (02:45): So, for some women, when we talk to them, they'll say, "My menstrual cycle's irregular, sometimes I have trouble sleeping, but my migraine is getting worse." So, we'll see a woman, perhaps in her early 40s, who's beginning to have a little bit more frequent migraine. Perhaps it's longer in duration; it's a little bit harder to get rid of. We have to take a different approach to the acute therapy, or maybe we have to think about prevention if she isn't already on preventative therapy.

Lisa Horwitz (03:09): Why are these hormonal migraines more intense or more difficult to treat, as you mentioned?

Dr. Lay (03:17): So, for a long time, that was not really proven, but in more recent years, diary studies and looking more specifically at this have shown that yes, in fact that menstrual migraine attack can be longer duration, more disabling, harder to get rid of with the usual medications. We don't fully understand why. It relates obviously to hormonal change, but along with hormonal change, we're now beginning to understand that CGRP [calcitonin gene-related peptide] — sort of the hot word in migraine in the last few years — probably also plays a role in that menstrual migraine attack being more burdensome.

Lisa Horwitz (03:50): Are the hormones fluctuating in a different way? Are the levels differently presented ... I'm just trying to fully understand. So I know I have my menstrual migraine; I've gotten used to that. Why in perimenopause is it different? Do I have less estrogen, less progesterone, or do the hormones just have a harder time switching back and forth?

Dr. Lay (04:13): So, there are probably a number of factors that play a role. One study suggested that for women with migraine, the drop in estrogen just before she experiences her period may be a more precipitous drop. It may be a faster drop; maybe it's dropping from a higher level. A very recent study this year also showed that during menstruation, women with migraine have higher levels of CGRP. That probably plays a role in that menstrual migraine attack, as well. And if we look back to the '70s when Somerville, the Australian neurologist, first discovered that the drop in estrogen before the onset of a period is what triggers a migraine, we have to really take a good look at that data.

Dr. Lay (04:52): A very recent study suggested, you know what, we're all relying on that; we're banking on that as the physiology. But in fact, if you look at those studies, they weren't really studies. They were observational tests in approximately six women. Another study was only 10 women; it wasn't a randomized control trial. So what we've been looking at all of these years as the cause of a menstrual migraine attack may not be the only factor. It's unlikely to be just estrogen that's playing a role here. So in the perimenopausal years, yes, the estrogen begins to change because the ovaries begin to burn out. There may not be the same … really, it's more of an orderly pattern. So, where a younger woman has this very clock-like type pattern to her menstrual cycle, in the perimenopausal years women lose that predictability.

Lisa Horwitz (05:39): We've heard in past Migraine World Summit interviews about protocols for menstrually-related migraine. How is the use of those protocols challenged during perimenopause?

Dr. Lay (05:51): It can be quite challenging because, for example, a woman in her 30s knows, “My period is coming on a particular day, I know my menstrual migraine attack is coming two days before that, and so I'm going to begin my mini-prophylaxis two days before that, and I'll be prepared and ready.” And along with other changes in the perimenopausal years, women begin to have those vasomotor symptoms. They have hot flashes, rushes of heat. Women will talk about feeling like somebody turned the heat up and then suddenly they're quite cold. And they also have difficulty sleeping — maybe related to the hot flashes — but sometimes just challenges with sleep in and of themselves. So as the sleep begins to change, then we're more vulnerable to migraine attacks being more frequent and more burdensome. So it's a real sort of chaos; it's just an avalanche that hits these women in those years. But with the right sort of education around it and the understanding of what's going on and looking at different tools, or using the same tools in different ways, we can generally help women pass through this time effectively managing their migraine.

Lisa Horwitz (06:53): Do you think this requires more keen awareness on the patient's part of their prodrome symptoms in order to treat these hormonal-based migraines, whereas before earlier in their age they might've just been able to rely on the calendar?

Dr. Lay (07:07): Yeah, they might've been able just to rely on "Oh, here's where it's coming, I'm going to treat." But you're absolutely right, Lisa. I think, even in general in migraine science we're now teaching people about the prodrome. If you have this reliable phase where you are bothered by light or feeling kind of irritable and you know a migraine is coming; jump on it, treat early to try and prevent it from happening at all or to prevent it from being more burdensome.

Dr. Lay (07:31): And so, for women who can't rely on those other cues, like a menstrual attack being predictable, or even for some women at ovulation, of course, they often had a reliable migraine attack. If they have an anovulatory cycle — so, they don't ovulate because they're going through perimenopausal times — they can't rely on those clues anymore. So we need to think about other clues. Now we may have to think about prevention because you can't necessarily rely on that predictability to plan your medications.

Lisa Horwitz (08:00): One last question tied to the migraine protocol for menstrual migraine: Why is it that during that time you can take triptans multiple times a day to prevent the onset of migraine when people are generally advised to limit triptan use throughout the month?

Dr. Lay (08:21): It can be confusing, and I think for many patients and even medical professionals, the real trouble with using triptans too often relates to the frequency of use. If women in this example use a triptan more than 10 days per month, they're increasing their chance potentially of medication-induced migraine or medication-induced headache. However, it's not 10 pills per month. So, for women who have reliably found that using mini-prevention with a triptan, for example, or potentially an NSAID, or in [the] recent era, the gepant — they can use those medications as mini-prevention, potentially taking one pill twice a day for five days approximately, and they've used up 10 pills and they think, "Oh my gosh, I'm over the limit of 10." They're not over the limit of 10 because they've only used it five days.

Lisa Horwitz (09:13): How does an actual migraine attack change during perimenopause and menopause? Are they longer? Does the aura change? Can the pain or the location of the pain change?

Dr. Lay (09:25): So many things can change. Women begin to notice they have more frequent attacks, they're more burdensome, they're harder to get rid of, they have to be more aggressive with their acute therapy to jump on it earlier, perhaps in that prodromal phase. And again, they're less reliable, they're less predictable. So there are a number of different changes that take place with that migraine. And many women will move from what perhaps was low-frequency or even higher-frequency episodic migraine, and now they're stuck in chronic migraine.

Dr. Lay (09:54): And if not well managed, then many women will get stuck with medication-induced migraine attacks. And we also see women who say, "You know what? I still have five or six attacks per month. I don't feel as well in between." That interictal burden has now gone up. And so instead of having a specified attack, taking the medication, and feeling great and well again, the interictal burden goes up. And so for women in perimenopause and menopausal years, they have more frequent attacks, and they also don't feel as well in between attacks.

Lisa Horwitz (10:25): I am speechless again because, as you're saying that I'm thinking about how that has so blatantly applied to my own life. It seems harder to treat that in-between period where you're not quite in extreme pain, but you're not quite yourself. Do you have any tips for making that period easier?

Dr. Lay (10:47): For many people, we first start with recording it, and so — many people know that at the University of Toronto, we follow what we created this Traffic Light of [Headache] system. So we want patients to manage their migraine, not just the headache phase. That's why we tend to stay away from pain scales because you may have a four out of 10 headache, but you're really disabled by light and sound intolerance, feeling unwell, cognitive fog. On the other hand, maybe you've got an eight or nine out of 10 headache, but you've taken your medication and everything else is well, so you're still able to go to work a little bit.

Dr. Lay (11:18): So first we start with tracking it: Red is, disabled, “I can't get out of bed, I have to stop”; yellow is, “I need to slow down”; green is, “Something's going on, but I'm going to try to go about my day”; then a clear day is, “Everything is great.” So we can look at this, and you can help identify perhaps for women that say, "You know what? Here's where I'm taking my triptan for example, or my gepant when I'm emerging into that red level." So we'll look at the calendar and go, "But you know what? The day before it was yellow and instead of taking your over-the-counter medication, then maybe we should start with an appropriate migraine medication and treat earlier."

Dr. Lay (11:55): We can also look at, what's your lifestyle like? So, going back to basics: How's your sleep? Do you have perimenopausal sleep disturbance? Are you busy with work and busy with life, and busy with family, and you're not looking after yourself? So you look at lifestyle, you look at your vitamins, you look at how aggressively you're treating. Are you getting on it early enough? Do we need prevention therapy? This is perhaps again the time we need to either adjust prevention, look at a more specific targeted migraine prevention therapy, and just being aware. That's really the first step of understanding, as you said, "You know what? I don't feel great in between these attacks." And talking to your provider about that to see if you can make some headway.

Lisa Horwitz (12:35): As people's symptoms change, at what point should they go back to their doctor to rediscuss their treatment plan? [Because] we know that migraine can vary from month to month. How big of a change before you try to readjust what you're doing?

Dr. Lay (12:54): If you notice over time — over three to six months — that, "You know what? I used to do this well; my traffic light of migraine score, or my HIT-6 [Headache Impact Test] score” — whichever scale you're going to use — "was better and now I'm seeing a pattern where things are worsening," you definitely need to talk to your doctor. Certainly for patients who perhaps did very well with older-school drugs and they haven't really touched base with their provider in the last three to five years, as you know, so many terrific new targeted migraine medications that are available that we can do better.

Dr. Lay (13:26): So it's important to talk to patients as a provider, or as a patient to tell your provider, "Yeah, this medication works pretty well. I take it, and I go have a nap for three or four hours, and I feel a little bit better by the end." That's not good enough. So you really want to be able to say, "I feel the prodrome, the symptoms start, I'm taking this medication, I'm repeating it in two hours." That's the other really key factor. If you don't feel well at two hours, as I say to patients: "Think of migraine like a fire; nobody would walk away from burning embers. The

migraine is the fire. You have to assess it at two hours, and if need be, take a second dose to really knock it out and get rid of it."

Lisa Horwitz (14:05): I really appreciate you saying as a physician, "This is not enough."

Dr. Lay (14:11): Yeah, it's not enough because we can do better, for sure. We now have this understanding, with all the science that's emerged, that there's this prodrome place where you can really look at identifying what's going on: "What am I feeling, what am I noticing?" And act earlier. And so to your point, people do worry, "Well, if I take a medication right away and two hours later I'm taking another one because they still have lingering symptoms, I'm going to get stuck in medication-induced headache," — but you might not.

Dr. Lay (14:39): And so we'll often look at the diary and say, "OK, here, here, and here you had six attacks, and they lasted three days each, and each time you took a triptan or a gepant." So you took — heaven forbid — 18 in the month because you had 18 days of headache. But if you back up and look at it and say, "OK, take one right away, a second dose in two hours, you reduce the risk of recurrence, and in all likelihood, that three-day migraine when you used maybe three or four of your medications might turn into a three- or four-hour migraine and you used one or two medications." So you [would] actually use less in most cases by treating earlier than you do by waiting.

Lisa Horwitz (15:20): At what point should someone seek emergency care? As your migraine symptoms change, how can you tell what's a dangerous change and what might just be a normal progression in perimenopause and menopause?

Dr. Lay (15:36): Yeah, that's another good question because, as a woman ages, of course she has an increased risk of other kinds of headache, and some of them are worrisome or problematic headache. So if there's any new associated symptoms or something is different about this particular migraine attack — it came on very suddenly, like a thunderclap headache, or it came on when they were straining, they were working out at the gym, they were engaged in sexual activity. If there's anything that's exertion-wise that triggered this sudden, severe thunderclap headache, they need to get to the emergency room to be checked out.

Dr. Lay (16:07): So, worsening migraine isn't always worsening migraine. And we often see women who will say, "Oh, I'm waking up in the middle of the night with this headache now," and you need to talk to your doctor about that. You need to look at it differently. Waking up in the middle of the night could be a problematic headache or could be a headache pattern of an older individual, such as hypnic headache, where they wake up with this alarm clock headache that's waking them in the middle of the night.

Dr. Lay (16:31): So, I think it's important to take power, be in control, keep track of your headache and migraine symptoms. And if you're the first person to say something's different, then you need to talk to your doctor about it. But certainly if it's more urgent or it's different, you have associated neurologic symptoms, then you don't wait to call your provider in the morning. You get yourself to the emergency room to be checked out.

Lisa Horwitz (16:55): Can migraine present for the first time during perimenopause or menopause? Is this common?

Dr. Lay (17:02): It definitely can. You need to dig into history more and find out, but there will be times when you really can't find a history of migraine in this individual. And so if a woman is in her 40s, we're probably more comfortable saying, "OK, it looks like migraine. There's all the migraine criteria. The pattern looks very routine and predictable. I'm confident that the neurologic exam is normal, that this person has migraine." Once a woman is menopausal and she presents, perhaps for the first time, with headache, that's more of a red flag because she's probably over 50. You really have to think about is this truly a migraine pattern. Does it look like migraine or something a little bit off? And you need to investigate a little bit further and look at that.

Dr. Lay (17:48): Many older women may find where they had migraine perhaps in their teens, or 20s, or 30s, and it "went away" at menopause. As they get a bit older, they may actually begin to experience aura where they didn't have aura before. So it could be even an aura episode without the headache that follows it. And that's something we see more commonly in the older woman. But again, you need to talk to your doctor about it and describe to them.

Lisa Horwitz (18:14): As a layperson, when I hear that hormone fluctuations are contributing to my attacks, I immediately want to have my hormones tested so I can try to fix them. Do you recommend this?

Dr. Lay (18:29): Generally, no, because you may get a random test when your hormones look just great, but in fact, you still could be in perimenopause. Because before the hormones die out and the ovaries shut down, there are fluctuations in the hormones. So checking hormones really isn't going to be helpful. It's more based on clinically how you're feeling. So if a woman says, "I'm having more frequent migraine attacks, I'm getting these rushes of heat, and I feel hot and sweaty. I'm having trouble sleeping at night." That really makes a clinical picture of a woman who's in perimenopause. And so I think it's more important to look at the clinical picture as opposed to rushing off to the lab to get your hormones tested.

Lisa Horwitz (19:07): Are there any hormonal-based treatments that are known migraine preventatives?

Dr. Lay (19:13): So, there are. I mean, definitely, this is an issue that comes up a lot and women will talk to their doctor, or the doctor will talk to their patients about considering hormone replacement therapy (HRT). So if we look at it on a big scale, most of us in the world of headache will not necessarily jump to HRT as a way to manage vasomotor symptoms in migraine; there's other nonhormonal therapies that we know can be helpful. Medications like venlafaxine or medications like gabapentin can be helpful for hot flashes and also be beneficial for migraine. But if it's determined that HRT is needed, then usually the patient should be in discussion with their family doctor and their neurologist or their gynecologist to look at what's the best way forward.

Dr. Lay (19:59): The data would suggest that the patch is probably the best tolerated and carries the lowest risk of stroke in that woman who's needing hormone replacement therapy. But we also have to look at other factors; we need to know a little bit more detail about this patient. Is she someone that had a history of unexplained miscarriage? Did her mother have miscarriage? Did someone in her family have sort of an unexplained clot in the lung, etc.? Is there a flavor that there could be a hypercoagulable clotting problem in this person? That needs to be looked at.

Dr. Lay (20:32): The other thing you need a more detailed history on is a history of cognitive issues or dementia. There's emerging evidence in a very recent study just published this summer. A Dutch group looked at what is the risk of dementia and are there factors that relate to this. And what they found is that the use of HRT — even for short periods of time, particularly in women who started it before the age of 55 — could be related to an increase in cognitive decline or dementia. We don't know that it's a cause and effect. So, in other words, it isn't necessarily that HRT causes dementia. That could be a possibility. But the other possibility is potentially women who have migraine and have a lot of vasomotor symptoms, and need HRT to control these symptoms, were already at risk of dementia. It's not well understood, but there's enough evidence there to tell us that we need to look at this more carefully; it needs further investigation. And as a physician, we need to talk to our patients more about other factors beyond their own personal history, potentially family history, that might help us make better-informed decisions.

Lisa Horwitz (21:43): Can taking birth control pills or other forms of birth control that limit your number of menstrual cycles improve migraine in perimenopausal women?

Dr. Lay (21:54): Yes. For some women, particularly if we use low-dose (so less than 30 micrograms) and monophasic formulations for those women, provided they don't have aura and they aren't a smoker, because smoking significantly increases the risk of stroke when that woman uses a birth control pill. But if all the other factors are clear and that woman wants to use a birth control pill (low-dose monophasic), in a continuous fashion, she can then have benefit because she will skip a menstrual cycle and therefore skip the menstrual migraine attack that normally would've happened with that.

Dr. Lay (22:28): For some women, also in the perimenopausal years when estrogen is fluctuating and there's chaotic variation in the estrogen, sometimes flattening that out in the perimenopausal years when she's still experiencing period, using the birth control pill can be helpful. In the later stages, when a woman is beginning to really skip her period, we don't find that it's necessarily as helpful, and it may carry a slightly increased risk of stroke over the patch therapies.

Lisa Horwitz (22:57): I've been told by my neurologist that my migraine attacks may drastically reduce during and after menopause. Is this true? Do you find this common in your experience?

Dr. Lay (23:09): So, it was believed for a long time, and many providers said to me, "Oh, once you hit menopause, everything will be better." And for many women, there is an improvement once menopause is reached and once the hormones have flattened out. But as I said earlier, perimenopause itself can be a very prolonged state. In some women, it begins in their late 30s. In most women, it's in the 40s; it goes through to the early 50s. While there is eventual benefit after menopause has been fully achieved, the transition time is often way too long to wait for that. So we have to be more forward-thinking, more aggressive in our treatment to help our patients.

Lisa Horwitz (23:49): Are there any predictors of whether someone is likely to experience a decrease in attack frequency after menopause?

Dr. Lay (23:58): So, for women who have had a menstrually related migraine attack most of their life — and that's small numbers, perhaps 6% or 7%; again, data around that is still looking at this, but that woman who always had a predictable menstrually related migraine attack will find

that once menopause comes in that she will have reprieve from that. But that same woman is also the one who will be more vulnerable to an initial increase in migraine as she enters the perimenopausal years and the period becomes more unpredictable.

Lisa Horwitz (24:32): Why do some people in menopause still experience a high frequency of migraine attacks?

Dr. Lay (24:40): Many women do, and it sometimes depends on how they entered perimenopause or the early menopausal years. Were they having a hard time? Did they have chronic migraine? Were they stuck, perhaps, in medication-induced headaches? So because the migraine itself becomes more disabling often — so, it's more frequent, it's harder to get rid of, it's longer in duration — if that woman hasn't been offered or didn't take proper medications, wasn't following lifestyle recommendations, or wasn't using herbal supplements, she's not going to find, as I said, this sort of sudden benefit of menopause coming in because she entered menopause in a tough place. But there are women who will do everything right, and then once those perimenopausal years come in or early menopausal years, they just find that things get worse. And that's because we know hormonally triggered migraine can be harder to manage.

Lisa Horwitz (25:34): For people experiencing frequent or chronic migraine and menopause, what treatment options are available?

Dr. Lay (25:42): So, there are many different treatment options available. So, it's important to talk to your doctor about whether you're having a hard time sleeping. There are many different medications. Again, lifestyle changes. Neuromodulation therapy can be very effective for patients. So, there are many devices, and these can often be a good option in that older patient who you're perhaps, as a physician, a bit worried about giving them a particular medication, or because of other comorbid conditions, and they have asthma, or they have hypertension, or they have depression, or whatever the comorbidity is. You're not comfortable using a particular medication, then neuromodulation therapy. It's a great time ... It's a great opportunity to introduce this to your toolkit.

Lisa Horwitz (26:23): Are there certain medications that can safely be used by younger migraine patients but are dangerous to patients in their 50s and up?

Dr. Lay (26:32): So, I think once upon a time we would've thought about things like triptans being dangerous, and there's been a lot of information that has come forward showing the absolutely outstanding safety profile of these medications. And so, we don't worry so much about age being a cutoff for these medications. As patients advance through their age, a lot of us are starting to think: Well, maybe a gepant in an older patient might be potentially a better option for them to consider. And while it's a challenging part of migraine, it's one of my favorite parts of managing migraine is that it's very individualized. There is no sort of recipe you can follow and say, "Oh, everybody gets X, Y, Z." You really have to look at the patient, get detailed information about all the other factors that are important to them in their life — what they do for a living, can they tolerate some side effect, or could they never tolerate that particular side effect? So it's very individualized, tailored treatment.

Lisa Horwitz (27:30): What lifestyle changes can reduce the number of attacks or the severity of the attacks during these phases of life?

Dr. Lay (27:38): Overall, like many, many people in this field, we do emphasize lifestyle factors. And so, it's important to be well hydrated; to be mindful of your caffeine; some form of mindfulness or meditation; walking if you can't exercise, or you can't do Pilates or you can't go to the gym. Even simple walking several times per week can be very beneficial for migraine. It can enhance brain health and for many individuals who suffer with anxiety or depression and has a positive benefit in that regard, as well. So, lifestyle factors are really important. I always say [that] one of the most important lifestyle factors is sleep. What time are you going to bed? How long does it take you to fall asleep? What are you doing before you fall asleep? Are you on your phone checking emails or Instagram? These things are problematic and lead to poor-quality sleep. And for women in these perimenopausal years, sleep is already problematic.

Dr. Lay (28:30): So you have to do everything you can to help improve your sleep quality, and that means keeping a routine. As you know, Lisa, many patients feel like they need to sleep in on a weekend and they have to catch up. They had a busy week, but sleeping in often leads to more migraine attacks. So routine is really important in sleep, and the quality of sleep that you're getting is important. Some women will experience sleep disorders as they enter these perimenopausal years, whether it's sleep apnea, restless legs, periodic limb movements of sleep. Talk to your doctor about your sleep if you don't feel like you're getting a good night's sleep and waking refreshed.

Lisa Horwitz (29:06): Where can we learn more about what you're doing or follow your work?

Dr. Lay (29:11): I'm based at the University of Toronto, so there's information there. And I'm currently chair of the American Migraine Foundation. So, the American Migraine Foundation has terrific resources for patients. And I'm also part of the Canadian Headache Society. And Migraine Canada has a lot of great resources for patients so that you can understand what's going on, recognize migraine is a brain disease, and be prepared for your appointments so that you can get the most out of those appointments.

Lisa Horwitz (29:39): I want to thank you so much for taking the time to speak with us today. We've really covered a wide array of information, but I think we can all come away with this knowing that if you're not getting sufficient relief from your current treatment plan, talk to your physician. You don't have to settle. The earlier you can treat your hormonal migraines during perimenopause and menopause, the likely better success rate you'll have at stopping an attack. And things can be unpredictable with your hormones, so work on the things you can predict, like your own routine and schedule. Is there anything else you'd like to add to that to kind of sum up what we've gone through today?

Dr. Lay (30:22): No, I think that's perfect. And to not lose hope because there are still new emerging medications and therapies on the horizon. If you haven't tried some of the more recent ones that came onto the market, go back to your doctor or provider and talk about getting on those medications.