CURE Epilepsy Webinar

Non-epileptic Seizures: Diagnosis, Treatment, and Management Strategies for Patients & Families

Presenter: Curt LaFrance, MD, MPH

Laura Lubbers:	00:00	Welcome, everyone, to today's webinar. I'm Laura Lubbers, and I'm the Chief Scientific Officer of CURE Epilepsy, and I want to thank you for joining us today. Today's webinar is entitled Non-epileptic Seizures: Diagnosis, Treatment, and Management Strategies for Patients and their Families. It's important to recognize that while the physical signs and symptoms of non-epileptic seizures, or NES, may be similar to epileptic seizures in some ways. People with non-epileptic seizures do not respond to anti-epileptic drugs, and therefore require different treatment options. Up to 20% of those diagnosed with that epilepsy actually have non-epileptic seizures.
Laura Lubbers:	00:40	This webinar is part of CURE Epilepsy's 2021 Leaders in Research webinars series, where we highlight some of the critical research that's being done on epilepsy. Today's webinar, like all of our webinars, is being recorded for later viewing on the CURE Epilepsy website, and you can also download transcripts of all of our webinars for reading. For over 20 years, CURE Epilepsy has raised millions of dollars to fund epilepsy research that supports our mission, which is to find a cure for epilepsy by promoting and funding patient-focused research.
Laura Lubbers:	01:14	CURE Epilepsy provides grants that support novel research projects that advance the search for cures and more effective treatments. Today's webinar will help viewers recognize the signs, symptoms, and understand the history associated with the presentation and diagnosis of non-epileptic seizures, and it will provide insights on treatment options for this condition.
Laura Lubbers:	01:38	This webinar is presented by Dr. Curt LaFrance, who is the Director of Neuro Psychiatry and Behavioral Neurology at Rhode Island Hospital, and Professor of Psychiatry and Neurology at the Warren Alpert Medical School of Brown University. He's also a staff physician at the Providence VA Medical Center, and the clinical lead for the VA national telemental health center teleseizures clinic. His research focuses on developing new biomarkers and treatments for neuropsychiatric aspects of epilepsy, traumatic brain injury, and more.
Laura Lubbers:	02:15	Before Dr. LaFrance begins, I'd like to encourage everyone to ask questions. You may submit your questions any time during the presentation by typing them into the Q&A tab located on your Zoom panel, and then click send. I also want to thank those who submitted questions in advance of today's webinar, and we'll do our best to get through as many of those questions as we can. We do want this webinar to be as interactive and

informative as possible. However, to respect everyone's privacy, we ask that you make your questions general, and not specific to a loved one's epilepsy. So with that, I'd like to turn it over to Dr. LaFrance.

Dr. Curt LaFrance:: 02:54 Thank you so much for the invitation to come and speak. It's an honor to speak to the people of CURE Epilepsy. I've known of the organization for a couple of decades. Every time I would go to the American Epilepsy Society annual meetings, I would always see a lot of buzz about what's happening with CURE Epilepsy, and I'm honored to be able to join your group to be able to speak today. So thank you, again, for the invitation.

Laura Lubbers: 03:26 Thank you.

Dr. Curt LaFrance:: 03:28 These are my disclosures. I'll be talking about some of the research that we've done. But also, this is a topic that for people in epilepsy, it's not a side topic, it's a main topic, and I'll tell you why. The research that we've done over the years has been with epilepsy and non-epileptic seizures, and other conditions. So hopefully, what you'll come away with in about a half hour of discussion is your understanding, that you'll learn about psychogenic non-epileptic seizures, and you'll be able to realize that there are what we call neuropsychiatric aspects.

Dr. Curt LaFrance:: 04:07 The neurology and the psychiatry elements of epilepsy includes, not just the comorbidities, like depression, anxiety, and cognitive issues, as many of you are familiar with, but also non-epileptic seizures. And then hopefully, with understanding what they are, you can understand what can be done for them.

Dr. Curt LaFrance:: 04:30 So, as a neurologist and a psychiatrist, I deal with the brain in the mind. Interestingly, it seems like it should be two sides to one coin. That's how I view the world. But not everybody does that, and sometimes in medicine, we'll split them out, this is brain, and this is mind, unfortunately. Because I tell my students, our patients don't read our textbooks, so they don't divide out brain and mind. Everything comes as a whole package.

Dr. Curt LaFrance:: 04:54 So here's a couple of ways to conceptualize non-epileptic seizures. One is that it's a nervous logical manifestation of an underlying psychological conflict, or a stressor, a life event. Another way to look at it is that it's a behavioral expression of neural network dysfunction. Again, these are two sides to one coin. It's not either or, it's both and. I've had the honor of working with some wonderful colleagues and friends over the decades, and some of this is summarized in the book, Gates and

Rowan's Nonepileptic Seizures, that Steve Schechter and I co-edited, and much of this information is there for your review, if you desire.

Dr. Curt LaFrance:: 05:43 So, here's what some of the great excitement is about monopolistic seizures. That in the past, we as clinicians, couldn't definitively make the diagnosis of psychogenic non-epileptic seizures. It's also referred to as a conversion disorder seizure, or a functional neurological disorder seizure, or functional seizures. Those are other terms that you might hear. But now we can make the diagnosis definitively. In the past, we couldn't... we didn't have a treatment for patients. While there were all these great advances for epilepsy, we had nothing for non-epileptic seizures. Now we do have treatments.

Dr. Curt LaFrance:: 06:17 Lastly, we didn't understand the mechanisms for what's happening in the brain for conversion disorders and for non-epileptic seizures, and now we're gaining some insight into that. So those three major... Those have been major leaps forward over the past couple of decades, and I'll let you in on some of that information. So, Laura's already mentioned that about 1% of the US, about 1% of the world population, is diagnosed with epilepsy. Not all of those people have epilepsy.

Dr. Curt LaFrance:: 06:55 So here's a key point. Each of these slides is a way... maybe a pearl that you might be able to come away with. If you or a family member is being treated for treatment refractory epilepsy, it may not be that the antiepileptic drug isn't working because the pill doesn't work, it's because it's not epilepsy. So, up to 20% of people who are diagnosed with epilepsy actually have non-epileptic seizures.

Dr. Curt LaFrance:: 07:23 Now, I've already told you that there's a difference between epilepsy and non-epileptic seizures. Many times people keep coming back to the seizure monitoring units, or to the emergency department, or to the clinic, saying, my seizures, they're just not responding to the fifth antiseizure medication. Unfortunately, it's not until we get the gold standard diagnosis, which is video EEG, that they realize, well, it's because we've been treating presumed epilepsy, and it's not.

Dr. Curt LaFrance:: 07:53 So interestingly, people say, well, epilepsy, that there's a high level of disability, unemployment, assistance, that kind of thing. It's equal in non-epileptic seizures. As you know, people who have seizures, what happens, they keep coming back to the emergency room, and they get more tests and labs and CAT scans and EEGS, and medication adjustments. Well, this lifetime cost for treating an individual with non-epileptic seizures can be

up to $100,000. And then if you add that up to all the people who have non-epileptic seizures, it can be up to a billion dollars a year, in the US alone. So it's a costly disorder, not only physically to the patients and family members, but also physically, monetarily, to the individuals, families, and to our society.

Dr. Curt LaFrance:: 08:44 So I mentioned earlier, there are... we can definitively make the diagnosis. Two of the reasons that we can is because we can use the physical exam. When you are examined by a clinician, then they will use physical signs, and using physical signs... Because it was an advisor to the book that's used in psychiatry, the DSM, the fifth version, fifth edition, to try and update conversion disorder, functional neurological disorders. So we made the recommendation to switch in version four to version five, incorporate physical signs that we use on exam. So now that's one of the diagnostic criteria. Also, because we have a lab, which is the video EEG, that's the other tool that we use in neurology and epilepsy to definitively diagnose the disorder.

Dr. Curt LaFrance:: 09:40 Some people will say, well, I've heard that the person is faking it. These people who have these seizures are not faking it. So malingering does exist. Now, malingering is about less than 5% of the people who come in to the emergency department, and those people are people who are trying to get out of prison, trying to get out of military service, trying to get on disability pay, and trying to get medicines inappropriately. That's a very small subset.

Dr. Curt LaFrance:: 10:17 So when you see somebody who's having a seizure, it may not be an epileptic seizure, but also, it's not faking it. This is a real seizure, and I intentionally use the term seizure. Some people don't agree with that, but I use the term seizure. But a seizure, as you know, just means to be taken hold of. So sometimes seizures are caused by abnormal brain cell firing, as in epilepsy, and sometimes they're caused by underlying psychological conflicts and stressors and life events, as in non-epileptic seizures. So having said that, when you see somebody who's having a seizure, I make the assumption, this is a real seizure. Maybe it's caused by abnormal brain cell firing, or maybe it's caused by a conversion disorder, but it's a seizure.

Dr. Curt LaFrance:: 10:57 I mentioned earlier about the importance of using video EEG. There's some great data that came out a while back that said, if you've got two seizures a week, and you have two normal EEG's, and you have failed two antiseizure medications and treatment, there's an 85% positive predictive value that you actually have non-epileptic seizures. So I would call that the rule

of twos. So when somebody has that kind of story, then we say, get them in the monitoring unit.

Dr. Curt LaFrance:: 11:27 And then getting them into the monitoring unit is where some of the work that's been done across seizure or epilepsy centers, that if you give the right story with the right video EEG, with the right image... You want the video, that's the third component that's so important, then you're going to have a high level of reliability between the different reviewers of the EEG. It's almost perfect, in fact, .94.

Dr. Curt LaFrance:: 11:56 Some people will say, well, I know that it was epilepsy, because it was a grand mall, and they were frothing at the mouth. One of the things I tell people is that any way that an epileptic seizure can present, a non-epileptic seizure can present. So just because it was generalized tonic-clonic seizure with tongue biting or incontinence doesn't... Many times, that's going to be epilepsy, but it doesn't necessarily mean it's going to be epilepsy.

Dr. Curt LaFrance:: 12:23 So people can have staring spells, like [inaudible 00:12:25], people can have generalized tonic-clonic people can have myoclonic jerks, all kinds that can be non-epileptic seizure, just as much as it can be epileptic seizure. What I'm trying to do is give you some data to challenge the dogma, the learning that we have. So here's another dogma. Well, it was a head injury, so it has to be epilepsy. Because you hear the term, oh, it's post traumatic epilepsy that happened after a head injury. A lot of people who have had injuries actually have non-epileptic seizures.

Dr. Curt LaFrance:: 12:59 So some of our studies showed that almost half of people who have non-epileptic seizures have a history of head injury, and up to three quarters of those patients actually had mild traumatic brain injury. This is what I call the double hit hypothesis, which is... or the double hit phenomenon, which is, I had a head injury in the car accident, or in the assault, or with the veterans who I see, and it was a mild traumatic brain injury. So they were awake, and aware, and conscious, maybe a little dazed and confused, but they were awake for the event. They had a physical hit, and then they also had a psychological hit, and that's where the PTSD, the post traumatic stress disorder, comes in. So we have to address the double hit in many of our patients with head injury and non-epileptic seizures.

Dr. Curt LaFrance:: 13:49 So some people will ask, well, we're talking about an either or, right? Well, sometimes it's both and, and what I mean by that is that 10% of patients with seizures have mixed epilepsy and non-

epileptic seizures. So when you are talking to your doctor, don't just tell them about my seizure, tell them about my seizures, plural. You may have two different types. There's one type, where you're staring off, and you're looking away, your eyes blink, but then there's the other one where your arm shakes, and then it generalizes, and you fall out of bed. Those are two different types of seizures. Make sure that your doctors know that you have two different types. They both may be epileptic seizures from different areas of the brain, or they could be. One is an epileptic seizure, and another is a non-epileptic seizure. So that's the importance of getting people into the unit to be able to distinguish and differentiate.

Dr. Curt LaFrance:: 14:40 I tell people a picture's worth a thousand words, while a video is worth a million words. So if you can, use your smartphone. Not everybody can get into the monitoring unit. So start to finish, capture the video, with the individual's permission, because we want to see that as clinicians. This is some of the research that we've done with some of our colleagues to say smartphone videos can help differentiate between epileptic and non-epileptic seizures. Now, it's not the gold standard of the video EEG but it gives us more information as clinicians to help us take care of our patients better.

Dr. Curt LaFrance:: 15:14 This really started to become... For the longest time, the term... There was a term in the past that used to be referred to as pseudo-seizures. Pseudo, as you know, means false or fake. I've already told you these aren't fake seizures, they're real seizures. The pseudo-seizures in the past were dismissed in neurology, unfortunately. In the 2000s, the National Institute of Neurological Disorders and Stroke, it got on their radar because many of our patients in the monitoring units don't have epilepsy, we're calling ourselves level four epilepsy centers, but we don't do anything for a third to a half of the people who come into our unit. What do we do for those patients?

Dr. Curt LaFrance:: 15:56 So the benchmarks were a way that allowed for the understanding... Benchmark one, basically, was diagnose epilepsy, benchmark two was treat epilepsy, and benchmark three, which got added in 2007, was, look at the comorbidities, also, which includes non-epileptic seizures. So it's on the radar for NINDS, which is great. It's also on the radar for International League Against Epilepsy. Not everybody has access to video EEG. So when you're talking with your clinician, you'll say, what level of certainty Do we have with my diagnosis? Documented, the highest level is right history, right witnessed event, and right EEG. No epileptiform activity, abnormal brain cell firing before, during or after the seizure.

Dr. Curt LaFrance::	16:46	If you don't have that level, then there's clinically established and other levels, lower levels. But that's how the ILAE, it's a way that... For countries that might not have access to video EEG, we can still talk about a common language of, how do you make the diagnosis, and what level of certainty? So, we talked a lot about diagnosis. The other piece of this, I want to talk about treatment. I mentioned earlier, now we can treat non-epileptic patients with non-epileptic seizures. So a lot of advances in the past two decades.
Dr. Curt LaFrance::	17:17	Here's how I organize it. The patient is at the center. A lot of times, people come to us as clinicians and say, well, you're the one who's supposed to fix me. I tell them, I don't have the power to fix you. But what I can do is I can walk with you as you go on this journey, and that's one of my roles as a clinician and a neurologist psychiatrists. But the patient is at the center, the individual's at the center, and then you've got a team around you. You've got your medical team, you've got people at home, family, and then you've got your community. So I tell people, family, friends, faith, those are part of your treatment group. And then you've also got your clinicians, who are part of that team, also.
Dr. Curt LaFrance::	17:52	So to organize that, we've tried to develop treatments over the past two decades, and even three, including my residency, where we've looked at, are there medications that can help? Are there therapies that can help? Are there combinations that can help? Are there other interventions? I'll just give a brief, brief overview of some of those treatments that we've studied to let you know that there are some options out there. One of my distance mentors is Orrin Devinsky, who was involved in my NIDSK 23, where we really started to look at the data.
Dr. Curt LaFrance::	18:26	In the past, in the early 2000s, there was only expert opinion. We didn't even have controlled trials to be able to inform evidence base. So now we've actually increased the evidence base. I'll tell you a little bit about that. So the National Institutes in Neurological Disorders and Stroke K23 that we did, the initial grant was looking at, can we do something with the medication? So what we found in a pilot trial... it's not the fully efficacy trial that you see with some of the anti-epileptic or anti-seizure medications. What we found is that using a serotonin medication, which is commonly used in depression and anxiety, there was a 45% reduction in patients who receive that. That was in contrast to people who received placebo or a sugar pill. They had an 8% increase in seizures.

Dr. Curt LaFrance:: 19:14 So that doesn't mean it cures non-epileptic seizures. What it means is it may help to reduce. Then we also started looking at... we called it cognitive behavioral therapy. It's not cognitive behavioral therapy. I'll tell you why in a little bit. But what about a psychotherapy? With our pilot studies, we found that a significant number of people had a full reduction in their non-epileptic seizures. So that was a big signal for us to keep going. Here's the way that we organize it in our minds. Somebody had a past injury or a trauma or an incident, and then they developed the non-epileptic seizures.

Dr. Curt LaFrance:: 19:51 There are other types of manifestations, also. I mentioned conversion disorder earlier, so it could be a tremor, or it could be a weakness, or it could be a walking gait disorder. All kinds of things happen after an injury or an event. It doesn't have to be immediate, like it just happened last week. It could have been remote, something from the past. We've got data to show that things that happened years ago can actually manifest later on, even decades later.

Dr. Curt LaFrance:: 20:16 So, some type of an event, life event, then seizures, then the term that we use is catastrophizing, and you're familiar with that, catastrophe, everything is going wrong or bad. My whole life has been taken away from me, and then they fear the next seizure, I don't know where it's going to come from. This happens in epilepsy, also, as you're aware. And then, they start to avoid events in the world, and then they start to attend to things going on in their body so much. Oh, what's this tremor that I'm having? What's happening here? And then they get into the cycle of disuse, and disability, and depression. This vicious cycle repeats itself in some of our patients.

Dr. Curt LaFrance:: 20:57 What we do with our treatment is we equip them with tools, so that they can make these links between this vicious cycle, then they use the tools to break the links. Once they've been empowered to do that, then they move out of this vicious cycle of non-epileptic seizures, into this virtuous cycle of confronting their fears and moving into recovery. It's such a beautiful thing to see patients get their lives back.

Dr. Curt LaFrance:: 21:23 So we've subjected this to higher levels of evidence. We did a multi-site, randomized controlled trial amongst three sites, and we found that the two therapy-containing arms, there was a significant reduction in seizures and in comorbid symptoms, like depression and anxiety, and improvements in quality of life and functioning. The medication alone, which was the serotonin medication, it's an antidepressant, so it would help depression, and it also... there was a trend and seizure reduction. Here's

one of the big takeaways. Standard medical care, what's delivered at the epilepsy centers around the country and around the world, showed no significant improvement in seizures or in secondary outcomes. So that was a big signal for us, we've got to do something about this, and we've got to start helping around the country.

Dr. Curt LaFrance:: 22:10 So having said that, some people would say, well, this all was great, but you're talking about epileptic seizures, right? No, I'm not. I'm actually talking about epilepsy and non-epileptic seizures, and here's the reason why I say that. This treatment was initially developed by Reiter and Andrews in the '80s and '90s in California for epilepsy. So you think, wait a minute, you're talking about a psychotherapy for epilepsy, how can you do that?

Dr. Curt LaFrance:: 22:37 Well, so what happens is, their initial approach was, identify your aura, use some of these behavioral interventions, and decrease the physiologic progression of the seizure. It's fascinating. It's fascinating neuropsychiatry in my mind. So I actually asked them permission to use their workbook, to modify it, to make it not just taking control of your epilepsy, but taking control of your seizures, and neutralize the term, so it can be used for epilepsy and for non-epileptic seizures. Because of our studies, Oxford University Press asked if they could use it in their treatments that work series, and they can. So it's available online, you can get it, Taking Control of Your Seizures, used for epilepsy or for non-epileptic seizures. The workbook is for the patient to do, to meet with the seizure counselor one hour a week to go over the information that the individual does.

Dr. Curt LaFrance:: 23:28 And then for those who are the clinicians, the therapist guide is used from the notes of the people that I've trained in the past, we put all those together to help the people who are going to be treating the individuals with seizures. So here's what the roadmap is if people do the treatment. There are different components, that's why I say this is not cognitive behavioral therapy. There are CBT elements to that, it's a big buzzword now, but there are also other types of therapies. Just like there are a number of different types of anti-epileptic, anti-seizure medications, there are different types of psychotherapies, also.

Dr. Curt LaFrance:: 24:03 So we took the best of the different therapies, and we put them, and we targeted the known struggles that patients with seizures have, and those targets are actually equipped with tools in each of the different sessions. So it's 12 sessions, it really is to equip the individual to be able to look at life differently, and to approach things on their own. So, I

mentioned earlier, people around the country are trained, and whether that's in the VA system for veterans, we've trained people, or whether it's in people clinicians in civilian hospitals. We've got people around the country who are now using the intervention to help with seizures.

Dr. Curt LaFrance:: 24:54 The last thing that I'll talk about, before we get ready to wrap up, is, one of the questions that came up with COVID was, well, people come into our office, can you do therapy with people who are remote, who aren't in your office? The National Telemental Health Center for the VA was already around, and they had asked me, in the early 2000s, to take the work that we had done in civilians to help out with veterans. In doing so, we established a teleseizures clinic in 2012. So I've been seeing veterans all around the country, even pre-COVID, and we've been using that information to say, hey, what does it look like if you use telehealth?

Dr. Curt LaFrance:: 25:34 What we found was that similarly, there was a similar reduction in seizures, and improvement comorbidities in people who came to the clinic, or people who were seen via telehealth around the country. So it can be delivered... The point of this, the [inaudible 00:25:48] of this is that can be delivered in clinic, in person, locally, or it can be delivered remotely. So, I'll close with this. Seizures has an impact on, not only the individual, but on the family, and this is epileptic seizures and non-epileptic seizures.

Dr. Curt LaFrance:: 26:08 Most of our research has been comparing two different seizure types, two different seizure groups, those with epileptic seizures, and those with non-epileptic seizures. So it's not just about treating the individual, it's about treating the individual in the context of their environment, and that may include family, also. So when I talk about, what are some of the treatment options, looking at the individual, but also looking at the social context, which includes the family. That may be of benefit, not only to patients with non-epileptic seizures, but also epilepsy.

Dr. Curt LaFrance:: 26:38 I'll skip ahead, because one part of the talk is on biomarkers, but that's... we can do that at another time. Only to say that we do have a study going on right now, where we have patients with epilepsy, and history of head injury, patients with non-epileptic seizures, and a history of head injury, and the third group is head injury alone and no seizures, and we're subjecting... we're taking these three groups, and we're getting FMRI before and after we administer this 12-session treatment for seizures, and we're looking at brain network changes before and after the treatment. We know that it works clinically, now we want to see

what happens physiologically and neurophysiologically. So that's a study that we're doing right now.

Dr. Curt LaFrance:: 27:28 I will forward to... This is a way to conceptualize at the end. If you're still having seizures, if you know somebody who's having seizures that are "treatment-resistant", or refractory, talk to your doctor and ask them, hey, do we need to look at this from another perspective? What I mean by that is, do we need to get an inpatient video EEG? Or video EEG, an ambulatory that you have in the outpatient setting, and add in... have the video, also. And then you get the proper diagnosis. Then, when you have the proper diagnosis, talk to, not just the individual with the seizures, but also to the family, so that people understand what the diagnosis is.

Dr. Curt LaFrance:: 28:10 Then, after that, you create what's called a problem list. It's not just about the seizure. To treat the whole patient, you have to look at them biologically, psychologically, socially, and spiritually. You have to look at the whole person. And then you come up with a formulation and a treatment plan, and you look at things that happened in the past, predisposing factors, you looked at when the seizure started, precipitating events, and then you look at things that might still be going on, perpetuating factors.

Dr. Curt LaFrance:: 28:37 So you address those three P's with medications, if appropriate, anti-seizure medications for epilepsy, tapering off anti-seizure medications, if you don't have epilepsy, using some other medications for depression and anxiety, which happens in epilepsy and in non-epileptic seizures, and also referring to appropriate therapy, which we talked about earlier. So there are a number of resources out there for you. We worked for almost a decade with the American Epilepsy Society to prepare the clinician formation sheet. You can go on this yourself and get some information on non-epileptic seizures, it's there available for you.

Dr. Curt LaFrance:: 29:15 To conclude, I'll just say that we didn't have a way to diagnose before, but we do. We didn't have a way to treat, but we do, and we're gaining insights into the neurophysiology, the brain workings, associated with these seizures. I will say this, if you're just going to a therapist who you go and talk with them about what's going on in life, and it's kind of a [inaudible 00:29:38] session, actually take that money and go out with a friend of Starbucks, because supportive therapy does not help this. Go for somebody who is familiar with the disorder, go to somebody who knows that they're actually evidence-based treatments,

and say, I'd like to increase the efficacy of what we're doing here. They've got resources that they can look into.

Dr. Curt LaFrance:: 30:04 Finally, to wrap up, I just... I want to thank all the people who are collaborators and friends around the country and around the world. It takes a big team to do some of the work that we're doing, and all of this is happening because of those great relationships. So I'm very thankful. If you do have somebody who has video EEG-confirmed non-epileptic seizures, or if they have epilepsy and a history of head injury, 18 to 60-year-old civilian or veteran, who's interested, feel free to contact my research coordinator, and she will be able to do a screen, and find out if you are interested or eligible in the study that's going on right now. With that, I will close and open to questions.

Laura Lubbers: 30:51 Thank you so much, Dr. LaFrance, that was fascinating. I learned so much on this important topic. It's so reassuring to know that there are things that can be done, because this is a real issue for people across the board. So thank you so much. We have a lot of questions. It has been great to see them coming through, and I can help field those. If you in the audience do have additional questions, please do put them into the Q&A tab. I know some of them are also showing up in the chat, and so we will work through that, as well, and we'll address as many of them as we can.

Laura Lubbers: 31:24 Again, fascinating topic. Why don't we go ahead and start with some of the questions that came in, in advance, because there was a lot of activity over the last couple of weeks once people found out about this. So question, a reoccurring thing, is, if non-epileptic seizures... It seems like epileptic seizures may come and go, based on the experience of our audience. If none-epileptic seizures reoccur, are epileptic seizures are also likely to reoccur? There seems to be an interest in understanding that connection, if there is one.

Dr. Curt LaFrance:: 32:05 So when you say we occur, I see... So we follow people over the course of time, and what we found, interestingly, is there can be periods... what we call periods of quiescence, or quiet periods, where there's no seizures. This can be for epilepsy or for non-epileptic seizures. In taking the history, in talking with people, we'll say... They'll come back, and they'll say, oh, I just had a flurry of seizures again. This could be epileptic or non-epileptic seizures. The question is, anything different recently?

Dr. Curt LaFrance:: 32:37 More times than not, what we'll hear is we'll hear, well, actually, I was getting ready for a final, and I pulled an all-nighter. And then after the final, whoo, I had the seizures again.

Again, this could be for epileptic or for non-epileptic seizures. As you're aware, sleep deprivation is one of the ways that we actually induce seizures, whether epileptic or non-epileptic seizures. So I'll see what we'll call environmental changes. That can be after a period of a quiet period, and then a flurry again, or recurrence, sometimes environmental. Sometimes it can be physiologic changes in the person.

Dr. Curt LaFrance:: 33:12 I see this from kids, to adolescents, to adults, I see this with other medications being added, bodily changes happening, all kinds of things. And then the physiology changes, and that has an effect on the way that the medications that the individual is taking is processed, what we call the pharmacokinetics and pharmacodynamics in the in the system of the of the [inaudible 00:33:33]. So a few different ways that seizures might recur.

Laura Lubbers: 33:37 Okay. That's fascinating, because there were some questions that came in, asking about whether there could be age-related, from childhood to adulthood, can that induce more non-epileptic seizures? There was also a question about whether trauma, for example, having wisdom teeth taken out, can that induce? That's a pretty big stressor in a young person's life. So it sounds like that, yes, those certainly can influence the occurrence of non-epileptic seizures.

Dr. Curt LaFrance:: 34:06 Yes. You said a very important word there, you said stressors in their life. So I'll hear this from some people, they'll say, but doc, I wasn't even stressed, and I had the seizure. So I'm not talking about stress-induced seizures, I'm talking about life stressors contributing to the formation. What I mean by that is, sometimes it's not in the ramped up period, where a lot of things are happening in life, or somebody just had a procedure, or a surgery, or something like that. They do happen postoperatively. I've seen them coming out of anesthesia, non-epileptic seizures.

Dr. Curt LaFrance:: 34:39 But also, after procedure, like wisdom teeth extraction... But it also happens in what I call the letdown period. What I mean by that is, I'm on the beach, and I'm with my family, and it's wonderful, and I had a seizure there. What's that all about doctor? So sometimes people, when they're in the ramped up stage, they've got their defenses up, and then they're when they're in the letdown stage, then their defenses are down, and that's where the seizure may occur. So there's not a one-to-one relationship of, I was stressed out, I had a seizure. It could be in different types of environments. So I refer to life stressors, life events... we've all got life events.

Laura Lubbers:	35:13	Right, right. Indeed. Great. I think that will be really helpful for people to have heard. One thing, another thing that people hear, is that well, we're not seeing an EEG signature, but it's because the the seizure is occurring deep in the brain, and we just can't pick it up. How would you respond to that?
Dr. Curt LaFrance::	35:30	I would say there are some seizures that... There are some locations, or foci, in the brain that elude scalp EEG signal. So what I mean by that is if you've got a what we call mesial temporal, or some frontal lobe seizures, epileptic seizures, they actually... you can have the epileptic seizure, and the scalp EEG is not going to pick up that abnormal brain cell firing, epileptiform activity. So in that case, it's not that it's not epilepsy, it's that the focus eluded the scalp electrode. So we've got a clue there, though.
Dr. Curt LaFrance::	36:13	So just because you haven't a normal EEG doesn't mean it's not epileptic seizures. We've got a clue, though, and we use the term semiology, ictal semiology, and all that means is the physical characteristics of the seizure. There are certain ways that frontal lobe epileptic seizures present, characteristically, that differ from psychogenic non-epileptic seizures. Even though both of those might have scalp negative EEG, we can look at the ictal semiology, the physical characteristics of the seizure, and we can make a comparison.
Dr. Curt LaFrance::	36:44	So that's why you heard me say earlier, the right history, with the right witnessed seizure, with the right EEG, those are the ways that we get the documented... That's how we get documented non-epileptic seizures. If we have the seizure characteristics, even though it's a scalp negative EEG we may say, hmm, this looks more like frontal lobe epilepsy than it does psychogenic non-epileptic seizure, just because I'm watching the seizure myself. That's the importance of the video EEG.
Laura Lubbers:	37:12	Fascinating, fascinating. Very helpful. So a number of people have asked, how do we find providers were trained to provide these therapies in our states or regions?
Dr. Curt LaFrance::	37:24	There are some people who... around the country. Some of it is, it's an email to your local... I would say start with your local epilepsy center, and say, do you have people who are trained in treatment for non-epileptic seizures? Now, that doesn't mean that they were trained with taking control of your seizures workbook, they may have their own approach. What I showed you was just one of a number of approaches. So this is not the be all and end all for everybody. There may be places around

		the country, who say yeah, we've got somebody who's been treating people for 20 years, and they use this approach.
Dr. Curt LaFrance::	38:04	So I would say start with your local seizure, with your local epilepsy center, your local epileptologist. If there's a neuropsychiatry department, sometimes they'll do overlap brain and behavior, and you can contact them. Those are the main... I would say start locally. And then, sometimes people will email and they'll say, do you have somebody trained in Michigan? Oh, yes. Well, there's actually Dr. [Baim 00:38:29], who's trained in Michigan, and this person's in Stanford, and this person... If you're talking about treatment with the workbook, then that's how that's listed.
Laura Lubbers:	38:39	Okay. I think that's a great suggestion, to start with the epilepsy center and move on from there. Of course, CURE Epilepsy is also helpful, willing to try to help find resources as well, if we can make connections. We know that this is an area of great struggle for people, and less identified providers. Another question is, are non-epileptic seizures ever a diagnosis that can be removed from a patient's problem list? This is something that needs to be on the radar now and indefinitely.
Dr. Curt LaFrance::	39:15	So that's a great question. I view seizures, whether epileptic or non-epileptic seizures, as a chronic medical illness.
Laura Lubbers:	39:28	Okay.
Dr. Curt LaFrance::	39:28	I'm thinking now of the International League Against Epilepsy's more recent definitions for epilepsy. Before, there wasn't a great definition for resolved, but now there's a category for resolved epilepsy. So just as there's a category for resolved epilepsy, you can have a category for non-epileptic seizures. That's not official from the ILA per se, but I'm thinking, in parallel, what's been done for the new diagnostic criteria for epilepsy and terminology, that could also be done for non-epileptic seizures.
Dr. Curt LaFrance::	40:03	Here's what I will say. Life events are still going to keep happening, life is going to keep happening. Somebody is going to get sick in the family, a bill is going to come due that you didn't expect, the car is going to break on the day that you don't want it. That's always going to keep happening. The treatment that we... The tools that patients get with the workbook, they have to keep applying those tools.

Dr. Curt LaFrance::	40:27	The way that I demonstrate that to patients is, if they have readers, then at the end of the treatment, I'll say, okay, read this sentence, and they'll read it. And I'll say, now take off your glasses and read the next sentence, and they can't read the sentence. And I'll say, the glasses didn't cure you. You have to have the glasses on for you to be able to read, you have to keep using the tools for you to be able to address the stressors, the ongoing life stressors.
Dr. Curt LaFrance::	40:51	So people can go for extended periods... I've had this and people who've been in our prior studies. They've come back two or three years later, and they've said, the stuff came back. And I said, ow are you doing with... what's going on in life, and how are you using the tools? And they said, life has gotten a lot harder, I just had two kids, and I'm not using the tools. I forgot about. So there's a little booster, and that booster is the thing that helps them to get back on track to use the tools again to address life events that are going to keep happening.
Laura Lubbers:	41:18	Okay. Great, great. A couple of people have asked about the role of psychogenic seizures, non-epileptic seizures, and post traumatic stress. I think you've already touched on this a bit. It's not just the current life events that are happening, but the sequelae, as well, and using these tools to address that. Correct?
Dr. Curt LaFrance::	41:38	Yeah. So people will refer to the various comorbidities or co-occurring illnesses. I didn't put the slide in, but you're probably already familiar. We're talking about epilepsy now. Anywhere from a third to a half of patients with epilepsy also have depression. Anywhere from 20 to 40% of individuals with epilepsy also have anxiety. Anywhere from a third to a half have cognitive issues with epilepsy. So, these are comorbidities, neuropsychiatric comorbidities that occur with epilepsy, very similar in non-epileptic seizures.
Dr. Curt LaFrance::	42:22	So you've got about half of the people have comorbid depression with non-epileptic seizures, about half have anxiety, about half of... 40% of civilians, and up to 70% of veterans have PTSD, as you would expect, with non-epileptic seizures. So a lot of comorbidities. So it's not just about treating the seizure. That's why I was saying earlier, you've really got to treat the whole patient.
Laura Lubbers:	42:46	Right. Great. Thank you. Thank you. So a recent question that just came in is, can there be a false diagnosis of non-epileptic seizures? Why and how?

Dr. Curt LaFrance::	42:57	The answer is yes, and it can go either way. You can be diagnosed with non-epileptic seizures, and it can be epilepsy, or you can be diagnosed with epilepsy, and it can be non-epileptic seizures. I've seen both of those. I've mentioned with one of my early distance mentors was Orrin Devinsky, and he said early on, Curt, you have to approach a patient with seizure with humility, because you can be fooled either way. So people can say, oh, well, I've seen that ictal semiology, I've seen the physical characteristics of that seizure, and that... That's got to be a pseudo seizure, they said in a dismissive manner.
Dr. Curt LaFrance::	43:33	You know what? Number one, it's not a pseudo procedure, and number two, it was actually a very odd manifestation of a frontal lobe epileptic seizure. Conversely, you can have somebody it's like, wow, that's a story for epilepsy, I'm going to treat them for two or three years with anti-seizure medications for presumed epilepsy. Nope. This was not epileptic seizures. The AED's are not going to help the individual.
Laura Lubbers:	43:59	Fascinating.
Dr. Curt LaFrance::	44:01	It keeps you honest as a clinician. You can't go and say, I've got... I wrote a textbook on it, and I'm still... Sometimes I'm scratching my head saying, hmm, I wonder about this. Let's take a tincture of time. Let's use a tincture of time to try and figure out, let's see what you've got. That sometimes is the best medicine.
Laura Lubbers:	44:21	Right. And really finding somebody who can work with you sounds like is important.
Dr. Curt LaFrance::	44:25	Yeah.
Laura Lubbers:	44:26	So here's an interesting question. They're all interesting, of course, but a different one. Do none-epileptic seizures present during sleep?
Dr. Curt LaFrance::	44:36	The answer is yes. The devils in the details here. So, epileptic seizures can arise out of physiologic sleep. Non-epileptic seizures can occur during the nighttime, when a person is sleeping. Those are two different statements. So, the way that we do that is... The way that we figure that out... So both of them can occur at night, both of them can occur while people are sleeping. But what I mean by that is, we look at the tracing on the EEG. As many of the individuals know, the EEG changes when we're in sleep and out of sleep stages.

Dr. Curt LaFrance::	45:14	So what happens is, we're watching somebody, and then there's an arousal, so they become awake, out of sleep, and then they have their non-epileptic seizure. That's how we see that. But we really need the EEG that corresponds to the video to be able to say, oh, you know what, there was an arousal, so they were awake, even though it was at nighttime, when they were sleeping, and it was a non-epileptic seizure, as opposed to literally coming out of physiologic sleep and treated to a seizure. More times than not, it's going to be epilepsy.
Laura Lubbers:	45:46	Fascinating, and complicated.
Dr. Curt LaFrance::	45:48	Yeah, yeah, it really is.
Laura Lubbers:	45:52	So here's a different question, as well. It's around frequency. Do you have to have regular events in order for them to be classified as non-epileptic seizures, or can very infrequent events still be characterized as such?
Dr. Curt LaFrance::	46:09	I've seen people who have them once a year, and I've seen people who have 30 in a day.
Laura Lubbers:	46:13	Wow.
Dr. Curt LaFrance::	46:15	Yeah. So I wish it was that simple, it would make my job a lot easier. But no, it's never that simple. So we really have to pay attention to how often are these occurring? When are they occurring? In the workbook, we have a thing called a seizure log, and that's where the individual really pays attention to their symptoms. So every day, they're documenting, I had one seizure at 12:00 PM, 12 noon, in the kitchen, after I was preparing breakfast, and it had this effect on me. So we get them to start paying attention, whether it's an epileptic or non-epileptic seizure.
Dr. Curt LaFrance::	46:54	And then when they start to pay attention to what's happening, and what might be a precipitant to the seizures, then they can use some of the tools to go back and say, when I have my aura, number one, I want to get to a safe place, first thing, I want to let somebody know, if I can, if I have the ability to do that, and then I want to use some of the tools that I've been learning to apply, to, hopefully,prevent the progression of the seizure into the full blown seizure. We've seen people with epilepsy and with non-epileptic seizures be able to take that approach.
Laura Lubbers:	47:25	Wow, wow. Wonderful, wonderful. Great tool. So you've talked about the workbook, and some of our audience members have

brought forward other types of potential treatments. Just wanted to get your perspective on this.

Dr. Curt LaFrance:: 47:42 Yep.

Laura Lubbers: 47:42 There's a project called Project Uplift.

Dr. Curt LaFrance:: 47:44 Yep.

Laura Lubbers: 47:45 Is this is something that's similar or different?

Dr. Curt LaFrance:: 47:49 Yeah. So Project Uplift is a great tool that used... So that's a self-management tool that was created by the Managing Epilepsy Well Network, some of my colleagues and collaborators, who in... funded by the CDC, the Center for Disease Control and Prevention. So Project Uplift addresses depression and epilepsy. This addresses the seizures and the comorbidities. So it's an inverse of the approach. They can both affect quality of life and improve quality of life, but the approach is a little bit different with Uplift, as it is with ours.

Dr. Curt LaFrance:: 48:31 The other thing that I say with our workbook is, it's not a self-help book. So it's to be done in concert with a clinician who knows how to treat people with seizures. So Uplift, you can get trained... or rather the clinician can get trained, and then be able to work with individuals with epilepsy. That's for Uplift. They've got a number of other things that Managing Epilepsy Well network uses, whether it's Hopscotch, which is used for cognition or thinking problems that can be associated with epilepsy. Yeah, a number of great resources that the MEWN has through the CDC.

Laura Lubbers: 49:08 That's a great way to explain the differentiation between those. Here's another one that somebody is asking about. So eye movement desensitization reprocessing therapy. Tell us about this.

Dr. Curt LaFrance:: 49:20 Now, EMDR is the acronym for that. People with histories of trauma can use EMDR to reduce some of their trauma-related symptoms. There are some case series that have been done for EMDR in individuals with non-epileptic seizures that showed a reduction in seizures. Those weren't controlled studies, so we can't attribute causation to say, well, that's what made it go down. But what I have heard is... I've got a number of patients with trauma histories, who say that EMDR was the thing that really helped me.

Laura Lubbers:	49:55	Okay.
Dr. Curt LaFrance::	49:56	Vastly, I've had people say, you know what, I started doing it, and it didn't really help. Nothing that we do in medicine is 100% effective, but I can say that some of my patients have anecdotally said, this has really helped me, and some have said-
Laura Lubbers:	50:12	Okay. Great. Not in like medications. [crosstalk 00:50:14]. Users have to keep trying and finding those resources.
Dr. Curt LaFrance::	50:17	They're trying.
Laura Lubbers:	50:18	So do these programs work for kids, as well? How do you include family members in this process?
Dr. Curt LaFrance::	50:25	Yep. It has not been studied in children 18 and younger, or rather, under 18. All of our clinical trials have been in 18 and older. So I'm only speaking from the published data. What I can say is, anecdotally, I've had a number of people say, yeah, I used the workbook with my 16-year-old, and it was fine. So when you say kids with epilepsy, are you talking about neonates, are you talking about 18-year-olds? That kind of thing.
Dr. Curt LaFrance::	50:56	When people ask me, hey, can it be used with kids? I say, it can be used for kids who have some self-awareness, and who have some maturity. For those who might be in their [tweens 00:51:14], they might not be ready for some of the ideas or the concept. But I've had some adolescents, who were very mature and had a lot of insight. So there's not a statement about it, it can only be used from this age to this age. There are people who do want to do a clinical trial in kids using the workbook, but that hasn't been done yet.
Laura Lubbers:	51:35	Okay. Okay. Great. Thank you. So, if there's nobody in the area in somebody's region that's an epilepsy specialist, what can they do? What can this person do? How can they find either remote resources, or is that possible? There are there lots of people in rural areas, or unable to get to an epilepsy center and see a specialist. What do they do?
Dr. Curt LaFrance::	52:05	They keep being an advocate for themselves.
Laura Lubbers:	52:08	Yes.
Dr. Curt LaFrance::	52:08	Here's what I mean by that. I tell people, my patients and family members, you are your best advocate. I'll hear statements like... sometimes they'll say, doctor, can you write me a letter, I'll say I

can, but I want you to write the letter, and I want you to write the letter to your doctor, your hospital, your congressman. I want you to write letters to the licensing boards. The reason why I say this is because I live in two different worlds on a number of fronts, so in neurology and psychiatry. I live in two different worlds at the same time. In the VA and in the civilian world, I live in two different worlds at the same time.

Dr. Curt LaFrance:: 52:47 So interestingly, with the VA system, being trained in telemedicine, I can treat veterans around the country. I go to my office in Providence, Rhode Island, and I see veterans all around the country, because the VA is a national system. So, one of the reasons that people can't treat across state lines is because for me to treat somebody in Georgia or Arizona, I have to have a license in the state of Arizona, and I'm not going to get 50 licenses to be able to do that. So that's why I'm saying, lobby. Go to the boards and say, you know what, telehealth has been helping people around the country and around the world, let's make sure that people who have specialties can treat people, or people who are primary care can treat across state lines, and not have that burden of the system that exists in the civilian world. That would be a way to really push the envelope, which I'm a big fan of.

Dr. Curt LaFrance:: 53:43 So that's what I would say, keep being an advocate for yourself, but also keep asking around. A lot of times people will say, well, I've got a local clinician, they're familiar. I view us in medicine as eternal students. So some people will say, I'll see you, and I'll read the workbook, and we'll work through this together. That's another option, is have the local people, whoever it is, to get equipped using the resources that are available. But I would say, like we've talked about earlier, Epilepsy Foundation, CURE Epilepsy, American Epilepsy Society, CDC, those are all places... Sometimes you'll see websites that will say, here, local clinicians. Keep advocating for yourself, is what I would say.

Laura Lubbers: 54:35 Absolutely, absolutely. People with epilepsy in their families have to be strong advocates. There are other networks. So we are aware that there's the Epilepsy Alliance, is available in certain states, and I know that they're able to sometimes get people two visits, if that's necessary, and help connect to different specialists in an area. So do be reaching out, if those resources are needed. We just have a few more minutes, and maybe we have time for another question, but I want to let people know that, once again, this is going to be posted on our website. Give us a couple of days to get the recording done and posted on our website. So if you want to view it again, please do come visit that.

Laura Lubbers:	55:25	Also, Dr. LaFrance, people are asking for the information related to your study, and so we'll make sure that that's visible. In the posting that we have, we do, again, have transcripts available, and we will be posting this information, so people can go back to our website and review and use those resources. Again, we can post information around the Epilepsy Alliance. We try to get as many resources out there as we can. So, again, this has been a fabulous presentation, a fabulous series of lots of questions, and more still coming in. Let's see if we can find one more that we can address.
Dr. Curt LaFrance::	56:17	While you're looking at that, I will say if people want to go to clinicaltrials.gov, they can look for epilepsy trials, and also for the trial that they're asking about now. So clinicaltrials.gov, and you can type in non-epileptic seizures, or LaFrance, or whatever you want to do, and that'll pull up the details of the clinical trial.
Laura Lubbers:	56:36	Fabulous. So one last question. Are non-epileptic seizures less dangerous to the brain than epileptic seizures?
Dr. Curt LaFrance::	56:44	People will ask, am I going to get brain damage from these? What I will say is that the effects of recurrent epileptic seizures... Sometimes people who have certain types of epileptic seizures, they can drop their oxygen level, and they can become hypoxic, and that can actually affect the brain, as you're aware, we don't see those same oxygen level drops in people who have generalized tonic-clonic non-epileptic seizures. So over time, we don't see the same brain energy risks that may be associated with some types of epileptic-seizures that we do with non-epileptic seizures.
Laura Lubbers:	57:23	Okay. Great. Great to know. That's very reassuring. So again, we want to thank you for your time and sharing your knowledge on this incredibly important topic. Thank you to the audience for your incredible participation, both before and during this presentation. It's been a phenomenal discussion. If you'd like to learn more about CURE Epilepsy, please go to our website. You'll also be able to review, again, this webinar, and upcoming webinars. Just want to let people know that our next webinar will be on October 21st, and it will recognize SUDIP Action Day, and it will discuss the important topic of sudden unexpected death in epilepsy or SUDIP, and cardiac function. So with that, again, I want to thank you, Dr. LaFrance, and our audience, and to everyone, please be safe.