

Narcolepsy Nerd Alert Podcast Episode 2
New & Upcoming Narcolepsy Treatments
Transcription by Mirela Starlight

Julie Flygare, JD is the President & CEO of Project Sleep, a leading narcolepsy advocate, speaker, published author, and Stanford Medicine X ePatient Scholar diagnosed with narcolepsy and cataplexy in 2007. She received her B.A. from Brown University in 2005 and her J.D. from Boston College Law School in 2009.

In today's episode, Julie Flygare talks with Dr. Anne Marie Morse, a board-certified and fellowship trained pediatric neurologist, specializing in sleep medicine at Geisinger Health System in Pennsylvania. Dr. Morse is certified by the American Board of Psychiatry and Neurology with special qualification in child neurology.

Julie and Dr. Morse discuss current treatment options, what's on the horizon in drug development, and how people with Narcolepsy can get involved to advance progress by participating in clinical trials. They also talk about non-pharmacological approaches like social support.

The Narcolepsy Nerd Alert series invites listeners to dive deeper into specific topics relevant to living with Narcolepsy. This is a written transcription of the podcast "New & Upcoming Narcolepsy Treatments" from Project Sleep.

Project Sleep is a 501-3c Non Profit Organization, dedicated to raising awareness and advocating for sleep health, sleep equity and sleep disorders.

All guests express their own opinions. While medical diagnoses and treatment options are discussed for educational purposes, this information should not be taken as medical advice. Each person's experience is so unique, which is why it's so important to always consult your own medical team when making decisions about your own health.

Julie talking in intro: What's next in Narcolepsy treatments? It's no secret that the prospect of novel Narcolepsy treatment options gives hope to many people and families living with Narcolepsy. The Narcolepsy Nerd Alert series invites listeners to dive deeper into specific topics relevant to living with Narcolepsy. For more on this topic, please check out our corresponding toolkit available for free on our website to download, print and share.

Julie: Hello, welcome everybody! We're really excited to talk about new and upcoming narcolepsy treatments today. We have a very special guest with us today, Dr. Anne Marie Morse— Hi, Anne Marie.

Dr. Morse: Hi, how are you? Thank you so much for having me today. I'm super excited to be here! I feel like I've reached celebrity status by being on the Narcolepsy Nerd Alert. I'm very, very impressed with everything that Project Sleep has done— but this I think has been a highlight and just really pleased to have the opportunity to be here with you today.

Julie: Well, we're so excited that you're with us. I think that you're definitely— probably, a little bit of a nerd.

Dr. Morse: Yes.

Julie: Yay! So Anne Marie, pediatric neurologist and sleep specialist. And you're at Geisinger, so that's— Central Pennsylvania?

Dr. Morse: Yes, it is. It's right smack in the middle. We cover 47 counties in Pennsylvania— so Janet Weis Children's Hospital is our children's hospital and Geisinger is our larger health care system.

Julie: Okay, and how long— So you just said that you think that we've known each other now for 7 years?

Dr. Morse: 6 years.

Julie: 6 Years!

Dr. Morse: Yep, I believe we met in 2015 at the Sleep Research Network Meeting which was a PCORI sponsored meeting and that was a period of time where you were sharing your passion already about narcolepsy and how to advocate for the patient and empower the patient in their journey. I was just a fellow under Dr. Michael Thorpe at that time where I was just becoming enamored with learning more about narcolepsy and the journey that patients are experiencing. So, that is definitely when we first got together! (laughs)

Julie: Yeah. Oh, so cool. Alright. So for today we're going to do an overview of treatment approaches and then we're going to talk about current medications and then new and upcoming medications and then also some non-pharmacological approaches.

So, at Project Sleep we really talk about these 4 pillars of narcolepsy treatment and that's why I'm so excited. I think medications are so super important and absolutely a foundational part of many people's treatment with narcolepsy. But we can't forget about some of the other coping mechanisms and strategies that can be extremely helpful as well. And so I include those things, are: naps, social support and lifestyle adjustments. So we'll get to some of those today as well hopefully but we will start with medications. Anne Marie, can you help break this down?

Dr. Morse: Sure. So when we're talking about current medication options, it is going to depend on whether the patient is pediatric aged or adult aged. I'm going to talk about it more globally and really focus a little bit more so on the adult population because I think it allows us to have more of a broad spectrum. When you look at the American Academy of Sleep Medicine's recommendations on, this is how you should take the approach to treatment of narcolepsy. There frequently are different tiers of approach and many times we're talking about alerting agents, we're talking about oxybate therapies, and then we're talking about traditional stimulants, and then some other cataplectic agents.

Dr. Morse: So when you're taking about alerting agents the ones that I think historically have been known the most are your modafinil and armodafinil. There's newer kids on the block, with pitolisant and solriamfetol. When you're looking at modafinil and armodafinil and even solriamfetol, they all have shared mechanisms by really working on your dopamine in your brain. Dopamine is a neurotransmitter that helps in maintaining wakefulness and really having that alerting effect. These are a little bit different from your traditional stimulants because they're more centrally acting. What that means is you're less likely to experience some of those side effects, like heart palpitations or appetite suppression or increase in blood pressure. Although those can still happen, they're less likely to occur.

Dr. Morse: Alerting agents are ones that are definitely considered first line therapies. One of the other ones that's a new kid on the block is that pitolisant which I had just mentioned, but it has a very novel mechanism of action. It works on your histaminergic system to enhance your wakefulness. It also has been found to be effective in treating cataplexy events. What is really important about this particular treatment is it's also a non-controlled substance, where most of the treatments that we're utilizing to treat excessive daytime sleepiness are controlled substances. When we go to the next types of therapies which are also considered another first line therapy, meaning that— if you have narcolepsy, these are the ones that your doctor may be offering you right off the bat— it's your oxybate therapies.

Dr. Morse: Sodium oxybate and low sodium oxybate. The reality is sodium oxybate has been available for a long period of time but it had a very high sodium concentration in it: about 1600 milligrams in a 9 gram dose that would be taken at night. The low sodium oxybate has a much lower amount of sodium in it— only about 131 milligrams in that same 9 gram dose, which is the reason why that is another option that has been available to help in navigating some of that sodium concentration. This is a medication that you're going to take at night, which is going to help in sustaining your ability to fall asleep and the result of that is going to result in improving excessive daytime sleepiness and we also see significant improvements in cataplexy events.

Dr. Morse: Now when you go with your second and third line therapies, you're looking at methylphenidates and amphetamines. These are your traditional stimulants that most people are familiar with in terms of ADHD treatments. So when you think of things like Ritalin, for example, that would be considered a methylphenidate class. Or Adderall, that would be considered an amphetamine. Methylphenidates are considered second line and amphetamines are considered third line. Again, they also are working on your dopaminergic system, but tend to have more systemic effects, and many times people can experience more of that heart palpitation and some of those undesirable side effects.

Dr. Morse: Finally when you look at your antidepressant medications, these are being used specifically for anti-cataplexy. The reason why is because we recognize that when we are adjusting a person's norepinephrine in their body, it helps in reducing the likelihood of experiencing cataplexy.

Dr. Morse: One of the particular points I always like to call out about the antidepressants is that we sometimes will utilize them for a dual benefit: We recognize 30-40% of individuals who have narcolepsy may also have comorbid psychiatric concerns such as depression or anxiety. So sometimes we'll utilize these for the intention of treating that comorbid psychiatric piece and the added benefit is that you may see that there's improvement on some of these others.

Dr. Morse: One of the things I do like to call out: because the fact that's a rate limiting step for patients' treatments is that sometimes insurances will say, 'you need to fail one of these medications before trying an oxybate therapy or something like pitolisant'. The reality is that pitolisant oxybate therapies are considered first line therapies.

Dr. Morse: Anti depressants are considered options but have no FDA indication for the treatment of cataplexy, and therefore those should be utilized and offered first before considering any of the anti depressants.

Julie: Wow, thank you for such a good overview. It's exciting to see that there are some new kids on the block in this area because for a while we didn't have any new kids on the block.

Probably since the early 2000s. I guess at one point I'd really like to just mention— because a lot of these are alerting agents or stimulants and something that took me many, many years to figure out was just— what anxiety is.

Julie: I'd heard that some of these different medications can cause anxiety, and for me, I'd thought of panic attacks and I'd had a friend who'd had panic attacks in college— I thought that was anxiety— and it was only in a support group many years into my diagnosis where someone described their anxiety as, this black cloud of darkness over them and nothing can be funny, and they just have this negativity that's not based in their sense of reality.

Julie: I just thought that was so powerful and I guess just wanted to mention it at some point today because I'm just afraid that other people might not know about some of the common— I don't think we talk about— some of the common side effects for some of these medications. I had that both with modafinil and I've had it with stimulants. But side effects are a part of it and obviously complications, too. When people can't take certain medications because they have complications of other conditions that gets really, really tricky really quickly too, I bet.

Dr. Morse: 100%. And I think you're right, I think a lot of people don't recognize anxiety. And I think one of the challenges when you're talking about individuals who are experiencing their journey with narcolepsy is that anxiety creeps into their life without them being aware of it because there's all these other symptoms that have occurred. So sometimes anxiety is truly another condition that is a part of their journey and sometimes it's just a consequence of how long their journey has taken to getting to the right diagnosis. So they're constantly waiting for the other shoe to drop: 'I went and I saw the endocrine doctor because I thought it was a thyroid problem, I went and saw the infectious disease doctor because I thought it was Lyme or because I had mono.'

Dr. Morse: And so there's all this anxiety of, 'do people believe me? Am I going to be able to actually meet that deadline?' A lot of people start to absorb that as, that's just a part of who I am. But you're right, there's that true anxiety that can be a part of the illness— but then there's also that anxiety that— you're 100% correct, can be a part of the experience of when a person is on a stimulant. Because I might be more awake and more alert— I might be less able to control my emotional response to changes in my surroundings.

Dr. Morse: So you're 100% correct and I do think it's really important because a lot of people still have a challenge in acknowledging mental health concerns and feel ashamed of those things and I do think it's a really important call to attention, to say that should be front and center. Because taking care of the whole person is critically important for any provider.

Julie: Yeah, for me I figured it out— that it was the medication— because of an error. Instead of getting the slow acting version, a pharmacy gave me the fast acting version of the same amount and so for two days it was hitting me so strongly that it was like it took over my life— I couldn't leave my house— And there was this dark cloud of negativity— and it was only seeing anxiety in an extreme form that made me then realize some of the lesser forms for me. And to be careful about how much coffee I had, too— if I had too much coffee in addition to stimulant that could also bring it out. Is there anything else before we move on to upcoming treatments?

Dr. Morse: One of the things that you've mentioned in regards to the increased number of players that we have in terms of treatment is a reflection of just improving— slowly but progressively— improving awareness in investment of trying to create more treatment options and more knowledge about the disease process. So I think that because of those

advancements in science and having a better understanding of the potential path of physiology contributing— or what is causing— to developing narcolepsy, I think you're going to see a reflection of changes in treatment modalities available.

Julie: Yeah. And really quickly, before we get to that too— I think that you have pointed out the AASM's guidelines— and we do have that in the resources at the end. It seems not all sleep doctors are maybe aware of some of the best line treatments— or familiar enough with them, or feel comfortable enough— so I think that's important that patients become educated about what is considered front line treatments, as you've discussed today. But we do have that guideline as well.

Julie: I don't know what you'd say, Dr. Morse, but if someone feels like they're maybe not getting access to front line treatments— because perhaps their doctor might not be as familiar with them— my advice would be to kind of consider getting a second opinion from another doctor, or trying to find out who treats a lot of people with narcolepsy in your area and who feels comfortable with the different options that are available. That's a concern of mine is that some sleep doctors still aren't super familiar with all these options.

Dr. Morse: I think you're correct and I think the challenge is that narcolepsy is technically considered a rare disease, correct? Even though my clinical experience would argue that it's not as rare as we potentially consider it to be. And what I would say is, you're correct— that different people have different levels of experience with the medication, different levels of experience with the disease— and therefore that might lead to discomfort.

Dr. Morse: You're 100% correct that most health care providers don't feel comfortable saying, 'I don't know,' and that, 'I'm uncomfortable,' or, 'you're the first patient who I'm going to be prescribing this medication to.' I very frequently see that as a rate limiting step for providers changing their behaviors.

Dr. Morse: But again, I think that's where as a patient it's really important to feel empowered and educated. I've found whether I'm wearing my neurology hat or my sleep medicine hat, that when I'm talking about rare diseases— that it's not uncommon that my patients, or the parents of my patients, are far more expert than most providers. I would say that if you're meeting a provider who is intimidated by that, that also may be a sign that you do need a second opinion.

Dr. Morse: And a second opinion doesn't mean that you don't like your doctor— it doesn't mean that you're necessarily going to have to change your doctor. It means that you're doing the scientific method, right? You have a hypothesis that you can do better, you're testing that hypothesis by seeking out an alternative treatment strategy— and then you're going to utilize that treatment strategy to see if that makes a difference. Right?

Dr. Morse: And so, I think that it is very important, through the work that you guys do, on a daily basis— to continue to educate and empower— and for patients to demand shared decision making with their providers.

Dr. Morse: The days of old of the provider always being right and, 'this is the only drug,' and, 'I'm smarter than you—' that is horrible. That is not the right way to care for patients. We need to take care of the full person in front of us, and really understand what's important to them.

Dr. Morse: Just because I maybe have 10 patients that did great with drug A, doesn't mean that my patient 11 is going to have that same response. And so I need to hear from them— as to, what is their priorities, what is the experience that they're having, and what are their fears.

Dr. Morse: That is where we have to work together to be able to develop a treatment plan and then also respond to, how are we going to monitor your response to that. I think that that sometimes is a fear for providers— to look like they chose the wrong drug— or that they're going to experience a side effect that they don't know how to navigate— and what I have found is that when I'm truthful with my patients and give anticipatory guidance of, 'these are the things that are possible, not necessarily expected—' that patients have a trust in that communication and are willing to enter that journey with me being the guide on the side.

Dr. Morse: No longer do I try to take that role of being the director or the captain of the ship. They're the captain of the ship. I'm the guide on the side that really is just helping with the navigation and giving all the options that I think may be helpful to them. But I always love when patients come to me and say, 'I saw that there was this new treatment.' A lot of people will tell you, "don't go to Dr. Google." I think it's a matter of, if you go to Dr. Google, have the opportunity and the communication capacity to speak with your doctor of, 'this is what I've read, can you tell me whether this is true or false— can you tell me what your experience has been with it.' And then be able to make those communications together.

Julie: Such a great point. Especially as there are new treatments available, coming to market— There's going to be more options. So, more to talk about.

Julie: So, walk us through the exciting things of what's coming in the future because this truly is so much hope for so many people.

Dr. Morse: I agree with you. So when we're looking at the different treatment options available I would say that what we have here is, first we have FT218. This is a once nightly oxybate therapy that has completed its phase 3 trial. Currently is going through open label extension. What that means is that patients who had previously been in a trial are able to continue taking that medication and then it may also be available to other people who had similar medications and wanted to transition to that.

Dr. Morse: Now we had talked about that there is oxybate therapy currently available. But that oxybate therapy that is currently available— both the sodium and low sodium oxybate— is twice nightly. You take one dose at bedtime and 2 1/2-4 hours later, you take a second dose. For many patients, that's fine. They do great.

Dr. Morse: But one of the conveniences that many patients will describe is that they would really prefer to be able to take one medication versus having to take it multiple times. So this is a once nightly sodium oxybate that is waiting for FDA approval to be able to become something that is clinically available. And so this is, again, something that is going to be taken at night time and does treat excessive daytime sleepiness and cataplexy.

Dr. Morse: Now when we're looking at the next treatments, the TAK-925, the TAK-861 and the TAK-994 — TAK is just standing for the name of the pharmaceutical company which is Takeda. They are all orexin agonists. So what is Orexin and why is that relevant? Well, when you're talking about orexin, or— also known as hypocretin— it's the neurotransmitter— or the brain signaler— that many patients who have narcolepsy are deficient in.

Dr. Morse: So, people who have narcolepsy type 1— or narcolepsy with cataplexy— have low levels of this neurotransmitter, which is responsible for the symptoms that they're experiencing. And the reason I specifically say that, is that with narcolepsy type 2 they tend to have normal levels of this. And so we don't fully understand the mechanism that is occurring for patients who are narcolepsy without cataplexy— or narcolepsy type 2. And we're looking at, what if we give people this neurotransmitter back? What if we allow them to have this self-signaling capability back, by giving them this replacement.

Dr. Morse: So, these are all very early phase studies. So when you're looking at the TAK-925, this is an IV formulation of that medication. When you're looking at 861 this is oral and so is the 994. The unfortunate news about the 994 is that, that clinical trial has been stopped due to a concern of a safety signal. However just because that trial has stopped does not mean that the 925 and the 861 may not come to fruition as being a treatment option that will be available for patients in the future.

Dr. Morse: These are all in early phase studies. So it's phase 1 and phase 2 studies. Which means that they're really looking at the safety, the tolerability, and the appropriate dosing before they go into the more advanced studies to do randomized control to say, 'this is the effect that we are seeing consistently,' in order to get that FDA approval.

Dr. Morse: When you're looking at the SUVN-G3031— which is samelisant— this is a histamine medication as well. This is working on that histaminergic system so this is similar to the medication that we already see that is approved— which is pitolisant— and this is in phase 2 trials right now.

Dr. Morse: AXS-12 is reboxetine. This is a norepinephrine re-uptake inhibitor. Remember on the last slide I had described to you that antidepressants are frequently used because it affects your norepinephrine. This is a medication that is being studied to specifically be a treatment for cataplexy alone. If you recall, none of those medications that I described have an FDA approval. So this is a company that is doing their due diligence to say, we not only want a treatment that is a norepinephrine affecting medication— but we want to make sure that we are getting you the dosing, and the titrations, and the safety— and getting that FDA approval. Which only makes it easier on the physician or the provider side to get these drugs approved for treatment.

Dr. Morse: THN102 is actually a combination of medications. So it's a combination of modafinil, plus another medication called flecainide. Flecainide historically is a medication that is utilized clinically in cardiology, as an arrhythmia problem. So trying to help people with cardiac rhythm problems. Many of you sitting here listening to this may go, well then what's the relevance to narcolepsy. Well, the reality is the relevance to narcolepsy is that when studied, they actually have found that it can affect what we call astroglia connections.

Dr. Morse: So basically what this is, is something that is very much involved in sleep regulation. And what they're identifying is that by affecting this, not only may it augment— or increase— the ability to have better sleep regulation and further enhance that modafinil's effect on alerting— but they also have identified that there may be some secondary gains in cognitive performance.

Dr. Morse: So one of the things that many many patients may describe to me is that they feel like they have brain fog. No matter how well I treat their sleepiness, even though I do the Epworth and I ask them about, 'are you falling asleep in this place, that place, etc— do you feel like you're dozing, do you feel like you can do all the things you want to?' They may say yes— they may still experience this inability to feel like they're processing the same way— and

focusing the same way— and really have a concern about their cognitive performance. What this drug is really looking to do is potentially say, not only can we keep you awake— but we can optimize your cognitive performance.

Dr. Morse: The final medication is one that is a very old drug, clarithromycin. It actually is an antibiotic. It's one that has been used very commonly and most commonly actually I've seen it coming out of Emory— from really, really incredible sleep scientists down there— in the use in idiopathic hypersomnia. They also now are extending this to the use in narcolepsy. The reason that they're using this antibiotic is not because people with narcolepsy have some unrecognized infection. But because the fact that one of the other things that are occurring is that they identified that this clarithromycin may have some impacts on our GABA system— so our inhibitory neurotransmitters. With that they're identifying that when they're giving this medication to individuals with central disorders of hyper somnolence— such as narcolepsy or idiopathic hypersomnia— that they are seeing an alerting reaction to it. And so that is currently in phase twos.

Dr. Morse: So a lot of these studies are in early stage research, so phase one or phase two. Phase one is typically looking at, again, that safety signal, that tolerability— and usually, that's not even in individuals who have the actual disease state— it may be in healthy volunteers.

Dr. Morse: It's in phase two and phase three where we really start to look at individuals who actually have the disease— so in this particular case, narcolepsy. We then identify what is the best dose that gives them tolerability without any side effects and how is their body metabolizing it and what is the best dosing and timing.

Dr. Morse: Then the phase three is usually saying, not only do we know the dose. Not only do we know the side effect profile. But we are demonstrating that there is improvement in excessive daytime sleepiness— cataplexy— or potentially, disturbed nocturnal sleep, or one of the other pentad symptoms that an individual may have.

Dr. Morse: Phase 4 studies generally are after there's FDA approval and is looking at real world evidence or post marketing analyses of, are there other side effects that maybe we didn't recognize or didn't come to light. And if after 5 years on the drug there's something else that we need to inform our patient population and our providers about.

Julie: This— is— so exciting! (laughs) Just— feel so grateful and hopeful that there are so many new options possibly coming down the road for people with narcolepsy— and I know patience is not my strong suit— I always say, I'm the most impatient patient. And so it's hard to sometimes think, “well, is this days, is this weeks, is this months, is this years, is this decades?” But I think by laying out this process and also just explaining how well studied each of these treatments, hopefully— if they go through the whole process to approval, and then, even more studied after that— that there is so much care to develop each one. It really gives you a lot of respect for such a big, rigorous process.

Dr. Morse: And a thing, I think— one of the other pieces that is so important is that when there's pharmaceutical companies who are looking at some of these targets— and developing these drugs— they don't go it alone. One of the things I've been repeatedly impressed by is that they will seek out expert opinion, to be able to help in better understanding— is this the right study design? Are we looking at the right outcomes? Are we looking at the right patient population?

Dr. Morse: And you're 100% correct in that, it's not— unfortunately— something that can happen over night, but that's for safety reasons. And so I do think that it's incredible that there are so many different companies that are developing treatment that are going to be extremely meaningful. And when you highlight the fact that this brings hope, I do think that that's so important.

Dr. Morse: Many times when I am giving talks about narcolepsy, I very frequently will make the analogy to another neuron-immunologic condition in neurology, which is multiple sclerosis. The reason I make that analogy is because there is so many similarities. The prevalence of the disease— so we talk about the worldwide prevalence of narcolepsy being 1 in 2,000— the same exact thing is true for multiple sclerosis. They're both considered neuron-immunologic processes.

Dr. Morse: The final piece that I like to highlight, in regards to hope— is that when I was training in neurology, there were really two main lines of therapy. You now look at the treatment landscape for multiple sclerosis and there's about 30 different treatments available. I think narcolepsy is on the same trajectory. And when I look at the impact it has had on patients of multiple sclerosis in terms of socio-economic disability, quality of life, functionality— it's been transformative. And I feel so, so privileged to be practicing in a time where I truly believe that that same type of transformative care is on the horizon.

Julie: Awww. That's— I love that. Okay, I'm going to try not to cry. Usually it's more storytelling that gets me crying, (laughs) but that was really beautifully said. I wanted to take a second to emphasize that as we talk about these new options— they can't come to market without people with narcolepsy, at some point, being part of that process. And so we're really thankful to all the people with narcolepsy that have been participating in clinical trials and clinical research. It's really amazing.

Julie: I just wanted to point out some of the reasons that people do decide to participate in clinical trials. It's really being part of history sometimes and helping to contribute to science moving forward. You also are doing something to support a broader narcolepsy community. Many of the clinical trials are happening in the US and Europe and so they're not even available for people in other parts of the world to be even a participant. So for those of us that are in places where these clinical trials are available, you know, it's really supporting the broader community.

Julie: Also you do get the possible opportunity to try novel treatments and to receive expert care from research staff and I just wanted to say that from talking to people that have been on clinical trials, they actually get to really learn more about their own experience with narcolepsy. They're often doing many surveys and all sorts of different things and it can be very educational to understanding ones own experience.

Julie: I just wanted to mention that because, again, often I've seen— not necessarily in the narcolepsy space, but more broadly with clinical trials— they're often slowed down because of trying to recruit people to participate. So it's really, really important for people to be willing to step up and participate. I don't know if there's anything else you wanted to add there, Anne Marie.

Dr. Morse: I think you're right and I think sometimes people are unaware of the fact that there's clinical research opportunities and they don't necessarily need to be occurring in the office that you're seeing your sleep provider.

Dr. Morse: There is many times that companies who are doing these clinical trials will have different posts on social media trying to just improve awareness. There's also the opportunity of going through something like clinicaltrials.gov where you're able to put in the disease state and it will give you some different options. Again, because there's different phases of it, it may have different participation criteria or different lengths of obligation.

Dr. Morse: Sometimes there is involvement of blood draws and sleep studies and things like that. And I do think that when looking at the participation in clinical trials, there is very frequently a sense of, "how will this help me?" but I think many patients— especially those who have rare disease— think, "how is this going to help the bigger community in general."

Dr. Morse: I think that when you are looking at different opportunities for clinical trials, you're 100% correct, Julie. We usually have very large teams that are working with our patients to ensure that all of their questions are answered and then that's in addition to the pharmaceutical company and research teams that they have there.

Julie: Yeah, perfect segue-way. (laughs) So if you want to learn more about the different opportunities, sometimes they post on social media through their own ways. But also on non-profits like Project Sleep or Wake Up Narcolepsy, Narcolepsy Network. Hypersomnia Foundation often will share announcements as well about clinical trials.

Julie: So we do highlight some research projects on our website, including some that aren't even clinical trials. Like currently we have one— a pediatric survey— through Children's Hospital in Boston. It's a great opportunity. So there are even some things you can just complete a survey or do an interview and really help the research process as well.

Julie: The map from clinical trials— I put in 'narcolepsy' and 'currently recruiting'—so, there are supposedly 14 currently recruiting in the US, 7 in Europe and one recruiting in Australia and Canada. But you can put 'narcolepsy' or 'idiopathic hypersomnia' into clinicaltrials.gov and it's kind of interesting to see too, some of the different stuff that's happening.

Julie: Just wanted to segue-way a little bit to some other aspects of caring for narcolepsy because we do have the medical management but also remembering as Dr. Morse said that, "looking at the whole picture." I like this quote from my own presentation back in 2015, "we may not have a cure for the condition today, but we do have a cure for the loneliness." Which is social support and being part of this community.

Julie: So just these reminders about some of the non-pharmacological approaches. Naps, and kind of even thinking about medications— if we think of sometimes, that the goal is to get rid of the nap, with medications— I think I originally thought that if my medications were working well I wouldn't have to nap. And I've still found that I do have benefit from my treatments but napping has continued to stay an important part of my treatment as well.

Julie: But social support has been absolutely huge for me and I know for a lot of other people. Emphasizing that is always important especially when I'm talking to doctors and health care professionals who may be thinking more about the medication— rightfully so, because that's what they're really empowered to help with— but also letting them know about the importance of connecting people to organizations like this, so that they can get more support for the social side. And knowing that they are not alone with all of these struggles. Just wanted to mention those important things.

Julie: And for me therapy was really important to process. Not that, because— I needed to like— It was just, dealing with a chronic condition. I think that it should be more, it should be normalized in our society that if you're taking on a major life changing thing— like a chronic disease diagnosis— that talking to someone on a regular basis can be helpful. I kind of happened upon that for the first few years which is really helpful.

Dr. Morse: I just wanted to comment on that. That is— I want people to actually hear what you just said. Is that being an individual who gets diagnosed with any chronic disease, including narcolepsy— It is okay to seek out support, because you have experienced something that is transformative to your life— and no one is born in this world completely equipped for something that just completely changes what their expectations are.

Dr. Morse: And I think that the fact that you had that realization— and ability, to seek out someone to help you— with augmenting your coping skills, and how to navigate, and how to be productive— obviously clearly has been demonstrated by your tremendous success in Project Sleep. But I do think it's something that is so important for people to hear, because again— I think that some people, when that suggestion is made— of, “seek out a psychologist or a counselor to help,” that we are saying that, “you're depressed because you have this condition,” and that's not what we are saying. It's saying, “we want you to be your best you.”

Julie: So I actually— So, thank you! But I actually didn't— That's not what happen— So what happened for me is that, before I found the terms, 'narcolepsy with cataplexy,' like, the week before— the primary care doctor had suggested depression. I didn't feel depressed— I felt tired— but I did feel out of control, and I was willing to try anything so I went to a therapist one week.

Julie: And then I found the word cataplexy, which led me to narcolepsy. And I forgot to cancel the next appointment with the therapist. And so I was like, “ah well, I'll just go,” and so I went and I just told her about, you know, “oh my god, I found this term, and this is what it is.” And I was like, “oh hey, I kind of like talking to you.” So I actually call it, sort of, you know— I don't think that I would have gotten the diagnosis and then thought I deserved it— but I kept her for the next two years.

Julie: And my therapist was just— so essential— to helping me, even thinking about changing my career a little bit— away from being a lawyer, to writing a book— and has been a huge part of my journey. But I actually, that's not what happened. I didn't seek it out that way— I call it kind of— the best, strange error— that happened in my process of finding narcolepsy, that ended up benefiting me.

Julie: Hoping that we can do better for other people, and that they don't have to go about it that way, but looking back— it's just amazing that I had her at that point in my journey for those two years— of getting through law school with narcolepsy. So, yeah. It is kind of strange. And I think there are some therapists now, that are having a chronic illness speciality, which is really exciting. There's a small list on Lauren's website— she's a therapist in San Francisco who has MS and a podcast and we will make sure to put that in our resources.

Julie: So, lifestyle adjustments. There's a lot of other things that people do because people often are so pro-active in trying to feel better and maybe don't get the benefits that they were hoping just from medication. Anne Marie, is there anything you wanted to share? I know that you've done a lot of work in the area of trying to help people in other ways.

Dr. Morse: First of all, I think these are all so critically important. I don't think it's just kind of taking one and running with it— I really do think that empowering a patient to be able to utilize all of these different options to maximize their day to day function and quality of life is critically important.

Dr. Morse: When looking at lifestyle adjustments for every single patient that we see we're always looking at sleep habits and making sure that they have optimal sleep hygiene: that they're entering a good bedtime routine so they have a healthy association with that. We also look a lot at diet and fitness and the reason why we look at that is because there is normal biologic changes that are occurring with optimal diet and fitness.

Dr. Morse: When we're exercising a lot people will refer to those endorphins that are being activated. Those are wake promoting neuron-chemicals that are making you have a much more natural development of being able to be awake and engaged, etc.

Dr. Morse: When we're talking about diet, there is some suggestion that different types of diets may contribute to improved wakefulness and decreased likelihood of lapsing into these sleep attacks or that sleep inertia that really drags many people down— even those who don't have narcolepsy. Very frequently people will describe after they eat a big meal that then they feel very sleepy. Well, that is a very common thing.

Dr. Morse: When we look at the different types of foods and what the diets can consist of, there is some suggestion that low-carbohydrate—or even ketogenic type diets—may provide some benefit in terms of wake promotion and improvement in sleep. Myself as a neurologist I can say that there is lots of data about ketogenic diet in the world of seizure disorders. Many times we're using that for seizure management, but one of the fallouts that we've identified is that many patients who take ketogenic diet, we also see have this benefit in their sleep.

Dr. Morse: I think that's not by accident, it's very much by design. Because when we're looking at the individuals who are on ketogenic diet— which if you consider this, please do so with a registered dietician, someone who is very familiar and making sure you enter it safely— we are generally achieving a goal where a person is producing ketones. Basically it's a different energy source than regular carbohydrates for your brain and your body.

Dr. Morse: The specific ketone that we usually are measuring is something called beta hydroxy butyrate. When we talked about those oxybate therapies earlier, the active metabolites that we're looking for there is gamma hydroxybutyrate. If I were to hold a mirror up to a gamma hydroxybutyrate, I would see beta-hydroxybutyrate. So it is an isomer, a mirror image of it. When we're looking at that I do think that the reason we're seeing this potentiation and improved wakefulness and good quality sleep is likely because of the fact that it's exerting similar effects of what we see with gamma hydroxybutyrate. So there are some clinical case reports that have been described of utilizing ketogenic diet in narcolepsy and some report that there may be some benefit, but in terms of large randomized controlled trials, or large case series, we're really lacking that kind of data.

Julie: Thank you so much for talking about that though because I think, even with social support— (laughs) as Dr. Morse knows, I'm a big proponent of social support— and I have had some doctors say to me, "well it hasn't been proven that that's going to improve someones outcomes." But I also don't think that there have traditionally been a lot of incentives to do big trials to look at whether— so just because there isn't the robust data today to support some of

these approaches, it doesn't mean they couldn't be effective for a lot of people or for some segments of people. It's just really, really important.

Julie: I always like to mention— I'll just say— I have heard, you know— I talk to a lot of people and parents of younger people with narcolepsy and one instance always stuck out to me though— where a child had been newly diagnosed, and still was having severe cataplexy, and the parent seemed afraid of traditional medications— of pharmacological treatments, and I just remember this mother saying, "I just try and get him with the trainer at least three times a week!" And that that was going to be, like—

Dr. Morse: A cure-all.

Julie: Yeah— and that really scared me and I just thought that, it's always important to remember that these can be great additions— but often, getting their medical management in better aligned somewhat, at first— should be probably a first priority, at least in that example. Just always want to mention that. And that usually, if anyone says they've found a "cure"—that it's going to do everything— it makes me a little bit skeptical. I'm much more interested when people say, "well here are some of the benefits," but, usually— I haven't found anything that's been, a full on— cure. For narcolepsy. But these are so important.

Dr. Morse: I think the points that you make in regards to support groups and really peer support in general, can be very critical and I think that when looking at this I also think some of the work that Project Sleep has done, like the Rising Voices of Narcolepsy should also be considered a part of that. Because even though that is a program that is dedicated to helping people to be able to speak more on their condition, I think it is a significant role for empowering people to feel more in control of the life that they're living, by just being able to communicate with others very effectively about the journey that they're having. And so I do think that there are so many tools that have been made available through Project Sleep and many other advocacy programs that do help in going this journey and not feeling alone.

Julie: Thank you. *(laughs)* We agree. *(laughs)*

(Dr. Morse laughing)

Julie: We'll probably have data someday to talk about how empowering it is. But yeah, definitely has been a big part of my journey— which is what has landed me, right here.

Julie: I wanted to close with a few beautiful poems because, you know, we always love our different ways of expressing things and different quotes. This is from Amanda who's in Scotland. Her instagram is mysleepystories and she had posted this the other day and it just is unforgettable and had resonated with me— this first stanza, of a longer poem. She says here, "take these twice a day, they'll keep you wide awake, you'll focus on everything trivial, they'll wonder what's wrong with your face."

Julie: She writes in the post where she shared this— and I did ask her permission to share this today. But on her post on Instagram, this was about her experience— with one of the wake promoting treatments— but I just thought, "you'll focus on everything trivial," *(laughs)* really resonated with some of the challenges of managing some of those stimulant, or wake promoting— treatments, and— feeling awake, but maybe not able to even focus on the right things. It just really was a powerful line there.

Julie: And, another poem by our esteemed poet laureate— I'd say, Project Sleep's poet laureate and board member— Anna. Anna Laura wrote this poem and I just wanted to share it with you today, "to buy myself time with my eyes open wide, I medicate in hopes to freeze time and extend my daylight. I buy off the shelf, what I can't make myself. Is this scrip made for me? Perhaps, we shall see. I'm feeling it now, freedom each time. When I take the pill, it's like I can fly. Damn it. I'm crying. The fog has dissolved. My icy skin thawed. To feel this sunshine brings tears to my eyes. Is this what it's like to be alive?"

Julie: (*crying*) Such a beautiful poem. And just reminds me of why we're trying to do this and so that more people can have more moments like this. Of being alive. Okay, sorry— (*laughs*) but, thank you Anna for your beautiful words and for letting us share them today. And Amanda.

Julie: Just a reminder of course about the different patient organizations that are out there. Project sleep is one of them but Hypersomnia Foundation, Narcolepsy Network and Wake Up Narcolepsy are three of the other ones here in the United States. There is an incredible group of organizations around the world as well. Please visit our world narcolepsy day webpage where we've outlined 20— I forget if it's 26, 29— I don't know, we have a lot of different partner groups around the world now. It's pretty awesome.

Julie: Please connect to these organizations for more information and education and resources. If you want to learn more about participating in research check out our webpage, check out clinicaltrials.gov. We did mention the AASM did just put out, really recently— in September— new clinical practice guidelines for hypersomnia and narcolepsy. So that's a really exciting resource that— I believe, yesterday I checked, you can download the PDF for free. So that's really nice when there's not a paywall keeping this information from us. And just really wanted to mention Anne Marie's website, can you describe a little bit about Wake Up and Learn?

Dr. Morse: Sure. So, Wake Up and Learn is actually a school-based sleep education and surveillance program that we developed that is free of charge for schools to participate in. The goal of it is really to try and break down that barrier between people who are suffering from sleep disorders, including narcolepsy, to appropriate time of diagnosis and treatment. So what we have done is sit screening in the school systems— so that this way, meeting the students where they are most of the time— rather than making them leave the school to have come to the doctor's office.

Dr. Morse: Allowing us to really provide universal education to all the key stakeholders in children's lives. We are very excited because we are planning to try and get additional grant funding to expand the program, so this way we can also— not only meet our middle school and high schoolers— but also college, medical school and resident physicians. So that this way we are further augmenting the awareness and ability to diagnose and get people appropriate treatment. Really the goal is to empower people and recognize the importance of sleep and the role in our overall wellness.

Julie: Amazing! We'll have to have you back for another broadcast about some of that. (*laughs*) That's so, so cool. Thank you for all your work! So in addition to being— You know, you just have so many hats you're wearing—

(*Dr. Morse laughing*)

Julie: —And this is just one of them, and the right person for the job.

Dr. Morse: Thank you.

Julie: Thank you everyone for tuning in and huge thanks to Dr. Morse for generously giving us this time for education and awareness and community. It's just— You're a huge part of my journey in this community, and— really lucky to work with you, in different ways and— especially today.

Dr. Morse: Thank you so much. I appreciate the opportunity to be a part of it.