Welcome everyone to today's webinar. My name is Laura Lubbers, and I am the Chief Scientific Officer of Citizens United for Research in Epilepsy or CURE. I'd like to thank everyone for joining us today. November is epilepsy awareness month, and we are very excited to present the second in our series of five webinars during this month that highlights some of the key research that's being done on epilepsy. Today's webinar will focus on epilepsy devices and technology presented by Dr. Bob Fisher. On November 15th, we will have Dr. Jeff Noebels from Baylor College, present on infantile spasms. On November 21st, Dr. Ramon Diaz-Arrastia, from the University of Pennsylvania, will present on post-traumatic epilepsy. During the last week of November on the 29th, Dr. Elizabeth Donner, from the University of Toronto will present on Sudden Unexpected Death in Epilepsy or SUDEP. All of these webinars are at 2:00 PM Eastern time.

For those of you who may not be familiar with CURE, our mission is to cure epilepsy, not just treat it. We seek to transform and save the millions of lives who are affected by epilepsy. We identify and fund cutting-edge research, challenging scientists worldwide to collaborate and innovate in pursuit of our goal. We are one of the largest private funders of epilepsy research in the world, funding over 200 research projects in 15 countries. CURE has been the pioneer in many areas of epilepsy research, including SUDEP, where we have invested over $4 million into research. CURE has also worked to accelerate the understanding of infantile spasms, a catastrophic form of childhood epilepsy that can significantly impact a child's development and leave lifelong disability. We also realize that anyone is at risk for developing epilepsy, because it can be acquired over time, and as a result of brain injury.

We have just launched a new project funded by a grant from the U.S. Department of Defense that supports a team approach to understanding post-traumatic epilepsy. CURE is also excited to support the development of an Apple iPhone app called EpiWatch. The first version of this app is already
available for download and helps people track their seizures, as well as allows the person to send an alert to a caregiver that a seizure is happening. It also helps track medications and potential triggers for seizures. CURE is partnering with investigators at Johns Hopkins University to help them develop the next generation of the app that will hopefully detect seizures and automatically send an alert to caregivers. Of course, the development of this version of the app requires research and data from those who have epilepsy.

Dr. Laura Lubbers: 03:03  
CURE is supporting this research by providing donated Apple watches to those who are eligible to participate in the research. Individuals must own an Apple iPhone that is capable of running the latest operating system, must be 16 years of age or older, have epilepsy and have had at least one tonic-clonic seizure in the past year. For the research study, it’s also important for participants have no physical or learning disabilities that would impair the ability to interact with the app. The family members and caregivers may be able to help you carry out some of the activities of the study. Please stay tuned for more information at the end of the webinar for details on how you or a loved one can learn more and potentially participate in the watch donation program and research study.

Dr. Laura Lubbers: 03:48  
EpiWatch is just one of the technologies that have been in development to improve the lives of those with epilepsy. Today, we have Dr. Robert Fisher, who will talk to us further about the newest devices and technologies that are in development. Dr. Fisher is the Maslah Saul MD Professor and Director of the Stanford Epilepsy Center and EEG lab. He's published over 200 peer-reviewed articles and three books. He's received numerous awards for his work, both nationally and internationally, and as a past president of the American Epilepsy Society. He's been involved in clinical trials on deep brain stimulation for epilepsy and on the next generation vagus nerve stimulation devices.

Dr. Laura Lubbers: 04:33  
His recent research is on new devices to detect and treat seizures. Dr. Fisher has won many teaching awards and also has an active clinical practice at the
Stanford Epilepsy Clinic. Before Dr. Fisher begins, I'd like to encourage everyone to be thinking about and asking questions. You may submit your questions anytime during the presentation, by typing them into the questions tab of the GoToWebinar control panel and clicking send. My colleague from CURE, Brandon Laughlin will read them aloud during the Q and A portion of the webinar. 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. We also want to mention that today's webinar as well as last week's webinar and the ones to come will be recorded and available on the CURE website. So with that, I would like to turn it over to Dr. Fisher.

Dr. Robert Fisher: 05:34
Thank you very much for joining us. For those of you who are wondering, I can see there are 77 of us online now, and that number keeps increasing, please do think of questions or comments. Please don't refer specifically as you heard to your own case, but make them general and try to keep them brief, and in turn I'll try to keep my answers brief, so that people have a chance to ask questions. We'll be talking today about devices for treating epilepsy. I wanted to make some disclosures because I have some relationships with the companies. I haven't actually had any income from any of these, but potentially I could. So take a moment to note the potential conflicts of interest, although I'm not selling any product here on this webinar. So we're talking about devices.

Dr. Robert Fisher: 06:30
Drugs are the mainstay of treatment for people with epilepsy, you all know that. But what's wrong with drugs? Well, they only work in two thirds of people with epilepsy. They have side effects, particularly memory problems, fatigue, moodiness, dizziness, gastrointestinal upset, et cetera. They have longterm side effects such as osteopetrosis, which is bone loss, sometimes weight gain or weight loss, cholesterol increases, in women of childbearing years, they sometimes can cause birth defects. They're inconvenient to take, there's a risk of forgetting to take them, and they can be quite expensive. Therefore, there are devices. On this slide, I gave
examples of six existing devices that can be used now, and on the next slide, I'll show you some future devices.

Existing devices include vagus nerve stimulation, shake watches, laser surgery, CyberKnife radiosurgery, seizure diaries, and the implanted responsive neurostimulator. Future devices, near future I hope, inhaled medicines, drug infusion directly into the brain tissue where the fluid surrounding the brain, seizure prediction devices, focused ultrasound, deep brain stimulation and transcranial magnetic stimulation. We won't have time to go into all of these in detail because it's a short webinar, but we can give a brief overview and then we can have some questions and answers on those that you wish to go into in more detail. So let's start with seizure alerting or predicting.

You heard at the beginning about the EpiWatch in association with Apple. There are several watches that are available that can detect the shaking of a seizure, one of them portrayed on the right and I'm intentionally avoiding brand names here, has the interesting characteristic of being able to record the electrodermal activity, which is the skin resistance or galvanic skin response, the same thing they use in lie detector tests, by the way, and it turns out to increase in many seizure. The problem with this shake detector philosophy is that it's good for the tonic-clonic seizures, what some of you may know as the grand mal seizures, but it's not good at picking up the complex partial seizures with the loss of awareness, the fumbling, the forgetting, the wandering sometimes, these seizures are now called focal impaired awareness seizures, by the way.

So the game is still not settled for having a bio detector, short of an EEG pasted on your head all the time, that can detect those smaller seizures. But we can detect shake detection seizures, we can then broadcast to your family member that you are having a seizure and where that seizure is taking place on a map. Now, that's a shake watch, there is a recent approved FDA device in the United States called the Brain Sentinel that detects rhythmical muscle contraction. You can see it stuck on the outside of
the arm and it picks up the rhythmical muscle contraction, so-called electromyogram EMG, there's no needles, it's a surface recording. It's approved in the United States as an adjunct to seizure monitoring in patients who are at rest, potentially at home.

Dr. Robert Fisher: 10:39
So, first question to think about, don't answer on your microphone, but you should be able to interact with the chat box. Have you tried one of the shake-detection watches or a shake-detection application on one of your smartphones? If so, how did it work? Seizure prediction, this has been a goal for a long time. Many of my patients tell me that one of the most difficult aspects of having epilepsy is the unpredictability of seizures. Can you imagine this scenario? Beep, beep, beep, a belt device tells you, you're likely to have a seizure in the next 10 minutes, make yourself safe and put a pill under your tongue. That is currently fantasy, but I think not for long.

Dr. Robert Fisher: 11:35
There has been a device which completed a clinical trial, the citation I listed above, Cook, in Lancet Neurology all the way back in 2013. This device is a seizure prediction device. It does involve implanting electrodes, not in the brain, but over the brain, under the bone, so it is an invasive monitor, and then it connects all under the skin to a device under the skin of the chest, which can radio broadcast to a belt paging device. Although it can give you a noise warning, it also can show you red for impending seizure, and blue for in the clear, with white being neutral. So here's a recording from the study by Cook. Each row is a day in the life of the patient wearing the monitor.

Dr. Robert Fisher: 12:38
You can see that there are several periods of red on the bar, these are warning periods, and the red arrows are times when there were actual clinical seizures. All of the red arrows in this patient happened at times when there was a warning. There are some other warnings that don't have red arrows and perhaps those were little electrical seizures that didn't really come to notice, but might have been seizures as well. So, this technology has not yet been brought to market mostly for business reasons, but my hope is that this and even better technology, because computers are getting smarter and faster all the time,
will soon be able to tell at least some of you when you are likely to have a seizure, so that you can do something about it, sit down, not drive, take an extra pill, et cetera.

Dr. Robert Fisher: **13:40**

There will soon be a variety of new EEG equipment that doesn't require pasting things on the head, it doesn't require wires, but will just be able to be worn like a cap. I imagine that may make monitoring quite a bit easier because an EEG monitor can pick up the smaller seizures, the focal impaired awareness seizures that don't involve shaking. It's just at the current time, not feasible to go around all the time with an EEG monitor on your head. Other detection devices, every time I give this talk, I get asked about seizure alert dogs. There are some people who are quite convinced that dogs can alert them of seizures, whether they can do that in significant advance of the seizure or just at the start of the seizure, I think is still a little bit debatable. It's possible that the cats could detect or predict seizures as well, I don't know, but I have a feeling if they could, they would probably not tell you anyway. So question, would it help you to be able to predict when a seizure will occur, and can you do this already?

Dr. Robert Fisher: **15:02**

Diaries, clinical information systems. There are several of them, My Epilepsy Diary and the Epilepsy Foundation My Seizure Diary seizure tracker, which the Moss family developed diaries with patients like me and several others. These are very important because the biggest problem that we physicians have in caring for people with epilepsy is poor information. We don't really know how many seizures you're having, most of the time. We don't know how strong they are, what type of seizure, what time of day they're occurring, what the triggering factors might be and whether they're happening because medication levels are low in your system. So, anything that creates better information or better recordkeeping will help us to take better care of our patients. Furthermore, this kind of information is critical as we do epilepsy research to try to invent better pills and better devices for seizures. If we don't know how well they're working, we don't know how to proceed.
The fallibility of diaries was brought home to me in a study that we did in the Stanford Epilepsy Monitoring Unit, a year or so ago, where we were looking to see if a shake watch could communicate with a diary in the sky automatically to record tonic-clonic seizures. We wanted to compare that with a bedside paper diary that we asked the patients to collect. Well, the watch captured 12 out of 13 of the shake seizures, and the number of those seizures that were recorded in the bedside diary amazingly was zero. In many cases the patients when asked said, "Yes, I had a seizure, but it just was not recorded in the diary." So I think we've got ways to go in order to get better information about people's seizures. I'm hopeful that technology in the near future may help us with that.

Possible future, I adapted a cartoon from McCracken, we're going to run a few tests to pin down the cause of your seizures. I made up the caption, but you see a patient with a shake detector on the wrist, which goes to automatic seizure tracking to the internet cloud. There's also some method of automatic tracking of medication blood levels, and that all comes together for information to give feedback to the doctor and the patient. And at some point this may be a closed loop where it even can give treatment to the patient on the basis of automatic tracking and detection, but that is somewhat off in the future. Questions then, do you always know when your seizures occur, and what are the issues that you have with logging in a diary? Why don't diaries work better than they do?

New ways of drug delivery. I think you all know about pills, about injections, about the rectal diazepam, more convenient will be coming up in the near future, I think some nasal sprays of medications and some inhaled medications like with asthma puffer kinds of devices. Some of these will work very quickly and will be of use in two circumstances. One, if you happen to be fortunate enough to have an aura or warning, and you're not immobilized during that time, you may be able to puff a medication to head a seizure off. And secondly, if you have seizure clusters, you know you have one seizure, you're probably going to have more, then you'll be able to take a medication that
would work quickly to head off the cluster seizures, what I call cluster busters.

Dr. Robert Fisher: 18:58 More intense than for people who obviously have severe and uncontrolled epilepsy, is the possibility of delivering seizure medications directly to the seizure focus in the brain. Doing this will enable a steady level of medication on a focus rather than the peaks and valleys that many people have when they take pills intermittently. And it also will allow relatively high concentrations of the medicines because you won’t be dealing with body side effects, blood pressure, kidney stones, nausea, but you can treat right where the problem is. Well, a pilot trial of this type of therapy injecting medicines into the cerebral spinal fluid, has been begun in Australia and is underway, initially promising but more to report in the near future when we see how this turns out. However, I think there’s a good chance that this may become a very useful therapy for a small number of people who can benefit by it.

Dr. Robert Fisher: 20:11 So, new ways of doing surgery, this could be a lecture in itself, but let me just mention three of them that have the feels somewhat excited. One is radiosurgery, radiation has been used for tumors for a long time. It’s been considered for epilepsy, but radiation can have damaging effects on the brain sometimes long term. So, there are new devices, gamma knife and the newest CyberKnife, a stereotactic radiosurgery that can focus the radiotherapy beam on the part of the brain that needs to be treated at very often a temporal lobe or the inner part of the temporal lobe, hippocampus in people with epilepsy. This has been shown in the study to be effective, although it is not caught on in a big way, because of the potential longterm risks of radiation.

Dr. Robert Fisher: 21:12 Surgery is increasingly being done in the epilepsy world and neurosurgery in general, with a laser fiber, I have been asked this for 30 years, “Can my surgery be done with a laser?” And the answer has always been no, until the past couple of years, and now the answer is yes. You see a glowing laser fiber, which becomes hot on the tip, it’s introduced typically if we’re, say, dealing with temporal lobe epilepsy, through a small opening in the back, a guide needle,
the laser fiber goes in and then heats up at the tip. This is done right in an MRI scanner. So the heat signature ball can be seen in real time in order to make sure that the laser fiber is in the correct place. Then you can pull back a bit, make another ball, that heat signature ball is actually removing the tissue just as a surgeon would. Then when you're done, you pull the laser fiber out. Typically, you're home the next day, a bone has not been opened and brain has not been removed in order to get down to the area where we want to do the surgery.

Dr. Robert Fisher: 22:27

Preliminary study of this, and this is available and happening in the United States now, suggests that at least for mesial temporal lobe epilepsy, causing complex partial or focal impaired awareness seizures that the outcome is almost as good as with open surgery. The recovery is much faster and the cognitive status, the thinking and the word memory afterwards and dominant hemisphere particularly are better with the laser fiber. If the laser fiber doesn't quite do the job, it is always possible to go back later and do a conventional open surgery to take out more. So, have any of you had epilepsy surgery with a new laser? How did it work? The last section to talk about today is the area of neurostimulation. There are several varieties of that. The one that's been around the longest has been vagus nerve stimulation.

Dr. Robert Fisher: 23:30

So, VNS or vagus nerve stimulation reduces seizures by about an average of 50% at two years. Some people are not helped at all, and a few people will become seizure-free. It's quite rare to be able to get completely off medications with VNS, even if it's working well, but often medications can be reduced. So, VNS has no drug like side effects, it does have some irritating effects sometimes on the throat, making hoarseness or a cough when the stimulator is on, it can be adjusted up or down for effect, like pill dosing. It can be removed if it's not effective. It's also helpful and licensed for treatment of depression. The battery device typically lasts about five years depending upon the setting, and then it has to be replaced. The usual stimulation is on for 30 seconds and off for five minutes on regular cycling.
If a person feels an aura, they can swipe a magnet over their chest where the device stimulator is and activate the on-cycle immediately. The new wrinkle with the vagus nerve stimulation is an additional ability to stimulate at a time when the heart rate increases. This is useful because most seizures cause a heart rate increase, and on this slide there's an example. This row at the bottom is the ECG for the heart rate, which increases from 80 beats per minute to 96 beats per minute. The device in this case is set at a threshold to detect that. So stimulation comes on, and the EEG here, which shows rhythmic activity of a seizure when the stimulator comes on, interrupts the seizure. Now, it doesn't always work that well, but it sometimes does.

So, this is what engineers called closed-loop or detect and stimulate mode. It detects the heart rate increase and then stimulates. Of course, it will detect many other times when the heart rate goes up, perhaps you're running up a flight of stairs, it turns out the heart rate increases faster at the start of a seizure than with many other activities such as exercise, and so the device takes that into account, but there's really no harm done if the device goes off as you're running up the stairs. So, have you tried vagus nerve stimulation, not necessarily the heart rate sensing newest form, but any form and how did it work for you? So now we've come to a couple of varieties of brain stimulation.

There's the Medtronic SANTE trial, which I led, Stimulation of the Anterior Nucleus of Thalamus for Epilepsy. The thalamus is a pacemaker area deep in brain that controls electrical activity of a lot of the brain, particularly temporal lobes and frontal lobes, which is where most seizures originate. So stimulation on a regular five minute cycle, actually six minutes cycle on for one minute and off for five minutes is what's done in the trial and in practice. This was shown to be effective versus placebo in a randomized large trial. By four years, the seizures on the average are reduced to about one third of what they were before, with some people becoming seizure-free. This treatment, which does require brain implantation and connecting the wires under the skin to a chest stimulator, is approved in 30 countries but
Dr. Robert Fisher: 27:44  This shows the improvement over time. In the double-blinded controlled scientific phase, there was a 40% improvement in seizures in the first three months of stimulation, which was more than the 15% improvement seen in a placebo group. It keeps getting better over time to about 70% improvement by five to seven years. Now, another type of stimulation is responsive neurostimulation, which is sometimes known by the company name NeuroPace. This device is approved and is currently being implanted in patients in the United States and it is covered by insurance in most cases. Instead of implanting the device in the chest, the company chose to build it directly into the skull. In order to do NeuroPace stimulation, your medical team needs to know where your seizures are coming from.

Dr. Robert Fisher: 28:47  They have to be no more than two places because there are two leads available on the device currently. And presumably it is a place that would not be amenable to being removed by surgery or you don’t want it removed. So in this case, the NeuroPace device is just implanted over a seizure focus or alternately you can use a depth wire to implant it in a seizure focus, for example, a hippocampus inside the temporal lobe. The device is then trained to recognize your specific EEG pattern during a seizure such as we see here, and then give an electrical stimulation to counteract the seizure. It’s rather analogous to the defibrillator device that you may have heard of in the heart that is implanted to detect an abnormal and dangerous heart rhythm and give the heart the shock to shock it back to a normal rhythm, similar thing, but done with the brain.

Dr. Robert Fisher: 29:49  So, this is a device that’s not curative and it does require a brain surgery, so it’s invasive, but it can sometimes be very helpful for seizures. This stimulator will last anything from two to 10 years, also, typically about five years depending upon setting, and then the whole thing needs to be replaced with an operation at the skull. This shows the results, the drop of the seizures in the blinded phase with use of stimulation and the maintenance and improvement.
to about the same level as when the thalamic deep brain stimulator by five years. This is important because if you had benefit for seizures just for a year or two, that then wore off, it would not be worth implanting a device, but the benefit seems not only to be lasting, but to improve over time.

Dr. Robert Fisher: 30:50

Now of course, these are devices in your head that we’re talking about, so there can be side effects. There’s a risk for bleeding, fortunately that hasn’t usually been a significant problem and the chances of serious bleeding are well under 1% in experienced hands. The device can be infected, which may require antibiotics or replacement of the device. The electrodes may need replacement, there can be tangling with stimulation, there is the need for battery device replacement. Sometimes it doesn’t help the seizures or rarely may make them worse. Question, have you tried a responsive neurostimulation device such as NeuroPace? Unless you’re from Canada or Europe, I don’t think you would have tried the deep brain stimulation device yet. And how did it work for you?

Dr. Robert Fisher: 31:43

I’d like to make mention to transcranial magnetic stimulation. This is not approved for treatment of epilepsy, it is approved in the United States for treatment of refractory depression. But the important feature of it is that it doesn’t involve drilling any holes in the head or putting any wires in the head or in or on the brain. It’s magnetic pulses externally, some studies have been positive, meaning favorable for epilepsy and some have been negative. Those of us in this research area are still working out how to make them most positive. This is an example of the most positive trial which was done in Beijing, China. You can see that a seizure frequency here when the two weeks of daily stimulation comes on plummets to about 20% of the baseline level, whereas the placebo fake stimulation does not have any effect on seizure frequency.

Dr. Robert Fisher: 32:47

So this is not yet ready for prime time, but this approach is a hopeful one, non-invasive neurostimulation. The conclusions then are that devices offer alternatives to medicines, devices and medicines are not mutually exclusive but can be used
together when a device works well it may be possible to cut down medicines and reduce side effects. The device side effects are different from the medication side effects. In the United States, several devices are available, and future neurostimulators, seizure predictors, local drug delivery devices and new neurosurgery methods are likely to emerge over the next five years, and should provide new opportunities for people whose epilepsy is not controlled by medications. At this point I will turn the program back over to CURE to organize any questions, answers and comments. Thank you very much.

Dr. Laura Lubbers: 33:55

Well, thank you Dr. Fisher, we really appreciate all of the information and the overview of so many different technologies. We'll now begin the Q and A session. Again, if you have questions, please submit them in the questions tab of the Go ToWebinar control panel and click send and Brandon can then go ahead and read them aloud. Hopefully there've been some questions that have already come on. Brandon, would you like to speak to those?

Brandon Laughlin: 34:22

Sure. Actually the first question made mention of some of your last slides there, Dr. Fisher, about FDA approval, and they wanted to know, do all devices have to undergo FDA approval, and why does the process seem to be much longer in the US?

Dr. Robert Fisher: 34:49

The FDA classifies devices as type I, II, or III. Type I might be a tongue depressor or a bedpan. Those devices do not have to go through approval processes. Type II has some risk. Type III is high risk. So, an implanted brain device would be in the type III category, which would be high risk, and those require pretty extensive evidence of safety and efficacy in medical trials. It probably does take the FDA longer to approve drugs and devices than may occur in some other countries. I can't speak really for the FDA, I can only say that they require a device to be safe, effective and that the benefit should be a clinically meaningful. I think that all of the devices that I talked about today have that potential but I can't promise that all of them will be approved and I can never really speak from the FDA's timeline.
Brandon Laughlin: 36:09  Great, thank you. Next question, is there any studies going on or do we know if wearable devices will ever be able to predict non-convulsive seizures?

Dr. Robert Fisher: 36:23  I think wearable devices will be able to predict non-convulsive seizures. We're looking for good ideas and good strategies on that, I think we can take advantage of tailoring an intelligent device to a person's particular seizure type. Let's imagine for example, that someone has a complex partial seizures and I apologize for the name change, seizure name just changed this year, and so that's also a focal impaired awareness seizure, could be a subject for another webinar, and the person might always say, "Help me, help me, help me." Or some stock phrase at the start of a seizure.

Dr. Robert Fisher: 37:06  So obviously then we could tailor a device to recognize that at the start. Now, in terms of prediction, it's a little bit harder. Mostly that seems to be based on EEG, some studies say measures of brain blood flow can be used for prediction. So, we're still looking for a way to have wearable predictive devices that are non-invasive. I think we can probably do it with invasive and maybe we can do in non-invasive.

Brandon Laughlin: 37:43  Great. Thank you. Along the same lines there, are there any statistics on actually how predictive wearable devices can be or is that information really not available yet?

Dr. Robert Fisher: 37:57  By wearable devices, mostly we're currently talking about shake detector watches or the shake detector Brain Sentinel EMG. Sentinel device had pretty good sensitivity for picking up seizures. The watches usually have pretty good sensitivity, meaning they pick up the shaking, but they also pick up a large number of non-seizure events like for example, brushing your teeth. When that's the case of the devices, can have a cancel button, because the watch can start beeping before it sends a broadcast that a seizure occurs and the person can say, "No, that's not a seizure, I'm just brushing my teeth." And hit the cancel button. So, if you use the cancel function, then both the sensitivity and the specificity of these devices in small studies can be above 75, 80%. Now, large
studies like the EpiWatch Apple study will give us the more definitive answer to the question you asked.

Brandon Laughlin: **39:12**

Great. Thank you. Do you know if after you’ve had invasive surgery, if laser surgery in the future would still be an option?

Dr. Robert Fisher: **39:24**

If there’s tissue remaining behind, then laser surgery is indeed an option. We’ve, at our institution, done laser surgery as repeat surgery, it’s worked out well. And in a few cases we’ve even used it to complete a corpus callosum resection, a split brain operation, where there were some remnant of the corpus callosum in the back part of the brain. So, the key to laser surgery is that you have to have a pretty localized area to remove, you’re not going to be able to use the laser to take out a whole lobe, for example.

Brandon Laughlin: **40:08**

Great. Next question, is NeuroPace approved for children such as under 12 years old?

Dr. Robert Fisher: **40:17**

I will let the NeuroPace people speak to that. I’m afraid I might get their indication wrong.

Brandon Laughlin: **40:25**

Okay. Next question, what is the reduction of VNS versus RNS at five years?

Dr. Robert Fisher: **40:33**

About 50%. In the controlled clinical trials, there were two, the reduction was statistically significant, but fairly small. It was in a 20 to 25% rate of reduction, but just like the deep brain stimulators, as the vagus nerve stimulator stays in for a year or two years, it becomes more effective. We’re not sure why that is, because for example, if you look at neurostimulators in the Parkinson area or in the tremor area, those are immediately effective within a minute of putting them in. So obviously different mechanisms, but by a couple of years, VNS, half of the people have their seizures cut in half or better and are satisfied with the results and most people vote in the real world to show satisfaction by usually having the stimulator replaced when the battery depletes.

Brandon Laughlin: **41:35**

Great, thank you. Next question, are there any good devices or perfect devices that can be used to prevent SUDEP?
Dr. Robert Fisher: 41:49 Oh boy, we really want, we really want those. The answer is no, the problem is not solved currently, there's much discussion on this, CURE is taking a major role if not the lead role. The Epilepsy Foundation has also just started something called the Epilepsy Innovation Institute EII, and has started tackling the problem of devices to predict seizures and to reduce the chance of SUDEP as well. Our sense is that it's not going to be one single modality device, but that it's probably going to be a device that combines a variety of measures, heart respiration, perhaps EEG, perhaps several other features that would be useful to mention, but we don't have the problem solved yet.

Brandon Laughlin: 42:58 Great, thank you. Next question, and some more general question. What is the difference between therapeutic devices and detection prediction devices?

Dr. Robert Fisher: 43:11 Yeah. So, detection prediction or diagnostic devices would be something like an EEG. So an EEG is a diagnostic device, it doesn't give therapy. I did talk mostly about therapeutic devices, but with respect to prediction, I crossed the line a little bit into detection devices because it's so obvious that if you can detect early or predict, then you will be able to take a next step soon after, which is to do something therapeutic about it. Perhaps turn on a neurostimulator, perhaps puff inhale antiseizure medicine or perhaps just sit down for safety.

Brandon Laughlin: 43:58 Great. I believe that is the majority of the questions that were asked by our audience today. I did get many comments that people loved your catch up, by the way, Dr. Fisher. So I did want to mention that as well.

Dr. Robert Fisher: 44:16 Okay. We may have a few minutes if you wish to share any of the comments since I did invite the audience to make comments, so I'll leave it up to you, but perhaps you could just read a few of those.

Brandon Laughlin: 44:33 I do not ... let me look at through here. I didn’t see any specific answers to any of those questions.

Dr. Robert Fisher: 44:42 Okay. People are being shy.
Brandon Laughlin:  **44:45**  People are being shy today, it looks like so.

Dr. Robert Fisher:  **44:49**  All right then.

Brandon Laughlin:  **44:49**  All right, I'll turn it back over to Laura.

Dr. Laura Lubbers:  **44:52**  Great. Thank you. Well, I think that there was a great set of questions that are very informative. This does conclude our webinar on epilepsy devices and technology, and I do want to thank everyone for joining us today and for your questions. I want to give a special thank you to Dr. Fisher for sharing your knowledge of epilepsy devices and technologies. If anyone has questions about CURE's research programs, please visit our new website at www.cureepilepsy, that's all one word, cureepilepsy.org. Or you can email us at info@cureepilepsy.org. That's I-N-F-O @cure.

Dr. Laura Lubbers:  **45:34**  You can ask us questions about our research programs and also get more information about the EpiWatch program that we're currently involved with. You can also find more information on the website about CURE events during epilepsy awareness month, including the My Shot at Epilepsy campaign. Please be sure to register for our next webinar one week from today on November 15th at 2:00 PM, Dr. Jeff Noebels from Baylor College will be joining us to discuss infantile spasms. So again, thank you all and enjoy the rest of your day.