CURE Webinar
Transforming Data Into Seizure Control with Learning Healthcare Systems
(Transcript)

Dr. Laura Lubbers: 00:02

Welcome, everyone, to today's webinar. I am Laura Lubbers, and I'm the Chief Scientific Officer at Citizens United for Research I Epilepsy, or CURE. I'm delighted to be with you today. Today's webinar is entitled Transforming Data into Seizure Control with Learning Healthcare Systems and it will discuss the progress and potential impact of The Pediatric Epilepsy Learning Healthcare System to people with epilepsy, their families, and to the entire epilepsy research community. This is our third installment of our 2020 Leaders in Epilepsy Research Webinar Series where we highlight some of the critical research that's being done on epilepsy. Today's webinar is being sponsored by our friends at the BAND Foundation.

CURE's mission is to find a cure for epilepsy by promoting and funding patient-focused research. CURE has been instrumental for over the past 20 years in supporting groundbreaking research from around the world. Before we get started with today's webinar, I'd like to take this opportunity to highlight CURE's new COVID-19 and Epilepsy Resource Hub that can be found on our CURE home page at www.cureepilepsy.org. This resource contains information on the impacts of the COVID-19 pandemic on the epilepsy community and resources to help families, patients, and caregivers stay safe and healthy.

Today's webinar is, again, focused on learning healthcare systems and will be presented by Dr. Zach Grinspan, who is the Associate Professor of Population Health Sciences and Pediatrics and Director of The Pediatric Epilepsy Program at Weill Cornell Medicine in New York City. He's the Primary Investigator of The Pediatric Epilepsy Learning Healthcare System Project and The Rare Epilepsies in New York City Project. He currently serves as the Chair of the Steering Committee for The Pediatric Epilepsy Research Consortium. His research includes investigations in comparative effectiveness research, epidemiology, health services research, and the role of computers in medicine.

Before Dr. Grinspan begins, I'd like to encourage everyone to ask questions. You may submit your questions anytime during the presentation by typing them into the Q&A tab located at the bottom of your Zoom panel and then click "Send". I want to thank those who have already submitted questions in advance of today's webinar. We will do our best to get through as many of them as we can. We do want this webinar to be as interactive and as 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.

I also want to mention that today's webinar, as well as all previous and future webinars, will be recorded and are available on the CURE website. With that, I'd like to turn it over to Dr. Grinspan.

Dr. Zachary Grinspan: 03:04

Great. Thank you, Dr. Lubbers. It's a real honor to speak to the CURE community and it's nice to see you, though virtually. We've had some really wonderful conversations about epilepsy and epilepsy research. I'm glad to continue those conversations today. Hello everyone in the audience. I am Dr. Zach Grinspan at Weill Cornell Medicine, and I'll be talking today about The Pediatric Epilepsy Learning Healthcare System.

Just first a thank you to the funders of this work. There's five that I want to give a shout-out to. Our institution, Weill Cornell Medicine, has provided funding. The Pediatric Epilepsy Research Foundation has provided a significant amount of funding to this effort. The BAND Foundation, The Epilepsy Foundation, and The Morris and Alma Schapiro Fund have also made significant contributions and I am deeply grateful to all of these funders for making this possible.

Let me start by talking at a high level about what a learning healthcare system is. The concept seems so straightforward. We should practice medicine, take notes about what we do, learn from that, and then change. The challenges in the current academic environment, that cycle can take 17 years, which when you pull in the data, you make your tables and figures, you write your paper, you get it out to the journals. Then, somebody hopefully somewhere reads it. It gets incorporated into statements and then slowly but surely people change their practice if what you have learned is actually important.

A learning healthcare system tries to make those cycles of improvement faster. The idea is that you capture data about what you're doing in real time when you're doing it and you have plans and a bunch of questions in place already as well as a system to pull that data and analyze so that you can learn from it, feed it back to all of the providers and the doctors and the nurse practitioners who are taking care of people with epilepsy and then change. Then, what's nice about having this cyclical approach is that you can do it in cycles again and again and continually move towards the best possible outcomes.

The model that we have been really excited about has been a group called Improved Care Now. These are not epilepsy

doctors. They're pediatric gastroenterologists and they take care of children with Crohn's Disease and ulcerative colitis. As the story goes, and I apologize, I am sure I am botching the details, but as the story goes, three or four of the experts in the field maybe 10, 12 years ago are sitting around a table. "How are your outcomes? How are your outcomes?" No one really knew, so they went back and they found out that about half of the time, kids with ulcerative colitis or Crohn's Disease were in remission.

At their first meeting, they say, "Okay, we think that the biologic ceiling", they say, "For our disease is like 64, 65%." They banded together. They started collecting data. They learned from it. They made changes in their practice. Their initial three sites are now more than a hundred across the country, and actually the Anderson Center out of Cincinnati Children's that runs this has now taught their methods to several other learning healthcare systems. These are there results and this is just through 2012. You can see here on the left, when they start they're at 50% remission, and then as they track their results, those are these blue dots, they gradually, gradually, gradually get up to over 75%. By 2012, they're almost to 80. Since then, they've blown past 80% and they've done better.To me, when I saw this data, I got very excited because, A, they blew past their own expectations, and then when I talked to the folks that started this, they clearly had the same passion that I've seen in my academic colleagues in the pediatric epilepsy world. I said, "Man, we got to do this for our disease." We weren't the only ones that had this idea. There are actually two Epilepsy Learning Healthcare Systems. I run one of them, The Pediatric Learning Healthcare System, but I do want to give a shout-out to our collaborator in this, The Epilepsy Learning Healthcare System that's run out of The Epilepsy Foundation, Brandy Fureman and Sue Herman are the leaders of that effort. Interestingly, there's a gentleman, Jeff Buchhalter, who's a giant of the field who is a leader for both of these efforts.

The Epilepsy Learning Healthcare System, they affectionately call it ELHS, is really quite collaborative and driven largely by advocacy efforts and brings together people with epilepsy, providers, community service organizations and researchers. They have a broad and broadening reach in partnership with the EF offices around the country. They have several epilepsy organization partners, and then they have sites in several states around the country. What I like to say is that we're parallel and

aligned. We're on a call with them fairly frequently and Dr. Buchhalter is always looking for ways for us to work together.

The Pediatric Epilepsy Learning Healthcare System, just by way of history, grew out of an organization called The Pediatric Epilepsy Research Consortium. Thanks for your patience with this alphabet soup. PERC is dedicated to collegial collaborative practice-changing research and there are more than 50 sites around the country. This map is a majority of them but we need to update it. That group has done a lot of really important research. We published an enormous series of children with infantile spasms in 2016. That was a project led by Kelly Knupp. Anne Berg has done really tremendous work looking at early-life epilepsies.

The thing about PERC is that the research we did was amazing, but it built this social foundation where there were a group of 50 to a hundred academic pediatric epilepsy doctors that all learned how to work together on these projects. That social glue really set the stage for The Learning Healthcare System in that we had preexisting relationships, we trusted each other, we knew how to work together, and this got us going.The Pediatric Epilepsy Learning Health System, our mission is to reduce seizures and their consequences for children with epilepsy through cycles of health data collection and analysis, dissemination of new evidence and practice change.

Our vision is that all children with epilepsy receive timely and optimal care according to standards that are continuously improved, and so it's inherently dynamic so that we always learn and are always trying to do better. I've had the honor of leading the effort and I have these amazing collaborators that round out our leadership team, Anup Patel in Columbus, Anne Berg in Chicago, Renee Shellhaas in Michigan, and I gave Jeff Buchhalter a shout-out already.

This is how it works at a high level. You can imagine that we have all of our sites, and I think we are 21 or 22 now and 13 of them have given us data. All of these sites have data in their electronic health record systems and that data just goes in there as part of routine care. When you register at the front desk, some of your demographic information goes into the computer. When the clinical team sees you in the office, they're taking their notes and sometimes their notes, they're pressing buttons and it's structured fields, "This is what the patient has." When a bill is submitted to the insurance companies, there are

additional pieces of information that are quite valuable that go along with that.

All of that data is just sitting there and the idea is is that we ask all of these sites to collect all of that data and send it to us. There's really three buckets of data that we're after. The first bucket is what I just described and what we call the structured data, demographics, insurance, visit history, your diagnosis codes, the medications prescribed, any procedures that are done, et cetera. Honestly, of the work that we're planning and the work that we're doing, this is the easiest piece. It's just there. You got to figure out who has it, how to get it out, how to move it, and how to process it. Each one of those steps is quite straightforward.

The second bucket is the hardest, the clinical data. There's no clear way in all of our electronic health record systems to know if a child is seizure-free. I might say, "Johnny had no seizures since last visit." Someone else might say, "Johnny's doing great." Someone else might say, "No seizures since last spring." It's always different and there's a million ways to say this. If we could figure out how to document that in some way that we all had that same information and we could learn from it, then the sky's the limit and you could really do a lot. In order to do that, we have to design a form for people to use and then we have to get them to use it.

The third bucket we know how to do, it's just expensive. I call it the fine phenotype, and that's, which voxel on the MRI is bright? Which lead has the spike on the EEG? What's the particular mutation? All of that data is there, but it's harder to get out because it's in these specialized areas. We're imagining that to get that data is going to require research assistants and large grants to get this data to merge with what we have.

We have our sights on five domains of research. The first domain is quality, which is to say we know what we're supposed to be doing, we're not doing it. Why? How can we be better? We also have our sights on comparative effectiveness research, which is to say we have some disease. Some people use drug X, some people use drug Y. Which one is better and by how much? Then, we're also interested in three other domains, surveillance and epidemiology, which is the incidence, prevalence, comorbidities, and mortality of disease; health services research, which is the organization, financing, and delivery of healthcare; and then clinical care of populations. How do we

know if people with epilepsy as a group are doing well? How do we measure that and move the needle? Then, what makes this a learning healthcare system is that all of the data that we collect and analyze we feed back to the sites so that we're always learning.

A brief word about governance just to kind of give everyone a sense of what we do and how we are structured. We have a leadership committee that I lead and the other folks that I mentioned before are on there. Then, we have three learning collaboratives. Each of these groups meets by phone one a month and I join all of the calls, and I got to tell you, those are some of my favorite calls every month because it's always a mix. You get clinical site leads that are often MDs and NPs from around the country. We have parents and advocacy group leaders that join these calls, and then we also have representatives from professional societies and those roll out. The leadership committee meets once a month and then we have an advisory group of experts and informatics, comparative effectiveness, and then in epilepsy-specific research.

We're off to the races. Just to give you a sense of where we are, there's 20 centers and I'm giving them all a shout-out. I won't go through them all. 13 of these sites have provided that first bucket of data, the standardized structured electronic health record data. To give you a sense of the scope, it's half a million people in this data set, 33 million medication events, 8 million outpatient visits, 300,000 inpatient admissions, and 2 million emergency department visits.

When we think about the research studies that we want to do, we realize that we have 60,000 neonatal visits, a hundred thousand infant visits, 200,000 early childhood visits, 200,000 school-age visits, and 130 visits, I mean adolescents. The scope gives us pause and gives us a sense of the potential of this network to really make a difference and to really help us understand how to do the best possible work.

I wanted to give the audience an example of something that we've started working on. Many of us are quite passionate about infantile spasms and so we started there. I mentioned PERC, one of our big early studies was that we put together a National Infantile Spasms Cohort, NISC, to look at what medications people were using and their outcomes. One of the things that we noted was that at our academic centers, one in

seven children was not receiving what we considered to be first-line care.

As you all know, there are really only three medications that have good evidence for use for first-line therapy for infantile spasms, ACTH, vigabatrin, and oral steroids, and if the oral steroids are going to be given, you have to use a good dose, four to eight milligrams per kilogram per day for those first few weeks. When we saw that one in seven were not getting one of those therapies, that was something that we needed to call attention to. Many of the names of folks who wrote this paper have been giving talks about infantile spasms and encouraging people to try to use one of those first-line drugs for several years now.

Here's how we studied this. We said, "Okay, each of those 12 sites, go ahead and go to your electronic health record and send us everything. Don't be shy, send us these huge files." They got these like hundred-megabyte files, a few are in the gigabyte range. We used secure transfer and they come to our secure data facility at Weill Cornell in New York City. Then, we do something called source-to-standard mapping. The data that we get, it's always different and we send all of the sites all of the specifications and no one listens to us. The data always looks different and we have to kind of harmonize it and make it all pretty. Then, we came up with a way with some reliability to find children with infantile spasms using some of those diagnostic codes.

Then, what we do is with free software... This is R, which is free software, we create these HTML reports, they're just websites, and we ship them securely to our colleagues essentially with a bunch of questions. Then, our colleagues use those reports to read up into the charts and we give them a REDCap database. This is an online secure platform for research with protected health information.

They fill out those REDCap surveys, send us that data, which we marry with the other data that we have, and then we're able to make reports. We can say, "Okay, you add 20 kids with infantile spasms and you use the right therapy for 17 of them." Well, we can do that for all of our centers. Then again, we're trying to learn, so we then return those reports to the sites. It's really two cycles, that initial transfer and processing and then the site review and validation.

Just to give you a sense of what we're sending back to the site, we have all of that electronic health record data, so we might give them a picture, something like this, and it's like, "Well, here's this child and there's a diagnosis in the chart for infantile spasms maybe at six months. We have all of the medication information and it looks like somebody wrote for ACTH, so is that right? Can you just confirm that?" Or, "I don't see any of the first-line drugs, so what happened?"

This is what we found and it doesn't quite show up but I think you get the idea. This is quarterly results from 15 through the end of 17 and these dots represent the rate or the percentage of children across, I think this was 12 centers at the time, the rate that was getting first-line therapy. What you can see is that across those three years of data, we were about 90%, 89.5%. We felt very mixed about this because on one hand it was better, one in 10 that we're getting wrong is better than one in seven, but we'd sure like to be perfect.

We did a little bit more investigation. I won't go through the details of what this particular visualization shows, but we tried to understand, where was the variation happening? What we found out is that a lot of the variation was by site, that whether you got first-line therapy didn't matter whether you had infantile spasms for unknown cause, whether it was from tuberous sclerosis or hypoxic ischemic encephalopathy. It didn't matter your race or ethnicity. The only thing that seems to determine whether you got first-line therapy or not was where you got care, but this was what we wanted. This is what makes a learning healthcare system work. This is 2017. If your dot is at the top, that means that you are perfect.

There were, let me see, one, two, three, four... there were six centers that were perfect in 2017, and then the rest of us were sort of lagging behind. What's lovely about having a nice social network where we all love and trust each other, I was going to say work with each other, but I said love which is sort of true. We really do. There's a lot of warts in the group. When you have that baseline, that social trust, it's very easy to say like, "Hey, you guys are doing something real good, so can you teach us? What are you doing so we can do it, too?" I've been part of so many of those conversations. It's really deeply rewarding.

The other thing is that there's some social pressure that we've taken advantage of. One of my favorite moments in this whole effort was that one of my colleagues was on rounds and one of

her residents said, "We have a child with infantile spasms. I think I'm going to start to Topiramate." She said, "You know, that's interesting that you said that because, A, that's not what we're supposed to do, and B, none of our peers are doing that, either, so maybe we should use something first line?" That kind of social nudge is quite powerful. This is data from '15, '16, '17, which we collected when we first started, and we'll do another round of this in the next year or two and see how this has improved. We also have more centers and as we've grown more folks are interested to see how they compare with others.

Let me talk a little bit about some of our ongoing work. One of the nice things about learning healthcare systems is one of the premises is that parents, advocates, and patients need to be part at every step of the process. We do that, too, so on all of our calls we have parents and sometimes people with epilepsy. One thing we heard again and again is that epilepsy is not just about seizures, that epilepsy is also about quality of life. We said, "Awesome. What do you mean? What is quality of life? How do you measure that?" The answers are sort of tough. The measures that are out there are long. The QOLCE 55 is called 55 because it's got 55 questions and, man, we're busy in clinic, so the idea of asking 55 questions in a 15-minute visit is just not feasible.

We said, "Okay, look, let's figure out what you mean by quality of life and then let's see if we can come up with something a little bit faster?" We decided through I think about 200 emails and several phone calls that a good quality of lfe measurement had to be understandable, actionable, trackable. It had to measure something distinct. It had to be meaningful, ideally something that was published so that it had been validated. It had to be anchored, meaning that there has to be some reference that you're comparing to. It has to be clear and it has to be feasible to answer in the context of clinical care.

Through those phone calls and, man, we got this wrong the first couple of times, but through multiple iterations we've come up with our solution and it's two questions. The first question says, "Think about the child's usual routines. How often in the past two weeks have seizures significantly changed those routines? Every day? Most days? Some days? Or never?" Then, there's a paired question. "Think about the child's usual routines. How often in the past two weeks have seizure medication side effects significantly changed those routines?" Believe me that we thought about just about every word. The word "usual" was

originally the word "typical" and we didn't like that. Two weeks was one month for a while and then people said, "I can't remember that far."

Then, we made it one week and they're like, "Well, let's make it a little longer." These were iterated quite a few times subjectively. Then, what's amazing is we've now piloted this at about 150 visits. That QOLCE 55 that I mentioned is our gold standard, so we measure that at the same visits, and what this graph is meant to show is that when you have more seizures, that's here at the left, so if every day seizures are disrupting your child's routines, then the QOLCE score tends to be low. As that becomes less true, the QOLCE score is higher.

The other thing we did is we had that question on side effects and so we looked at a measure called PESQ. This is a standardized score for medication side effects in children and we see a similar correlation. We are continuing to work on this. I was talking to our statistician this morning. I'll probably have an abstract to AES describing this work in more detail.

The other thing that we're working hard on is that we want to make sure that at the point of care we get that middle bucket of data. I want as a learning health system to know which children are still seizing and which children are seizure-free and I want to know lots of other things as well. If there are any clinicians in the audience, you'll recognize this is Epic, which is one of the main electronic health record vendor systems that are in use at most academic centers across this country. We're working with them. They have built a button, PELHS, which anyone with Epic will be able to use when they're seeing a child with epilepsy. When you click the button, this is a mock-up because it's much smaller, they'll get a bunch of epilepsy-specific questions.

For example, "When was the child's last generalized tonic-clonic seizure? Oh, it was one to four weeks ago." Then, it asks, "Okay, well, recently what is the frequency of generalized tonic-clonic seizures?" Then, you have some questions there. What's lovely about having these buttons with these standardized questions is that we'll be able to collect it. We'll have the IT folks extract this data directly from the notes, add it to our database, and then we can actually know who's seizing and who's not. That will help us learn, figure out what's working and what's not and pass it on to the clinicians in our group.

We've got several other projects we're working on, so the quality of life measure I mentioned. We're also interested in other quality of care measures, so for example, we want to make sure that children who have refractory epilepsy that continues despite two medications, that they're getting seem by epilepsy specialists. Then, we're very interested in status epilepticus and we want to make sure that children who show up in the emergency department with unremitting seizures are given the correct therapy at the right time at the dose. We're developing some measures for that.

We have our sights on comparative effectiveness. One of the PERC studies that we published a year or two ago was that we found that phenobarbital... We compared phenobarbital and levetiracetam for infantile epilepsy and in that data set levetiracetam seemed to be a lot better, but we were using a data set that was not designed for comparative effectiveness. We really want to answer this question more definitively so we have a big grant under review trying to figure out, if funded, we'll help us use the network to answer that question.

Then, we've started our surveillance and epidemiology work. We're quite interested in mortality in epilepsy, particularly in children with epilepsy. Our idea there is not that we're going to be able to provide population-based estimates, but rather that we'll create a process by which all of the clinicians in our group can systemically review the deaths among the kids with epilepsy that we take care of so we can try to understand, "Well, man, is there something we could have done differently? Was there something that we can learn from this case?" There is a deep emotional resonance that often happens at those kinds of conferences when you're facing mortality, particularly in children, and so we think that if we launch this that this will really motivate people to make change in their practice.

That's the end. I just wanted to reiterate our mission, which is, again, to reduce seizures and their consequences for children with epilepsy through cycles of health data collection and analysis, dissemination of new evidence, and practice change. Thank you to the funders and to all of the amazing people who have helped make this happen, and to all of you out there in the audience, thank you for listening.

Dr. Laura Lubbers: 32:28 Thank you, Dr. Grinspan. We'll now begin the Q&A session. I know a number of questions have already come in. If you have questions, please do submit them in the Q&A tab located at the

bottom of the Zoom panel and click "Send". We'll do our best to get through everything that arrives. We got a number of questions here. One, which is a big data type of question. "From a digital perspective, for gathering your data, what are your biggest needs at this point?"

Dr. Zachary Grinspan: 33:00

Oh, what a great question. Let me be a little wordy with my response and that it depends a little bit on which kind of data that we have. For the electronic health record data, a lot of it is we have so many conversations with IT groups around the country, and so the need there is as we're imagining going to scale is figuring out, how do we... I was going to say McDonald's-ify it. That's not quite the right term, but how do we standardize that process? Other groups have done that and I think we need to get better at that.

Right now, it's a lot of phone calls and a lot of specifications. It works. We're getting there, but we could certainly be more efficient. We have a good system to transfer the data. Now that we have the data, I think we're starting to run into some bottlenecks with the processing. We have one analyst who's sort of working through it. I think as we scale up we'll need more, people just kind of processing the data and getting it ready. A lot of the technology is free, so we have a good pipeline to get the reports out.

Then, for the other buckets, the electronic health record system questionnaires, they're going to get deployed over the next few months. Epic is going to release our questions this month. Cerner is not far behind, and someone has already built it out in Athena. We'll want to expand that to other electronic health record vendors. We really want to be vendor agnostic. Then, we'd like to bring more data in.

The EEG, the MRI, patient-reported outcomes would be amazing, devices. There are some people who are walking around collecting data moment to moment with an RNS or a VNS, and so partnering or working together to figure out how to get that data in, you need people. Some of it is human-ware. I think technology is relatively straightforward. It's just a matter of all of the conversations and figuring out how to get the data out, move it, and link it.

Dr. Laura Lubbers: 35:34

Okay. A lot to happen, still, but it's great to see it already underway and with so many plans moving forward. Here's a question that sort of touches on what you were just talking

about. "With the advancements of implants, watches, and other devices, has this helped you understand more about medication efficacy for patients? Has this increased the whole picture of an epilepsy patient's day and changed the way you view potential individual versus multi-drug prescription regimens?"

Dr. Zachary Grinspan: 36:03 Yeah, it's a great question, and what it gets at is in the digitized world, you have people who are creating oceans of data and, can we do anything with it? For some individual patients, absolutely. There are some patients that come in and you look at their VNS data, you look at the RNS data, and you can make very targeted changes. The question is, how do we scale that and how do we learn from it? I think that the vision that the question asking her... That's a weird term. The individual who asked the question posed is really very compelling. We are not there yet because I don't think we know how to do this yet at scale. It's a long-term goal of ours.

Dr. Laura Lubbers: 36:54 Okay, okay. Along the same lines, "Is this aggregated data that is collected data that can be individualized? Or data that can be used to provide a service to doctors and patients for a fee? For example, if RNS data is collected, would somebody need to pay in order to see their own data?"

Dr. Zachary Grinspan: 37:17 That's interesting. There's so many pieces to that. I don't have any patients who have RNS, but I do for VNS and I've never had anyone ask me for a copy of their data. It's certainly doable and it's coming from you. I don't see any obstacle to that. For the data that we're collecting, other learning health systems have ingested identified data, so like ImproveCareNow that I started with, their database, they know your name, they know your date of birth, they know everything. They actually do provide as the questioner poses direct services. Here is a patient-level report about how your patient is doing.

We shied away from that really for privacy reasons. Data breaches can be devastating for so many reasons, and so we opted to use less personalized data. We don't anyone's names. We do know dates of birth, we do know zip codes, and we have a study ID, but we don't know where you live, we don't know your medical record number. That was intentional. Our idea is that we can send information to each center. The center knows who you are and we might say, "Patient ABC had this happen", and then the center will have... we call it a crosswalk, but they'll be able to say, "ABC is actually John Smith." They have to do that extra step. I don't know it's John Smith. I know it's ABC.

We get around it a little bit and it helps make the data a bit more secure, but we're very much about data sharing, and so we have promised all of our collaborators that they can have their own data essentially with no questions asked. We'll just give it back to you. We've crunched it and processed it a little bit because we want to promote your new faculty, we want to promote residents and fellows who do research projects. Then, for the network, if one investigator says, "I have an idea. It works on my own data. Can I do it on everyone else's data?" Then, we have a very straightforward process to allow that to happen, too. We really all want to learn together.

Dr. Laura Lubbers: 39:44 That's pretty. It's great, and actually, it's a great segue into the next question. "You've talked about data sharing. Will data sets be made publicly available?"

Dr. Zachary Grinspan: 39:53 That's a wonderful question. I don't think we've thought about that really. The data sets we have qualify as limited PHI. It's a technical term from federal privacy offices, which means that we have dates of birth and zip codes, so we would not be able to release that to the general public, but fully the identified data, I mean, theoretically we could. I think we'd have to talk and think a bit more about that. What a lot of networks do is they want to make sure that when data goes out that it's being used for a purpose that's aligned with the mission of the organization, and so there's often a process. We don't have such a process in place right now, but if that became something that was of interest to the community, there's no reason we couldn't start planning.

Dr. Laura Lubbers: 40:54 Okay, great. Here's another sort of process question. "How have you had to overcome the barriers of institutions not wanting to share their data with other institutions?"

Dr. Zachary Grinspan: 41:06 I thought that was going to be a huge problem. It doesn't seem to be a problem. Everyone's so happy to share. It's really nice. I think that as much as I'd like to say I'm a pioneer, I'm not. People have been working on this in other fields for more than a decade, so I think that the ground has really shifted and we're just in a new world. The Pediatric Hospital Inpatient System has data from like 45 centers and they highlight like non-competing hospitals, but Cornell data's in there, Columbia data's in there, NYU data's in there, and you can walk from one to the next in an hour. I think that the culture, particularly in pediatric hospitals, is very mission-driven and that these issues of

competition and "you can't have my data" has just not been an issue.

There's some centers that have stricter privacy requirements than others, but it's kind of a bunch of phone calls and, especially in the Zoom era, they see your face and they see that you're mission-drive and you want to do the right thing. People are really more than happy to help out.

Dr. Laura Lubbers: 42:19 That's wonderful. That's great news. Here's a question about a specific area of epilepsy. "What are you doing to monitor and measure the impact of diet on seizure control?"

Dr. Zachary Grinspan: 42:31 Great question. The structured data that we have does not include... It's not easy, rather, to figure out who is on an epilepsy-related diet and who isn't. I showed you that one question about the seizure frequency, but we built in some questions also about diet. It's pretty epilepsy-specific, so it's ketogenic diet and modified Atkins, low glycemic index or other. That'll give us some high-level information about who's getting the diet, does it work, things like that. More detailed information about specific foods and specific exposures would mean a whole different level of data collection.

Dr. Laura Lubbers: 43:18 Okay, but it's certainly sounds like something that this system could evolve to-

Dr. Zachary Grinspan: 43:21 Absolutely.

Dr. Laura Lubbers: 43:22 And it... Okay, great. Here's a question about a different data resource. "Are you familiar with the Observational Health Data Sciences and Informatics, OHDSI?"

Dr. Zachary Grinspan: 43:35 Yes. Yeah, so let me nerd out for a bit. One of the major questions that we've had is, "What does a tables look like in the database?" A lot of people have spent careers thinking about that for health data. There are two major models of how you do that. One is called OMOP, and I think I'm going to mess up the OHD... I'm feeling guilty because I can't remember exactly what it was, but I think the organization, Dr. Lubbers, that you just mentioned uses the OMOP standard. Then, there's another standard that PCORI, the Patient-Centered Outcomes Research Institute, has advocated called PCORnet, the PCORnet Common Data Model.

I think our data looks a little bit more like PCORnet, with the OMOP there's a lot of linkages you have to do and when you're looking at the files, it's a little harder to kind of figure out what stuff is, but we ended up kind of doing it a little bit idiosyncratically. Currently, our data model is our own, which could be sort of seen as a simplified version of OMOP and PCORnet. What we told our sites is that, "Look, if you have the data in PCORnet or if you have the data in OMOP, just send that. Don't reinvent the wheel." No one's taken us up on the offer, so it seems like operationally, a lot of the sites are finding it easier just to kind of make a custom extract for us and just sending us what we want, which we've been fine with.

Dr. Laura Lubbers: 45:25 Great, great. Sounds like a very collaborative approach. Here's another question. "Would it be beneficial for a healthcare provider to have the PELHS questions answered before the visit versus during the visit?"

Dr. Zachary Grinspan: 45:42 What a good question, I love that. Yeah, so yes and no. We really want curated data where a clinician's eyes have been on it. The workflow that the questioner is proposing is a good one, which is that the parents or the young adult or whatever it is enters the data in prior to the visit, and then the clinician and the family review it together, and that would be lovely and fine. That would be totally okay.

The linked idea there is that we'd had a lot of really nice conversations with Rob Moss, who runs SeizureTracker, and he's very excited about this idea. He's been working to link his application with Epic, which is one of the electronic health record vendors and we've been talking like, "Well, if you get that workflow there, can the SeizureTracker data like populate the learning healthcare system data?" We're agnostic. If the data gets in there and the clinician vouches for it, then we're good.

Dr. Laura Lubbers: 47:01 Okay. I want to talk more about the role of the patients and how they interact. First, "Are patients and their families aware that you are collecting these data? How do they feel about participating?"

Dr. Zachary Grinspan: 47:13 That's a good question. Let me answer that in two ways. One is we've been very deliberate from the beginning in making sure that we're in communication with advocacy groups and that we have parents and people with epilepsy involved at the highest levels until all of the pod calls typically will have a parent and

then sometimes there's a few people with epilepsy who will join the calls also, so there are representatives. What is not true, though, is if you bring your child to one of the centers that are involved, you wouldn't know that the information from that visit is being brought into Learning Healthcare System.

We don't do consent and the reason is that we argued successfully to our institutional review board that the labor required to get the consent was too much work for this kind of data. The way that electronic health record data is used for research in this country tends to support that. Institutional review boards have these exemptions where you can get an exemption from the federal regulations from HIPAA and we applied for that and got it. What that allows us to do is we're allowed to look at the data without a hundred thousand people's explicit permission to do so.

One of the things that makes us comfortable with is that we feel like that the good that we're going to learn far outweighs the risk to loss of privacy. We've been quite intentional, as I said, about making sure that the data that we have doesn't have a lot of personal information, no names, no addresses. We have dates of birth, but lots of people share same dates of birth. Then, when we've spoken to advocacy groups, most people are in agreement with this philosophy that the labor required, it's so much work to get those consents. We'd spend all of our effort doing it and they would rather us do the learning rather than the consent. We got all of the approvals. We have data use agreements. We have all of the legal and ethical infrastructure, but it's true that you wouldn't know that your data is going to be in there necessarily.

Dr. Laura Lubbers: 49:57 Okay, okay. That's helpful. "You have talked about a role in patients in designing the system to some degree. How have you involved patients in doing this and the process and the governance? You've already touched on that a little bit and wonder if you can comment on whether there are differences between the Pediatric Epilepsy Learning Healthcare System and the other system that you mentioned?"

Dr. Zachary Grinspan: 50:18 Yeah. I think both systems are quite deliberate about it and both have made a big effort. The ELHS, the Epilepsy Learning Healthcare System, is really run out of the Epilepsy Foundation, which at its heart is an advocacy organization, so I think the DNA there I think is much more about patients' perspectives. We were aware of that. We wanted to make sure that we were

listening and that that voice was there, which is why we bring everyone on the calls.

I can give you some very specific examples and when we put our forms together, we wanted to have a scale like, "How often are you having seizures?" The original scale, the most you could say was multiple per day. We're like, "Okay, that's the most you can, multiple per day." A couple of parents were like, "My kid has more than that." "What do you mean? Multiple per day, that's it." They're like, "Yeah. I can't even count because there's so many."

We said, "Oh, okay. We missed something important." Now, the highest level is too many to count. It was originally innumerable, and then one of our researchers were like, "That's a weird word? What does it mean?" We changed from innumerable to too many to count. It's a little bit easier to understand. Then, honestly, our whole quality of life line of research was very much inspired by parents where they said, "This is important. You have to measure this." Our pushback was like, "I don't know what to measure." Our solution to that was like, "Well, let's just come up with some questions that we can agree on", and then we did.

Dr. Laura Lubbers: 52:09 Okay, great. Lots of learning, lots of iterative learning in this process.

Dr. Zachary Grinspan: 52:15 Absolutely.

Dr. Laura Lubbers: 52:17 "You've mentioned the example of the ulcerative colitis. Did those researchers identify factors about that experience, the GI experience, that allowed for the increase in remission? How are you applying that thinking?"

Dr. Zachary Grinspan: 52:35 See, that's a good question.

Dr. Laura Lubbers: 52:35 That you're doing.

Dr. Zachary Grinspan: 52:37 That's a good question. I've had several conversations with leaders in that group and the things that have resonated the most deeply were, number one, to focus on outcomes. Part of the reason that we worked so hard with the electronic health record vendors is that the most important outcome is seizure control and you can't measure that with normal electronic health record data. Right now if you want to figure that out, someone has to open the chart and that takes forever, so we

from the beginning made that a priority. We did this whole prioritization process. What are the outcomes that people care about? Seizure control was clearly the number one, and then we realized that the only way to measure that was to get it into the electronic health record.

We also learned from them how to work with the vendors, with Epic, Cerner, Athena, et cetera. They had good relationships and we learned what works, what doesn't work, how to sort of finesse those relationships. The idea of the pods, Peter Margolis, that's the guy I talked to, so he's sort of one of the leaders. I was at a conference with Peter Margolis in D.C. It's got to be three or four years ago, and at that time like, "Oh, I'll just sort of call like each center once a week and kind of, you know"... He's like, "Zach, that's too many calls. You can't do that." We were just sitting around a table and like, "Well, maybe we could do like learning collaboratives or pods. It was just like a, "What if?"

He kind of nodded his head and then we launched it. These are some examples of how we've learned from them. We had done some things differently than them. For example, they take... as I said, know all of the protected health information. They have a very robust but somewhat rigid database system that has worked well for them for more than a decade, but we wanted to be a little bit more flexible, and so the system that I described was really a custom decision by our network to allow us to answer lots of different questions.

What else? Those are some examples. I think we learn a lot from those other networks and we have been in communication with them.

Dr. Laura Lubbers: 55:14 That's great, and it's great to have a network to help support this and inform this. I think there's time for two more questions. One is, "Is there the possibility for an international collaboration? Could it be even better with hundreds or thousands in the wider group?"

Dr. Zachary Grinspan: 55:32 I love that. Whoever wrote that question, we are like mind meld. We've had some conversations. Weill Cornell has an academic collaboration with a medical school in Qatar in Doha and the leader of the epilepsy program there actually trained in Columbus, Ohio, where Anup Patel is. Khaled Zamel is a great guy, and so they may come onboard at some point. I trained with this wonderful guy who now practices in Beirut in Lebanon,

and they had Epic, so if we get into Epic, they'll be able to get it. I've been trying to pitch Ingrid Scheffer on this who's in Australia. I lured Helen Cross, who's in the UK, she uses Epic, so I think the potential is there.

What's nice now working with the vendors is that if you build it into the vendor system, then all of their customers, and it's an international group, can then use your form. Then, if you get a collaborator, then the data's already there. He's got to pull it out.

Dr. Laura Lubbers: 56:43 Great, great. Well, that answer was very much appreciated by the person who asked the question. Actually, maybe we can fit in... Well, we are running low on time. I do want to ask, somebody has a final question. "How do I encourage my neurologist to participate in The Pediatric Epilepsy Learning Healthcare System?"

Dr. Zachary Grinspan: 57:04 Oh, I love that. I think just tell them to email me. I don't know what else to say. We have some funding and we were able for our 20 sites to provide some seed funding. That money has run out, but some sites are willing to join with internal resources, and so we've actually had some interest there. Then, the ImproveCareNow, they have a fee-for-service model, so every site that's in ImproveCareNow pays $20,000 into the system every year. We haven't done that. At present, if there are sites that are enthusiastic, they can just find me and I can have a conversation with them.

The other thing is that 54 of the U.S. Pediatric Epilepsy Centers are part of PERC, and I am pitching and giving updates on this through all of our PERC calls. We just had our annual meetings virtually, unfortunately, last week, and we have calls every other month. Finding out if your center is part of PERC, finding out who the PERC representative is, and then having that person reach out to me could also be effective.

Dr. Laura Lubbers: 58:24 Great, great. Thank you so much. Thank you so much for sharing information on The Learning Healthcare System and how it's being used to help provide better care for people with epilepsy and their families. I also want to thank the BAND Foundation for sponsoring today's webinar and our entire webinar series, and I'd like to thank the audience for the terrific questions that came in. If you have any other questions, please do email them in and we will do our best to get those addressed.

If you have any additional questions about CURE's research programs or future webinars, please do visit our website at www.cureepilepsy.org. Also, please stay tuned for announcement for our summer webinars that will be coming out in the near future. With that, thank you and please be safe.

Dr. Zachary Grinspan: 59:13 Thank you.