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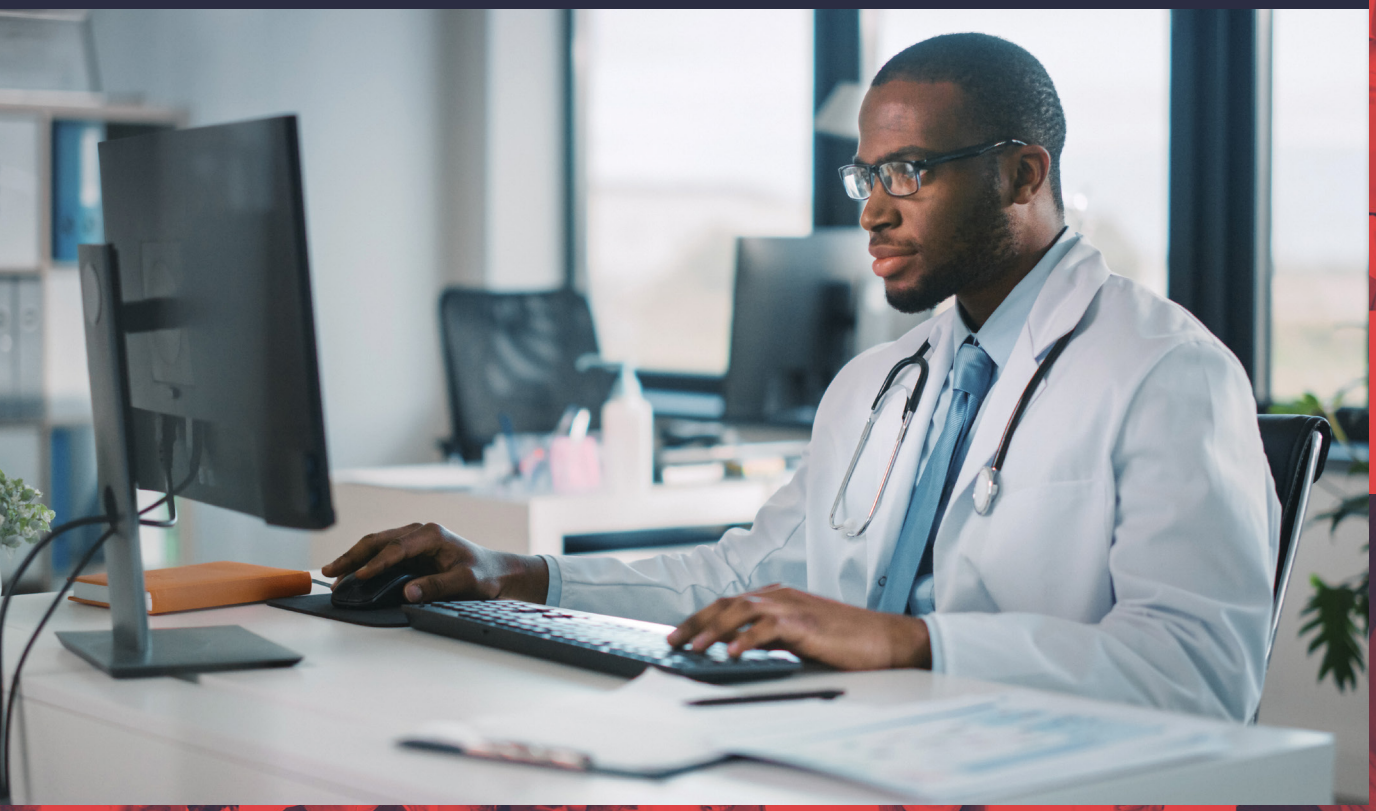
HEALTH RESEARCH

MONOGRAPH

ONLY ELLIGO ACCELERATES CLINICAL TRIALS THROUGH HEALTHCARE

Elligo Elite Learning Series Monograph — Beyond the EHR: Clinical Trials in the Age of Abundant Data

Only Elligo provides direct access to known patients with their trusted physicians, along with research practice management solutions to accelerate the development of new pharmaceutical, biotechnology, and medical device and diagnostic products.



BEYOND THE EHR: CLINICAL TRIALS IN THE AGE OF ABUNDANT DATA

The amount of electronic health record (EHR) data we've amassed is immense. Similarly, clinical research has never needed access to such specific or large patient populations as it does today. Data-sharing partnerships can harness EHR data to bring more patients into research and improve research processes.

Michael Ibara, Pharm.D., Chief Data Officer at Elligo Health Research®, presented an Elligo Elite Learning Series roundtable with Xtalks, entitled, "Beyond the EHR: Clinical Trials in the Age of Abundant Data." This roundtable was a deep dive into what data partnerships can accomplish in the research space. It featured industry experts Michael R. Fronstin, Global Head of Clinical Research and Consulting, Cerner Enviza; Doug Lee, Vice President of Operations and Chief Data Officer, Harris Computer; and Seth Hopkins, Ph.D., Executive Director of Translational Medicine, Sunovion Pharmaceuticals Inc.

In the roundtable's first section, Michael Fronstin explored the concept of a data-sharing network of healthcare systems and how EHR data gathered from such a network can inform patient-centric trial designs, lead sponsors directly to the patients they need, and increase diversity in any given trial. Doug Lee then described how his company solved data-sharing problems to ultimately provide a complete longitudinal view of a patient's healthcare journey. Next, Seth Hopkins used the work he did on a psychiatry trial as an example of how EHR data are already enhancing research. Finally, Michael Ibara led the group in a discussion about the challenges of implementing EHR data in clinical trials and how data literacy is becoming an essential part of bringing efficiency to research.

AYESHA RASHID

Good day to everyone joining us, and welcome to today's Xtalks webinar. Today's talk is entitled, "Beyond the EHR: Clinical Trials in the Age of Abundant Data." My name is Ayesha Rashid, and I will be your Xtalks host today.

Today's webinar will run for approximately 60 minutes. This presentation includes a Q&A session with our speakers. This webinar is designed to be interactive, and webinars work best when you're involved. So please feel free to submit questions and comments for our speakers throughout the presentation using the questions chat box, and we will try to attend to your questions during the Q&A session. This chat box is located at the bottom

INDUSTRY EXPERTS

MICHAEL IBARA, PHARM.D.

Chief Data Officer,
Elligo Health Research®

SETH HOPKINS, PH.D.

Executive Director
Translational Medicine,
Sunovion Pharmaceuticals Inc.

MICHAEL R. FRONSTIN

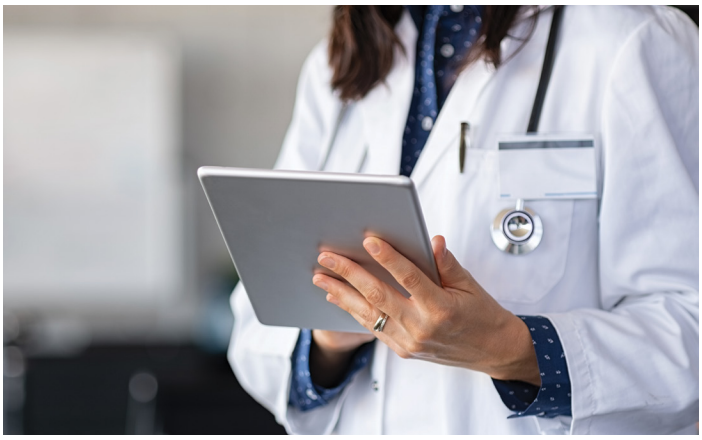
Global Head of Clinical Research and Consulting, Cerner Enviza

DOUG LEE

Vice President, Operations and Chief Data Officer, Harris Computer

of your Go-to-Webinar control panel. If you require any assistance, please contact me at any time by sending a message using this chat panel. At this time, all participants are in listen-only mode. Please note that this event will be recorded and made available for streaming on Xtalks.com.

At this point, I'd like to thank Elligo, who developed the content for this presentation. Elligo Health Research accelerates clinical trials through healthcare with access to over 150 million known patients and their HIPAA-compliant healthcare data, the company's IntElligo® Research Stack technology, and their Patient*Select* identification and engagement model. Coupled with the largest Known Patient Access Network, Elligo's Site Solutions enable healthcare practices and research sites to participate in clinical trials. By adaptive engagement of known patients and physicians, Elligo accelerates the development of new pharmaceutical, biotechnology, and medical device and diagnostic products.



And now it's my pleasure to introduce our speakers for today's event. Michael Ibara has more than 20 years of experience in clinical research and development. Throughout his career, Michael has sought to improve healthcare by bringing together healthcare data and digital technologies. His interests include regulatory and policy implications for digital healthcare, exploring the factors needed to allow interoperability of healthcare data for all stakeholders involved, and implications for the use of big data, machine learning, and natural language processing to improve our ability to perform regulated clinical research. Before joining Elligo, Michael Ibara was Head of Digital Healthcare for the Clinical Data Interchange Standards Consortium, or CDISC. There, he led the FDA eSource project and Healthcare Link efforts with registries, clinical trials, and mobile health to enable use of real-world data from healthcare for regulated research and decision making. Prior to his time at CDISC, Michael was Head of Business Development, Coordination, and Innovation and also Head of Pharmacovigilance Innovation at Pfizer, where he worked for 15 years in various positions, leading implementations of global systems and large-scale technologies.

Michael Fronstin joined Cerner Enviza, formerly Kantar Health, in 2005, and currently leads the organization's clinical regulatory and safety team. Michael's team is responsible for delivering high-quality, regulatory-grade work to support pre/peri-approval clinical research and post-approval safety surveillance. The clinical regulatory and safety team also leads global harm-reduction partnerships and separately, public health partnerships in Germany. In addition to overseeing the global team, Michael is accountable for supporting corporate development and product innovation. Michael's prior roles include Global Health of Offer and Innovation, General Manager of the Real-World Evidence Group, Chief Operating Officer, and Head of Life Sciences Business Development. Prior to joining Cerner Enviza, he held various leadership roles spanning industry, payer, and consulting organizations. Michael is a member of the Cerner Enviza leadership team and is proud to serve as a board member for International Guardian Ltd. Michael earned a Master of Business Administration from the University of Miami with a certification in healthcare administration. He has a Bachelor's Degree in sociology from the State University of New York at Albany.

Seth Hopkins is the Executive Director of Translational Medicine at Sunovion Pharmaceuticals. In his work at Sunovion, he has led and advanced new treatments for CNS disorders from discovery to regulatory submissions. Prior to his role in translational medicine, Seth served in a variety of roles, including those involving

computational chemistry, pharmacology, and preclinical and clinical development. During his tenure, he has advanced programs through clinical development, applying clinical pharmacology, experimental medicine, neuroimaging, modeling, and simulations at Sunovion. His current research interest is the application of advanced mathematics and analytics to improve the efficiency of clinical development of breakthrough treatments for psychiatric disorders. Seth was a key contributor to the initiation, clinical development, and submission of IMDs, NDAs, and psychiatric indications. Seth completed his postdoctoral training at the University of California, San Francisco, and earned his Ph.D. in biophysics from the University of Pennsylvania.

With over 20 years of experience in business, technology, and innovation leadership, Doug Lee has emerged as a change agent. Through precise strategy and dynamic culture development, Doug has demonstrated the ability to help businesses weaponize their data to drive top-line growth and profitability. In his roles as Vice President of Operations and Chief Data Officer, Doug is responsible for data strategy, data commercialization, innovation, and operational excellence. He is active in related professional organizations, serving on various boards within the private and public sectors. And now without further ado, I'd like to hand over the mic to our speakers. You may begin when ready.

MICHAEL IBARA

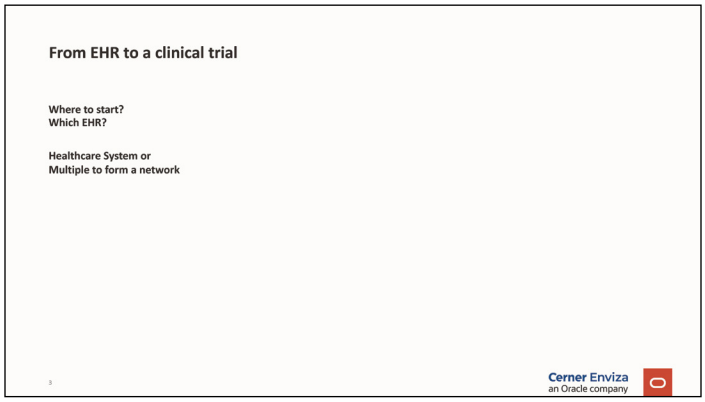
Thanks very much, Ayesha. I'm Michael Ibara. Thanks to everyone for attending this webinar. This is a fascinating webinar — to me, personally, as I work with all of our speakers here. When you look at the breadth of what we have, this is what it takes to run clinical research these days. I think there are several epochs in the history of using EHRs. I remember years back when they first were introduced, when I learned about them, and from the industry side, I thought, this can be a great boon to clinical research. But at the time, I think a lot of us thought of it as being like hooking up one machine to another. And that's going to get us where we need to go. Then we started to realize that achieving interoperability is much harder than we thought. So we started working on that, and then we realized, well, we need to get all of the data together, because we have to standardize it to a lot of things before it can work. So we started collecting large amounts of data, and then to our surprise, again — I suppose we shouldn't have been surprised by then — collecting all the data in one place didn't necessarily do it, because now we all have collections of data, and they're normalized within their own silos.

But a fascinating thing has happened in the last several years in clinical research. Whereas I thought we would basically be solving more and more of the problem, as clinical research has progressed, we now actually have a two-sided problem. On the one hand, we have much more specific requirements to go after specific populations, because drugs today are able to target more specific conditions and populations of patients, meaning we're finding smaller numbers of patients whom we need to target more specifically. At the same time, we've got studies running across 1,000, 5,000, 10,000, or 20,000 patients, where we need the volume. Amazingly, we end up with a continuing need to find more patients for trials. I believe this will be an ongoing trend. This panel represents the types of relationships I think we need to bring together, because no one group can really do it alone anymore. We've got folks representing development of an individual EHR and bringing the sites in for that, we've got individual companies holding many EHRs, we've got sponsors working on leveraging EHRs, and Elligo has relationships with all these folks. What it shows me personally is that when you digitize a field, you sort of bring everybody into the same room, and that's what I think we're doing today. Besides talking about using an EHR, how do you really use EHR data to place your patients into trials and improve your trials? That's what we're about today. Each speaker has a little bit to say on that, and then we can open it up for discussion and Q&A.

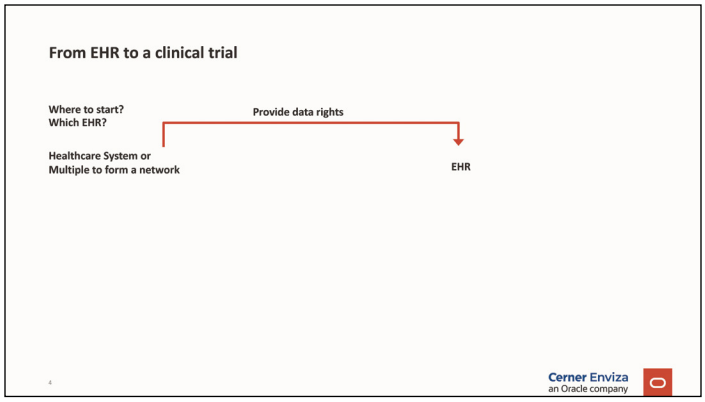
So I'd like to start with you, Michael. From the perspective of Cerner, having a single EHR and developing that and developing a learning health network, what are your perspectives on the topic?

MICHAEL FRONSTIN

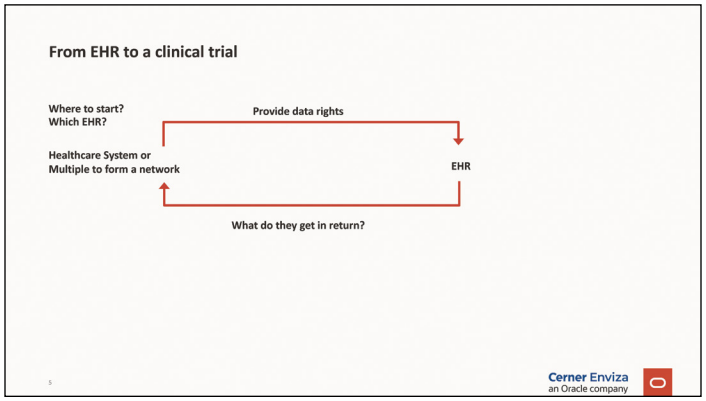
Thanks, Michael. First, let me say thank you, to you and to Elligo, for inviting me to join you in this discussion. And to Xtalks. I'm humbled to be with such great people and speakers here. What backgrounds — wow. The age of abundant data on that first slide. ... We are not lacking in data, that's for sure. Getting to the data is the challenge, right? And it's even more difficult when it comes to electronic health record data. But where do you start?



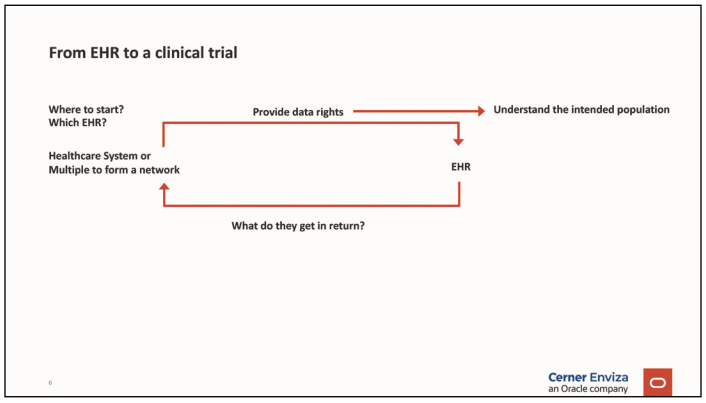
From an EHR perspective, if you want to get the data, have it harmonized, curated, and appropriate — fit for purpose, if you will, to use for a clinical trial — there are 200 to 300, I think, EHR systems in the U.S. There are aggregators, and there are other sources that you can go to in partners, so you have to start out by saying, "Where do I go? Which EHR?" Often, it starts with



healthcare systems, or multiple healthcare systems combined to form a health network or a learning health network, as Michael mentioned. And that's not an easy task. There are a lot of considerations around these networks. What do they represent? What is their heterogeneity? What do they look like? It's obviously all U.S. right now, because of GDPR. You can't get to the EHRs in Europe, or it's very difficult to, so you have to determine where to go and how to get there as a starting point.

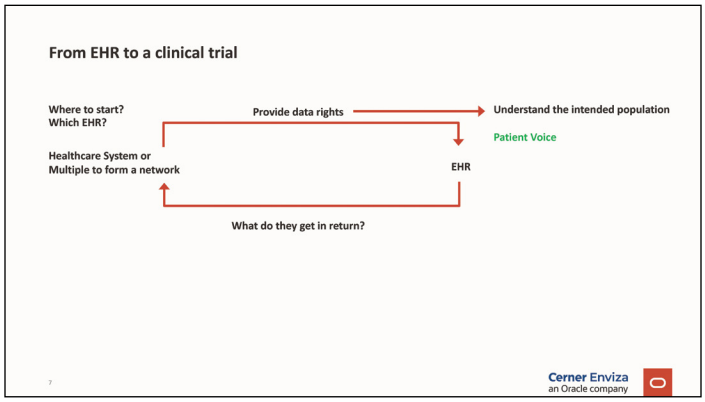


Then, really what you're looking for is for the healthcare system to provide data rights to their EHR to you so that you can use it. But then the data are very messy — not set up for research purposes or to identify the populations intended to be enrolled in clinical trials. There are a lot of challenges here. Why would they give you data rights? It's their bread and butter, their gold mine, if you will. What is it that they're going to get in

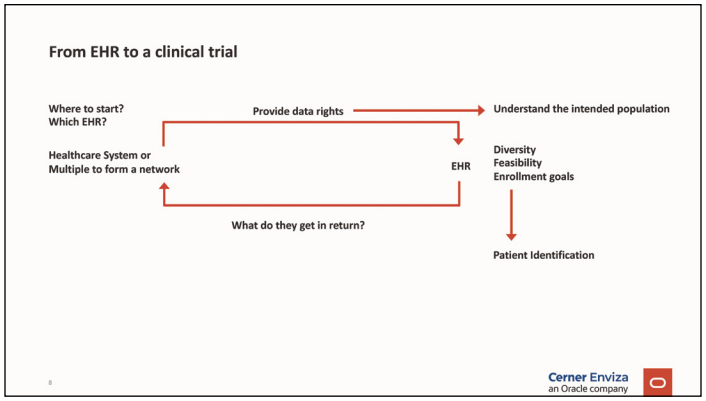


return? You have to determine that upfront. You've got to talk to them about that — negotiate and find out what's important to them. Is it bringing back clinical trials to them? Is it access to de-identified data across the entire network, if it is a multihealthcare system network, which will vary depending on what health

system you're looking at? If you're looking at a small community hospital that's never done clinical trials or research in the past, their incentives will be very different from an academic medical center or some large, independent delivery network. You really have to have those conversations to determine what they want to get in return.

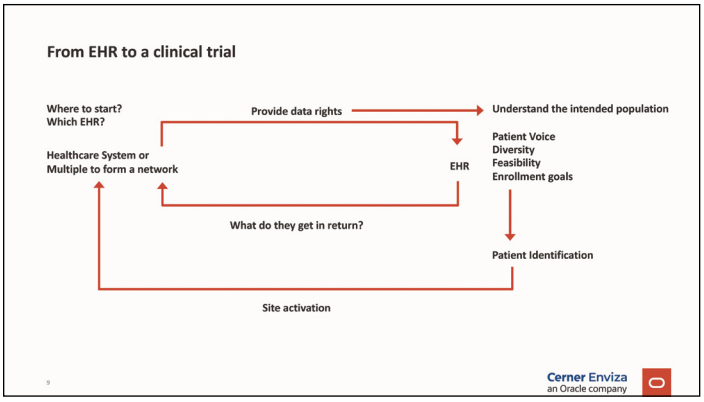


Once you figure all that out, and they do provide data rights to you, and you've now cleaned the data, organized the data, de-identified the data — and there's a boatload of steps occurring during this process — then you can start to understand the population you want to include in your clinical trials. And of course, the inclusion/exclusion criteria are critically important. Life science, medical device, and genomic companies are all going to tweak and massage their I&E criteria — relax it or make it more rigid, depending on what they want and what they're studying. Before you even dig into that next step of the EHR data specifically, you really need to take a step back and understand the patient's voice. We've seen the FDA in particular talking a lot about patient-centric clinical trials, and we talk a lot about patient experience and patient voice. But if clinical trials don't objectively measure what's important to patients, caregivers, and their families, then perhaps all that discussion isn't serving its purpose. A lack of understanding of patients' specific needs — their priorities, the experiences that they're living every day based on their disease — can really negatively impact clinical trials and their results. It could result in worse or lengthened enrollment periods, lower retention and recruitment, lots of amendments. ... It really could just derail your clinical trial. It's really important to understand these things. Then you can dive into the EHR or whatever data set you're using to reflect and find what's important or most important to the patients, caregivers, and their families.

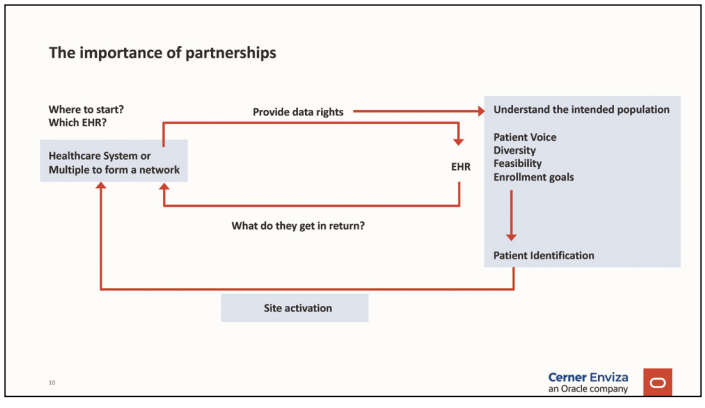


Now we start delving into the EHR data. There are so many different ways you can leverage the data to help establish what your clinical trial protocol is going to look like. You see, diversity, feasibility, and enrollment costs are just three of many things I've listed here, and diversity is at the top. There have been two sets of guidance rolled out by the FDA a couple of years ago, and most recently in April. And diversity is a part of everything from social determinants of health, and demographics, race, and ethnicity, to things like comorbidities, disability, and transplant patients, and where they are located. From a geographical perspective, it used to be that we were only doing clinical trials in the largest cities, but prioritizing diversity and health equity means not just getting to the underserved populations who may not have access, but also to those who don't have access because they're just not in the proximity of a research site. Using the EHR for protocol, optimization, and feasibility to understand what we can do out there — not even knowing necessarily if some of these patients are already enrolled in a clinical trial, and therefore the feasibility may be worse than we're led to believe — based on the data, you would use all this information to set up what your enrollment goals will look like, based on some stratification of all these variables. So you have targets that represent the disease itself and not

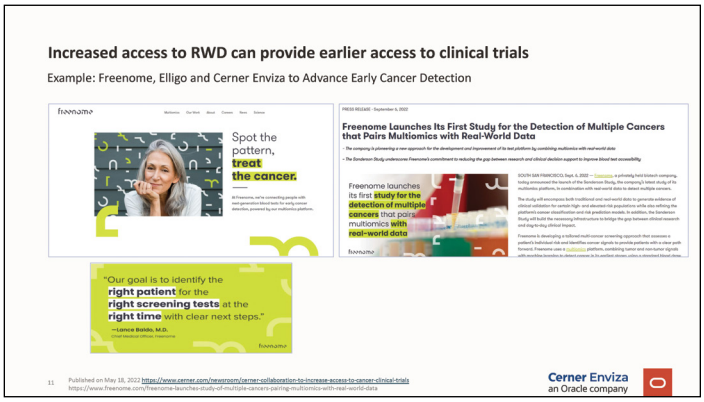
necessarily just the U.S. census, because certainly some diseases will occur in a disproportionate way among some specific group of people. Once you do all that, then you look in the EHR data to identify the patients, and when I say identify, what I mean is, where are they located? How do we get to them so we can start enrolling them into our clinical trials and activate them into the trial itself? And to do that, you need to start site activation. You go out to those sites back at that same healthcare system where you've identified these eligible patients based on the ID and any criteria, and you start



working with these systems. And again, based on the system itself, and whether it's an academic center or community health center, an IDN, or so forth, they may or may not have done research in the past. That's where it's important to have partners like Elligo at your side, to help you get this done in some of these research-naive settings.



I emphasize the importance of partnerships, because at each of these steps, having or lacking the right partners with the right experience is going to make your jobs and lives either easier or harder, set you up for success or failure. Now we're in a position where we need to accelerate clinical trials or recruitment into clinical trials the right way with the right patients, so that we can get these newer treatments into the hands of the people who need them the most, especially when you think about rare diseases and oncology. It's important to have partners every step of the way to think about that. The last thing I'll discuss is, how does this come to life?



Here's a real example, and a way that we're working with Elligo. The title says, "Increased Access to Real-World Data Can Provide Earlier Access to Clinical Trials." In this case, Elligo and Cerner Enviza leveraged the partnerships I just described in the Learning Health Network at Cerner. We're working with multigenomics and multiomics, and this has just been released in a press release. This is all public information, and the idea here is that we use the EHR data to identify newly diagnosed cancer patients and then, working with Elligo and working on behalf of the sites, we reach out to these patients before they get their first treatment, to enroll them into the clinical trial so they can get a blood draw. If you think about it, you have a very short window to get in there and do this. Working with EHR data, not only are you able to identify who the appropriate patients are in real time, depending on how you access the data and the rights that you have, you're also able to leverage certain aspects of the EHR data. We can see the patients' appointment schedule and call them up,

saying, “Hey, I’m calling on behalf of Dr. so-and-so, and I see you’re scheduled for your next appointment in two weeks,” or whatever it is. The use of EHRs to help accelerate this enrollment is really fascinating. It’s come a really long way, and it’s leverageable if you know how to leverage it. This is a real story, and we’ve already started enrolling our first few patients this last month or this month... the beginning of this month. It’s going to be great. And with that, let me pass it back to Michael, and thank you again for the opportunity.

MICHAEL IBARA

Thanks very much, Michael. You laid out a great road map from EHR to clinical trials and experience and things like that. Thank you. Next up, Doug, if you could address the challenges of starting a company within a company with a wide variety of EHRs and data stores, and then realizing that you want to bring clinical research to that sort of research-naive population.

DOUG LEE

Absolutely. Thank you. So I’ll take a huge step back. I’m a part of Constellation Software — that’s our parent company. Then we have Harris Computer, which is the next layer. My company is a startup within Harris computer called Sidus Insights. Our brief, as Michael suggested, is to take a network of EHRs with EHR data and inpatient data and figure out how we pull it together into a central store. How do we gain insights from it, and how do we enable clinical research? It’s been a long journey — 16 months since we first started. We had to jump through a lot of hoops. Of course, it all started with legal regulatory privacy and security. We started out with a lot of conversations on those issues, but with our sister business units, as well, and on data rights, as Michael touched on earlier. In this case, we were stuck: Do our EHRs have data rights from their providers? So there was that extra step that we needed to have in place in order to make our legal teams happy.

But at the same time, we also looked at how to build a system that could take all these disparate EHR data and inpatient data and pull them into a platform that made sense and that we could use to compute capabilities at a high level of performance. So we ran a bunch of POCs. At the end of the day, we ended up with a platform that was 12,000% higher performing than our previous one. To quantify that, with our previous system, one data set took five days to run, around the clock. With the new platform, the same data set took 45 minutes. So we definitely found something there, but from that, the hard part really started. We had to standardize the data, we had to transform the data, and we had to normalize the data. We had a master data model, and we wanted to make sure that we preserved data utility as much as possible. We cast a wide net, and we created our own master data model. Now we had a little bit of everything from each data source.

Each EHR records data differently, and there is no global standard out there. As it was, there was a lot of noise. The cleansing, the standardization — that transformation was huge for us. We were trying to get everybody to speak the same language. At the end of the day, there were data and identification that we had to build in-house. And we worked really hard. It took us over a year to run it through expert determination. We now have our expert determination certification for all our unstructured and structured data sets.

Ultimately, the goal was to pull together a longitudinal view of Patient X. It didn’t matter if they went to this EHR or that EHR within our network — we wanted to make sure that we could tell their story. Usually, that story is between 15 and 20 years long, which provides a pretty good view of a patient. From there, the last problem to solve was really just data sharing at the end of the day. So how do we look at that problem? There were a few different ways we looked at it, and we have a few different solutions in place, but one of them I’m most proud of is working with Michael at Elligo — being able to have a direct share with Michael, so his team can have a view of the data. When we share the data with

them, it's a live view. For his team to be able to run queries directly on that data set was huge. I'm most proud of that. It's just a way for us to enable clinical research with our partners.

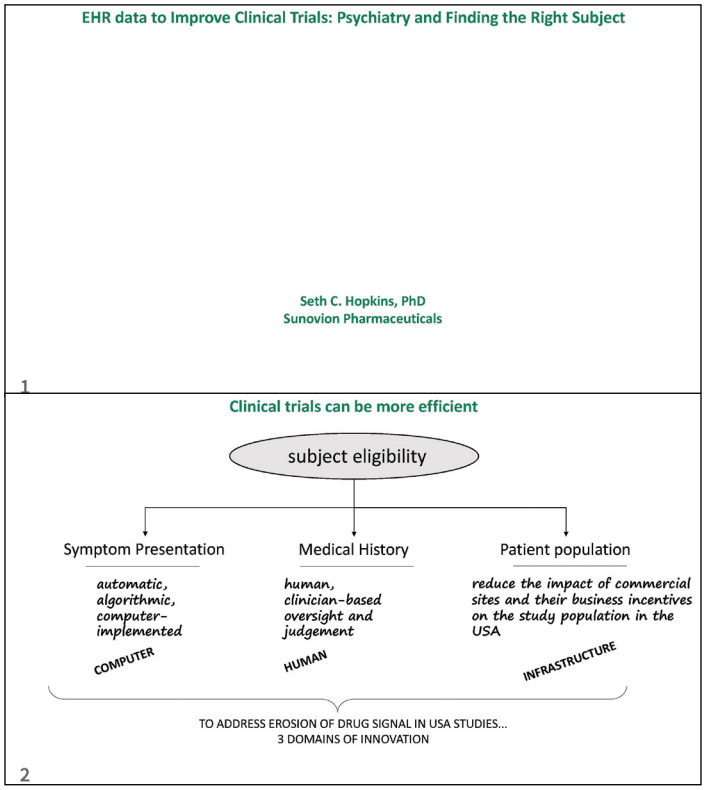
MICHAEL IBARA

Thanks very much, Doug. And thank you for speaking on a topic near and dear to my heart, which is the heterogeneous EHR environment in the U.S. Honestly, usually, for clinical folks who are starting a trial and want to use an EHR, the last thing you think about is the thing that stopped you dead in the water, which is, oh, we can't merge the data. We need to clean it, or we need to standardize and things like that. You guys have done all of that with such a large amount of data. It's very impressive. As you've heard from Michael and Doug, doing the trial is the tip of the iceberg, and everything underneath there on the use of EHRs is a tremendous amount of work. Our next speaker can provide a great testimony as to why we would want to do all this. I'm very excited, Seth, about what you have to talk about in terms of showing that there is a payoff, at the end, of trying to use medical records. So I'll turn it over to you.

SETH HOPKINS

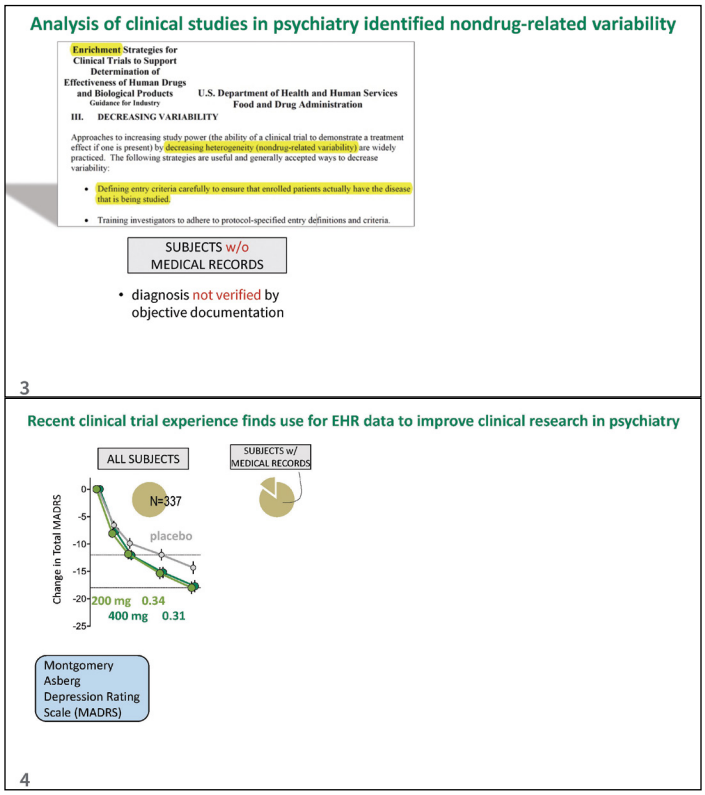
Thank you, Michael, and thank you, Doug. I want to focus on some data — some actual clinical trial data and some approaches we're taking to incorporate medical records in the conduct of Phase III regulatory, FDA-adequate, and well-controlled trials for the registration of new drugs.

As I think Michael mentioned, we're in this epoch in which no one group can do it alone anymore. When we thought about our Phase III programs in psychiatry, we realized that, particularly in the U.S., our clinical trials could be more efficient. In the U.S., we've seen an erosion of drug signal. What I mean by that is this notion of a clinical trial effect, or you can think of a placebo response: an inability to detect whether a

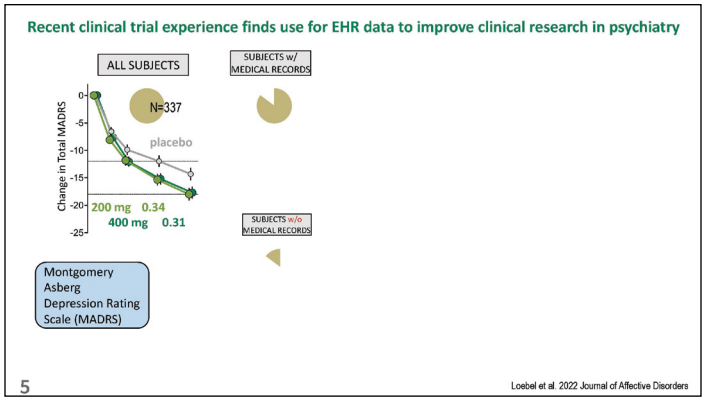


drug is active in comparison to a placebo. So by no one group, we've focused on subject eligibility, as I think Michael pointed out, as well. I'm dividing subject eligibility across three domains. One is around symptom presentation. One is around medical history, which is where the medical records come in, and the other is around the infrastructure or the patient population who shows up for clinical trials, particularly in the U.S., where there are business incentives influencing the study population in which we study our drug effects.

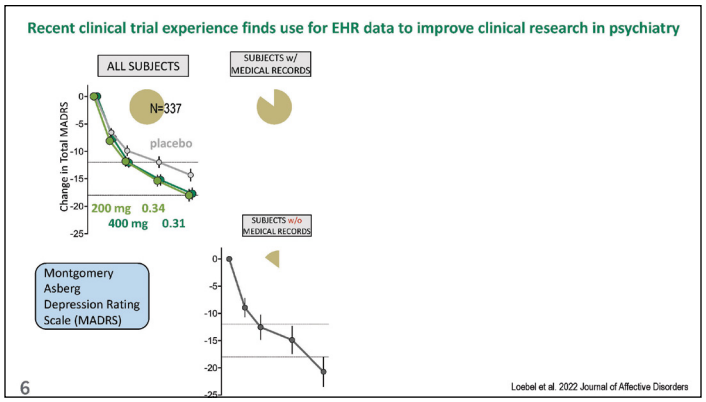
One of the key guidances we focused on, particularly around the erosion of drug signal, is the enrichment guidance issued by the FDA. One of the first elements of that guidance centers on defining entry criteria carefully to ensure that enrolled patients actually have the disease being studied. I want to take you through some recent data we've published around that erosion, particularly in subjects lacking a medical record and objective verified documentation of their condition.



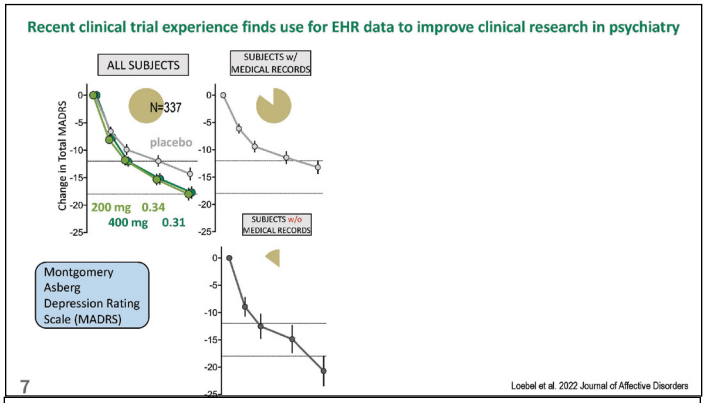
We're studying psychiatry, and in particular, bipolar depression. This was a Phase II study, where we were measuring improvement in total symptoms of depression over six weeks, and the scale we use is called Madras. What I'm showing you is the intent-to-treat population, the 337 subjects entering the trial, and the change in symptoms. I'm marking those dashed lines around "12-point change" versus around "18-point change." That's the window in which we can detect drug effects across all compounds that have been developed in depression over the last 15 years, and when placebo change is greater than that top dashed line, around -12 points. It's a ceiling effect — we've suppressed our ability to detect drug-placebo separation. This trial does have an effect size shown there, at about 0.3, and it was able to show a separation, but you can see that the effect size is relatively small, meaning that clinical trials dedicated to showing drug-placebo separation need to be very large, which is not an efficient way to develop new treatments for patients who need them. We noticed though, especially in the U.S., that there's a fraction of the subjects who did not have medical records that could document a diagnosis of bipolar depression, and who were currently experiencing depression prior to entering the trial. Once they enter the trial, the assessments are all very thorough, but we rely on the investigator and the patient volunteers to accurately portray their medical history.

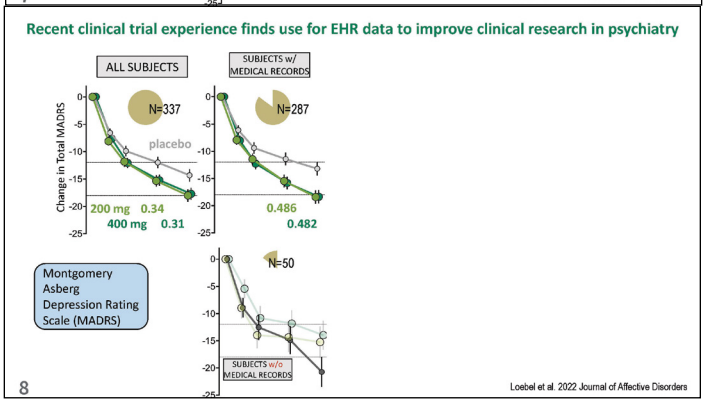


So we've separated out those subjects without medical records from those who had records supporting their diagnosis. In the bottom curve, look at what happens



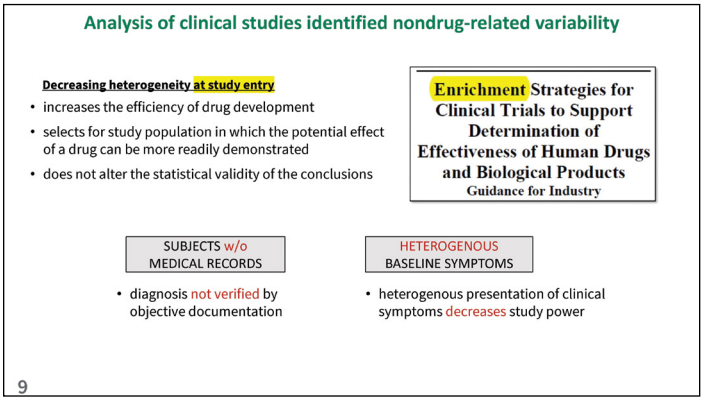
to the subjects who came in without medical records. That's a placebo curve, where the change on placebo is enormous. It's difficult to detect any drug-related improvement when all the subjects are getting better. The placebo change for those who had documentation of their diagnosis in their medical records was much more modest. You can see they're around 12 points. So the 10, the drug effect, and the top panel is now almost 0.5. That means clinical trials can be smaller and more efficient, and drugs can be approved more effectively. In the bottom panel of 50 subjects who didn't have medical records, the overall change even on the drug was very high.



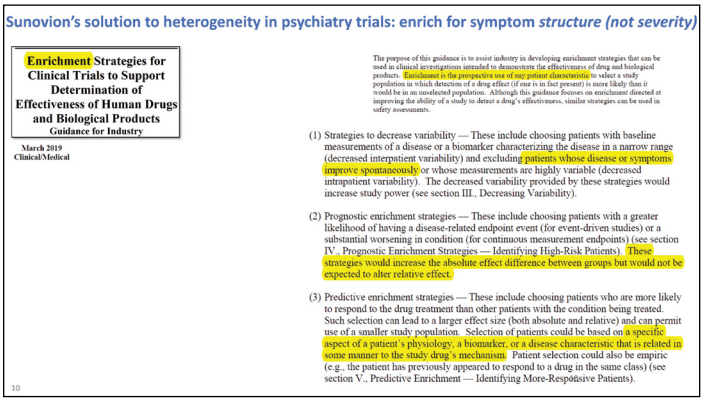


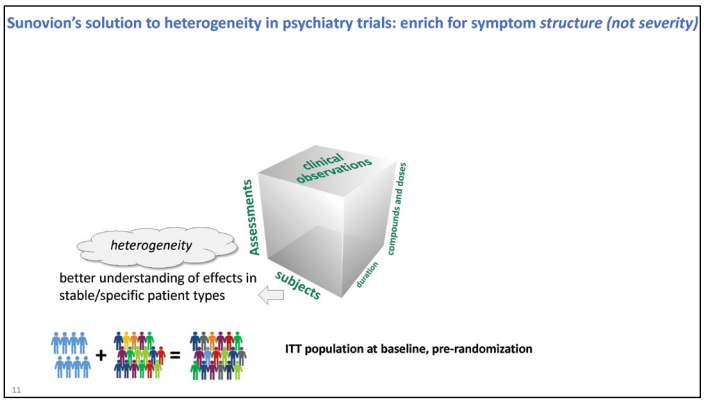
Going back to this enrichment guidance, that is a very important way to communicate the design of our trials, and the appropriateness and adequacy for regulatory submission we gained by making reference to this guidance. One of the ways to improve drug signal is to decrease heterogeneity, which increases the efficiency of drug development. This selects a study population for whom the potential effects can be more readily demonstrated, and in general, it's not considered to alter the statistical validity of the conclusions.

I just want to take a few moments to talk about an approach we've taken recently in psychiatry trials, and then I'll come back and relate it to infrastructure and patient population. Traditionally, when we write inclusion/exclusion criteria in our trials, we talk about symptom severity. We want to be able to detect the drug effect in a population of patients who have relatively severe symptoms in psychiatry, who are

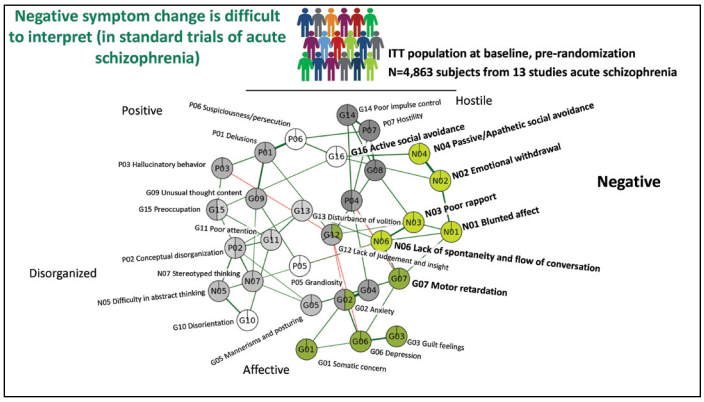


relatively disabled by their symptoms. In their guidance, the FDA describes three strategies. One is to decrease variability — and I just showed you an example of that, where in those patients without medical records, there really was a prompt resolution of symptoms, and they improved spontaneously. Another two strategies focus on prognostic enrichment. These are ways to find subjects who have more likelihood of presenting with a disease-related endpoint, if it's an event-driven study, or who have a substantial worsening condition. Then the last one is the holy grail of predictive enrichment strategies, where you have an additional measure of some aspect of the patient's physiology that's related in some manner to the drug's mechanism. That's an approach that would ultimately shift benefit-risk calculations by identifying a marker and a patient. That's where this concept of right patient, right drug, comes from.

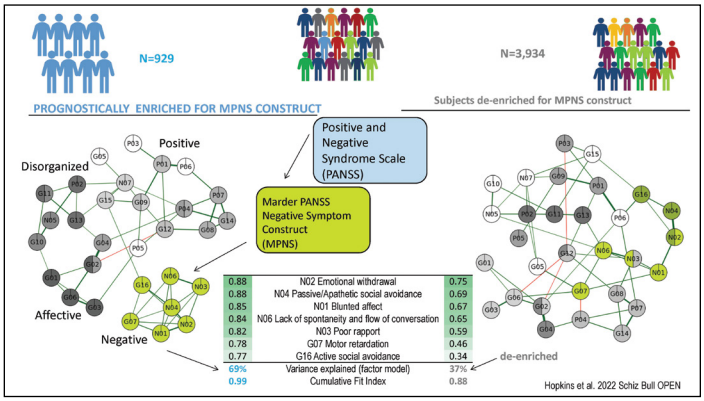




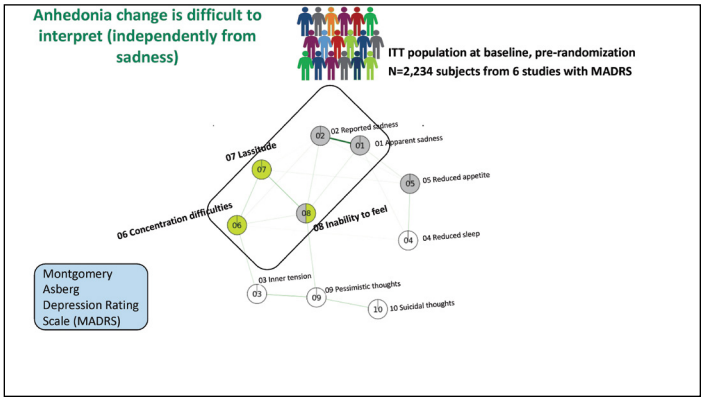
So this gets back to what Doug was talking about inside a drug company. We have a very large collection of clinical observations from our clinical trials, which have been standardized, and we collect clinical observations under very regulated conditions. So we looked back in our data sets from the past 15 years of trials in psychiatry and decided we could approach heterogeneity around patient type in a way that would help in the prospective use of inclusion criteria — one that wouldn't just be around symptom severity but around symptom structure. What you're looking at



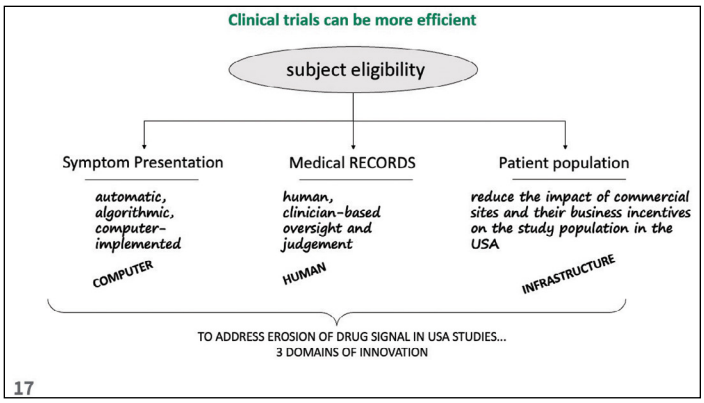
here is the constellation of symptoms in schizophrenia. This is acute schizophrenia. We had run 13 studies, four to six weeks long. In the hospital, we had almost 5,000 subjects at baseline. These are the 30 symptoms of the scale used to register new treatments for schizophrenia. Each symptom is a node, and their relatedness is represented by the lines between them or the edges in the diagram. They're organized around symptoms that are positive, disorganized, negative, hostile, or affective. We want to develop and describe the effects of novel treatments on the constellation of symptoms, but in this heterogeneous population, that's very difficult to assess. We've discovered ways



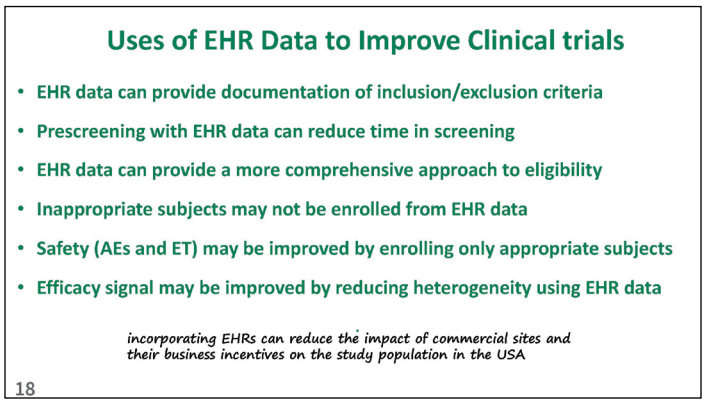
to prognostically enrich for particular patient types, defined by a constellation of negative symptoms, for example, as shown here. On the left side, we found approximately one-quarter to one-fifth of our patients had a very coherent community of symptoms associated with their disorder, which could be more readily measured with our existing scales. On the right side are the heterogeneous patients, in whom those measurements would be less reliable. We're working on inclusion criteria to enroll subjects in whom the endpoints can be more reliably measured.



That's where EHRs are very important. This approach can be applied in other psychiatric disorders, particularly in depression, and we can enrich for symptom presentation in various psychiatric



disorders. On the left side of this slide, with the "no one group or one approach can do it alone," we have this concept of enrichment, where symptom presentation and medical records go hand in hand. This next slide focuses on eligibility. Here on the right side, it's around access to clinical research as care, which gets to the patient population and infrastructure. Some of the uses of medical records from our perspective, which aims to improve clinical trials, really center on the documentation of the inclusion/exclusion criteria and confidence in the diagnosis and presentation of symptoms that actually can reduce time and screening. Incidentally, in the U.S., we've noticed a phenomenon where we screen far more subjects who ultimately don't get enrolled than we do outside the U.S. So there's a business incentive that's influencing how we enroll our patient population.



Medical records can provide a more comprehensive approach to eligibility in our protocols. Our protocols can help prevent inappropriate subjects being enrolled if we cannot access and incorporate that data. Overall, when we develop drugs, we need to very carefully describe safety in terms of adverse events and early terminations. For that reason, the inclusion criteria are very important around enrolling appropriate subjects who warrant treatment and participation in a research study, and the medical records help there. And ultimately, I think I've shown you how the efficacy signal can be improved by reducing heterogeneity. That revival requires access to patients' histories and medical records. So I'll end it there. Thank you. Back over to you, Michael.

MICHAEL IBARA

Thank you very much, Seth. As I mentioned before, I think this is tremendously exciting, drawing a straight line from the use of record-based information, which is more factual, to impacts on efficacy, which, like I said, are the payoff for all of us in talking about all this. So thanks very much for that.

From my point of view as the Chief Data Officer at Elligo, the speakers who have gone before are all part of my journey in what we've been working on at Elligo. Elligo's business model is to bring clinical research into healthcare and to those sites that may be research-naive or need help with that. Because of that, the emphasis is on standing up the research infrastructure at a site, let's say. But what is the role of working with data and data science in that organization? My remit is to get value from the data we collect, and the value is defined as bringing a patient into a trial, right? I've been at Elligo for years now, and in the time between when I started and now, I've learned two major lessons. The first is the topic of this of this webinar, which is that you need to form partnerships in order to execute research. In today's world, as you heard from Michael and Doug, the challenges that they have to go through, just focused on the data long before you try and bring it to clinical research, are immense. And as I said, this is typically the part of the iceberg that you don't see — that's underwater. So if we want to stand up research at a site, there's 100 things to be done before that, and

it can take up 90% of the attention of a data partner like Cerner, or Harris and Sidus. The first thing my group had to do was learn how to work with other groups. If you're a data science group, in addition to looking at analysis and things like that, we had to learn not just our own data, but learn our data partner's data, because we need to make things as easy as possible for them so that they can concentrate on what they have to do. And they do have so much to do, just in working with the data. Now we want to stand up clinical research.

What I found, to my surprise, is that data science becomes a link between partnering for the data and executing on the final product, which for us is getting a patient into a trial. You heard Doug talk about the fact that we have direct access to their de-identified data, and we have the same thing with Cerner. That's hours and hours of discussion and work spent on understanding the history of the data; the way the data rights are set up, as Michael mentioned; the operating principles in both companies; and the endpoint we want to get to. In addition, working out the process and the cycle time, because as you know, standing up something, getting a query out understanding the protocol, all of that moves at a very accelerated pace these days. So very quickly, we switched data science into a collaborative group, where we're working as much outside as inside the organization. That was a lesson for me in the way I needed to set up a group.

The second lesson has been more recent. That's about a general shift from a primary population approach to finding patients, for example, to more of a precision approach, to coin a term from precision medicine, where we're finding records at a patient level. So for a few years now, a lot of us have been finding patients by going over a large number of medical records — hence the reason for the partners we've chosen. You find that at a population level, and then you have the individual patients to look at. But now there's an increasing need, I think, to find all the records for any given patient. Seth and Sunovion give us a great example of that. For us, I realized we have to create a turnkey sort of operation to do that. For any given patient at an individual level, let's find all the records associated with them. So we set up a service, and if you're familiar with it, there's no one way to get all the medical records for a single patient. Many times, they may come in in a PDF format, and you can't search those very easily at all. So we had to set up a system where, simply to get all the data into a structured format, you're going to have to run it through OCR and NLPD. All these terms basically mean you can take a PDF form and turn it into a structured data set — sort of an Excel spreadsheet.

In the end, the goal is to collect all the encounters from all the providers for any individual patient and have that available. We're working with our data partners to do that, as well. We're also working with other vendors, because if you're going to your primary care physician, and then you find out you have cancer, you're going to go to an oncologist. You may be traveling and going to a different provider, and you may be seen by an emergency department. So I feel like that's the next step, and it's happening much quicker than I thought it would.

We got into a conversation with Sunovion. Seth showed us what he was doing, and I realized, okay, so while we initially designed this system to work for a volume of 5,000-10,000 patients, now we see another direct use is what Seth and Sunovion are doing: to be able to find, upfront in a trial, medical records that you can use to

confirm and clarify patients' suitability for inclusion/exclusion, so you can improve the outcomes of the trial. To me, that's the second lesson. Those two things I said were not in my purview when I first started, and they're not necessarily the way I grew up thinking about clinical research, or even thinking about EHRs. So those are the takeaways for me, from what it means to do clinical research now that we have most clinical sites having EHRs and producing data. There's always one more step you have to do. But I feel like we're getting much closer to closing that gap between what you have to do to get the data ready and how you can use the data to impact your trial. From Elligo's perspective, that's what I've seen so far.

I'd like to open it back up now for discussion by our panelists. I had a couple of questions for the group, one concerning the past and one future-facing. The first question is something we all alluded to a little bit, from each of your perspectives — Michael, working to get this setup to run smoothly; Doug, introducing the idea of clinical research; and Seth, introducing this idea of using medical records. I imagine you've all run into some change management issues, some skepticism, some concern, things like that, because we're changing the model. I'd love to hear your perspectives on what sort of problems you run into as you're trying to do the work you're trying to do. Seth, you could start us off?

SETH HOPKINS

Yeah, I would. I smile, but it's a tragedy that what is enabling our adherence to this new way around requiring medical records is that we can no longer run trials in Ukraine or Russia. There's a reason we were running trials in those countries, and it comes from access to medical history. Before we lost that capacity, that volume that you speak of, change management was not possible in U.S. We sought to minimize their exposure to the heterogeneous access to psychiatric care in the U.S., but that's not a path forward anymore. So there's a huge hurdle to change. But it got accelerated by the war.

MICHAEL IBARA

Very interesting. Doug, what is your perspective?

DOUG LEE

I always say that, in this data world, changing is like moving sands. There's always a new regulation popping up on the radar, be it at a state level or elsewhere. GDPR is looking at the next iteration and how it's going to affect HIPAA. At the end of the day, will there be a new standard that will pop up on the radar? I think we're always chasing the goal posts, and they keep moving for us. But I think it's just being plugged in, right? You know, I see data as a community, and it takes all of us — like those of us right on this call — to jointly create something meaningful. It starts from all of us, and it flows through this app. That's sort of how I see the workflow. In the end, what I really hope for is a global standard that we can all stand on. If we can get there, that will be magical.

MICHAEL IBARA

I have to say, I've been hoping for that for most of my career, but I'm still with you, Doug. Michael, I was going to say you have a foot in both worlds, but actually, you're in more worlds — you have more worlds that you're in than you have feet. So from your perspective, how's the challenge been? What do you see as the sort of resistance to we need to overcome to get there?

MICHAEL FRONSTIN

You know, I sort of wish you'd asked me to talk first because he answered in the way I would have, at least for part of my answer. Certainly, anything that's new is always a challenge when it comes to change management, and in healthcare, we're always the last to change. In every way. It's just how we are, because people's lives are at stake. It's just so important, right? But I'll tell you, the introduction of the 21st Century Cures Act opened up a lot of possibilities. And we talked

about interoperability. While it's encouraged — mandated, or whatever you want to say there — many health systems are doing it, many data companies are doing it, but not all of them are enabled or ready to do it. There are so many things going on right now, you might say it's just a mess. You have to figure out how to navigate that mess, to be specific and know exactly what you're looking at, what you're doing, what you're pulling in. I think that's part of the challenge. Michael, you and Seth said it really well, using a little different wording, about bringing the patient into clinical research. Seth, I think you took it a little bit further when you talked about bringing the right patient into clinical trials, but to do that, you've got to know where you're starting and what you're doing. If you do that, if you bring the right patient in, then everybody wins. And you'll also avoid the AES and other things that have been talked about so much. New things are really tough for a lot of people, and you've got to figure out how to navigate the sea of information that we have.

MICHAEL IBARA

I agree completely with all these statements. A divide that I've seen is if you ran a clinical trial, sort of on the front end of it, for the last 10 years or so, you needed to know what a medical record was in concept, probably seeing it sort of as paper, but you haven't had to be data literate, as it were. And what I see is what you guys represent right now: data literacy as part of bringing efficacy to clinical trials. Every so often I think about the fact that when I'm in discussions with folks like you, we lay out all the terms that we use when we're talking. I'll bet my clinical colleagues may understand less than 10% of those terms. The same is true when they're talking about patient care and things like that, if you're on the ground working with data. When I first had my group, they understood less than 10% of the clinical terms. I had to literally recruit people who had both of those skill sets, and they're very hard to find these days.

So I agree on all that change management has to do with the ability to see across from being data literate over to being clinically literate. That's something our industry is still going through, I think. We used to think of technology as something we laid on top of a process that we figured out, and now we're actually recognizing that if we understand the data from the beginning, we can directly influence the clinical results.

MICHAEL FRONSTIN

Can I add something to that? Even though we've been working with real-world data now for, I'd say, 5-10 years, depending on who you're talking about — long enough for many of us — why is it that every webinar you go to about using real-world data, except this one, starts with a slide defining real-world data? Why is it that people still don't know what it is, or claim EHR is being used interchangeably with RWD? You know, oh, it's the same. It's not the same. So we have a long way to go. Yes, we've come a long way, but we still have a long way to go. And I think the fastest-growing jobs are data scientists and biostatisticians as a result of that. So yeah. We'll get there, we're in a good place.

MICHAEL IBARA

We've one more comment, but either Seth or Doug, I didn't know if you had any further comments on that?

SETH HOPKINS

Sure, I'll jump in. I do agree with your aligning of all the terms and the inability to translate between the various disciplines. Another phenomenon that I think stems from that is those who maybe don't understand the set of terms from one view to the other. We may be on the clinical side and be like, isn't there a gadget out there that you guys can press a button on? And then it's just impossible to narrow it down. We have that on our side, too, where often we refer to a biomarker, for example, as what we were measuring. And we wouldn't call it a marker, we would actually name what we're measuring. So there are aspirational terms, there are actual terms, and a lot gets lost in translation.

DOUG LEE

I fully agree. I think terminology is large for our business at the end of the day. And Seth, I get that all the time — what, don't you have some AI bot that you built? To translate this, I go, "No, that's why we have data scientists and biostatisticians." Going back to Michael Fronstin's point, I think it's an ongoing education. I think everybody's learning at their own pace. I know in healthcare, sometimes it's a little bit slower. And going back to Michael's point, again, it all starts with a definition of what real-world data are. More and more, I'm seeing the definition starting to become clearer, you know — everybody's starting to speak the same language. That's a positive, so I think we're evolving. We're moving in the right direction.

MICHAEL IBARA

Absolutely. So I'd like to thank everybody for attending. I especially want to thank the panelists here, because I think what we demonstrated here is that we're doing the actual work in this area. I encourage you to reach out to Doug, Michael, and Seth about the work they're doing. I think this proves that even though it's hard, it is happening in today's world. I'll turn it back over to you, Ayesha.

AYESHA RASHID

Thank you very much, Michael, and thank you to all our speakers for that very insightful presentation and discussion. We've now reached the end of the question-and-answer portion of this webinar and the webinar itself. If we couldn't attend to your questions, the team at Elligo may follow up with you, or if you have any further questions, you may direct them to the email address displayed on your screen. Thank you, everyone, for participating in today's webinar. You will be receiving a follow-up email from Xtalks with access to the recorded archive for this event. In addition, a survey window will be popping up on your screen. Your participation is appreciated, as it will help us to improve our webinars. Now I'm about to send you a link in your chat box to where you will be able to view the recording of this event, and you can also share this link with your colleagues when they register for the recording. I do encourage you to do so. Now please join us in thanking

today's speakers Michael Ibara, Michael Fronstin, Seth Hopkins, and Doug Lee. We do hope you found this webinar informative on behalf of the team here at Xtalks. Thank you for joining us. Please take care and bye for now.

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