The Rise of Big Data Registries in Rheumatology – Part 1

Transcript

Jeff Greenberg, MD (Guest): Big data is a term, I think, that many people interpret in different ways.

Meghna Rao (Host): Welcome to Rheum Advisor on Air, the official podcast of *Rheumatology Advisor*, one of Haymarket Media's leading publications that focuses on the latest news and research in rheumatology to inform clinical practices. I'm your host, Meghna Rao, the editor of *Rheumatology Advisor*.

In this podcast series, we will be looking at emerging topics in the field of rheumatology from various experts. These perspectives may be related to the diagnosis and treatment of rheumatic diseases, current guidelines, practice management, patient care, and much, much more. So let's dive in.

Meghna: The potential for big data and data registries in rheumatology is immense. In this 2-part series, we're getting updates and talking about the future plans of some of the big data registries in rheumatology.

Now in 2016, CreakyJoints collaborated with leaders in rheumatology to launch ArthritisPower, a patient led, patient centered research registry for the management of patients with rheumatoid arthritis [(RA)] and spondyloarthropathies.

To learn more, I'm speaking with Dr Michael George, an assistant professor of medicine at the Hospital of the University of Pennsylvania, and assistant professor of epidemiology, and a Penn Medicine physician.

Hello Dr George, and thank you for joining me today.

Michael George, MD (Guest): Thanks so much for having me.

Meghna: You know, it's been approximately 5 years since the inception of ArthritisPower. Could you provide some updates, Dr George, on where the registry currently stands in terms of informing research studies and using these patient-generated data as real world evidence, which I believe is one of the objectives of the registry?

Dr George: That's right. So yes, I think ArthritisPower is incredibly exciting. I mean, this now includes nearly 30,000 patients, about 20,000 of [whom] have either rheumatoid arthritis or spondyloarthritis, and these are patients that are very engaged and interested in research. And this is a partnership between patient advocacy groups, patient governors, and the patient participants and researchers, so it's a chance for us not only to hear the patient voice in terms of answering research questions, but also helping to

define what the important questions are to look at.

The registry has been able to look at a range of things such as response to treatments, how patients weigh the risks and benefits of treatments, [r]ecruitment of patients for more standard studies, and a number of different things that have been really exciting to see.

Meghna: You know, that's wonderful. The registry may be especially beneficial in this area, since patient-reported outcomes [(PROs)] as studying points have become such an important aspect of the newer clinical trials, right?

Dr George: That's right. I think that there's certainly a push for us to move beyond just using some of our standard measures, but also capturing patient-reported outcomes that help us understand the impact of treatments on some of the things that are especially important to patients – impacts on fatigue, on ability to interact socially with other people, to do daily activities, all of these things that may not be fully captured in some of our standard measures.

ArthritisPower is great in this respect, through the app, patients can easily report their PROs, and research in the registry has helped define what our important PROs that should be measured in clinical trials are, as well as the performance of some of the [Patient-Reported Outcomes Measurement Information System] (PROMIS) measures. That's been really important in the registry.

Meghna: Dr George, what can you tell us about one of the other goals of the registry, that is, its impact on the improvement of patient care and management?

Dr George: I think there's been large strides here, and there's certainly still so much to do, but the registry is able to impact patient care and management in a number of ways. First, as we've talked about, identifying PROs and how treatments and medications are really affecting patients. There's a lot of potential here to look at comparative effectiveness of different treatments, also adverse events of different medications and how this is really affecting patients.

Actually, we're hoping to launch a study fairly soon kind of looking at common infections. We've been doing ongoing work about the impact of the pandemic on patients. And there's also other ways that the registry can be helpful on [affecting] patient care and management.

It's been used to help recruit patients for more standard studies such as studies of zoster vaccination, and also, we're now looking at vaccine hesitancy and telehealth as well. So all important areas that have a direct impact on patients.

Meghna: I'd like to also talk a little bit more about how ArthritisPower, a direct-to-patient registry, so to speak, compares with the collection of data

from say, electronic health records [(EHRs)]?

Dr George: There's a number of differences here. I guess the 2 main differences are that here the data [are] being collected specifically for research purposes with specific questions and hypotheses in mind, whereas [i]n EHR data, this is primarily for patient care or for billing or some combination of that.

The second is that this is primarily patient-reported data rather than data from clinicians, so we're sort of getting the patient voice and patient report on their symptoms and other things. Although there is the potential to link this to other data sources, to even link EHR data potentially [and] collect laboratory data; we're doing more with wearables and collecting data in other ways remotely from patients.

Meghna: Yeah, and you know, I'm also curious about how efficient the data collection process is, again, in comparison with these other databases. And also, what can potentially be better than how can this be achieved?

Dr George: One of the big aspects of efficiency is in patient recruitment. We have this very large population of patients who are also quite engaged in research and want to be part of research studies. And so, there's substantial efficiency when launching a study above, you know, that where you're sort of waiting for patients to come to clinic and trying to recruit people face-to-face.

[A]s an example, when the pandemic broke out, we launched an initial study, which is still ongoing, and within a couple of months had several thousand patients doing this longitudinal study, reporting their symptoms, and how they're doing during the pandemic. That's just a small example. There's many other projects they're doing, and that recruitment is a huge asset.

Now, of course, the other thing, and I think what ArthritisPower continues to work on, is making sure that patient voice is expanded, and we're getting the full voice of patients broadly. This is a subset of patients who are very interested in research, who are part of this online patient network, and that may not reflect all patients with rheumatoid arthritis and spondyloarthritis.

So one of the big pushes for the registry is outreach and making sure that we're getting a full sense of patients out there. For example, one of the things right now is launching a Spanish version of ArthritisPower to make sure to capture that population that has not been represented traditionally.

Meghna: But with something like this, I can definitely see how registry design is so crucial, right, as well as addressing challenges such as generalizability of data, the procurement and collection of longitudinal data, and, of course, keeping in mind the potential for bias.

Dr George: That's right. I mean, I think this is true of all studies, and the important thing is identifying what the potential biases are and then figuring

out what other questions you can answer, and then if need be, find other sources of data to address those biases.

Meghna: Absolutely. What's next for ArthritisPower? You know, I had spoken with you earlier about the Autoimmune [COVID-19] project, a collaborative effort by several different entities to track the consequences and outcomes of [COVID-19] and autoimmune disorders.

Dr George: I think there [are] a number of things. One of the things that I think is exciting is that ArthritisPower has a strong collaboration with other patient-powered research networks – the Autoimmune Research Collaborative includes ArthritisPower, the Vasculitis Patient-Powered Research Network, IBD Partners for patients with inflammatory bowel disease, and iConquerMS for multiple sclerosis.

So this collaborative kind of allows us to do research that expands across these areas and do a better job of coordinating, and I think that has high potential to do things that broadly affect patients with autoimmune conditions.

There's also, I think, a lot of interesting things using wearables to collect data, linking to other data sources, collecting labs from commercial labs. There's so much that can be done to kind of further expand the reach and the scope of what a registry like ArthritisPower can do.

Meghna: I think that's all we've got time for today, Dr George. Thank you for spending your morning talking with us, despite all the logistic challenges we've had.

Dr George: Yes, well thank you, and thanks for your interest.

Meghna: To tell us more about CorEvitas, formerly known as the CORRONA Registry, we're joined today by Dr Jeff Greenberg, the chief medical officer at CorEvitas and a clinical associate professor of medicine at New York University School of Medicine.

It's a pleasure to have you on this episode, Dr Greenberg.

Dr Greenberg: Thank you, it's a pleasure to join.

Meghna: [W]e've been getting updates from leaders who are affiliated with the different registries in rheumatology. So I'd like to start the conversation there – The CORRONA, now CorEvitas, registry with which you are affiliated is now more than 20 years. I'm curious to know what prompted the name change, first of all?

Dr Greenberg: Well, as you say, after 20 years, and after a 100-year pandemic hit us that's got a very similar name to CORRONA, we thought it was time to change. But we also realized, and had been planning to change

our name as we've expanded our registries. Not just beyond RA to other rheumatic conditions, but to other specialties, including dermatology, gastroenterology, and neurology.

Meghna: Yeah, that makes sense. And you know, the registry was conceptualized with the objective of advancing medical research and improving the quality of patient care in rheumatic and other chronic diseases. Dr Greenberg, we're seeing so much news regarding the registry at conferences and as studies in the various research journals. But could you maybe provide an excerpt of the most recent and important updates from the registry?

Dr Greenberg: Sure, I'd be happy to. We're constantly generating new publications. It's sometimes hard to pick your favorite study, but I'll pick 2 to focus on that I think have some real clinical relevance to rheumatologists.

The first update is that we recently published the results of a 5-year postauthorization safety study that compared the safety of tofacitinib, the first [(Janus kinase)] JAK inhibitor that was approved, vs biologic drugs.

In the study, we used propensity scores and multivariable regression statistical methods to compare the safety of tofacitinib vs biologics, and adjust for differences in characteristics of patients who were starting tofacitinib vs biologics. And the methods are important because patients starting a new therapy, like tofacitinib, particularly in the early years after approval, might have had higher disease activity [and] greater disease severity than some of the older biologics that were in the comparator arm.

So, we were able to carefully measure these differences with the data collecting in the registry, and then adjust for those differences along with a range of other clinical variables. And so in the study, we examined the risk [for] major adverse cardiovascular events or MACE, malignancy, serious infection, herpes zoster, and all-cause mortality. We found that the safety of tofacitinib compared [with] biologics was similar across all of these outcomes, with the exception of the risk [for] herpes zoster, which had a 2-fold increased risk for tofacitinib vs biologics.

In the second study, which was really a collaboration with a group of researchers from the University of Nebraska, led by Ted Nichols, collaborated with the CorEvitas team, examining whether patients [with RA] who have multiple serum autoantibodies are more likely to respond to biologic drugs.

The team, together, leveraged a nested substudy in the registry called the CERTAIN study, [which] collected samples on about 2800 patients who started a biologic for the first time and were followed clinically. And in the study, we found that patients were more likely to respond to biologics if they were seropositive for all 3 of the autoantibodies studied, with [anticyclic citrullinated peptide] (anti-CCP) being the strongest of the 3 antibodies as a predictor of response, but there was really a nice dose response in terms of

patients with all 3 of the autoantibodies having the highest likelihood of responding.

Meghna: That's very compelling data, you know, and just going back to the roots of the registry itself, could you maybe elaborate the difference in the data collection models between traditional databases and CorEvitas, which seems more like a collaborative database, and, of course, the difference in the fact that it is an independent registry without links to the pharmaceutical industry. But Dr Greenberg, what challenges are commonly encountered with such a model and how are they being addressed?

Dr Greenberg: Well, I think the traditional model, as most people know, is to use administrative claims datasets. Those datasets, for some types of studies, can be very impactful and have really strong statistical power, but for studying outcomes like real-world effectiveness, I think that's where the challenges lie.

So typically, those studies will look at persistence on drug, how long patients stay on a drug based [on] refills to a pharmacy; and that is a good surrogate measure of response, perhaps, but it's not really measuring clinical response, and there are a number of limitations with just looking at drug persistence.

So registries, including CorEvitas, really look at the actual clinical outcomes, ask the physicians to measure those clinical outcomes that are traditionally measured in phase 3 clinical trials, do it as part of routine clinical care, and then be able to analyze the real-world effectiveness with validated outcome measures and not surrogate measures.

Meghna: Yeah, and I know you alluded to this before but the CorEvitas Rheumatoid Arthritis Registry, which is now the largest real-world prospective cohort study in the world, collects data from both physicians and patients during [a] first clinical encounter and then longitudinally as well. So what lessons were learned from this registry and how can it be, sort of, extrapolated to the other disease states in rheumatology?

Dr Greenberg: Yeah, we've learned a lot of lessons over our 20-year history. Much of how we run our registries really reflects how our founder, Dr Joel Kremer, interacted with his colleagues, his friends, and as rheumatologists who were investigators in the registry.

I think lessons one was always to put ourselves in the shoes of a busy clinician filling out the questions as part of a super busy day of clinical practice. The lesson is really to take the time to design the form the right way, not to be in an ivory tower, to minimize the work for the physician, and make it as logical and pain-free as possible, while collecting what is really research-grade outcome measures that are needed for the studies.

Lesson number 2 was equally simple. If we expect or ask a busy clinician to report very granular clinical assessments and detailed safety data, you really have to reward them commensurate with the effort that you're asking them

to put in above and beyond their clinic notes. So if you increase the workload and add another page to the questionnaires, you have to pay more to the sites.

Meghna: Now may also be a good time for us to discuss what we were talking about earlier when I first mentioned big data and the CorEvitas registry. Do you consider CorEvitas to fall under the umbrella of big data, Dr Greenberg, and why or why not?

Dr Greenberg: Big data is a term, I think, that many people interpret in different ways. I think that in general, our registry data would not be considered big data. We do have over 70,000 patients across our registries collecting hundreds of variables, potentially generating millions of genomic data points for patients who have genetic markers and genetic samples, but, in general, I think big data frequently uses machine learning and, kind of, unsupervised methods to analyze the data.

Whereas we are doing some studies with machine learning, but the vast majority of our work really focuses on using the clinically rich, clinically deep data, testing specific clinical hypothesis using traditional robust statistical techniques, which is different than how much big data analyses data to derive new insights.

Meghna: Yeah, I think that makes sense. I also saw some recent information that the CorEvitas registry may be involved in data collection on COVID-19 outcomes among enrolled patients. This is very exciting, and honestly the need of the hour.

Dr Greenberg: About 3 months after the pandemic really hit the United States, we developed and then rolled out a very detailed questionnaire for patients who developed suspected or confirmed [COVID-19] infections. And we asked our physicians to report on a range of the clinical risk factors, the detailed clinical presentation, drug treatments that were tried to treat [COVID-19], and, of course, the prognosis and outcome. We do this for all of our safety outcomes, but we did this very tailored for COVID-19 infection.

Then as the vaccine started rolling out to the US, we launched an additional module that collects information about the [COVID-19] vaccines that the patients are receiving, specifically what [COVID-19] vaccine did they receive, what was the date of each dose, and who was the manufacturer.

So, with all this data, which is part of the clinical registry now, we're able to characterize what risk factors exist for patients with RA and autoimmune conditions for developing severe [COVID-19], as well as what is the impact of [COVID-19] infection on longer-term outcomes in RA and autoimmune conditions.

Meghna: Interesting. [I]'m sure this is very useful for informing research and therapeutic options in the future as well. Well, Dr Greenberg, thank you so much for sharing your insights. I wish you and the registry nothing but a lot

of success.

Dr Greenberg: Thank you so much.

Meghna: To give us further insight into the [American College of Rheumatology] (ACR)'s RISE registry, we have with us Dr Christie Bartels, the division chief of rheumatology and associate professor at the Department of Medicine at the University of Wisconsin.

Thank you for speaking with us, Dr Bartels.

Christie Bartels, MD (Guest): Well, thank you for the invitation.

Meghna: Now getting straight to the point. The ACR's Rheumatology Informatics System for Effectiveness, or RISE registry, is now the largest rheumatology registry in the world, with data of more than 2 million individuals and 1000 providers. When it was initiated in 2014, the registry was intended to address and navigate federal reporting requirements for reimbursement and incentive payments, and, of course, allow for data sharing across rheumatology practices.

But Dr Bartels, with the buzzword these days being big data and large databases and all that, where are we today with the RISE registry? Could you describe to us what the registry currently encompasses?

Dr Bartels: That's a great question. So, you know, the terrific thing about RISE is it has continued to grow since 2014, as you mentioned, that there are now 310 different practices enrolled. You mentioned there were 1000 providers. That actually encompasses 2.5 million patients and over 25 million visits.

So there's an enormous wealth of information that's encompassed in that registry, which is really exciting. You also mentioned that, you know, MIPS was one of the original and some of the advanced payment models or one of the impetus to go ahead and create the registry to help support practitioners for submitting their quality reports.

And the great thing that we can tell you right now is that 155 different, either practices or providers, just submitted, just this last cycle through the RISE registry system.

The other great thing is that the registry provides a platform where we can have ongoing data where we can really gauge the quality of care; we can innovate and be ahead of [Centers for Medicare & Medicaid Services] (CMS) Medicare so that we can have the rheumatology specialty driving what those quality measures will be for new programs. And we can also really innovate and think about how we can support practices with practice improvement and CME opportunities, as well as supporting research.

So really, the registry has many different missions and is continuing to grow and thrive, which is really exciting.

Meghna: That's incredible! [S]eeing this as a medical journalist, what I thought to be especially exciting is how the RISE registry can now be used in the study of rare diseases and populations and rheumatology. In fact, I think it also goes nicely along with some of the content in our previous podcast episodes about ultra-rare and novel rheumatic diseases.

Dr Bartels: The great thing is they've been able to dive into some rare diseases already. There was a nice abstract on [Behçet] disease at the last ACR conference in 2020. There also have been projects that have come through RISE to look at systemic sclerosis or to look at sarcoidosis and vasculitis, and again, some more rare diseases that they're anticipating in the future, you know, even opportunities for even more rare things than that.

In the future, they're really hoping that they can do some clinical trial queries through this as well. And, so again, I think it's really exciting to think about, again, how to serve patients with rare rheumatic diseases like you're saying. It's great.

Meghna: Yeah, and, you know, towards the second half of 2020, I also came across ex-ACR president Dr Ellen Gravallese's note on the RISE registry being a tool for rheumatology professionals in terms of capturing critical data and thus furthering research studies. Could you tell us more about the impact of the registry, specifically on research?

Dr Bartels: And I'm glad you asked that as well. You know, there have been a number of research studies supported through this registry, and again, those studies have included investigator-initiated studies, as well as some pharma studies as well.

I think our new vendor also is going to have some opportunities where even individual practices might be able to look at a few projects and/or even things that they could create ACR abstracts or small projects out of using the new interface.

Some other exciting things that are happening in the research realm include the [Centers for Disease Control & Prevention] (CDC) grant that was just funded with ACR to look at lupus, to define new lupus core data elements, and possibly, even look at prospectively gathering PROs and how we can support practices or how we could support collection of patient-centered information, which I think would be really exciting.

Jinoos Yazdany and Will [inaudible] are leading a charge right now to do personalized medicine projects, so that, again, is another really exciting future proposal.

Meghna: Amazing! You know, I think you kind of answered my next few questions, but, you know, just to get a little bit more into it – based on the

evolving needs of the rheumatology community and the scope of the RISE registry that you just spoke about, what lies ahead for the future of the registry and how will it continue to impact and potentially improve patient management and care?

Dr Bartels: We're really at a terrific threshold where you can see through the [A]CR/CDC grant where we're really looking at ways that we can interactively use the registry to figure out baseline data. We have some new capabilities of linking with Medicare data, so we'd have both peer information as well as practice information for Medicare-age patients or patients enrolled in that program.

And then other future things that are out there are, you know, we're trying to get more involvement with academic practices. There have been some barriers to that, including things like greater barriers for data security through academic centers and other factors. But again, we're working to reduce those barriers and increase participation through academic centers. There are a few academic centers that are currently participating.

I think the other fantastic thing is, even beyond the research space, for everyday care of patients and practice. I really am excited about the possibility that this new vendor could have better patient engagement and also, could directly feedback information to practices so that they can benchmark their own [quality improvement] (QI) efforts and/or participate in practice improvement projects through the ACR that could be supported by the registry as well. So, a lot of exciting things, I think, both for research and also for clinical care.

Another fantastic opportunity would be to look at health disparities through the RISE registry, which is work that has begun. We look at race/ethnicity, we can look at geography, a payer mix, other factors that contribute to health care disparities, as well as health outcome disparities. And then we could also look at interventions and changes over time, which really makes RISE a fantastic platform to address health disparities.

Meghna: The RISE registry definitely seems to have great potential in precision medicine, making provision for individualization of therapeutic options, right?

Dr Bartels: Absolutely; which is really an exciting threshold. So, I think it will be exciting to see what happens in the next chapter. Absolutely.

Meghna: [T]he registry's focus on improving quality of care in rheumatology is incredible, to say the least, and I hope to continue to see these wonderful things. Dr Bartels, thank you for your time today, it's been an absolute pleasure.

Dr Bartels: Thank you so much, Meghna.

Meghna: Please stay tuned for more episodes in this series. For more information on *Rheumatology Advisor* and this podcast, you can reach out to us at editor@rheumatologyadvisor.com. We, at *Rheumatology Advisor*, look forward to delivering timely evidence-based news to you. You can also sign up for our free e-newsletters on the site.