Discussion Summary

Real World Evidence in Life Sciences: What Happens After Clinical Trials?

August 2015

Interview Featuring:

**Jamie Powers, DrPH, Principal Consultant and Practice Lead,
Health & Life Sciences, SAS Institute Inc.**

Introduction

In the pharmaceutical industry, the overarching goal is to bring drugs and devices to market faster that improve health outcomes for patients. But what happens once those drugs are in the market and clinical trials conclude? Real World Evidence (RWE) provides deep insight into how a drug is actually used and how it performs in the "real world" with all its variety of settings and circumstances. IIA spoke with Jamie Powers, a Principal Consultant and Practice Lead with the Health Analytics Practice, Health & Life Sciences at SAS Institute Inc. to discuss the impact of RWE in the pharma ecosystem, including the benefits and opportunities RWE provides, as well as some of the challenges associated with implementation.

Q: Please summarize the role of analytics in drug development.

To get a compound or device to market – or from "bench to bedside" – you're looking at potentially an 8 to 12 or even 15-year process. Data and analytics have a critical role at every step, but their role is typically most visible in the clinical trials process. The very regimented and tightly regulated process mandated by the FDA and other regulating agencies is data-intensive. Anybody in the industry, not just the statisticians and analysts, will agree that the data generated is the most critical output of clinical trials. That's how we track safety and measure efficacy. Then commercialization of a product is also a very data-intensive process where we start pulling in data from other sources to make projections about the market performance and make a variety of go-to-market decisions.

Q: What's changed in recent years?

Technology has improved dramatically – data storage, computational power, Hadoop and big data capabilities generally. We can do things faster and cheaper. We can bring a greater variety of data sources together and analyze them sooner. The analytics process used to be constrained by technology infrastructure because, quite frankly, it was expensive. Today, data and analytics technology is driving innovation and productive change in the drug development process.

One of the biggest innovations and opportunities is in "real world evidence" (RWE). This idea is not necessarily new because clinical evidence for approved products has always been of interest. Maybe ten years ago we started seeing journal articles about making the health care system more efficient by better understanding more proactively how medicines and devices are used and perform in actual clinical practice – after they're in the market. And really starting to talk about how we can integrate evidence into development strategy.

Clinical development programs have very specific parameters around what the drug was approved for, but in the real world the uses of that medicine or therapy may be slightly different. Do we really have a good and deep insight into prescribing practices, given that physicians have the discretion to do "off label prescribing" of drugs for slightly modified reasons? And, of course, the efficacy may be greater or lower than anticipated in specific populations of patients. That's where the term "real world evidence" came from.

Q: To a layman the term "real world" sounds a little odd – as though clinical trials have been operating in a less than real world. Would you care to comment?

The objective of clinical trials is to represent the "real world," but they're constrained. Companies recruit physicians who recruit patients with a very specific persona of characteristics and conditions – lab parameters, age range, free of specific diseases, and so on. For the sake of demonstrating safety and efficacy, approval is targeted to a certain type of patient. That's kind

of the real world, and that's the regulatory world we live in right now. But there's a duality in this system. Pharma companies are very focused on patient populations and inclusion criteria and trials which may not necessarily represent the full spectrum of usage in actual medical practice.

That's why we're starting to see a lot more discussion around so-called "real-world" and "pragmatic" clinical trials. These have larger sample size and simpler eligibility criteria targeted more towards that "real world" setting. This supplemental evidence and analysis may prove valuable in Phase 3 of clinical trials that take a "big picture" look at safety and efficacy. There's going to be debate over the coming years about integrating some of this evidence into the current process, or gathering the evidence in parallel. I feel we're approaching a transition point, and someday we'll look back and say, "That's when clinical development programs and real world data started to come together." But for now, typically, "real world evidence" comes into play after a drug or device has been approved.

Q: What can we learn and do with RWE that we couldn't do before?

We can do database studies and quickly generate analyses around certain cohorts of patients. For example, for a compound in diabetes we can interrogate claims and EMR databases to find out, "What's really happening with these patients?" That might help decide whether to change course in a clinical development program.

We can also do more observational studies in the real-world setting, for example, learning about different types of subgroups. If a certain subgroup of patients really respond well to a therapy, that knowledge can inform both marketing and further development plans. A company could also confirm or reject the hypothesis that it should try to get approval for a slightly different set of criteria for the drug.

And we can generate more insightful competitive analysis and commercialization strategies. For example, beyond the standard sales forecasting, a company might pick up on signals that a drug may have stronger potential in one geography than another.

Finally, researchers are making a distinction between efficacy and comparative effectiveness, trying to understand all the different phenomena influencing different disease areas. RWE is central to their efforts.

In short, we have more and better data, plus better tools in the analytic ecosystem to work with that data and make the outputs easily digestible. So with RWE we can do better science and get better results quicker.

Q: How does RWE accelerate analysis and decisions?

Compiling a set of real world evidence does not, in and of itself, accelerate the process. It's what we do with the data and analysis that can create efficiencies and speed.

We have use cases that are both compelling and disruptive. The analyses of the performance of drugs and devices can be extremely complex and time-consuming. Suppose we are trying to analyze and document how beneficial a compound is to certain people. We'd typically bring in clinical and claims data, plus some EMR data, and we might have observational studies as well. Then there's an iterative cycle of sorting through those data sources, programming specific analyses, then changing our minds or asking new questions, and the cycle goes on.

We're getting very close to being able to get the stakeholders together to look through all the data and try different hypotheses in real time. Maybe we can rule out lines of inquiry that would have cost us months of effort, or perhaps discover more productive new things to investigate. We can use today's technology to shorten cycle times and do in a few hours what used to take weeks. That's a pretty exciting innovation.

But it's also potentially disruptive because people are used to doing things a certain way. They assume that analysis takes a long time and "that's just the way the world works." So we try to impress on people that this is a very real scenario – and a meaningful contribution to pharmaceutical analysis and science.

Q: What are some of the main challenges in establishing RWE programs?

One of the biggest challenges is dealing with that disruptive innovation, coming in with a fresh point of view that things don't have to operate the way they always did. Doing analyses faster, cheaper and more efficiently in no way compromises completeness or quality. What we're actually doing is increasing the bandwidth of analysts (who are in short supply) so we can do more with the same resources. There's a technology side to this challenge because people have assumptions about how fast – or rather slowly – they can work.

The pharmaceutical industry is well behind financial services and online businesses when it comes to real-time analytics. So we argue by analogy: "How do you think Amazon knows instantly what purchase suggestions to make to you? It's all algorithms in the background being processed on state-of-the-art technology. That's possible in health and life sciences, too." But seeing is believing, so we're doing lots of demonstrations to help people push the "I believe" button.

People tend to assume that data presents a major challenge, especially assembling and preparing a variety of data sources for analysis. But they're underestimating the capability of data management today. On the one hand, master data management and data quality and ETL software is very powerful, and it needn't be mysterious. People commonly bemoan the fact that health care data is so fragmented; however, more and more of the structured data in health care is well managed. On the other hand, Hadoop and the related technologies of "big data" enable large and disparate data sets, structured and unstructured, to come together for analysis.

We advise customers to take data management seriously, and scrutinize the data you get from third parties. But don't delay in putting your data to work and challenging the status quo regarding what you can accomplish.

Q: What are some of the best practices and necessary components of an RWE program?

We've already touched on the data management, analytics, and technology components. Another thing that's really important is ensuring that RWE initiatives align very closely with clinical development, commercial pharma, global regulatory affairs, and other stakeholder groups. A pharma company is a diverse enterprise, and a successful RWE program can support many parts of it. Clinical is the primary focus, but RWE can drive better questions and answers for other business functions as well.

If these other interests are not part of the RWE mix, I'd suggest that the leaders of those functions need to come together and form a sort of consortium because everyone's interested in maximizing the value of the huge investments made in R&D. So the key question for the leaders of RWE initiatives is: "Are we continually aligning with the concerns of the other business partners?" I think that's high on the recommended best practice list.

Q: What are the bottom-line benefits of RWE for biopharma companies?

The overarching goal in this industry is to improve patient outcomes and bring drugs and devices to market faster. That has the biggest impact on the bottom line. Data, analytics, and technology enable companies to accelerate the "bench to bedside" process and make it more efficient. Specifically with RWE, they can make faster and better decisions about strategy for compounds and create a "virtuous cycle" of feedback into the R&D pipeline. As you expand the informational scope of RWE, you can inject that feedback into R&D at earlier stages. And as already mentioned, if you have a seamless technology and data platform for RWE, all the concerned parties can be at the table discussing and evaluating hypotheses and scenarios.

Q: What are the associated benefits to payers, providers and ultimately patients?

RWE creates an opportunity for pharma companies and insurers to collaborate as never before. They are interested in much the same analyses, but from slightly different angles. Pharma companies want the evidence that gets their products on the insurance companies' formularies. Payers want continuing evidence that the products are delivering cost-effective results. Then add in providers, who are generating much of the new data, and who very much want to better understand their clinical and financial performance, and you complete the loop. Pharma companies want to supply health systems with new therapies and devices, and payers want claims and payments to work smoothly. The players simply have a lot of data and analytics needs in common, and RWE can enable collaboration across the health care ecosystem.

In the center, and the most important stakeholder, you have the patient. RWE aims to generate the insight to improve clinical care through cost-effective therapies. It could also generate information of direct value to patients – information about how best to manage their "journey" through the system and participate in their care. After all, the whole ecosystem is really centered around the patients and the data they generate. A feedback loop can serve them, too.

Q: How do you see RWE and its value evolving over the next few years?

I see more heightened awareness of the possibilities and increasing demand for RWE. I see more investment coming from different types of companies in the ecosystem. In a few years (I don't know how many), we're going to see regulatory agencies really take a closer look at these large, simple, pragmatic trials and perhaps even rebalance the whole clinical development paradigm. Other countries have been innovating in the regulatory space and I hope we see that trend take hold in the United States. The FDA is becoming more flexible in special cases, such as fast tracks for "orphan" disease categories where there's no compound available, and

iianalytics.com

"compassionate use" trials of oncology compounds. And the spheres of RWE and "Phase 4" post-approval trials (primarily focused on measuring safety) may converge somewhat. The core question remains, "Can we make regulatory decisions on data earlier, hence bring therapies to patients more quickly?"

I also see the market demanding more out of their data and analytics technology providers, including SAS. Companies are not just looking for technology foundations. They want help, playbooks and recipes, for putting data to work in new ways. That's why SAS is so focused on business use cases and scenarios for RWE. We want to enable and empower pharma companies, and the rest of the health care ecosystem, to succeed through analytics.

Q: Who needs to appreciate the power of RWE, and what's the top thing they need to understand?

There are many internal stakeholders in pharma companies who should be listening to the story, in commercial as well as R&D and clinical development. There should also be interested players in health economics, epidemiology, and academic health care research. And as we've discussed, the entire ecosystem can benefit from collaborating around more "real world" evidence.

What these stakeholders need to know is that technology can speed the delivery of information and insight, and accelerate decisions, in ways that enable – and in no way compromise – the science. And the non-technical person can work more directly than ever before with the data, the analytics, the evidence.

Additional Information

To learn more about this topic, please visit **www.sas.com/lifesciencs**

About the Interviewee

Jamie Powers, DrPH, is a seasoned analytics professional with a doctoral degree in biostatistics and more than 10 years of experience in the clinical R&D analytics space. He is a member of the SAS Health & Life Sciences division, which works with pharma, biotech and CRO customers to discover the power of SAS big data analytics and machine learning. Beginning as a phase 2-4 biostatistician and later taking a leadership role in a predictive analytics group, he developed techniques to drive value in many topics in pharma R&D. Powers also recognized the trend in harnessing big data from various sources to inform clinical R&D decision making. He empowers SAS software users by combining business knowledge with technical expertise.