The Power to Pivot: Decoding CNS Trials with Data Analytics

Jesse Kooker, MPH

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An Interview with Jesse Kooker, MPH, VP of Clinical Data Sciences, WCG's MedAvante-ProPhase

Jesse Kooker is not what you'd expect from a self-proclaimed "data geek." In his charming and self-effacing way, he makes data seem undeniably cool.

"It's an exciting time to be a geek," says Kooker. "It's not that data are suddenly compelling. They always have been. It's just that now the world is finally catching up."

Kooker is a former US Army captain. He has an undergraduate degree in Quantitative Methods and graduate degrees in both Epidemiology and Biostatistics. During his 20-year-career in the clinical research industry, he's worked for a number of top tier biopharmaceutical companies and contract research organizations. Today, he's MedAvante-ProPhase's VP of Clinical Data Sciences.

When Kooker looks at the clinical development industry, he sees increasing competition for the best and the brightest talent. Especially for "data dorks" like him, who are helping biopharmaceutical companies to transform copious amounts of data into valuable, actionable information.

"It's no surprise that data play a critical role in clinical development," says Kooker. "What's interesting is how our industry is finding more impactful ways to use that data. For example, right now we gather a ton of data from clinical trials. We understand when a drug has been effective and can measure how effective it has been. But we don't always understand why it has been effective. We don't completely understand the physiological impact of our intervention. What lever did we pull and why did it work? I think answering these questions will be the future of clinical data science."

Today, through his work at WCG's MedAvante-ProPhase, Kooker is helping clients to get a clearer picture of what's happening with the patients in their clinical trials. He leverages data to reduce the noise, the bias, the masking of signals and the placebo effect that can negatively impact the results of central nervous system (CNS) studies.

"The collection of high-quality, reliable data is critical in any trial," said Kooker. "But in no therapeutic area is it more important than in CNS, where the consequence – and likelihood – of collecting poor quality data is so high."

In therapeutic areas other than CNS, objective biochemical measurements resulting from lab work, urine cultures, and radiological studies can be

used to diagnose illness and, in clinical studies, quantify the effect of a new drug or therapy. In CNS, the measurements are often subjective – left to the interpretation of the individual investigator. And these observations are not clear cut. Physicians and researchers rely on patient interviews and examinations to diagnose and monitor the effects of their treatment. For example, consider the challenges of measuring the memory loss of a patient suffering from Alzheimer's Disease, the degree of muscle tremor in a patient afflicted with Parkinson's Disease, or measuring a change in the symptoms of someone with Schizophrenia. These are all subjective assessments – open to individual investigator bias. The clinicians of MedAvante-ProPhase provide expert advice, standardization scales, and supporting technology to mitigate the subjective bias associated with CNS trials.

The clients of WCG's MedAvante-ProPhase tend to have strong, vocal scientific and clinical leadership teams who value the expertise and experience that thought leaders like Kooker bring to the support of trials with subjective endpoints, like those in CNS. Research sponsors bring the company in early to assist in protocol design, scale selection, endpoint determination and site selection; activities which can all be optimized by incorporating MedAvante-ProPhase's clinical expertise and deep experience with data analytics.

"There are literally thousands of measurement scales for CNS, and yet most biopharma clients keep using the same four," said Kooker. "They use them because they're comfortable with them. They've used them in the past. We've used a lot more scales than they have, and we've used them across a number of client studies. We participated in the development of the influential PANSS scale and have the most experience using it. We can guide our clients to the use of better, more appropriate scales for their purposes. Or to more appropriate primary endpoints and better secondary, supporting endpoints. We can even say, 'What claims do you want to make in your marketing materials? Here is the scale that has worked best to achieve what you want, in this particular population.'"

WCG's MedAvante-ProPhase uses data in another unique way: to inform our clients' selection of investigators for a study. In addition to information on patient population, previous research experience, competing trials and even contract and budget negotiation timelines, MedAvante-ProPhase can show sponsors past performance for a given investigator in the CNS specialty. Our specific investigator information informs clients in their selection of the most appropriate sites for their studies: the highest

enrolling investigators with the highest quality clinical performance. Adds Kooker, "With CNS, perhaps more than in other indications, site quality metrics matter – often more than enrollment data. Since in CNS studies you can't get objective data, clients must have consistent and high quality data from investigative sites – this is the outcome of our solution".

Of equal importance to site selection, the clinical experts of WCG's MedAvante-ProPhase advise clients on protocol design. Using advanced principles of Adaptive Trial Design, new protocol designs allow sponsors to optimize trial outcomes through real time pivots or adjustments in the course of their trial. In no indication are these real-time adjustments more important than in CNS, where trials can last up to six years. As for assuring the highest quality of data, during the conduct of the trial, MedAvante-ProPhase provides clients our proprietary technology and administers training to investigative sites – all intended to reduce the noise of the placebo effect (especially prominent in CNS trials), amplify signal detection, and get a clearer picture of what's happening to patients so they can adjust the trial accordingly.

"As a member of military and a scientist, the logic, order and precision of data analysis appeals to me. Analytics tell you, quantifiably, if there is a relationship between two points and what that relationship is. If you compare enough data points, you begin to understand the relationship to a degree of reliability that allows you to predict what's coming next. With that predictability comes knowledge, which we use to inform our clients' trials."

Biopharmaceutical organizations recognize the extraordinary power of data but vary significantly in how they put it to use. Kooker has identified four subgroups—or archetypes— that seem to define the attitudes and approaches of research sponsors across the clinical development industry:

1) The Uber Conservative

This group is comprised of the largest, most conservative companies. They leverage data in all aspects of their business. They implement costly technologies and build massive infrastructures to support the collection and analysis of their data. Drawbacks of the Uber Conservative approach include significant expense, competition for talent, and being limited to one's own data set (MedAvante-

ProPhase clients enjoy the peer benchmarking and industry-wide metrics that only an external partner can provide).

2) The Cautious Mover

Large and mid-sized biopharmaceutical companies that struggle with the idea of outsourcing. Cautious, careful and slow to change, they are also reluctant to spend money to build an expensive internal infrastructure that will require considerable maintenance and support. Their internal debates are fierce.

3) The Nimble Outsourcer

Small to mid-sized companies that only have a few compounds in their pipeline. These companies maximize their data, using it to make adjustments in real-time because they cannot afford to waste time or money. They are nimble, with management teams that are attracted to innovation and efficiency.

4) The All or Nothing.

Very small, single-compound companies. Everything is riding on the success or failure of a single compound, and decisions are made by just a few people in management. Data is everything, and these companies either can't afford it, or can't afford to live without it.

Clinical and scientific teams tend to grasp the value of the WCG MedAvante-ProPhase offering pretty quickly, but operations executives, who are more familiar with using analytics to improve trial performance, are starting to catch up. They recognize the competitive edge that real-time analysis of trial results can give them.

"The point of a clinical trial is to change something. To intervene, to measure impact, and quantify the effect created," said Kooker. "It's not just about collecting and organizing data. It's about collecting the right data. Having the clinical context to understand your data. Being able to draw accurate, reliable conclusions from that data. And using the knowledge gained from analysis to intervene in trials, in real-time, to change their course. At MedAvante-ProPhase, we give sponsors the power to pivot. With sophisticated technology and the best scientific minds in the field, we generate the highest quality of data. Because in the absence of truly objective data, the quality of the data you generate is everything".

About the Author

Jesse C. Kooker currently serves as the Vice President of Clinical Data Sciences for WCG's MedAvante-ProPhase. His previous experience includes leading global data science teams in both the sponsor and CRO sides of the industry, with a focus on efficient operational delivery. Jesse has significant regulatory experience and has overseen the submission of multiple compounds across several FDA divisions, from a data submissions perspective. Jesse holds a dual Masters in Public Health (Epidemiology/Biostatistics) from Rutgers University.

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