CLINICAL INFORMATICS NEWS

Using Real World Data to Enhance Clinical Trials

13**JAN**2017
By Sujay Jadhav

Randomized clinical trials (RCT) remain the trusted standard for assessing pharmaceutical drug and medical device safety and efficacy. An RCT uses a carefully planned experimental framework to compare an intervention/ treatment with a control, investigating the effect of each treatment option on a defined outcome. Patients participating in an RCT are carefully screened based on precise clinical criteria, and usually have very similar characteristics. Unfortunately, life does not always mirror the idealized world of an RCT.

Patients often have characteristics, experiences, and treatment protocols that differ from the controlled environment of RCTs, and therefore the information gained from the RCT may not “generalize” to a broader group of patients. To evaluate real world product effectiveness, more information is often needed on how specific treatments perform within different age groups, genders, races, and ethnicities, as well as how they perform when patients have differences in disease severity and/or co-morbid conditions that require other medications.

Healthcare is experiencing an avalanche of electronic data with sources including social media, smart phones, activity trackers, electronic health records, insurance claim databases, patient registries, health surveys, and more all having the potential to deliver vast amounts of accessible patient health and medical care data from outside of the controlled RCT environment.

This real world data (RWD) can provide important health information about patients in the social context of their day-to-day lives. To fill the knowledge gap between clinical trials and actual clinical practice, research using RWD is being conducted to help understand how treatments work when applied in clinical practice environments. The hope is that properly analyzed RWD can provide key insights that will help drive down medical costs, as well as improve both product safety and effectiveness.

Real World Evidence as the ‘New Normal’

RWD can best be described as data collected under normal day-to-day circumstances found outside of a randomized clinical trial. By itself, the data is meaningless but becomes real world evidence (RWE) when context about what is being measured is added, and the data is analyzed within that context. What is ultimately required is RWE that can be used to evaluate treatment effectiveness in daily settings to guide clinical decision-making and answer scientific questions.

RWD support for pharmaceuticals and medical devices is increasingly becoming the new normal. Acknowledging this trend, the FDA recently released its draft guidance document entitled "Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices." In this document, the FDA clarifies how they "evaluate real-world data to determine whether it may be sufficiently relevant and reliable to generate the types of real-world evidence that can be used in FDA regulatory decision-making for medical devices."

Proving safety and efficacy through an RCT prior to product launch is no longer enough to guarantee success and profitability in an increasingly competitive healthcare environment. Pharmaceutical and device companies must now demonstrate evidence of successful real world outcomes to differentiate their products in a saturated and competitive environment, while also satisfying the additional scrutiny and demands of regulators, insurance companies, healthcare providers, and individuals to whom the products will be prescribed.

Real World Studies

Real world studies determine how new drugs or devices perform beyond the scope of clinical trials. Using a variety of data sources, pharmaceutical companies, healthcare providers, and insurance companies can determine the effectiveness, safety, and cost benefit of a medicine by mining the records of tens of thousands of patients. While accessing and analyzing large amounts of data can be unwieldy, generations of RWE is becoming easier thanks to advances in data management and analytics. Technologies such as Hadoop, for example, enable large and disparate data sets (structured and unstructured) to come together for analysis.

Another way of generating RWE is via practical clinical trials that relax some of the constraints of a normal RCT to better reflect the daily conditions of clinical practice. In practical trials, patients may be randomized to various treatments under study, with additional or subsequent care being determined by the doctor based on their clinical judgment. Instead of a placebo control group, practical trials usually include a comparison group receiving standard care.

Because there is more room for variability in real world studies, proper study design is especially important and care must be taken to assure quality data sets are utilized for analysis.

One example of a real world study evaluated the performance of Sanofi's diabetes drug Toujeo in patients who switched to this medication from another form of basil insulin. In this study, the U.S. Predictive Health Intelligence Environment (PHIE) database, containing a substantial amount of patient level information, was analyzed to assess changes in average blood sugar levels (HbA1c) and presence of hypoglycemia in patients up to six months following the switch. Results demonstrated a successful switch to Toujeo in a real-world setting. Sanofi is following up with 3 other practical clinical trials that are designed to demonstrate product effectiveness.

Another example of the utility of RWE comes from the world of Transcatheter aortic valve replacement (TAVR) devices. TAVR devices are a new and innovative class of medical devices that allow treatment of patients with diseased aortic valves who are judged too-high a risk for conventional aortic valve replacement. In 2011, two professional societies involved in cardiovascular care, the American College of Cardiology (ACC) and the Society

of Thoractic Surgeons (STS), worked together with the FDA and the Centers for Medicare and Medicaid Services (CMS) to create a new pathway for the approval of TAVR devices in the U.S. that would ensure the most safe and effective adoption for patients in need. The cornerstone of the strategy is a new TAVR registry that builds on the pre-existing registries administered by both societies. The ACC and STS have developed common data formats and data collection methods that have expedited use of the registry to conduct prospective, randomized, post-market trials of different valve products. Evidence generated by the registry has already resulted in the 2013 FDA approval of expanded indications for the Sapien Transcatheter Heart Valve.

Finally, The Salford Lung Study, currently being conducted, is the world's first Phase 3 pragmatic randomized clinical trial of a novel drug therapy. This study compares the use of a once-per-day inhaled corticosteroid against normal course of care for both COPD and asthma patients. Patients are treated and monitored through use of electronic medical records. The drug trial will test both the clinical effectiveness of treatments and their impact on patients' ability to adhere and realize long-standing benefit.

Benefits of Real World Evidence

The generation of RWE provides numerous benefits:

- **More Accurate Conclusions about Medications:** RWE is often derived from medical data gathered from thousands of patients in real time. This larger dataset allows industry stakeholders to form more accurate conclusions about the effectiveness and ROI of a medication as it's being prescribed.
- **Provide New Insights:** As data from multiple, disparate sources is integrated and analyzed, new insights can be uncovered - such as discovering that a slightly less effective but significantly less expensive medicine is the most cost effective option for a certain patient population. In addition, RWE can provide insight into disease epidemiology.
- **Better Health Outcomes:** The ability to transform RWD sources such as claims data or electronic medical records into RWE can improve health outcomes for patients by helping pharmaceutical firms be more efficient in drug development and smarter in commercialization.
- **Satisfy Payer Demands:** Payers - whether they are private insurers, Medicare, Medicaid or other government programs - require evidence that establishes the cost-effectiveness of a medicine before they agree to pay for it. Studies generating RWE can easily satisfy this demand.
- **Reduce Medical Costs:** Studies generating RWE can provide important information about how best to use medications, thereby reducing medical costs.
- **Increase Patient Safety:** By collecting post-RCT information about a drug in real time, RWE helps researchers identify medication side-effects and contraindications, thus limiting harm to patients.
- **Increase Personalization of Medical Care:** RWE can help researchers identify classes of patients who can benefit the most from a medication, due to their illness, their genetics, or other factors.
- **Discover New Indications for Existing Treatments:** Large datasets inherent in RWE generation allow researchers to discover patterns that were not visible with smaller samples sizes. These patterns may reveal new indications for medications.

- **Identify New Markets and Patient Populations that are Underserved:** Using population data on disease trends and medical outcomes, real world insights can be gleaned that inform the development of new products to serve new markets.
- **Gain Payer Approval of Expensive Treatments:** Pharmaceutical companies can use RWE to demonstrate that expensive therapies can provide real value relative to cost for specific populations, thereby winning payer acceptance of these therapies in these cases.
- **Improve ROI for Pharmaceutical Companies:** RWE insights can speed the development of new therapies, provide verifiable evidence for payers and help pharmaceutical companies differentiate their brand in the health care market.

Technological advances are providing a trove of data sources for researchers, which hold enormous potential for improving the quality, safety, efficiency and cost effectiveness of treatments. RWE studies are useful complements to RCTs, because they reflect the day-to-day utility of drugs, devices and other products, providing a more comprehensive view of patient response to medications, a better understanding of disease patterns, additional safety data, as well as data for economic analyses. RWE can also help to better inform healthcare decision makers and policy leaders. Pharmaceutical companies and Contract Research Organizations need to stay at the forefront of new developments in RWE, data sources, analytical techniques, and study methodologies to ensure they remain competitive and maximize ROI on new products.

Sujay Jadhav
CEO | goBalto

Sujay Jadhav *Sujay has over 20 years of experience with leading Silicon Valley software providers with a life sciences focus. Sujay was most recently Senior VP of Global Corporate Strategy and Development at Model N, where he filled multiple roles, from corporate development to overseeing their life sciences analytics and SaaS business unit. Sujay started as employee #6 and was instrumental in the growth of Model N to 600 employees, over $100M in revenue, and its eventual IPO (NYSE: MODN). His career has also included strategy consulting at Booz Allen Hamilton, product strategy at CommerceOne, and general management roles at Singapore Telecom. Sujay received his undergraduate degree from the University of South Australia and an MBA from Harvard University.*