Achieving More Precise PATIENT RECRUITMENT

Secondary data and advanced analytics offer evidence-based approach to improving protocol validation, site allocation and investigator recruitment.

Contributed by

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While pharmaceutical market researchers have benefited from comprehensive, secondary data sources and sophisticated analytics for years, the R&D functions and clinical research organizations (CROs) were on the outside looking in when it came to access to this information and analytical approach.

However, today R&D pharma executives and CROs can tap into these rich data resources to improve their patient recruiting productivity by identifying the most relevant patient populations around the globe.

Using tools and methodologies of the pharmaceutical marketer, R&D personnel and CROs can now base their recruitment decisions on evidence of physicians' patient populations and treatment practices. This will allow for R&D and CROs to avoid costly protocol amendments, mitigate limited patient populations, speed the investigator recruitment process, improve recruitment success rates, and reduce the risk that investigators will miss their targets.

A Better Understanding of Patient Populations

Sharper insight into patient populations is made possible by three key databases and a two-stage process that uses these databases to complement one another. Through this methodology, it is possible to: determine if the study protocol will yield enough patients to meet the required end points; and identify the physicians who are most likely to have a sufficient patient pool for the study.

The first database is of integrated hospital, medical and pharmacy claims on millions of anonymized patients. It is "longitudinal" or follows patients' activity over time and is gathered from nearly 90 health plans in the United States, featuring inpatient and outpatient treatment claims, diagnoses, procedures, prescriptions and demographics. Findings are projected to the total insured population. The second, available in Europe, is a longitudinal data set comprised of electronic medical records (EMR) gathered from medical practices, while the third is a longitudinal database of anonymized prescription transactions gathered from pharmacies and traced back to the prescriber. Capturing details on 65 percent of all retail prescriptions filled in the United States, the database provides physician's specialty, patient year of birth and gender, product form and strength, quantity dispensed, days of treatment supplied, and method of payment. It also allows for tracking of anonymized individuals over time by a HIPAA compliant encryption.

Successful Trial Execution

There are three important steps in successful trial execution:

1. Protocol Validation: Applying an evidence-based study design using longitudinal patient data enables researchers to assess the impact of inclusion and exclusion criteria on patient populations. And, because different types of secondary databases yield sample sizes much more robust than those acquired through primary research, results are usually far more accurate. This allows companies to understand quickly and easily if there are enough of the right types of patients to support their clinical trial needs.

Evidence-based trial design can be conducted on a trial-by-trial or on an ongoing basis by the clinical development organization. Through the longitudinal health plan integrated claims and physician practice EMR databases, it is possible to quantify the number of patients with a specific profile, as defined by age, gender, diagnosis, disease severity, treatment pattern, co-morbidities, drugs prescribed, adherence, prior hospital stays, associated procedures, laboratory tests, economic burden, and the treating physician's specialty.

For example, a large global pharmaceutical manufacturer needed to know how many patients diagnosed with multiple sclerosis would fit its study criteria in Germany. By systematically applying exclusion criteria to the 291,256 patients initially identified through the physician practice EMR database, the company learned that there were 12,740 German patients suitable for its trial. (See chart on opposite page.)

2. Site Allocation: An evidence-based approach to trial site allocation improves the decision-making process and provides tangible documentation for patient prevalence, market value and expected country performance.

Additional benefits include upfront feasibility evidence, the ability to standardize and shorten the allocation process, proper allocation to the right low-cost emerging markets, increased reliability of trial allocations, and consistent risk management. Adding value to the trial allocation process opens up significant cost-saving opportunities during the trial execution. This allows for researchers to increase the productive portion of initiated sites (>1 patient), shorten the recruitment period, mini-

mize the need for back-up countries and sites, avoid expensive late-stage protocol amendments, optimize utilization of resources, and reduce time to market.

Allocating clinical trials more strategically and tactically delivers better informed decisions. By utilizing a combination of global data sources that track worldwide drug sales and prescriptions as well as physician surveys that help size local patient populations diagnosed with certain conditions and provide a view of the existing standard of care, it can show where patient groups treated for specific diseases are clustered geographically. Further, potential market values for each country can be assigned to help in the decision making on where to place clinical trials.

3. Investigator Recruitment: Developing a target list of clinical investigators takes some additional time up front, but greatly reduces the chances that a CRO or pharma R&D function will select an investigator who cannot deliver in the end. CROs have long reasoned that the most expedient way to meet a study's quota is to enlist clinical investigators who've successfully completed prior trials.

To identify other prospective investigators, CROs purchase physician lists, access data from the Food & Drug Administration on other studies, and consult publicly available population data. However, these sources only reveal high areas of concentration for a condition. They offer no visibility to patients' prior medication use, which can be an exclusion criterion, nor do they link medication use with disease states and patient demographics.

In an ideal world, longitudinal prescription data collected from pharmacies would include the diagnosis for which the prescription was filled – indicating precisely the physicians who had the best patient populations for a study. However, since pharmacy prescription data do not include the diagnosis, it must be inferred from what is known. If a disease is treated almost exclusively by one physician specialty, or if a drug is used for a single indication, then the physicians in the pharmacy prescription transactions database can simply be sorted into deciles to find those with the highest volume of: prescriptions written, therapy initiation, and treatments in a certain drug class for first or second-line therapy. However, there are times when it is necessary to create a predictive model to estimate the number of patients whom individual prescribers are seeing for a particular condition. In such situations, the clue to the diagnosis can be found in the physician specialty, combined with other attributes such as the patient age and the average daily dose of a medication.

Another predictive modeling approach involves using health plan data to isolate anonymized patients with a clean diagnosis. Those patients and the physicians who treat them are then profiled using an array of attributes from patient age and gender, to physician specialty and geography, to medication history, daily dose, and payment method. At this point it is possible to identify those factors that are both high and low predictors of the diagnosis.

The next step is to create a statistical model capable of predicting the diagnosis in question when applied to the longitudinal prescription data. The goal is to be able to place individual physicians listed in the pharmacy prescriptions transactions database into deciles based on their estimated volume of patients having the particular diagnosis and desired patient demographics. To test how well the model performs, it is applied to the subset of this database for which claims data also exists, comparing what the model predicted with the diagnoses actually contained in the claims database.

MS Patients in Germany Reduced by Exclusion Criteria

Diagnosis of Multiple Sclerosis

		Patients in Germany: 291,256
Exclusion factors	***Excluded***	***Remaining***
Ages under 18 and over 55 years	-79,870	211,386
Pregnancy	-392	210,994
Manifestation of MS other than RRMS	-129,507	81,487
Corticosteroid treatment	-19,257	62,230
Other chronic disease (ICD: D80-89)	-637	61,593
Diabetes mellitus	-490	61,103
Active systemic infections	-294	60,809
IFN- or glatiramer acetate	-28,861	31,948
Immunosuppressive medications	-1,372	30,576
Immunoglobulins	-294	30,282
Cladribine or cyclophosphamide	-245	30,037
Myocardial infarction	-49	29,988
History of angina pectoris	-392	29,596
History of symptomatic bradycardia	-392	29,204
History of sick sinus syndrome	-637	28,567
Class III antiarhythmic drugs	-196	28,371
History of chronic disease of the immune system other than MS	-637	27,734
Uncontrolled hypertension	-490	27,244
Active pulmonary disease	-294	26,950
Chronic therapies for asthma	-735	26,215
Chronic liver or biliary disease	-539	25,676
History of substance abuse	-11,417	14,259
Progressive neurological disorder, other than MS	-1,519	12,740
Remaining patients for clinical trial		**12,740**

Source: IMS LRx Longitudinal

A Welcome Solution

Today, when drug sponsors and CROs alike are faced with rising study costs and mounting time pressures, a well-established method for speeding and perfecting trial design, allocation and investigator recruitment is a welcome solution. PV

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