GNS HEALTHCARE

Subpopulation and Biomarker Discovery for Precision Medicine

Identifying patient populations for precise drug targeting to improve drug development success and optimize commercial strategy

Precision medicine is increasingly focusing the biopharma industry on better outcomes at lower costs. Given the high failure rate of novel therapies in clinical development and the increasing need to prove the value of newly approved drugs in the real world, biopharma companies are charged with identifying the subpopulations of patients who benefit most from a new or existing treatment. The dramatic decrease in sequencing costs and the ability to measure a variety of '-omics' from the smallest amount of tissue, now provides the ability to identify these subpopulations in an unbiased, data-driven way.

According to a survey from BIO, the world's largest biotech trade association, drug development programs that included selection biomarkers saw their Likelihood of Approval (LOA) rate from Phase I through approval increase by a factor of three compared to those who did not (25.9% to 8.4%).[1]

It's important to discover relevant biomarkers in patients who respond positively to a drug in early clinical trials in order to optimize and streamline later trials. Uncovering these pertinent biomarkers enables biopharma to precisely recruit patients, calibrate inclusion criteria and develop a companion diagnostic.

Defining populations for clinically meaningful benefit

Analyzing the complete dataset from phase two clinical trials typically yields inconclusive results regarding the efficacy of the drug. In order to extract value from this data and discover which patients benefit, it's crucial to understand the cause-and-effect relationships within the data. This requires identifying common biomarkers for those patients who benefit from the drug in relation to the trial population as a whole.

By identifying biomarkers and subpopulations during the clinical trials process, biopharma can more accurately define the inclusion and exclusion criteria for Phase 3. Recruiting the right patients can not only improve the probability of success, but also provide insights into how the drug would perform in the real world.

Once the drug has been delivered into the hands of physicians and patients, real world data is generated based on its effectiveness for both primary indications and off label use. By analyzing this RWE, biopharma can identify subpopulations for whom the drug is more beneficial, as well as potentially discovering new indications for its use.

In order to deliver value-based therapeutics, biopharma needs to leverage the vast data sets available and utilize powerful AI technology to speak the language of precision medicine.

The challenge of biomarker discovery

Developing a drug without a known biomarker, or the wrong biomarker, can lead to trial failure and unnecessary expense. Therefore, discovering a biomarker as early as possible is key to accelerating the drug development process. Unfortunately, identifying relevant biomarkers is labor intensive, time consuming, and expensive.

Common statistical methods that rely on predictive modeling do not allow analysis of the complicated correlation structure in the clinical and preclinical data simultaneously to identify biomarkers and potentially may lead to inaccurate patient stratification. Without a clear understanding of the confounding relationships among these variables, those statistical methods might result in mistakenly selecting a confounder rather than a true driver of the clinical outcome or treatment effect for further study.

1 *Clinical Development Success Rates 2006-2015, BIO Industry Analysis, June 2016*

The GNS subpopulation solution

GNS Healthcare's Subpopulation tool allows biopharma to run a complete trial dataset and quickly identify predictive biomarkers to select patients with a high probability of treatment benefit in a follow-up trial. It also prioritizes prognostic biomarkers that could identify disease drivers that when perturbed show a change in the outcome of interest.

The GNS Subpopulation tool:

- Identifies a set of predictive response biomarkers
- Determines confounding variables and removes them from analysis
- Allows the user to optimize the set of biomarkers by varying cut- points and the ability to visualize the impact on the corresponding hazard ratios and information on the biomarker prevalence
- Prioritizes prognostic biomarkers to identify disease drivers

The Subpopulation tool eliminates the time-consuming current methods of biomarker selection, allowing scientists to explore all potential biomarkers and select the most relevant predictive biomarkers for a trial. The tool accelerates the process of preparing for later phase trials by reducing biomarker discovery from months to weeks.

The REFS Advantage

The REFS causal machine learning platform can be an integral part of your subpopulation identification process by:

- Using retrospective analysis to generate biomarker hypotheses
- Identifying predictive biomarkers to enrich patients in clinical studies
- Using data to understand disease progression and treatment impact
- Performing interim analysis to refine biomarker choice and adjust trials
- Employing causal models to improve clinical trial analysis
- Continuously validating and improving causal models using additional clinical data

Our clients frequently turn to GNS as a source of analytics, data science and machine learning expertise. Our expert REFS team has been deployed and embedded in leading analytics teams across the biopharma industry. Our experts can partner with your internal teams on subpopulation analysis to impact results.

Rigorous Math, Powerful Science

REFS uses Bayesian network inference to learn causal models directly from data. In doing this instead of trying to learn a single or 'best' model, REFS learns how trillions of small sets of variables can be connected, and evaluates how these sets of variables may be assembled together into network models, across thousands of these models simultaneously.

The platform then evolves these models, rapidly iterating through trillions of possible configurations, to discover which configurations better describe a process or underlying structure that is consistent with the data.

About GNS Healthcare

GNS Healthcare solves healthcare's matching problem for leading health plans, biopharma companies, and health systems. We transform massive and diverse data streams to precisely match therapeutics, procedures, and care management interventions to individuals, improving health outcomes and saving billions of dollars. Our causal learning and simulation platform, REFS, accelerates the discovery of what works for whom and why.

To learn how GNS Healthcare can help support your initiatives, email us at *info@gnshealthcare.com*.