GNS HEALTHCARE

Subpopulation and Biomarker Discovery from Clinical Trial Optimization to Comparative Effectiveness

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

With the availability of artificial intelligence (AI) technology and the expectation of precision medicine, attention has turned to how clinical trials can be redesigned. Increasingly, biopharma firms are focusing on producing better outcomes at lower costs, but the questions that arise during the drug discovery and development process are only becoming more difficult. Given the mounting cost and high failure rate of novel therapies in clinical trials, it is time to revisit how technology can streamline and speed up the development process. With the dramatic decrease in sequencing costs and the increase in availability of various '-omics' data, there is a mountain of information to be leveraged. What you need is the right technology to sort through it all.

The Challenge of Biomarker Discovery and the GNS Healthcare Approach

Developing a drug without known biomarkers, or the wrong biomarkers, can lead to trial failure and add needless costs and delays. The earlier key biomarkers can be identified and leveraged, the higher the probability of success. However, the identification process can be labor intensive, time consuming, expensive and still relies primarily on common statistical methods. Without the power of causal modeling, it is hard to tackle the complex correlation and causation structures necessary for preclinical and clinical data simulation. The chance of acting on false-positives and mistakenly selecting a confounder instead of the true driver of clinical outcomes or treatment effect is high.

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]

GNS Healthcare is the pioneering force behind causal AI in pharma. Our proprietary platform, REFS, uses Bayesian network inference to learn causal models directly from data. 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 networks across thousands of models simultaneously.

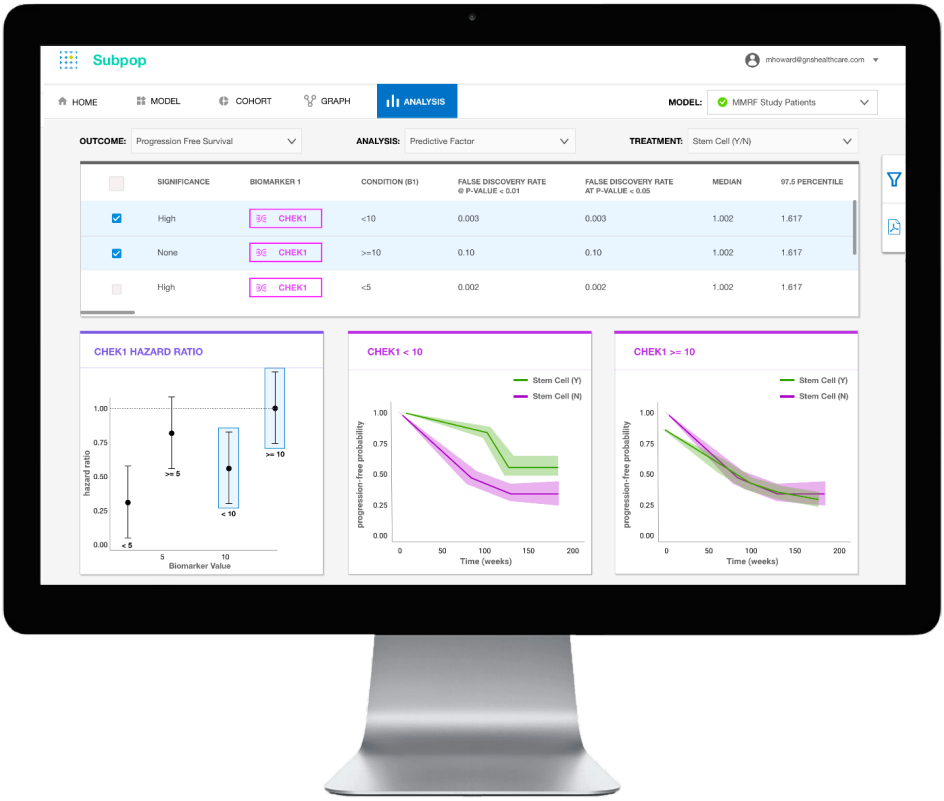
The platform then evolves these models, rapidly iterating through trillions of possible configurations, to discover which configurations better describe a process or underlying structure that is consistent with the data. This approach identifies biomarkers and subpopulations earlier in the development process.

Now the power of our reverse engineering and forward simulation engine also works behind the scenes of the GNS Subpopulation Tool, providing non-computational users easy access to dynamic models specifically for subpopulation exploration.

The GNS Subpopulation Software Product

GNS Healthcare's Subpop tool is a web application, powered by REFS, which allows non-programmer users, including clinical trial researchers, principal investigators, and clinical biostatisticians, to explore causal REFS models built based on any combination of diverse sets of data modalities, including molecular, clinical trial, real world, survey, etc. The software automatically discovers key predictive (treatment impacting) and prognostic biomarkers (disease drivers). With a simple click, users can run the Subpopulation tool to predict the probability of treatment benefit for patients with one or more predictive biomarkers, obtain statistics on such patient populations and more. Similarly, they can explore outcome modifying effects of one or more prognostic biomarkers simultaneously.

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



Analysis screen of the Subpopulation tool. A user can see the significance of the CHEK1 biomarker on progression free survival for multiple myeloma patients who have received a stem cell transplant. Example is meant to illustrate the tool. Results have been modified to obscure clinical insight.

Answering Key Questions with Subpopulation Analysis

The Subpopulation tool augments the current time-consuming methods of biomarker selection, allowing scientists to explore all potential biomarkers and select those most relevant for a trial. Accelerate the process of preparing for later phase trials by using the Subpopulation tool for the following key findings:

- **Predictive biomarkers**: identify which groups of patients would benefit the most from a particular treatment by segmenting the most relevant biomarkers or drivers for specified outcomes of interest.
- **Prognostic biomarkers:** determine a prioritized list of disease drivers which act as potential drug targets in clinical trials. With forward simulation, show modulation in outcomes of interest given single or multiple biomarker conditions and identify underlying subpopulations.
- **Hypothesis testing:** ask any number of 'what if?' questions and see what effects one or multiple biomarkers have on outcomes regardless of treatment or when considering treatment.

Supporting clinical researchers and investigators in their quest for informed decisions during clinical trial design is paramount for improved probability of success. Using the Subpopulation tool web-based workflow, users can establish key **predictive** and **prognostic** biomarkers and analyze the causal effects of any biomarkers on outcomes.

Licensing Subpopulation for BioPharma

Effective use of the Subpopulation tool within an organization relies on having REFS models built. Customers can either license REFS platform and have their data scientists build models or rely on GNS experts to build the models. Customers can then separately license the Subpopulation application so that non-programmer users can explore the REFS-generated models and discover insights using the web application.

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.

For pricing information or to learn more, please contact **info@gnshealthcare.com**