



## Precision HEOR to Support Drug Discovery and Clinical Trials

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### Perspective

Journal of Personalized Medicine has recently reported a concept of Precision Health Economics and Outcomes Research (HEOR) [1]. This concept is bringing traditional HEOR to a more precise level yet not altering the health sector decision contexts in which precision HEOR will play a supporting role, namely, 1) intervention development, 2) health technology assessment (HTA), 3) clinical guideline development, 4) patient-physician shared decision making, and 5) reimbursement decision making. While the applications of 2-5 are activities post launch of a drug, in the pre-launch stage precision HEOR also plays a role to increase the efficiency of drug development that traditional HEOR is ever able to.

It is not new that HEOR is an integral part of clinical R&D and impacting clinical trial design. This is because the economic value of a drug is becoming equally important as its clinical value in the context of an inevitable tradeoff between increasing healthcare demand and limited healthcare resources. A good example is that US regulators have been increasingly putting emphasis on patient reported outcomes (PRO) data for making drug approval decisions: “findings measured by a well-defined and reliable PRO instrument in appropriately designed investigation(s) can be used to support a claim in medical product labeling if the claim is consistent with the instrument’s documented measurement capability”, stated by the U.S. Food and Drug Administration (FDA) [2]. Based on these considerations, drug developers have understood the imperative to develop comprehensive and robust HEOR strategy from the beginning of drug development throughout its life cycle. Traditionally, HEOR tasks in early R&D phase include initial value proposition, selection of PRO instruments, economic evaluations based on trial data, etc. The “Go” or “No-go” decision for a drug also uses HEOR analysis as a reference to forecast the risk-benefit (Figure 1). As we move into the big data era, we hold a strong belief that HEOR holds promise to be incorporated more closely into the R&D process by utilizing many more data from different dimensions to identify a more refined match of clinical and economic value as early as possible, and it can be called “precision HEOR”. Indeed, with the advent of big data, drug discovery and development is evolving into relying on systems pharmacology which 1) uses biological and clinical data at multiple temporal and spatial scales to develop actionable and interpretable mechanistic or predictive models, and 2) the output from the model leads to novel hypotheses and biomedical knowledge, as well as supporting decision making in drug discovery and clinical practice [3]. Precision HEOR is evolving in the same direction utilizing big data technologies, e.g. patient similarity analysis and machine learning for risk prediction modeling, in order to predict the economic risk and benefit of a drug in precisely defined patient cluster subgroups as early as a new drug is in its R&D stage. In the next section I will discuss two perspectives of precision HEOR in drug discovery and clinical trials.

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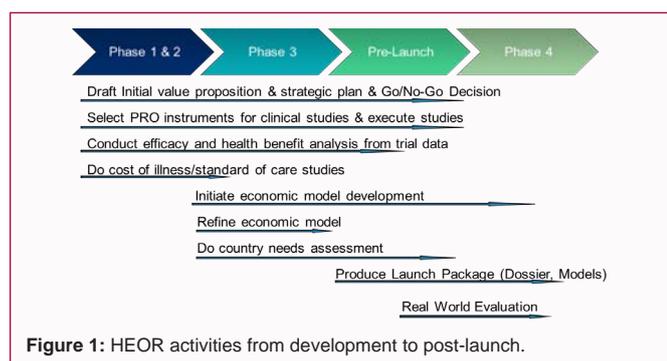
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### Precision HEOR in Drug Discovery

There is an increasing trend that researchers use big data analytical tools for identifying disease biomarkers for drug discovery from large sets of genomics and other omics data [4]. It is well known that one of the important benefits of biomarker identification is developing personalized medicine and we argue that considering HEOR as early as this stage might lead to a more nuanced value story of the potential drug than taking it into account later, say, clinical stage.

Nowadays, a drug is considered successful not only because of its improved safety and efficacy profile, but also its reasonable price and budget impact which convince the payer for favorable reimbursement decision making. As long as a disease biomarker is identified, it will be farseeing to estimate the economic impact of a potential new drug will have on the healthcare system, especially the potential size of patient population. Benefited from the current advances big-data-based prediction of a drug response phenotype, health economists will be able to construct a more



precise prediction model corresponding to patient populations with different response level implying differentiated post-launch market access strategy which is in turn valuable information to inform the direction of drug discovery and development.

### Precision HEOR in Clinical Trials

As Chen *et al.* reported, precision HEOR can be separated into its precision health economics (HE) part and precision outcomes research (OR) part [1]. Both of them will play a more important role in drug development stage, leading to a more efficient and targeted R&D process than traditional HEOR is able to. As stakeholders are increasingly relying on HEOR information to fully understand product value in healthcare and its potential in real-world clinical practice, maximizing the therapeutic value is particularly critical for a product to reach the market faster at an optimal price.

Traditionally, HEOR analyses are performed alongside or shortly after clinical trials using the efficacy and safety data as clinical inputs in HEOR studies. Precision HEOR tends not to “passively” use data from clinical trial, but interactively inform clinical trial design in the way to yield best clinical outcomes in the trial population. We propose a stepwise approach as shown below:

1) To conduct an outcome-driven patient similarity analysis once the primary results of a clinical trial are obtained. Instead of using a pre-defined cut-off for treatment success or failure, we create a machine learning model to classify heterogeneous patients into several clusters, each of which contains patients with similar clinical outcomes.

2) To identify the characteristics, both phenotypic and genotypic, of each cluster and try to identify what characteristics drive the difference in patient response rate to a drug. This information

holds promise to stratify patients by using factors even not known to researchers before and uncover the characteristics of patients likely to benefit most from this drug.

3) To use this information to make a seamless connection of pre-clinical and clinical phases, and inform pricing and market access strategy in precisely stratified patient population in order to ensure the new drug will provide the best possible benefits to the most correct patients and to support optimal allocation of healthcare resources from a societal perspective.

For example, precision HEOR studies during the initial phase of trials give precise assessment of the burden of disease, and those conducted in comparator trials will demonstrate stratified effectiveness of the new drug in corresponding patient populations. It has particularly merit in providing evidence for supporting payers to make precise reimbursement decisions, e.g. differential reimbursement level in patients with same disease but with different underlying phenotypic and genotypic characteristics.

At the same time, we do realize that there are challenges galore in conducting precision HEOR alongside R&D of new drugs. Apart from the universal challenges associated with big data analytics, e.g. data quality, stability, privacy, storage, standardization, etc., it is critical to complement data-driven analytics with knowledge-driven approaches because using data-driven analytics alone we risk obtaining correlations without true causal relationships thus misleading subsequent economic modeling and data interpretation. Nevertheless, we very much look forward to piloting a precision HEOR study early in R&D of new drugs to foresee the combination of clinical and economic benefit of our innovations and to gradually develop a nuanced value story from societal perspective at every point in the R&D process.

### References

1. Chen Y, Guzauskas GF, Gu C, Wang BC, Furnback WE, Xie G, et al. *J Pers. Med.* 2016; 6: 20.
2. FDA Guidance for Industry Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims. 2009.
3. Xie L. *Annual Review of Pharmacology and Toxicology. Annu Rev Pharmacol Toxicol.* 2017; 57: 1-26.
4. Szezák N. Over-the-counter Acne Treatments. *Clin Pharmacol Ther.* 2014; 95: 492-495.