Potential of Pharmacometricians beyond Quantitative Pharmacology: Future Looks Promising!

Shailly Mehrotra[1], BPharm and Jogarao Gobburu[1], PhD, MBA, FCP

Center for Translational Medicine, School of Pharmacy, University of Maryland, Baltimore, Maryland, USA

Health care industry is undergoing metamorphosis as the payor expectations have substantially changed. Pharmaceutical companies are struggling to discover promising assets. These challenges are opportunities for Pharmacometricians beyond Quantitative Pharmacology (Figure 1). Our role in quantitative pharmacology has been on the rise for the past two decades, but the growth seems to have plateaued. The experience we have gained over this time, however, is valuable for us to create new opportunities for the future scientists. In fact, if we position ourselves well the future opportunities will dwarf the past.

Precision Therapeutics & Real World Evidence

There is a movement away from the pay-for-service to a pay-for-performance model. Optimization of health care delivery hence is receiving big investments. Enhancing quality requires dealing with large electronic medical records, heterogeneous data, dynamic forecasting, integration with financial and pharmaco-economic modeling and technology. Pharmacometricians are trained to find best solutions based on not-so-perfect data by using science to impute missing information.

Drug development and regulatory practices are designed to find an average drug for an average patient. Precision Medicine (PM) advocates usage of drug in an accurate manner for each patient (not to be confused with pharmacogenomics which also strives to find average doses in most cases). With the announcement of "Precision Medicine Initiative" by President Obama in 2015[1], more investments in Precision Medicine can be expected. Using millions of medical records as priors and the particular patient's data as the likelihood to deliver precise health care management requires Bayesian forecasting. Because the Bayesian approach has to have a mechanistic underpinning, Pharmacometricians (or Clinical Pharmacologists) are best suited to lead the analytics component. New innovative methods for PM are much required.

A related application is to utilize real world data to infer efficacy and safety outcomes. Real World Evidence (RWE) is a rapidly growing discipline which holds promise in deriving effectiveness and safety from real world patient data as opposed to data obtained from controlled clinical trial.[2] An extended use of the quantitative analyses of real world data is to guide cost-effectiveness and comparative-effectiveness decisions. Pharmacometricians can easily acquire pharmaco-economic skills to contribute meaningfully in the RWE realm.

PM and RWE are the two most promising immediate opportunities for our scientists.

Quantitative Systems Biology

For our purpose, we define systems biology models as elaborate models that capture the entire biological cascade.[3] With the advent of advanced understanding of the physiological systems, predictive systems biology models can be developed that can be utilized to answer questions pertaining to target identification, target optimization, identifying biomarkers and understanding drug effects. However, a typical Pharmacometrician will require training on biology to engineer systems biology models. An alternative would be for Pharmacometricians to be involved in bridging the systems biology model predictions with clinical outcomes and trial design. But that would be a limited role.

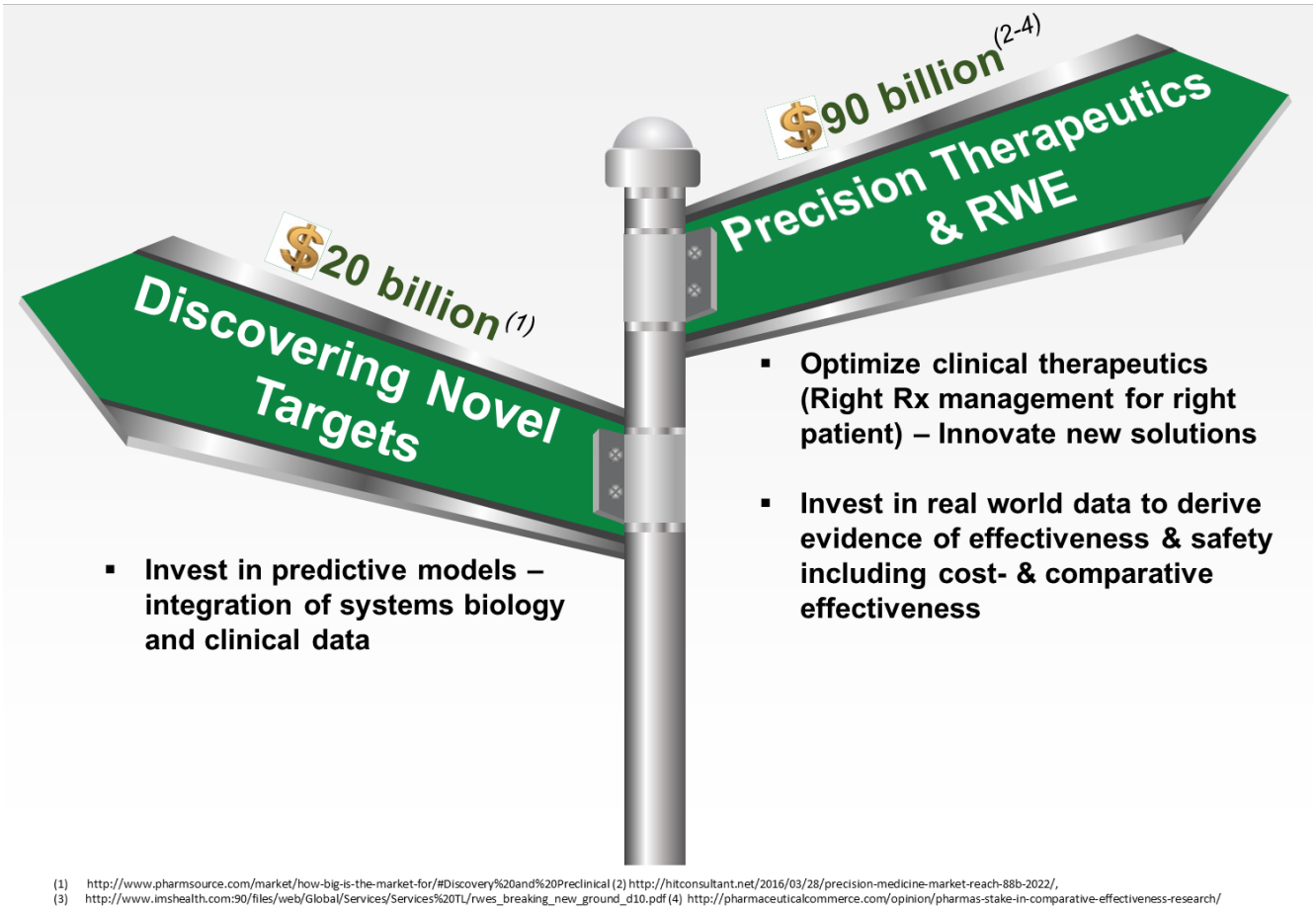
References

1. The Precision Medicine Initiative, https://www.whitehouse.gov/precision-medicine.

2. PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2018 Through 2022,http://www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM511438.pdf.

3. Peterson MC, Riggs MM. FDA advisory meeting clinical pharmacology review utilizes a quantitative systems pharmacology (QSP) model: A watershed moment? *CPT Pharmacometrics Syst Pharmacol*. 2015;4(3):189-192. doi:10.1002/psp.20.

Figure 1: The payor pressure and poor R&D productivity led to heavy investments in Precision Therapeutics, real world evidence and identifying novel targets.



The dollar value at the top of each box denotes the market share. RWE- real world evidence