EE421

Integrating Payer Reimbursement Strategies into Modeling and Simulation (M&S)-based Methods to Redefine Drug Development

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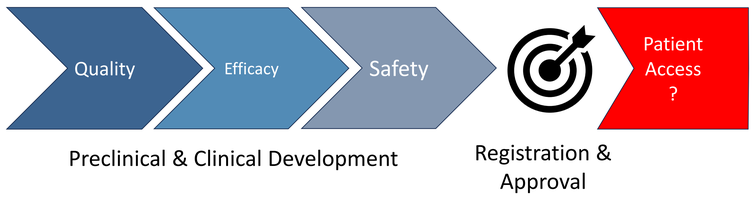
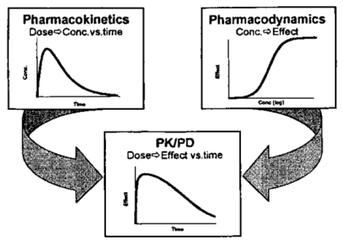
Background

"Drug development" is **typically perceived as a *sequential* process of data collection** that **is completed when regulatory "hurdles"** of quality, efficacy, and safety are satisfied.

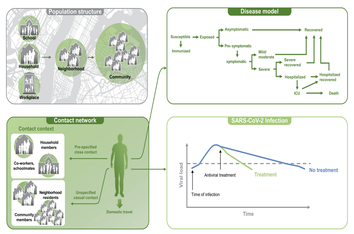


- Addressing the **"fourth hurdle", i.e., patient access / payer reimbursement)** is often **neglected during clinical development** due at least two factors:
  - The **perception of insufficient data** to formulate rigorous economic evidence to develop payer reimbursement strategies **prior to later stage trial readouts**, and
  - A **historical preference from regulatory agencies** for patient data from randomized controlled trials **(RCTs)** as the primary evidentiary basis for authorization.

Today, however, **mechanistic and population-level methods** for **model-informed drug development (MIDD) to generate evidence** are well-accepted by the industry and regulatory bodies and can provide **evidence of clinical outcomes and safety**.



Pharmacokinetic / Pharmacodynamic (PK/PD)[1]

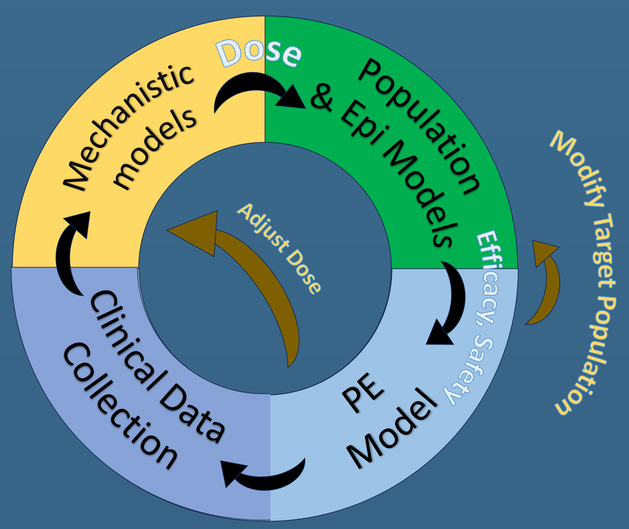


Agent-based (ABM) or Epidemiological[2]

Quantitative Systems Pharmacology (QSP)

Concept

- There is quantifiable evidence on the impact of **challenges in payer reimbursement,** reflecting the need to proactively **consider payer strategies during early drug development**
  - Only **~30% of approved drugs were covered by Medicare insurance plans** without restrictions unless "fast-tracked" by the FDA after three years[3]
- These data suggest that **early planning for evidence generation** to support post-reimbursement payer discussions is of substantial importance
  - To facilitate this, perceived challenges related to insufficient availability of human data to enable early economic modeling must be surmounted
- **MIDD approaches** can generate early insights into clinical outcomes and safety
  - These methods **have shown success in the clinical and regulatory setting** (*lower left column*) and recent published successes when applied to **facilitate early pharmacoeconomic (PE) modeling** *(upper right column)*
- We propose industry researchers employ a paradigm of **extended MIDD to integrate these approaches** as part of **iterative research programs** to identify material evidence gaps, guide clinical and real-world data collection**,** and mitigate risks of challenges during payer discussions



Extended MIDD Successes & Potential

- **An extended MIDD approach in follicular lymphoma** used outputs of a **PK/PD model** linking rituximab concentration to progression-free survival as inputs into **a PE model** to compare the predicted cost effectiveness of rituximab to trial-based estimates.
  - Concordance between simulation- and trial-based estimates of cost effectiveness was found,[4] illustrating that a proactive use of extended MIDD may have provided powerful early insights if performed earlier.
- An extended **MIDD approach** was developed to **investigate the economic impact of oseltamivir for influenza,** including PK/PD, epidemiology, and PE decision analytic modules.
  - Oseltamivir reduced # of infected patients, increased quality-adjusted life years (QALYs) and was cost-effective under most scenarios and doses compared to no treatment.[5]
- **Extended MIDD has significant untapped potential to impact rare diseases**, where data are scarce
  - A Spanish consortium has funded the development of AI-facilitated QSP model to identify drug candidates in 100 rare diseases and successfully identified 20 potential novel targets for Fanconi anemia.[6]

Conclusions and Future Directions

- The notion of "drug development" should include early consideration of payer strategy and informed data collection during clinical development
- Extended MIDD approaches have already demonstrated the ability to "do more with less data" to mitigate developmental risks and inform payer strategy.
- Payer relevant endpoints are a natural extension to MIDD, but application of extended MIDD is not a current research standard because of siloed research coupled with low awareness of the value of the wide-ranging and impactful applications[7], e.g.,
  - Identifying key evidence gaps that impact economic value
  - Guiding prioritized real-world data collection
  - Understanding the economic impact of variations in dosing regimens and subpopulations
  - Informing drug differentiation strategies from both a clinical and economic perspective.

(1) Derendorf H. and Meibohm B. Modeling of Pharmacokinetic and Pharmacodynamic Relationships: Concepts and Perspectives. Pharmaceutical Res. 16(2): 176-185, 1999.

(2) Kamal M. et al. Assessing the Combined Public Health Impact of Pharmaceutical Interventions on Pandemic Transmission and Mortality: An Example in SARS CoV-2. Clin. Pharma. Thera. 112(6): 1224-1235, 2022. https://doi.org/10.1002/cpt.2728

(3) Shaw D.L., Dhruva S.S., Ross J.S. Coverage of Novel Therapeutic Agents by Medicare Prescription Drug Plans Following FDA Approval. J. Man. Care Spec. Pharm. 24(12): 1210-1294, 2018. https://doi.org/10.18553/jmcp.2018.24.12.1230

(4) Pink J., Lane S., and Hughes D.A. Mechanism-Based Approach to the Economic Evaluation of Pharmaceuticals. Pharmacoeconomics 30(5): 413-42, 2012.

(5) Kamal et al. Interdisciplinary pharmacometrics linking oseltamivir pharmacology, influenza epidemiology and health economics to inform antiviral use in pandemics. Br. J. Clin Pharm. 83(7): 1580-1594, 2017. https://doi.org/10.1111/bcp.13229

(6) http://https://www.clinbioinfosspa.es/projects/holiRD/

(7) Kamal M., Ganguly S., Kadambi A., and Smith P. (Extended) Model Informed Drug Development: Beyond Clinical Trials and Regulatory Approval. Clin. Pharma. Thera., submitted April 2024.