RWD with a focus for R&D use - *challenges and opportunities in research and early development*

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Abstract

Research and Development has largely focused on using data from Clinical Trials to assess the safety and efficacy of New Molecular Entities (NMEs). However, recent advances in the availability and accessibility of Real World Data (RWD) sources have led to opportunities to leverage RWD to improve the efficiency of research and development. This discussion will focus on some of these innovative uses of RWD for improving the targeting and execution of clinical development programs including: target selection and prioritization based on unmet clinical need; on identification of high-risk patient sub-groups for early POC analysis, and on the use of RWD for testing clinical trial design, country and site selection.

Perspective

I bring a number of different perspectives to today's discussion

- Academic
  - PhD Economist
  - Post Doc Health Services Research
  - MBA Marketing & Finance
- Industry:
  - Merck – Outcomes Research & Management
  - Merck – Financial Evaluation & Analysis
  - J&J Device & Diagnostics – Healthcare Informatics
  - **Astellas – Real World Informatics, Strategic Capabilities & Alliances**
- Vendor
  - Medstat – Pharma Information Products & Services
  - Wolters-Kluwer – Brand Analytics
  - Ingenix – Pharma Informatics
- Healthcare Provider
  - Ingenix – Data Management & Analytics
  - Optum – Advanced Analytics
- IT Services
  - HCL – Lifesciences & Healthcare Solutions

Fundamental Goal of Drug Development

Answer the question, "What will be the outcome if I give Patient A, Drug 1, on Outcome a?" It's a classic counter-factual.

$$\text{Effect}(A,1,a) = E(O^A_a \mid D^A_1 = 1) - E(O^A_a \mid D^A_1 = 0)$$

In the era where data was difficult and costly to collect, and computing power was slow and costly, the RCT evolved as a way to answer the question, so long as the Effect Size was large and we were willing to overlook the Heterogeneity of patients.

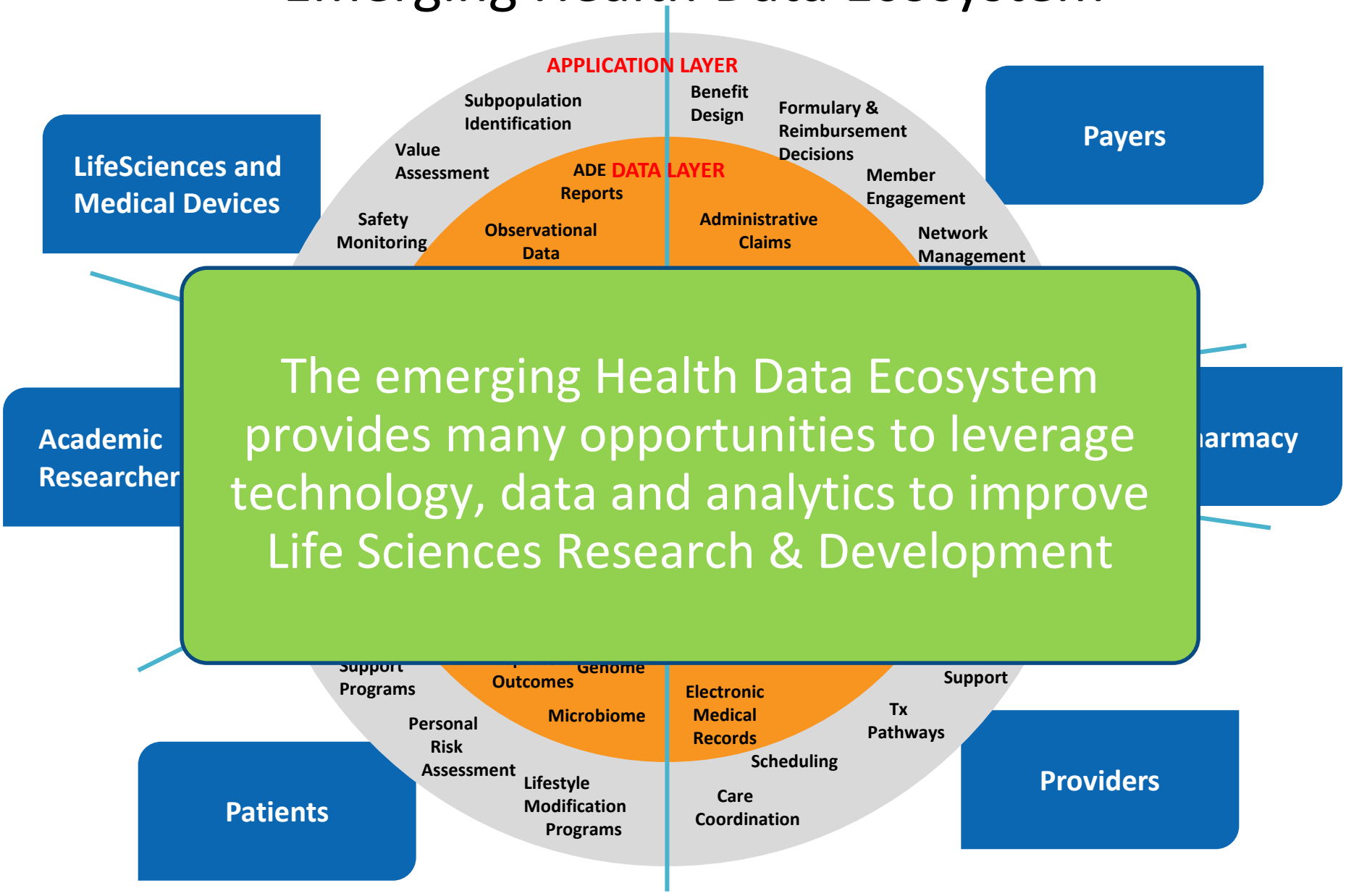
With randomization…

$$\text{Avg Effect}(A,1,a) = \text{Avg}\{(O^A_a \mid D^A_1 = 1)\} - \text{Avg}\{(O^B_a \mid D^B_1 = 0)\}$$

What's Changed?

- Data is cheap, easy to collect, store and analyze.
- Computing power / speed growing exponentially.
- Heterogeneity is becoming ubiquitous, as we learn more about the genome, micro-biome, exome and all the other 'omic's

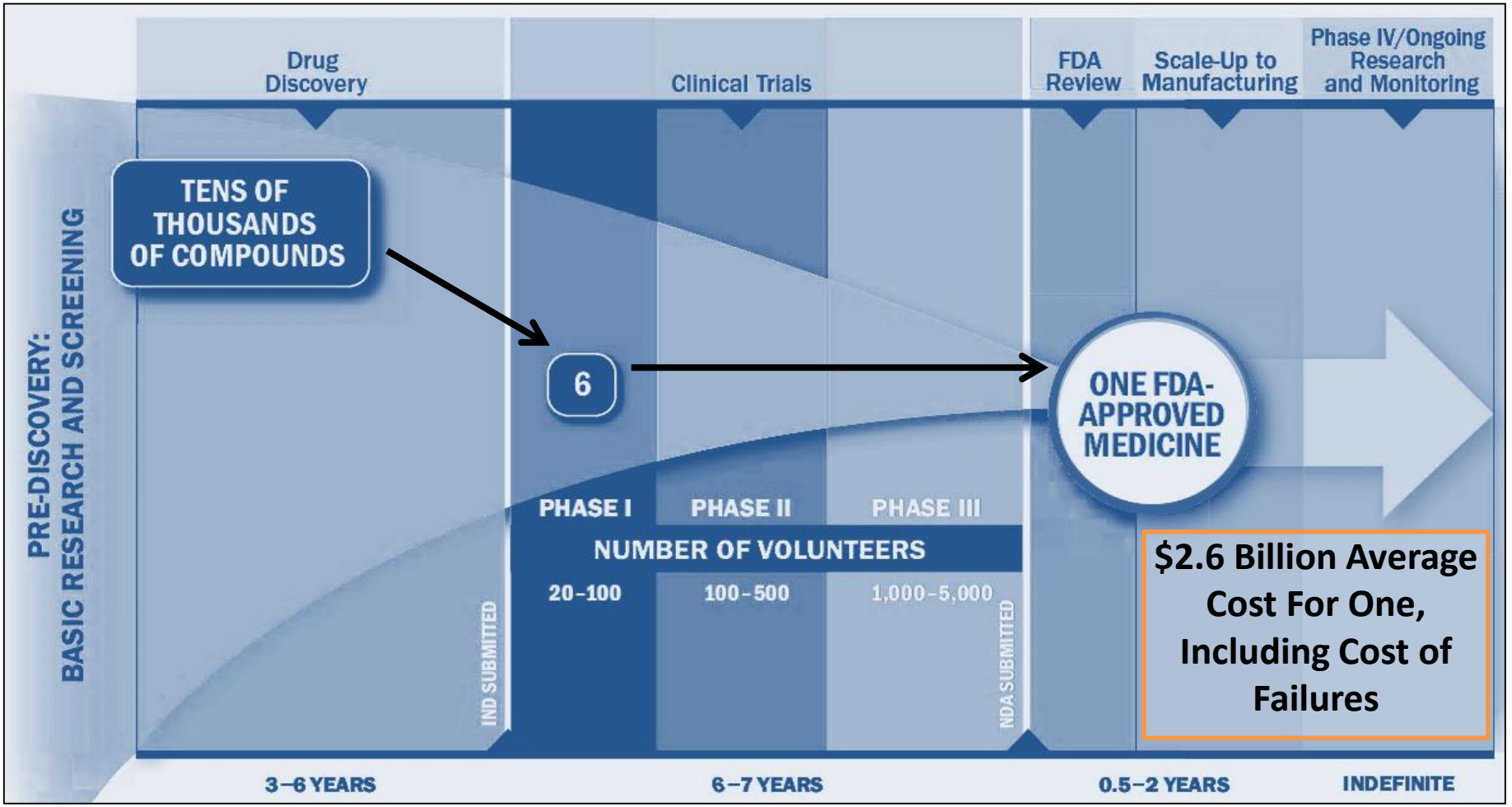
Emerging Health Data Ecosystem



Implications

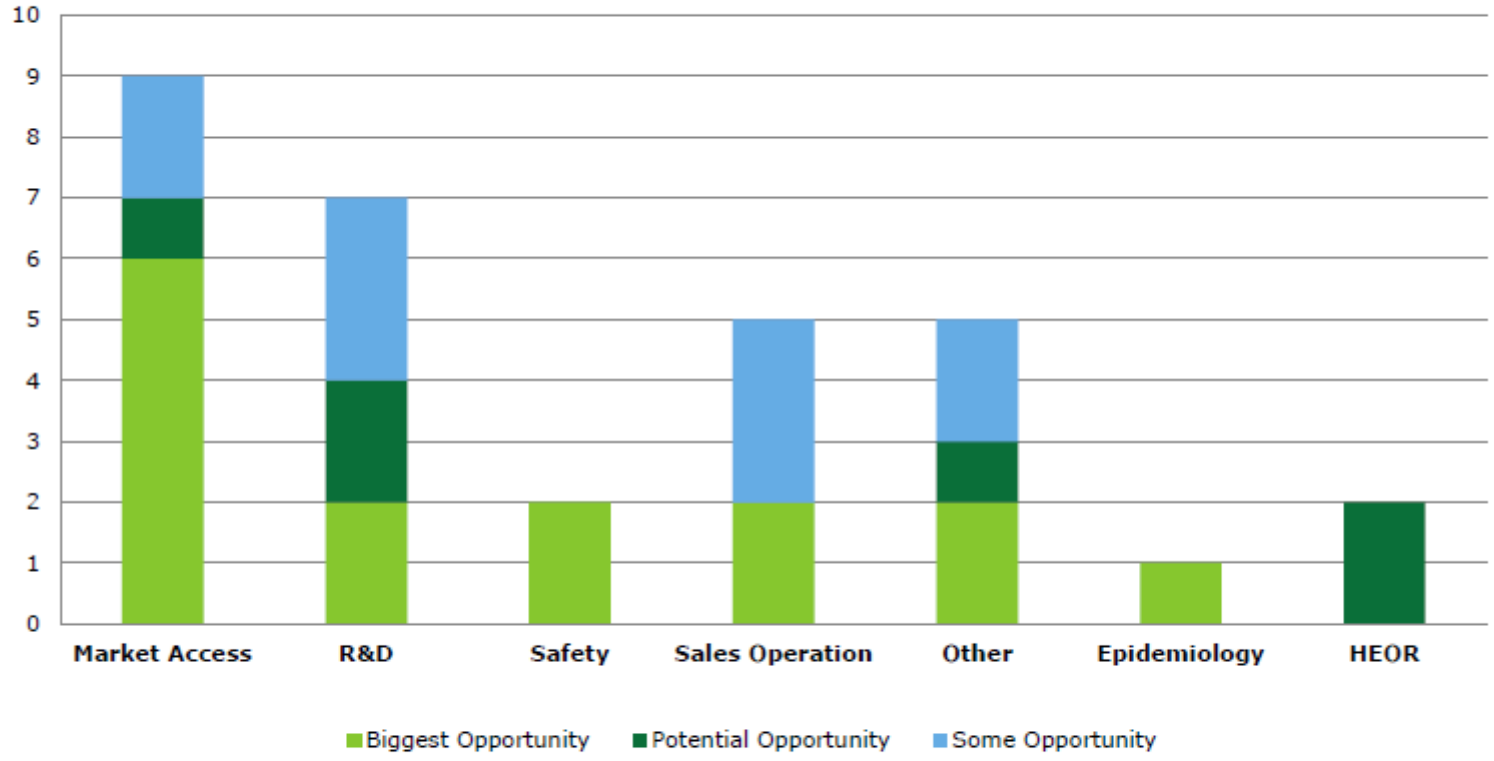
- We can make the existing process for answering the fundamental question more efficient.
  - Improving Drug Discovery
  - Improving Clinical Trial Execution
- We can radically change the way in which we answer the fundamental question.

The Biopharmaceutical R&D Process
$2.6 Billion to Bring One Drug to Market



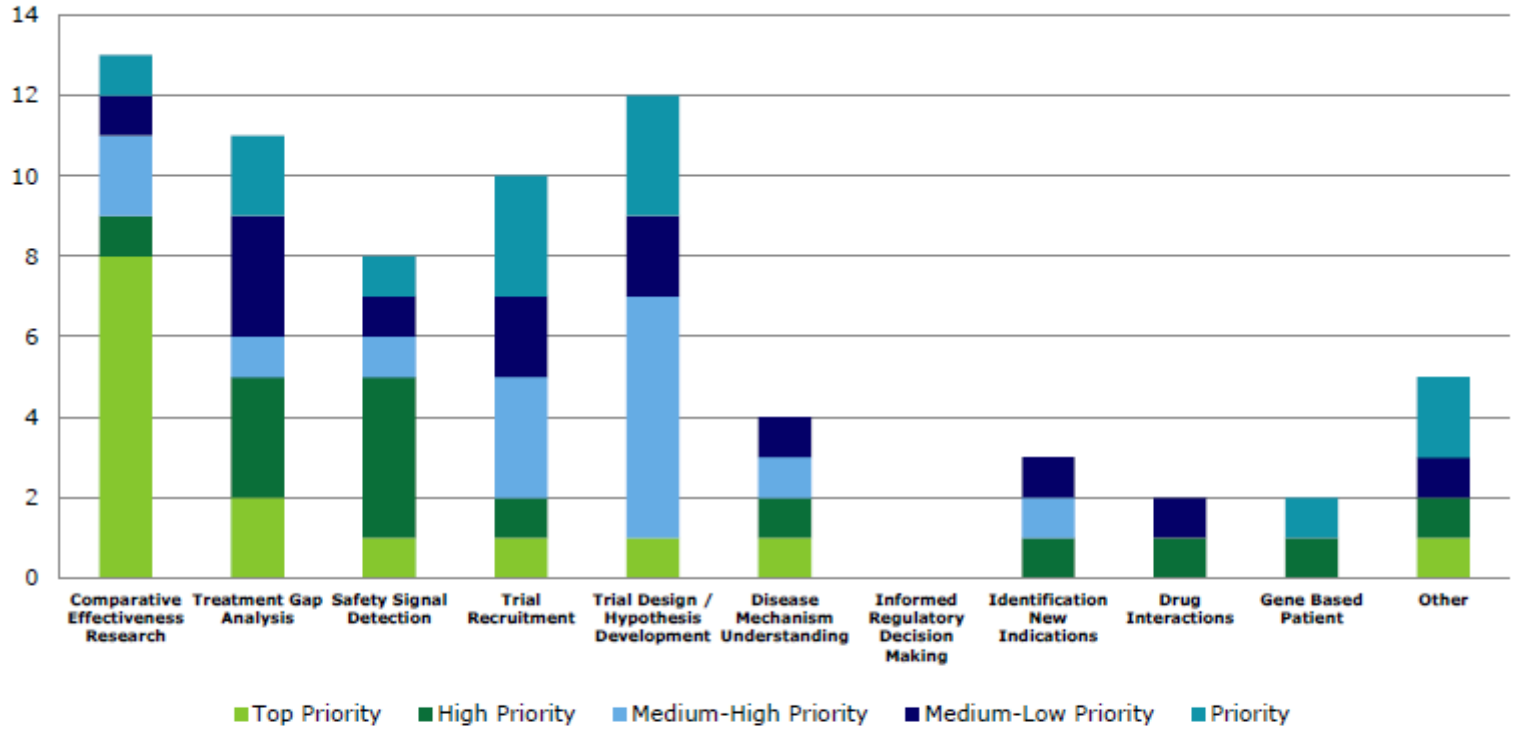
Source: *2015 Profile, Biopharmaceutical Research Industry*, Pharmaceutical Research Manufacturers Association (PhRMA), p.37. PhRMA lists multiple industry, academic, and government sources.

Where are the biggest opportunities to leverage RWE?



Key finding: Market access and R&D were ranked as the biggest opportunities for leveraging RWE.

Which use cases are top priorities?

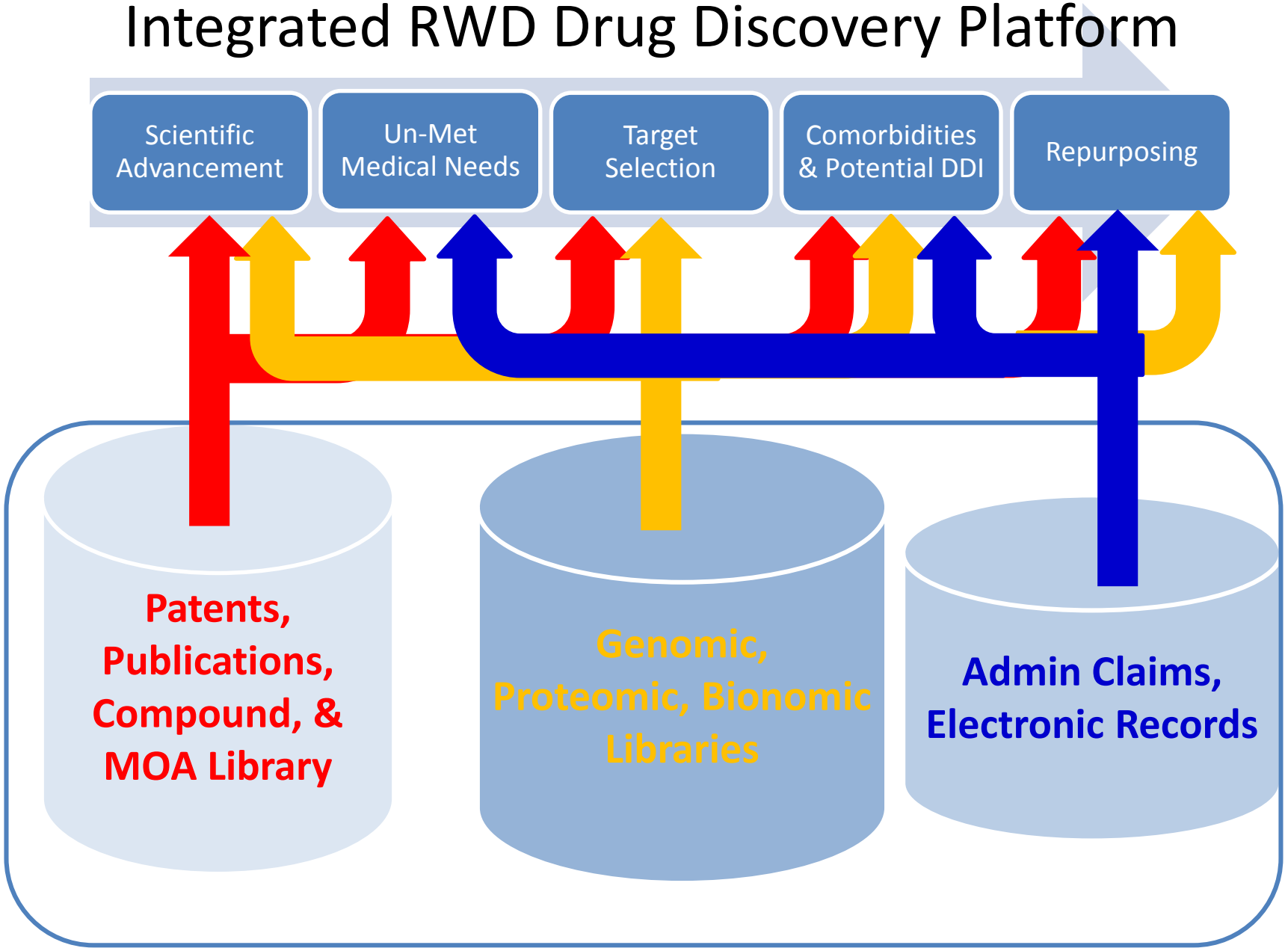


Key finding: CER and treatment pathway/gap analysis are still the top priority – a reflection of demand from payers and providers for RWE to demonstrate the value of products in real-world settings. R&D use cases of trial design and recruitment were the next highest priority. Increased pressure from manufacturers to accelerate the development process may drive the focus on trial design and recruitment.

Improving Drug Discovery

- Identify novel compounds and associated MOA
- Associate MOA with diseases of interest
- Evaluate compounds for proposed use in-vivo or in animal models
- Identify potential AE profile
- Assess unmet medical need in that disease

Integrated RWD Drug Discovery Platform



Improving Traditional Clinical Development

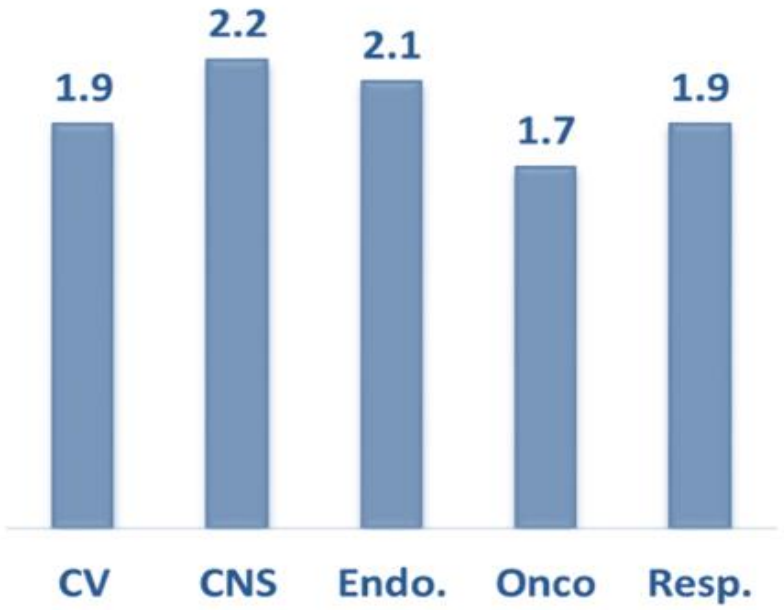
- Identify the right Target Population(s)
- Optimize Protocol Design
- Identify Countries, Sites, and Investigators
- Execute, Execute, Execute

- Avoid unnecessary delays or changes

Trials Run Late
Poor Site Enrollment Is a Root Cause

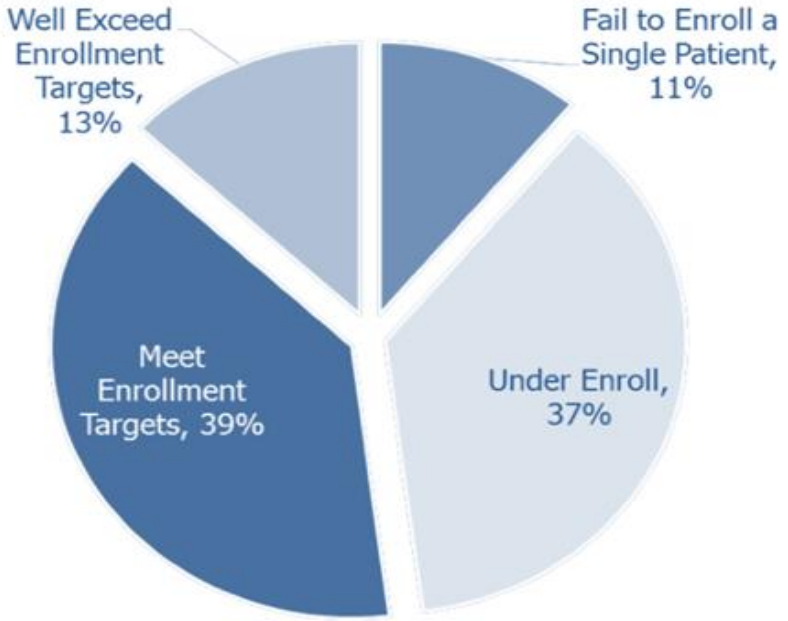
Study Enrollment Cycle Times

Typical Multiplier of Planned Duration to Reach Target Enrollment



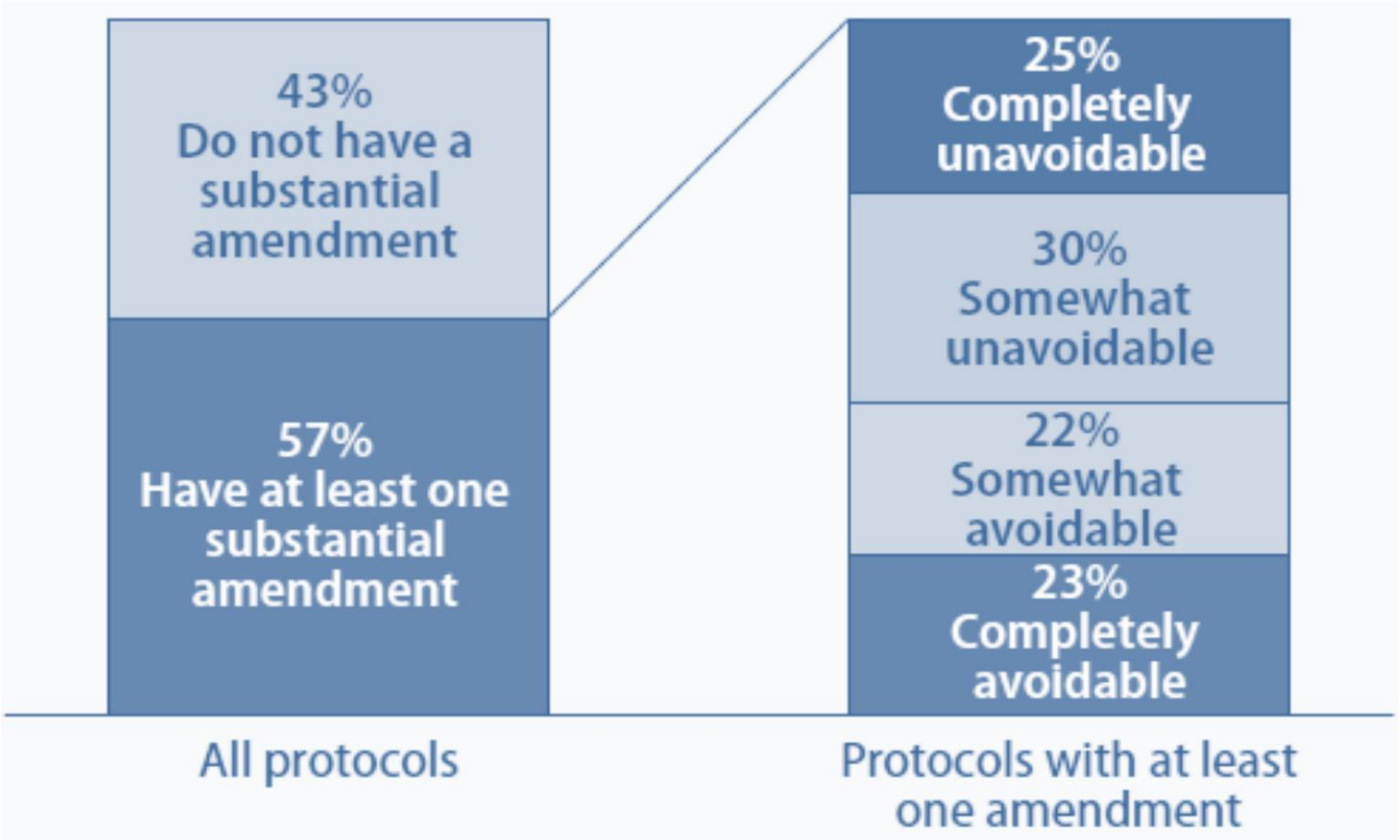
Source: Tufts CSDD, 2013

Site Enrollment Achievement



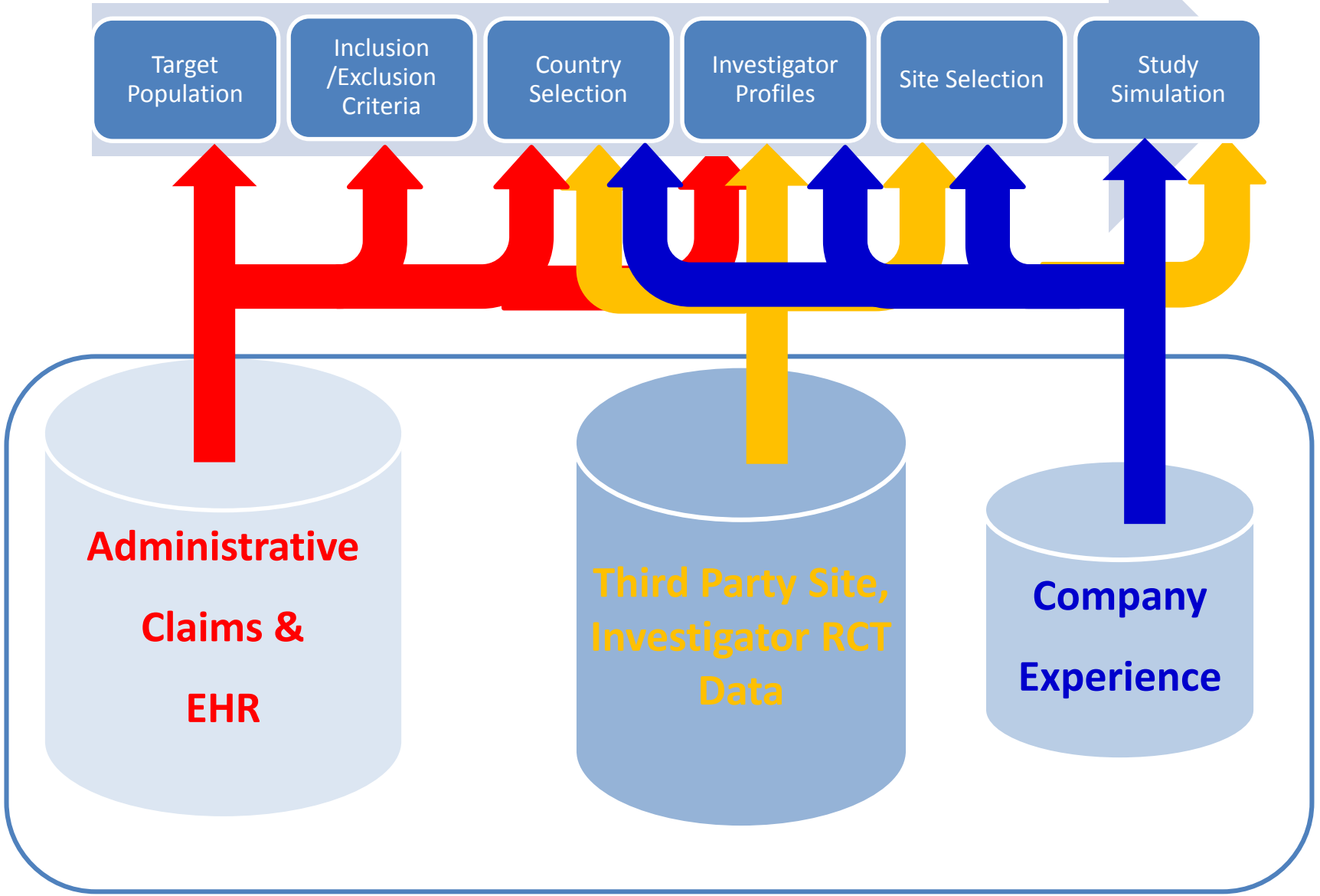
CenterWatch Clinical Trials Data Library

57% of Protocols Have Amendments Most Were Avoidable



Source: "Facing Protocol Amendments Head-On," *The CenterWatch Monthly*, April, 2016, p. 1.
CenterWatch's Source: Tufts Center for the Study of Drug Development, 2016 <csdd.tufts.edu>

Integrated RWD Clinical Trial Optimization Platform



Innovative Trial Designs
Based on Real World Data

- Large Simple Trials
  - Randomizing patients at practices and capturing follow-ups through EMRs can provide valuable information about real-world outcomes.
- One-Armed Trials
  - Matching patients from a single armed study to “Real World Controls” from databases could reduce the costs of trials, particularly in orphan conditions.
- Observational Studies
  - Using statistical methods from epidemiology and economics, analyzing non-randomized observational data can provide critical insights into how drugs are actually used and real-world outcomes.
- “Synthetic” Trials
  - Creating matching cohorts of exposed and un-exposed patients can often provide evidence of a drugs effects in situations where clinical trials are not reasonable to conduct.

Changing the Paradigm

With all this additional data about patients (Z^A) we are now in a position where every patient experience can become part of the corpus of knowledge.

$$Effect(A,1,a|Z^A) = (O^A_a \mid D^A_1 = 1, Z^A) - Pred(O^A_a \mid D^A_1 = 0, Z^A)$$

With the inclusion of Big Data and Machine learning, we are in a position to directly compare the actual outcome for patient A treated with Drug 1, to the predicted outcome of the patient in the absence of treatment based on what happened to all the other patients who didn't take Drug 1.

Summary

- Real World Data provides valuable insights which can speed up and improve the likelihood of success across the early drug discovery and development process.
- Integrating data from multiple sources, across multiple types is necessary to achieve maximum impact.

Key Area's for Collaboration

- Data Integration & Vendor Collaboration
- Data Models & Ontology Development
- Analytic Method Development & Standardization
- Text Analytics / Unstructured Data
- Machine Learning / Artificial Intelligence
- Regulatory Acceptance