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LEAPS

Learning Ecosystems Accelerator for
Patient-centered, Sustainable innovation

Design Lab

Day 2 – July 18, 2018

MIT CENTER FOR BIOMEDICAL INNOVATION

Massachusetts Institute of Technology

Evidence Generation Platforms: Through the LEAPS Lens

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Framing the Need for a New Approach to Evidence Planning & Production

"High-quality evidence is what we use to guide medical practice. **The standard approach to generating this evidence** — a series of clinical trials, each investigating one or two interventions in a single disease — **has become ever more expensive and challenging to execute**…The common denominator is a **need to answer more questions more efficiently and in less time**."

(Woodcock & LaVange, Aug 2017)

What is a Platform?

Microsoft Office

General Platform Definition*

A foundation (physical or virtual) that brings together different people or organizations for a **common purpose** or to share a **common resource**

**Michael A. Cusumano, MIT Sloan School of Management*

Product Platform Definition

- A foundation (physical or virtual) that brings together different people or organizations for a **common purpose** or to share a **common resource**
- Enables innovations **within an organization or supply chain** using common components & architectures
- Generates value from sales of related products or services

Industry Platform Definition

- A foundation (physical or virtual) that brings together different people or organizations for a **common purpose** or to share a **common resource**
- Enables innovations or transactions **inside AND outside the organization (the "ecosystem")** that might not otherwise occur
- Generates value from "**network effects**" that help make platform-related products & services increasingly useful

Additional Platform Definition

There are three broad properties of a platform*:

- Magnet: A platform needs to get both producers and consumers on board
- Toolbox: A platform needs to provide the tools required for producers and consumers to interact (and transact)
- Matchmaker: A platform needs to match producers and consumers, leveraging data

*Sangeet Paul Choudary is co-author of Platform Revolution and the author of Platform Scale. He is the co-chair of the MIT Platform Strategy Summit at the MIT Media Labs, an Entrepreneur-in-residence at INSEAD Business School, and an executive educator with Harvard Business School Publishing

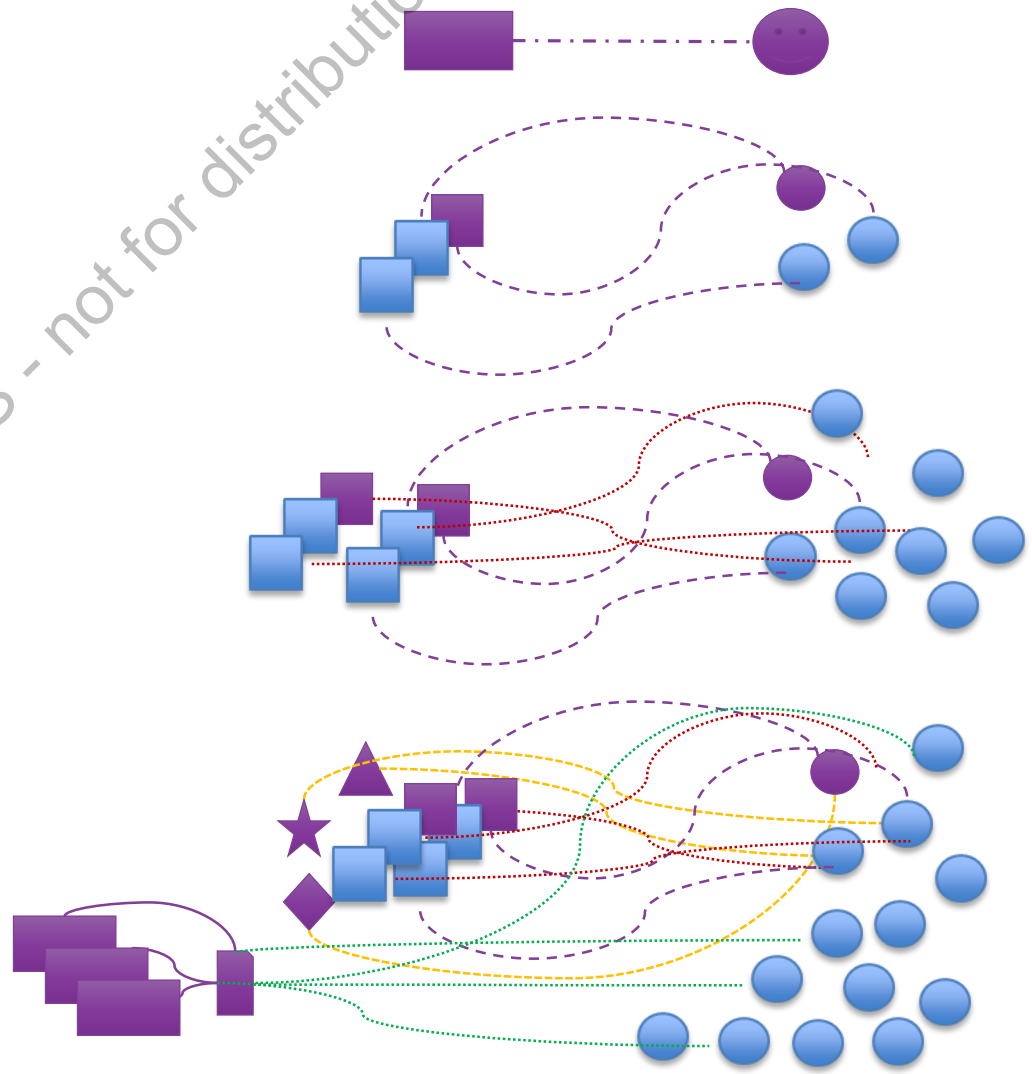
What is a “network effect”?

Platforms are also often associated with “network effects”: that is, the more users who adopt the platform, the more valuable the platform becomes to the owner and to the users because of growing access to the network of users and often a set of complementary innovations. (Gawer & Cusumano, 2012)

Network Effects: Amazon

Amazon is recognized as one of the most successful platforms

- Not a platform at the start. It was online retailer of books, an alternative to brick and mortar stores.
- End user reviews started the evolution to platform. No longer limited to formal ‘book reviewers’, customers authored and consumed reviews.
- The next step was ‘users who liked this also like this’, helped to match consumers with products.
- Next, they created the Marketplace to include other vendors
- And introduced Kindle device with a kit for encourage development of new products.



Network Effects: Amazon Acquires PillPack

It didn't stop at Kindle… (partial list)

- **Amazon Web:** Cloud Storage and Computing
- **Whole Foods:** Grocery Chain
- **Alexa:** Voice Assistant
- **Partner w/ JP Morgan and Berkshire Hathaway:** Healthcare coverage for 1.2M employees
- **PillPack:** Online Pharmacy

- *PillPack is a specialty online pharmacy, offering home delivery of convenient daily packages for monthly prescriptions for chronic disease patients*

Consider the possibilities of putting all this together!

Evidence Generation Platforms

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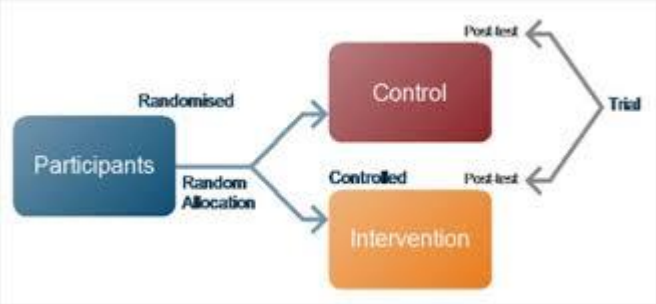
All key stakeholders generate relevant data in our daily lives/work, but need more than just our own data to make good decisions

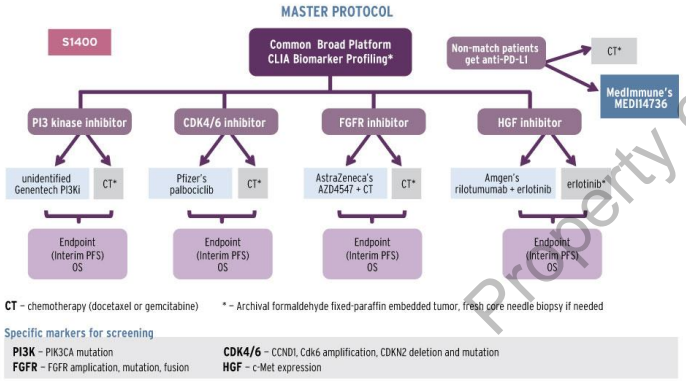
Evolution of Evidence Generation Platforms

Pre-Market (R&D)

Randomized Controlled Trial (RCT)



Adaptive Platform Trial



Post- Market (Real-World Evidence)

Individual Product Registry

- One industry sponsor
- Only enrolls patients taking drug X
- Indirect comparator data from RCTs or other cohorts

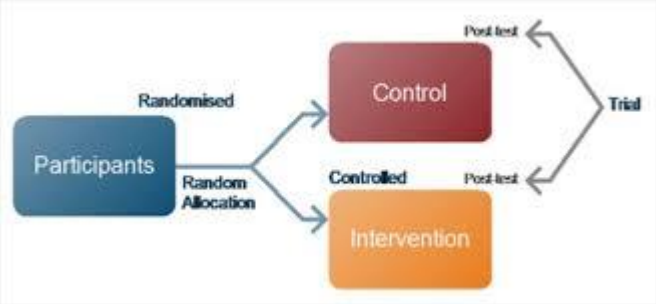
Disease Registry

- Multiple sponsors (cost sharing)
- Patients and physician groups can jointly sponsor
- Enrolls patients with Disease Y
- Outcomes for similar patients prescribed products with indication Y can be compared
- Enables recruitment into future targeted RCTs

Evolution of Evidence Generation Platforms

Pre-Market (R&D)

Randomized Controlled Trial (RCT)



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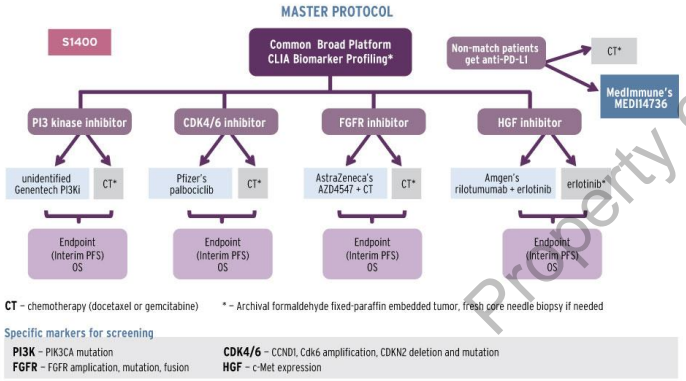
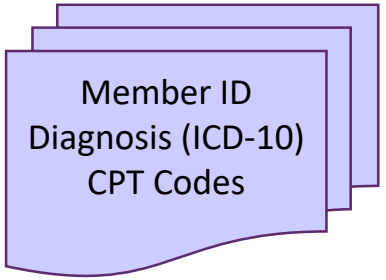
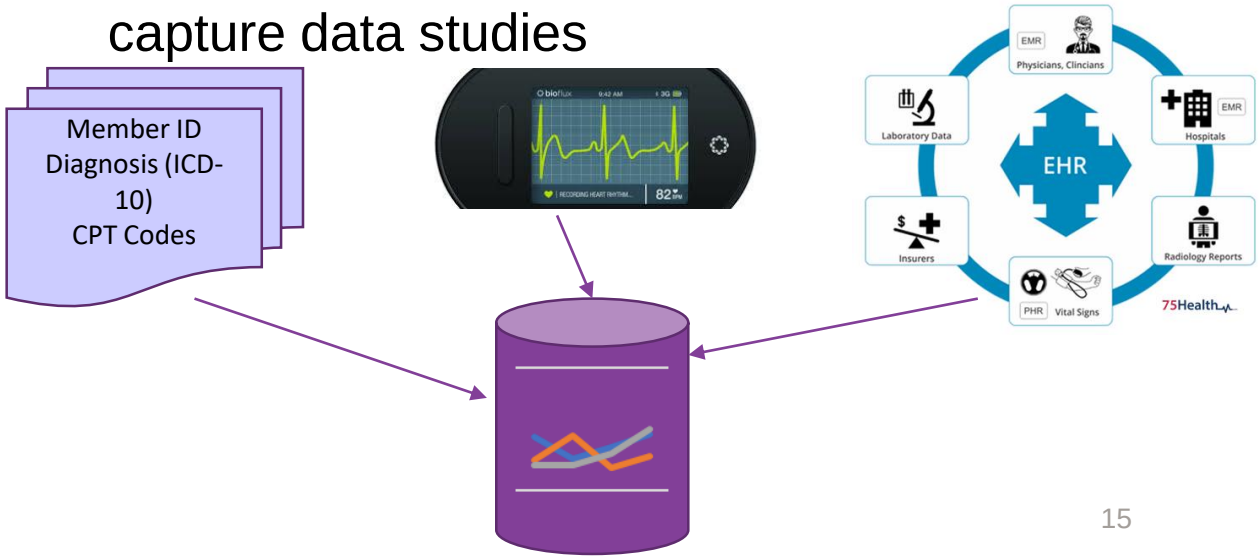


Post- Market (Real-World Evidence)

Claims Data Studies



Integrated EHR, Claims Data and digital remote-capture data studies



The PIPELINEs Vision

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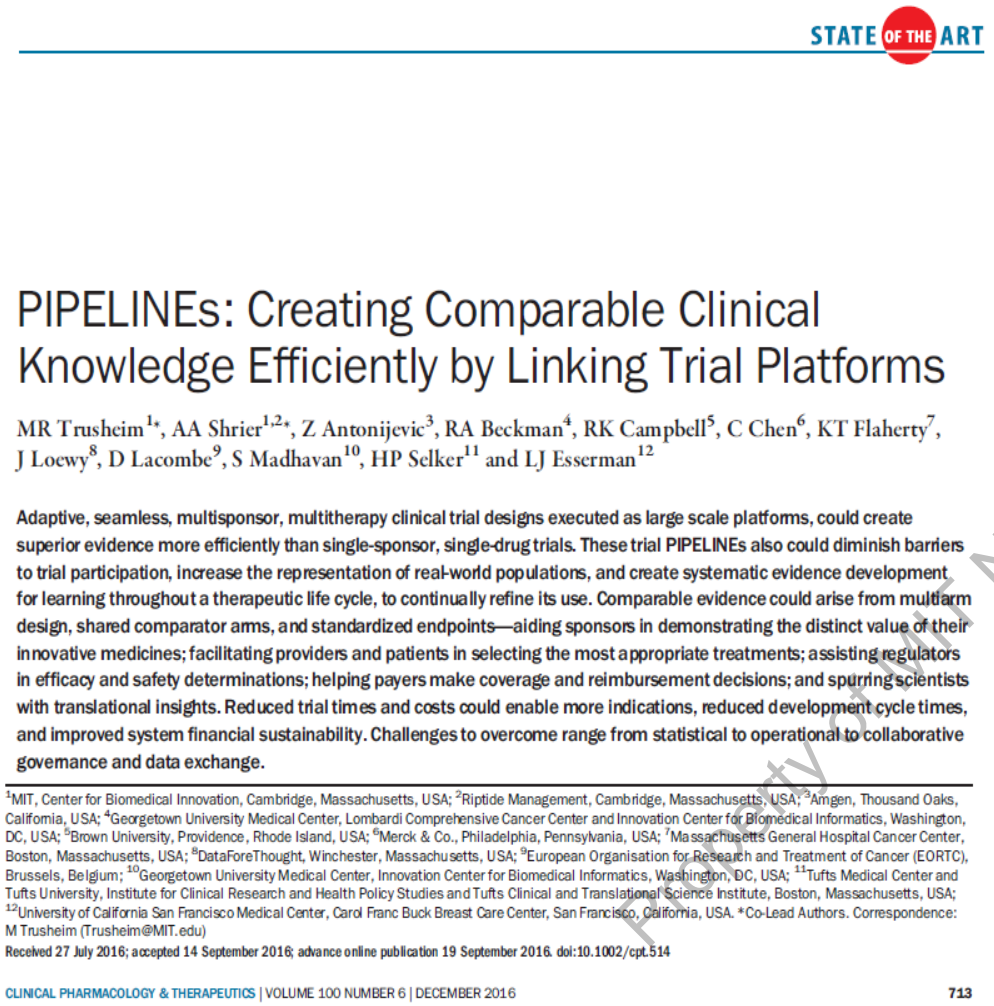
PIPELINEs of Platforms: Challenging Opportunities



STATE OF THE ART

PIPELINEs: Creating Comparable Clinical Knowledge Efficiently by Linking Trial Platforms

MR Trusheim[1]*, AA Shrier[1,2]*, Z Antonijevic[3], RA Beckman[4], RK Campbell[5], C Chen[6], KT Flaherty[7], J Loewy[8], D Lacombe[9], S Madhavan[10], HP Selker[11] and LJ Esserman[12]

Adaptive, seamless, multisponsor, multitherapy clinical trial designs executed as large scale platforms, could create superior evidence more efficiently than single-sponsor, single-drug trials. These trial PIPELINEs also could diminish barriers to trial participation, increase the representation of real-world populations, and create systematic evidence development for learning throughout a therapeutic life cycle, to continually refine its use. Comparable evidence could arise from multiarm design, shared comparator arms, and standardized endpoints—aiding sponsors in demonstrating the distinct value of their innovative medicines; facilitating providers and patients in selecting the most appropriate treatments; assisting regulators in efficacy and safety determinations; helping payers make coverage and reimbursement decisions; and spurring scientists with translational insights. Reduced trial times and costs could enable more indications, reduced development cycle times, and improved system financial sustainability. Challenges to overcome range from statistical to operational to collaborative governance and data exchange.

[1]MIT, Center for Biomedical Innovation, Cambridge, Massachusetts, USA; [2]Riptide Management, Cambridge, Massachusetts, USA; [3]Amgen, Thousand Oaks, California, USA; [4]Georgetown University Medical Center, Lombardi Comprehensive Cancer Center and Innovation Center for Biomedical Informatics, Washington, DC, USA; [5]Brown University, Providence, Rhode Island, USA; [6]Merck & Co., Philadelphia, Pennsylvania, USA; [7]Massachusetts General Hospital Cancer Center, Boston, Massachusetts, USA; [8]DataForeThought, Winchester, Massachusetts, USA; [9]European Organisation for Research and Treatment of Cancer (EORTC), Brussels, Belgium; [10]Georgetown University Medical Center, Innovation Center for Biomedical Informatics, Washington, DC, USA; [11]Tufts Medical Center and Tufts University, Institute for Clinical Research and Health Policy Studies and Tufts Clinical and Translational Science Institute, Boston, Massachusetts, USA; [12]University of California San Francisco Medical Center, Carol Franc Buck Breast Care Center, San Francisco, California, USA. *Co-Lead Authors. Correspondence: M Trusheim (Trusheim@MIT.edu)

Received 27 July 2016; accepted 14 September 2016; advance online publication 19 September 2016. doi:10.1002/cpt.514

PIPELINEs Project Timeline

- Summer-Autumn 2015: Concept formation
- Autumn 2015: DIA ADSWG engagement
- June 2016: Submission to CP&T
- December 2016: CP&T Publication

Why Change from Individually Crafted RCTs?

“One drug, one population, one indication, one phase“ reaching limits

- **Patients** urgently need new treatments but are increasingly resistant to classic RCT participation
- **Uncertainties** (scientific, clinical, operational, and financial) remain unresolved even years after approval
- **Increasing Evidence Demands** from patients, providers, payers, public, policy makers and regulators
- **Expense and Time** required are high
- **Financial Sustainability** for many stakeholders is threatened

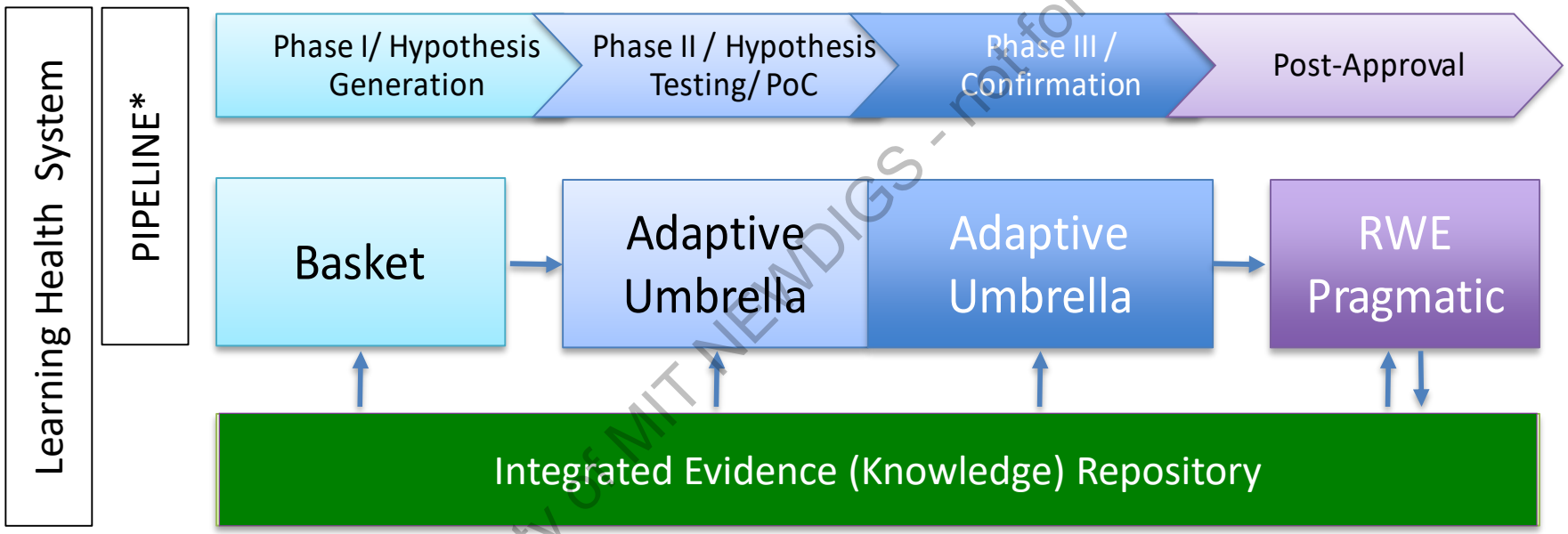
Why Change from Individually Crafted RCTs?

“One drug, one population, one indication, one phase“ reaching limits

- **Success** requires balance among:
  - **Generating knowledge** to reduce uncertainties
  - **Providing patient access** early, appropriately and sustainably
  - **Aligning outcomes** (clinical, operational and financial) **and incentives** in ways acceptable to all stakeholders
  - **Engaging all key stakeholders** in the processes

PIPELINEs Connects Platforms into an Evidence Generation Engine

PIPELINEs could create more credible, comparable evidence faster and cheaper for the benefit of all players (developers, regulators, payers, providers and patients)



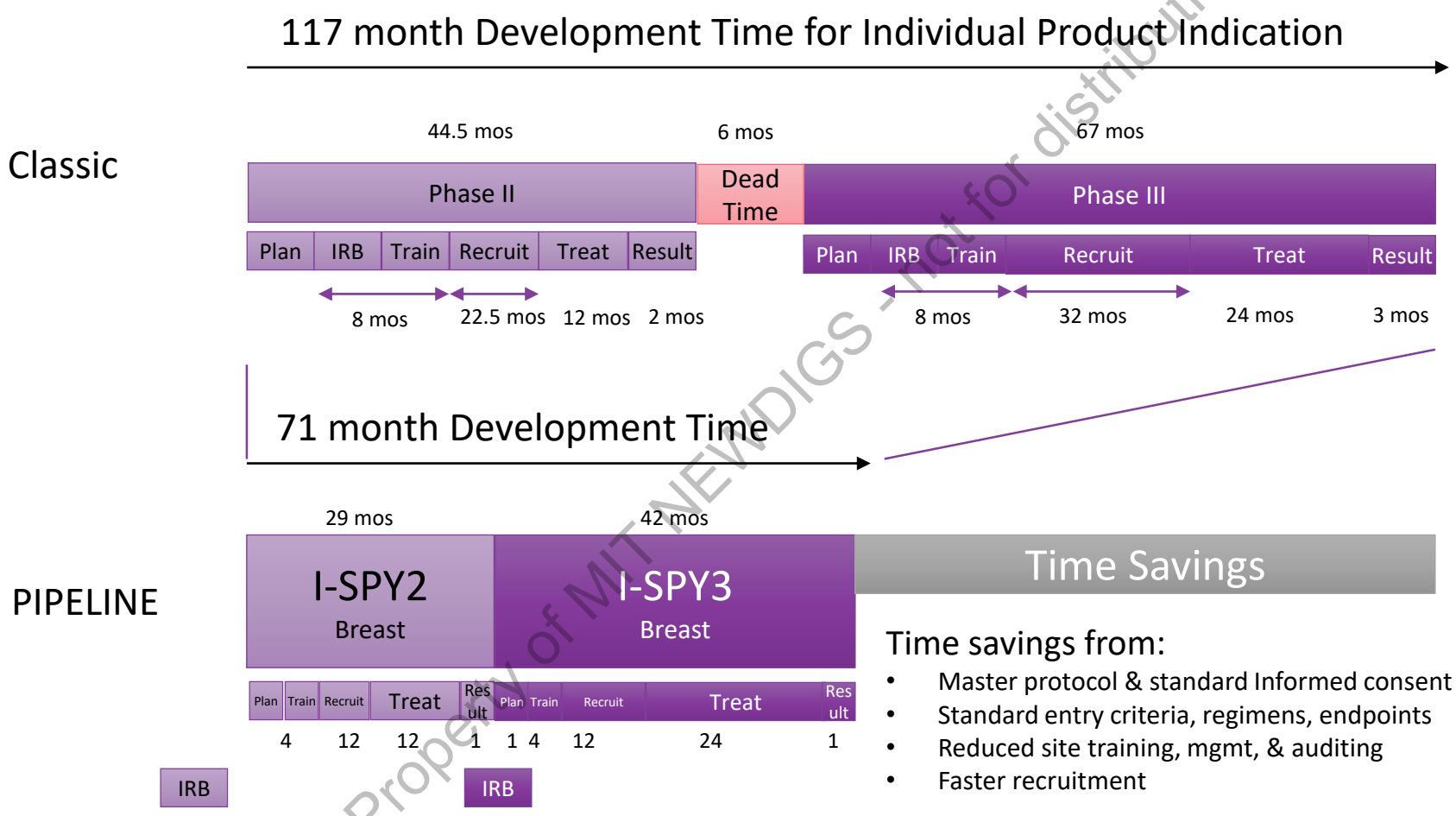
*PIPELINE: Portfolio of Innovative Platform Engines, Longitudinal Investigations and Novel Effectiveness

(Modified from Trusheim et al, PIPELINEs/CP&T December 2016)

PIPELINEs Could Benefit All

Stakeholders	Potential Benefits
Patients	**Faster Access, reduced toxicity exposure in trials & practice** **Increased options and improved regimens over time**
Payers	**Credible, comparable evidence at initial access & in RW setting** **Continued learnings to optimize utilization over time**
Regulators	**Credible, comparable evidence including post-approval monitoring** **Lower auditing burdens**
Developers	**Faster to market at lower cost** **Comparability benefits superior products**
Providers	**More options, indications including patient sub-population info** **Continued learnings to optimize utilization over time**

PIPELINEs Can be Cheaper and Faster

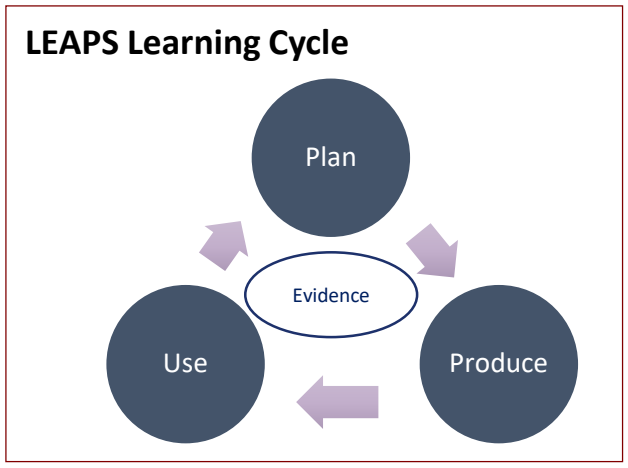


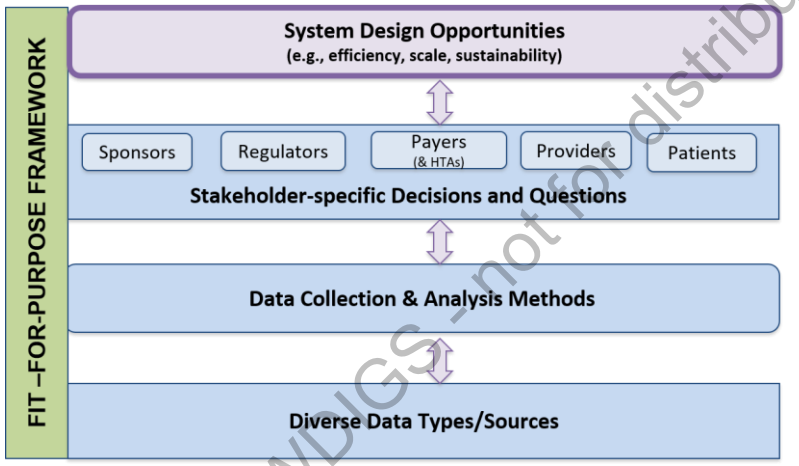
Time savings from:

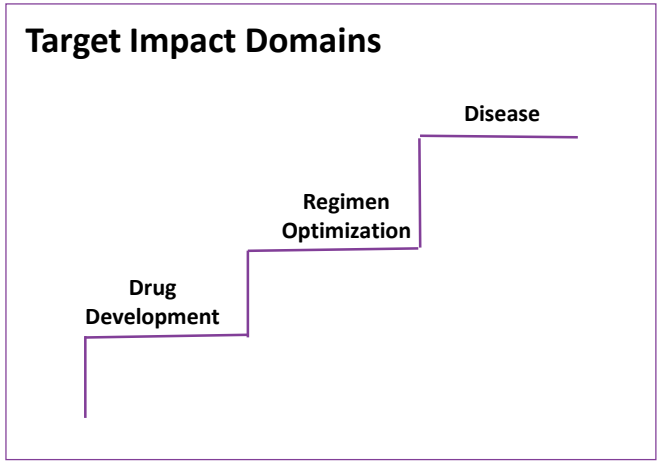
- Master protocol & standard Informed consent
- Standard entry criteria, regimens, endpoints
- Reduced site training, mgmt, & auditing
- Faster recruitment

Connection between PIPELINEs and the Value of Evidence

Tools







	Question	Opportunity to Enhance VoE
Plan	How to produce evidence for downstream stakeholders?	Validated biomarkers, identified subgroups, comparative effectiveness
Produce	How can we reduce time/cost of evidence generation?	Adaptive nature of studies, early read-outs from trials, faster recruitment
Use	How to extend the learnings from platform trials into the real-world environment?	Provide meaningful communications from platform trial to providers and patients in real-world environment