

NEW DIGS

LEAPS

Learning Ecosystems Accelerator for
Patient-centered, Sustainable innovation

Bringing Precision Medicine to life

LEAPS modernizes the downstream system to catch up with the science

Precision Medicine offers the promise of “getting the right treatment to the right patient at the right time.” Yet this aspiration falls short in most diseases, where the standard of care too often remains trial-and-error prescribing. Approved drugs, studied as monotherapies under ideal experimental conditions, face a more diverse population of patients and are used in therapy regimens (combinations and sequences) often not studied via clinical trials once on the market. Our inability to understand the drivers of treatment response variability and predict which drug to use for any given patient at the point of care drives enormous clinical and economic waste/inefficiencies. There are also existing drugs on the market whose value is not fully captured, largely because we lack the evidence needed to guide their use.

Historically most effort and investment in support of Precision Medicine is directed into scientific discovery (‘upstream’). As is often noted by Janet Woodcock (FDA), “systematic learning about new drug therapies stops at the point of regulatory approval.” This must change. LEAPS fuels **Downstream System Innovation** to connect research and clinical practice, to enable vital the real-world use of the products. **The promise of Precision Medicine will never be fully realized without transforming how we produce and use real-world knowledge regarding drug therapy regimens.**

LEAPS, a major project of the MIT NEWDIGS initiative, was launched in 2018 to advance the knowledge and practice of Precision Medicine by modernizing how we Plan, Produce, and Use real-world evidence (RWE). We take a systems approach to enhancing the efficiency and scalability of real-world learning to ensure that the right drug therapies are delivered to the right patient at the right time. Our participatory design approach involves stakeholders in the system who hold the data, use the evidence, and only together have the power to ensure that healthcare is both patient-centered and economically sustainable.

METHODS AND INFRASTRUCTURE INNOVATION

Knowledge production: From cottage industry to industrialization

Precision Medicine should be supported by industrializing RWE production through new flexible, scalable, inter-operable, sustainable RWE generation infrastructures (platforms) that, unlike their traditional predecessors, can address more than one question at a time and adapt their capabilities as new uncertainties emerge.

Standardizing and sharing RWE via Master or Core Protocols, centralized IRBs, and shared bio-specific repositories, for example, will be critical for fueling efficiencies and economies of scale. Leveraging insights from early examples in the marketplace¹, we in LEAPS have designed and prototyped a Real World Discovery Platform, and conceptualized an Adaptive Point of Care (APoC) and a Learning Hub (see Fig 1) for the centralized archiving and curation of evidence. We continue to push the boundaries with the new Predictive Outcomes Platform that will leverage predictive modeling to support Precision Medicine in clinical practice.

1. Angus, D. (2015). Fusing Randomized Trials with Big Data: The Key to Self-learning Health Care Systems. JAMA, 314:767-8.

PROCESS & POLICY INNOVATION

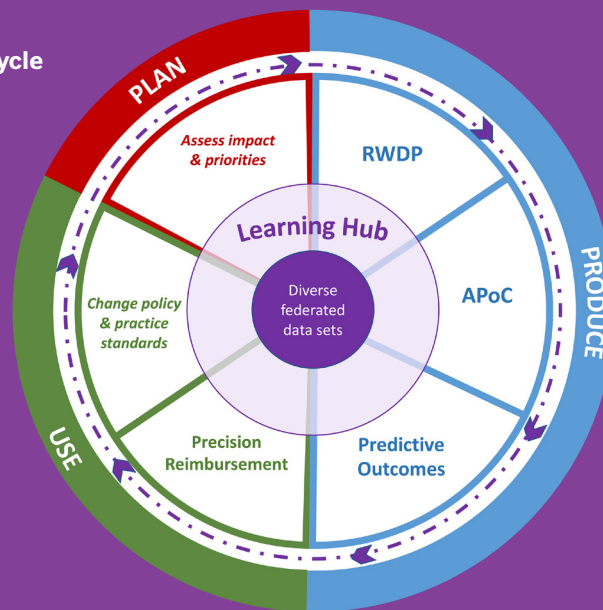
Enabling a Learning Health System: Moving from proprietary silos to collaboration & collective intelligence

The sharing of patient-level data in healthcare is costly and time-consuming, constraining current efforts to scale ongoing RWE production. LEAPS' principles address this in at least three ways:

- **Recognize and exploit RWE production as a value driver for all key stakeholders.** Downstream stakeholders (payers, providers, and patients) generate Real-World Data (RWD) as

OUR EVOLVING BLUEPRINT

Figure 1: The LEAPS Learning Lifecycle



REAL WORLD DISCOVERY PLATFORM (RWDP)

RWDP is an infrastructure of diverse, federated real-world data sources, analytic capabilities, and partnerships focused on discovering insights with potential predictive value for patient-centered decisions and outcomes. In LEAPS, the power of an RWDP is channeled toward optimizing drug therapy regimens for a target disease.

PRECISION REIMBURSEMENT (PR)

The Precision Reimbursement (PR) workstream of the MIT NEWDIGS LEAPS Project is addressing the need for new financing and payment approaches to ensure appropriate access for patients to drug therapies and economic sustainability for the system while progressively strengthening the availability and use of real-world evidence (RWE) for treatment optimization. PR structures align incentives across all stakeholders to achieve these goals in scalable, sustainable ways. PR pilots optimize collaboration value via generalizable learnings while supporting organizational autonomy to tailor specific design elements for pilot partners.

ADAPTIVE POINT-OF-CARE (APOC) PLATFORM

An APoC Platform integrates elements of adaptive clinical trials and point-of-care studies into an embedded, perpetual learning platform designed to assess the comparative effectiveness of regimens of medicines (combinations and sequences).

PREDICTIVE OUTCOMES PLATFORM

The Predictive Outcomes Platform workstream focuses on the need for a new capability for identifying clinically meaningful patient sub-populations of a target disease, and the associated predictive features that support the targeted use of drug therapy treatment regimens for optimal treatment outcomes. The platform will enable iterative cycles of predictive analytics applied by a network of federated evidence generation partners and coordinated by a neutral, centralized third party. The platform is designed to scale efficiently, leveraging the sharing of evidence rather than patient-level data to refine the emergent predictive models.

a by-product of their work/life, but they all need more than just their own data to improve decisions about drug therapies.

- **Minimize the need for patient-level data sharing** using distributed data sources and **Federated Evidence Production** process innovations.
- **Enable pre-competitive collaboration** among stakeholders to reduce RWE production costs and scale.

Through our work in the RWDP and ongoing efforts in Precision Reimbursement and the Predictive Outcomes Platform, LEAPS is defining **new collaborative spaces for RWE production** where the shared need for specific types of RWE is addressed faster, better and cheaper together than alone, with no proprietary risk to any individual party.

RWE standards should emphasize fit-for-purpose thresholds for decision-making, with the flexibility to adapt requirements to context (stakeholder, decision, disease).

We challenge the assumption that RWE for effectiveness must always meet the same evidence standards set by regulators for the assessment of safety and efficacy of new drugs and instead assert that downstream stakeholders each possess unique evidence and must meet different knowledge needs. The gold standard of randomized controlled clinical trials (RCTs) may not be necessary to improve the current state of trial-and-error use of drug therapies in some cases. LEAPS extends “learning for regulatory approval” to address critical knowledge gaps identified by payers, providers, and patients for their decisionst.

INCENTIVE REDESIGN AND INNOVATION

Improving patient outcomes: From conflicting to aligned rewards

The current healthcare system depends on biopharma companies to produce most of the evidence about their products. However, in most cases, the current incentive model in healthcare rewards developers by paying for volume, not actual clinical value delivered. Consequently, the evidence produced emphasizes target average population responses to drugs rather than the individual variations that lie at the core of Precision Medicine.

Payers are interested in evolving toward value-based payment models but are challenged by the lack of high-quality RWE to inform meaningful contract designs as well as to adjudicate payment using such models. Different types of RWD are produced and held by different downstream stakeholders and yet there is no incentive for them to collaborate to generate the RWE they all need. LEAPS is spearheading use cases and pilots in Precision

A SEAT AT THE TABLE

Design Labs² embody the ‘secret sauce’ of NEWDIGS. These participatory design events catalyze transformational system solutions focused on leverage points that lie in the white space between stakeholder silos. They provide a safe haven environment for the collaborative discovery of new ways to share risk, reduce complex uncertainties, and align incentives, together empowering sustainable, patient-centered biopharmaceutical innovation.

Our collaborators can expect to:

- Gain strategic insights into next generation RWE production
- Generate high-impact RWE to fill critical knowledge gaps better, faster, cheaper (with no proprietary risk to any party)
- Influence the next generation of outcomes- and value-based reimbursement models
- Benefit from high-value, cost-efficient R&D associated with downstream innovation
- Gain access to multi-stakeholder thought leaders

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Reimbursement (PR) that will tackle the incentives problem, rewarding treatment regimens tailored to specific patient sub-populations and fueling the production and use of RWE that is critical for the design and implementation of these contractual agreements. As PR becomes more routine, the need for more efficient, scalable RWE production will incentivize this vital collaboration among stakeholders.

Stakeholders are at the center of LEAPS’ innovations

The central tenet of LEAPS is that **all stakeholders benefit from the RWE produced** in the LEAPS Learning System: As uncertainties about the real-world performance of products are progressively reduced, stakeholders face better, more accessible evidence for improved decision making:

2. Baird L, Hirsh G, Adaptive licensing: creating a safe haven for discussions, Scrip Regulatory Affairs, 20 August 2013

LEAPS Project at MIT NEWDIGS

- Patients and providers can more readily benefit from Precision Medicine by optimizing drug therapy regimens to improve patient outcomes based on the best available evidence;
- Payers can mitigate the financial risk in the coverage and reimbursement of drug therapies;
- Developers that understand real-world performance are well-positioned to improve the probability of success for existing and future pipeline products; and,
- Regulators have an enhanced ability to protect public health through real-world learning.

The LEAPS participatory design methodology, guided by our Learning Lifecycle Framework, engages all RWE stakeholders to ensure that the knowledge produced by learning health systems is fit-for-purpose for impact and sustainability.

LEAP WITH US!

LEAPS priorities in 2021/22 focus on two central innovation pillars:

1. Precision Reimbursement: Pilots are demonstrating how to align and connect incentives across stakeholders to fuel the clinical application of RWE.
2. Predictive Outcomes: Creating a platform using a federated approach for predictive modeling to integrate evidence, not data, to improve outcomes through more targeted drug therapy regimens.

We welcome your engagement, support, and input as we continue to innovate and catalyze change.

ABOUT MIT NEWDIGS

MIT NEW Drug Development ParadIGmS (NEWDIGS) is an international “think and do tank” dedicated to delivering more value faster to patients, in ways that work for all stakeholders. NEWDIGS designs, evaluates, and catalyzes the real-world implementation of system innovations that are too complex and cross-cutting to be addressed by a single organization or market sector. Its members include global leaders from patient advocacy, payer organizations, biopharmaceutical companies, regulatory agencies, clinical care, academic research, and investment firms. For more information, visit <http://newdigs.mit.edu>.