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LEAPS

Learning Ecosystems Accelerator for
Patient-centered, Sustainable innovation

RESEARCH BRIEF

By MIT NEWDIGS
LEAPS Project
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Precision for Whom? Partnering with Patients to Ensure that Precision Medicine Targets What Matters.

Despite decades of growth and adaptation in patient engagement, knowing or being able to find guidance for which model or approach will be most impactful in which healthcare or research context can be challenging. Bringing Precision Medicine to life will require that we more fully leverage patient-generated health data (PGHD) and the lived ex-perience and expertise of patients in the co-design and implementation of a next generation learning system. This Research Brief explores the unique role that LEAPS could play as an incubator in advancing "precision patient en-gagement" for Precision Medicine.

BRINGING PRECISION MEDICINE TO LIFE

At the core of LEAPS is a commitment to accelerate Precision Medicine to improve our collective ability to 'get the right treatment to the right patient at the right time' for a target disease. Our strategy focuses on modernizing how we plan, produce, and use real world evidence (RWE) across the biopharmaceutical/healthcare value chain for more efficient, continuous learning and improvement. While most efforts and investments in Precision Medicine center around upstream R&D, LEAPS was launched to systematically strengthen these efforts with connected and scalable real-world (post-market) learning.

LEAPS takes a systems approach to the design of these new learning capabilities, believing that it is critical to engage key stakeholders—those who will benefit from the knowledge created to improve their decisions and outcomes—in the design process. The success of LEAPS will require that we understand how to effectively engage patients as design partners in this new kind of learning system that will both benefit from, and propel, Precision Medicine.

Key takeaways

LEAPS is developing a blueprint for a next generation learning health system that advances Precision Medicine in order to optimize the timely and targeted use of drug therapy regimens for patients within any specific disease area.

While scientific and financial investment priorities for Precision Medicine to date have been channeled to R&D, LEAPS is focused on modernizing the downstream (post-market) system in ways that accelerate, de-risk, and amplify the impact of upstream advancements.

Success in "Downstream System Innovation[1, 2]" will require a deep understanding of how to effectively engage patients in the design and implementation of this new system that both benefits from and propels Precision Medicine.

Building on our experience to date, LEAPS has an exciting and unusual opportunity to advance the field of patient engagement.

PATIENT ENGAGEMENT: HOW DID WE GET HERE?

The basic construct of patient engagement—that patients should be integral partners and purveyors of data in efforts to better diagnose, manage, and treat disease—is not new. Notions of patient engagement can even be seen in the Hippocratic *Epidemics* from thousands of years ago.[3] In the absence of a fully formed nosology for disease and illness, the patient herself was the most important data point. Fast forward a few millennia, and Dr. William Osler is imploring his students to observe the same principle; "Listen to the patient, he is telling you the diagnosis."

Beyond the critical role patients can play in the diagnosis and management of *their own care*, is the role a patient can play in providing the lived experience of disease and illness to research or healthcare innovation. Constructs like Community-Based Participatory Research[4], a cousin to today's patient engagement, first became popular in the 1940s, originally envisioned for initiating social change, but since then adapted to clinical and public health research.

However, the evolution of patient engagement hit its still-current explosive pace with the HIV/AIDS crisis in the 1980s and 1990s. With the creation of the AIDS Coalition to Unleash Power (ACT UP), and similar patient and advocate groups, patients and family members who felt disenfranchised and unheard took steps to learn the science and identify the best ways to insert themselves into the research, development, and regulatory process.[5] From there, the list of initiatives and innovations grows exponentially, both domestically and internationally. The table below provides a snapshot of some of these efforts, which are too numerous to list. Notably, patient engagement efforts now exist in nearly every facet of healthcare and research including but not limited to patient safety and quality improvement, health technology assessment, health services research, clinical research, drug and device

> "With regard to diseases, the circumstances from which we form a judgment of them are by attending to the general nature of all, and the peculiar nature of each individual… to the patient's habits, regimen, and pursuits; to his conversation, manners, taciturnity, thoughts, sleep, or absence of sleep, and sometimes his dreams, what and when they occur; to his picking and scratching; to his tears; to the alvine discharges, urine, sputa, and vomitings; and to the changes of diseases from the one into the other…"
>
> *Epidemics, Book I, Section III*

Patient and Public Involvement (PPI), United Kingdom	The National Institute for Health Research (NIHR) Patient and Public Involvement Programme[6], and "INVOLVE", are governmental and public/private arrangements to incorporate patients and members of the public in the research funding and priority-setting processes and increasingly, in the research process.
Patient-Focused Drug Development, FDA, US	PFDD[7] is "a systematic approach to help ensure that patients' experiences, perspectives, needs, and priorities are captured and meaningfully incorporated into drug development and evaluation."
The Patient-Centered Outcomes Research Institute, United States	The first funder of clinical research to require meaningful partnership with patients and families in the planning, conduct, and dissemination of research.
EUPATI, Pan-Europe (now headquartered in the Netherlands)	EUPATI, the European Patients' Academy[8], formed through the Innovative Medicines Initiative in 2012, has long facilitated and trained patients for authentic partnership in the development and evaluation of therapeutics.
Patvocates, Germany	Patvocates[9], a patient-run, patient-founded coalition to support engagement across healthcare and research.
The Institute for Patient- and Family-Centered Care, U.S.	IPFCC provides training and support for hospitals and health systems, Patient and Family Advisory Councils, and patient and family partners to work together to improve the quality and safety of healthcare.
CADTH, Canada	The Canadian Agency for Drugs and Technologies in Health partners with patients and families throughout the Health Technology Assessment process, to ensure the lived experience of patients is taken into consideration.

Table 1: Snapshot of International Patient Engagement Practices

development and regulation, digital health, and pre and post-graduate clinical training.

GLEANING "HOW-TOS" FROM THE UNIVERSE OF ENGAGEMENT ACTIVITY

As with any type of culture change, progress has been slow and difficult, but over time many promising practices have emerged within specific domains of activity such as comparative effectiveness research (PCORI), and drug and device development (FDA, EMA). These practices share some commonalities but given that engagement approaches necessarily must adapt to the task at hand, they also differ from one another.

Among the most universal of promising or best practices in engagement are: a) building patient engagement infrastructure as early in a process as possible, including at the point of ideation, b) honoring concepts of transparency and trust, c) embracing the idea that each stakeholder can learn from one another, regardless of formal academic training, and d) facilitating the process of engagement, which often requires training or onboarding for patients as well as for the other experts on the team. Many of these practices are captured in the six engagement principles in PCORI's seminal Patient and Family Engagement Rubric.[10]

Accepting and even embracing these concepts may not seem like a big lift, but just how does one *do* this work? Despite a great deal of published literature[11], widely disseminated tools from entities like PCORI[12], and the National Health Council[13], and massive repositories of methods and approaches like the Patient-Focused Medicines Development's repository known as Synapse[14], a critical gap remains supporting stakeholders to identify which engagement approaches work best for which diseases and patient groups, and for what types of projects or activities. This takes on particular significance for an effort like LEAPS, in which multiple activities are combined—including but not limited to health services research, data science, and health information technology optimization.

The translational challenge of applying learnings or models of engagement to a new or unique project exists at a few levels. The first is simply the orientation of the term "engagement". Many engagement efforts are designed and described to engage the patient *as the end-user* rather than as a *partner*; for example, the patient as a clinical trial participant rather than as an advisor on the clinical trial team. Some concepts will apply to both orientations of "engagement", but the majority will not, making the challenge of identifying the best roadmap for a given effort even more difficult. Another challenge in application of promising practices is the frequent need to invert or reframe the learnings as action items. Seeing how another project was able to harness and use the partnership and insight of patients can prove that engagement is worth doing, but it may not *demonstrate* how it was done. Finally, even the best available "how-to" examples can be difficult to reimagine for a new context such as a new topic or a new population. These descriptions are not intended as a criticism of the immense body of domestic and international engagement work and ensuing published guidances and examples. On the contrary, the hope of this discussion is that we can provide a detailed description of our own approaches for developing or applying patient engagement strategies in the moment or over weeks and months of work.

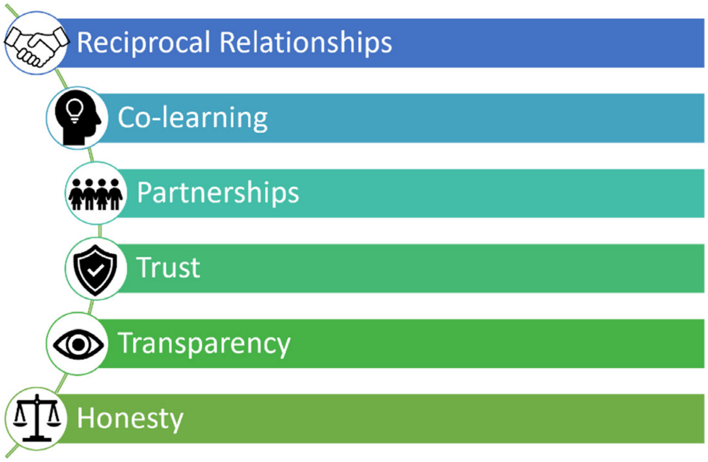

Figure 1. PCORI Patient / Family Engagement Principles

BUILDING IT WHILE WE FLY IT?

The goal of the LEAPS Project is to design and pilot a next generation learning health system for one disease—beginning with Rheumatoid Arthritis—that is empowered to reliably get the right treatment to the right patient at the right time. This system is being designed to propel both the creation and capture of value from Precision Medicine, and focuses on three strategic levers:

- **Multi-stakeholder Collaboration**: Define a new collaborative space for real-world evidence (RWE) production that is better, faster and cheaper together than alone, without any proprietary risk to any party.
- **Industrialization of RWE Production**: Apply platform strategies to the design of new data and analytic infrastructures that enhance the efficiency and scalability of RWE generation.
- **Incentives Alignment**: Develop and align innovative incentives to foster collaborative, patient-centered RWE production.

Underlying each aim and the overall project focus is the notion that patients with lived experience have a critical role to play in this project.

Our undertaking at LEAPS might be one of the most ambitious patient engagement experiments yet. The schematic in Fig. 2 conveys a foundational principle at the heart of our work in LEAPS since its launch: all key stakeholders in biopharma and healthcare generate data as a byproduct of their daily work/life, but they all need more than just their own data to make effective decisions about drug therapies. The LEAPS participatory design approach to Downstream System Innovation engages

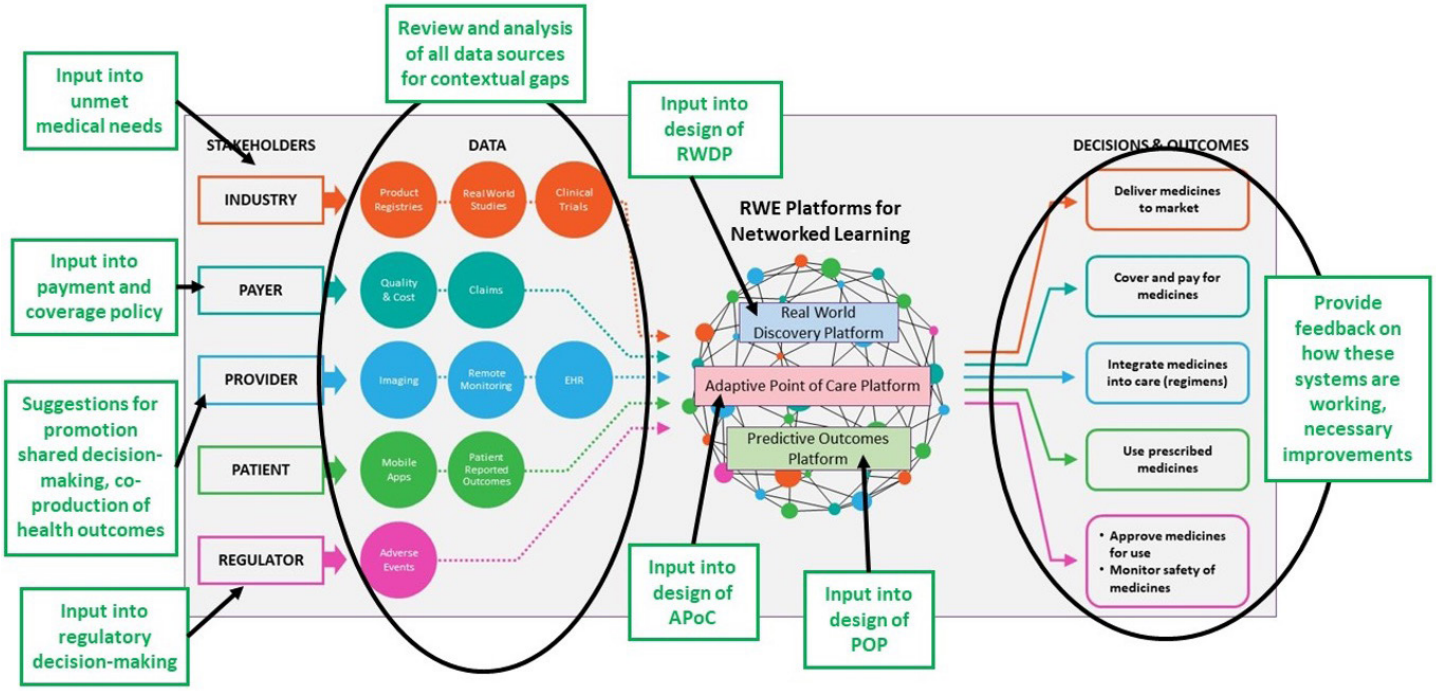

Figure 2 : Functions for Patient Partners in Downstream System Innovation: Patients are a key stakeholder in the healthcare system, actively participating in shared decision-making with providers while also being uniquely impacted by decisions made by all other stakeholders. As such, they play a critical role across all aspects of the design of a LEAPS learning health system, drawing from their lived experience and expertise to better inform inputs and outputs. The green boxes show the many, and still growing, roles they play as design partners as our work advances.

all stakeholders who hold the data, use the evidence, and only together have the power to ensure that healthcare is both patient-centered and economically sustainable. Patients play a unique role in the healthcare system as they alone are ultimately impacted by the decision of all stakeholders. As such, they are not only a key stakeholder, but also a critical design partner across all aspects of the system.

In effect, LEAPS involves the collaborative design of a complex adaptive learning health system. The scope, complexity, and interdependence of design elements provides a valuable opportunity to explore in real time which models of patient engagement work best for which types of tasks/initiatives—and the activities for which no known approaches apply. Patients were rightly identified as a key stakeholder from the very beginning, as contributors to the LEAPS team, and as generators of PGHD and end-users of the therapeutics and best practices generated through the learning platform. Since the launch of this work however, the scope and function of patient engagement has grown significantly, and we have continued to rework and refine the roles for patients and their data. The figure below identifies the key functions for patient partners—both individuals and communities—in both the inputs and outputs of the workstream.

FINDING—OR CREATING—OUR OWN HOW-TOS

A precise recounting of the methodology we used and developed during this work is forthcoming in a publication, but what follows is a snapshot of some key steps in the recent workstreams and the roles that patient partners played in each one. The table below provides examples of these key steps with the related patient activities and impacts. To oversimplify, we relied over and over again on the lived experience of patients, from planning, through conduct, and then to evaluation of each project phase. Depending on the activity, we may rely on the insights of one or two patients who could provide a representative perspective from years of interactions with the broader patient community, a large set of patients long connected to LEAPS, or an even larger set of patients who were unconnected to LEAPS and could provide a "fresh" look. Regardless of the manner in which patients were involved, there was always a unique perspective provided that either served to inform, confirm or modify our next steps.

Perhaps the most novel aspect of the patient engagement activity across all of the work to-date is the real-time development of patient engagement approaches for reviewing, analyzing, categorizing, and drawing conclusions from claims and EMR data. Typically the purview of data scientists, health economists, and large health system experts, inviting patients—and clinicians—to look under the hood at this data and evolving evidence is, to our knowledge, groundbreaking. Given that there is no one-size-fits-

Step	Engagement	Impact
Overall project management	Patients in project leadership roles contributed to planning and execution of tasks	Having patients in leadership roles ensures the patient perspective is always present
Design Lab agenda setting and activities	Patients provided feedback about, presented at, and contributed to discussions at Design Labs.	Patients offered fresh insights into key issues such as valid reasons for non-adherence to medication.
Formulating patient journey “maps”	Patients helped to develop a longitudinal accounting of disease course from their lived experiences and those of their community members.	Patients helped identify key pivot points where decision-making, access, effective therapy, and other weighed most heavily.
Using patient journey maps	Patients vocalized appropriate and inappropriate use of patient journey maps as static tools.	Patients voiced concern about heterogeneity of patient experience may not be apparent in static maps.
Identifying treatment optimization questions and hypotheses for data queries	Patients elucidated the sometimes difficult realities of treatment decision-making and access/cost.	Patients pushed hard to include a focus on the issue of repeat exposure to TNF-alpha therapy, versus solely immediate switching to JAK-inhibitors, more reflective of the experience of the patient community
Formulating data queries to test the hypotheses	Patients helped select patterns in treatment and other care to help identify trends	Patients offered suggestions for proxies of treatment efficacy such as co-therapy, reduction in steroid use, and reduction in frequency of visits
Analyzing the initial data query responses	After being presented with initial data findings, patients reviewed, reflected, and asked clarifying questions to test the validity of the data being presented	Patients identified things in claims data like stops or gaps in treatment that were a familiar and normal part of disease management, not to be misinterpreted as a signal of inefficacy
Reformulating the query or suggesting different “cuts” of data	After the initial data query and presentation to the team, patients helped identify additional ways to cut the information or decipher the findings	Patients helped to refine and account for things like comorbidities or changes in insurance that might influence data findings

Table 2. Patient Engagement Across Data Analytic Activities in LEAPS

all approach to patient engagement, we have had to tailor existing engagement strategies and methods to this concentrated data query and analysis work. This real-time approach to rapid-cycle prototyping and iterative refinement of engagement methods “as we go” could afford an opportunity for LEAPS to serve as an engagement “incubator” of sorts.

A few key practices served as the bedrock for our patient engagement applications, all of which will be important to carry forward in future LEAPS work.

- Accepting that data (claims, EMR, etc.) is not necessarily valid on its face; it may require clean-up or context
- Recognizing that a diversity of both patient perspectives and approaches to involvement is necessary
- Creating an environment where disagreements between patients and other stakeholders do not automatically default toward the non-patient experts and instead aim for thoughtful compromise
- Driving toward compromises that represent the “sweet spot” between what is meaningful and true-to-life for patients AND feasible for rigorous and robust research
- Not penalizing or stewing over assumptions or ideas that do not pan out; the team learns from the experiment what it can, and moves forward

LOOKING AHEAD

Each testbed activity within LEAPS offers an opportunity to experiment, refine, document, and learn about the tailoring of patient engagement. As such, LEAPS offers a unique “incubator” environment for fueling the evolution of patient engagement in the specific context of Precision Medicine.

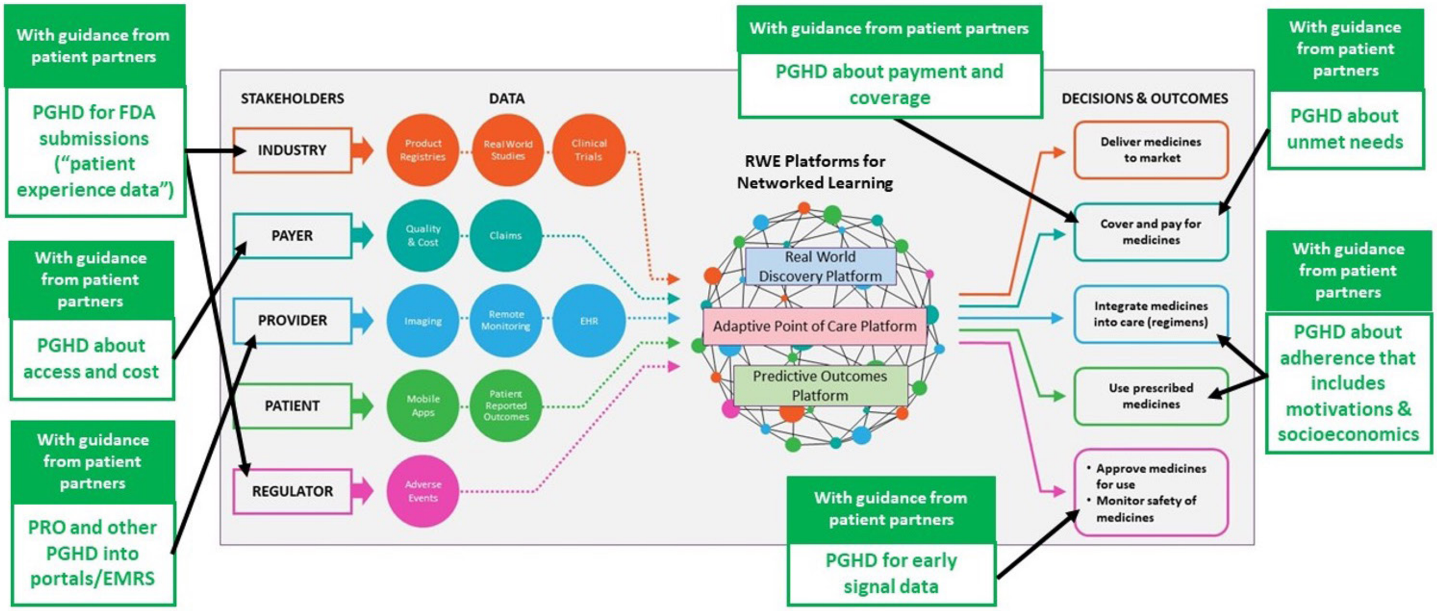

Figure 3 : Enhancing the Value of PGHD with Patient Engagement: In addition to the many key activities for patient partners, there are multiple intersection points for PGHD, both as inputs and as outputs to validate learnings and inform revisions and improvements.

One emerging focus within LEAPS that may offer fertile ground for patient engagement innovation is the incorporation of PGHD into some of our RWE generation platforms. As the utility of "big data" has been increasingly recognized, so too has a precarious practice of siloed and presumptive analysis; drawing conclusions from data from administrative claims or EMRs without input or context from members of the relevant patient community. More problematic, is the belief that because the data *came from* patients, it represents the patient perspective fully and validly, regardless of who did – or did not—do the analysis. This belief is further amplified, though still faulty, when the health data is patient-generated.

Over the past several months the process we have developed ensures patients are partners and critical purveyors of context and insight. For example, something as simple as the frequency with which patients stop and start medications (for a variety of reasons) would not be obvious to those without lived or clinical experience, who might incorrectly interpret that stopping and starting pattern to mean the harvested data was damaged or incomplete. We believe our model could be further developed and described for others to use in their patient engagement efforts, particularly in projects leveraging big data.

The figure above, a second version of Figure 2 above, shows the multiple points of intersection of PGHD with the many LEAPS inputs and outputs. Importantly, anywhere there is a function for PGHD, there is a function for patient partners to help determine how to collect, analyze, and report that PGHD.

CONCLUSION

Patient engagement is not a new phenomenon, but as healthcare innovation—particularly Downstream System Innovation—continues to evolve, patient engagement must evolve too. Our experiences with developing or modifying patient engagement approaches to this workstream has provided a launchpad for further tailoring engagement mechanisms to leverage the full value of patient partnership in contextualization and analysis of data. Furthermore, our opportunity to document what we did and learned in real-time allows us to codify our engagement approaches in a more step-wise manner than other guidances or tools which we believe will mitigate many of the translational challenges referenced above.

ACKNOWLEDGEMENT

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ABOUT LEAPS

LEAPS, a major project of the MIT NEWDIGS initiative that advances 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. For more information, visit https://newdigs.mit.edu/programs-projects/leaps.

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