

NEW DIGS

LEAPS

Learning Ecosystems Accelerator for
Patient-centered, Sustainable innovation

RESEARCH BRIEF

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Baking the Cake: A decision driven framework for planning fit-for-purpose evidence across stakeholders. The LEAPS methodology begins by answering two structured questions: *what* evidence to produce, and *how* to produce it, as outlined in this two-part Research Brief series:

- Part I: Baking the Cake: A Decision Driven Framework to Planning Fit-for-purpose Evidence Across Stakeholders (WHAT)
- Part II: Evidence Generation Platforms: Enhancing the Efficiency & Scale of Evidence Production (HOW)¹

INTRODUCTION

The MIT NEWDIGS “LEAPS Project” is transforming how we plan, produce, and use real world evidence (RWE) to systematically improve patient outcomes. The NEWDIGS 3-Layer Cake framework guides a multi-stakeholder process for determining what evidence is needed for which impactful decisions and suggests latent synergies for generating that evidence.

Applying biomedical innovations in value-based healthcare demands joint decision making informed by targeted evidence generated at scale. Clinical use of biomedical innovations must advance from “trial-and-error” to “predictive” medicine—in which patients, providers and payers are all confident that the right treatment is available to patients as needed. Today, critical knowledge gaps undermine healthcare’s ability to achieve this goal because the current approach to biomedical evidence generation is expensive, inefficient, fragmented, and narrowly focused on addressing one question, for one drug, for one stakeholder decision at a time. The 3-Layer Cake methodology targets these gaps that prevent biomedical innovation from delivering its full value.

KEY TAKEAWAYS

Value-based healthcare requires filling knowledge gaps that undermine the ability to provide the right treatment at the right time to patients.

Stakeholders working together across traditional silos can fill these gaps more efficiently and effectively than working individually.

The NEWDIGS 3-Layer Cake provides a framework that begins with stakeholder decisions and then connects to the minimal ‘fit for purpose’ evidence needed to make them.

The LEAPS pilot for Rheumatoid Arthritis (RA) in Massachusetts (MA) will demonstrate the approach in a real world setting.

The challenge

In traditional biomedical innovation, clinical trials supporting regulatory decision making typically focus on one product, with perhaps one comparator. Systematic learning generally stops at regulatory approval. In addition,

downstream stakeholders may define value differently from regulators. Thus, clinical trial evidence designed for regulatory submissions is often inadequate for downstream decision-making by payers, providers, and patients regarding access to and use of products, both individually and in regimens.

Delivering ‘fit-for-purpose’ evidence requires understanding what evidence is needed by whom, and with what research rigor to be deemed actionable, for their decisions that impact patient access and outcomes.

BAKING THE CAKE

The NEWDIGS “3-Layer Cake” is a strategic framework proven in the NEWDIGS Adaptive Licensing Project² to help develop coordinated product lifecycle evidence plans in multi-stakeholder contexts. It helped stakeholders interact across silos and anticipate evidence needs over time, rather than their traditional insular, step-wise approach to evidence planning and decision-making.

This evidence planning methodology leverages the principle that while *science evolves “from left to right”* on the innovation value chain, (i.e., from Discovery to Development to Delivery), *evidence should be planned “from right to left”* with downstream decision makers (patients, providers and payers) guiding an early understanding of likely real world value drivers for the new product. LEAPS adds the principle that “*Downstream innovation requires explicitly planned evidence generation*”. This transformation lies at the heart of the NEWDIGS LEAPS Project and its first pilot, focused on creating a next generation learning ecosystem for Rheumatoid Arthritis (RA) using Massachusetts (MA) as a statewide testbed, the “RA MA Pilot”.

This strategic framework considers evidence planning in three interdependent layers: each key *decision* (layer I) faced by one or more stakeholders defines the evidence required to answer questions that the stakeholders’ weigh in making that decision. Those requirements drive the *design and analysis methods* (layer II) necessary to generate the ‘fit-for-purpose’ evidence (as determined by the particular stakeholder) from appropriate diverse *data types/sources* (layer III) (Figure 1). In this manner, the totality of the evidence generated is actionable for the stakeholders’ decisions.

I. STAKEHOLDER-SPECIFIC DECISIONS AND QUESTIONS

Key to the process is *defining the impactful decisions* each stakeholder will make and *the multiple questions* needing answers to make those decisions regarding the development of, access to, and/or use of biomedical innovations. This level also defines the evidence requirements that would be considered acceptable for actionable decision-making by the target stakeholder.

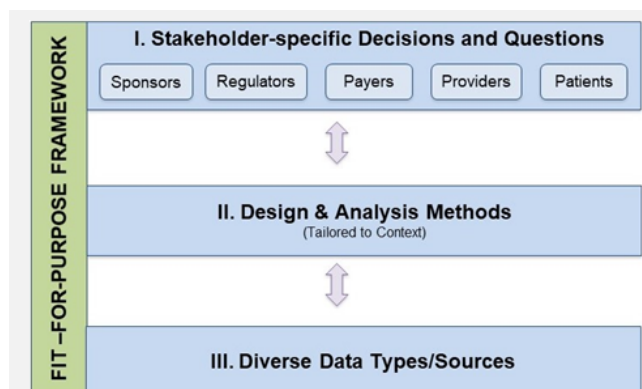


Figure 1. NEWDIGS 3-Layer Cake provides a structured framework for planning evidence that will be fit-for-purpose for decision making by stakeholders in the ecosystem context.

For example, in the LEAPS RA pilot the critical regimen optimization decisions concern access to therapies at a given stage/step/line of therapy, the order of those therapies and in the context of patient preferences, payer costs and clinical sub-population considerations from the molecular to the comorbidities. The evidence requirements regarding endpoints to examine, the sub-populations to examine and the research rigor required to be an improvement over evidence used for current decision making then guide the Level II Design and Analysis Methods selection process.

II. DESIGN AND ANALYSIS METHODS

Once the decisions, the open questions and the strategic evidence required by stakeholders are identified, the specific methods by which to generate the needed ‘fit-for-purpose’ evidence can be determined. Evidence is differentiated from data, as evidence is the product of data collection and analysis methods, not the raw data itself. Fit-for-purpose evidence is gained by consideration of the appropriate study design, endpoints, populations, statistical analyses, and data collection methods. The methods considered include all available in the clinical evidence toolkit. They may range from retrospective to prospective, from randomized to not, from pre-authorization RCTs to Real World to meta analyses and novel approaches. An individual study is unlikely to meet all the needs. The result of this level is likely a multi-pronged evidence development plan that anticipates phases and revisions over time.

III. DIVERSE DATA TYPES/SOURCES

Finally, once the methods to generate the totality of ‘fit-for-purpose’ evidence needed for stakeholder decisions are determined, the data sources (i.e., clinical trial data, medical and pharmacy claims, patient registries, electronic medical records) can be identified or commissioned. This may involve leveraging existing data sources where possible, either “as is” or by a hybrid approach in which existing data sources are augmented with additional data collection or linkages to

other sources. Prospective studies may also be executed as part of the Level II Design which could range from traditional RCTs to adaptive RCTs to pragmatic trials or other real-world study designs. Indeed LEAPS envisions ongoing evidence generation platforms capable of serving multiple evidence needs (See Part II).

While the 3-Layer Cake was originally designed to support evidence planning for a single product, the framework is flexible and can be extended to include multi-product treatment regimens. The initial emphasis in LEAPS is use of real world evidence generation to transform decision making in RA care to tangibly impact patient outcomes. Utilization of the 3-Layer Cake methodology is core to this LEAPS pilot and will be instrumental in the future as LEAPS is expanded to additional diseases and geographies.

Part II of this Research Brief series will focus on ways to implement these evidence plans that not only ensure that the outputs are fit-for-purpose, but also enhance the efficiency, cost, and scale of the associated production processes.

REFERENCES

1. Publication in Fall 2019
2. Eichler, H-G., et al. “Adaptive licensing: taking the next step in the evolution of drug approval.” *Clinical Pharmacology & Therapeutics* 91.3 (2012): 426-437.

ABOUT LEAPS

LEAPS (Learning Ecosystems Accelerator for Patient-centered, Sustainable innovation) is advancing the mission of the MIT NEWDIGS consortium—to deliver more value from biomedical innovation faster to patients, in ways that work for all stakeholders—through a new collaborative systems approach to the planning, generation, and use of evidence across R&D and healthcare delivery. LEAPS is tackling the challenge of delivering on the promise of biomedical innovation in the world of value-based healthcare, which means advancing from “trial-and-error” to “precision” medicine, where patients are confident that they are receiving the right treatments at the right time for their situation. Achieving this goal will require transforming the current approach to evidence generation and use, leveraging emerging LEAPS “downstream innovation” principles to enhance the value of therapeutics for all stakeholders. To this end, a model system for rheumatoid arthritis (RA) will be piloted in Massachusetts (2020 launch), and will inform related efforts in other disease areas and geographies. Success in LEAPS targets better patient outcomes while reducing waste and inefficiency across systems.

This is the second in a series of Research Briefs for LEAPS to document the pilot, describe the tools utilized in its design and implementation, and disseminate generalizable insight to accelerate innovation in other disease ecosystems.

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