

NEW DIGS

LEAPS

Learning Ecosystems Accelerator for Patient-centered, Sustainable innovation

RESEARCH BRIEF

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Rheumatoid Arthritis (RA) chosen as target for LEAPS

Massachusetts (MA) Pilot (RAMA) to demonstrate the feasibility and impact of a sustainable and patient-centered healthcare learning ecosystem to optimize care regimens through evidence generation and coordinated implementation.

GENERAL SELECTION CRITERIA

The target disease for the LEAPS pilot project was selected from four diseases (RA, asthma, type 1 and type 2 diabetes) that met the following general criteria:

Sufficient patient population size in target geographic area (MA). This selection criterion rules out orphan diseases as well as cancer, given the targeted nature of oncology.

Sizeable commercially insured population. The predominant insurer of the target population should not be Medicare; particularly at age of disease onset (<65 years) when treatments are selected.

Biomedical optimization opportunities. Pharmacotherapy is a requisite primary component of disease management, and there *must* be an unmet need in currently available treatments. Excludes diseases with surgery as a first-line treatment.

Critical knowledge gaps exist that prevent delivering the right treatments to the right patients at the right time.

Active biopharmaceutical pipeline to provide ongoing regimen optimization needs.

KEY TAKEAWAYS

RA has high patient outcomes variability along with limited evidence for treatment selection and ordering.

RA outcomes and costs are driven by biomedical interventions, which aids both learning and implementation of a disease-focused ecosystem.

Successfully implementing a learning ecosystem in RA should generalize to other conditions such as asthma and diabetes, among others.

CHARACTERISTICS OF RA

RA is a chronic autoimmune disease that causes progressive irreversible functional impairment due to inflammation of the joint lining (synovium) and erosive damage to the bones. RA is common, with prevalence estimates of 1.6 million patients in the US and approximately 60,000 patients in MA.^{1, 2, 3} Typical age of onset is between 30 and 60, and commercially insured.

Biomedical knowledge gaps on existing agents and anticipated new agents create multiple regimen optimization opportunities for both patients and payers:

- **Pharmaceuticals represented 55% of direct spending** in 2005, but this has likely increased with increased availability and use of biologics.^{4,5}
- **Current clinical guidelines contain limited evidence to differentiate 2nd-line treatments and predict response, and therefore lack a directed treatment algorithm.** As such, treatment decisions by providers are often driven by external factors such as insurance coverage and patient preference rather than strictly by clinical evidence. Disease-modifying anti-rheumatic drugs (DMARDs) are the mainstay of treatment, with methotrexate being the gold-standard, first-line medication. Most patients have an inadequate response to methotrexate over time and warrant the addition of conventional synthetic or biologic DMARDs. Despite many available biologic agents, the ACR70 patient response rate to any of the biologics, following an inadequate response to methotrexate, is only 20-30%.⁶
- **Significant near-term pipeline** of 5 RA drugs in phase 3 trials and 25 RA drugs in phase 2 trials⁷ is expected to yield 8 new approved drugs.
- **The degree of heterogeneity of disease and treatment response is great with clinical validation of biomarkers proceeding slowly.** There are no defined subpopulations other than patients with “mild” or “moderate to severe” disease and there is a lack of comparative effectiveness data. While many RA biomarkers have been identified, their clinical validation has thus far proven to be challenging. Success will likely require a broad and coordinated effort across diverse data sets; this is difficult to implement in the current healthcare system.

Additionally, RA represents a disease area in which the LEAPS pilot has the potential to drive significant impact for all stakeholders.

- **The stakes of ineffective treatment of patients with RA are high, having substantial individual, family, and societal impact.** Delays in effective treatment often lead to disease progression and irreversible joint damage. There is tremendous burden from costs related to co-morbid conditions, diminished quality of life, costs of caregivers, and lost work productivity.
- **Currently, patient access to specific therapies does not yield high clinical value.** An average 30% response rate in 2nd line therapies translates into a 70% cost burden of treatments that are reimbursed by payers but are not clinically effective. This represents substantial waste in the healthcare system that can start

to be addressed through generation of better evidence to support clinical care decisions.

- **The RA drug market is crowded and poorly differentiated,** which increases commercial risk for manufacturers. Without reducing current knowledge gaps, additional products will likely make the treatment landscape more confusing.

SELECTION OF RHEUMATOID ARTHRITIS

Any of the four finalist conditions could have excelled as the MA pilot target disease. The participants at the July 2018 LEAPS Design Lab examined the suitability of each finalist. Considering their findings, the MIT CBI Leadership Team, the LEAPS Strategic Advisory Network, and the LEAPS Steering Committee selected RA as the target disease for the MA pilot project due to its strengths on the general selection criteria, as well as the following factors.

- **Strong patient and provider community.** MA has a broad network of 7 RA Centers of Excellence, as well as highly active local patient groups and American College of Rheumatology leadership.
- **Higher patient adherence background.** RA patient adherence to drug therapies is relatively high with lower variability compared to inhaler use in asthma and insulin management in diabetes.

GENERALIZING BEYOND RHEUMATOID ARTHRITIS

RA offers a powerful exemplar for the initial LEAPS pilot project in MA because of the degree to which complex knowledge gaps 1) undermine effective decision-making for stakeholders within a value-based system; 2) fuel morbidity for patients; and 3) drive waste and inefficiency.

A priority for the LEAPS project is to not only bring solutions to the many stakeholders in MA involved in the care of patients with RA, but to also synthesize generalizable learnings for application by innovators working in other geographical regions and applying the LEAPS principles to other disease targets. The systematic evaluation of knowledge gaps in a target disease area and their resulting impact on patients and other stakeholders in the healthcare system is broadly applicable to identifying the evidentiary needs of any target disease.

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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 first 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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