NEW DRUG DEVELOPMENT PARADIGMS INITIATIVE

TuftsMedicine
Tufts Medical Center

LEAPS

Learning Ecosystems Accelerator for
Patient-centered, Sustainable innovation

DESIGN LAB SUMMARY

June 2023

CONFIDENTIAL

Tufts Medical Center Institute for Clinical Research and Health Policy
Center for Biomedical System Design

LEAPS

Learning Ecosystems Accelerator for
Patient-centered, Sustainable innovation

The LEAPS Project seeks to modernize how we plan, produce, and use real world evidence (RWE) in order to optimize drug therapy regimens for patients. LEAPS seeks to improve patient outcomes in economically sustainable ways through new patient-centered learning healthcare system designs, RWE platform infrastructures, and alignment of incentives across stakeholders. Design collaborators in LEAPS include patient advocacy groups, clinicians, provider systems, healthcare payers, biopharmaceutical and diagnostics companies, regulators, and academic researchers in data science, informatics, biostatistics, epidemiology, and healthcare policy, financing, and reimbursement.

NEWDIGS at Tufts Medical Center 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 initiates advancements 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 https://newdigs.tuftmedicalcenter.org.

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Learning Ecosystems Accelerator for
Patient-centered, Sustainable innovation

DESIGN LAB, JUNE 2023

Executive Summary

On June 13th, NEWDIGS' LEAPS (Learning Ecosystems Accelerator for Patient-centered, Sustainable innovation) Project held a Design Lab exploring innovation in healthcare payment models and used a synthetic oncology case study to explore the utility of value-based contracting (VBC) data for Accelerated Approval products to inform decision-making beyond immediate contract adjudication. The Design Lab was preceded by a special morning session, co-hosted by NEWDIGS and the Innovative Medicines Initiative's Health Outcomes Observatory (H2O), on "How an RWE Infrastructure Could Enable Payment Innovation." Proceedings for the special session will be prepared separately.

Methods Innovation: Federated Learning Landscape

The Methods Innovation team presented an update on the federated learning landscape in healthcare. An evolving approach, federated machine learning, represents an opportunity to train machine learning models collaboratively without having to share data among participating entities. An open-source software tool and training datasets available to researchers were reviewed.

As is often the case, solutions to multi-party incentive problems lag technical capabilities. Currently, there is a lack of incentives for validation of machine learning models, and in some cases, disincentives for participation in FL exist. Pilot activities catalyzed by work completed by the Methods Innovation team are now underway at Merrimack College.

Payment Innovation Framework

The Payment Innovation Roundtable held by NEWDIGS in September 2022 refined and ratified the framework for innovative payment models. Core principles for payment innovation include:

- Ensuring patient-centric, equitable access
- Connecting access and reimbursement to patient benefits received
- Reducing financial volatility
- Achieving operational efficiency
- Designing to learn over time

Possible actions to further payment innovation were discussed, with most Design Lab participants agreeing that education was a suitable focus for NEWDIGS efforts. As a multistakeholder con-

sortium, NEWDIGS is well situated to develop and support internal champions that can educate colleagues, in order to catalyze a tipping point in the adoption of payment innovations.

Accelerated Approval Case Study

To explore how VBCs could address the pressing patient access challenges for Accelerated Approval Program (AAP) products, a fictitious case study was presented of an oncology therapy, "Astrotuminib." Breakout group discussions were intended to push beyond the dynamics of negotiating VBC parameters, to begin to imagine the potential uses of VBC data collected in real-world settings for patient access, payer value assessments, and the regulatory totality of evidence. In each group, participants felt that the data generated from VBCs would be useful for the stated purpose, despite its inherent limitations. Nearly all the groups wanted to collect more data than the VBC would need for simple adjudication and settlement of contract terms. This desire for more data sets up an inherent struggle, constrained by available resources to perform and pay for additional data collection.

- *VBC Outcomes Data CAN Improve Appropriate Patient Access.* By reallocating some financial risk to the manufacturer, VBCs may make "day 1" commercial insurance coverage of Astrotuminib more feasible in the period between accelerated approval and traditional approval. The evidence collected for the VBC may also enable refining the use/dosing/regimen of Astrotuminib. Where the drug is not working for patients, VBC data could improve the appropriate use of AAP-approved products and may enable more timely transition to the alternate treatments. At the same time, it is likely that additional data would be required to confirm patient responses, beyond that which would be collected for the VBC (e.g., discontinuation via claims data). Importantly, the thorny issue of who will pay for collection of additional data was left unresolved.
- *VBCs WILL Impact Payer Value Assessment (PVA) Processes*. VBC data was anticipated to be fit-for-purpose in designing successive iterations of the VBC. With more clarity on patient outcomes, coverage (e.g., expansion from only RCT-like populations to those in the gap between the label and the trial population) and even reimbursement rates could evolve from one version of the contract to the next. In addition, any subsequent payer value assessment (PVA) could review the VBC data as an additional source of knowledge, allowing payers to best ascertain treatment protocols and payer value recommendations. The group grappled with ways for patients to own and control their data, and ways to easily aggregate claims and clinical data upon affirmative permission from the patient. This kind of system change could vastly reduce barriers to implementation.
- *VBC Outcomes Data CAN Contribute to the AAP Regulatory Totality of Evidence*. VBC evidence was felt to be a potential complement to confirmatory trials in regulatory packages for AAP-approved drugs (not on its own). A more robust assessment of prescriber demand, geographic diversity beyond trial sites, and safety, especially in a broader patient population, were the strengths that this type of RWE could bring to the regulatory environment. Given the tension between the desire to expand data collected within VBCs and the constraints of financing that data collection, further work is needed to explore how to identify the minimal data needed and how to align incentives to allow richer evidence.

NEWDIGS Forward Planning

Moving forward, FoCUS and LEAPS will form a new combined project called Payment Innovation for Value and Outcomes for Therapeutics (PIVOT). PIVOT will extend the application of innovative payment models designed within FoCUS beyond CGT to other therapeutic areas and product classes, and beyond the US to global markets. It will explore opportunities to learn from payment innovation data to inform other types of decisions, while also broadening the coalition for change. The first joint Design Lab for PIVOT will be help in Boston on September 26-27, 2023.

Strategic planning for the Tufts Center for Biomedical System Design will continue in 2023 and will center around new activities/programs that accelerate and amplify the impact of NEWDIGS in the US and globally. We look forward to reaching out to many in our collaborator community for your input.

LEAPS

Learning Ecosystems Accelerator for
Patient-centered, Sustainable innovation

LEAPS DESIGN LAB REPORT

June 2023

Introduction

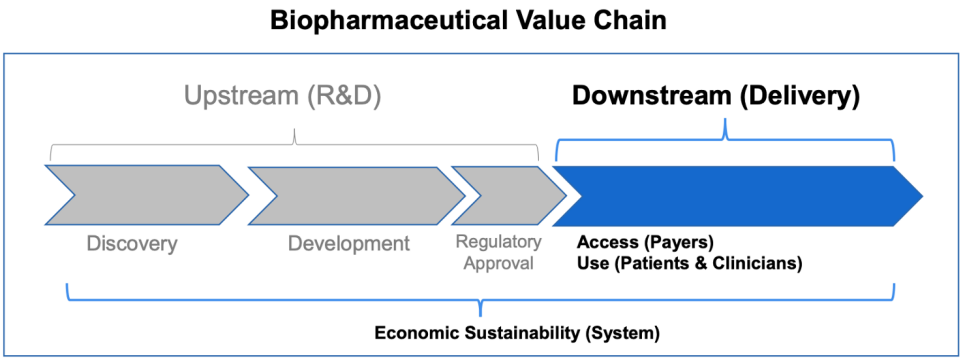
The New Drug Development Paradigms (NEWDIGS) Initiative, a multi-stakeholder design consortium now housed at Tufts Medical Center, has a mission to improve health outcomes by accelerating appropriate and timely access for patients to biomedical products, via innovation in the downstream biopharmaceutical value chain (Figure 1). NEWDIGS has been engaged in linking real-world evidence (RWE) to innovation in healthcare payment models. On June 13th, NEWDIGS' LEAPS (Learning Ecosystems Accelerator for Patient-centered, Sustainable innovation) Project held a Design Lab which continued these efforts, in part by exploring a unique hypothetical case related to value-based contracting (VBC).

The Design Lab was preceded by a special morning session, co-hosted by NEWDIGS and the Innovative Medicines Initiative's Health Outcomes Observatory (H2O), on "How an RWE Infrastructure Could Enable Payment Innovation." Proceedings for the special session will be prepared separately and distributed to participants.

Objectives for the Design Lab included:

- Explore concerns around Accelerated Approval Program (AAP) products in the context of their value, appropriate patient access, and long-term performance.
- Investigate the potential for value-based contracts to address these concerns, while also contributing to the totality of AAP regulatory evidence and supporting Payer Value Assessment approaches.
- Update participants on NEWDIGS work on Methods Innovation and Payment Innovation.

Figure 1. NEWDIGS focuses on downstream system innovation



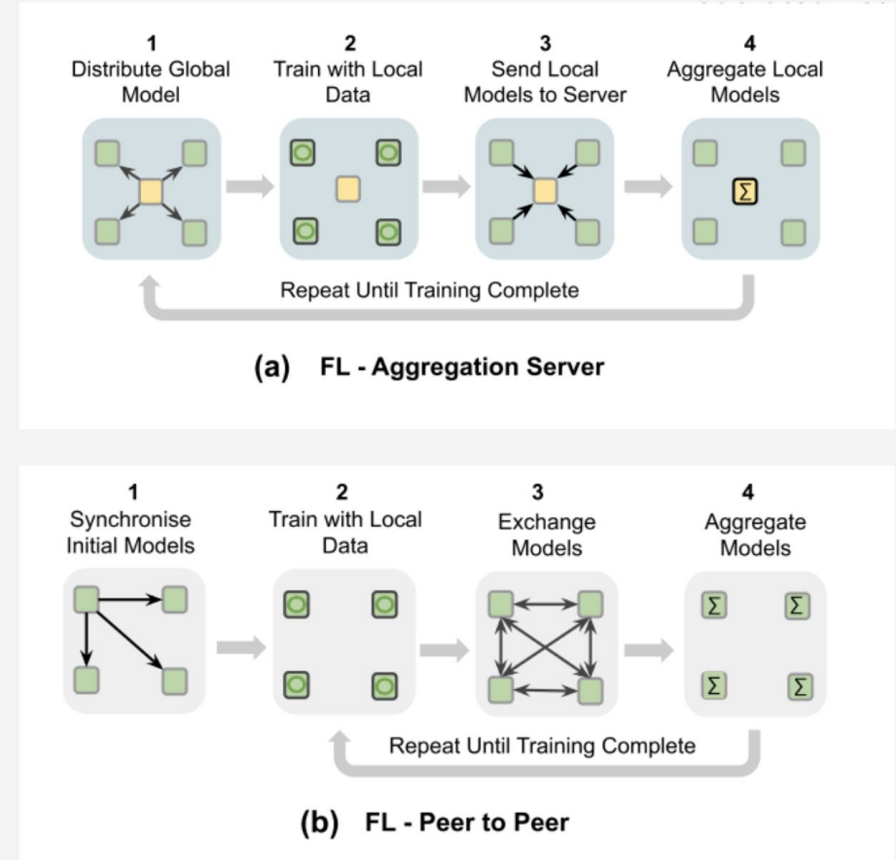
Methods Innovation: Federated Learning Landscape

An important goal of NEWDIGS has been to better understand the rapidly evolving landscape of predictive algorithms, with the goal of driving change in the targeted use of drug therapy regimens, while mitigating disparities in care. To this end, the Methods Innovation team has been pursuing a better understanding of the strengths, weaknesses, and current applications of federated learning in healthcare. Representatives of the Methods team presented an update on this work at the June Design Lab.

In healthcare, machine learning has been used for image processing (e.g., tumor detection) and

other diagnostics, for drug discovery, and for detection of fraud and errors, including prescription errors. The sheer size of the datasets and the need to protect confidential patient information have presented challenges and fostered a tendency for hospital systems to limit themselves to their own collected data. These precautions can lead to bias as each hospital system is exposed to non-uniform influences, such as geographical differences, differences in social determinants of health, or technical capacity differences between the systems. Siloed data can then exacerbate systemic and self-reinforcing "exclusion cycles" [Bracic, *et al*. Science 2022; 377:1158-60] that can drive disparities in research, care, and outcomes. While an evolving approach, federated machine learning represents an opportunity to train machine learning models collaboratively without having to share data among participating entities. Instead, models are exchanged and fitted on local datasets, which can be heterogenous in size and composition, and either aggregated to form a consensus model on a central server, or independently aggregated on a peer-to-peer network (Figure 2).

Figure 2. Federated machine learning frameworks



Design Lab participants learned about Substra, a software tool to enable training and validation of machine learning models on distributed datasets. The software is a ready-to-use federated learning (FL) application developed by Owkin, now open-source and hosted by the Linux Foundation for AI and Data. Also under the Owkin aegis are open-source datasets (FLamby) that are available to the research community and technology partners.

As is often the case, solutions to multi-party incentive problems lag technical capabilities. Currently, there is a lack of incentives for validation of machine learning models, and in some

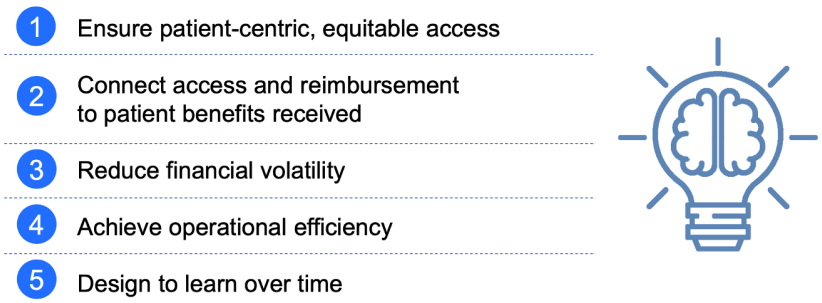
cases, disincentives for participation in FL exist. Data owners / holders may have business models which rely on sales of large data sets for one-off projects. How to value data that is used for FL but remains housed with the data owner is not well established. Other questions centered around how bias mitigation might apply to under-representation of providers as well as of patients, the role of artificial intelligence (AI) in decision support, and ways to ensure accuracy of models and security of data.

Final insights from the Methods Innovation Team will be shared with the NEWDIGS community in an upcoming 3-part series of Research Briefs in the NEWDIGS newsletter. We are pleased to announce that pilot activities that build on this team's work have now been launched at Merrimack College. Further details are available upon request; contact Keileen Hopps (keileen.a.hopps@tuftsmedicine.org).

Payment Innovation Framework

The NEWDIGS Payment Innovation team provided an update on the Payment Innovation Framework. NEWDIGS convened senior decisionmakers from payer and developer communities in September 2022 to discuss what it would take to encourage the use of payment innovation, specifically for durable cell and gene therapies and transformative chronic therapies. The roundtable addressed challenges for innovative payment models, including uncertain effectiveness and safety, high upfront payments and uncertain durability (in cell and gene therapy space), and adherence issues (relevant to chronic therapies). Five core principles were agreed upon for payment innovation efforts (Figure 3).

Figure 3. Five core principles for payment innovation



Possible actions to further payment innovation were discussed at the Design Lab, extending previous conversations from the September roundtable. To reach a tipping point, roundtable participants mentioned critical areas for adoption of Payment Innovation: policy and regulatory innovation, education (e.g., within companies, for all parties needing to sign off on agreements and initiatives), simple and specific solutions, stakeholder alignment, and payment performance transparency. Of these, Design Lab participants agreed that education was the area most suitable to NEWDIGS efforts. As a multistakeholder consortium, NEWDIGS is well situated to develop and support internal champions that can educate colleagues involved in initiating, evaluating, and approving innovative payment models. NEWDIGS resources such as the Paying for Cures Toolkit, webinars, and white papers have already proven valuable in advancing Payment Innovation. Audi-

ences to date have included self-insured employers, reinsurers, stop-loss, and consultants working in these areas. Proceedings from the Next Generation Payment Innovation Roundtable were developed and refined at the November 2022 LEAPS Design Lab and have now been finalized and disseminated.

Accelerated Approval Case Study

In the US, pharmaceutical products with regulatory approval granted through the Accelerated Approval Program (AAP) present specific concerns about how to reduce the uncertainties of benefit and harm that remain at the time of launch (see Box). The AAP process authorizes access to high-potential treatments for small patient populations without viable treatment options. Yet, these conditions themselves create challenges for developing a timely and robust data package. Finding it difficult to assess value, payers may restrict patient access, seek price reductions, or even deny coverage entirely until traditional approval is granted based on confirmatory trial evidence. AAP-approved products are thus a fertile area for innovative payment approaches such as value-based contracts (VBCs). The breakout group discussions were intended to push beyond the dynamics of negotiating VBC parameters, to begin to imagine the potential uses of VBC data collected in real-world settings for patient access, payer value assessments, and the regulatory totality of evidence.

The Accelerated Approval Program & recent updates

In 1992, the US FDA initiated an Accelerated Approval Program (AAP) to address concerns that new medicines for diseases without adequate therapies were not reaching patients quickly enough. Since that time, the FDA's Center for Drug Evaluation and Research (CDER) has approved 278 new medicines via the AAP[1]. The pace of AAP approvals has increased over time, with a quarter of these approvals (70 drugs) granted between 2020-2021.

Through the AAP, medicines that have shown promise to advance care are allowed to go to market with data limited to surrogate endpoints, and an agreement that confirmatory trials would be conducted after market entry to confirm clinical benefit. The confirmatory trials have been a consistent feature of the AAP agreement between CDER and manufactures.

Unfortunately, 1/3 of all AAP-approved medicines (104 drugs) have not completed the confirmatory trials in the agreed upon timeframes. According to the Office of Inspector General report estimates, Medicare and Medicaid spent more than $18 billion for AAP-approved drugs with incomplete confirmatory trials between 2018-2020[2].

There are many reasons why confirmatory trials are so difficult to complete, including limited incentives for patients to join the trials, insufficient resource allocation by manufacturers (or transfer of ownership of a drug), and insurer's interest in negotiating additional endpoints to be included in the confirmatory trials[3]. In response, the FDA has initiated specific changes to the AAP in December of 2022 under the Consolidated Appropriations Act, including:

1. A mandate that confirmatory trials are underway prior to AAP approval decisions.
2. A more streamlined process to take drugs off the market if clinical benefit is not proven.

[1.] U.S Dept. of Health and Human Services, Office of Inspector General, Data Snapshot. "Delays in Confirmatory Trials for Drug Applications Granted FDA's Accelerated Approval Raise Concerns" September 2022 OEI-01-21-00401, p.1.
[2.] Ibid., p.5.
[3.] Kaltenboeck, A., et al, "Strengthening the Accelerated Approval Pathway: An Analysis of Potential Policy Reforms and Their Impact on Uncertainty, Access Innovation and Costs," Institute for Clinical and Economic Review White Paper, April 26, 2021. (Accessed online March 23, 2023), p.18-22.

To illuminate stakeholder issues in VBCs and assess the utility of evidence produced, a synthetic case study was presented of an oncology therapy, "Astrotuminib." Astrotuminib was described as an oral, small molecule therapeutic which was granted accelerated approval for the treatment of Astrorenoma, a malignant kidney tumor not related to renal cell carcinoma. Patients with the grave yet imaginary disease typically face onset between the ages of 35 and 65 years, with a high risk of occurrence in both kidneys (Figure 4). Because of the design of the initial Astrotuminib trial, clinical evidence is available for first-line treatment of patients aged 40-55, with involvement of a single kidney, no metastatic disease, and no history of heart disease; the FDA label is for treatment of non-metastatic Astrorenoma, without regard to age. A confirmatory trial of Astrotuminib is already underway, with 5-year overall survival as the primary endpoint.

Figure 4. Astrotuminib for Astrorenoma

	Astrotuminib for Astrorenoma
Condition	• Malignant tumor of the kidney, unrelated to renal cell carcinoma • Propensity for occurring in both kidneys or early metastasis • Late metastasis to brain primarily • Current standard of care is kidney removal/transplant
Population	▪ Onset at 35-65 years old, gender agnostic ▪ Commercial insurer population ▪ Prevalence in this population is 1 in 30,000
Product	▪ Daily, oral small molecule targeting the "Metaphor Pathway" ▪ Used as first line treatment
Clinical Evidence	▪ 40-55 years old with involvement of a single kidney; no metastasis ▪ Responses split between dramatic responders (30% sub-population) with 24-month PFS and non-responders (70%) ▪ Possibility of preventing life-long dialysis or transplant ▪ No history of heart disease
Label	▪ Granted an Accelerated Approval ▪ Indication: For treatment of non-metastatic Astrorenoma
Payer Segmentation, Coverage & VBC	▪ Commercial population (majority in commercial insurance, including ACA) ▪ Price set at $240k/year, $20K/month, in use as first-line therapy ▪ The VBC would track **discontinuation at <24 months** and provides a **pro-rata performance rebate** of total net spend (100% if discontinued in months 1-3, with linear reduction to 0% if discontinued in month 24).

Several key assumptions framed the case study discussion:

- Responses to Astrotuminib are split between dramatic responders (30%) with 24-month progression-free survival, and non-responders (70%)
- No demographic characteristics or biomarkers have been found to predict which patients will respond to treatment
- Coverage and reimbursement for Astrotuminib has been established for the initial trial population (Figure 5), with a price of $20,000/month and a VBC with rebates to the payer based on a patient's performance on the medication over time
- The VBC tracks discontinuation via filled scripts claims data, with sliding scale rebates based on the time of discontinuation (and presumed failure): 100% rebate if prior to 3 months, decreasing linearly to no rebate at 24 months
- The terms of the VBC have already been negotiated, however, new versions of the VBC are expected annually (Figure 6)

Figure 5. Astrotuminib for Astrorenoma: Trial Population and Labeled Indication

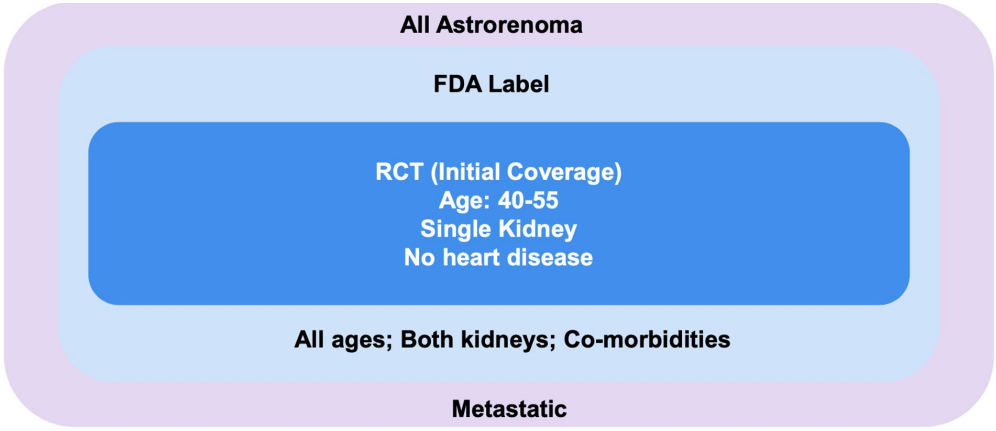
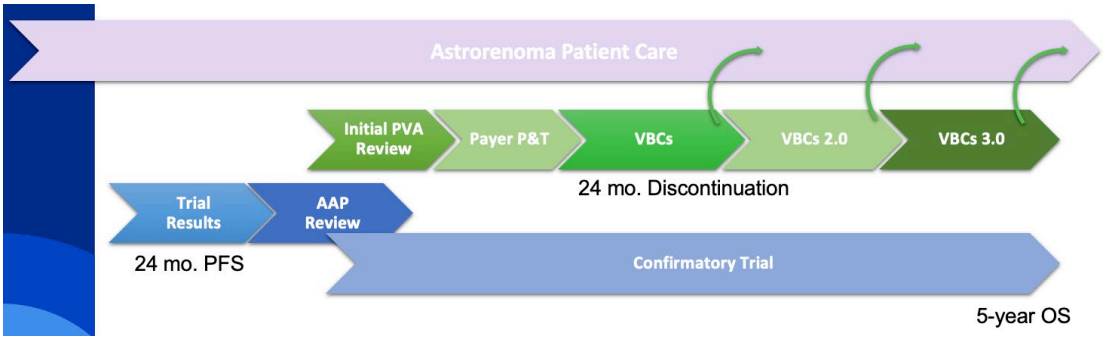


Figure 6. Patient Care Process Refinement
Purple = patient, green = coverage and reimbursement, blue = regulatory process



Accelerated Approval Case Study: Breakout Groups

Breakout groups were divided to consider the utility of VBC outcomes data, as outlined in the hypothetical case example, from 3 perspectives: patient access, payer value assessment, and the regulatory totality of evidence. In each group, participants overall felt that the data generated from VBCs would be useful for the stated purpose, despite its inherent limitations. One commonality in the group discussions was the desire to collect more data than was specified in the VBC of the case, based on discontinuation alone. With many players poised to use the VBC data, a tendency towards "scope creep" may surface, as these users make requests for additional data points or linkage. In the absence of a realistic way to fund this additional collection, this tendency could lead to friction in utilizing VBC data.

*Can VBC Outcomes Data Improve Appropriate **Patient Access**?*
From the patient perspective, patients would be understandably eager to try a first-in-class treatment for this disease. VBCs may make "day 1" commercial insurance coverage of Astrotuminib more feasible in the period between accelerated approval and traditional approval by sharing risk with the manufacturer. Additionally, the Patient Access group decided that one overarching goal was to work towards shifting the 70/30 split of treatment failure to success by learning to better target Astrotuminib treatment. Where the drug is not working for patients, improved prediction may enable more timely transition to the standard treatment protocol, including kidney explantation along with dialysis and/or kidney transplant.

For refinement of patient risk assessment to work, additional data may need to be generated around the prior authorization process which would be richer than claims data alone. This "breaks" the constraints and assumptions laid out in the case. How much richer the data would need to be, and, importantly, who will pay for the data collection were also discussed. Pharmacy benefit managers generate data during prior authorization and could be an important part of the solution; however, a variety of stakeholder incentive issues remain unresolved. Addressing some of these thorny issues will form Part 2 of the AAP case study, during the upcoming September Design Lab.

Ideally, risk sharing leads to differentiation which leads to "right patient, right time" treatment. The potential benefit to patients is obvious; risk sharing in the VBC (i.e., 70% of the population might be eligible for a sizable rebate) means that developer and payer interests are more aligned with those of patients, to rapidly discover who will benefit from treatment. Breakout group participants felt that the more precise the VBC is, the more the parties can be open with each other.

*Might VBCs Impact **Payer Value Assessment (PVA)** Processes?*
The PVA breakout group was overall optimistic that evidence generated from VBCs would be a worthwhile shared decision-making tool, potentially improving overall care. As in the patient access group, VBC data was anticipated to be useful in designing successive iterations of the VBC on an annual basis. Coverage (e.g., expansion from only RCT-like populations to those in the gap between the label and the trial population) and even reimbursement rates could evolve from one version of the contract to the next. There was some hesitation on discontinuation alone as an endpoint in a narrow indication without alternative medications. On the other hand, discontinuation is a simple and clear endpoint, which was felt to be critical in avoiding payment disputes. It also has the advantage of accounting for both lack of effectiveness or safety/tolerability in a single metric. For patients outside of the trial-eligible population (not covered by the initial VBC under this scenario; see Figure 5), some participants felt richer, registry-type data would be needed at the outset.

Cost sharing with patients was seen as a potential confounder for the discontinuation endpoint, i.e., patients unable to afford co-pays or deductibles may discontinue even if they drug is working. The group therefore agreed cost sharing should not be part of a VBC which uses discontinuation as a proxy for effectiveness (and it was not, in the presented case). The particulars of the Astrorenoma case, specifically the special situation of dialysis with regard to Medicare coverage, added complexity to the payer assessment of cost, budget impact, and value.

Looking more broadly at potential system change requirements, the group sought ways for patients to own and control their data, and ways to easily aggregate claims and clinical data upon affirmative permission from the patient. Once that machinery is in place, the information may be so valuable that there would be demand to expand the data collected in future iterations, to help examine the sources of variability. The burden of collecting data from clinicians to support each VBC (especially when and if they become more common) was seen as a significant barrier to implementation, compared to current automated methods of data collection, even if imperfect. Pushback from the commercial payer and developer participants about increasing VBC complexity and cost, even minimally, means that players who would want more data are many, while those willing to fund its collection are few.

*Can VBC Outcomes Data Contribute to the AAP **Regulatory Totality of Evidence**?*
Two groups examined whether VBC outcomes data might contribute to the totality of evidence for AAP-approved drugs, using the synthetic case. The perspective provided by considering "totality of evidence" was a useful one, since the VBC data was felt to be a potential complement to confirmatory trials in regulatory packages (not on its own). A more robust assessment of prescriber demand, geographic diversity beyond trial sites, and safety, especially in a broader patient population, were the strengths that this type of RWD could bring to the regulatory environment.

Another, practical point in favor of utilizing VBC data was that a large proportion of the patient experience may be captured from contracts with only a few major market players (the top 3 pharmacy benefit managers represent ~80% of prescriptions, according to a participant). The opportunity to work across fewer institutions would allow for less variability in reporting processes and more efficient data sharing practices, especially where small patient populations are involved. Similar to the patient access and payer-oriented groups, some participants in both regulatory-focused breakout groups expressed the desire to modify future iterations of the VBC in order to collect more contextual data, such as reasons for discontinuation and need for dialysis.

From a developer perspective, participants wondered if collecting outcomes data in a VBC posed a risk to regulatory submission, e.g., for expanded indications or for full approval. Lack of data ownership could lead to hesitation on part of developers to participate in VBCs. For data sharing, one group intended that the payer should publish the evidence while holding the raw data and could submit data directly to FDA. Others felt it appropriate for the drug manufacturer to report all data to FDA as part of a submission package, meaning data transfer would be necessary at some point. As a counterpoint, several participants pointed out that the pharmaceutical industry's track record for fulfilling confirmatory trial requirements has not been good, leading to skepticism by providers and guidelines groups that additional data sharing requirements would be met. If timely VBC data becomes a routine part of the available evidence for AAP-approved products, that could mitigate these concerns.

LEAPS Forward Planning

The Design Lab closed with a discussion of NEWDIGS priorities moving forward. NEWDIGS started in 2011 with work in Adaptive Licensing – while the topic was regulatory, the success story involved process, more than policy, innovation. At the core of Adaptive Licensing was a fundamentally different way for stakeholders to work together across the product lifecycle to share risk and progressively reduce uncertainty. This project also elucidated capability gaps in the downstream (post-market) system that represented barriers to the adoption of Adaptive Licensing, including (1) the need for more flexible payment models that

In Case You Missed It
LEAPS Activities

As an outgrowth of previous Design Lab work, LEAPS teams recently released:

- White paper from the METRICS team on a practical approach for defining outcomes and thresholds for predictive healthcare algorithm development using real-world data
- A Research Brief series from the Methods Innovation team
- The LEAPS Lipids Management team held a webinar in December 2022

NEWDIGS is continuing to work to accelerate next generation outcomes tracking. We are exploring the opportunity to develop a generalizable set of principles to enhance system readiness for outcomes tracking to support payment innovation for biomedical products and patient value.

rewarded clinical value demonstrated, and (2) the need to improve the efficiency RWE production. These identified gaps led to the launch of the FoCUS and LEAPS projects, respectively.

In ensuing years, NEWDIGS has been running FoCUS and LEAPS as two separate projects, yet it has become clear that they represent two sides of the same coin and need to evolve together. Payment innovation solutions require RWE to implement, and incentives (including financial incentives) must be aligned in order to ensure the sustainability of RWE production.
Moving forward, activities within FoCUS and LEAPS will be integrated under the name **Payment Innovation for Value and Outcomes for Therapeutics – PIVOT** (Figure 7).

PIVOT will extend the application of innovative payment models designed within FoCUS beyond durable cell and gene therapies to other therapeutic areas and product classes, and beyond the US to global markets. It will explore opportunities to learn from payment innovation data to inform other types of decisions, while also broadening the coalition for change.

FoCUS will continue to operate as a special interest group within PIVOT, maintaining its focus on durable and curative therapies in the US (Figure 8). The overarching goal of PIVOT will remain accelerating appropriate and timely access to biomedical products, in ways that work for all stakeholders.

Figure 7. NEWDIGS introduces PIVOT: Payment Innovation for Value and Outcomes for Therapeutics

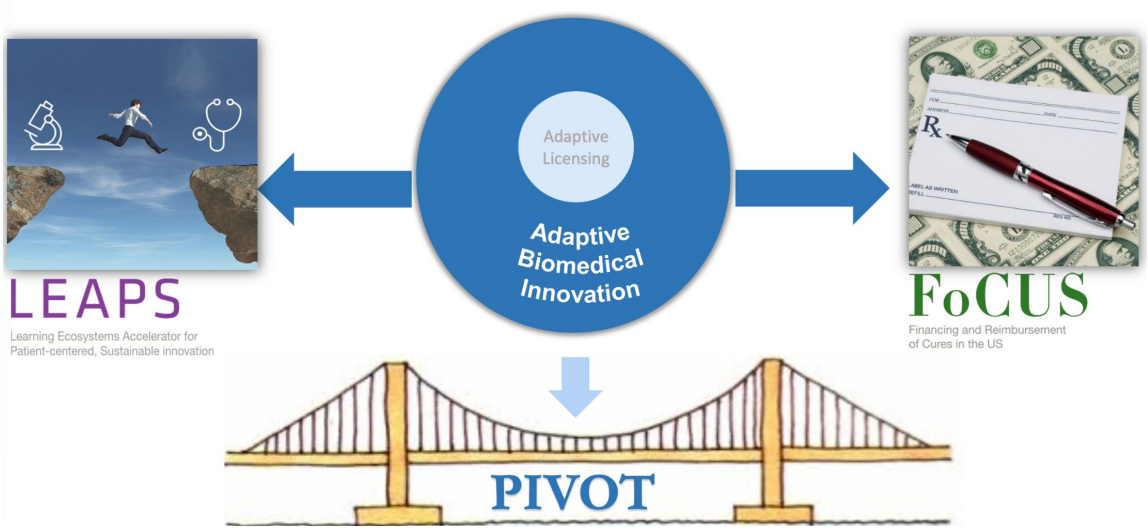
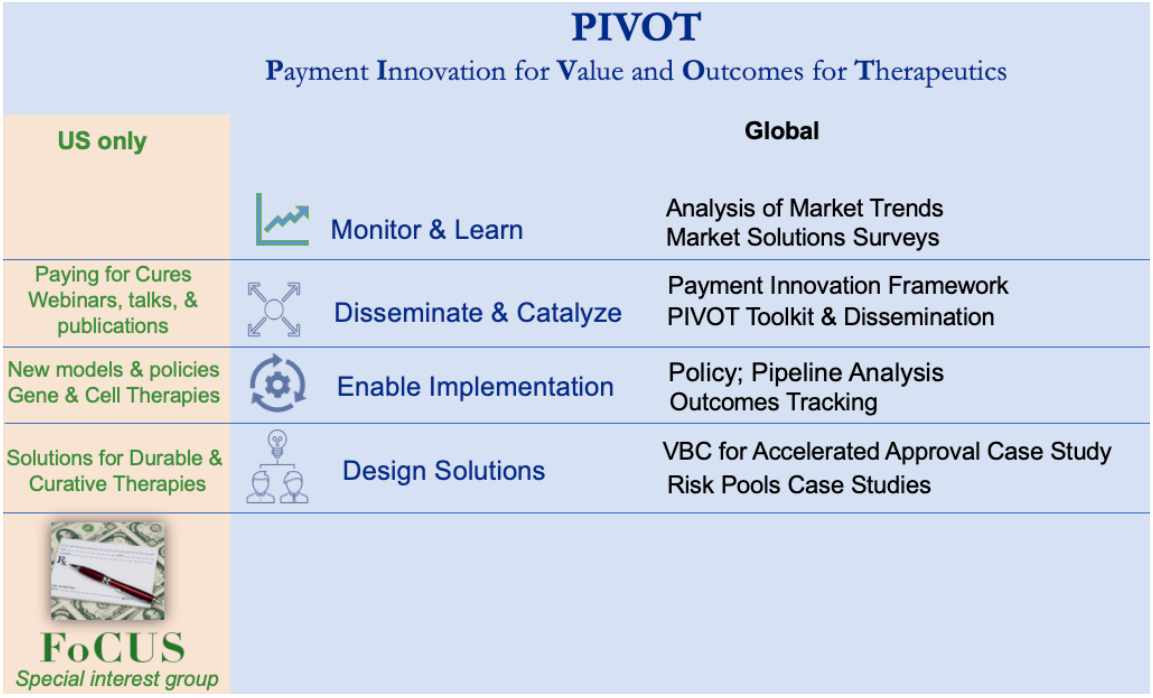


Figure 8. Current activity areas within PIVOT



A three-year strategic plan is now under discussion by the PIVOT Team. Priorities will address challenges across key components of the NEWDIGS payment innovation lifecycle, including:

- Design solutions
- Enable implementation
- Disseminate and catalyze
- Monitor and learn

We will hold the first NEWDIGS PIVOT Design Lab in September 2023. Part 2 of the Accelerated Approval Case Study will be explored at that Design Lab, scheduled for September 26-27, 2023. Two Design Labs, in April and September, are planned for 2024 in Boston. Additional case studies are under discussion for 2024.

See Figure 8 for activities now underway in PIVOT, and Appendix A for a list of current team-based engagement opportunities. Additional engagement opportunities (team membership, new case studies, research projects, communication & educational activities, etc.) will be announced as they are defined, so stay tuned for updates!

Appendix A

Teams seeking new members

PIVOT Team
Team Lead: Mark Trusheim
Provides input into the strategy and implementation planning for all activities across the PIVOT project including those associated with:

- Monitor & Learn
- Disseminate and Catalyze
- Enable Implementation
- Design Solutions

Monitor & Learn

Analysis of Value-Based Contracting Market Trends
Team Lead: Mark Trusheim

Exploring the evolving market trends in Value-Based Contracts (VBCs) to demonstrate and identify patterns of expanding use of VBCs globally. By leveraging existing data sources and proprietary database solutions, the team is investigating issues of patient access, clinical efficacy and categorize by disease type rather than products. Establishing a repository for CGT Outcomes-Based Contracts is also potentially of interest to the group, particularly with a focus on collecting data and outcomes that show clinical efficacy.

Disseminate & Catalyze

FoCUS Catalyst Communications
Team Lead: Tsega Meshesha

Leads the publication efforts, speaker engagements, and preparation of resources for presenters across different platforms. Proactively disseminating FoCUS thought leadership and education, the team will focus on guiding stakeholders in integrating the findings into their strategies and operations, with a particular emphasis on promoting the Paying for Cures Toolkit.

Paying For Cures Toolkit: Navigation and Design
Team Lead: Karen Geary

Responsible for maintaining the Toolkit website with industry updates and all relevant briefs and progress notes from FoCUS. Other Toolkit activities will include the development of visual presentations of information as downloadable infographics and/or slides.

Enable Implementation

Policy Team

Team Leads: John Glasspool, Mark Trusheim

Currently focusing on several key policy areas, including

- Examining, in the context of Accelerated Approvals, the potential for VBC outcomes data to improve patient access, reimbursement decisions, and the totality of evidence for regulatory decisions.
- Regulatory barriers in value-based pricing (VBP) and the Medicaid Best Price (MBP) program, as well as the mechanics of the Average Sales Price (ASP) system.
- Engaging with the Center for Medicare and Medicaid Innovation (CMMI) and exploring topics related to Cell and Gene Therapies (CGT) and their relationship to Accelerated Approval.
- Studying patient shifting dynamics, such as the impact of the State Innovation Waivers (e.g., for self-insured employers), the Affordable Care Act (ACA), Patient Assistance Programs, and Medicaid.
- Evaluating pooling approaches, both their own and those initiated by CMMI, to identify opportunities for collaboration and knowledge-sharing.

Medicaid Best Price (MBP) Research team

Team Lead: Mark Trusheim

Developing a research paper to provide a comprehensive explanation of the phenomenon of 340B and ASP interactions with VBCs. This analysis aims to examine the dynamics between Average Sales Price (ASP) and the 340B program, specifically focusing on their impact on VBCs.

Pipeline Analysis and Modeling: Predictions and Insight on the Health Ecosystems' Capacity for CGTs

Team Leads: Claire White, Colin Young

Generating an overview of current and anticipated practices regarding the infrastructure and ability to administer cell and gene therapies in both in- and out-patient settings. Our study aims to identify what is feasible and acceptable to enable timely patient access, while illuminating best practices, issues or challenges that impact providers' capability. Work will be done in a multi-stakeholder setting to enable patients to engage in and suggest patient-centered solutions.

Design Solutions

New team engagement opportunities will be announced as the PIVOT Team defines strategic priorities and associated case studies.

Appendix B

List of abbreviations

AAP	Accelerated Approval Program
AI	Artificial intelligence
FDA	Food and Drug Administration
FL	Federated learning
FoCUS	Financing and Reimbursement of Cures in the US
H2O	Health Outcomes Observatory
LEAPS	Learning Ecosystems Accelerator for Patient-centered, Sustainable innovation
NEWDIGS	NEW Drug Development ParadIGmS
PIVOT	Payment Innovation for Value and Outcomes for Therapeutics
PVA	Payer value assessment
RCT	Randomized controlled trial
RWD	Real-world data
RWE	Real-world evidence
VBC	Value-based contract