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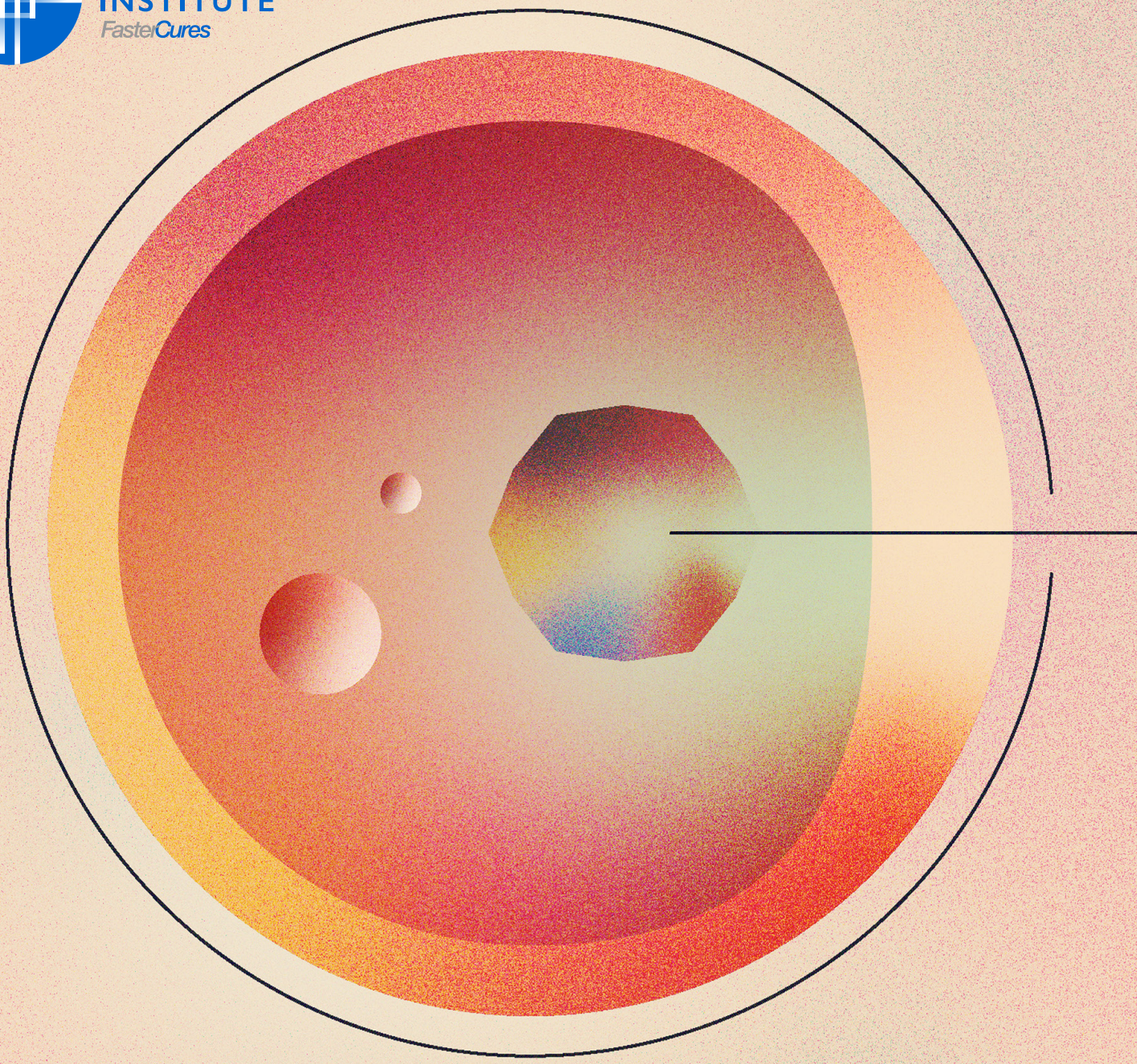
FasterCures



Cures for Life: Long-Term Follow-Up Data Collection for Cell and Gene Therapies

ANITA NOSRATIEH, PHD, AND RACHEL TUNIS

About the Milken Institute

The Milken Institute is a nonprofit, nonpartisan think tank.

For the past three decades, the Milken Institute has served as a catalyst for practical, scalable solutions to global challenges by connecting human, financial, and educational resources to those who need them. Guided by a conviction that the best ideas, under-resourced, cannot succeed, we conduct research and analysis and convene top experts, innovators, and influencers from different backgrounds and competing viewpoints. We leverage this expertise and insight to construct programs and policy initiatives.

These activities are designed to help people build meaningful lives in which they can experience health and well-being, pursue effective education and gainful employment, and access the resources required to create ever-expanding opportunities for themselves and their broader communities.

About Cures for Life

In 2019, FasterCures launched the Cures for Life project to elevate the patient voice in the new and rapidly evolving landscape of cell and gene therapies. We conducted interviews and workshops with a variety of stakeholders, with an emphasis on the participation of patient organizations, to identify common challenges to ensuring that patients have access to life-saving cell and gene therapies. Throughout 2020, FasterCures will host a series of issue-specific workshops to discuss emerging areas of focus where we can help amplify the patient perspective.

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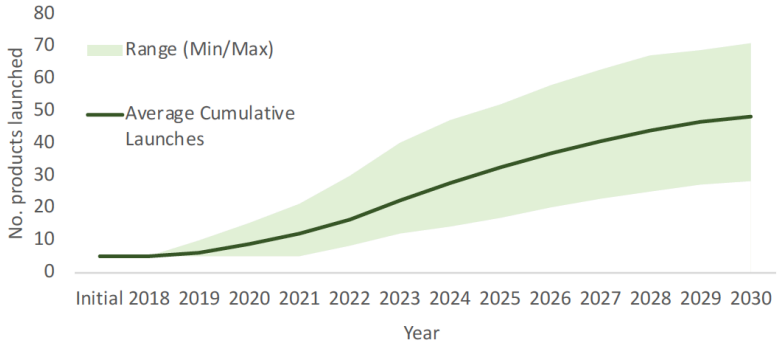
INTRODUCTION AND OVERVIEW

Advances in biomedical innovation have given rise to new transformative therapies, including cell and gene therapies, with incredible potential to improve the lives of patients dramatically. These innovative treatments may treat or even cure debilitating genetic, oncologic, and other diseases once thought incurable.

FIGURE 1: PROJECTED CUMULATIVE PRODUCT LAUNCHES - 2017 TO 2030



Source: "Projections from the Existing Pipeline of Cell and Gene Therapies," MIT FoCUS, Research Briefs (2018)

In 2017, the first cell therapy was approved in the US. Currently, four products are approved in the US, and six products are approved in Europe.[1] These therapies come with price tags of hundreds of thousands to millions of dollars, leaving the health-care system scrambling to figure out how to pay for these treatments efficiently and sustainably while ensuring patient access.

1. "Approved Cellular and Gene Therapy Products," US Food and Drug Administration, March 29, 2020, https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/approved-cellular-and-gene-therapy-products; "Gene Therapy Medicinal Products," Paul-Ehrlich-Institut, last modified April 6, 2020, https://www.pei.de/EN/medicinal-products/atmp/gene-therapy-medicinal-products/gene-therapy-node.html.

TABLE 1: CURRENT FDA- AND EMA-APPROVED THERAPIES[2]

Company	Product	Type	Disease	List Price	FDA Approval	EMA Approval
Novartis	Kymriah	CAR-T	Acute Lymphoblastic Leukemia	$475,000	August 2017	June 2016
Kite	Yescarta	CAR-T	Diffuse Large B-Cell Lymphoma	$373,000	October 2017	May 2016
Spark	Luxturna	Gene therapy	Inherited Retinopathy	$425,000/eye	December 2017	November 2018
Novartis	Kymriah	CAR-T	Diffuse Large B-Cell Lymphoma	$373,000	May 2018	August 2018
Bluebird Bio	Zynteglo	Gene therapy	Transfusion-Dependent B-Thalassemia	$1.3-1.4 million	N/A	June 2019
GSK	Strimvelis	Gene therapy	ADA-SCID	$665,000	N/A	May 2016
Amgen	Imylgic	Gene therapy	Melanoma	$65,000/week	N/A	October 2015
AveXis	Zolgensma	Gene therapy	Spinal Muscular Atrophy	$2.125 million	May 2019	N/A

The currently approved cell and gene therapies target rare diseases with smaller patient populations who may have few or no other treatment available. The US Food and Drug Administration (FDA) requirements for approvals do not require the hundreds of thousands of patients needed for traditional drug approvals, thus shortening the time to market and enabling earlier patient access. Because the datasets are less mature, FDA requires post-approval data collection for up to 15 years.

2. Ibid.

Only four cell and gene therapy treatments have been approved in the US, but many more promising treatments are in the pipeline. By 2020, FDA anticipates receiving more than 200 Investigational New Drugs per year and, by 2025, approving 10-20 cell and gene therapy products covering a wide range of therapeutic areas per year.[3] These therapies are designed to instigate permanent or long-acting changes in the body, which pose higher risks of delayed adverse events, uncertainties about the full range of benefits, and unknown implications for a larger patient population over an extended period.[4]

Collection of long-term follow-up data is needed to address the many unanswered questions about the effects of these therapies. Because this field is rapidly evolving, the outcomes data collected now will serve to extend the understanding and applications of cell and gene therapies far into the future. Patient groups, regulators, health-care providers, health insurance plans, developers, and research groups are all grappling with uncertainties that could be answered through post-market data collection.

3. "Statement from FDA Commissioner Scott Gottlieb, MD, and Peter Marks, MD, PHD, Director of the Center for Biologics Evaluation and Research, on new policies to advance development of safe and effective gene and cell therapies," US Food and Drug Administration, January 15, 2019, https://www.fda.gov/news-events/press-announcements/statement-fda-commissioner-scott-gottlieb-md-and-peter-marks-md-phd-director-center-biologics.

4. James Huang and Stephen Huang, "Gene therapy – high promise, high risk?" *PharmaTimes*, April 2019, http://www.pharmatimes.com/magazine/2019/april/a_state_of_confusion2.

STAKEHOLDER DATA COLLECTION NEEDS

Patients, Caregivers, and Patient Organizations

From the patient perspective, high-quality data are crucial for navigating treatment options and making a variety of health and lifestyle decisions. The outcomes that matter most to patients do not always align with those that matter to clinicians, researchers, or other stakeholders, although recent efforts, such as FDA's Patient-Focused Drug Development initiative, have tried to incorporate patient perspectives more systematically into their activities.[5] Recipients of cell and gene therapies and their families, for example, might be most interested in outcomes such as improved mental health, productive workdays, less pain and fatigue, or fewer necessary appointments with a specialist or physical therapist. Patients with comorbidities may also want to leverage patient-reported data to understand how cell and gene therapy treatments might impact their other underlying diseases and how patients like them have responded. In addition, because treatment can be costly and time-consuming for caregivers, it is also important to collect data on the effects of treatment on caregivers so that patients can make fully informed decisions about their treatments, such as whether to seek new cell or gene therapies or remain on medicines where they are well managed.

To collect direct input from patients on their lived experiences with treatment, health-care stakeholders can leverage patient-reported outcomes (PROs). A variety of tools already exists to collect PROs directly from patients in a user-friendly and understandable way. For example, the National Institutes of Health's (NIH) Patient-Reported Outcomes Measurement Information System (PROMIS) collects data directly from patients about their physical, mental, and social health and functioning.[6] This information can then be linked to clinical data through patient registries.[7]

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5. Leah Howard, et al, "Taking Stock of PFDD: Envisioning a Vibrant Future for Patient-Focused Drug Development," Food and Drug Law Institute, February 2020, https://www.fdli.org/2020/02/taking-stock-of-pfdd-envisioning-a-vibrant-future-for-patient-focused-drug-development/.

6. "PROMIS – HealthMeasures," HealthMeasures, accessed March 13, 2020, http://www.healthmeasures.net/explore-measurement-systems/promis.

7. "CIBMTR Manual of Operations, Version 6.1 (2019)" (Center for International Blood & Marrow Transplant Research, 2019), https://www.cibmtr.org/About/AdminReports/Documents/CIBMTR%20Manual%20of%20Operations%20Version%206.1.pdf.

The more holistic the data captured from patients, the clearer the picture will be for future patients as they navigate their health-care journey.

US Food and Drug Administration (FDA)

In January 2020, FDA's Center for Biologics Evaluation and Research (CBER) released updated guidance on long-term follow-up after the administration of gene therapies, recommending monitoring of gene therapy recipients for up to 15 years.[8] The guidance focuses on collecting data to refine safety labeling to inform patients and the development of future products; it also outlines a risk assessment strategy to determine what long-term follow-up should occur based on product characteristics, patient-related factors, and more. In most cases, post-approval monitoring will be required, although perhaps not for the full 15 years, and the burden of developing a monitoring plan lies with the developer. CBER encourages but does not require product developers to engage patients when writing protocols for long-term monitoring, given the prevalence of data siloes within the health-care system.[9] Most efforts to collect real-world data ignore the outcomes that matter most to patients. Thus, conversations to develop metrics reflecting patient preferences are critical.

Payers

The combination of uncertainty about clinical risks and benefits at the time of product approval and in the long term, as well as daunting upfront costs, have led to an industry-wide exploration of novel payment arrangements between health insurance plans and product developers.[10] In the face of these high costs for therapies whose benefits will accrue over time, precision financing solutions may help to ensure both patient access and sustainability. Novel payment models include milestone-based contracts, performance-based annuities, and payments over time, which hold product developers accountable for the performance of their products and enable health insurance providers to share risks and/or spread out the cost.[11]

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8. "Long Term Follow-Up After Administration of Human Gene Therapy Products," US Food and Drug Administration, January 2020, https://www.fda.gov/regulatory-information/search-fda-guidance-documents/long-term-follow-after-administration-human-gene-therapy-products.

9. "Center for Biologics Evaluation and Research Patient Engagement Program," US Food and Drug Administration, accessed April 1, 2020, https://www.fda.gov/vaccines-blood-biologics/development-approval-process-cber/center-biologics-evaluation-and-research-patient-engagement-program.

10. "Bill Cassidy, "How will we pay for the coming generation of potentially curative gene therapies?" *Stat News*, June 12, 2019, https://www.statnews.com/2019/06/12/paying-for-coming-generation-gene-therapies/.

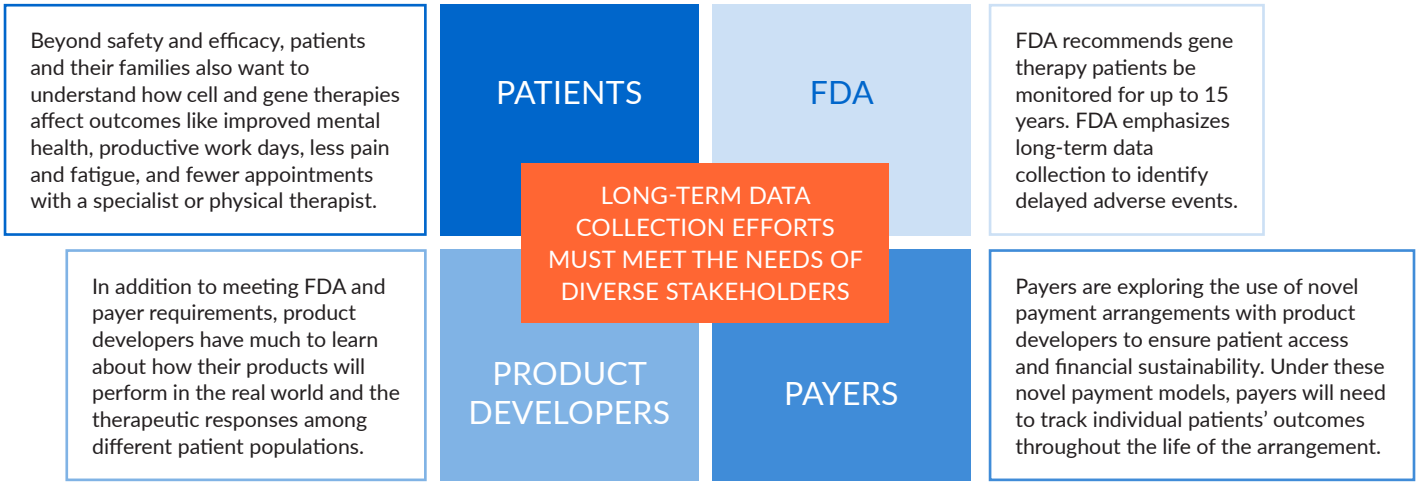
11. "Precision Financing Solutions for Durable / Potentially Curative Therapies" (MIT NEWDIGS, January 24, 2019), https://newdigs.mit.edu/sites/default/files/MIT%20FoCUS%20Precision%20Financing%202019F201v023.pdf.

These new payment models create a variety of post-market data collection challenges. For example, an individual patient's response to therapies must be tracked through the life of the contract between the developer and payer. In addition to fulfilling contractual terms, this response data can be used to refine which sub-populations should receive preferred access and to assess value. The current process of tracking each patient through contract life is manual. This approach is neither scalable nor sustainable, especially because many more cell and gene therapies are expected to enter the market, which would result in the implementation of many more outcomes-based contracts.

Product Developers

In addition to meeting FDA and payer requirements, product developers must study how their products perform in real-world and scaled-up settings. By collecting long-term data, they can learn how different patient populations respond to their treatments and then pursue expanded indications based on this real-world evidence. Data on therapy performance can also inform the pipeline through research, development, and manufacturing. In addition, data stratified by specific patient populations can guide negotiations for outcomes-based contracts.

FIGURE 2: DIVERSE DATA COLLECTION NEEDS OF DIFFERENT STAKEHOLDERS FOR LONG-TERM FOLLOW-UP



Source: FasterCures, Milken Institute (2020)

POTENTIAL DATA COLLECTION SOLUTIONS

Currently, patients' experiences with new therapies are tracked and recorded through a variety of methods. From traditional sources such as patient registries to recently developed data platforms specific to newly approved cell therapies, each data repository has its strengths and limitations. In the coming years, as more cell and gene therapies receive approval, it will be crucial to leverage the strengths of existing platforms to expand on solutions that are working, incorporate missing data elements, and ensure the ability to scale to meet all stakeholders' needs.

Patient Registries

One traditional platform for collecting patient data over time is the disease-specific patient registry in which data are managed by the corresponding patient organization and used for a variety of purposes, including creating care guidelines, improving treatment, and/or contributing to research. Some registries can incorporate and link a variety of data elements within the registry, such as PROs, clinical data, and/or genetic data. They can also utilize data standards or common data elements that make interoperability with other data platforms possible. For example, Cure SMA, the patient organization representing spinal muscular atrophy patients, for which Zolgensma is a recently approved gene therapy, is able to integrate its Clinical Data Registry with electronic health records from health-care centers in the Cure SMA Care Center Network.[12] However, patient registries tend to be leveraged by other stakeholders on a case-by-case basis for a specific research purpose or post-market commitment.[13] As such, patient organizations can be inundated with requests from external stakeholder groups to leverage their registries. The current format of most patient registries is, therefore, not scalable to meet the needs of an efficient global research ecosystem. However, data captured in registries through direct partnership

12. "Cure SMA Care Center Network." Cure SMA, accessed June 15, 2020, https://www.curesma.org/sma-care-center-network/.

13. Kristin Schneeman, Valerie Barton, and Brenda Huneycutt, "Advancing Models of Patient Engagement: Patient Organizations as Research and Data Partners" (Milken Institute, December 2019), https://milkeninstitute.org/sites/default/files/reports-pdf/Full%20Series_Advancing%20Models%20of%20Patient%20Engagement-%20Patient%20Organizations%20as%20Research%20and%20Data%20Partners%20copy.pdf.

with patient organizations offer one strong advantage: Patients often have a unique trusted relationship with these organizations, increasing their willingness to share their data and engage with and drive research in these contexts.[14] This element of patient registries must not be lost as wider-scale systemic solutions are devised.

Cell Therapy Registry: The Center for International Blood and Marrow Transplant Research

The Center for International Blood and Marrow Transplant Research (CIBMTR) is a research collaboration between the Medical College of Wisconsin and the National Marrow Donor Program/Be The Match with more than 40 years of experience documenting patient experiences, including outcomes. In 2016, CIBTMR launched a registry to capture data on both acute care quality and long-term follow-up from recipients of gene and cell therapies. Since launching this registry, CIBMTR has contracted with product developers of the two approved commercial CAR T-cell therapies to use its infrastructure to comply with FDA's 15-year follow-up requirement.[15] As of January 2020, the registry has enrolled more than 2,000 patients.[16] In addition to facilitating both long-term follow-up of approved cell therapy products and post-approval safety studies, CIBMTR data can inform outcomes-based reimbursement and serve as a resource for the biomedical and clinical research communities.

CIBMTR was designed to collect data following transplants for annual, population-level, or anonymized reporting. Its functionalities have already been extended to collect data on CAR T-cell therapies. Scaling to meet all stakeholders' data collection needs for every anticipated approved product beyond those administered in transplant centers may not be feasible. In addition, new payment approaches often require monthly reporting on individual patients reaching payment milestones. The current model of contracting with specific developers may be burdensome for providers who must meet data entry requirements that are product-specific. It may be advantageous to consider a disease-specific approach where there is an opportunity to develop a set of core data elements, as this would make it possible to capture the same data elements relevant to a specific patient population regardless of the product.

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14. Ibid.

15. "CIBMTR Announces Collaboration with Kite to Track Long-Term Outcomes Data for Yescarta," Be The Match Biotherapies, May 17, 2018, https://bethematchbiotherapies.com/newsroom/cibmtr-announces-collaboration-with-kite-to-track-long-term-outcomes-data-for-yescarta/; "CIBMTR To Track Long-Term Outcomes Data for Kymriah," Be The Match Biotherapies, September 14, 2018, https://bethematchbiotherapies.com/newsroom/cibmtr-to-track-long-term-outcomes-data-for-kymriah/.

16. Marcelo Pasquini, "Capturing Real-World Data on Patients Receiving CAR T cells in the US," presentation at Cures for Life Data Collection workshop, FasterCures, Washington DC, February 2020.

However, as a functional registry tracking patient outcomes in the long term, several qualities of CIBMTR should be replicated in other registries or databases that expand or emerge. CIBMTR allows any center of a clinical institution to participate, including multiple centers at a single institution, and data requests are disseminated at a clinical level to the sites that administer treatments.[17] It also allows the personnel at the treatment site with the most access to and familiarity with the data to manage the data in the registry. CIBMTR also collects PROs using the NIH Patient-Reported Outcomes Measurement Information System, which is linked to patients' clinical data.[18]

Global Disease Registry: World Bleeding Disorders Registry

Launched in January 2018, the World Bleeding Disorders Registry (WBDR) provides a platform for Hemophilia Treatment Centers (HTCs) around the world to collect standardized data on people with hemophilia.[19] The WBDR is a prospective, longitudinal, observational registry of patients diagnosed with hemophilia A and B. It is a privacy-protected, web-based, data-entry system that enables collection of individual patient data, thus providing a clinical profile for each person. Implementation of the WBDR began with a global rollout in 2018, with a five-year goal of enrolling 10,000 people with hemophilia, from 200 HTCs representing 50 countries.[20] The first WBDR Data Report was published in May 2019 and includes data entered into the WBDR in 2018.[21] A WBDR committee has outlined recommendations for patient data and privacy, data collection fields, and educational materials for patients and caregivers. Future data platforms should draw from the WBDR model in several ways, namely that the registry is created by patients, allows data collection at the individual level, and ensures patient privacy. Additionally, the outcomes collected are based on a standardized, disease-specific, patient-driven core outcome set. Participation, however, is completely opt-in and voluntary, which can create challenges around missing data on patients and possible bias if certain patients are more or less likely to participate. Additionally, it may be a costly endeavor for each individual disease organization to replicate. Finally, because data is de-identified and data elements do not specifically include adverse events or other outcomes of interest to the FDA or payers, global disease registries like WBDR may not directly meet the needs of these stakeholders.

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17. Ibid.

18. CIBMTR, Manual of Operations.

19. "World Bleeding Disorders Registry," World Federation of Hemophilia, accessed March 10, 2020, https://www.wfh.org/en/our-work-research-data/world-bleeding-disorders-registry.

20. Ibid.

21. "2018 Data Report," World Federation of Hemophilia, accessed March 10, 2020, http://www1.wfh.org/publications/files/pdf-1718.pdf.

Cloud-Based Solutions

Patient data for long-term follow-up could be collected through a cloud-based platform in which information is stored, managed, and analyzed on a network of remote servers rather than a specific physical location. Cloud environments are relatively cost-effective options and enable more secure and easy data sharing among different stakeholder types.

In January 2019, the Harvard-MIT Center for Regulatory Science, along with MIT's Center for Biomedical Engineering, proposed a framework called the Dynamic Dossier in the Cloud. This framework outlines how biopharmaceutical companies might share data with stakeholders.[22] Its goal is to transform data sharing by collaborating with the FDA, patient groups, and product developers to aggregate data and enhance decision making across stakeholders. For example, the longitudinal tracking of clinical data and PROs for cell and gene therapies could improve the process of evaluating new products and enable the implementation of performance-based contracts between product developers and payers. Proponents of cloud-based solutions are focused on analyzing stakeholder-specific functional requirements, including policy, process, and technology changes, and identifying a roadmap for development and implementation. Cloud-based solutions may overcome many of the infrastructure challenges that exist in current registries. However, they come with a heightened need to ensure data security. While a single cloud platform will likely not be able to meet data collection needs for all cell and gene therapies and their relevant stakeholders, a cloud-based format makes a platform more nimble and able to accommodate updates, changes, and evolution of functions. Stakeholders should work to align their efforts to avoid duplication.

22. "Dynamic Dossier in the Cloud to Transform Data Sharing, Starting with Federal Regulators," MIT NEWDIGS, January 30, 2019, https://newdigs.mit.edu/news/"dynamic-dossier-cloud"-transform-data-sharing-starting-federal-regulators.

TABLE 2: COMPARISON OF DATA COLLECTION MODELS

	Benefits	Limitations
Patient Registries	• Directly incorporate patient-reported data through a trusted platform • Patients have more opportunities to drive research	• Lack of infrastructure to be used on a wide scale for research studies spearheaded by different stakeholders • Work best on a disease-by-disease basis
The Center for International Blood and Marrow Transplant Research	• Platform demonstrated to successfully track long-term follow-up data for approved cell therapies, in accordance with FDA requirements • Data are collected during clinical care	• Scalability may be a challenge for future approvals • Contracts are product-specific rather than disease-specific
Global Disease Registry	• Collected data are based on a disease-specific, patient-focused, and standardized core outcome set • Global platform created and driven by patients, with all participants on an opt-in, voluntary basis	• Not designed to capture data relevant to post-market safety studies or outcomes-based payment models and thus do not meet FDA or payer data needs
Cloud-Based Dossier	• A convenient option for sharing data between stakeholders • Could improve the evaluation of new products and enable the implementation of outcomes-based payments between product developers and payers	• Pilots are in early stages of development, with no mature model currently in use

DISCUSSION

On February 13, 2020, FasterCures held an in-person workshop focused on strategies to promote data collection for long-term patient follow-up for cell and gene therapies. Approximately forty stakeholders attended the workshop, with the majority representing patient organizations. We asked participants to imagine an ideal system for cell and gene therapy patient data collection. Responses included the following:

- Infrastructure should allow for scalability, the incorporation of data standards and common data elements, and interoperability with other platforms. One approach could be to start with smaller modules (e.g., to collect core outcomes or PROs) and build from there.
- Registries should be disease-specific rather than product-specific and be organized around disease-specific needs and outcomes. Having multiple independent data collection initiatives for the same disease is less informative and efficient than coordinated programs.
- Continued multi-stakeholder engagement could accelerate the development of a core set of data elements with built-in flexibility to meet disease-specific needs.
- Leveraging the use of wearables, telemedicine, and digital health could enable active patient engagement and increased adherence to data collection. It could also decrease patient burden, freeing the patient from the obligation to travel and attend frequent, time-consuming, in-person appointments.

There has been some recent progress made in collecting health data that is standardized and interoperable. In March 2020, the Office of the National Coordinator for Health Information Technology released rules mandating interoperability and requiring public and private entities to collect specified core data elements in electronic health records. These rules also require the adoption of specific data standards to enable data exchange between different platforms and applications through secure APIs.[23] However, important questions remain related to data governance, access to health data, and legal uses of collected data. Workshop participants underscored the importance of protecting the data and privacy of patients whose data are included in registries, especially for an extended time. Data use and sharing agreements should acknowledge that data may be used in different ways at different times, and should clearly outline what data uses are and are not permitted. These agreements should also outline policies for sharing data with third

23. "HHS Finalized Historic Rules to Provide Patients More Control of Their Health Data," US Department of Health and Human Services, March 9, 2020, https://www.hhs.gov/about/news/2020/03/09/hhs-finalizes-historic-rules-to-provide-patients-more-control-of-their-health-data.html.

parties, again specifying upfront conditions for circumstances in which data may be shared and for what purposes. All centers or organizations that report data to a registry should have an ethics board and a dynamic consent process so that patients understand the agreements in place. All of these processes should comply with the Health Insurance Portability and Accountability Act (HIPAA) and other applicable laws and regulations. However, meeting regulatory requirements should be the minimum bar, because HIPAA protections are weak in certain areas, such as third-party uses of data.[24] Since data sharing is the most promising path toward meaningful multi-stakeholder collaborations that can generate evidence and lead to greater patient access, effective guardrails around its use are paramount.

24. Deven McGraw and Vince Kuraitis, "Health Data Outside HIPAA: The Wild West of Unprotected Personal Data," The Health Care Blog, August 12, 2019, https://thehealthcareblog.com/blog/2019/08/12/health-data-outside-hipaa-the-wild-west-of-unprotected-personal-data/.

KEY CONSIDERATIONS BY STAKEHOLDER GROUPS

Patient Organizations, Patients, and Caregivers

Patients and caregivers should be fundamental participants in all partnerships and collaborations to ensure the inclusion of their preferred outcomes. Patient input should be built into any proposed tool to streamline and standardize data collection, such as the development of core outcome sets.[25] Patients should also provide feedback about novel methods of data collection, such as wearable sensors or digital health tools. There should be mechanisms in place to reduce the high level of effort and resources needed for sustained involvement of patients and patient organizations during data collection, study design at the early stages, and review of data sharing and re-use policies after data have been collected. Patients should see the value of their participation returned to them, perhaps through the return of results in a comprehensible format.

FDA

FDA should facilitate and require early dialogue between stakeholder groups and ensure that patient groups are included in initial discussions of potential long-term effects of new treatments. The Patient-Focused Drug Development program has already shown success in incorporating the patient's voice in drug development and evaluation. This program could be expanded to promote conversations between more stakeholders and publish learnings about patient needs and preferences for long-term follow-up data collection. Engaging with payers remains a challenge; however, other models within FDA exist to potentially be built upon. The Center for

25. A. Iorio, et. al., "Core outcome set for gene therapy in haemophilia: Results of the coreHEM multistakeholder project," Haemophilia, Vol. 24 (4), (May 20, 2018), https://doi.org/10.1111/hae.13504; Erin McCallister, "Patients at the core," *BioCentury*, May 25, 2018, https://www.biocentury.com/article/295625/how-patients-payers-companies-identified-core-outcomes-for-hemophilia-gene-therapies.

Devices and Radiological Health's Payor Communication Task Force is a voluntary program that facilitates communication between device developers and payers to shorten the time between FDA approval and coverage decisions.[26] CBER, which regulates cell and gene therapies, could implement a similar program to encourage early conversations among product developers, payers, and FDA to ensure that their individual data collection needs are built into the study design, potentially leading to quicker access to therapies for patients. The FDA should also partner with disease organizations to develop core data elements, standards, and disease-specific outcome sets to be collected post-approval that adhere to safety and efficacy requirements. Learnings from this process should be disseminated widely. Finally, the FDA should consider approaches to incorporating real-world data collected in the clinical setting or through digital health devices into its evidence base.

Payers

Payers can develop data standards and core outcome sets to standardize evidence generation to the extent possible. As value assessors for the health system, payers should work to identify therapies in the pipeline that lack supporting evidence and then work with other stakeholders to develop a plan to generate real-world data to build an evidence base. Further, payers should work with other stakeholders to translate the learnings from these efforts into guidance. For example, payer engagement during pivotal clinical trial development periods for FDA submission may help product developers design studies that meet both FDA and payer evidence requirements. The payer community typically does not engage in the activities described here. Further consideration is needed to determine how to seek and secure the community's buy-in.

Product Developers

Product developers can position themselves at the intersection of patients, FDA, and payer communities. In this way, they can generate learnings about: (1) patient needs and desired outcomes, (2) what outcomes will be used to prove efficacy, (3) how efficacy will be compared to that of other products, (4) how long-term effectiveness will be assessed and verified, and (5) how findings will be publicly and transparently disseminated. Knowing this information, they can develop effective long-term monitoring strategies. Further, developers should keep patient communities informed of therapies in development and potential clinical trials that may benefit them.

26. "Payor Communication Task Force," US Food and Drug Administration, accessed April 27, 2020, https://www.fda.gov/about-fda/cdrh-innovation/payor-communication-task-force.

TABLE 3: SUMMARY OF KEY CONSIDERATIONS FOR EACH STAKEHOLDER GROUP

Patients	FDA	Payers	Developers
• Provide input about the tools used to streamline and standardize data collection (e.g., core outcome sets) • Provide input about any novel proposed methods of data collection (e.g., wearables or other digital health tools) • Seek a feedback loop so that findings of any data collection activities are shared with patients who contribute their data	• Develop programs that facilitate early dialogue prior to the design of a pivotal study between developers and payers to meet data-collection needs (such as the Payor Communications Task Force which already exists within the CDRH) • Expand the Patient-Focused Drug Development program to include patient preferences on data collection • Partner with disease organizations to develop core data elements and standards for data collection • Incorporate real-world data collected in the clinical setting or through digital health devices in decision making	• Leverage data standards and core outcome sets to standardize the evidence generation process and develop guidelines accordingly • Support the development of a real-world evidence base for cell and gene therapies • Develop a mechanism to incorporate direct feedback from advocates/patients into their medical policy process	• Engage with patient communities to learn about their needs and determine the best outcomes to prove efficacy and demonstrated improvement over other treatments • Develop a plan to assess and verify long-term effectiveness • Keep patients informed of therapies and potential treatments that might benefit them

CONCLUSION

Ultimately, data collection processes that generate evidence to inform all stakeholders, serve patients' needs, and promote patient access to therapies will be more effective if established through multi-stakeholder collaborations and partnerships. Some elements of these processes may require some degree of government mandating.[27] Any data collection initiative should engage all stakeholders to ensure that the collected data are mutually fit for purpose and serve patients' needs and preferences. Such initiatives should also strive to reduce patient and clinical burden wherever possible, moderating the amount of time and energy required from patients and limiting redundant requests. The use of digital health products, wearables, and online tools such as computer-adaptive testing could help to achieve this aim. The ecosystem as a whole should strive to develop standardized assessment and collection tools so that interoperability requires minimal extra effort.

Exploration of collaborative strategies to efficiently collect long-term data needed to inform decisions by patients, clinicians, regulators, payers, and policymakers will be an ongoing effort. Continued multi-stakeholder engagement, partnerships, and collaborations will be essential to develop and drive feasible solutions forward. The work presented here is intended to be leveraged and built upon as we address the challenges involved in data collection together. Recognizing that health-care providers are critical partners in long-term data collections, FasterCures will host a workshop focused on provider-specific challenges and needs in the summer of 2020.

27.` "Cornerstones of Collaboration: Foundation-Led Partnerships to Accelerate R&D" (Milken Institute, 2017).

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About the Authors

Anita Nosratieh is an associate director at FasterCures, a Center of the Milken Institute, primarily leading the Cures for Life project. Nosratieh is passionate about patient access to novel medical products and has a background that spans preclinical research, clinical trials, and regulatory affairs. She holds a doctorate from the University of California, Davis, in biomedical engineering.

Rachel Tunis is an associate at FasterCures, a Center of the Milken Institute, primarily providing research support to core program areas related to health data and technology. Tunis enjoys using social science research approaches to better understand complex problems in the biomedical research system. She holds a BA from the College of William & Mary in sociology and French.


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