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The Current Landscape of the Science of Patient Input

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ABOUT US

About the Milken Institute

The Milken Institute is a nonprofit, nonpartisan think tank focused on accelerating measurable progress on the path to a meaningful life. With a focus on financial, physical, mental, and environmental health, we bring together the best ideas and innovative resourcing to develop blueprints for tackling some of our most critical global issues through the lens of what's pressing now and what's coming next.

About FasterCures

FasterCures, a center of the Milken Institute, is working to build a system that is effective, efficient, and driven by a clear vision: patient needs above all else. We believe that transformative and life-saving science should be fully realized and deliver better treatments to the people who need them.

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INTRODUCTION

In the last decade, FasterCures, along with many stakeholders across the biomedical research ecosystem, has driven initiatives to ensure that patients' perspectives and input are appropriately represented across the product-development continuum and post-approval phase. These activities, generally classified as patient engagement or efforts to advance the science of patient input, have been driven by various stakeholders and legislation. In the US, the Food and Drug Administration (FDA) has provided the regulatory impetus and guidance for patient engagement activities, bolstered by legislation that calls for greater involvement of patients in research, development, and delivery of medical products. The FDA Safety and Innovation Act (FDASIA), recent iterations of the Prescription Drug User Fee Act (PDUFA), and the 21st Century Cures Act all contain specific provisions and recommendations around patient engagement, patient data, and patient-focused drug development. Nonprofit organizations have also been instrumental in developing tools and resources to fill in knowledge gaps, and patient advocacy organizations have served as bridges between patient communities and industry.

In 2016, FasterCures released a report, Expanding the Science of Patient Input: Pain Points and Potential (the "Pain Points and Potential" report), which provided a set of 25 stakeholder-developed and informed priorities to advance patient input in the R&D ecosystem. One of the preeminent issues identified in that report was the need for common language that encapsulates the definition of the science of patient input. Terms such as patient-centered, patient-focused, and patient engagement, which have been used interchangeably to define the involvement of patients in health-care research and delivery, appear to cause more confusion than clarity because they are interpreted differently by various stakeholders. The report called for a glossary of terms to harmonize definitions associated with patient engagement and patient centricity. The rest of the 25 high-priority activities, tools, and products identified in the report to advance the science of patient input were categorized into seven groups of initiatives covering communications, development of tools and frameworks, training, methods development, addressing legal challenges, improving measurement, and a combination of the preceding categories.

Approximately five years after the release of the "Pain Points and Potential" report, several developments uncovered a need to assess the current state of the science of patient input and patient engagement. For example, the Cures 2.0 Act, which is currently under consideration by Congress, will have impacts on how patient data could be used in the research process and how patient input will be leveraged in the future. The COVID-19 pandemic has revealed glaring inequities in biomedical research and has heightened the emphasis on ensuring that R&D engages and serves diverse populations to ensure that the needs of the entire patient community are addressed.

Also, as work has continued on patient engagement over the past several years, the need has arisen to survey the disparate efforts in progress to identify challenges that persist and priorities that must be addressed now to ensure the success of future efforts. To address that need, FasterCures embarked on a series of activities to gather information about current advances in patient engagement and opportunities for action to drive meaningful progress (see sidebar).

This report summarizes our assessment of the science of patient input, including areas that have seen the greatest progress, opportunities for action to accelerate the inclusion of patients' perspectives in research, and the next steps for stakeholder action.

To inform the development of this report, we conducted interviews with stakeholders from industry, patient organizations, regulatory agencies, and other related organizations with current patient-engagement initiatives, to gather their perspectives on progress to date and gaps that remain. We supplemented these interviews with a review of publicly available information and key takeaways from participant discussions at patient engagement sessions held as part of the Milken Institute "Partnering for Patients Forum" in December 2021.

DEFINING AND CHARACTERIZING PATIENT ENGAGEMENT AND THE SCIENCE OF PATIENT INPUT

A key theme from the "Pain Points and Potential" report, which recurred in our assessment, was the need for better definitions around patient engagement and the science of patient input. "Patient engagement" and related terms, while used interchangeably throughout health care, are interpreted and operationalized differently by various stakeholders. This leads to confusion around the terminology, with calls for standardization. This is especially true for patient engagement in biomedical R&D, where patients have conventionally been regarded as research subjects. Patient engagement aims to promote a more active role for patients as partners in clinical research, regulatory activities, and other aspects of the drug-development and approval process.

The National Health Council's (NHC) glossary of patient-engagement terms defines patient engagement as "the active, meaningful, authentic and collaborative interaction between patients and other stakeholders across all aspects of the health ecosystem, where decision-making with regard to an activity or process is guided by patients' contributions as partners, recognizing their unique experiences, values and expertise."[1] Other organizations have produced taxonomies to capture patients' involvement in health care and research, including an ISPOR (The Professional Society for Health Economics and Outcomes Research) taskforce, which defined patient engagement as "the active, meaningful, and collaborative interaction between patients and researchers across all stages of the research process, where research decision making is guided by patients' contributions as partners, recognizing their specific experiences, values, and expertise."[2]

FasterCures developed a report in 2016, *Expanding the Science of Patient Input: The Power of Language*, that explains the myriad ways in which patient engagement and the science of patient input are described in the R&D space. Despite definitions from various organizations that seemingly align with the underlying concept, confusion still surrounds terminology used to describe patient engagement. Other terms—such as the science of patient engagement, defined as "the development and use of systematic approaches and tools to collect, analyze, and apply patient input to medical product R&D lifecycle and regulatory decision-making," which aims to systematize the process for collecting and using patient input in medical product R&D—may have added to the confusion, as "science of patient engagement" is now used interchangeably with patient engagement, patient-centeredness, and other related terminology.[3]

Although numerous definitions of patient engagement have been proposed, stakeholders with whom we engaged in the landscape analysis for this report continue to call for clarity around defining patient engagement.[4] Our assessment indicates that calls for better definitions seem to reflect the need to operationalize concepts to consider and align the goals of key stakeholders, and recognize the various levels from which stakeholders may engage, as well as the diverse activities stakeholders may participate in along the continuum of the biomedical research process. Persistent lack of clarity around the terms and process of involving patients in biomedical activity could stall progress and remains a critical issue for action.

EVIDENCE OF PROGRESS

Notwithstanding confusion around definitions, we found evidence of meaningful progress towards incorporating patients' perspectives in the R&D process. This progress is corroborated by regulatory developments, as well as the recent proliferation of tools and resources to address gaps hampering the advancement of patients' involvement in biomedical research.

Regulatory: FDA Leadership and Guidance

In the last five years, decision-makers—especially regulatory bodies—have indicated strong interest in considering patient preference and experience data (PPED) as part of the decision-making process. The FDA is at the forefront of providing regulatory impetus for the collection and use of PPED as part of medical product development. The FDA's patient engagement activities can be traced back to the 1980s with the HIV/AIDS advocacy movement. Still, it wasn't until 2012 that the agency was obliged by legal mandate to "develop and implement strategies to solicit the views of patients during the medical product development process and consider the perspectives of patients during regulatory discussions."[5]

As part of the Medical Device User Fee Amendments (MDUFA) and Prescription Drug User Fee Act (PDUFA) reauthorizations, the FDA introduced several programs, including the Patient-Focused Drug Development (PFDD) program. The FDA has held at least 24 PFDD meetings since 2012 to hear perspectives on various diseases directly from patients and caregivers. These meetings have been supplemented, since 2015, with more than 55 meetings externally led by patient communities to enable the FDA to hear from those with a broader variety of conditions.[6] The FDA has also released a series of PFDD guidance documents, as mandated by the 21st Century Cures Act and the Food and Drug Administration Reauthorization Act of 2017 Title I. At the time of this report's development, the FDA had finalized two of the guidance documents, released a third in draft version, and was finalizing the fourth and final guidance.[7]

In addition to the PFDD methodology guidance, the FDA has released other guidance documents on patient engagement. Two final guidance documents were released in early 2022. One is focused on principles to consider when using patient-reported outcome instruments in evaluating medical devices and providing recommendations about ensuring that measures are fit-for-purpose. The other is focused on applications of patient engagement in the design and conduct of medical device clinical studies.[8]

Other activities by the FDA supporting patient engagement in medical product development and the regulatory process include the release of an FDA-commissioned report on the use of patient experience data in regulatory decision-making and efforts by the FDA to promote global harmonization in patient engagement.[9] This review found that although the FDA's commitment to advancing PFDD was evident to stakeholders, perspectives varied as to whether and how the FDA uses patient experience data in its approval decision-making.[10] As of August 2022, the FDA had

indicated that it would use the report's findings to "support its efforts to enhance the use of patient experience data in regulatory decision-making" but had not offered any specific next steps.[11]

The FDA has also been instrumental in driving efforts to promote global harmonization of patient engagement. In 2016, the FDA and the European Medicines Agency (EMA) Patient Engagement cluster, a workgroup to focus on patient engagement, was created to allow the two agencies to share best practices for engaging patients along drug and biologic regulatory life cycles.[12]

The FDA's patient engagement activities have sent a clear signal to stakeholders that the agency is interested in, and dedicated to, incorporating patients' perspectives in drug approval decisions. There is, however, a need for the agency to state how patient experience data submitted as part of applications will be considered in decision-making and to provide case examples of the use of patient experience data in regulatory decision-making.

Tools and Resources

In addition to regulatory drivers of patient engagement, we found that several other stakeholders were leading the charge to develop tools and resources to compensate for gaps. We highlight four case studies to illustrate the types and breadth of existing tools. Several more tools have been developed, and numerous others are underway.

Example 1: Patient-Centered Outcomes Research Institute Funding Opportunities

Since its establishment, the Patient-Centered Outcomes Research Institute (PCORI) has been at the forefront of driving patient-engagement efforts. PCORI makes funding available and provides other resources in generating and disseminating information to advance the relevance and quality of evidence helping patients and other stakeholders make informed decisions about their health. In 2019, Congress reauthorized PCORI's funding for another 10 years to continue supporting comparative clinical effectiveness research of treatments or other remedial approaches to health and health care. PCORI's National Research Priorities for Health are the core of its research agenda and other activities. Among the national priorities—reflected in the research funding PCORI makes available—are enhancing the infrastructure to promote patient-centered outcomes research and achieving health equity.

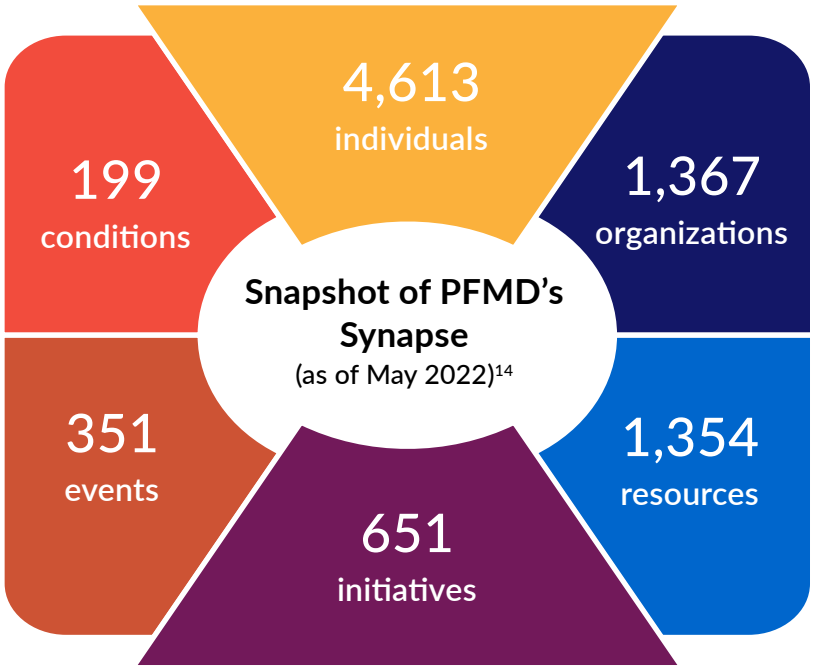
In 2022, PCORI announced funding projects to address methodologic gaps in the research of patient-centered outcomes and comparative effectiveness, including the use of artificial intelligence and machine learning in clinical research and other methods to enable the integration and use of large amounts of data from different sources. PCORI also announced a funding opportunity to promote the implementation of the results of PCORI-funded research. In the most recent funding cycle, researchers can obtain up to $2.5 million by proposing studies to implement results from four previous studies funded by PCORI.

In addition to research and implementation/dissemination funding, PCORI provides funding to enhance the meaningful involvement of patients, caregivers, clinicians, and other health-care stakeholders in patient-centered outcomes research and comparative effectiveness research. PCORI has made $25 million available for such capacity-building awards in FY 2023. In the funding announcement, PCORI encourages studies that address health equity, another of its National Priorities.

These examples illustrate the breadth of PCORI's investments in filling important methodological gaps in patient-centered research and exploring approaches for building capacity among stakeholder communities to engage in patient-centered research. PCORI's focus on implementation addresses a compelling need to identify and pilot initiatives that work. PCORI's investment in patient engagement research has significant implications for the broader health system—beyond biomedical research.

Example 2: Patient Focused Medicines Development Patient Engagement Synapse

Patient Focused Medicines Development (PFMD) developed Synapse, a user-driven tool, as a hub for globally collating and disseminating patient-engagement efforts. Individuals and organizations can sign up on Synapse to showcase their patient-engagement activities, share models and frameworks, post patient-engagement events, and connect with experts and organizations actively involved in the field.[13]



Source: Milken Institute, using data from Patient Focused Medicines Development (2022)

Synapse currently has a global reach, with majority participation from the US and European countries. Synapse fills a crucial gap for knowledge sharing by disseminating information on how other organizations are involved in patient engagement, as well as sharing tools and frameworks that have proved useful to their peers. Users can navigate the Synapse tool first by sorting by disease area, narrowing the focus to a specific geographic area, identifying upcoming events and sorting through initiatives that span clinical trials to regulatory and approval processes, and finally, to value assessments and post-marketing activities.[15] Synapse is one of the most comprehensive patient-engagement repositories and, as such, is a valuable resource to organizations interested in or pursuing patient-engagement activities.

As with any user-curated tool, there is as yet no general rating of the quality and value of the information in the hub. The onus is thus on users to navigate the myriad resources to assess the utility of the information. Additionally, there is no guidance for users at various stages of the patient-engagement journey to navigate the information in the tool effectively. This is especially important, as feedback in our stakeholder conversations suggested that organizations interested in ramping up patient-engagement efforts often lack guidance on how to start.

Example 3: National Health Council Fair Market Value Calculator

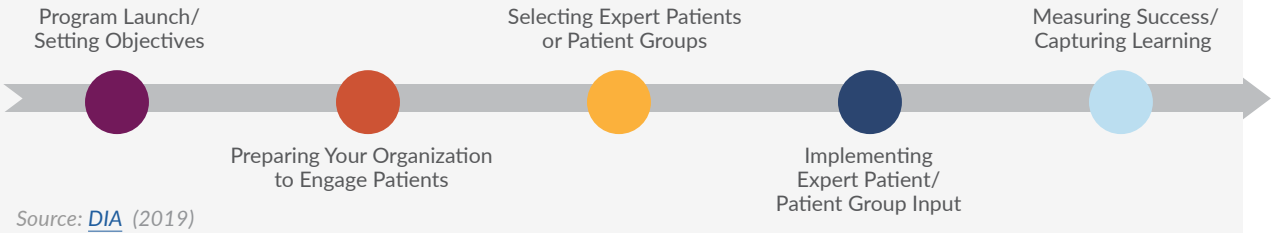
The Fair Market Value (FMV) calculator is a tool to assess fair compensation for patients and patient groups, providing information and valuable insights to product sponsors.[16] The calculator is part of a suite of patient-compensation tools that includes a guide as well as a framework for patient-engagement activities. The FMV calculator can estimate the appropriate hourly rate for an individual patient, caregiver, or group involved in a range of activities with medical-product manufacturers. After the user completes a brief questionnaire about the type and level of engagement, the tool provides a range of FMV compensation, excluding applicable expenses.

A key finding from our landscape review is the tension between, on the one hand, the increasing demand for patients' insights as part of the research process and, on the other, the need to build capacity, in both resource level and expertise, in the patient community. The NHC FMV calculator is a practical third-party tool to calculate appropriate remuneration—for time, effort, and expertise—of the patient community, especially unaffiliated patients and smaller patient organizations that are venturing into patient engagement activities with the private sector. The tool could help these patients access much-needed financial resources to develop their capacity to engage in research and the medical product-development process.

Example 4: Drug Information Association Considerations Guide to Implementing Patient-Centric Initiatives in Health-Care Product Development

Several guides are available to support medical product manufacturers in incorporating patients' perspectives in R&D. One such resource is the Drug Information Association's (DIA) Considerations Guide, developed as part of a DIA study of patient-centric initiatives in drug development. The Considerations Guide is intended to help pharmaceutical companies develop customized patient-centric initiatives while referring them to other available resources. The Considerations Guide is organized as a roadmap with the following categories:

FIGURE 1: Roadmap to Patient-Centric Pharmaceutical Product Research



Source: DIA (2019)

The guide recommends a list of contributors and considerations for each category, including organizational readiness, program support, guiding principles for patient-centricity, and engagement plan.

Example 5: EveryLife Foundation Guide to Patient Involvement in Rare Disease Therapy Development

The guide informs stakeholders of efforts to promote patient-focused drug development and explains how related FDA guidance can be leveraged to promote patient engagement in rare disease therapy development. The guide was a joint effort of the EveryLife Foundation for Rare Diseases, Biotechnology Innovation Organization (BIO), NHC, and Pharmaceutical Research and Manufacturers of America (PhRMA); it was derived from a series of four virtual Patient-Focused Drug Development Guidance Compendium workshops.[17]

The guide is designed to be applied to all types of therapies across all rare diseases. It is organized into eight topic areas where stakeholders may take action to involve patient perspectives in the development of rare-disease therapies. Each section documents actions for patient advocacy leaders and product sponsors, as well as collective actions that offer opportunities for collaboration among multiple stakeholders. The guide also includes an appendix summarizing the four workshops held by the EveryLife Foundation, with links to resources, including the FDA PFDD guidances.[18] The EveryLife PFDD compendium and guide adapts FDA guidance documents specifically for application within the rare-disease context, thereby lending actionable value to the information.

The examples highlighted in this report indicate the breadth of resources for patient engagement. There are many more, such as frameworks developed by the Clinical Trials Transformation Initiative (CTTI); the European Patients' Academy on Therapeutic Innovation (EUPATI), which explains how patient engagement is used throughout the R&D lifecycle; and the PFMD *Book of Good Practices* (2020 edition), which presents case examples of organizations conducting effective patient engagement. Despite the availability of these tools and resources, the need for more—especially how-to guides and case examples—was a recurrent theme in our stakeholder conversations and information-gathering activities. This finding may underscore the need for dissemination and uptake of existing resources or highlight the need for tools that address knowledge gaps not filled by existing tools. The next section discusses the challenges identified in the landscape analysis.

SEVERAL OLD AND NEW CHALLENGES REMAIN

Though progress in engaging patients in research has accelerated over the last few years, many gaps and challenges persist from five years ago, when FasterCures last assessed the state of the science of patient input. In some cases, efforts and activities in progress have allowed for better engagement of patients in certain contexts, but specific organizational progress does not always translate to broad, systemic progress. The following is a list of persistent challenges, with examples where incremental change is occurring.

a. Patient Organizations Experience Challenges with Being Effective Conduits for Patient Input

Patient organizations are often the main stewards connecting the patient community to researchers. Many continue to characterize the patient journey, capture patients' lived experiences and preferences, advocate for their needs, and connect them to needed resources. In a 2022 FasterCures Capacity-Building and Patient Engagement Needs Assessment Survey (unpublished), some responding patient organizations indicated they may not prioritize engaging patients comprehensively across the spectrum of R&D activities because they lack the capacity, experience, and know-how to respond to the growing demand for patient engagement. Thus, some efforts may be ineffective in meaningfully incorporating patients' perspectives or may produce data that are not usable, representative of those with the disease, or meeting the standards required for regulatory decisions or coverage determinations.[19] Instances such as these can jeopardize the integration of patient engagement data to inform decisions, for both present and future submissions.

Grants, donations, and event revenue are traditional, primary, and reliable sources of financial support, but sometimes patient organizations may also receive support from industry partners to collaborate on specific research efforts.[20] However, these funding sources only partly serve the collective needs of all patient organizations with research missions, which leaves many organizations with inadequate resources for building and sustaining research-oriented patient-engagement programs. The COVID-19 pandemic exacerbated demands on patient organizations and negatively impacted many traditional funding streams these organizations rely on to fuel their efforts in research and engagement.[21]

Beyond the financial support critical for capacity building, many nonprofit umbrella organizations—such as NHC, PFMD, DIA, Milken Institute, Genetic Alliance, Global Genes, Medical Device Innovation Consortium (MDIC), BIO, National Organization for Rare Disorders (NORD), and others—offer resources that help grow organizational capacity to engage patients in research. However, the sheer multitude of resources across many websites can create obstacles for patient organizations with limited time and means for identifying and using helpful resources.

In the 2022 FasterCures Capacity-Building and Patient Engagement Needs Assessment, some patient organizations indicated experiencing challenges with engaging representatives of

the greater patient community (though patient organizations may have better outreach into diverse patient communities than other actors in R&D). In some instances, organizations may repeatedly draw from the same pool of patients or "expert patients," thus failing to collect diverse views reflecting the spectrum of people with the condition of interest.[22] Historically, engaging more diverse patient populations has been challenging for reasons such as concerns over trust, difficulty with communication, cultural considerations, computer literacy challenges, home instability, the difficulty of accessing research centers, or the means or awareness of participating in research studies.[23] This has particularly affected patients in rural areas and patients of color.

The lack of representativeness in engagement can pervade the continuum of R&D efforts, from preclinical research through clinical trials, regulatory engagement, and post-market activities. Organizations aiming to attain representative engagement must make conscious, sustained efforts over time to build trust and relationships with the communities they engage. They must also hire staff who reflect the diverse patient populations they aim to recruit.

b. Lack of Understanding of the Value of Patient Engagement

While the scope and breadth of patient engagement activities have increased through new policies, programs, and practices, many research sponsors still do not fully understand the value of patient engagement.

Some may resist changing existing processes and paradigms; others only do enough to comply with the minimum regulatory requirements.[24] However, evidence increasingly demonstrates that patient engagement can improve the conduct of clinical trials, such as through faster planning, approval, and enrollment and fewer protocol changes. Improvements in outcome may include more positive volunteer-subject feedback and savings in long-term drug development.[25]

A 2016 report on patient involvement in 10 research studies noted improvements in recruitment, retention, and acceptability.[26] A recent literature review and meta-analysis identified evaluative measures that companies could use to evaluate engagement efforts. The consortium, Patients Active in Research And Dialogues for an Improved Generation of Medicines (PARADIGM), has a framework and metrics to measure patient engagement from various stakeholder perspectives.[27]

Further dissemination and promotion of existing studies and examples—together with results that demonstrate positive returns on investment in terms of speed, cost savings, and value—can help make the case for shifting organizational practices towards a more patient-centric perspective on research. Our assessment showed that stakeholders, especially product sponsors, are increasingly convinced of the utility of patient engagement in research and product-development activities. There is, however, a need to document and disseminate the value of such activities systematically, especially as it pertains to research outcomes and regulatory and payment decision-making.

As previously discussed, regulators, including the FDA, have signaled their support for including patients' perspectives in research. However, payers, another key stakeholder group, may require more evidence to establish the utility and value of patient engagement efforts.

Regulatory agency reviews focus on a treatment's safety and efficacy, whereas payer decisions focus on whether the use of the treatment is reasonable and necessary to improve health outcomes. Evidentiary needs vary between the two stages of review. The ways patients can be engaged and the data that can be used from those engagement activities vary and are not fully aligned. Payers often base their analyses on claims data and may not consistently and uniformly engage patients or consider their preferences to inform coverage determinations. The use of patient data better aligned with payers' specific evidentiary needs could encourage payers to use patient data more consistently in reaching their decisions.

In the research sponsor and payer cases outlined, there may be a lack of positive incentives to integrate patient data, perspectives, and preferences—or few negative consequences for not doing so. For sponsors, the unwillingness may stem from the perceived cost in time, money, and resources, as well as the risks of undertaking engagement activities deviating from accepted drug-development models and of developing robust engagement programs.[28]

c. Underuse of Measures, Guidance, and Frameworks

Although many new tools and frameworks have been developed in the past five years to target methodological gaps, our landscape analysis found that those tools are not being promoted and adopted for systemic changes. In fact, it appears that the proliferation of tools and resources may contribute to the problem, as organizations often lack the bandwidth to identify the resources best suited to their specific needs. In addition, some resources are not scalable, others may be proprietary and thus not widely available, or they may not be the right tools to address current gaps.

Needs persist for additional patient-engagement guidance documents. Though new guidance is available from the FDA on patient-focused drug development and patient engagement in medical device clinical studies, regulatory information is not yet available on what successful patient engagement looks like from a variety of perspectives.[29] Additionally, though the FDA developed a patient experience data table for submission with new drug applications, comprehensive guidance for industry is not yet available to guide the development of data for consideration in the FDA regulatory decision process.

d. Need for Additional Widely Promoted Case Examples and Best Practices

Many research organizations are making strides to integrate meaningful patient engagement into the R&D continuum.[30] Wide dissemination of both successes and failures in engaging patients in research activities would create a more efficient R&D ecosystem, where

less-resourced research organizations could apply the learnings of their peers in designing their own engagement efforts. However, some organizations may view their patient-engagement efforts as a competitive advantage when successful or as harmful to brand or investment prospects when delays in research progression or regulatory failures occur, thus setting up an environment that is not conducive to sharing.

Some progress has been made towards documenting examples of patient engagement practices by PFMD in its series *The Book of Good Practices*. Many organizations also produce webinars on the topic, highlighting specific examples. However, these resources need further promotion, and more organizations need encouragement to share resources, examples, case studies, and templates pre-competitively whenever possible.

Webinars Highlighting Patient Engagement in Research

The following webinars show various approaches to patient engagement in biomedical R&D:

1. Patient-Focused Medical Product Development: Real-World Case Examples, National Health Council, 2020
2. Effective Engagement with Patient Groups around Clinical Trials, Clinical Trials Transformation Initiative, 2015
3. Involving Patients in Clinical Outcome Assessments Strategy and Development, Patient Focused Medicines Development, 2020

e. Lack of Alignment

Lack of alignment of patient engagement activities both within a disease area and among regulatory bodies was identified as a persistent challenge in our research, though efforts underway could achieve progress in these fields.[31] This can be the case at the international level among regulatory bodies of different countries, between federal and national-level organizations within a country, and within organizations themselves. For instance, within a research organization, different teams may have various levels of patient engagement activities, and such efforts may not be aligned or complementary, which can sap efficiency and increase the burden on patients.

Internationally, progress in engaging patients in research happens at different rates, and specific regulatory guidances and processes are often not fully aligned between countries. This can make data collection challenging for research organizations and increase the burden or reduce the efficiency of patient data collection, particularly when the patient pool is limited in size.[32] While the FDA and EMA are working to align on patient engagement, those two regulatory bodies still have a long way to go, as do corresponding agencies in other countries, in developing complementary processes.[33]

RECOMMENDATIONS

Considerable progress has been made in advancing the science of patient input to ensure that the voices and perspectives of patients and caregivers are heard in biomedical research and medical-product development. Substantial barriers remain before the full benefit of engaging patients as part of the biomedical research system can be realized. We identified priorities and overarching opportunities for immediate action that could address one or more of the gaps discussed in the preceding section.

1. Establish How Patient Information Is Used in Decision-Making

Medical product sponsors acknowledge the enormous cost—which is admittedly beneficial to product development—involved in intentionally ensuring patients' input at every step of the research and manufacturing process. Some sponsors have already invested in making their organizational focus and practices more patient-centric. Still others need more information to understand how decision-makers—primarily regulatory bodies like the FDA—are using patient-provided and patient-preference information as part of their decision-making and eventual labeling of products. One of the key findings from the recent report commissioned by the FDA to assess its use of patient experience data was that while the agency reported actively using patient experience data, various external stakeholders—including patients, caregivers, and product manufacturers—lacked clarity on how the FDA uses such data. The report also found that the FDA's use of patient experience data in decision-making varies widely; it recommended approaches the FDA might take to indicate clearly how patient experience data submitted as part of product applications is used. The report further called for the FDA to provide examples of patient-experience data submitted with product-marketing applications.[34]

Other recommendations called for the FDA to continue to expand information on acceptable and not-yet-acceptable patient-experience data and tools, and broach discussion with product sponsors early in the application process. The three PFDD guidances released by the FDA have provided much-needed information to product sponsors, and the agency has highlighted how information in the first two PFDD guidances facilitated recent FDA approvals (e.g., Sanofi's Dupixent [dupilumab] indicated in the management of eosinophilic esophagitis).[35] More examples like these, along with the impending fourth PFDD guidance, will continue to inform product sponsors in the collection and submission of patient-experience data as part of their applications.

The FDA leadership has cited the lack of standardization in the quality and reliability of patient input currently being accrued as a barrier to utility in regulatory decision-making. The PFDD guidance documents should help to address this challenge. However, the FDA needs to publish guidance on how it specifically considers and weighs patient-experience data alongside other clinical data submitted as part of product applications.

2. Build a Pre-/Non-Competitive Space for Knowledge Sharing

There are likely many undocumented examples of how various organizations successfully engage patients and the patient community along the research continuum. There is currently little incentive for organizations to share such examples and any lessons learned. In fact, the competitive advantage elicited by pursuing effective patient engagement discourages sharing of information.

A valuable example of a collaborative venture is the Rare Disease Cures Accelerator-Data Analytics Platform (RDCA-DAP), launched by the FDA to "support innovation and quality in rare disease drug development."[36] The RDCA-DAP "facilitate(s) a cooperative approach and common standardized platforms to better characterize rare diseases, incorporate the patient's perspective in clinical outcome assessment measures, and build clinical trial readiness in the precompetitive space." The RDCA-DAP provides a hub for knowledge-sharing to inform understanding of rare diseases, research, and other critical areas. Disease-specific examples can be modified to guide how patient-experience data are collected and used in various therapeutic instances. The FDA can lead in establishing a program like this, just as it did for rare diseases.

3. Invest in Building Capacity in the Patient Community

As the roles of patients and their caregivers expand in drug development and research, patient organizations will continue to be invaluable stakeholders. They will need to build the necessary capacity for resources and expertise to respond adequately to the growing demand for patients' perspectives.

Many organizations, established with the primary goal of advocating for the needs of particular patient populations, have to build the requisite expertise to engage effectively in the R&D sphere. Patient organizations frequently struggle with chronic underfunding and must balance competing priorities for the populations they serve. Other stakeholders can be part of the solution by ensuring that patient organizations are well positioned to meet the increasing demand for patient input.

NHC's FMV estimator offers a good starting point to assess appropriate remuneration for the patient community when partnering with industry in research. However, as indicated earlier, there is a need for more sustained funding for these organizations and for a better approach to collecting the required patient perspectives. Medical product manufacturers, federal agencies, nonprofit organizations such as PCORI, and disease-specific foundations that partner with patient groups for research are important sources of means and support for capacity building in patient organizations.

There is a need for a paradigm shift in how the patient community is engaged in research: moving away from individual requests to collective efforts. One way to achieve the goal is through transforming patient-registry development practices. Registries can be designed with a

patient-centric emphasis while providing the necessary information to researchers and product manufacturers. For instance, the RDCA-DAP is beginning to leverage collective patient-generated health data over many different and related conditions to build predictive models, assist in trial design, and accelerate clinical development across disease-state contributors. Because disease registries have the potential to benefit multiple stakeholders, the impetus to establish one will have to emerge from a philanthropic initiative or a public-private partnership.

In addition to greater investment in expanding the efficiency and analytical power of patient-derived data, additional resources must be committed to patient organizations for building the necessary capacity, infrastructure, and workforce to align with the recently released and forthcoming guidance provided by the FDA to advance patient engagement in research. For instance, similar capacity-building grant programs exist for state and local health departments and other nonprofit entities to meet federally issued guidance issued by the US Department of Health and Human Services. Similar investments and grant programs could be implemented to support patient-organization capacity growth in response to the burgeoning demand for patient input and according to the FDA recommendations and criteria.

CONCLUSION

There is excitement and momentum for the inclusion of patient input in research. This landscape assessment found that compared to five years ago, stakeholders are convinced of the utility of patient engagement but are struggling with defining and capturing the value and identifying the right approaches for forging ahead. There are, however, organizations leading the charge in the conduct of patient engagement and the development of tools and resources. Highlighting these examples of progress, sharing their best practices, and better aligning stakeholders who collect and use patient-experience data are critical to maximize the impact of patient-engagement efforts and improve their efficiency and effectiveness. In addition, more clarity is needed on how decision-making bodies use patient data; how to encourage a more pervasive, precompetitive knowledge-exchange environment to share best practices; and how we can sustainably expand patient-organization capacity to meet the growing demand for patient-engagement initiatives arising from increased industry and regulatory interest and newly issued federal guidance.

FasterCures is continuing work in patient engagement as a convener, bringing thought-leaders together to explore current issues and challenges further and discuss solutions. Over the course of 2022, we brought industry experts together, providing a platform to share their progress in demonstrating the value of patient-engagement efforts and obtaining leadership and organizational buy-in to expand such efforts. We will continue bringing leaders together to explore solutions to issues related to stakeholder alignment of patient-engagement efforts and capacity building, addressing growing demands and requirements to engage the patient community. We hope these efforts will help drive R&D ecosystem efforts, policies, and practices toward a research environment where all stakeholders can better incorporate patients' perspectives, experiences, and needs into research efforts and decisions.

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