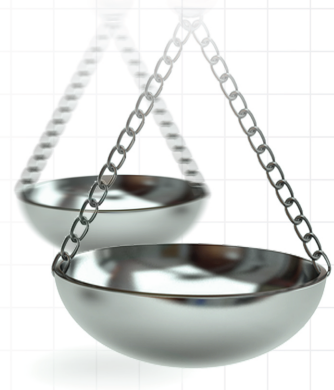
Perspective



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A proposed framework for patient engagement throughout the broader research enterprise

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Patient engagement in clinical research refers to the involvement of patients beyond the role of research subject. To date, the goals of patient engagement have not been clearly defined for each stage of the research enterprise, which, when viewed broadly, encompasses stages such as setting research priorities, interpreting and incorporating research results in clinical guidance, and translating study results into insurance coverage policies. This article presents a new framework for patient engagement by first describing the goals of patient engagement at each stage of the research enterprise and then establishing how to prioritize the types of patient expertise that are needed to achieve these goals.

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Patient engagement in clinical research is intended to foster a more accountable research agenda, enhance the usefulness and relevance of findings, and increase the uptake of evidence in clinical care [1]. On these grounds, researchers, research funding organizations and policymakers in the USA have rapidly adopted patient engagement efforts. For example, the Patient-Centered Outcomes Research Institute (PCORI) has required active patient participation at every step of its sponsored studies [2,3]; medical journals have encouraged authors to 'co-produce' research with patients [4]; and the 21st Century Cures Act has directed the US FDA to significantly develop its use of patient engagement in drug development [5].

There is widespread agreement about the general importance of incorporating patients' perspectives in research. However, there is also doubt about the exact goals of patient engagement at each stage of the research enterprise and about how to select patient representatives to accomplish these goals [6–8]. Viewed broadly, the research enterprise includes many activities worthy of patient input that extend beyond the core activities of clinical trial design and implementation. From prioritizing possible research questions to translating the results into clinical guidelines and insurance coverage policies, patient engagement can serve important goals. To date, however, a description of how the goals of patient engagement vary at these different stages of research has been lacking.

In 2014, PCORI developed a rubric intended to guide patient engagement across the three stages of research: study design, study conduct and dissemination of findings. However, this rubric sets cryptic goals for patient engagement for these stages (i.e., reciprocal relationships, co-learning, partnerships and transparency), and a dimension that is not represented in the rubric at all is 'what patient expertise would be needed to achieve them' [9–11].

Thus, there is need for a clear framework that provides the normative goals of patient engagement at each stage of the research process and how to prioritize the patient expertise most needed 'at the table' at each stage. We believe such guidance would improve the ability of researchers, patient groups and policymakers to select and train patients in order to achieve meaningful and actionable input for all types of clinical research.

In this article, we will first briefly outline five major types of patient expertise that are important for effective patient engagement. Then, we will provide a framework prioritizing these types of expertise within five stages of clinical research: priority setting within disease area; study design and oversight; making regulatory decisions; translating findings into clinical practice; and application to insurance coverage policy. Finally, we discuss ethical

Future Medicine

Table 1. A proposed framework for patient engagement throughout the research enterprise.

Stage of clinical research	Purpose of patient engagement	Type of patient expertise
Priority setting within disease area	To generate knowledge that can benefit patients	Patients with expertise in a condition's clinical diversity
Study design and oversight	To influence trade-off decisions around study conduct To mitigate roadblocks to study completion	Patients with expertise in clinical trial design Patients with expertise in clinical trial participation
Making regulatory decisions	To reach acceptable drug review decisions	Patients with expertise in a condition's clinical diversity
Translating findings into clinical practice	To set relevant clinical guidelines	Patients with expertise in clinical care
Application to insurance coverage policy	To influence deliberations about coverage policy and system affordability	Patients with expertise in insurance coverage policy Representatives from patient advocacy groups

implications of our approach, including potential negative consequences of prioritizing certain kinds of expertise over others, and how this effort can be reconciled with general goals for diversity among patient representatives.

Types of patient expertise

All patients have knowledge from their direct personal experience that can be useful to researchers and policymakers. Even academic experts and seasoned clinicians stand to gain from patients' knowledge because of the distinct insights that can accompany their lived experience. However, some patients also have specialized knowledge beyond their personal experience, that is, expertise, that can offer especially crucial insight to the research process when only a limited number of patients are engaged by researchers or policymakers. In particular, five types of expertise are relevant for patient engagement at different stages of research: expertise in a condition's clinical diversity; expertise in clinical trial design; expertise in clinical trial participation; expertise in clinical care; and expertise in insurance coverage policy (Table 1). We will briefly describe each in turn.

First, patients with expertise in a condition's clinical diversity can offer an account of the breadth of patients' clinical experiences of a condition. Often, people with the same condition experience that condition differently. For example, in conditions like autism, individuals may have milder or more severe forms on a broad spectrum of severity. For other conditions, such as multiple sclerosis, individuals may vary in the clustering and progression of their symptoms. Patient representatives could gain this expertise through working extensively as advocates and thus having extensive contact with a broad range of other patients. Ideally, because it may be difficult for patient representatives to appreciate the full clinical and political diversity among patients, formal surveys or interviews of other patients would ground their views. Patient representatives endowed with this type of expertise can serve a critical role at different points in the research enterprise by describing a condition's diverse clinical presentations and the corresponding effects on patients' interests.

Second, patients with expertise in clinical trial design have a detailed understanding of clinical research methodology and can speak to a study's methodological strengths and limitations. These patients can be a resource to researchers in addressing the more technical details of trial methodology from a patient perspective. They could be research scientists by training, but they could also be self-taught 'lay experts' who have accumulated the scientific knowledge themselves.

Third, patients with expertise in clinical trial participation can represent the diverse experience of patients participating in various types of clinical trials. The patient experience in trials varies dramatically based on multiple factors, and true expertise in this area requires a patient representative who can share perspectives from patients who have participated in everything from phase one trials, to randomized trials, to registries. These patients are likely to emerge from backgrounds as research coordinators, social workers or affiliates of patient advocacy organizations.

Fourth, patients with expertise in healthcare delivery and patient care can foresee the implications of alternative courses of clinical management, which is indispensable when deciding how to interpret and integrate research findings into clinical guidance. These patient representatives could be clinicians by training, but they could also be self-taught 'lay experts'.

Finally, patients with expertise in insurance coverage understand how research findings are translated into coverage policies, as well as how patients with different insurance plans and income levels experience healthcare. Only with this expertise can patients effectively engage at the final stage of the broader research enterprise: applying the study results to insurance coverage decisions. These patient representatives are likely to have backgrounds working within the insurance industry and/or close ties to an advocacy group that has had experience working on behalf of patients with diverse forms of insurance.

Naturally, these types of patient expertise will be more or less useful at different stages of the research enterprise. And since no single patient or even a group of several patients is likely to be endowed with all these dimensions of expertise, priorities must be made regarding which patients to engage at each stage. We turn to these concerns next.

Linking patient expertise with stages of the research enterprise

Priority setting within disease area

In establishing a research agenda, researchers must choose which scientific questions to pursue, and life science companies, nonprofit organizations and governments must decide how to allocate scarce resources among alternative scientific projects. As a result, the research agenda for a condition like breast cancer may emphasize particular areas of research (e.g., causation and prevention) at the expense of other areas (e.g., optimal treatment and recovery). Such allocation decisions will be inevitable so long as research funds remain finite.

At this research stage, the principal goal of patient engagement is to increase the likelihood that the research agenda for a condition will yield benefit for patients with that condition. Through engagement, patients can evaluate the relevance of a proposed research agenda to their population's interests, and they can highlight important but underfunded areas of research. For instance, research funders might find that the majority of the HIV patient community wants to prioritize research toward potential cures, or, conversely, that they prefer to prioritize research on noncurative but less toxic antiretrovirals and new treatments for HIV co-infections. In this context, patient engagement can help prevent commercial or other interests from driving research priorities.

To achieve this goal, the most important priority for researchers and research funders is to recruit patients who have expertise in a condition's clinical diversity. These individuals can ensure that the range of patients' symptoms, responses to treatment and other experiences are taken into account when setting priorities for a clinical research program. Meanwhile, at this stage of the research enterprise it is unnecessary to call on patients to make technical judgments about the analytic design of competing research proposals. As a result, patient engagement at this stage does not require any specific expertise in study design.

Study design & oversight

Researchers and Institutional Review Boards (IRBs) must make several tradeoffs in setting the parameters of a clinical study. For example, if researchers and IRBs favor restrictive clinical criteria for enrolling research subjects, a study can generate stronger statistical findings but does so at the cost of reducing the generalizability of findings to patients outside of the clinical trial setting. Tradeoffs also occur for other components of study design, such as the choice between study end points that are easy to measure (e.g., the level of a muscle enzyme) and those that represent a desired clinical outcome (e.g., improved muscle function and quality of life).

The main goal of engagement during study design is to involve patients in making these kinds of trade-off decisions. Patients can shine light on the potential benefits, costs and inconveniences of a particular study design and help researchers weigh their importance. It is therefore critical at this stage of research to engage patients with expertise in the design and conduct of clinical research studies. These patients are familiar enough with the basic elements of study design and oversight to provide feedback on the advantages and disadvantages of different design options; they have basic knowledge of research methods, statistics and IRB review, and thus are well positioned to have leverage in the connected debates. In this context, patients with some expertise in study design and oversight will be able to serve more effectively as a liaison between the research team and the patient community.

A subsidiary goal of engagement at this stage of research is to mitigate roadblocks to study completion. For example, patients can help guide efforts to refine consent language, suggest ways to reach underrepresented populations in research, alert investigators to problems with their recruitment plan and articulate which safety issues may deter enrollment. For this goal, patients with expertise in clinical trial participation are well positioned for engagement, as they can point out barriers to participation and outline information that potential study participants would want to know.

Making regulatory decisions

The FDA assures the safety and efficacy of drugs and regulates their manufacturing, marketing and distribution. The FDA's approval of new drugs is based on a risk–benefit assessment, which is informed by scientific evidence about the drug, the severity of the condition and how well current therapies meet patients' needs [12]. In accordance with the Prescription Drug User Fee Act (PDUFA) and the 21st Century Cures Act, FDA has committed to engaging patients in these risk–benefit assessments [13,14].

Through its engagement efforts, FDA should seek to understand patients' quality of life, their tolerance for risks and their views on available therapies. For example, because antipsychotics inadequately control symptoms and cause adverse reactions in certain patients with schizophrenia, a new treatment option may be valuable to these patients despite unique safety concerns [15]. In this kind of situation, engagement can enhance FDA's understanding of how clinically significant a new treatment would be to all patients or to a specific subset of patients, thereby helping FDA making decisions that balance tradeoffs among a treatment's benefits, risks and uncertainties.

Because FDA will need information about the impact of a disease and its treatment on patients, the agency should prioritize recruiting patients who have expertise in the condition's clinical diversity.

Translating findings into clinical practice

One prominent way in which research results are translated into medical practice is through clinical practice guidelines. To develop clinical guidelines, a panel of scientific and clinical experts appraises the scientific evidence on a health condition, and then decides upon a generally recommended course of clinical management [16]. However, the available evidence may support several treatment pathways, as is reflected in the conflicting guidelines issued by different organizations on Type 2 diabetes, breast cancer screening and hypertension [17].

At this stage of the broader research enterprise, the purpose of patient engagement is to account for patients' preferences in defining appropriate care, especially when the research evidence is limited or supports a range of management options. For instance, patients who have genetic variants that significantly elevate their risk of developing breast and ovarian cancer face treatment choices ranging from prophylactic surgery to increased surveillance [18]. In this case, patients could have disparate views about when and how to initiate optimally aggressive treatment, and if so, they could help inform the development of a clinical guideline that suggests that multiple courses of clinical action are appropriate [19].

When drafting clinical practice guidelines, experts should engage patients with expertise in clinical care, for example, doctors, nurses and lay experts who have an appreciation of clinical nuance and thus can anticipate the range of possible guidelines consistent with reasonable medical practice. Patients with this kind of expertise in clinical care are better equipped to interpret new scientific data and participate in discussions establishing patient-centered clinical strategies.

Application to coverage policy

Another way in which research results are translated into healthcare delivery is through insurance coverage policies. Health insurers have internal procedures whereby a group of experts review the scientific evidence on a new medical intervention in order to develop coverage criteria for the intervention. Coverage criteria include patient characteristics (e.g., age) that determine eligibility, prescriber restrictions (e.g., the prescribing physician must be an oncologist), coverage duration (e.g., 1 year) and clinical benchmarks (e.g., improved pulmonary function) that must be met before renewal of coverage.

At this final stage of the broader research enterprise, health insurers should engage patients in order to make sure that insurance coverage provides reasonable access to appropriate medical interventions for different kinds of patients. Patients can help clarify the comparative value of a new therapy by pointing out unique benefits or disadvantages that are not captured in the clinical evidence for the 'average' patient. In addition, health insurers should develop opportunities to engage patients with special expertise whenever coverage is being designed that might ask clinicians for substantial documentation of clinical eligibility or that involves a procedural requirement for step therapy or for switching from more expensive to less expensive medications. Patients with the right expertise can describe the broad effects of these types of coverage options on their patient community and call attention to broader financial and administrative burdens related to the management of their illness.

It seems likely that to possess the requisite expertise in this area a patient would have to come from an insurance background, but it is also possible for senior leaders of patient advocacy organizations to gain enough experience with these issues over time. These leaders may be burdened with conflicts of interest due to financial relationships with the life-science community [20], yet insurers developing important coverage policies should still seek to gain the benefits that patients with this expertise can bring. It has been a missed opportunity for health insurers not to view patient engagement as a central component of the stage of the research enterprise that culminates with translation of research results into coverage policy.

Discussion

The goal of this article has been to distinguish among different stages of a broader view of the research enterprise and suggest how to prioritize specific types of patient expertise in order to maximize the beneficial impact of patient engagement. In contrast to this approach, some scholars have suggested that random sampling would be a better and more fair way to identify patients for engagement [21,22]. Though a random sample of patients would be more representative in a technical sense, we believe this approach can run counter to patients having an appreciable effect on the research. At the level of individual clinical research studies, there is evidence that researchers are frequently unable to implement patients' input during engagement due to patients' lack of adequate preparation and training, which can leave patients unsure as to how to contribute in a substantive way to the research [23]. To boot, investigators traditionally select only a handful of patients to serve as advisors for the entire duration of a project, meaning that they cannot tap the full range of patient expertise at discrete stages of research. We think it is a mistake to assume that a single patient would be equally adept at advising investigators on how to apply research findings and how to structure research protocols.

We believe a more tailored approach of matching patient expertise with the specific goals of each stage of the research enterprise will maximize the input of patients and improve the chances that the important goals of patient engagement are achieved. It would help reduce the risk of tokenism, where researchers endorse engagement and set up some form of generic 'patient advisory group' for the purposes of improving their chances of getting research funding while achieving little else. It would also demand more extensive training for patient representatives than has been given as standard and may initially strain patient groups and researchers whose patient representatives do not arrive 'fully formed'.

We therefore would deny the oft-cited concern that patients who contribute to health research may lose the 'outsider' perspective that engaging them is supposed to offer. In many cases, the goals of patient engagement do not call for an outsider perspective *per se* but rather for a patient perspective and the unique insights that receiving care for a condition confers. Patients with appropriate expertise and training are often better positioned to communicate these insights to researchers and policymakers.

We would also argue that it is important not to sacrifice the effectiveness of patient engagement for a noble yet vague goal of fairness defined primarily by representativeness. To cite a paradigmatic case, AIDS activists were successful in securing a fast-track policy for promising drugs at FDA precisely because over time they marshalled the expertise of specific individuals who had learned the nuances of clinical research design [24–26]. This case suggests that relying on patients who have acquired the relevant expertise can, at least in certain circumstances, be critical for effective engagement.

However, the two goals of effectiveness and representativeness are not mutually exclusive. More work is needed to supplement the effort to identify and train individual patients who can bring specific expertise to the table with direct efforts to understand the views of the broader patient community. Expertise-focused patient engagement alone is unlikely to reveal the full range of patients' perspectives and, consequently, it will be important to combine the sustained engagement of individual patients with wider efforts to gather the community's views through surveys and requests for written testimony.

Our framework has left out stages of research where patients occupy nontraditional roles, including that of data collection and analysis. And there are potential goals of patient engagement that we have not discussed, like that of respecting patients by folding them into the research process at every stage. Rather than providing a complete laundry list, our framework has homed in on the specific areas of clinical research where we believe patient input is both underused and especially of high value.

Conclusion

As patient engagement efforts continue to gain momentum, it will become increasingly important to establish models of best practice and to explore new ways to bring the perspective of patients not only into research design but into every stage of the broad research enterprise. This article has argued that researchers, patient groups and policymakers should consider the specific goals of engagement at each stage and select patient representatives with specific expertise needed to achieve those goals. Patient engagement cannot be left to become a simple bumper sticker, a box to be ticked by plugging in the same types of patient advocates and representatives into any and all efforts. If patient engagement is going to become a serious part of the research paradigm, placing patients with the right kind of expertise at the table is the best way to enable all patients to benefit.

Summary points

Background

- The literature lacks a clear framework for the goals of patient engagement and the patient expertise most needed at each stage of the research process.

The Framework

- Patients with knowledge of their condition's diverse clinical presentations can help research funders evaluate the relevance of a proposed research agenda to their population's interests.
- Patients with knowledge of clinical research methodology can help researchers weigh the potential benefits, costs and inconveniences of a particular study design.
- Patients with knowledge of their condition's clinical presentations can help the US FDA make risk–benefit assessments of new drugs.
- Patients with knowledge of healthcare delivery can help experts integrate research findings into clinical guidance that better matches patients' needs.
- Patients with an insurance background can help health insurers make coverage decisions that do not excessively burden patients.

Discussion

- Our framework contradicts the popular belief that patients should be randomly sampled for engagement.
- Our framework is inconsistent with the common practice of engaging the same small group of patients at every stage of the research process.
- Our framework contradicts the belief that the purpose of engaging patients is primarily to collect an outsider's perspective.

Conclusion

- Patient engagement is a growing practice in clinical research. To prevent tokenism, researchers and policymakers should bring patients with expertise to the table.

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