Patient-Engaged Research

Choosing the "Right" Patients to Avoid Pitfalls

BY EMILY A. LARGENT, HOLLY FERNANDEZ LYNCH, AND MATTHEW S. MCCOY

Including patients' perspectives in the design and conduct of clinical research is thought to be useful for aligning health care with patients' needs and priorities. But which patients are engaged—and which should be? Engaging the "wrong" patients might even be detrimental.

The U.S. Congress's 2010 authorization of the Patient-Centered Outcomes Research Institute[1] represented an inflection point in the long normative push toward including patient perspectives in the design and conduct of clinical research: a major research sponsor would now require such patient engagement as a foundational condition of funding. Thus, PCORI is a useful case study for understanding and evaluating patient-engagement efforts more broadly. PCORI's mission is to "help . . . people make informed healthcare decisions, and improve . . . healthcare delivery and outcomes, by producing and promoting high-integrity, evidence-based information that comes from research guided by patients, caregivers, and the broader healthcare community."[2] One of PCORI's animating beliefs is that patients have knowledge and insights that researchers lack. Thus, research meaningfully informed by the patient perspective will be more relevant to the complex choices individuals face when it comes to their health care, allowing them to make better decisions in line with their own goals and priorities.

To ensure that the information resulting from PCORI-funded research is relevant to patients, PCORI eschews the "traditional health research" paradigm, in which investigators drive all aspects of research, in favor of one in which patients assume the role of research partner.[3] To effectuate this paradigm shift, PCORI requires that the research proposals it funds include patients and other stakeholders at every step of the research process—"from proposal development to research design and dissemination of the study results."[4] Patient engagement can take many forms, from offering information, advice, and

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feedback to serving as a coinvestigator participating in recruitment, data collection, and data analysis.[5]

Further empirical analysis is needed to determine the effects of patient engagement on research and whether PCORI's stated goals are being achieved.[6] Yet if we accept the premise that patient engagement can offer fresh perspectives that shape research in valuable ways, then at least two important sets of questions present themselves. First, *how* are patients being engaged—and how should they be engaged? PCORI has devoted substantial energy to addressing these questions, and it requires all applications to include an "engagement plan" detailing how patients will be engaged at each phase of research.[7] In addition, there is a small but growing body of research that examines different methods of patient engagement employed by PCORI-funded researchers.[8]

The second set of questions, which has received relatively less attention, is *which* patients are being engaged—and which patients should be? This neglect is somewhat surprising, given that the "who" question is conceptually prior to the question of "how." For if the "wrong" patients are engaged in research—even if they are engaged in the "right" ways—their input will have less value and might even be detrimental. In light of that possibility, we suggest that not all patient engagement should be treated as equal and, perhaps controversially, that patient engagement is not necessarily an unmitigated good.

Given these concerns, this article focuses attention on the "who" of patient engagement in research. First, we provide background on the rationale for patient engagement, underscoring the importance of ensuring the representativeness of engaged patients. Second, we present what little is known about patients engaged in PCORI-funded research. Third, we identify and discuss the ethical implications of ways in which current practices of patient identification and recruitment may lead to a lack of representativeness. These practices include reliance on the well-connected and well-informed, reliance on patients who are not well trained or well-informed, and reliance on patient advocacy organizations. Finally, we consider several strategies for addressing these pitfalls in order to maximize the positive goals of patient engagement. Patient engagement is intended to address the inability of researchers, funders, and others to fully represent patient views and priorities, but without sufficient attention, the patients selected for this role may still leave important gaps.

Goals and Motivations of Patient Engagement

Patient engagement is central to PCORI's mission,[9] but it is not, of course, an end unto itself. Rather, patient engagement is a means of ensuring that research is "patient centered, useful, and trustworthy," leading to "greater use and uptake of research results by the patient and broader healthcare community."[10] Why believe that patient engagement will have these salutary effects? The premise behind this idea is that patients are meaningfully different from researchers by virtue of their firsthand experience with a particular disease or condition, which in turn gives them unique knowledge and insights. For example, patients can help researchers better understand not only what it is like to live with a particular condition but what sorts of interventions might make the greatest contribution to their well-being. They can identify unmet needs facing patients as well as problems that cause existing interventions to fall short. Moreover, as relative "outsiders" to the research enterprise, patients can raise relevant questions and concerns about aspects of research that "insiders" on the research team might take for granted, such as what might make research participation more or less attractive for members of a particular patient community.

If the purpose of patient engagement is to help researchers better understand the perspectives of a given patient population, then the patients engaged should reflect the range of characteristics, experiences, and interests of the people in that population. We can think of representativeness in this context not as a statistical benchmark to be achieved but as a regulative ideal that is realized when a variety of voices are heard. The closer engaged patients come to reflecting the full diversity of a population of interest, the greater the likely value of their input. By contrast, when the engaged patients are a narrow and relatively homogenous sample of the people in a patient population, then their input will be of limited value and may even compromise research. We will examine the problems associated with a lack of adequate representation in patient engagement in greater detail below, but first we review what is known about who is presently being engaged in patient-centered outcomes research.

Patients are individuals with distinct traits, experiences, interests, goals, and relationships. A choice to engage some patients instead of others will have consequences for which perspectives inform research.

Who Is Being Engaged Now

Unfortunately, little is known about those currently engaged in patient-centered outcomes research. In 2017, Lauren Ellis and Nancy

Kass published findings from interviews of thirty-three patients engaged in PCORI-funded research, offering some of the most comprehensive demographic information available to date.[11] They found that "[m]ore than two-thirds of patients . . . were female; the majority were white, with a wide age range represented . . . . More than two-thirds were employed and held a college or graduate degree . . . . [M]ore than one-third had previously engaged in research."[12] This data has obvious limitations, coming as it does from a small qualitative study, but it suggests high levels of homogeneity among engaged patients across important parameters.

Slightly more is known about how patients are selected for engagement. Research suggests that many patients are recruited based on longstanding relationships with the principal investigator or through the PI's personal network. Ellis and Kass, for instance, found that in more than half of the projects they studied, the PIs and patients had "preexisting relationships, often from prior engagement or professional interactions, including working at the same institution or shared membership in an organization."[13] In other words, there is strong reliance on convenience sampling as the method to identify patients for engagement in research. Other investigators doing patient-centered outcomes research have reported forming new relationships for purposes of patient engagement—recruiting patients from clinics, national patient associations, local disease groups, their hospital's patient advisory council, or their professional network.[14] While some of these "new" connections seem to reflect outreach to individuals outside the investigators' existing circles, others do not. This data, too, is suggestive of relative homogeneity in the patients selected for engagement.

Potential Pitfalls

As the push intensifies to think of patients as coequals in the research process, we must think about the "who" of patient engagement in a more systematic and critical way. Patients are not a monolithic group. They are individuals with distinct traits, experiences, interests, goals, and relationships. Accordingly, a choice to engage some patients instead of others will have important consequences for which perspectives inform research. These choices not only affect the instrumental value of patient engagement but also have downstream ethical implications that deserve greater attention than they have received to date.

If the patients engaged do not adequately reflect the range of diversity within a target patient population, some perspectives may be emphasized while others get ignored. An apt analogy can be drawn to clinical trial recruitment: researchers seek to avoid collecting data from too homogenous a group because that will prevent them from generalizing the results in the desired way. Similarly, in patient-engaged research, if only a narrow range of patient voices are heard, then researchers will gain a partial—and potentially misleading—sense of the concerns and needs of patients in the population of interest. More problematically, this kind of skewed representation will often benefit the relatively well-off at the expense of socially marginalized groups, therefore "perpetuating disadvantage to other groups of patients whose perspectives continue to be excluded," as Ellis and Kass note.[15]

If research is guided by patient engagement, then which patients are involved will determine which questions are asked, how they are asked, and how data is interpreted to answer them. These decisions at the research phase can have far-reaching effects when research is used to shape health policy. For example, one of PCORI's national priorities is to address health disparities by "identifying potential differences in prevention, diagnosis, or treatment effectiveness, or preferred clinical outcomes across patient populations and the healthcare required to achieve best outcomes in each population."[16] Yet if patient-centered outcomes research is disproportionately influenced by the perspectives of a narrow, relatively well-off segment of patients, then the treatment and policy decisions it informs are likely to reflect this bias and may fail to address or even exacerbate existing disparities. Ultimately, then, concerns about the representativeness of engaged patients are closely associated with concerns about justice and who benefits from research.

There are at least three ways in which practices of patient identification and recruitment currently used by PCORI-funded researchers can lead to lack of representativeness.

Relying on patients who are well-informed and well connected. As detailed above, engaged patients are often recruited via convenience sampling. Patient engagement requires commitment from both the researchers and the engaged patients to maintain contact and participation, and trust has been described as a key factor in sustaining engagement over time.[17] Thus, it is not surprising that PIs would turn to individuals with whom they have preexisting relationships or who are referred to them via their professional networks. Longstanding relationships are likely to be based on some degree of trust and to allow PIs insight into the potential quality of a working relationship. Furthermore, researchers may find it difficult to establish new partnerships with patients under the time pressure of writing a research proposal.[18] Similar considerations explain why investigators often collaborate with professional colleagues they already know rather than initiating new collaborative relationships.

Yet patients engaged via convenience sampling are unlikely to be sufficiently representative of the range of patient experiences relevant to the research. For instance, we might reasonably hypothesize that convenience sampling yields engaged patients with higher health literacy than the general population.

Health literacy is, according to a report from the Institute of Medicine, "[t]he degree to which individuals have the capacity to obtain, process, and understand basic health information and services needed to make appropriate health decisions."[19] If patients are engaged on the basis of preexisting connections with investigators and health care institutions—institutions of the kind that are competitive for PCORI awards—they are probably able to navigate the health care system with comparative sophistication and ease. Findings regarding the number of college and graduate degrees held by engaged patients, detailed above, support this hypothesis; educational attainment is often used to estimate health literacy.[20]

Low health literacy is associated with differential use of health care services and health-related outcomes.[21] Hard-to-reach patients will have unique experiences, perspectives, and understandings of the barriers they face, which seem to be particularly relevant to PCORI's goal of ensuring that research will meaningfully contribute to real-world improvements in patient care. What those improvements will need to look like for savvy consumers of health care as compared to those who are more marginalized is probably substantially different. Achieving representativeness among engaged patients is, therefore, a means of combating disparities and promoting health equity.[22]

Beyond health literacy, there are a number of relevant traits that could be expected to influence the sort of input engaged patients might provide. For example, for reasons similar to those driving health literacy, patients engaged via convenience sampling are more likely to have trust in the health care system, in their clinicians, and in researchers. The majority of engaged patients interviewed by Ellis and Kass were white, and race is known to correlate with trust both in the health care system and in research.[23] Relative levels of trust will be particularly important if engaged patients are being used to gauge, for instance, how comfortable prospective study subjects will be with certain research-related risks, the acceptability of elements of study design, or what recruiting methods would be most effective. It may also skew the perceived acceptability or responsiveness of the intervention being tested. Furthermore, the types of patients that have the time and money to engage with researchers—in addition to working, caregiving, or fulfilling other obligations—are likely to be relatively better off. Preferentially including well-connected, well-informed, and well-off patients in research may perpetuate disadvantages experienced by marginalized groups.

As long as ties between patient advocacy organizations and industry remain prevalent, researchers who engage patients affiliated with PAOs may hear patient voices filtered through an industry lens.

Relying on patients who are not well trained or well-informed. PCORI-funded investigators are steeped in the Western-medicine and research paradigms. Patients may have different frameworks for thinking about health and wellness and are likely to be much less familiar (if they are familiar at all) with research methods.[24] Patient engagement will be reduced to mere tokenism if patients are not capable of meaningfully contributing to the research enterprise due to a lack of preparation and training.

In a sense, bringing individuals who cannot be effective collaborators into patient-engaged research creates the inverse of the problem described in the previous section. Choosing the "model" patient may lead to confirmation bias because investigators are engaging with patients so enmeshed in the health care system that they do not offer sufficiently distinct perspectives to be valuable. By contrast, relying on patients who may have unique, relevant perspectives to share but who lack the understanding and confidence to express those perspectives in a clear and constructive manner may result in PIs' hearing nothing at all or receiving input that is impractical or out of place. For example, patients may be hesitant to contribute or may not understand how best to contribute if the study team speaks to them in a rush of acronyms—"INDs," "IRBs," "RCTs," "DSMBs"—that are familiar to researchers but for which most patients (reasonably and predictably) have no context. In these scenarios, patient involvement becomes an exercise in "checking the box" simply to satisfy PCORI's technical requirements.[25] Without training, notes Rebecca Dresser, engaged patients "are likely to become frustrated and cynical about researchers' motives for including them,"[26] which can damage trust or have other negative effects on research, potentially causing more damage than if patients had not been engaged at all. Outsider perspectives are essential, but the outsiders must be adequately supported.

Overreliance on patient advocacy organizations. A third consideration is that patients selected for engagement at present often have close ties to patient advocacy organizations. PAOs are formally organized nonprofit groups that, as one of us (Matthew McCoy) and colleagues describe them, seek "to combat a particular disease or disability or to work toward improving the health and well-being of a particular patient

population."[27] The organizations play an influential role in shaping health policy and are obvious allies for investigators doing patient-centered outcomes research. However, PAOs often differ in systematic ways from the broader patient population. To the extent that patients affiliated with PAOs share the values and interests of their organizations, their perspectives on research are likely to reflect these differences. There are at least three ways in which the views of PAO-affiliated patients can diverge from those of other patients.

First, the broader population of persons affected by a particular disease or disability may not speak with one voice, and PAOs may champion research priorities not shared by all patients. For example, the autism community faces schisms over how to direct funding for research, and Autism Speaks, a leading autism advocacy organization, has repeatedly been criticized by outsiders and by people who have left the organization for its research priorities. In the past, the organization was criticized for continuing to support vaccine research despite mounting evidence that vaccines were not a cause of autism (although the organization is now clear that "[v]accines do not cause autism"[28]), and others have criticized its emphasis on curing autism.[29] Similar observations can be and have been made about advocacy movements around breast cancer,[30] mental health,[31] and other health issues. Ethical problems arise when groups with the best access to researchers gain a disproportionate advantage, as the imbalance promotes unfair and inequitable allocations of research funding and prioritization of some research goals at the expense of other equally valid (indeed, perhaps more valid) goals.

Second, many PAOs have well-documented financial and governance relationships with drug, device, and biotech companies. As a recent study showed, "among 104 of the largest U.S.-based [PAOs], at least 83% received financial support from drug, device, and biotechnology companies, and at least 39% [had] a current or former industry executive on the governing board."[32] These relationships give rise to institutional conflicts of interest that can influence PAOs to act in ways that benefit their industry backers at the expense of the patients they purport to serve. While there have been reports of overt pressure on industry-funded PAOs to adjust their priorities to suit donor interests, COIs need not result in this type of demonstrable pressure to raise ethical concerns.[33] Institutional COIs are a result of circumstances in which an organization's financial interests pose a risk of unduly influencing the organization's pursuit of its primary mission. Thus, a COI can exist even without the actual occurrence of undue influence.[34] Many PAOs are mindful of these conflicts and recognize that more substantial efforts to manage them are needed. For example, a 2017 survey of PAO leaders found that "most . . . believe that industry [COIs] are relevant to PAOs [and] acknowledge that their policies need to be strengthened."[35] However, as long as ties between PAOs and industry remain prevalent, researchers who engage patients affiliated with PAOs may hear patient voices filtered through that lens.

Third, while some PAOs may be biased by industry ties but still function more or less independently, some groups presenting themselves as PAOs are essentially industry fronts. "Astroturfing" is the creation of a fake grassroots organization to create the perception that there is public support for an industry agenda.[36] For example, Sprout Pharmaceuticals created what was widely regarded as a sham organization called "Even the Score" to shill for Addyi, its antidepressant-turned-female-aphrodisiac.[37] Addyi, which twice failed to get U.S. Food and Drug Administration approval, received approval (albeit with a black-box warning) after Even the Score mounted an ostensibly grassroots campaign linking Addyi's approval to women's sexual health equity. Consumer groups paid by Even the Score advocated for FDA approval, but consumer groups that were not paid by Even the Score opposed both Addyi's approval and use. Although "Female Viagra," as Addyi is sometimes called, has not been successful in the marketplace, commentators have expressed concern that the Even the Score campaign taught companies to manipulate the FDA through patient advocacy.[38] The development of Addyi is not an example of patient-engaged research, but it vividly illustrates how patient engagement can be hijacked by industry for its own ends. One could easily imagine a similar example in which companies—motivated by the obvious and growing political influence of patients—hire patients to advance

RECOMMENDATIONS

- Engage more patients—Involve larger numbers of patients to capture a wider variety of perspectives and experiences.
- Purposively engage patients—Use purposive sampling to ensure representativeness along relevant dimensions.
- Reduce barriers to engagement—Identify and address obstacles to engagement of a representative range of patients.
- Offer training to facilitate engagement—Make training on research and research methods available to any patient interested in engaging.
- Manage engaged patients' conflicts of interest—Require disclosure of COIs and consider further steps to mitigate them.
- Conduct further research on who is engaged—Determine which patients are presently engaged in research and assess their representativeness.

their agendas through collaboration with PCORI-funded investigators.

The sympathetic nature of patients imparts credibility to their recommendations about research. But the prospect of PAOs with research agendas that are not broadly shared by the patient community, of conflicted PAOs, and of sham patient organizations suggests the danger of assuming that every organization that purports to represent patient interests truly does. Instead of ensuring patients an independent voice in the development of research priorities and projects, the involvement of PAOs could be used to give industry additional avenues for promoting its agenda. Some investigators may be able to discern these issues when they arise, but it would be naïve to assume that they will be able to recognize and avoid such outside influence reliably.[39]

Recommendations

In the previous section, we identified ways in which representativeness may be compromised by current patient-engagement strategies. These shortcomings are more concerning in instances where engaged patients are granted a substantial role in shaping research. Nevertheless, we should promote diversity in patient engagement. In what follows, we offer several suggestions for more conscientious selection of patients for engagement (see the table). Some of these strategies may have cross-cutting effects and increase representativeness broadly, while others, though important, are likely to have a more limited effect.

Engage more patients. The number of patients engaged may help address the problems of nonrepresentativeness. One study found that although 15 percent of projects reported engaging only one patient, more than half of projects reported engaging six or more patients.[40] These numbers are encouraging. While every patient's experience is important, experiential knowledge is necessarily both limited and idiosyncratic;[41] as Dresser notes, "Personal experience cannot in itself confer knowledge of 'what it is like' for others in similar situations."[42] Therefore, including more patients is a first step toward collecting the desired variety of perspectives.

Purposively engage patients. Numbers alone cannot ensure that engaged patients are representative of the target patient population along all relevant dimensions. It is also necessary to use purposive—rather than convenience—sampling. The limited available evidence suggests this is not presently happening in patient-centered outcomes research. As noted above, it appears to be quite rare for research teams to recruit patients for engagement with the aim of balancing competing viewpoints or with the goal of achieving socioeconomic or other types of experiential diversity.

When patients are engaged in research, representativeness needs to be considered along a number of axes. In most cases, it is necessary to consider the typical indicators of diversity, such as gender, race, educational attainment, and socioeconomic status. Ultimately, however, representativeness must be understood contextually, in relation to the population of interest for the research. For example, breast cancer disproportionately affects women, and the majority of sickle cell patients are black. Achieving a 50-50 mix between men and women engaging with researchers about a breast cancer study is probably not desirable, just as proportioning racial diversity in accordance with U.S. census numbers is probably inappropriate in a sickle cell study. Representativeness should also account for heterogeneity in disease progression or along the spectrum of illness—such as the autism spectrum, which captures a wide range of conditions—because individuals may reasonably be expected to have different interests depending on where they fall on the continuum. It is also important to recruit from subpopulations that are often underrepresented in research, such as people sixty-five and older.[43]

Further, investigators have an obligation to understand reasonable debates and disagreements within the relevant patient community and to engage with patients embodying these diverse views. For example, members of the Alzheimer's community have different views on the relative importance of cure versus caregiver support.[44] But it is not necessary to give credence to unmeritorious viewpoints in an attempt to achieve a veneer of balance. It would be inappropriate, for instance, to engage antivaxxers in research on the causes of autism, given the current state of the science.

Investigators have an obligation to understand reasonable debates and disagreements within the relevant patient community and to engage with patients embodying these diverse views.

PCORI has sought to overcome barriers to patient engagement in research. For example, PCORI's Pipeline to Proposal awards program focuses on building the community of patients and other stakeholders who can participate in patient-centered outcomes research by providing funding to build capacity and engage people around health care research.[45] It would be useful if these funds were awarded with a preference for inclusion of diverse patient perspectives, as with university research grant programs that seek to promote interdisciplinary work by conditioning funding on the inclusion of faculty

members from different university departments and schools.

As a further step, PCORI should ask all funded investigators to report how patients were chosen for engagement and why. PCORI currently requests that funding proposals include "a plan to ensure representativeness of [research] participants."[46] PCORI should request a similar plan for patient engagement.

Reduce barriers to engagement. Serving as an engaged patient will impose opportunity costs for everyone. Barriers to participation are, however, likely to be higher for some patients than for others. Because these barriers are not randomly distributed, they can be expected to affect representativeness.

Offering payment to engaged patients could address a financial barrier to engagement for some individuals. PCORI offers a compensation framework that emphasizes the importance of fair financial compensation as a means of recognizing the contributions of all members of the research team, including patients.[47] Such acknowledgment is an important function of payment.[48] Yet payment may have an additional benefit here if it expands the pool of patient partners who are willing and able to engage. It may also be necessary to hold meetings during evenings and weekends, or whenever more patients are able to come, and to find other ways to be flexible, such as using conference calls for patients who may be too ill to reliably attend in-person meetings or ordering rides for participants via ride-sharing apps.

Offer training to facilitate engagement. To be effective research partners, engaged patients will need some understanding of the science and the research process. Training may, therefore, appear to be part of the "how" of patient engagement, a question we have set to the side in this article. Yet we would argue that, unless training is made readily available for all engaged patients, researchers will continue to rely disproportionately on the most well-educated and well-informed patients, creating the risks of confirmation bias discussed above.

Theoretically, a number of stakeholders in the research could offer such training. There are barriers to having PCORI-funded investigators do it, however, such as lack of time and resources, the inefficiency in having every PI reinvent the wheel to develop and offer training, and the possibility that the investigators might, even if unintentionally, impart knowledge that conforms with their views, diluting the value of patient engagement. At present, some patient groups are able to provide their members with the necessary education. For instance, the Parkinson's Disease Foundation has a Parkinson's Advocates in Research program that has trained more than 280 volunteer patient advocates "to work on the frontlines with the professionals seeking better . . . treatments" for Parkinson's disease since 2008.[49] The foundation explains that, when advocates from disease communities "are primary partners in research alongside scientists, industry, and government," research can be made more efficient and effective. Some patients cannot, however, access training, and some organizations cannot offer it. For these individuals and groups, reliance on an ad hoc system of training may limit meaningful participation—or perhaps preclude any participation—resulting in marginalization. The gold standard should therefore be training that is available to any patient and delivered by an institutional stakeholder.

PCORI is an obvious candidate for developing and delivering this information, even recognizing that PCORI-funded projects are heterogeneous and that a PCORI-developed program may not be perfectly tailored to all projects' needs. PCORI would benefit from economies of scale and from its own considerable institutional knowledge. Further, PCORI is already taking steps in this direction.[50] For example, the PCORI Ambassador program "equips, trains, connects, and mobilizes patients, organizations, and other stakeholders to share PCORI's vision and mission, . . . participate as full partners in research, and help ensure the sharing and use of information generated from PCORI-funded projects."[51] All ambassadors, who are volunteers, must complete PCOR 101 and PCOR Science Training and fill out a COI disclosure form, although mechanisms for subsequent conflict management are unclear. At the end of 2014, PCORI had trained eighty-two ambassadors from stakeholder communities—not just patients but also caregivers, researchers, clinicians, purchasers, payers, industry representatives, and others.[52] The long-term goal is to have ambassadors in every state. This is an important effort but of limited effectiveness given the small reach of the program at present.

A longer-term but nonetheless salient concern associated with training is that it may turn engaged patients into "insiders," thereby depriving them of the "outsider" perspective that is implicitly their contribution to patient-centered outcomes research. If one's expertise depends on a relative lack of knowledge about the nature and details of research, does acting as an engaged patient undermine the patient's "outsider" expertise over time? Comparisons can be drawn to the community member on an institutional review board—a lay person who often fulfills the regulatory roles of a nonscientific member and unaffiliated member. The longer these individuals are exposed to IRB deliberations, the less likely they are to act as outsiders.[53] U.S. regulations do not require the IRB's community member to be representative of the community, however; the concept of patient-engaged research does demand representativeness and suggests that participation as an engaged patient may need to be time limited. Rather than engaging the same patients on multiple studies and over time, researchers, with the assistance of PCORI, should strive for reasonable turnover in the population of engaged patients.

Manage engaged patients' conflicts of interest. Many see the involvement of PAOs in PCORI-funded research as making a valuable contribution to research rather than as compromising it. And given that PAOs often unite many patients under one umbrella, these organizations may indeed offer important perspectives. To maximize these benefits, however, it is important to actively manage the COIs previously described.

Disclosure of COIs has become a widely accepted norm in science and medicine. Engaged patients, who are being held up as important contributors to research, should be held to the same standards as researchers in this regard. Thus, it is important that patients disclose both individual COIs and the COIs of organizations with which they are affiliated. This two-step disclosure is important so that it is possible to identify when patients are affiliated with an industry-funded advocacy organization. Requiring disclosure is not the same as assuming that PAOs would knowingly let their financial ties bias their judgment. Rather, requiring disclosure is an effort to achieve transparency and promote trustworthiness.[54]

Disclosure is not a complete solution to COIs. Compelling engaged patients to provide full information about their COIs is, however, a first step to enabling additional solutions to ensure that industry interests do not unduly influence patient engagement. A further step would be to limit the engagement of PAO-affiliated patients to those from PAOs that receive less than a certain percentage, perhaps 10 percent, of their total funding from industry. Limiting industry funding in this way is a means of splitting the difference between prohibiting PAO involvement (which is likely a nonstarter and would sacrifice some benefits) and allowing egregious cases in which PAOs become de facto advocates for industry. A further step would be to cap the number of engaged patients who are involved in industry-funded PAOs in a given study.

Conduct further research on who is engaged. Finally, more research is needed to determine which patients are being engaged. Ideally, to assess the full extent to which the potential pitfalls discussed here are encountered in practice, it would be helpful to gather more individual-level information about engaged patients and also more information about how researchers identify these patients for engagement and why they select some patients over others. In addition, PCORI should continue funding research on patient engagement, with a focus on how to effectively recruit patients from hard-to-reach populations.

Taking Patient Engagement Seriously

PCORI aims to increase the quality of information available to patients in their health-related decision-making, both through its own funding and by influencing health care research funded by others to be more patient-centered. Moreover, there is a general trend toward patient engagement in health-related decision-making.[55] Patient-centered outcomes research is therefore a useful case study for drawing lessons about high-quality patient engagement in research that can apply more broadly. Even if the problems we have identified are infrequent, the obvious potential for bias, injustice, and the erosion of public confidence in research makes it important that PCORI and other bodies supporting patient engagement create robust policies to address them. If we are going to take patient engagement seriously as a goal, we need to take seriously the question of who the patients are and ought to be.

Notes

1. Patient Protection and Affordable Care Act, 2010.
2. "About Us," Patient-Centered Outcomes Research Institute, March 21, 2017, https://www.pcori.org/about-us.
3. "Our Story," Patient-Centered Outcomes Research Institute, August 5, 2014, https://www.pcori.org/about-us/our-story.
4. "How We Select Research Topics," Patient-Centered Outcomes Research Institute, May 1, 2014, https://www.pcori.org/research-results/how-we-select-research-topics.
5. E. A. Largent et al., "Patient-Centered Outcomes Research: Stakeholder Perspectives and Ethical and Regulatory Oversight Issues," *IRB: Ethics & Human Research* 40, no. 1 (2018): 7-17.
6. L. Esmail, E. Moore, and A. Rein, "Evaluating Patient and Stakeholder Engagement in Research: Moving from Theory to Practice," *Journal of Comparative Effectiveness Research* 4, no. 2 (2015): 133-45.
7. L. Frank et al., "Conceptual and Practical Foundations of Patient Engagement in Research at the Patient-Centered Outcomes Research Institute," *Quality of Life Research* 24, no. 5 (2015): 1033-41.
8. S. R. Morain et al., "Deliberative Engagement Methods for Patient-Centered Outcomes Research," *The Patient—Patient-Centered Outcomes Research* 10, no. 5 (2017): 545-52.
9. J. V. Selby, A. C. Beal, and L. Frank, "The Patient-Centered Outcomes Research Institute (PCORI) National Priorities for Research and Initial Research Agenda," *Journal of the American Medical Association* 307, no. 15 (2012): 1583-84.
10. "What We Mean by Engagement," Patient-Centered Outcomes Research Institute, August 12, 2014, https://www.pcori.org/engagement/what-we-mean-engagement.
11. L. E. Ellis and N. E. Kass, "How Are PCORI-Funded Researchers Engaging Patients in Research and What Are the Ethical Implications?," *AJOB Empirical Bioethics* 8, no. 1 (2017): 1-10.
12. Ibid., 3.
13. Ibid., 5.
14. L. P. Forsythe et al., "Patient and Stakeholder Engagement in the PCORI Pilot Projects: Description and Lessons Learned," *Journal of General Internal Medicine* 31, no. 1 (2016): 13-21.
15. Ellis and Kass, "How Are PCORI-Funded Researchers Engaging Patients in Research and What Are the Ethical Implications?," 8.
16. "National Priorities and Research Agenda," Patient-Centered Outcomes Research Institute, May 1, 2014, https://www.pcori.org/research-results/research-we-support/national-priorities-and-research-agenda.
17. D. Cukor et al., "Patient and Other Stakeholder Engagement in Patient-Centered Outcomes Research Institute Funded Studies of Patients with Kidney Diseases,"

Clinical Journal of the American Society of Nephrology 11, no. 9 (2016): 1703-12.

18. J. V. Selby, L. Forsythe, and H. C. Sox, "Stakeholder-Driven Comparative Effectiveness Research: An Update From PCORI," *Journal of the American Medical Association* 314, no. 21 (2015): 2235-36.

19. Institute of Medicine, *Health Literacy: A Prescription to End Confusion* (Washington, D.C.: National Academies Press, 2004).

20. L. D. Chew, K. A. Bradley, and E. J. Boyko, "Brief Questions to Identify Patients with Inadequate Health Literacy," *Family Medicine* 36, no. 8 (2004): 588-94.

21. N. D. Berkman et al., "Low Health Literacy and Health Outcomes: An Updated Systematic Review," *Annals of Internal Medicine* 155, no. 2 (2011): 97.

22. R. Hasnain-Wynia and A. C. Beal, "Role of the Patient-Centered Outcomes Research Institute in Addressing Disparities and Engaging Patients in Clinical Research," *Clinical Therapeutics* 36, no. 5 (2014): 619-23.

23. L. E. Boulware et al., "Race and Trust in the Health Care System," *Public Health Reports* 118, no. 4 (2003): 358-65.

24. M. Tai-Seale et al., "The Language of Engagement: 'Aha!' Moments from Engaging Patients and Community Partners in Two Pilot Projects of the Patient-Centered Outcomes Research Institute," *Permanente Journal* 20, no. 2 (2016): 89-92.

25. Largent et al., "Patient-Centered Outcomes Research."

26. Rebecca Dresser, *When Science Offers Salvation: Patient Advocacy and Research Ethics* (Oxford University Press, 2001), 41.

27. M. S. McCoy et al., "Conflicts of Interest for Patient-Advocacy Organizations," *New England Journal of Medicine* 376 (2017): 880-85, at 880.

28. "What Causes Autism?," Autism Speaks, July 25, 2012, https://www.autismspeaks.org/what-autism/learn-more-autism/what-causes-autism.

29. E. Shire, "'Autism Speaks'—but Should Everyone Listen?," *Daily Beast*, June 13, 2014.

30. P. Orenstein, "Our Feel-Good War on Breast Cancer," *New York Times*, April 25, 2013.

31. N. Tomes, "The Patient as a Policy Factor: A Historical Case Study of the Consumer/Survivor Movement in Mental Health," *Health Affairs* 25, no. 3 (2006): 720-29.

32. McCoy et al., "Conflicts of Interest for Patient-Advocacy Organizations," 884.

33. K. Thomas, "Furor over Drug Prices Puts Patient Advocacy Groups in Bind," *New York Times*, September 27, 2016.

34. M. S. McCoy and E. J. Emanuel, "Why There Are No 'Potential' Conflicts of Interest," *Journal of the American Medical Association* 317, no. 17 (2017): 1721-22.

35. S. L. Rose et al., "Patient Advocacy Organizations, Industry Funding, and Conflicts of Interest," *JAMA Internal Medicine* 177, no. 3 (2017): 344-50, at 348.

36. S. Perry, "New Patient-Advocacy Group 'Outed' by Minnesota-Based Website as 'Astroturf' Campaign," *MinnPost*, February 16, 2016, https://www.minnpost.com/second-opinion/2016/02/new-patient-advocacy-group-outed-minnesota-based-website-astroturf-campaign.

37. A. Hogenmiller, A. Hirsch, and A. Fugh-Berman, "The Score Is Even," *Bioethics Forum* (blog), June 14, 2017, https://www.thehastingscenter.org/the-score-is-even/.

38. J. Block and L. Canner, "The Grassroots Campaign for 'Female Viagra' Was Funded by Its Manufacturer," *The Cut*, accessed June 14, 2018, https://www.thecut.com/2016/09/how-addyi-the-female-viagra-won-fda-approval.html.

39. E. Silverman, "McCaskill Bill Would Make Pharma Report Payments to Patient Advocacy Groups," *STAT*, June 6, 2018, https://www.statnews.com/pharmalot/2018/06/06/mccaskill-payments-advocacy-groups/.

40. Forsythe et al., "Patient and Stakeholder Engagement in the PCORI Pilot Projects."

41. G. P. Martin, "'Ordinary People Only': Knowledge, Representativeness, and the Publics of Public Participation in Healthcare," *Sociology of Health & Illness* 30, no. 1 (2008): 35-54.

42. R. Dresser, "The Role of Patient Advocates and Public Representatives in Research" in *The Oxford Textbook of Clinical Research Ethics*, ed. E. J. Emanuel et al. (New York: Oxford University Press, 2011), 234.

43. K. S. Kauffman et al., "Engaging Hard-to-Reach Patients in Patient-Centered Outcomes Research," *Journal of Comparative Effectiveness Research* 2, no. 3 (2013): 313-24.

44. J. Graham, "Alzheimer's Activists Splinter in Angry Fight over Priorities," *STAT*, March 2, 2016.

45. "Pipeline to Proposal Awards," Patient-Centered Outcomes Research Institute, August 5, 2014, https://www.pcori.org/funding-opportunities/research-support-funding-opportunities/pipeline-proposal-awards.

46. "PCORI Methodology Standards," Patient-Centered Outcomes Research Institute, November 12, 2015, at https://www.pcori.org/research-results/about-our-research/research-methodology/pcori-methodology-standards.

47. "Financial Compensation of Patients, Caregivers, and Patient/Caregiver Organizations Engaged in PCORI-Funded Research as Engaged Research Partners," Patient-Centered Outcomes Research Institute, June 10, 2015, www.pcori.org/sites/default/files/PCORI-Compensation-Framework-for-Engaged-Research-Partners.pdf.

48. L. Gelinas et al., "A Framework for Ethical Payment to Research Participants," *New England Journal of Medicine* 378 (2018): 766-71.

49. "Become a Research Advocate," Parkinson's Foundation, October 12, 2017, http://parkinson.org/research/Patient-Engagement/Advocate-for-Research.

50. L. Gelinas et al., "Oversight of Patient Centered Outcomes Research: Recommendations from a Delphi Panel," *Annals of Internal Medicine* (forthcoming).

51. "Pipeline to Proposal Awards," Patient-Centered Outcomes Research Institute.

52. L. Frank et al., "Conceptual and Practical Foundations of Patient Engagement in Research at the Patient-Centered Outcomes Research Institute," *Quality of Life Research* 24, no. 5 (2015): 1033-41.

53. C. W. Lidz et al., "The Participation of Community Members on Medical Institutional Review Boards," *Journal of Empirical Research on Human Research Ethics* 7, no. 1 (2012): 1-8.

54. S. L. Rose, "Patient Advocacy Organizations: Institutional Conflicts of Interest, Trust, and Trustworthiness," *Journal of Law, Medicine & Ethics* 41, no. 3 (2013): 680-87.

55. "Learn about FDA Patient Engagement," U.S. Food and Drug Administration, accessed August 9, 2018, https://www.fda.gov/ForPatients/PatientEngagement/default.htm.