



Patient-Centered Outcomes Research Institute

Funding Announcement:

***Assessment of Prevention, Diagnosis, and
Treatment Options***

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Opportunity Snapshot

It was the most important health decision that she had faced in the 68 years of her life. She needed information about the risks and benefits of the treatment options she was asked to choose among. She needed information that applied to patients like her, and she needed information on a range of clinical outcomes that she felt were important to consider. Unfortunately, the information she needed was not available.

Purpose

Every day, patients and their caregivers are faced with crucial healthcare decisions while lacking key information that they need. The needed information does not deliver verdicts or tell people what to do, but informs them of the trade-offs associated with the options they have—and helps them make better decisions for themselves in collaboration with their clinicians—based on the facts, perhaps even personalized for them, and their own values, preferences, and goals.

We at the Patient-Centered Outcomes Research Institute (PCORI) are entrusted by the public to fund research that will matter to patients and their caregivers, and we now turn to you to help us. We have designed five national priorities and a research agenda for the projects we will fund that is focused on producing knowledge that is useful to patients, their caregivers, and clinicians. This knowledge is also expected to be useful to health system leaders, payers, and regulators who make decisions that impact patients. We have not specified the questions or the conditions. We believe that the important gaps in knowledge are pervasive and that, rather than dictate which conditions and questions are more important than others, we have chosen to seek wisdom from around the country in the form of applications for funding in the five priority areas. We also have identified some areas, such as rare conditions, and the needs of patients with multiple chronic conditions that are often neglected to be sure they are covered among our funded projects.

In this PCORI Funding Announcement (PFA), we seek to fund projects that address critical decisions that face patients, their caregivers, and clinicians every day and with too little information. These decisions must be consequential, be occurring now without key evidence about the comparative effectiveness of two or more options, and patients/caregivers must benefit from new knowledge in ways that are clear and important. The premise of this research is that new knowledge will support critical choices by patients, caregivers, and their clinicians, not that it will deliver a verdict that will lead us to dictate a choice. This knowledge will provide insight about the comparative benefits and harms of the options and provide information about outcomes that are experienced by patients and important to patients.

We are seeking to change how research is done by emphasizing the role of strong research teams that include varying perspectives. PCORI seeks to distinguish itself by supporting research in which patients, caregivers, and practicing clinicians are actively engaged in generating the research questions, conducting the research, and using the results of that research to truly understand and address patient needs. In the end, PCORI will be held accountable for whether this model succeeds in producing knowledge that patients need and use. We hope that you—patients, caregivers, clinicians, health plans, product manufacturers,

policy makers, and researchers from around the country—will join us in producing an unprecedented portfolio of truly patient-centered outcomes research that will transform the ability of patients, their caregivers, and clinicians to seek, find, and use practical information in the decision making process.

Funds Available

We anticipate that approximately 54 contracts totaling up to \$48 million in total costs may be funded under this PFA in this funding cycle, assuming receipt of a sufficient number of high quality applications. PCORI anticipates additional funding cycles related to this announcement. However, funds available may vary, and PCORI reserves the right to modify or terminate this announcement at any time.

Budget and Project Periods

Direct project costs are limited to a maximum of \$500,000 per year.

Organizational Eligibility

Applications may be submitted by any private sector research organization, including non-profit and for-profit organizations, any public sector research organization, universities, colleges, hospitals, laboratories, healthcare systems, and units of state and local governments. All US applicant organizations must be recognized by the Internal Revenue Service. Foreign organizations and nondomestic components of organizations based in the United States may apply, as long as there is demonstrable benefit to the US healthcare system and US efforts in the area of patient-centered research can be clearly shown. Individuals may not apply. Foreign organizations should consult the PCORI Application Guidelines because there is an extra step for such organizations to register within the PCORI online system.

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Assessment of Prevention, Diagnosis, and Treatment Options

If you are interested in applying for an award under this program, follow PCORI's five-step process.



- ✓ **Review the Program Detail:** Get familiar with the program announcement and PCORI's areas of interest. Look at the example questions.
- ✓ **Consider the Components:** Consider the applicant eligibility requirements and PCORI's specific requirements to see if your organization, your interests, and your project fit within this program.
- ✓ **Develop Your Application:** Design the project. Determine and document who will be involved, the research strategy, and the budget needs. To see the Application Guidelines, go to <http://www.pcori.org/assets/PFAguidelines.pdf>.
- ✓ **Know the Review Criteria:** Understand the PCORI merit-review assessment criteria. The criteria are provided at the end of this document.
- ✓ **Submit Your Application:** Compile and submit your application. To see the Application Guidelines go to <http://www.pcori.org/assets/PFAguidelines.pdf>. You can register for the online system and submit a Letter of Intent (LOI) or an application beginning September 17, 2012. A link to the online system will be available on the PCORI Funding Announcements (PFAs) web page at <http://www.pcori.org/funding-opportunities/funding-announcements/>.

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Step 1: Review Program Detail Overview

We are soliciting studies comparing the effectiveness of alternative strategies for prevention, treatment, screening, diagnosis, or management.

We are looking to fund projects that address critical decisions that patients and their caregivers face every day, for which the information available today is inadequate. These decisions must be consequential and must be occurring now without key evidence about the comparative effectiveness of possible options. The potential of the research to benefit patients and their caregivers must be clear and important.

Research Areas of Interest

We are interested in the following broad topical areas:

- Studies that compare the effectiveness of two or more strategies for prevention, treatment, screening, diagnosis, or management that have not been adequately studied against alternative options. Topics are not limited to medical or surgical therapy and may include a range of strategies including self-care. Special emphasis is placed on studies conducted in typical clinical populations considering the full range of relevant patient-centered outcomes and possibilities that results may differ among patient groups based on patient characteristics (understood broadly as possibly including clinical, psychosocial, demographic, and other domains) or preferences.
- Studies that compare the use of prognostication/risk-stratification tools with usual clinical approaches to treatment selection or administration.
- Studies that investigate the key determinants of the outcomes patients experience following treatment decisions, with attention to various patient factors, including demographic, biological, clinical, social,

Once [my daughter] got diagnosed, I really wanted to know what the most effective treatment was or which way we should go. There are so many different medicines. It is pretty much a trial- and-error type of thing, but dealing with your kids, you are extra sensitive about it; and then I didn't know if she was able to actually deal with her pump at school, carrying it around or losing it.

—Parent of pediatric patient

With the diagnosis and all this, I'm like, when am I going to get better? When is this going to end? I questioned myself. Should I be really cautious about all of this, or should I just go with what was recommended? Should I maybe go get a second opinion, third opinion, or should I just do it? They really do scare you. Basically, my question is, when is it ever going to get better?

—Patient with recurring needs

As far as exercise goes, is there something non-medical like yoga or breathing exercise, or should [my son] be doing anything? Is there anything he can do other than take medicine, or will he be on medicine for the rest of his life?

—Parent of pediatric patient

[My doctor] doesn't like pills, but he wants me to take several months off work, and I can't really do that.

—Patient with recurring needs

A rheumatologist would say let's try to treat it conservatively. We'll try different therapy, we'll try drug treatment, and we'll try to stay away from invasive treatment. If you go to an orthopedic, he's going to say right away arthroscopic, knee replacement, and so on and so forth. Each of them knows what it is, but they have completely different views.

—Patient with recurring needs

Whenever I do any kind of research about treatment, illness, or whatever, it's really nice to know if this is the profile [of the patients] and these are the three things that work best.

—Patient with recurring needs

Does my doctor know about every single drug and its interactions and side effects? I have seen enough with family members and myself to say no. It doesn't mean he is a bad doctor, but it is probably a tough call to know everything about every drug.

—Patient with arthritis

It used to be accepted that we screen everyone for prostate cancer who is a candidate. Now we don't know what to do.

—Primary care physician



economic, and geographic factors that may influence the outcomes that follow a specific treatment.

Strategies may focus on patient populations with a single condition or involve patients with a range of conditions. Strategies addressing care for patients with rare conditions are of interest. Rare diseases are defined as life-threatening or chronically debilitating diseases that are of such low prevalence in populations that special efforts, such as combining data across large populations, may be needed to address them. The term *low prevalence* is defined as meaning conditions that affect fewer than 200,000 individuals in the United States or have a prevalence of less than 1 in 1,500 persons.

Background

Patients, caregivers, and clinicians often lack the appropriate evidence on which to make the best choices regarding prevention, screening, diagnosis, monitoring, or treatment. This gap in knowledge may be for a variety of reasons. Even when new therapies or technologies have been approved and marketed, there are often gaps in research comparing its effectiveness with that of another clinical option being offered. In some cases, the research may not have included outcomes that are important to patients and their caregivers. In addition, the existing evidence base for prevention, diagnosis, and treatment options may not be relevant for certain patient populations, such as those at the extremes of age or with multiple comorbid conditions.

Comparative clinical effectiveness research (CER) compares the effectiveness and safety of preventive, diagnostic, and treatment options to create a foundation of information for personalized decision making. This research places emphasis on the practical utility of the comparisons; the examination of all outcomes that may be important to patients; and the possible differences in outcomes across patient subgroups, both in terms of outcomes and preferences.

Prevention

Individuals, clinicians, health plans and other payers, as well as policymakers need longitudinal comparative data to evaluate the benefits and possible risks of preventive measures. The U.S. Preventive Services Task Force (USPSTF) is formally charged with reviewing the evidence and making recommendations for or against use of clinical preventive services. The Task Force has found sufficient evidence to identify 45 clinical preventive services, including tobacco use counseling and screening for colorectal cancer, for which the evidence suggests a high certainty of net benefit in certain populations. The Community Preventive Services Task Force (Task Force), which complements the work of USPSTF and also uses evidence-based methods to formulate recommendations, examines community-based preventive services and has identified 109 services with evidence sufficient to support a recommendation for implementation. These include patient reminders for breast, cervical and colorectal cancer screening and collaborative care for the management of depression. For a smaller number of measures, there is sufficient evidence of either a lack of benefit or actual harm to support recommending against use.

However, for numerous preventive strategies and services, these task forces have concluded that current available evidence is insufficient to recommend either for or against. The absence of such evidence leaves

patients and clinicians in a state of uncertainty with respect to what to recommend or what to do. Services lacking sufficient information include many for conditions presenting a high burden of disease, such as screening for asymptomatic coronary artery disease or for Hepatitis C infection. Another notable gap in the available evidence is on strategies to prevent obesity and promote weight loss and physical activity in clinical and community settings.

Diagnosis

Diagnostics continue to evolve in tandem with advances in science and technology that enhance understanding of biological systems and disease. Emerging today are entirely new categories of diagnostics, based on full continuum of care and personalized medicine approaches. The rapid pace of introduction of new diagnostics and the diversity of new technologies raise questions about the role and added benefit of these new options for guiding clinical decisions and changing patient outcomes. Examples include the role of molecular diagnostics in managing the care of patients with cancer. Some new diagnostic technologies have potential uses for a wide range of conditions, but the evidence base demonstrating benefit for these new indications fails to keep pace with use. For example, there continues to be a desire for evidence to support the use of PET imaging, MRI, and CT for a number of conditions, including oncology and lower back pain. Finally, questions sometimes remain about the long-term safety of well-established modalities, even some modalities perceived traditionally as having relatively little risk, such as dental x-rays.

Treatment

To obtain and maintain regulatory approval and payer coverage in the United States, manufacturers of drugs and, to a lesser extent, devices must establish through clinical investigations the safety and effectiveness of their products. Evidence developed as a result of these pre- and post-market requirements yields important information for therapeutic decision making. However, given the breadth of treatment options and the dynamic nature of clinical practice, many research questions continue to be raised following approval. These questions go well beyond those typically addressed by regulatory agencies and focus particularly on the comparative real-world effectiveness of possible treatment choices for a wide variety of clinical options. There is a need for research that can better enable patients to make treatment decisions reflective of their individual values and preferences. In some situations, comparison to no treatment may be most relevant for patients.

Using prostate cancer as an example, an array of treatment strategies may each present distinct and significant trade-offs. The body of evidence on the comparative benefits and risks of these options leaves remaining questions for the individual who must make a treatment decision. Particular types of treatments, such as complementary and alternative medicine approaches, surgical options, and treatment options that involve behavioral modification, remain understudied. In addition, often because of the difficulty in recruiting certain patient populations, such as patients with multiple chronic conditions, the elderly, and children, there is a gap in knowledge for the treatment choices that are most appropriate for them.

Definition of Patient-Centered Outcomes Research

PCORI has defined patient-centered outcomes research, posted the definition for public comment, and incorporated these comments into the revised definition. Applications for research projects to PCORI must align with this definition, which is provided here and available at www.pcori.org/what-we-do/pcor/.

Patient-centered outcomes research (PCOR) helps people and their caregivers communicate and make informed health care decisions, allowing their voices to be heard in assessing the value of health care options. This research answers patient-centered questions such as:

1. “Given my personal characteristics, conditions and preferences, what should I expect will happen to me?”
2. “What are my options and what are the potential benefits and harms of those options?”
3. “What can I do to improve the outcomes that are most important to me?”
4. “How can clinicians and the care delivery systems they work in help me make the best decisions about my health and healthcare?”

To answer these questions, PCOR:

- Assesses the benefits and harms of preventive, diagnostic, therapeutic, palliative, or health delivery system interventions to inform decision making, highlighting comparisons and outcomes that matter to people
- Is inclusive of an individual’s preferences, autonomy and needs, focusing on outcomes that people notice and care about such as survival, function, symptoms, and health related quality of life
- Incorporates a wide variety of settings and diversity of participants to address individual differences and barriers to implementation and dissemination
- Investigates (or may investigate) optimizing outcomes while addressing burden to individuals, availability of services, technology, and personnel, and other stakeholder perspective

Example Questions

The following research questions are meant as examples of the types of questions that patients, clinicians, or other stakeholders might ask about prevention, diagnostic, or treatment strategies, and which your research might help answer. They are expressed from the perspective of an individual patient, emphasizing the notion that information must lend itself to tailoring for a range of individuals with varying characteristics and circumstances. The list is by no means exhaustive.

- A 48-year-old woman has recently completed radiation for a small growth in her breast. Her doctors currently see no signs of disease, but recommend that she continue to be monitored for potential recurrence. What is her optimal management strategy?

- A 56-year-old man has chronic kidney disease requiring dialysis. He also has hypertension, diabetes, obesity, and chronic headaches. He develops atrial fibrillation with intermittent rapid heart rates. What are his options and the trade-offs between them?
- A 50-year-old woman is diagnosed with Parkinson’s disease. Given who she is, what is the comparative effectiveness and harms of the strategies available to her, especially with regard to cognitive and physical functioning?
- A 30-year-old woman, diagnosed with bipolar disorder and a history of psychotic mania and episodes of suicidal thoughts, learns that she is pregnant. What are her options for protecting fetal development while managing her mental illness?
- An 8-year-old girl who is obese has signs and symptoms of metabolic syndrome. What is the optimal preventive and clinical management strategy for her and her parent(s) or caregiver(s)?
- A 34-year-old woman newly diagnosed with depression has read about the possible benefits of pharmacogenetic testing to guide treatment choices.
- A 64-year-old man is recently diagnosed with myelofibrosis, a rare disorder of the bone marrow that affects blood cell production. He is currently showing no signs of liver or spleen swelling, which can be an indicator of advanced disease. What strategies are available to potentially help slow progression of the disorder, as well as help him maintain his stamina throughout the work day?
- A 58-year-old woman is the caretaker for her 82-year-old mother with moderate Alzheimer’s disease, osteoarthritis, and chronic pressure wounds that limit her mobility. What are the most effective wound care options the woman should consider for her mother, given her mother’s cognitive and physical functional impairments?
- A 43-year old worker for an express package delivery firm developed very severe low back and left leg pain that began shortly after unloading a heavy package. Her family doctor recommended taking NSAIDs and if that didn’t help, suggested she see a physical therapist. She also called an orthopedist who recommended she might benefit from some stronger pain medications should the NSAIDs be inadequate, and if that didn’t work she may need an MRI to evaluate whether she needed surgery. One of her neighbors is a chiropractor who treated two of her coworkers successfully for on-the-job back injuries. The chiropractor recommended that she avoid narcotic medications, stay active and try a course of spinal manipulation for a few weeks before considering an MRI or surgery. An acupuncturist whom the worker has consulted for temporary relief of neck pain in the past also recommended a series of treatments. The worker is perplexed and does not know which of the treatments are safe, what the risks are, and which might be of greatest benefit.



Deadlines and Submission

This is a standing announcement, with three application deadlines per year. For this round, applicants must submit a Letter of Intent to PCORI no later than 5:00 PM EST on the due date shown in the Key Dates table (<http://www.pcori.org/funding-opportunities/funding-announcements/apply/>) via PCORI's online system. Full applications must be submitted to PCORI no later than 5:00 PM EST on the due date shown in the Key Dates table via the PCORI online system.

Funding and Project Period Limits

We expect to fund approximately 54 projects totaling up to \$48 million in total costs under this PFA. Because the nature and scope of the proposed research is expected to vary widely from application to application, it is anticipated that the size and duration of each award will also vary.

Projects may not exceed three years in duration. Budgets may not exceed \$500,000 in direct costs per year. It is expected that, within these limitations, project budgets and duration will vary substantially, depending on the study design, needs for recruitment and/or primary data collection, required length of follow-up, and analytic complexity. To that end, PCORI will reserve a portion of funding for smaller (less than \$500,000 in total costs) and intermediate sized projects (less than \$1 million in total costs). PCORI encourages studies that can deliver findings promptly, including studies that take advantage of research infrastructure already in place and of longitudinal studies already underway. Currently funded CER studies may be considered for PCORI funding to support distinctive work related to extending follow-up, adding additional outcomes, or examining outcomes in key patient subgroups. Efficient use of research resources is a criterion that will be considered by merit reviewers and will also be reviewed by PCORI staff. The total amount awarded and the number of awards will depend on the quality, duration, and costs of the applications received.

Applicants wishing to propose prospective randomized trials or other complex studies that they believe will require more funding or longer duration may contact PCORI before the required deadline for the Letter of Intent to request permission to increase the budget beyond \$500,000 in direct costs in any project year or to extend the study duration beyond three years. PCORI does not guarantee that permission will be granted, and applicants should expect that the deliberative process may result in delaying the submission for one or more cycles.



Step 2: Consider the Components

Now that you understand the research focus and priorities, you will need to determine if your organization and approach meet PCORI’s other eligibility requirements. To do that, please consider the following important issues.

Organizational Eligibility

Applications may be submitted by:

- Any private sector research organization, including any:
 - Non-profit organization
 - For-profit organization
- Any public sector research organization, including any:
 - University or college
 - Hospital or healthcare system
 - Laboratory
 - Unit of state or local government

All US applicant organizations must be recognized by the Internal Revenue Service. Foreign organizations and nondomestic components of organizations based in the United States may apply, as long as there is demonstrable benefit to the US healthcare system and US efforts in the area of patient-centered research can be clearly shown. Individuals may not apply.

In addition, investigators may serve as Principal Investigator (PI) on only one application for any individual PFA per cycle. An individual who is a PI may, however, participate in other applications (from the same or other organizations) in a different role, such as co-investigator or consultant.

Characteristics of PCORI-Funded Research

Successful applicants for PCORI funds must:

1. Have a research team that includes patients and/or caregivers, as well as clinicians, health system managers, or other potential end-users of the study findings, along with researchers—each contributing the expertise that they have and participating actively in the design and implementation of the study and the dissemination of its results. A key concept here is ensuring that the research remains true to the interests of those who would use it.
2. Be familiar with the four questions of our patient-centered outcomes research definition. These questions articulate the needs of people as they make health care decisions. Applicants must clearly explain how their proposed research aligns with one or more of these questions.

3. Demonstrate that the proposed research question and project has the potential to provide truly important information that patients need to make decisions but that is not currently available. Think about what kind of information or support patients, clinicians, or health systems may need to effect interventions and changes that will bring us closer to the elimination of these disparities—or about interventions that may make it feasible to adopt this information widely. What information would make the biggest difference to those who seek this change?
4. Propose to use PCORI resources efficiently in producing new knowledge. We aim to stretch our resources as far as possible because we recognize the vast information needs of patients. Research budgets will be used as one component to evaluate the use of resources, as detailed in Review Criterion #8 (see PCORI Review Criteria on pages 17-18). We are looking for approaches that are highly efficient without sacrificing methodological rigor. We are also interested in the potential for findings to be applied in multiple areas, independent of the disease studied.
5. Make clear how you are accounting for individual differences among patients and patient groups. Average results are useful, but we are also very interested in providing evidence that can be tailored to patient subgroups and individuals based on their clinical and demographic characteristics. We want products of the research that are scalable and generalizable—and can be customized for sites. We recognize that there are challenges in seeking evidence at these levels, but we hope that many applications will seek to provide insights about how individual patients may make use of the products of the research.

PCORI is interested in research that can be rapidly disseminated and implemented into clinical and community settings, yielding prompt improvements in patients’ decisions and the outcomes experienced. To that end, projects of shorter duration and projects that take advantage of existing research infrastructure and data are of great interest. Applications must include a dissemination and implementation assessment that discusses prospects for dissemination and considers possible barriers as well. For projects that produce important findings deserving dissemination, PCORI will consider subsequent applications that evaluate additional dissemination and implementation efforts.

A variety of study designs and analytic methods may contribute valid new knowledge. These include evidence syntheses, randomized comparisons at either the individual or cluster level, or various observational approaches (e.g. quasi-experimental studies). Qualitative methods may also be employed, either in mixed methods approaches or, potentially, as qualitative comparative studies. Evidence syntheses should follow rigorous standards accepted in the field, such as those published by the Agency for Healthcare Research and Quality (AHRQ) or the Institute of Medicine (IOM). Issues of possible heterogeneity of treatment effects must be considered and discussed. Any planned analyses of subpopulations should be discussed. Inclusion of previously understudied population groups, including the elderly, children (if appropriate), and vulnerable populations, is particularly important. Randomized evaluations must be generalizable either by virtue of considering entire populations or by efficiently recruiting highly representative study populations rather than selected volunteers. Observational comparisons must employ study designs and analytic methods that convincingly protect against selection bias and other threats to validity. Applicants should specifically discuss the need to measure factors such as

differential adherence to chosen treatments that could create apparent differences in effectiveness in clinical populations. Regardless of the particular methods employed, proposals are expected to use rigorous methodology. Applicants are encouraged to refer to the contents of the PCORI draft Methodology Report, which is posted at <http://pcori.org/assets/MethodologyReport-Comment.pdf>, in developing their research plan. However, since the draft report will not be finalized integrating feedback from public comment before November 30th, 2012, applications for this funding cycle are not required to adhere to the Report's standards. Adherence to the finalized Methodology standards will be required in future funding cycles.

Comparisons must be to relevant alternatives, which may include other interventions or clinical strategies designed to treat the same need, or to "usual care," or in some instances to no therapy. The research will ideally provide information about the range of outcomes that are experienced by and important to patients. These outcomes may include quality of life, ability to participate in desired activities, degree of suffering from pain or other symptoms, ability to live independently, and satisfaction with health care.

Comparisons should examine the impact of the strategies in various subpopulations with attention to the possibilities that the effects of the strategy might differ across various populations. Populations of interest include those that are less frequently studied (e.g. the elderly; children, if appropriate; patients with multiple chronic conditions; patients with rare conditions) and other vulnerable populations, including those of low socioeconomic status, low literacy and/or numeracy, and patients groups known to experience disparities in health care and outcomes, such as racial/ethnic minorities. Alternatively, the study may focus primarily on comparative effectiveness of strategies for prevention, treatment, screening, diagnosis, or management in one or more of these populations of interest.

Please note that your application will be organized by and scored against the eight PCORI review criteria found at the end of this document.

Relevance to Patients

Research proposals should clearly identify the relevant patient population, the health decision(s) examined in the proposed study, and the patient outcomes that will be affected by the research, as outlined in PCORI Review Criterion #4. As patient-centered research, the focus should be on the identification of the primary concerns and questions of patients and their caregivers.

Details of the required plan for patient and stakeholder engagement are described in the Application Guidelines (<http://www.pcori.org/assets/PFAguidelines.pdf>).

Patient and Stakeholder Involvement

Persons representative of the population of interest, referred to here as patients, their caregivers, and clinicians, should be engaged in all phases of the research process, as outlined in PCORI Review Criterion #7: Research Team & Environment. Patients may include individuals who have or had the condition or who are at risk of the condition under study; it may also include patient surrogates or caregivers. In some instances, representatives of patient advocacy organizations may be appropriate research collaborators. Clinicians who face these decisions in collaboration with their patients are also relevant team members.



Engagement should include participation in formulation of research questions; defining essential characteristics of study participants, comparators, and outcomes; monitoring of study conduct and progress; and dissemination of research results. In essence, patients and stakeholders must be important contributors throughout the research enterprise.

A key goal of patient engagement in research is to produce information that will best support health decisions for patients, their caregivers, and clinicians. As a result, patients and other key stakeholders must be meaningfully involved in the research team throughout the process. The members of the team will vary depending upon the research area or focus of study.

Details of the required plan for patient and stakeholder engagement are in the Application Guidelines (<http://www.pcori.org/assets/PFAguidelines.pdf>).

Dissemination and Implementation Assessment

PCORI is interested in funding studies that produce findings that can be readily disseminated and implemented—and are highly likely to be valued by patients and caregivers. To that end, it is important that potential facilitators and barriers to dissemination and incorporation into practice be assessed and anticipated. Applicants must provide a dissemination and implementation assessment as described in the PCORI Application Guidelines (<http://www.pcori.org/assets/PFAguidelines.pdf>).

Reproducibility and Transparency of Research

The ability to replicate potentially important findings from PCORI-funded studies in other datasets and populations is essential to building confidence in the accuracy of these findings. To that end, we will support policies to promote sharing of study documentation (e.g. study protocol, programming code, data definitions) so that other researchers may replicate the findings in other populations. For large studies—those with direct costs greater than \$500,000 in any year—we will also require that applicants propose a plan for sharing of de-identified data, so that results may be reproduced by others in the same dataset. Whether data sharing is ultimately requested will depend on study findings and the availability of funds to support the process. Details of both requirements are in the Application Guidelines (<http://www.pcori.org/assets/PFAguidelines.pdf>).

Inclusiveness of Different Populations

PCORI seeks to fund research that includes diverse populations with respect to age, gender, race, ethnicity, geography, or clinical status. PCORI recognizes that some proposed studies may represent important PCOR opportunities even in the absence of a broadly diverse population. However, the burden is on the applicant in such cases to justify the importance of the study given the absence of diversity. Alternatively, PCORI is interested in the inclusion of previously understudied populations for whom effectiveness information is particularly needed, such as ““hard-to-reach”” populations or patients with multiple conditions.

Protection of Human Subjects

PCORI adopts, by reference, the Human Subjects requirements of 45 CFR Part 46.

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Step 3: Develop Your Application

There are three main parts of designing your project: (1) defining your research question and research strategy, including the study population and analytic approach; (2) describing the people who will comprise your research team and the institutions, organizations, and locations that will be involved; and (3) determining the budget. To better understand each of these steps and to find and complete the application forms, please see the PCORI Application Guidelines (<http://www.pcori.org/assets/PFAguidelines.pdf>).

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Step 4: Know the Review Criteria

It is PCORI's goal to make its funding decisions in a way that best supports our mission of improving patient-centered outcomes and in the most fair and transparent way possible. Below is an overview of PCORI's review and decision making process.

The PCORI review process includes four stages:

- Completeness, Compliance, and Eligibility Check
- Merit Review
- PCORI Deliberations
- Business Review

You should carefully read and thoroughly understand the PCORI review criteria, at the end of this document, before applying.

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Step 5: Submit Your Application

To apply with PCORI, you must register with PCORI's online system and submit both a timely Letter of Intent and a timely application. To learn more about the application process, go to the Application Guidelines at <http://www.pcori.org/assets/PFAguidelines.pdf>.

PCORI Review Criteria

PCORI Criteria	Brief Description
RESEARCH STRATEGY: Background and Significance	
1. Impact of the condition on the health of individuals and populations	Refers to the current impact of the condition on the health of individuals and populations. Is the condition or disease associated with a significant burden in the US population, in terms of prevalence, mortality, morbidity, individual suffering, or loss of productivity? A particular emphasis is on patients with chronic conditions, including those patients with multiple chronic conditions.
2. Innovation and potential for improvement	Refers to the potential that the proposed research may lead to meaningful improvement in patient health, well-being, or quality of care. Is the research novel or innovative in its methods or approach, in the population being studied, or in the intervention being evaluated, in ways that make it likely to change practice? Does the research question address a critical gap in current knowledge as noted in systematic reviews, guidelines development efforts, or previous research prioritizations? Has it been identified as important by patient, caregiver, or clinician groups? Do wide variations in practice patterns suggest current clinical uncertainty? Do preliminary studies indicate potential for a sizeable benefit of the intervention relative to current practice? How likely is it that positive findings could be disseminated quickly to effect changes in current practice?
3. Impact on health care performance	Refers to the potential that the proposed research could lead to improvements in the efficiency of care for individual patients or for a population of patients. Does the research promise potential improvements in convenience or elimination of wasted resources, while maintaining or improving patient outcomes?
RESEARCH STRATEGY: Relevance to Patients	
4. Patient-centeredness	Is the proposed research focused on questions and outcomes of specific interest to patients and their caregivers? Does the research address one or more of the key questions mentioned in PCORI's definition of patient-centered outcomes research? Is the absence of any particularly important outcomes discussed?
RESEARCH STRATEGY: Approach	
5. Rigorous research methods	Refers to the use of appropriate and rigorous research methods to generate patient-centered evidence, including appropriate choice of study design and of analytic methods. How likely is it that the proposed study population, study design, and available sample size will yield unbiased, generalizable information with sufficient precision to be useful and reliable for patients, their caregivers, and clinicians
RESEARCH STRATEGY: Inclusiveness of Different Populations	
6. Inclusiveness of different populations	Does the proposed study include a diverse population with respect to age, gender, race, ethnicity, geography, or clinical status? Alternatively, does it include a previously understudied population for whom effectiveness information is particularly needed?



	Does the study have other characteristics that will provide insight into a more personalized approach to decision making based on a patient’s unique biological, clinical, or sociodemographic characteristics.
PEOPLE AND PLACES	
7. Research Team and Environment	The research team must be appropriately trained and experienced to carry out the planned studies. Does the study team have complementary and integrated research expertise in implementing the study? Are relevant patients and other key users of the study information (e.g. caregivers, clinicians, health system, community, or policy makers) appropriately included on the team? Will the research environment contribute to the probability of success? Are features of the research environment, such as health system or community involvement or collaborative arrangements, described? Are institutional and community investment in the success of the research described?
BUDGET	
8. Efficient use of research resources	Does the budget appear to be reasonable in relation to the potential contribution of the research? Does the justification address the efficiency with which PCORI resources would be used? Are there opportunities to make the study more efficient? Are there additional benefits to a PCORI investment in this study through the creation of common data or infrastructure that could support future research?

About PCORI

The Patient-Centered Outcomes Research Institute (PCORI) is an independent organization created to help people make informed health care decisions and improve health care delivery. PCORI will commission research that is guided by patients, caregivers, and the broader health care community and will produce high integrity, evidence-based information.

PCORI is committed to transparency and a rigorous stakeholder-driven process that emphasizes patient engagement. PCORI will use a variety of forums and public comment periods to obtain public input throughout its work.

Our Mission: PCORI helps people make informed health care decisions and improves health care delivery and outcomes by producing and promoting high integrity, evidence-based information that comes from research guided by patients, caregivers, and the broader health care community.

Our History: PCORI was created by the Patient Protection and Affordable Care Act of 2010 as a non-profit, nongovernmental organization. PCORI's purpose, as defined by the law, is to help patients, clinicians, purchasers, and policy makers make better informed health decisions by "advancing the quality and relevance of evidence about how to prevent, diagnose, treat, monitor, and manage diseases, disorders, and other health conditions."

The statutory language defining PCORI is broad and authorizes research that will support a strong patient-centered orientation, inform better choices among alternative treatment and prevention strategies, and direct attention to individual and system differences that may influence strategies and outcomes. PCORI was designed to produce knowledge through the analysis and synthesis of existing research or the support of new research.