August 2013 Cycle

PCORI Funding Announcement: Assessment of Prevention, Diagnosis, and Treatment Options

Published May 22, 2012
Revised July 1, 2013
About PCORI: PCORI is committed to transparency and a rigorous stakeholder-driven process that emphasizes patient engagement. PCORI uses a variety of forums and public comment periods to obtain public input to enhance its work.

Our Mission: PCORI helps people make informed healthcare decisions and improves 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.

Our History: PCORI was authorized 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.”

Questions Regarding PCORI Funding Announcements: Please email (pfa@pcori.org), phone (202-627-1884), or contact us online (pcori.org/funding-opportunities/programmatic-inquiry/) if you have any questions regarding this PCORI Funding Announcement or would like to schedule a call with program staff. PCORI will provide a response within 72 hours. However, PCORI cannot guarantee that all questions will be addressed 72 hours prior to a Letter of Interest or application deadline.

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1. INTRODUCTION

1.1. Purpose
In this PCORI Funding Announcement (PFA), we seek to fund projects that address critical decisions that face patients, their caregivers, and clinicians every day without adequate information. These decisions must be consequential and be occurring now without key evidence about the comparative effectiveness of two or more options. 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.

1.2. Funds Available
PCORI expects to fund projects totaling up to $32 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. PCORI reserves the right to change the funds available at any time.

1.3. Budgets and Project Periods
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. 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 (LOI) 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.

1.4. Organization 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 or manufacturer
- 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. Organizations may submit multiple applications for funding. Individuals may not apply.

1.5. Questions Regarding PCORI Funding Announcements
Please email (pfa@pcori.org), phone (202-627-1884), or contact us online (pcori.org/funding-opportunities/programmatic-inquiry/) if you have any questions regarding this PCORI Funding Announcement or would like to schedule a call with program staff. PCORI will provide a response within 72 hours. However, PCORI cannot guarantee that all questions will be addressed 72 hours prior to a Letter of Interest or application deadline.

2. OVERVIEW

PCORI seeks to fund projects that address critical decisions that face patients, their caregivers, and clinicians. These decisions must be consequential and lack key evidence about the comparative effectiveness of two or more options. The premise of this research is that new knowledge will support critical choices by patients, caregivers, and their clinicians. This knowledge will provide insight about the comparative benefits and harms of the options and provide information about outcomes that are important to patients.

The Patient-Centered Outcomes Research Institute (PCORI) is entrusted by the public to fund research that will matter to patients, their caregivers, and stakeholders (defined as clinicians and clinician societies, hospitals, and health systems; payers [insurance]; purchasers [business]; industry; researchers; policy makers; and training institutions). PCORI seeks to change how research is conducted by emphasizing the role of diverse research teams that include varying perspectives. PCORI distinguishes itself by supporting research in which patients, caregivers, practicing clinicians, and the broader stakeholder community are actively engaged in generating the research questions, reviewing the proposals, conducting the research, disseminating the findings, promoting the implementation of the findings, and using the results to understand and address patient and stakeholder needs.

2.1. Background
Patients, caregivers, and clinicians often lack the appropriate evidence required to make the best choices regarding prevention, screening, diagnosis, monitoring, or treatment. Even when new therapies or technologies have been approved and marketed, there are often gaps in research comparing their effectiveness with that of other clinical options. In some cases, prior research may not have included outcomes that are important to patients and their caregivers. In addition, the existing evidence base may not be relevant for certain patient populations, such as those at the extremes of age or with multiple comorbid conditions.
**Prevention**

Individuals, clinicians, policymakers, health plans and other payers 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 USPSTF has found sufficient evidence to identify 45 clinical preventive services for which the evidence suggests a high certainty of net benefit in certain populations. The Community Preventive Services 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.

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 on what to do. Well planned research that fills these evidence gaps potentially can reduce uncertainty about effective methods to prevent disease.

**Diagnosis**

The rapid pace at which new diagnostic methods are introduced and the diversity of new technologies raise questions about the role and added benefit of new options for guiding clinical decisions. 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. Whether some of these new diagnostic technologies will ultimately benefit patients in a meaningful way will need to be determined.

**Treatment**

Given the breadth of treatment options and the dynamic nature of clinical practice, many patients face decisions about choosing among alternative treatments. While published placebo-controlled trials provides some of the evidence base informing such decisions, there is a broad need for better comparative evidence. Because of the difficulty in recruiting certain patient populations, such as patients with multiple chronic conditions, the elderly, and children, there also may be gaps in evidence about treatment outcomes for these groups.

### 2.2. Research Areas of Interest

Under this PFA for Assessment of Prevention, Diagnosis, and Treatment Options, PCORI seeks studies comparing the effectiveness of alternative strategies for prevention, treatment, screening, diagnosis, or management.

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 compared in previous studies.*
The topics are not limited to medical or surgical therapy and may include a range of strategies including self-care. Studies conducted in typical clinical populations and that address the full range of relevant patient-centered outcomes are of particular importance to PCORI.

**Studies that compare the use of prognostication/risk-stratification tools with usual clinical approaches for selecting treatments or adhering to management programs.**
Such studies should include tools that are based on robust evidence and organize the evidence in an innovative fashion.

**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, economic, and geographic factors that may influence those outcomes.**
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.**
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 conditions that affect fewer than than 200,000 individuals in the United States or have a prevalence of less than 1 in 1,500 persons.

**Strategies to deal with insufficient information to inform a medical decision.**
When sufficient evidence about effectiveness is lacking, it is paramount that patients be actively engaged in shared decision-making with their providers. Even when a good evidence base is available, there may be no large difference in effectiveness between two alternative treatment or management strategies. PCORI is interested in innovative methods to help optimize shared decision making in such settings. For example, comparative studies could be undertaken to assess the use and adoption of alternative decision aids or other tools for facilitating shared decision making. PCORI also is interested in determining the parameters that best reflect the real-world effectiveness of such tools.

### 2.3. Sample Questions

The following research questions are meant as examples of the types of questions that your research may 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.

- A 48-year-old woman has recently completed radiation therapy 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 50-year-old woman is diagnosed with Parkinson’s disease. Given her personal characteristics, what are 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, has a history of psychotic mania and episodes of suicidal thoughts. She now 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 64-year-old man was recently diagnosed with myelofibrosis, a disorder of the bone marrow that affects blood cell production. What strategies are available to help slow progression of the disorder and also help him maintain his stamina throughout the work day?

- 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 non-narcotic pain medications and suggested she see a physical therapist. She also called an orthopedist who recommended she might benefit from 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.

2.4. Other Programmatic Considerations

Applications to this PFA will be considered nonresponsive if research is proposed that:

- Conducts a formal cost-effectiveness analysis in the form of dollar-cost per quality-adjusted life-year (including non-adjusted life-years) to compare two or more alternatives.

- Directly compares the costs of care between two or more alternative approaches as the criteria for choosing the preferred alternative.

However, PCORI does have an interest in studies that address questions in conditions that lead to high costs to the individual or to society. This is included in our criterion on impact of the condition on the health of individuals and populations. PCORI is also interested in studies that examine differentials in healthcare resources or costs as a determinant of, or barrier to, good outcomes. Examples include ways in which out-of-pocket costs may constitute a barrier to the receipt of care. PCORI also considers it important for applicants to discuss cost-related issues such as resources needed to replicate or disseminate a successful intervention. Also, PCORI is interested in evaluation of interventions to reduce health system waste or increase health system efficiency. Proposals that include studies of these issues without utilizing a formal cost-effectiveness analysis or directly measuring and comparing costs of care of alternatives will be considered responsive.

2.5. Definition of Patient-Centered Outcomes Research

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

- Assesses the benefits and harms of preventive, diagnostic, therapeutic, palliative, or health delivery system features to inform decision making, highlighting comparisons of 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 burdens to individuals, availability of services, technology, and personnel, and other stakeholder perspectives.

PCORI funds PCOR, a type of comparative effectiveness research. The research PCORI funds requires inclusion of the patient perspective in the research. To be considered responsive to PCORI, applications to this PFA must describe research that:

- Studies the benefits and harms of different interventions and strategies, which can be delivered in actual settings. By “actual settings” we mean that the research evaluates treatments as they are delivered and received in typical clinical settings, not just in restricted trials of experimental care or at selected academic centers. PCORI is interested in innovative studies that can help patients and other stakeholders make informed decisions about their health care and health outcomes.

- Compares at least two alternative approaches. The types of interventions examined can include specific drugs, devices, and procedures, as well as other types of alternatives, such as medical and assistive devices and technologies, diagnostic testing, behavioral change, and delivery system strategies. “Usual care” or no specific intervention may be an appropriate comparator, if this is a realistic choice faced by patients and other stakeholders (e.g., choosing not to have a PSA test).

- Compares health outcomes that are meaningful to the patient population under study.

3. ELEMENTS OF PCORI-FUNDED RESEARCH

3.1. Technical Requirements and Review Criteria

Now that you understand the research focus and priorities, you will need to determine if your organization, proposed study, and approach meet PCORI’s technical requirements and review criteria for a successful project, which are described below:

1. The application demonstrates that the condition imposes a significant burden on the health of
individuals and/or populations.

2. The application explains how the results of the proposed study:
   • Would likely improve health care and patient outcomes
   • Would likely improve the efficiency of health care

3. The application demonstrates strong technical merit, including:
   • A clear research plan with rigorous design and analytic methods
   • Key project milestones clearly articulated
   • A strong research team
   • A supportive research environment
   • A diverse population with respect to age, gender, race, ethnicity, clinical status; OR
   • A defined population for which effectiveness information is particularly needed

4. The application demonstrates patient-centeredness through:
   • Including outcomes that are meaningful to patients and other stakeholders
   • Research that addresses one or more questions of clear importance to patients

5. The application demonstrates a commitment to patient and stakeholder engagement through the integration of patients and stakeholders in key elements of the proposed project including:
   • Participation in formulation of research questions
   • Defining essential characteristics of the study, participants, comparators, and outcomes
   • Monitoring study conduct and progress
   • Dissemination of research results

The specific research questions, specific populations to which the research is intended to apply, and the specific research settings will all inform the nature of appropriate patient and stakeholder engagement.

3.2. Additional Guidance and Characteristics

Dissemination and Implementation Potential

In addition to the elements described above that represent the criteria by which we review proposed projects, PCORI is interested in research that can be rapidly disseminated and implemented into clinical and community settings, facilitating improvements in patients’ and other stakeholders decision making about health care. Therefore, applications should include a section that describes the potential for disseminating and implementing the results of your work in other settings. We also request that you describe possible barriers to dissemination and implementation of your work in other settings. Please note, we are asking you to describe the potential for dissemination and implementation. PCORI does not expect you to undertake this dissemination and implementation work at this juncture. For projects that produce important findings, PCORI will consider subsequent applications that support dissemination and implementation efforts through
separate funding announcements.

Methodsological Considerations
Regardless of study design, proposals must adhere to all relevant PCORI Methodology Standards\(^1\). A variety of study designs and analytic methods may contribute valid new knowledge. These include 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. Issues of possible heterogeneity of treatment effects must be considered and discussed. 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. Comparisons must be to relevant alternatives or to “usual care”—such as other interventions or clinical policies designed to address the same need in the same or in a different healthcare system, or to a previous approach used within the same system.

Populations Studied
PCORI seeks to fund research that includes diverse populations with respect to age, gender, race, ethnicity, geography, or clinical status, so that possible differences in comparative effectiveness may be examined. 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. Thus, 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. PCORI has developed the following list of priority populations to guide our efforts in research and engagement, which includes:

- Racial and ethnic minority groups
- Low-income groups
- Women
- Children (age 0–17)
- Older adults (age 65 and older)
- Residents of rural areas
- Individuals with special healthcare needs, including individuals with disabilities
- Individuals with multiple chronic diseases
- Individuals with rare diseases
- Individuals whose genetic make-up affects their medical outcomes
- Patients with low health literacy/numeracy and limited English proficiency

\(^1\) Available at pcori.org/assets/PCORI-Methodology-Standards.pdf
Lesbian, gay, bisexual, transgender (LGBT) persons

Reproducibility and Transparency of Research
The ability to replicate potentially important findings from PCORI-funded studies in other data sets and populations is essential to building confidence in the accuracy of these findings. PCORI 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—PCORI requires that applicants propose a plan for sharing of de-identified data, so that results may be reproduced by others in the same data set.

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

If the proposed research will involve human subjects, refer to the Supplemental Instructions for Preparing the Protection of Human Subjects Section of the Research Plan in Part II of the Instructions for the PHS 398 Form, as found on the National Institutes of Health (NIH) website.2

Note: PCORI requires engagement in the research by patients and/or other stakeholders, as research partners. Research subjects’ protection requirements do not apply to co-investigators, members of the research team, or research partners.

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2 Available at http://grants.nih.gov/grants/funding/phs398/phs398.html
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<th>PCORI Criteria</th>
<th>Brief Description</th>
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| **1. 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?  
• Does it impose a significant burden on a smaller number of people who have rare diseases?  
• A particular emphasis is on patients with chronic conditions, including those patients with multiple chronic conditions. |
| **2. Potential for the study to improve health care and outcomes** | Refers to the potential for the proposed research to lead to meaningful improvement in the quality and efficiency of care and to improvements in outcomes that are important to patients.  
• Does the research question address a critical gap in current knowledge as noted in systematic reviews, guideline 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?  
• 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 improve care?  
• 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 and affect changes in current practice? |
| **3. Technical merit** | Refers to inclusion of the following:  
• Clear research plan with rigorous methods and key milestones clearly articulated  
• Research team has appropriate expertise, and project organizational structure is appropriate for the study  
• Research environment is sufficient to support conduct of the work; appropriate resources are available  
• Includes diverse population with respect to age, gender, race, ethnicity, and clinical status as appropriate for the study  
• Focuses on defined population for whom effectiveness information is particularly needed |
4. **Patient-centeredness**

- Is the proposed research focused on questions that affect 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?
- How credible are the application’s claims that engaged patients and stakeholders will exert meaningful influence on the design and conduct of the research, to ensure patient-centeredness of the questions and outcomes addressed?

5. **Patient and stakeholder engagement**

- Does the proposal describe how patients and stakeholders were or will be identified and engaged in the research?
- What are the roles of patients and key stakeholders in formulating the study’s hypotheses and design and in the study’s conduct and dissemination of results?
- What roles do patients and stakeholders have in any planned dissemination or implementation plans?

**Applications need to demonstrate patient and stakeholder engagement** through the integration of patients and stakeholders in the development of the research plan and in key elements of the proposed project including:

- Participation in formulation of research questions.
- Defining essential characteristics of the study, participants, comparators, and outcomes.
- Monitoring study conduct and progress.
- Dissemination of research results.

If the project has not included patient and stakeholder engagement (for example, in the area of analytic methods), has the application justified their non-inclusion?

If engagement is not applicable, explain why it is not.

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### 4. APPLICATION AND SUBMISSION GUIDELINES

#### 4.1. Submission Procedures

To apply with PCORI, you must register with the PCORI Online System and submit both a timely and required LOI and a timely application for each cycle that you are applying. To learn more about completing your application, please see the PCORI Application Guidelines.

#### 4.2. Funding and Project Period Limits

This is a standing announcement. Applicants must submit an LOI and application to PCORI, in accordance with the published dates and times listed in the PCORI Funding Center.