Winter 2014 Funding Cycle*

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

Published September 5, 2013  
Latest Revision October 15, 2013

This PCORI Funding Announcement applies to the funding cycle that closes January 21, 2014. Application guidelines, templates, and other resources are available at pcori.org/PFA/options.

*Previously released as the December 2013 Funding Cycle
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. 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.

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.”

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Follow us on Twitter: @PCORI
## Overview

<table>
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<tr>
<th>Published Letter of Intent Due</th>
<th>September 5, 2013; revised October 16, 2013 October 15, 2013 by 5:00 pm ET</th>
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<tr>
<td>PCORI is seeking applications for comparative effectiveness research designed to provide information that would inform critical decisions that face patients and caregivers, clinicians, policy makers, and health care system leaders. These decisions must be consequential and be occurring now in the absence of sound evidence about the comparative effectiveness of alternative approaches. There must be substantial potential that patients/caregivers will benefit from the new knowledge in ways that are important to them. The premise of this research is that the new knowledge will inform critical choices by patients and stakeholders in health care. This knowledge will provide insight about the comparative benefits and harms of the options and provide information about outcomes that are important to patients.</td>
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### Applicant Resources

- **Online System Opens**: September 16, 2013
- **Letter of Intent (LOI) Due**: October 15, 2013 by 5:00 pm ET
- **Applicant Town Hall Session (Event webinar will be archived post event)**: To Be Announced
- **Applicant Training Programs**: To Be Announced
- **Application Deadline**: January 21, 2014
- **Merit Review Dates**: May 2014
- **Awards Announced**: June 2014
- **Earliest Start Date**: August 2014

### Key Dates

- **Maximum Budget (Direct Costs)**: $1,500,000 total direct costs
- **Maximum Project Period**: 3 Years
- **Funds Available Up To (Direct Costs)**: $32 Million

### Eligibility

Applications may be submitted by any private sector research organization, including any non-profit or for-profit organization and 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.

### Review Criteria

1. Impact of the condition on the health of individuals and populations
2. Potential for the study to Improve healthcare and outcomes
3. Technical merit
4. Patient-centeredness
5. Patient and stakeholder engagement
Other

Deadlines are at 5:00 PM ET. If deadlines fall on a weekend or a federal holiday, the deadline will be the following Monday or the next day after the federal holiday. To propose a project budget that is greater than the direct costs or maximum project period listed for a PFA, submit a request by the LOI deadline using the templates provided above.

Contact Us

Please email (pfa@pcori.org), phone (202-627-1884), or contact us online (http://www.pcori.org/PFA/inquiry) if you have 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 Intent or application deadline.
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1. Request for Proposals

Summary
Under this funding announcement, the Patient-Centered Outcomes Research Institute (PCORI) invites applications for comparative effectiveness research designed to provide information that would inform critical decisions that face patients and caregivers, clinicians, policy makers, and health care system leaders. These decisions must be consequential and be occurring now in the absence of sound evidence about the comparative effectiveness of alternative approaches. There must be substantial potential that patients/caregivers will benefit from the new knowledge in ways that are important to them. The premise of this research is that the new knowledge will inform critical choices by patients and stakeholders in health care. This knowledge will provide insight about the comparative benefits and harms of the options and provide information about outcomes that are important to patients.

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.

PCORI is entrusted by the public to fund research that will matter to patients, their caregivers, and other 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 research questions, reviewing research proposals, conducting research research, disseminating research findings, promoting the implementation of research findings, and using the results to understand and address patient and other stakeholder needs.

Research Areas of Interest
PCORI seeks to fund investigator-initiated research that:

- Compares 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 complementary medicine and self-care. PCORI is particularly interested in studies that are conducted in typical clinical populations and that address the full range of relevant patient-
centered outcomes. Randomized trials that compare clinical interventions are particularly encouraged.

- Compares 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 offer innovative ways of organizing the evidence to inform decision-making.

- Investigates various factors that account for variation in treatment outcomes, with attention to demographic, biological, clinical, social, economic, geographic, and other factors that may influence those outcomes in the context of comparing at least two treatment approaches. Strategies may focus on patient populations with a single condition or involve patients with a range of conditions.

- Investigates strategies that address 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 200,000 individuals in the United States or have a prevalence of less than 1 in 1,500 persons.

Investigators are encouraged to propose studies that leverage existing resources, such as adding PCOR to an existing large clinical trial or analyzing existing large databases that contain valuable, relevant information that may be used to answer important clinical effectiveness research questions.

**Sample Research Questions**
The following questions are examples of the types of questions that your research may help answer. This list is by no means exhaustive. *All questions must have a comparative component.*

- 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?

- An 11-year-old boy who is obese has signs and symptoms of metabolic syndrome. What is the optimal preventive and clinical management strategy for him and his parent(s) or caregiver(s)?

- An 80-year-old man was recently diagnosed with myelodysplasia, 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?
Certain physiological/surrogate measurements (e.g., blood pressure, serum cholesterol) are strongly linked to outcomes, such as stroke and coronary ischemia, which patients care about. Therefore, a study that proposes to compare the effect of alternative interventions on these types of outcomes, in addition to patient centric outcomes (e.g., treatment-related symptoms, functioning, and health status), would be considered in alignment with PCORI’s focus on patient-centeredness. To be competitive for a PCORI contract, an application must make the case that its proposed research question(s) and outcomes will matter to patients and/or other stakeholders.

2. What Research Does PCORI Fund?

Research Priorities

PCORI funds patient-centered outcomes research, a type of comparative effectiveness research. The studies PCORI supports must include 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 that 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. Certain physiological measurements, such as blood pressure and serum cholesterol, are strongly linked to complications or other outcomes that patients care about. Therefore, an application to PCORI which proposes to conduct a study comparing two approaches to helping people control their blood pressure would be well-aligned with PCORI’s focus on patient-centeredness, assuming that the study would also compare the two approaches’ effects on any other relevant outcomes that are important to patients, such as treatment-related symptoms (side effects).

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

- 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 about conditions that lead to high costs to the individual or to society. This is included in our review 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. 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.

Definition of PCOR
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, personnel, and other stakeholder perspectives.

Review Criteria
Criterion 1. Impact of the condition on the health of individuals and populations
The proposal addresses the following questions:

• 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?
• Alternatively, does the condition or disease impose a significant burden on a smaller number of people who have a rare disease?
• Does the proposal include a particular emphasis on patients with one or more chronic
Criterion 2. Potential for the study to improve health care and outcomes
The proposal has the potential to lead to meaningful improvement in the quality and efficiency of care and to improvements in outcomes that are important to patients. It addresses the following questions:

- 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?

Criterion 3. Technical merit
The proposal has the technical merit to ensure that the study goals are met. It includes:

- A clear research plan with rigorous methods and key milestones clearly articulated
- A research team with necessary expertise, and an appropriate project organizational structure
- A research environment sufficient to support the conduct of the work with appropriate resources
- A diverse study population with respect to age, gender, race, ethnicity, and clinical status as appropriate for research
- A focus on a defined population for whom effectiveness information is particularly needed

Criterion 4. Patient-centeredness
The proposal demonstrates patient-centeredness at every stage of the research. It addresses the following questions:

- Is the 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 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?
Criterion 5. Patient and stakeholder engagement

The proposal integrates patients and stakeholders in the development of the research plan and in key elements of conducting the research. It addresses the following questions:

- Does the proposal describe how patients and stakeholders were or will be identified and engaged in the research?
- Are the roles of patients and key stakeholders significant in formulating the study’s research questions, hypotheses and design and in the study’s conduct and dissemination of results?
- Are the roles proposed for patients and stakeholders in any planned dissemination or implementation plans meaningful and likely to be effective?
- If engagement is not applicable to the proposed research, does the application justify why it is not?

Dissemination and Implementation Potential

PCORI is interested in research that can be rapidly disseminated and implemented in clinical and community practice, facilitating improvements in patients’ and other stakeholders’ decision-making about health care. Therefore, applications should include a section that describes the potential for disseminating your findings and facilitating their widespread use in practice. We also request that you describe possible barriers to dissemination and implementation the results 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.

Methodological Considerations

Regardless of study design, proposals must adhere to all relevant PCORI’s Methodology Standards. A variety of study designs and analytic methods may contribute valid new knowledge. These include randomized trials, at either the individual or group/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 made to relevant alternatives. If an application proposes to make comparisons to “usual care,” then the aspects of that care must be well-specified. PCORI’s Methodology Standards include four categories that apply to all planned research:

1 Available at pcori.org/assets/PCORI-Methodology-Standards.pdf
• Patient-Centeredness
• Formulating Research Questions
• Crosscutting Methods for PCOR
• Preventing and Handling Missing Data

The Methodology Standards also include seven other categories that apply to specific types of data sources or study designs. These standards should be followed in all cases when they are applicable. The additional categories include:

• Causal Inference
• Heterogeneity of Treatment Effects
• Data Registries
• Data Networks
• Adaptive and Bayesian Trial Designs
• Studies of Diagnostic Tests
• Systematic Reviews

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 study 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/or limited English proficiency
• Lesbian, gay, bisexual and transsexual (LGBT) persons.

3. How to Submit a Proposal

PCORI Online System
To submit a proposal, you must register with the PCORI Online System and submit both a Letter of Intent and an application for each cycle in which you are applying. See the PCORI Funding Center for applicant resources, including application guidelines and templates.

Additional Guidelines

Submission Dates
This is a standing announcement. Applications must be submitted in accordance with the published dates and times listed in the Overview of this document and in the PCORI Funding Center.

Organizational Eligibility
Applications may be submitted by any private sector research organization, including any non-profit or for-profit organization, and any public sector research organization, including any: university or college; hospital or healthcare system; laboratory or manufacturer; or 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.

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, and data definitions) so that other researchers may replicate the findings in other populations. For large studies—those with total direct costs greater than $1,500,000 and those with durations of more than three years—PCORI requires that applicants propose a plan for sharing of de-identified data, so that others may analyze 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 provided by the National

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2 Available at https://pcori.fluxx.io/user_sessions/new
3 Available at pcori.org/funding-opportunities/funding-center
4 Available at pcori.org/funding-opportunities/funding-center
Institutes of Health. 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.

Applicant Resources

PCORI Funding Center: Assessment of Prevention, Diagnosis, and Treatment Options  pcori.org/PFA/options

PCORI Online System  https://pcori.fluxx.io/user_sessions/new

PCORI Funding Awards
General: pcori.org/pfaawards
Past Awards by Priority Area: pcori.org/pfaawards/?viewby=priority

PCORI Methodology Standards  pcori.org/assets/PCORI-Methodology-Standards.pdf

Contact Us
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5 Available at http://grants.nih.gov/grants/funding/phs398/phs398.html