



PATIENT-CENTERED OUTCOMES RESEARCH INSTITUTE

Spring 2014 Funding Cycle

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

This PCORI Funding Announcement applies to the funding cycle that closes May 6, 2014, at 5:00 p.m. (ET). Application guidelines, templates, and other resources are available at pcori.org/pfa/spring-2014/options



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 nonprofit, 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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Overview

Published	February 5, 2014
Letter of Intent Due	March 7, 2014, by 5:00 p.m. (ET)
Summary	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.
Applicant Resources	See pcori.org/pfa/spring-2014/options
Key Dates	Online System Opens: February 5, 2014 Letter of Intent (LOI) Deadline: March 7, 2014, by 5:00 p.m. (ET) Applicant Town Hall Session: To Be Announced Application Deadline: May 6, 2014, by 5:00 p.m. (ET) Merit Review: August 2014 Awards Announced: September 2014 Earliest Project Start Date: December 2014
Maximum Project Budget (Direct Costs)	\$2 million
Maximum Project Period	Three years
Funds Available Up To (Direct Costs)	\$32 million
Eligibility	Applications may be submitted by any private sector research organization, including any nonprofit 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 local, state, or federal government. All US applicant organizations must be recognized by the Internal Revenue Service. Non-domestic components of organizations based in the United States and foreign organizations 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 are not permitted to apply.
Review Criteria	<ol style="list-style-type: none">1. Impact of the condition on the health of individuals and populations2. Potential for the study to Improve healthcare and outcomes3. Technical merit4. Patient-centeredness5. Patient and stakeholder engagement



Budget	\$2 million Note: If your proposed budget is more than \$2 million in direct costs and is a head-to-head comparison of two or more interventions or strategies (and not an evidence synthesis study or a project to develop and evaluate a decision support tool), you may wish to apply under PCORI's Large Pragmatic Studies to Evaluate Comparative Clinical Effectiveness Funding Announcement
Contact Us	<p>For programmatic questions, please email (pfa@pcori.org), phone (202-627-1884), or contact us online (http://www.pcori.org/PFA/inquiry). PCORI will provide a response within three business days. However, PCORI cannot guarantee that all questions will be addressed three business days prior to a Letter of Intent or application deadline.</p> <p>Please email (pfa@pcori.org) for any administrative, financial, or technical questions. PCORI will provide a response within three business days. Please note that during the week of the application deadline, response times may exceed three business days. Applicants may call the helpdesk (202-627-1885) within a week prior to the deadline for technical or administrative support. Applicants are asked to plan accordingly. It is the applicant's responsibility to submit the application or before the application deadline.</p>

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I. Introduction

Summary of Program

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, disseminating research findings, promoting the implementation of research findings, and using the results to understand and address patient and other stakeholder needs.

Research 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 are known to be efficacious but 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.

- Among compared groups, 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.

For this current funding announcement, PCORI welcomes applications that provide new evidence to help guide decision making but does not encourage new projects that have the primary goal to develop and test decision aids. PCORI will consider resubmissions of previously reviewed projects on decision aids, but the number of new awards will be limited. Please also refer to PCORI's [Communication and Dissemination Research Funding Announcement](#)¹ for further information.

II. Guidance for Proposing Research

Research Priorities

PCORI funds patient-centered outcomes research (PCOR), a type of comparative clinical effectiveness research. The studies PCORI supports must include the perspectives of patients and other healthcare stakeholders. To be considered responsive, applications must describe research that:

- Studies the benefits and harms of interventions and strategies delivered in actual settings. By “delivered in actual settings,” we mean delivered and received in typical “real-life” clinical settings, not just in restrictive trials of experimental care or at selected academic centers. PCORI is interested in innovative studies that provide practical information 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 tested 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 a wide variety of strategies for improving delivery systems, but the studies must be comparative. “Usual care” (or no specific intervention) may be an appropriate comparator if this is a realistic choice faced by patients and other stakeholders, but the clinical characteristics must be specified.
- Is based on health outcomes that are meaningful to the patient population under study.
- While most patient-centered outcomes directly impact the patient’s quality of life, certain physiological measurements, such as blood pressure and serum cholesterol, are strongly linked to complications or other outcomes that patients care about and have become outcomes of interest to patients because of increased awareness. Therefore, an application to PCORI that 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-

¹ Available at pcori.org/apply

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).

Non-responsiveness

Applications will be considered non-responsive if the proposed research:

- Conducts a formal cost-effectiveness analysis in the form of dollar-cost per quality-adjusted life-year to compare two or more alternatives.
- Directly compares the costs of care between two or more alternative approaches as the criterion for choosing the preferred alternative.

PCORI does have an interest, however, 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.

Further, PCORI considers it important for applicants to discuss cost-related issues such as the resources needed to implement, replicate or disseminate a successful intervention. PCORI also is interested in evaluation of interventions intended 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 comparing the costs of alternatives are considered responsive.

PCORI discourages proposals that include studies of the natural history of disease, instrument development, pharmacodynamics, and fundamental science or study of biological mechanisms. It also discourages studies that have the primary purpose of developing and evaluating new decision aids or clinical prognostication tools.

Features of 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 the choices 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, functioning, 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.

- Directly compares clinical interventions that are generally available in the clinical settings that people use to access health care.
- Obtains the perspectives of stakeholders to address the burdens to individuals, availability of services, and requirements for technology and personnel.

Comparative Clinical Effectiveness Research

Applications submitted in response to this funding announcement should evaluate the comparison of two or more clinical interventions. The efficacy of each intervention must be known prior to the initiation of the proposed project. The application must provide information from systematic reviews or credible literature reviews on the nature of the research gap being addressed and the data about efficacy of the clinical interventions that will be compared. Projects that aim to develop new or novel interventions will be considered out of scope.

Leveraging Existing Resources

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 comparative clinical effectiveness research questions. PCORI is also interested in seeking proposals for meta-analyses that use individual participant data.

Preliminary Data and Use of Accepted Measures

PCORI encourages investigators to design their research using valid patient-centered outcomes measures. Include preliminary data that supports the proposed measures. Investigators are encouraged to consider those measures described in the [Patient Reported Outcomes Measurement Information System \(PROMIS\)](#).²

Documentation of Assumptions

PCORI specifically seeks studies that are sufficiently powered to detect clinically meaningful effects. To that end, please justify the proposed sample sizes by explaining the assumptions used in all study power calculations. The application should clearly state all the necessary assumptions (i.e., the primary outcome measure, the estimated difference in the mean value of this measure between study arms, standard deviation of the measure, type I error rate, and any other assumptions). All such estimates must be justified by referring to prior published research or preliminary data.

Studies in Rare Diseases

PCORI is interested in the investigation of 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

² Available at nihpromis.org

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.

Review Criteria

PCORI's review panels rate all submitted applications on the following five 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 condition?

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 and implemented quickly, resulting in improvements in practice and patient outcomes?

Criterion 3. Technical merit

The proposal has sufficient technical merit to ensure that the study goals will be met. It includes:

- A clear research plan with rigorous methods that demonstrates adherence to PCORI's Methodology Standards
- A realistic timeline that includes specific scientific and engagement milestones
- A research team with the necessary expertise and an appropriate 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 the proposed research

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 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?

Criterion 5. Patient and stakeholder engagement

The proposal demonstrates that people representing the population of interest and other relevant stakeholders are engaged in ways that are appropriate and necessary in a given research context.

- Are patients and other stakeholders engaged in:
 - Formulating research questions
 - Defining essential characteristics of study participants, comparators, and outcomes
 - Identifying and selecting outcomes that the population of interest notices and cares about (e.g., survival, function, symptoms, health-related quality of life) and that inform decision making relevant to the research topic
 - Monitoring study conduct and progress
 - Designing/suggesting plans for dissemination and implementation activities
- Are the roles and the decision making authority of all research partners clearly stated?
- Does the proposal demonstrate the principles of reciprocal relationships, co-learning, partnership, trust, transparency, and honesty?

Patient and Stakeholder Engagement

PCORI encourages all applicants to clearly describe the patient and stakeholder engagement in their research proposals. PCORI understands that patient and stakeholder engagement in research can take many forms; it is not seeking one particular type or method of engagement. Rather, applicants should communicate how patients (those with lived experience), family members, caregivers, and the organizations that represent them, as well as any other relevant stakeholders, will be involved in study activities. Because this type of engagement in research is a relatively new concept, PCORI has developed a Patient and Family Engagement Rubric (see the appendix to the Engagement Template) to guide both applicants and merit reviewers. Additionally, studies are expected to adhere to PCORI's Methodology Standards Associated with Patient-Centeredness and to the PCOR Engagement Principles found within the rubric. These and additional resources are available in [PCORI's Funding Center](#).

Methodological Considerations

Regardless of study design, proposals must adhere to all relevant [PCORI Methodology Standards](#). These include 47 individual standards that fall into eleven categories. The first five categories are cross-cutting and are relevant to most PCOR studies. Researchers should refer to all of these standards when planning and conducting their research projects. These categories are:

- Standards for Formulating Research Questions
- Standards Associated with Patient-Centeredness
- Standards on Data Integrity and Rigorous Analyses
- Standards for Preventing and Handling Missing Data
- Standards for Heterogeneity of Treatment Effect (HTE)

Six other categories of standards will be applicable to particular study designs and methods. The standards in each of these categories should be used for guidance when they are relevant to a particular study. These categories are:

- Standards for Data Registries
- Standards for Data Networks as Research-facilitating Infrastructures
- Standards for Causal Inference Methods
- Standards for Adaptive and Bayesian Trial Designs
- Standards for Studies of Diagnostic Tests
- Standards for Systematic Reviews

Most of these standards should be considered “minimal” standards. Additional best practices, including guidelines for the conduct of clinical trials developed by other organizations, should be addressed in the application for PCORI funding.

All applicants should specifically discuss their capacity to measure factors such as differential adherence to chosen treatments (or participation in intervention programs) that could create or explain apparent differences in the effectiveness of the alternative interventions being compared in clinical populations.

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 clinical effectiveness research 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 in 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 years)
- Older adults (age 65 years 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

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 Institute of Health](#).³ 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.

Budget and Project Duration

The maximum budget for this PFA is \$2 million total direct costs. The maximum period of performance is three years. This program does not consider exceptions to the budget and period of performance limits.

III. How to Submit a Proposal

Submission Dates

Letters of Intent and applications must be submitted in accordance with the published dates and times listed in the Overview and in the [PCORI Funding Center](#).⁴

PCORI Online System

To submit a proposal, you must register with the [PCORI Online System](#)⁵ and submit both a Letter of Intent (LOI) and an application for each cycle in which you are applying.

Applicant Resources

PCORI Funding Center	pcori.org/pfa/spring-2014/options
PCORI Online System	https://pcori.fluxx.io
PCORI Funding Awards	pcori.org/pfaawards

³ Available at <http://grants.nih.gov/grants/funding/phs398/phs398.html>

⁴ Available at pcori.org/funding-center

⁵ Available at <https://pcori.fluxx.io>

Contact Us

Programmatic Inquires: Please contact the PCORI Helpdesk via email (pfa@pcori.org), phone (202-627-1884), or online (<http://www.pcori.org/PFA/inquiry>). PCORI will provide a response within three business days. However, we cannot guarantee that all questions will be addressed three business days prior to a Letter of Intent or application deadline.

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