



PATIENT-CENTERED OUTCOMES RESEARCH INSTITUTE

Fall 2014 Funding Cycle

PCORI Funding Announcement: Improving Methods for Conducting Patient-Centered Outcomes Research

Published August 6, 2014

This PCORI Funding Announcement applies to the funding cycle that closes November 4, 2014, at 5:00 p.m. (ET). Application guidelines, templates, and other resources are available at <http://www.pcori.org/fall-2014-methods/>.



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

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|---------------------------------------|--|----------------------|----------------|----------------------------------|--------------------------------------|------------------------------|--|-----------------------------|--------------------|-----------------------|-------------------------------------|---------------|---------------|-------------------|----------------|----------------------|------------------|
| Published | August 6, 2014 | | | | | | | | | | | | | | | | |
| Letter of Intent Due | September 5, 2014, by 5:00 p.m. (ET) Letters of Intent will be screened for responsiveness of fit to program goals, and overlap with projects in the existing portfolio. Only those selected will be permitted to submit full applications. Notification of request to submit full application will occur no later than September 19, 2014. PCORI encourages prospective applicants to contact us with questions prior to the deadline. See “Contact Us” below for additional details. | | | | | | | | | | | | | | | | |
| Summary | In this PCORI Funding Announcement (PFA), we seek projects to address gaps in methodological research relevant to conducting patient-centered outcomes research (PCOR). Results of these projects will inform future iterations of PCORI’s Methodology Report. The improvement of existing methods will benefit all stakeholders, including researchers planning investigations, policy makers weighing the value of healthcare interventions, and patients, clinicians, and caregivers facing healthcare decisions. | | | | | | | | | | | | | | | | |
| Applicant Resources | See http://www.pcori.org/fall-2014-methods/ | | | | | | | | | | | | | | | | |
| Key Dates | <table border="0"> <tr> <td>Online System Opens:</td> <td>August 6, 2014</td> </tr> <tr> <td>Letter of Intent (LOI) Deadline:</td> <td>September 5, 2014, by 5:00 p.m. (ET)</td> </tr> <tr> <td>Applicant Town Hall Session:</td> <td>August 13, 2014, 11:00 a.m. (ET)</td> </tr> <tr> <td>LOI Screening Notification:</td> <td>September 19, 2014</td> </tr> <tr> <td>Application Deadline:</td> <td>November 4, 2014, by 5:00 p.m. (ET)</td> </tr> <tr> <td>Merit Review:</td> <td>February 2015</td> </tr> <tr> <td>Awards Announced:</td> <td>April/May 2015</td> </tr> <tr> <td>Earliest Start Date:</td> <td>July/August 2015</td> </tr> </table> | Online System Opens: | August 6, 2014 | Letter of Intent (LOI) Deadline: | September 5, 2014, by 5:00 p.m. (ET) | Applicant Town Hall Session: | August 13, 2014, 11:00 a.m. (ET) | LOI Screening Notification: | September 19, 2014 | Application Deadline: | November 4, 2014, by 5:00 p.m. (ET) | Merit Review: | February 2015 | Awards Announced: | April/May 2015 | Earliest Start Date: | July/August 2015 |
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| Awards Announced: | April/May 2015 | | | | | | | | | | | | | | | | |
| Earliest Start Date: | July/August 2015 | | | | | | | | | | | | | | | | |
| Maximum Project Budget (Direct Costs) | \$1 million | | | | | | | | | | | | | | | | |
| Maximum Project Period | Three years | | | | | | | | | | | | | | | | |
| Funds Available up to | \$12 million 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. | | | | | | | | | | | | | | | | |
| 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. The Internal Revenue Service must recognize all US applicant organizations. Nondomestic components of organizations based in the US 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. | | | | | | | | | | | | | | | | |

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| Review Criteria | <ol style="list-style-type: none"> 1. Identifies evidence gaps noted in the PCORI Methodology Report or other comparable sources 2. Potential for the study to improve PCOR methods 3. Technical merit 4. Patient-centeredness 5. Patient and other stakeholder engagement |
| Budget/Time Limits | Applicants must submit a Greater Than Time/Budget Request with their Letter of Intent if the proposed project's budget or duration exceed limits specified in this funding announcement. |
| Contact Us | <p>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.</p> <p>Administrative, Financial, or Technical Inquiries: Please contact the PCORI Helpdesk at pfa@pcori.org. PCORI will provide a response within two business days. Please note that during the week of the application deadline, response times may exceed two business days. One week prior to an application deadline, applicants may also call the PCORI Helpdesk (202-627-1885). Applicants are asked to plan accordingly. It is the applicant's responsibility to submit the application on or before the application deadline.</p> |
| Other | *Deadlines are at 5:00 p.m. (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. |

New or Revised for the Fall 2014 Funding Cycle:

- Increase of award size from \$750,000 to \$1,000,000 in direct costs.
- Revised section on methods for patient and other stakeholder engagement in research, articulating programmatic intent to advance the science of engagement—see pages 7–8.
- New section on general analytic methods related to treatment adherence—see page 9.
- New section for improving methods of recruitment and retention of participants into PCOR/CER (comparative effectiveness research)—see page 10.
- Revised Special Topic of Interest on research related to patient-centered outcomes and patient-reported outcomes. Notably, the current PFA does **not** include a special emphasis on PROMIS-related projects. We will still consider projects that include PROMIS measures, provided they align with the priorities articulated in this PFA—see pages 7–12.
- New Special Topic of Interest focusing on methods for network-based data in research, including methods related to distributed data network analytics and methods related to linkage of data sources—see page 12.
- Removed section on methods for generating, selecting, and prioritizing topics for research and for including patients and stakeholders in the peer review process—this topic may be re-introduced into this PFA in future funding cycles.
- Removed section on methods for conducting systematic reviews in PCOR/CER—no longer a programmatic priority.



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I. Introduction

Summary of Program

In this PCORI Funding Announcement (PFA), the Improving Methods for Conducting Patient-Centered Outcomes Research program seeks projects to address gaps in methodological research relevant to conducting patient-centered outcomes research (PCOR). Results of these projects will inform future iterations of [the PCORI Methodology Report](#). The improvement of existing methods will benefit all stakeholders, including researchers planning investigations, policy makers weighing the value of healthcare interventions, and patients, clinicians, and caregivers facing healthcare decisions.

Background¹

The availability of multiple options for treatment, prevention, and diagnosis in health care presents a significant challenge to patients and clinicians trying to make informed care decisions. Deciding between alternative options in health care requires an understanding of how to balance the benefits and risks of each treatment option and understanding how each option may apply differently to patients, given their unique personal characteristics. PCORI was created with the promise of enhancing the ability of people who are making decisions about health care to fully understand and weigh these options.

To address this challenge, PCORI seeks to fund projects emphasizing research into the methods used in the conduct of PCOR. PCORI and its Methodology Committee recognize the need to better understand and advance the appropriate and efficient use of these methods. Strong methods will support the generation of research findings that can be trusted to directly improve patients' healthcare outcomes.

The importance of understanding the methods underlying research findings for all healthcare stakeholders involved in making healthcare decisions can be illustrated in several ways. First, patients' healthcare issues have become more complex, in part due to an aging population and patients living with multiple conditions. Second, the availability of different types of treatment options has increased markedly over the past decade, offering a sometimes bewildering number of options to patients and their clinicians. Other developments, such as the increasing use of research findings by healthcare delivery systems to inform their policies, as well as the advances in personalized medicine, present further methodological challenges to PCOR. Together, these factors contribute to making decisions for patients and their clinicians more complex and underscore the importance of understanding the methods behind the research findings. An understanding of how the research study was designed and conducted is critically important in determining whether the research finding should be used by patients and caregivers in making healthcare decisions.

PCORI was created to support research that provides relevant information to patients and clinicians. Research findings that can be trusted must be based on valid, rigorous, patient-centered methods.

¹ This background section borrows from the following article published on behalf of the PCORI Methodology Committee: "Getting the methods right—The foundation of patient-centered outcomes research by Gabriel and Normand. *NEJM* August 2012," available at nejm.org/doi/full/10.1056/NEJMp1207437.



PCORI's founding legislation contained a provision to set up a 17-member Methodology Committee, whose charge is "to develop and improve the science and methods of comparative clinical effectiveness research" and to produce "methodological standards for research." These standards are intended to support the generation of patient-centered health interventions. The PCORI Methodology Report describes the rationale behind creating standards for patient-centeredness; for prioritizing topics for research; for choosing a study design (including the first edition of the translation table); and for designing, conducting, and reporting PCOR. It also highlights gaps in the evidence that PCORI's program of methodological research should address.

Research Areas of Interest

PCORI is interested in supporting research that has the potential to impact the field of PCOR methods and has the potential to provide methodological advances that will generate information that patients need to make decisions. Proposed research should be justified with specific references to gaps identified in the PCORI Methodology Report or published scientific literature. Applicants are further encouraged to refer to PCORI's Methodology Standards to develop their research question(s) and research plan.

Below are the research topics that PCORI seeks to support. Many of these were identified as gaps in need of further research in the PCORI Methodology Report. The list is not exhaustive, and applicants may submit other proposals that advance the field of PCOR.

1. Development of methods for patient and other stakeholder engagement in research

PCORI is interested in funding innovative methods projects that advance the science of engagement in PCOR/comparative effectiveness research (CER). We are particularly interested in projects that examine the best methods for involving patients and stakeholders (e.g., clinicians, employers, private and public payers, the life science industry, hospitals and health systems, and policymakers) in PCOR/CER. This will include research on the most effective methods for engaging patients, clinicians, and other stakeholders throughout the research process, including identification of meaningful research questions and outcomes to be measured, study governance, data collection, development of analysis plans, interpretation of findings, and dissemination of results. The Methods program is interested in the following broad topical areas:

- Methods for engaging patients and stakeholders who are under-represented, are hard to reach, have low health literacy, or are in different settings (e.g., hospitals, healthcare systems, community organizations, public health departments, schools), and methods to understand the appropriate role of surrogates and advocates
- Methods for building trust with patients and organizations and for partnering with organizations and communities; methods for engaging patients and stakeholders in all phases of research; and methods to translate, scale up, and sustain successful local engagement processes
- Research on methods to balance and reconcile input from various stakeholder groups, including patients, surrogates, clinicians, payers, and policymakers in the design, conduct, and dissemination of PCOR

- Research on methods for ensuring study questions, outcomes, and interventions that are meaningful to the end users including patients, surrogates, clinicians, payers, and policy makers
- Research on the impact of engagement on research, including value of outcomes recommended by patients and other stakeholders for advancing knowledge of the research topic, speed of dissemination of research results, and speed and comprehensiveness of uptake of relevant research findings into clinical practice by target populations

2. Development and refinement of general analytic methods

A variety of analytic methods may contribute valid new knowledge. PCORI is interested in supporting research that aims to improve the validity and/or efficiency of analytic methods for PCOR and CER.

Analytic methods of interest include:

Methods related to causal inference:

- Development of innovative ways to identify and recruit new users of interventions for research studies
- Development of methods to study complex interventions in experimental and observational research
- Comparison of the validity of different methods for reducing confounding and bias using randomized controlled trials (RCT) and registry studies
- Development and dissemination of software needed for sensitivity analyses and approaches to evaluating the assumptions underlying complex analyses, such as instrumental variable analyses
- Development and dissemination of methods for adequate analysis of data in cases where the treatment/exposure varies over time
- Development of a consensus for the types and quantity of target parameters causal inference should estimate in order to be most informative for a range of decision makers, including patients, providers, payers, and industries/manufacturers
- Instrumental variables

Methods related to heterogeneity of treatment effect (HTE):

- Development of analytic approaches to help support methods guidance for predictive approaches to HTE, as well as for subgroup analysis with a focus on their use for PCOR
- Development of methods to help support guidance for HTE analyses in comparative effectiveness trials
- Development and evaluation of methods for HTE analyses that consider the predicted level of non-adherence to a given healthcare intervention
- Research on methods to help support the development of guidance on the use of Bayesian methods in HTE analyses and appropriate outcome scale for HTE analysis (e.g., risk difference, risk ratio, log of odds-ratio)
- Research on methods to help support the development of guidance for analyses for HTE in observational studies
- Review of standards for decision analysis and simulation modeling with respect to HTE analysis

Methods related to missing data:

- Development and refinement of methods for missing data in RCTs and observational studies, including registries
- Development of software to reduce barriers that inhibit the use of more rigorous methods for handling missing data
- Development and refinement of methods to address erroneous data, inconsistent data, uninterpretable data, and other noncoded data

Methods related to adherence:

- Research on generalizable methods to measure treatment adherence in PCOR
- Development of innovative methods to account for non-adherence across different study designs
- Research on interventional methods to improve adherence which are generalizable and scalable (i.e., not treatment-specific)

3. Development and refinement of design-specific analytic methods.

In addition to the general analytic methods described above, PCORI is interested in supporting research on design-specific analytic methods, including but not limited to:

Methods related to cluster-randomized trials:

- Development of methods for improving the conduct of cluster-randomized trials with specific attention to their application in PCOR

Methods related to adaptive trials:

- Research to help support methods guidance on adaptive trials specific to PCOR, especially those using Bayesian approaches
- Development of software for adaptive trials that can simulate complex designs

Methods related to registries:

- Development of innovative ways to reduce loss to follow-up as registries encompass longer time periods, and ways to improve follow-up rates and test these strategies in different types of registries and among different patient populations
- Development of improved strategies for linking data while maintaining privacy protections and ensuring that linked data do not lead to re-identification in de-identified data
- Development of methods to enable routine, inexpensive nesting of clinical trials into existing registries (also known as “clinical registry trials”)
- Development of innovative methods to measure treatment adherence in registries or to build registries with generalizable measures of treatment adherence

Methods related to diagnostic tests:

- Development of improved methods for measuring the impact of diagnostic testing on patient outcomes, including methods for improving their predictive value, given patient heterogeneity

Methods related to devices:

- Development of improved methods for assessing the impact of devices on patient outcomes

Methods related to decision analysis and simulation models:

- Review of standards for best practices in the development of decision analysis and simulation models for patient-centered comparative effectiveness questions
- Development of methods to use simulation models to address questions on HTE

Methods related to complex interventions:

- Development of methods for improving the measurement and analysis of contextual influences and other effect modifiers
 - Development of methods for improving the measurement and analysis of mediators and mediation effects
 - Development of strategies for managing adaptation while retaining internal validity
 - Development of methods (both qualitative and quantitative) to assess mechanisms of action (What are the “active ingredients” in complex interventions and how are they exerting their effect?)
4. Research on **issues related to human subjects protections**, including but not limited to Institutional Review Board (IRB) review of PCOR studies and novel approaches to informed consent. Research on ethical issues arising in the context of particular CER study designs (e.g., cluster randomized trials, pragmatic randomized trials) or the use of particular data sources for CER (e.g., electronic clinical data). Research on the ethics of randomization of standard clinical interventions. Proposals responding to this interest area must include an empirical component; strictly conceptual/theoretical work will be considered nonresponsive.
5. Research on **novel methods, interventions, or strategies for increasing recruitment and retention** of participants (e.g., patients, caregivers, clinicians, hospitals and health systems) in PCOR/CER randomized trials, observational studies, and registries. Examples include but are not limited to: open-trial designs, opt-out strategies, monetary and nonmonetary incentives, and educational and communications interventions. Proposals designed to compare and rigorously evaluate two or more recruitment or retention strategies in the context of real studies are of particular interest. Novel strategies for patient, family, clinician, community, or public engagement in the context of research recruitment and retention are also encouraged. Proposals focused on *hypothetical* studies (e.g., where potential participants are asked if they would take part in a trial if it were run, but where no trial exists), will be considered nonresponsive. Proposals examining ways to increase survey/questionnaire response rates will also be considered nonresponsive.

SPECIAL TOPICS OF INTEREST:

Special Topics of Interest are created to signal to potential applicants the research topics of particular scientific and/or strategic importance to PCORI. Special Topics may occasionally be supported by dedicated, additional funds in a given funding cycle. For the Fall 2014 Cycle, however, no additional funds will be made available. There are two Special Topics of Interest:

1. Research related to patient-centered outcomes (PCOs) and patient-reported outcomes (PROs)

An explicit focus on PCOs is a defining characteristic of PCOR. When patients or people at risk of a condition are the best source of information regarding outcomes of interest, then the study should employ PROs in lieu of, or in addition to, measures derived from other sources. Pain, for example, cannot reliably or accurately be assessed by any means other than direct patient report, so inclusion of

PROs is often essential to patient-centeredness.

PCORI's Methodology Standards require the use of psychometrically sound PRO instruments when they are available. To that end, we have established methodological research related to PCOs and PROs as a Special Area of Interest in this PFA. We are interested in proposals that address the following topics:

- Research on methods for PRO development, including open-platform, web-enabled qualitative research, and other innovative methods for identifying concepts relevant to patients and generating items to measure those concepts
- Research on usefulness of patient-reported data in clinical care, by therapeutic area, patient population, and/or type of measure (e.g., adaptive vs. static). Issues impacting measure usefulness that may be included in this research are psychometric performance, usability and variation by platform, concordance between patient-report and other data sources, and respondent burden.
- Research on PRO score interpretability with a focus on clinical meaningfulness
- Strategies for minimizing missing data, and statistical methods for improving score interpretation of missing PRO data
- Research on the collection of PRO data for multiple purposes (clinical care, care quality assessment, effectiveness research)
- Research on methods to elicit patient preferences, as they relate to patient valuation of the benefits and harms of alternative interventions
- Research on integrating PROs into clinical practice, including clinician use and acceptance of PRO data; relationship with clinical outcomes (utilization, hospitalizations, medications); comparison between clinic-based and home-based PRO reporting to understand differences. Health systems-level incentives and disincentives to incorporating patient-reported data into clinical care may also be included.
- Research on the use of PROs in registries (feasibility assessment, approaches for enhancing completeness and reducing missing data, measuring improvement vs. progression, estimating ideal follow-up time frames).

For the purposes of this PFA, development and validation of new disease-specific instruments, as opposed to research on methods related to the development and validation of instruments, will be considered nonresponsive. Note: Studies that include refinement of an existing measure (e.g., evaluation of psychometric performance in an understudied population) are acceptable if the study has one of the areas noted above as the primary aim.

2. Development of methods to support data research networks

PCORI is interested in funding innovative methods projects related to the use of data from multiple sources in PCOR and CER. We are particularly interested in methods to improve distributed analyses in data research networks (e.g., automated distributed regression analysis). We are also interested in methods to obtain longitudinal and complete data in data research networks, such as:

- Methods to establish optimal linkage of multiple data sources, such as electronic health records (EHR), claims, and national registry data
- Development and refinement of innovative ways to link to information captured from patient-reported outcomes, mobile and smart phone technology, or patient-generated data



- Methods to conduct patient-level disambiguation for de-identified linkage of data across networks
- Methods related to missing and incomplete data within networks

Evidence to Action Networks

PCORI is interested in ensuring communication and engagement between awardees with similar needs and interests and end users to help refine and improve the research and facilitate dissemination of research findings that will help patients and the public to make better and informed healthcare decisions. To meet this goal, PCORI has set up Evidence to Action Networks, where PCORI facilitates engagement among awardees and cross-learning between projects and teams comprising researchers, patients, caregivers, and other stakeholders. In addition, PCORI facilitates exchanges between awardees and end users (e.g., patients, caregivers, and other stakeholders such as payers, employers and purchasers, clinicians, professional societies, policy makers, and training institutions) for dissemination and implementation of important research findings.

Awardees are encouraged to participate in these Evidence to Action Networks as they become available.

II. Guidance for Proposing Research

Research Priorities

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. For more information on PCORI's research priorities, see our [National Priorities and Research Agenda](#).

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 (including non-adjusted life-years) to compare two or more alternatives.
- Measures the relative costs of care of two or more alternative approaches as the primary criteria for choosing the preferred alternative.

Proposals that include studies of these issues may measure and report utilization of any or all health services, but may not employ direct measurements of costs of care.

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. Thus, PCORI is also interested in studies that:

- Examine the effect of costs on patients, such as patients' out-of-pocket costs, hardship or lost opportunity, or costs as a determinant of or barrier to access to care;
- Address cost-related issues such as the resources needed to replicate or disseminate a successful intervention; or



- Evaluate 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 comparing the costs of alternatives are considered responsive.

Features of PCOR

Patient-centered outcomes research 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.

Methodological Considerations

Regardless of study design, proposals must adhere to all relevant [PCORI Methodology Standards](#). These include 47 individual standards that fall into 11 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)

Five 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:

- 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

Most of these 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.

Patient and Stakeholder Engagement

Applicants must complete this section of the [Research Plan](#) to outline how patients and other stakeholders will participate as partners in various phases of the proposed research. To assist applicants, PCORI provides [sample methods engagement plans](#) from previously funded methods projects. The sample methods engagement plans are not intended to be comprehensive or prescriptive. Instead, they provide examples of options to incorporate engagement, where relevant, into the research process.

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 CER may be examined, otherwise known as heterogeneity of treatment effects. 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 and to discuss which subgroups are most important and how they will be analyzed, including whether there will be power to examine the question of effectiveness in subgroups. 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 a 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 makeup affects their medical outcomes
- Patients with low health literacy/numeracy and/or limited English proficiency
- Lesbian, gay, bisexual, and transgender (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 Institutes of Health](#).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.

Replication and Reproducibility of Research and Data Sharing Plan

PCORI is committed to maximizing the utility and usability of data collected in our funded projects. Describe the ability to replicate and reproduce potentially important findings from PCORI-funded studies in other data sets and populations. This is essential to building confidence in the accuracy of these findings. PCORI will also 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. Also, propose a method for sharing data, if such activity is later requested. The ability to reproduce important findings from the original data is critical to establishing trust in PCORI findings.

III. How to Submit a Proposal

PCORI Online System

To submit a proposal, you must register with the [PCORI Online System](#)³ and submit both a Letter of Intent (LOI) and an application for each cycle in which you are applying.

Upon receipt of Letters of Intent, PCORI program staff will screen the LOIs for programmatic fit. An applicant whose LOI does not meet program areas of interest will not be invited to submit a full application. Applicants will receive notification accepting or declining their LOI prior to the system opening for application submission. This process will take two weeks. PCORI encourages prospective applicants to contact us if you have any questions prior to the deadline.

See the [PCORI Funding Center](#)⁴ for applicant resources, including application guidelines and templates.

Letter of Intent

Applicants should download the [Letter of Intent template for the Improving Methods for Conducting Patient-Centered Outcomes Research](#) PFA from the PCORI Funding Center. They must complete the document and convert it to a PDF with a limit of three pages. All references should be included as in-text

² Available at grants.nih.gov/grants/funding/phs398/phs398.html

³ Available at <https://pcori.fluxx.io>

⁴ Available at pcori.org/apply

citations. Letters of Intent that exceed the page limit will not be reviewed. Do not upload additional documents as part of your LOI, including letters of endorsement or support, as they are not requested at this stage. Their inclusion will result in LOI rejection without review. Please visit the PCORI Funding Center for additional applicant resources, including the PFA and required templates.

To submit an LOI, upload the completed PFA-specific LOI into the PCORI Online System and complete the required fields. Provide a thorough description that allows the scientific community to understand the project, including the aims and study design, without reviewing the full application. Letters of Intent should be a maximum of three pages and should follow the formatting guidelines found in the [Application Guidelines](#). The LOI must include the following sections:

- **Background**—State the problem or question the research is designed to address and indicate the specific topic in the funding announcement to which the proposed project is responsive. Describe why this is of interest to patients, caregivers, researchers, and/or other stakeholders.
- **Objectives**—Describe briefly the specific aims of the study, including specific research question(s) and the long-term objectives. Please note that proposals that include objectives to conduct cost-effectiveness analysis in any capacity will be deemed nonresponsive.
- **Methods**—State the problem or question the research is designed to address and indicate the specific topic in the funding announcement to which the proposed project is responsive.
- **Outcomes (Projected) and Anticipated Impact**—Specify the study outcomes and state briefly why these are important to the field of PCOR. Please address how this project will help to advance PCORI’s mission.
- **Patient and Stakeholder Engagement**—Provide a description of the plan for engaging patients, caregivers, and/or other stakeholders over the course of the project. If you believe that patient and caregiver engagement is not appropriate given the technical nature of the proposed research, consider whether engagement of other **stakeholders and/or end users** (data architects, clinicians, domain experts, health services researchers with different expertise than members of the research team, policy makers, etc.) in both the methodological process and the dissemination and implementation plans would be of value. Provide a clear and concise justification of both the types of patients, caregivers, and stakeholders that will be engaged and how those individuals will contribute to the research.

When complete, save this document as a PDF and upload into the PCORI Online System.

Greater Than Time/Budget Request

Applicants must submit a [Greater Than Time/Budget Request](#) with their Letter of Intent (LOI) if the proposed project’s budget or duration exceed limits specified in this funding announcement. If applicable, combine the completed [Greater than Time/Budget Request](#) with the completed LOI, save as a PDF, and upload into the PCORI Online System.

Although both subcontractor direct and indirect costs are considered to be direct costs to the prime, subcontractor indirect costs should not be included when determining if the budget exceeds the total direct cost limit.

Letter of Intent Review

Letters of Intent are evaluated on the following criteria (note that PCORI does not score the LOI):

- Importance and relevance of the topics to PCORI priorities, as evidenced by critical gaps identified by clinical guidelines developers and/or recent relevant systematic reviews
- Clarity and credibility of applicants' responses to the LOI questions
- Prior relevant experience
- Programmatic fit and balance, taking into consideration whether the proposals significantly overlap with previously funded studies or concurrent proposals or, conversely, whether the proposal fills a gap in the portfolio of proposals with certain characteristics, including disease category, topics, priority population, methodologies, and other variables.

Only Letters of Intent deemed most responsive to this PFA will be invited to submit a full application. Notification of request to submit full application will occur no later than September 19, 2014. Please refer to the [Application Guidelines](#) for due dates and information on how to submit your LOI in PCORI Online.

Note: An individual may submit only one LOI per PFA as a Principal Investigator (PI). While a PI may submit an LOI to other PFAs, the research topic/project must be distinct. Letters of Intent with scientific overlap or that appear to be duplicate submissions will be removed during the LOI screening process.

Project Budget and Duration

Proposals submitted under the Methods research funding stream may be granted an exception to the project budget limit of \$1,000,000 in direct costs and/or the project duration limit of three years. Note that although both subcontractor direct and indirect costs are considered to be direct costs to the prime, subcontractor indirect costs should not be included when determining if the budget exceeds the \$1,000,000 limit. Applicants must submit a [Greater Than Request](#) form with a justification for the increased budget and/or extended project duration with the LOI. The request will be reviewed by the program staff, and applicants will receive a notification for approval or denial within two weeks of the LOI deadline.

Methods Project Symposium

PCORI will hold an annual convening of all our Methods projects, including PROMIS. Applicants should label travel funds allocated for attendance to this convening as "PCORI Methods Projects Symposium" in the travel section of their budget. You should budget for up to three project team members (the PI is required to attend and can select up to two additional individuals from the project team). We recommend that you calculate your budget based on travel costs for a two- to three-day trip to Washington, DC, based on the travelers' locations. The costs of travel for these purposes do not count against the scientific and programmatic travel caps. Although there is no limit on these costs, PCORI will closely review these budgets for reasonableness.



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](#).

Applicant Resources

| | |
|-----------------------------|---|
| PCORI Funding Center | http://www.pcori.org/fall-2014-methods/ |
| PCORI Online System | pcori.fluxx.io |
| PCORI Funding Awards | pcori.org/pfaawards |

IV. Merit Review

PCORI Merit Review is a multiphase process that includes: evaluation of Letters of Intent; preliminary review of full applications by review panels; in-person panel discussion of a subset of full applications (identified by PCORI’s Research Priority Area Program Staff, based on the preliminary review and program priorities); Selection Committee recommendation of applications for funding; and finally, Board of Governors award approval (no later than May 2015).

Preliminary Review

PCORI conducts rigorous merit review of the full applications it receives. Note that applications may be eliminated from the review process for administrative or scientific reasons (i.e., non-responsiveness). An application may be administratively withdrawn if it is incomplete or submitted past the stated due date and time, or it does not meet the administrative or formatting criteria outlined in [the Application Guidelines](#), in the PCORI templates, and in the PCORI Online System. An application may be scientifically withdrawn if it is not responsive to the guidelines as described in this PFA, describes research that is not comparative, includes cost-effectiveness analysis, or otherwise does not meet PCORI programmatic requirements.

Administratively and scientifically responsive applications will be reviewed by one or more specially convened Merit Review panels. Each panel is recruited by PCORI Merit Review Officers, who identify the Chair; scientist reviewers who are clinical experts familiar with the clinical content of submitted applications; methodological and statistical experts familiar with pragmatic clinical trials and large database analyses; patient representatives trained in review of scientific proposals; and representatives of other stakeholder groups.

The following are PCORI’s Merit Review criteria. These five criteria are used by PCORI’s review panels during the preliminary and in-person phases to score and evaluate all submitted applications:

Criterion 1. Study identifies evidence gaps noted in PCORI Methodology Committee Report⁵ or other comparable sources

Refers to whether the proposed study explicitly identifies gaps noted in the report or other sources. The proposal addresses the following questions:

- Does the research question identify a critical gap in current methodological understanding as noted in the Methodology Committee Report or in other sources? Which particular gap(s)?

**Please note that proposals that do not explicitly identify a gap noted in the Methodology Committee Report will still be considered. However, applicants should provide strong support for their claims that their proposal does address a current gap in PCOR methods.*

Criterion 2. Potential for the study to improve PCOR methods

Refers to the potential of the proposed methodological investigation and its results to change methodological practices in ways that improve PCOR and ultimately support the decisions made by patients and their clinicians. The proposal addresses the following questions:

- Do existing methods weaken the validity of PCOR studies, and would improved methods therefore increase the validity of PCOR findings?
- How often would these methods be used, and how many PCOR studies would benefit from these improved methods?
- Is the proposed approach feasible and likely to result in new standards or in the improvement of existing standards?

Criterion 3. Technical merit

Refers to the technical merit of the proposal. The proposal addresses the following questions:

- Is there a clear research plan with rigorous methods that demonstrates adherence to PCORI's Methodology Standards?
- Does the proposal delineate a clear conceptual framework/theory/model that anchors the background literature and informs the design, key variables, and relationships being tested?
- Do the study methods reflect state-of-the-art thinking and practice in the methodological area, so that results are likely to be accepted and heeded?
- Is the project timeline realistic, including specific scientific and engagement milestones?
- Does the research team have the necessary expertise to conduct the project? Is the organizational structure and are the described resources appropriate to carry out the project?
- Will the proposed methods help support the inclusion and study of diverse populations with respect to age, gender, race, ethnicity, geography, or clinical status, or, alternatively, do the methods support the inclusion of previously understudied populations in PCOR?

Criterion 4. Patient-centeredness

⁵ Available at pcori.org/assets/2013/11/PCORI-Methodology-Report.pdf

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. It addresses the following questions:

- Are patients and other stakeholders engaged in:
 - Formulating research questions
 - Defining essential characteristics of study participants, comparators, and outcomes
 - 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?
- If engagement is not applicable to the proposed research, does the application justify why it is not?

In-Person Review

After preliminary review is completed, panel scores and critiques are evaluated by PCORI program staff to identify a subset of applications to be discussed at the in-person review meeting. Not all submitted applications move forward to in-person review, but all applications are evaluated and scored based on PCORI's Merit Review criteria, which include evaluation of adherence to PCORI's Methodology Standards.

During the in-person review, panels meet to discuss applications and further clarify the merits of the proposed research along with identifying areas for improvement. Additionally, each application is re-scored based on the content of discussion. The in-person panel meeting is led by a Chair and a PCORI Merit Review Officer, who ensure that all applications receive a fair and thorough review informed by the standards outlined in the PFA.

Post-Panel Review

Following the in-person panel review, meritorious applications are reviewed by PCORI program staff, who review merit review scores and comments, identify duplication or synergy among funded projects, and consider the fit of applications within the programmatic vision. Program staff then recommend projects to a Selection Committee that includes members of PCORI's Board of Governors. The Selection Committee considers recommendations and works with staff to identify a slate of applications for



possible funding based on merit review scores, programmatic balance and fit, and PCORI's strategic priorities. This slate is proposed to PCORI's Board of Governors for its consideration and approval.

Funding Recommendations: Factoring in the total available funds allotted for this announcement, high scoring applications that fit the programmatic needs and satisfactorily address reviewers' critiques and adhere to PCORI's Methodology Standards will be considered for funding by the PCORI Board of Governors. Applicants will receive notification of the funding status of their application no later than April/May 2015.