PATIENT-CENTERED OUTCOMES RESEARCH INSTITUTE



## Spring 2014 Funding Cycle

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

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/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 | February 5, 2014 |
| Letter of Intent Due | March 7, 2014, by 5:00 p.m. (ET).<br><br>Letters of Intent will be screened for responsiveness and fit to program goals. Only those selected will be permitted to submit full applications. Notification of request to submit full application will occur no later than March 21, 2014. PCORI encourages prospective applicants to contact us with questions prior to the deadline. See "Contact Us" below for additional details. |
| Summary | In this PFA, we seek projects to address gaps in methodological research relevant to conducting 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. Additionally, we seek projects that focus on Patient-Reported Outcome Measurement Information System (PROMIS) – related research. |
| Applicant Resources | See pcori.org/PFA/spring-2014-methods |
| Key Dates | Online System Opens: February 5, 2014<br>Letter of Intent (LOI) Deadline: March 7, 2014, by 5:00 p.m. (ET)<br>Applicant Town Hall Session: To Be Announced<br>LOI Screening Notification: By March 21, 2014<br>Application Deadline: May 6, 2014, by 5:00 p.m. (ET)<br>Merit Review: August 2014<br>Awards Announced: September 2014<br>Earliest Start Date: December 2014 |
| Maximum Project Budget (Direct Costs) | $750,000 for Methods projects<br>$500,000 for PROMIS-focused projects |
| Maximum Project Period | Three years for Methods projects<br>Two years for PROMIS-focused projects |
| Funds Available Up To (Direct Costs) | Up to $12 million for Methods projects<br>Up to $5 million for PROMIS-focused projects<br><br>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. |

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| 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 | 1. Addresses evidence gaps identified in The PCORI Methodology Report or other comparable sources<br>2. Potential for the study to improve PCOR methods<br>3. Technical merit<br>4. Patient-centeredness<br>5. Patient and other stakeholder engagement |
| 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.<br>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 | **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.<br><br>**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 or before the application deadline. |

**New or Revised for the Spring 2014 Funding Cycle:**

- New research area of interest focusing on research related to the Patient-Reported Outcome Measurement Information System (PROMIS)—see page 7
- New research area of interest focusing on the protection of human subjects and ethical issues arising in PCOR—see page 8
- New section on methods for complex interventions—see page 10
- New section on nonresponsive and non-priority research areas—see page 8
- Revised and expanded section on research related to Patient-Centered Outcomes (PCOs) and Patient-Reported Outcomes (PROs) to signal prioritization of research on these topics—see page 12
- Revised and expanded section on methods for patient and stakeholder engagement—see page 16

- Revised Merit Review criteria—see page 15

## Contents

# 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 PCOR. Results of these projects will inform future iterations of The PCORI Methodology Report.[1] 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.

## Background[2]

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 patient-centered outcomes research (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 decades, 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.

[1] Available at pcori.org/assets/2013/11/PCORI-Methodology-Report.pdf

[2] 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 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. 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.

PCORI is releasing this PFA to address the methodological gaps in PCOR identified in The PCORI Methodology Report and findings from these projects will inform future iterations of this report. The improvement of existing methods will benefit all stakeholders, including researchers; policy makers; and patients, clinicians, and caregivers facing decisions.

### Research Areas of Interest

The Improving Methods for Conducting Patient-Centered Outcomes Research program is interested in the following broad topical areas:

- Research in patient and stakeholder engagement. This will include research that identifies optimal methods for engaging patients and other stakeholders in the research process, and methods for evaluating the impact on research outcomes of engagement in the research process. This also includes research that determines methods for ensuring study questions, outcomes, and interventions are meaningful to patients and other stakeholders.
- Research in generating, selecting, and prioritizing topics for research, as well as research into the inclusion of patients and stakeholders in the peer review process.
- Research that aims to improve the validity and/or efficiency of analytic methods for comparative effectiveness research (CER), for example, approaches for strengthening causal inference in observational and randomized studies; approaches to identifying and confirming heterogeneity in risk factors, disease prevalence, and treatment effects.
- Research that determines the validity and efficiency of data sources commonly used in PCOR. For example, research that seeks to improve the volume, completeness, comprehensiveness, accuracy, and efficiency of use of clinical data collected across healthcare systems, clinical data networks, registries, or payer databases, and the utility of this data for conducting longitudinal studies of patient outcomes; or research that develops and promotes the utility, performance, and efficiency of large clinical data networks or registries for supporting patient-centered outcomes research for patients with rare diseases.

- Research to support the routine and systematic collection of key patient-reported and patient-centered outcomes. Research on methods related to PRO development, reliability, validity, and utility. Research on methods to elicit patient preferences in regard to how they value the benefits and harms of alternative interventions.

- Research with and on PROMIS measures. Specific areas of interest are integration of PROMIS measures in clinical care, research on clinically meaningful change and clinically meaningful differences in PROMIS scores, PROMIS item bank expansion, cross-calibration between PROMIS and other PRO measures, and exploration of predictive value of PROMIS measures.

- Research on issues related to human subjects protections, including but not limited to 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 not be considered for funding.

### Nonresponsive and Non-Priority Research Areas

Applications 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

While PCORI considers it important for applicants to discuss cost-related issues such as the resources needed to implement, replicate, or disseminate a successful intervention, proposals that include methodological studies of these issues without utilizing a formal cost-effectiveness analysis or comparing the costs of alternatives are considered responsive.

The following areas are not considered priority areas for funding:

- Development and validation of disease-specific instruments rather than research on methods related to the development and validation of instruments
- Development or maintenance of clinical data networks
- Development of tools to measure and enhance medication adherence

Areas not explicitly identified in The PCORI Methodology Report as critical methods gaps may be considered less of a programmatic priority than areas that are explicitly addressed in the report.

### Sample Research Topics 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 examples of the research topics that PCORI seeks to support. Many of these topics 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**
    - Development of comprehensive typologies or inventories of methods for achieving effective patient and stakeholder engagement.
    - Identification of best practices in research engagement by stakeholder type and by research phase.
    - Evaluation of models for overcoming engagement barriers.
    - Research on the most effective methods for engaging patients and stakeholders in the research process, with attention to factors such as clinical condition, care setting, study design, or other relevant factors. Specific examples may include 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 and scale successful local engagement processes.
    - Research on methods for partnering with patients and stakeholders for engagement in the research process. Specific examples may include: methods for engaging patients and stakeholders who are underrepresented or hard to reach, or who are in different settings (such as primary care, long-term care, acute care setting, hospices), and methods to understand the appropriate role of surrogates and advocates.
    - Research on methods to balance and reconcile input from various stakeholder groups in design, conduct, and dissemination of PCOR.
    - Research on methods for assuring study questions, outcomes, and interventions are meaningful to patients and other stakeholders.
    - Quantitative and qualitative data on the impact of engagement on research, including value of patient-recommended outcomes for advancing knowledge of research topic, speed of dissemination of research results, and speed and comprehensiveness of uptake of relevant research findings into clinical practice by target populations.
    - Quality indicators for engaged research from the perspective of researchers, patients, other stakeholders, and end users of the research.

2. **Research in methods to conduct systematic reviews of patient-centered CER**
    - Research on methods for improving the validity of systematic reviews of CER.
    - Research on methods for improving the efficiency of systematic reviews without compromising validity.

3. **Development of methods for generating, selecting, and prioritizing topics for research and for including patients and stakeholders in the peer-review process**
    - Review or development of methods for patient and stakeholder engagement in topic generation.
    - Evaluation of the employment of research gap analysis to continue to develop the empirical evidence on its use.
    - Development of methods to improve and/or compare research prioritization methods, including Value of Information (VOI) approaches. Given the limited evidence available in the area of prioritization, PCORI is particularly interested in applications on this topic. The evaluation of different stakeholder panel sizes and compositions in prioritization is also of interest.

- Research on the effect of alternative approaches to managing bias and conflict of interest in topic prioritization and peer review of proposals.

**4. Development and refinement of general analytic methods**

**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.

**5. Development and refinement of design-specific analytic methods.**

**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.
- 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 testing these strategies in different types of registries and among different patient populations.
- Development of improved strategies for linking data while maintaining privacy protections and assuring 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").

**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-centered 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 heterogeneity of treatment effect.

**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?).

**6. Research that determines the validity and efficiency of data sources commonly used in PCOR.**

- Methods to improve the use of clinical data collected across healthcare systems, clinical data networks, registries, or payer databases and the utility of this data for conducting longitudinal studies of patient outcomes.
- Methods to integrate randomized trials directly into clinical care;

- Methods to enable patients to enter their own data via web and mobile technologies; methods to enable passive collection of certain patient-centered data from mobile technologies.
- Research that develops and promotes the utility, performance, and efficiency of large clinical data networks or registries for supporting PCOR for patients with rare diseases.

**SPECIAL AREA OF INTEREST:**

**Research related to Patient-Centered Outcomes (PCOs) and Patient-Reported Outcomes (PROs).**
An explicit focus on patient-centered outcomes 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 are establishing methodological research related to patient-centered outcomes generally and PROs specifically 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, particularly methods for establishing meaningfulness of score changes over time and/or score differences between groups.
- Strategies for minimizing missing data, and statistical methods for improving score interpretability for missing PRO data.
- Development of new measures and/or refinement of existing PRO measures for use in treatment intervention trials, including testing of new drugs or devices, and inclusion of measures in comparative effectiveness studies. PCORI highly encourages networks of investigators to collaborate in this area.
- Research on the collection of PRO data for multiple purposes (clinical care, care quality assessment, effectiveness research).
- Development of methods to enhance the understanding of the impact and burden of disease, in specific diseases, from the patient's point of view. This includes identifying, in collaboration with patients, which symptoms or other disease characteristics are most important to them and which benefit-risk trade-offs are acceptable to patients when receiving treatments.
- 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; impact on clinical outcomes (utilization, hospitalizations, medications); comparison between clinic-based and home-based PRO reporting to understand differences; approaches for handling

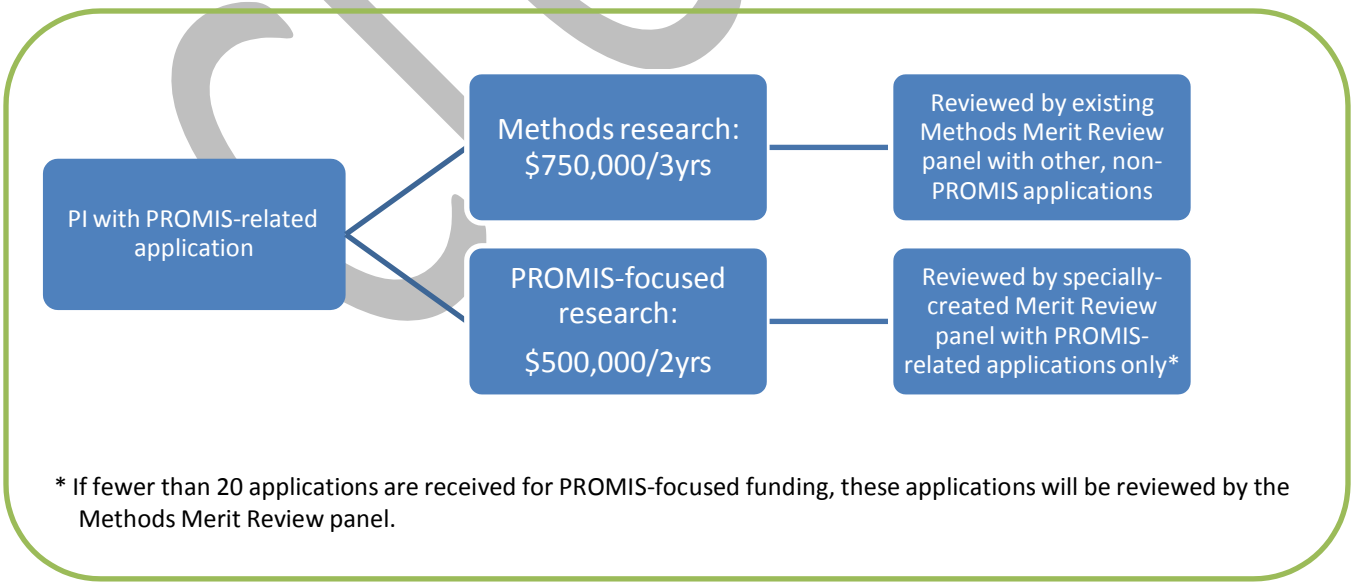
missing data. Health systems-level incentives and disincentives to incorporating patient-reported data into clinical care may also be included.

- 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 timeframes).

**As part of this Special Area of Interest, PCORI is making available an additional and separate funding stream to support PROMIS-focused projects.** The following topics are particular priorities:

- Integration of PROMIS measures into clinical care: developing and testing methods for incorporating data collection into existing electronic health record systems, which may include
- Optimizing data collection and use across different clinical care settings and with different types of patients; and/or notifying patients and clinicians of data collection need in relation to clinic visits;
- Optimizing interpretability and use of PROMIS-generated data by clinicians and patients, which may include development and testing of "dashboards" and other tools to improve usefulness of PROMIS data for all users.
- Research on clinically meaningful change/differences by disorder, by patient type. Of particular interest is the relationship of clinical meaningfulness to clinical management.
- Expanding item bank development to pediatric, geriatric, and under-researched populations.
- Establishing cross-calibration between PROMIS and other PRO measures.
- Exploring predictive value of PRO data. This may include examination of the relationships between PROMIS measure data and biomarker and/or other clinical variables.

Proposals that include PROMIS measures may be submitted to the Methods **OR** PROMIS-focused funding streams described in this PFA, but not both, as indicated in the figure below.




* If fewer than 20 applications are received for PROMIS-focused funding, these applications will be reviewed by the Methods Merit Review panel.

# II. Guidance for Proposing Research

### Research Priorities

The Patient-Centered Outcomes Research Institute (PCORI) helps people make informed health care decisions, and improves health care delivery and outcomes, by producing and promoting high integrity, evidence-based information that comes from research guided by patients, caregivers and the broader health care community. For more information on PCORI's research priorities, see our National Priorities and Research Agenda.[3]

### Features 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 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.

### Review Criteria

All applications are evaluated by reviewers external to PCORI based on the five merit review criteria listed below. In addition, PCORI program staff evaluate top scoring applications for programmatic fit relative to the existing PCORI portfolio of awarded Methods projects, based on topic area, population studied, and methods used.



[3] Available at http://www.pcori.org/what-we-do/priorities-agenda.

**Criterion 1. Study addresses evidence gaps identified in PCORI Methodology Committee Report[4] or other comparable sources.**

*Refers to the extent that the proposed study explicitly addresses gaps identified in the Report or other sources. The proposal addresses the following questions:*

- Does the research question address 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 address a gap identified in the Methodology 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?
- 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 research team appropriately trained and experienced to carry out the planned studies?
- Is the research environment sufficient to support the conduct of the work, and are appropriate resources available?
- 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?



[4] Available at http://www.pcori.org/assets/2013/11/PCORI-Methodology-Report.pdf

**Criterion 4. Patient-centeredness**
Refers to the level of patient-centeredness of the proposal. The proposal 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**
Where applicable, proposals need to demonstrate patient and stakeholder engagement through the integration of patients and stakeholders in the development of the research plan and in key elements of the proposed project. The proposal addresses the following questions:

- Are patients and other stakeholders engaged in:
  - Formulating research questions and hypotheses
  - Defining essential characteristics of study design, including, as applicable, 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?



## Methodological Considerations

Regardless of study design, proposals must adhere to all relevant PCORI Methodology Standards. PCORI Methodology Standards 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 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 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.

# III. How to Submit a Proposal

### PCORI Online System

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

Upon receipt of Letters of Intent (LOIs), PCORI program staff will screen the LOIs for programmatic fit. An applicant whose LOIs 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 one week. PCORI encourages prospective applicants to contact us if you have any questions prior to the deadline.

See the PCORI Funding Center[6] for applicant resources, including application guidelines and templates.

### Additional Guidelines Specific to this PFA

**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.[7]

**Project Budget and Duration**
Proposals submitted under the Methods research funding stream may be granted an exception to the project budget limit of $750,000 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 $750,000 limit. Applicants must submit a Greater Than Request form with a justification for the increased budget and/or extended project duration with the Letter of Intent (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.

Proposals submitted under the PROMIS-focused funding stream are not permitted to exceed $500,000 in direct costs or two years in project duration.

[5] Available at https://pcori.fluxx.io
[6] Available at pcori.org/apply
[7] Available at pcori.org/apply

**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.[8] 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

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| **PCORI Funding Center** | pcori.org/PFA/spring-2014/methods |
| **PCORI Online System** | pcori.fluxx.io |
| **PCORI Funding Awards** | pcori.org/pfaawards |
| **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.<br><br>**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 or before the application deadline. |



[8] Available at http://grants.nih.gov/grants/funding/phs398/phs398.html