



Cycle 2 2015 Funding Cycle

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

Published June 29, 2015

This PCORI Funding Announcement applies to the funding cycle that closes on November 3, 2015 at 5:00 p.m. (ET). Application guidelines, templates, and other resources are available at <http://www.pcori.org/Cycle-2-2015-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 Act, is to help patients, clinicians, purchasers, and policy makers make better-informed health decisions by "advancing the quality and relevance of evidence about how to prevent, diagnose, treat, monitor, and manage diseases, disorders, and other health conditions."

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Overview

Published	June 29, 2015
Letter of Intent Due	July 29, 2015, by 5:00 p.m. (ET) Letters of Intent (LOIs) will be screened for responsiveness of fit to program goals and for overlap with projects in the existing portfolio. Only those selected will be invited to submit full applications. Notification of request to submit full application will occur no later than September 8, 2015. 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 to fund projects to address gaps in methodological research relevant to conducting patient-centered outcomes research (PCOR). 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/Cycle-2-2015-methods/
Key Dates	Online System Opens: June 29, 2015 Letter of Intent (LOI) Deadline: July 29, 2015, by 5:00 p.m. (ET) Applicant Town Hall Session: July 8, 2015, 11:00 a.m. – 12:30 p.m. (ET) LOI Screening Notification: September 8, 2015 Application Deadline: November 3, 2015, by 5:00 p.m. (ET) Merit Review: February 2016 Awards Announced: April 2016 Earliest Start Date: June 2016
Maximum Project Budget (Direct Costs)	\$750,000
Maximum Project Period	3 years
Funds Available up to	\$12 million Because the nature and scope of the proposed research are 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 U.S. applicant organizations. Nondomestic components of organizations based in the United States and foreign organizations may apply, as long as there is demonstrable benefit to the U.S. healthcare system and U.S. efforts in the area of patient-centered research can be clearly shown. Organizations may submit multiple applications for funding. Individuals are not permitted to apply.
Review Criteria	<ol style="list-style-type: none">1. Identifies evidence gaps noted in the PCORI Methodology Report or the published scientific literature2. Potential for the study to improve PCOR methods3. Technical merit4. Patient-centeredness5. Patient and other stakeholder engagement

<p>Contact Us</p>	<p>Programmatic Inquires: Please contact the PCORI Helpdesk via email (sciencequestions@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 an LOI 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. Applicants may also call the PCORI Helpdesk (202-627-1885). It is the applicant’s responsibility to submit the application on or before the application deadline.</p>
<p>Other</p>	<p>*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.</p>

New or Revised for the Cycle 2 2015 Funding Cycle:

1. PFA restructured
 - Research Areas of Interest are renumbered and organized into tables
 - Changes in content and shifts in priorities
2. PFA no longer includes 3 Special Topics of Interest
 - Research related to Human Subjects Protections
 - Previously Special Topic of Interest #1, now Research Area of Interest #3
 - Research related to Recruitment and Retention
 - Previously Special Topic of Interest #2, now part of Research Area of Interest #1
 - Methods To Support Data Research Networks
 - Previously Special Topic of Interest #3, now Research Area of Interest #6

Moving forward, the PFA will not include Special Topics of Interest unless dedicated additional funds are provided to address that topic.

3. Extra scrutiny for projects overlapping with current portfolio

The Methods program portfolio has now funded a number of projects addressing analytic methods, such as heterogeneity of treatment effect and causal inference. With this cycle, we would like to encourage applications that seek to foster advancements in study design. While we will still consider applications related to analytic methods responsive to this PFA, these applications will undergo substantial scrutiny to ensure that the proposed research does not significantly overlap with previously funded projects or concurrent proposals. See Research Areas of Interest #4 and #5 for more details.



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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 aims to fund high-priority methodological research topics in patient-centered outcomes research (PCOR). Studies should address gaps in methodological research, supporting PCORI's Methods Strategic Imperative to develop and promote rigorous patient-centered outcomes research methods, standards, and best practices.

Background¹

The availability of multiple options for prevention, diagnosis, and treatment 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 an understanding of 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 understand and weigh these options fully.

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

Research Areas of Interest

PCORI is interested in supporting research that advances methods relevant to PCOR and comparative effectiveness research (CER). Proposed research should be justified with specific references to gaps identified in the PCORI Methodology Report or published scientific literature. Applicants are encouraged to refer to PCORI's [Methodology Standards](#) to develop their research question(s) and research plan.

Below are the six research areas of interest that the PCORI Methods Program seeks to support. Many were identified as gaps in the PCORI Methodology Report. This list is **not exhaustive**, and applicants may submit other proposals that advance the field of PCOR/CER methods by addressing significant methodological gaps that have been sufficiently justified with respect to the scientific literature.

¹ This background section borrows from the following article published on behalf of the PCORI Methodology Committee: Gabriel and Normand. (2012, August). "Getting the Methods Right—The Foundation of Patient-Centered Outcomes Research." *NEJM*. Available at nejm.org/doi/full/10.1056/NEJMp1207437.

1. Methods for patient and stakeholder engagement

The Methods Program is primarily interested in funding projects that identify impactful methods of patient and stakeholder engagement for the planning, conduct, and dissemination of PCOR/CER across different patients, settings, and/or health conditions. We support the identification and assessment of engagement methods that are ethical, feasible, sustainable, and account for existing capacity and resources among academic researchers and their patient and stakeholder partners. Patient engagement partners may include patients, caregivers, family members, and patient advocacy groups. Stakeholder partners may include clinicians, employers, private and public payers, the life science industry, hospitals and health systems, and policy makers.

The following topics are considered priorities for Research Area of Interest #1:

<p>a. Methods of patient and stakeholder engagement that are relevant to end-users (e.g., patients, caregivers, advocates, clinicians, payers, and policy makers) and PCOR/CER researchers</p>	<ul style="list-style-type: none"> • Development of methods to evaluate impact of engagement • Development of methods to evaluate uptake of relevant research findings into clinical practice or PCOR/CER • Development of methods to discern appropriate engagement at each phase of research, priority population, or health condition • Development of methods to balance and reconcile input from various patient and stakeholder perspectives in PCOR/CER • Development of methods to identify factors outside of patient and stakeholder engagement that have contributed or hindered the uptake of relevant findings for end-users, such as structural or institutional factors or temporal trends
<p>b. Methods of patient and stakeholder engagement to improve representation of populations, settings, and phases of PCOR/CER</p>	<ul style="list-style-type: none"> • Development of methods of patient and stakeholder engagement to improve participation of underrepresented and hard-to-reach populations (e.g., ethnic/racial minorities, low-literacy and/or -numeracy, non-English-speaking, stigmatized behavioral risk groups) • Development of methods of patient and stakeholder engagement to expand inclusion of underrepresented settings (e.g., hospitals, healthcare systems, community organizations, public health departments, and schools) • Development of methods to increase patient and stakeholder engagement in underrepresented phases of research, such as data collection, data analysis, and interpretation of findings <p><i>Proposals focused on developing new methods of patient and stakeholder engagement that do not contain an impact evaluation component will be considered nonresponsive.</i></p>
<p>c. Methods of patient and stakeholder engagement to improve recruitment and retention of patients into trials, observational studies, and</p>	<ul style="list-style-type: none"> • Development of methods including, but not limited to, opt-out strategies, monetary and nonmonetary incentives, and patient and clinician education and communication (e.g., opportunities for clinicians to enroll patients at the point of care)

registries	<p><i>Proposals focused on hypothetical studies (e.g., where potential participants are asked if they would take part in a study if it were conducted, but where no study exists) will be considered nonresponsive. Proposals examining ways to increase survey/questionnaire response rates will also be considered nonresponsive.</i></p>
<p>2. Methods for Patient-Centered Outcomes (PCOs) and Patient-Reported Outcomes (PROs)</p>	
<p>For the purposes of this PFA, the Methods Program is <u>not</u> interested in funding narrowly focused instrument development projects, which would result in products limited to a specific disease, health condition, behavior, or therapeutic area. Such applications will be considered nonresponsive.</p> <p>The following topics are considered priorities for Research Area of Interest #2:</p>	
<p>a. Methods related to PRO interpretability, value, and use</p>	<ul style="list-style-type: none"> • Development of methods to evaluate feasibility and acceptance of PRO into routine clinician use • Development of methods to evaluate relationships between PROs and clinical outcomes (utilization, hospitalization, medications) • Development of methods to evaluate PRO score interpretation and longitudinal assessment
<p>b. Methods related to PRO integration into clinical care and research</p>	<ul style="list-style-type: none"> • Development of methods to identify and address barriers and facilitators for incorporating PRO into clinical care and research • Development of methods to evaluate integration of PROs into electronic medical records, clinical care, care quality assessment, PCOR/CER, clinical data research networks (CDRNs), patient-powered research networks (PPRNs), and registries
<p>c. Methods related to PRO variation by mode of administration, platform, and setting</p>	<ul style="list-style-type: none"> • Development of methods to compare and integrate PRO reporting from multiple settings (e.g., clinic-based, home-based, mobile data collection) • Development of methods to evaluate patient and surrogate reports in comparison to other data sources, including identification of factors that affect concordance/discordance (e.g., respondent burden, health literacy, patient vs. caregiver report) • Development of methods to address and reduce discordant data

<p>d. Methods related to PRO data collection and completeness</p>	<ul style="list-style-type: none"> • Development of methods to enhance completeness and reduce missing PRO data • Development of methods to measure both positive and negative change (e.g., symptoms, function) • Development of methods to estimate optimal measurement time points (e.g., set time, health episode)
<p>3. Research related to Human Subjects Protections</p>	
<p>The Methods Program is interested in funding projects on 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); and research on the ethics of randomization of standard clinical interventions. Proposals responding to this research area of interest must include an empirical component; purely conceptual/theoretical work will be considered nonresponsive.</p>	
<p>4. Methods to Improve Study Design</p>	
<p>The Methods Program is interested in funding projects that foster improvements in study design to address CER/PCOR questions.</p>	
<p>The following topics are considered priorities for Research Area of Interest #4:</p>	
<p>a. Methods related to cluster-randomized trials</p>	<ul style="list-style-type: none"> • Development of methods to improve the conduct of cluster-randomized trials with specific attention to their application in PCOR/CER
<p>b. Methods related to adaptive trials</p>	<ul style="list-style-type: none"> • Development of methods for adaptive trials specific to PCOR, especially those using Bayesian approaches • Development of methods for simulation models to improve adaptive trial design for PCOR/CER
<p>c. Methods related to registries</p>	<ul style="list-style-type: none"> • 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 methods to build registries with generalizable measures of treatment adherence
<p>d. Methods related to recruitment and retention</p>	<ul style="list-style-type: none"> • Development of novel trial designs to improve recruitment and retention of participants (e.g., patients, caregivers, clinicians, hospitals and health systems) in PCOR/CER randomized trials, observational studies, and registries, such as open-trial designs

<p>e. Methods related to complex interventions</p>	<ul style="list-style-type: none"> • Development of methods to improve the measurement and analysis of contextual influences and other effect modifiers • Development of methods to improve the measurement and analysis of mediators and mediation effects • Development of strategies to manage 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 effects?)
<p>f. Methods related to medical devices and diagnostic tests</p>	<ul style="list-style-type: none"> • Development of methods to capture and evaluate the use of medical devices or diagnostic tests across ranges of effectiveness such as accuracy, precision, sensitivity, specificity, and patient characteristics • Development of methods to evaluate the impact of medical devices or diagnostic tests on PCOs, PROs, adherence, and treatment effectiveness

5. Methods To Improve Validity and Efficiency of Analyses

The Methods Program is interested in funding projects that develop, refine, and disseminate analytic methods to improve causal inference in PCOR/CER.

NOTE: The Methods Program has funded a large number of projects on methods related to heterogeneity of treatment effect (HTE) and the validity of methods for reducing confounding and bias in RCTs and observational studies. Applications that aim to study these types of analytic methods will undergo substantial scrutiny to ensure that the proposed research does not significantly overlap with previously funded projects or concurrent proposals and that the proposals fill a gap within the program's portfolio.

The following topics are considered priorities for Research Area of Interest #5:

- a. Methods to address missing data in RCTs and observational studies, including registries
- b. Methods to improve the use of instrumental variables
- c. Methods related to time-varying factors (e.g., treatments / exposures or potential confounders)

6. Methods To Support Data Research Networks

The Methods Program is interested in funding projects that improve the capacity for high-quality multisite PCOR/CER using horizontally and vertically partitioned data. Due to diversity in the methods used to optimize the use of large amounts of data, additional research is needed to understand distributed analytics while preserving the privacy of patients and the security of data.

The following topics are considered priorities for Research Area of Interest #6:

<p>a. Methods to improve distributed analyses in data research networks</p>	<ul style="list-style-type: none"> • Development of methods to evaluate optimal network designs with respect to distributed analysis and statistical approaches currently used (e.g., propensity scoring, distributed regression, and meta-analysis) • Development of methods to determine the robustness of methods via an analytical stress test, such as evaluating meta-analysis methods as well as propensity scoring in distributed research networks • Development of methods to evaluate heterogeneity in claims and electronic health record (EHR) data (e.g., process to identify the type of heterogeneity within databases and across databases) • Development of methods to preserve privacy while enabling research (e.g., comparison of privacy-preserving methods using distributed analytics) • Development of methods to compare complete data-sharing (pooling of data) vs. networks with limited sharing capabilities, leveraging both the empirical evidence from current networks and simulation analyses
<p>b. Methods to obtain longitudinal and complete data in data research networks</p>	<ul style="list-style-type: none"> • Development of methods to evaluate optimal linkage of multiple data sources, such EHRs, claims, and national registry data • Development of methods to capture and link data from multiple sources (e.g., PROs, mobile and smart phone technology, or patient-generated data) • Development of methods to conduct patient-level disambiguation for de-identified linkage of data across networks • Development of methods to address missing, incomplete, erroneous, and/or non-coded data within networks

II. Requirements for PCORI 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](#).²

Nonresponsiveness

Applications to PCORI's Funding Announcement for Improving Methods for Conducting Patient-Centered Outcomes Research that propose the following types of research will be considered non-responsive:

- Cost-effectiveness 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
- Non-methodological Research
 - Develops a discrete intervention or healthcare practice
 - Compares the efficacy of two or more health interventions
 - Develops best practices for healthcare delivery
- Narrowly Focused Research
 - Development, refinement, and/or validation of a disease- or condition-specific measure

Proposals **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 criteria on impact of the condition on the health of individuals and populations. Thus, PCORI is 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
- 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.

² Available at <http://www.pcori.org/content/national-priorities-and-research-agenda>.

Consistent with PCORI's [authorizing law](#),³ PCORI does not fund research whose findings will include:

- Coverage recommendations
- Payment or policy recommendations
- Creation of clinical practice guidelines or care pathways
- Establishing efficacy for a new clinical intervention
- Pharmacodynamics
- Study of the natural history of disease
- Fundamental science or study of biological mechanisms

Avoiding Redundancy

PCORI intends to balance its funded portfolio to achieve synergy where possible and to avoid redundancy. Potential applications are encouraged to review funded research on [PCORI's website](#).⁴

Methodological Considerations

Regardless of study design, proposals must adhere to all relevant [PCORI Methodology Standards](#).⁵ These include 47 individual standards that fall into 11 categories. The first five categories are cross-cutting and 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 HTE

Six other categories of standards will be applicable to certain types of 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
- Standards for Systematic Reviews

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

³ Available at http://www.pcori.org/sites/default/files/PCORI_Authorizing_Legislation.pdf.

⁴ Available at <http://www.pcori.org/research-results>.

⁵ Available at <http://www.pcori.org/research-we-support/research-methodology-standards/>.

All applicants should specifically discuss their capacity to measure such factors 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](#) demonstrating clear and concise justification of the types of patients, caregivers, and stakeholders that will be engaged and how those individuals will contribute to the research. To assist applicants, PCORI provides an [Engagement Rubric](#) and [sample Methods engagement plans](#)⁶ from previously funded methods projects. The sample plans are not intended to be comprehensive or prescriptive; instead, they provide examples of options to incorporate engagement, where relevant, into the research process.

If patient and caregiver engagement is deemed inappropriate in the planning, conduct, and/or dissemination of research given the technical nature of the proposed project, clearly justify why. Highly technical proposals should consider whether engagement of other stakeholders and/or end-users (e.g., data architects, clinicians, domain experts, health services researchers with different expertise than that of members of the research team, policy makers, etc.) in both the methodological process and the dissemination and implementation plans would be of value.

Leveraging Existing Resources

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

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 HTE. 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 the importance of subgroups and how they will be analyzed—including whether there will be statistical power to examine the question of effectiveness in subgroups. PCORI is particularly interested in the inclusion of previously understudied populations for whom effectiveness information is especially 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 different subpopulations. To guide our efforts in research and engagement, PCORI has developed a list of priority populations which includes:

- Racial and ethnic minority groups

⁶ Available at <http://www.pcori.org/assets/2014/08/PCORI-Sample-Methods-Engagement-Plans.pdf>.

- 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

This component (up to five pages) is included in the Research Plan Template. Describe the protection of human subjects involved in your research. PCORI follows the Federal Policy for the Protection of Human Subjects (45 CFR part 46), including the Common Rule. For more detailed information, please see Section 5 “Human Subjects Research Policy” from the [Supplemental Grant Application Instructions for All Competing Applications and Progress Reports](#),⁷ issued by the U.S. Department of Health and Human Services (DHHS). PCORI does not require that applicants comply with sections of this policy that refer to requirements for federal-wide assurance (FWA), or that refer to standards for inclusion of women, minorities, and children. PCORI also requires applicants proposing clinical trials to include a data- and safety-monitoring plan. Awardees must also comply with appropriate state, local, and institutional regulations and guidelines pertaining to the use of human subjects in research.

PCORI merit reviewers will examine plans for protection of human subjects in all applications and may provide comments regarding the plans (see [How to Evaluate Human Subjects Protections](#)⁸). Reviewers’ comments on human subjects research are not reflected in the overall application score but may be used by PCORI staff during any potential funding negotiations. Final determinations about adequacy of human subject protections rest with the Institutional Review Board (IRB) or IRBs that have jurisdiction for the study.

The awardee institution or organization, whether domestic or foreign, bears ultimate responsibility for safeguarding the rights and welfare of human subjects in PCORI-supported activities.

Required Education of Key Personnel on the Protection of Human Subject Participants

PCORI requires all applicants to adhere to the National Institutes of Health (NIH) policy on education in the protection of human subject participants in the conduct of research. This applies to all personnel listed as “key personnel” in the application. The policy and FAQs are available [from the NIH website](#).⁹

⁷ See <http://grants.nih.gov/grants/funding/424/supplementalinstructions.docx>.

⁸ See <http://www.pcori.org/sites/default/files/PCORI-Checklist-for-Evaluating-Human-Subjects-Protections.pdf>.

⁹ See <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-08-054.html>.

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. This is essential to building confidence in the accuracy of these findings. PCORI supports 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. Please propose a method for sharing data and appropriate documentation on request.

Recruitment (if applicable)

Include information about the potential pool of patients from which recruitment will occur and the expected participation rate. Recruitment targets must be specified in the milestones and will be monitored closely by PCORI in the funded research.

Peer Review and Release of Research Findings

PCORI has a legislative mandate to ensure the scientific integrity of the primary research it supports and to make study findings widely available and useful to patients, clinicians, and the general public within a specific timeframe. The PCORI Board of Governors adopted the following process for peer review and public release of the results of all funded studies.

Awardee Institutions are required to submit to PCORI for peer review a draft final research report that provides the methodological details, describes the main study results, and properly interprets the findings in clinical or other decisional contexts. Subject matter experts, individuals with expertise on research methodology or biostatistics, as well as patients, caregivers, and other healthcare stakeholders, will review the draft final research report. After awardees have responded to reviewers' comments to PCORI's satisfaction, the report will be accepted and considered final. PCORI will then prepare a 500-word abstract summarizing the study results for patients and the general public, which the Awardee Institution will review and approve.

PCORI will post the following materials on its website no later than 90 days after the draft final research report is accepted: a 500-word abstract for medical professionals, a standardized summary of the study's results for patients and the general public, and a link to the study record on ClinicalTrials.gov (as applicable). The final research report, along with anonymized reviewer comments, will be made publicly available on the PCORI website no later than 12 months after its acceptance, except by prior mutual agreement with the Awardee Institution.

III. How To Submit a Proposal

PCORI Online System

To submit a proposal, you must register with [PCORI Online](https://pcori.fluxx.io)¹⁰ and submit both a Letter of Intent (LOI) and an application for each cycle in which you are applying.

¹⁰ Available at <https://pcori.fluxx.io>.

Upon receipt, LOIs will be screened by PCORI program staff for responsiveness and programmatic fit. An applicant whose LOI is not responsive to this PFA or 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 approximately five weeks. Applicants should contact PCORI if they have any questions prior to the deadline.

See the [PCORI Funding Center](#)¹¹ 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 citations. LOIs 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.

To submit an LOI, upload the completed PFA-specific LOI to the PCORI Online System and complete the required fields. Provide a thorough description of the research that allows the scientific community to understand the project, including the aims and study design, without reviewing the full application. LOIs 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 methodological gap the research is designed to address and indicate the specific topic in the PFA to which this project responds. Describe how this project will advance PCOR and methodological research and why it would be of interest to patients, caregivers, researchers, and/or other stakeholders.
- **Objectives:** Describe how the overarching research questions are answered by the specific aims of the project, including the specific research objectives linked to each aim.
- **Methods:** Provide a detailed description of the methodological work that is planned and the specific ways in which it addresses the identified methodological gaps and the specific aims of your project. Include a detailed description of the following:
 - Study design
 - Study population (if applicable)
 - Sample size (if applicable)
 - Data sources/datasets (if applicable)
 - Analytic methods
- **Outcomes (Projected) and Anticipated Impact:** Identify and explain the specific anticipated contributions and applications of the methodological advancement to PCOR as well as the

¹¹ Available at pcori.org/apply.

patients and/or stakeholders who will benefit from it.

- **Patient and Stakeholder Engagement:** Describe and justify the plan for engaging patients and stakeholders over the course of the project. If patient and stakeholder engagement is deemed inappropriate in some or all phases of research, justify why.

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

Letter of Intent Review

LOIs are evaluated on the following considerations (note that PCORI does not score the LOI):

- Responsiveness to the specific PFA
- Importance and relevance of the topics to PCORI priorities, as evidenced by critical gaps in current methodological understanding as noted in the Methodology Committee Report or in the scientific literature
- Clarity and credibility of responses to each section of the LOI
- Sufficient detail and scientific rigor of the proposed methods
- Programmatic fit and balance, taking into consideration whether a proposal significantly overlaps 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 applicants whose LOIs are deemed **most responsive** to this PFA will be invited to submit a full application. Notification of the request to submit full application will occur no later than September 8, 2015. Please refer to the [Application Guidelines](#) for due dates and information on how to submit your LOI via PCORI Online.

You are invited to submit an application based on the information provided in the LOI. Any changes to the following require PCORI's approval:

- Research question(s)
- Specific aims
- Study design
- Comparators (if applicable)
- Principal Investigator
- Institution

If you need to change any of this information or have any questions, email pfa@pcori.org.

Note: A PI may submit multiple LOIs in a cycle but the research topics/projects should not be similar. If a PI submits an LOI to multiple PFAs, LOIs with scientific overlap or that appear to be duplicate submissions will be disqualified. PCORI will contact the PI and give them an opportunity to choose which PFA they would like to apply to. An individual listed as a PI on one LOI may be listed and serve in another role (e.g., co-investigator, co-PI) on other LOIs within the same PFA during the same cycle.



Project Budget and Duration

Proposals submitted under the Methods research funding stream will not 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 whether the budget exceeds the \$750,000 limit.

Submission Dates

This is a standing announcement. Applications must be submitted in accordance with the published dates and times listed in the Overview section of this document and in the [PCORI Funding Center](#).

Applicant Resources

PCORI Funding Center	http://www.pcori.org/Cycle-2-2015-methods/
PCORI Online System	pcori.fluxx.io
PCORI Funding Awards	http://www.pcori.org/research-results

IV. Merit Review

PCORI Merit Review is a multiphase process that includes: PFA development; staff evaluation of LOIs; 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 (Board) award approval (no later than April 2016).

Preliminary Review

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

PCORI Merit Review Officers (MROs) recruit each panel based on the number and topic areas represented by invited LOIs. MROs recruit the panel Chair, scientist reviewers who are subject matter experts familiar with the scientific topics represented by submitted applications, methodological and statistical experts, patient representatives trained in review of scientific proposals, and representatives of other stakeholder groups. All panel members receive training during the review cycle, to ensure that all understand the programmatic and organizational goals of review.

Below are PCORI's merit review criteria. PCORI's merit review panels use these criteria during the preliminary and in-person review phases to evaluate and score all submitted applications:

Merit Review Criteria

The following are PCORI's Merit Review criteria for Methods Projects. PCORI's review panels use these criteria 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 Report or the published scientific literature.

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 the scientific literature? Which particular gap(s)?

Criterion 2. Potential for the study to improve PCOR methods

The proposal addresses the following questions:

- Would the development, refinement, or comparison of methods in this area produce more valid, trustworthy, and useful 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

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 relevant 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? Are the organizational structure and 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

The proposal addresses the following questions:

- Would the research improve processes to address questions about 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

PCOR?

- “Given my personal characteristics, conditions, and preferences, what should I expect will happen to me?”
- “What are my options, and what are the potential benefits and harms of those options?”
- “What can I do to improve the outcomes that are most important to me?”
- “How can clinicians and the care delivery systems they work in help me make the best decisions about my health and health care?”

Criterion 5. Patient and stakeholder engagement

The proposal addresses the following questions:

- Are patients and other stakeholders engaged meaningfully in appropriate phases of the research? 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; and trust, transparency, and honesty?
- If engagement is deemed inappropriate in some or all aspects of the proposed research, does the application justify why it is not?

In-Person Review

After the preliminary review is completed, PCORI program staff members evaluate panel scores and critiques 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 to further clarify the merits of the proposed research as well as to identify areas for improvement. Additionally, each application is re-scored based on the content of discussion. The Chair and PCORI MRO lead the in-person panel meeting and ensure that all applications receive a fair and thorough review informed by the standards outlined in the PFA.

Post-Panel Review

After the in-person panel review, PCORI program staff review meritorious applications’ merit review scores and comments, identify duplication or synergy among funded projects, and consider the fit of applications within the programmatic vision. Program staff members then recommend projects to a Selection Committee, which includes members of PCORI’s Board. The 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 then proposed to PCORI’s Board for its consideration and approval.

Summary Statements and Funding Recommendations

Summary statements and funding decision notifications are provided to applicants contemporaneously. If an application progresses to in-person discussion, the applicant will receive a summary statement



inclusive of the panel discussion notes, the final average overall score, and preliminary reviewer critiques. Summary statements for applications that do not progress to in-person discussion include only the preliminary reviewer critiques.

Funding recommendations are made by identifying meritorious applications that fit the programmatic needs and that satisfactorily address the merit review criteria while adhering to PCORI's Methodology Standards. Programs also consider the funds allotted for the current funding announcement when deciding which applications to recommend to PCORI's Board for approval. Applicants will receive summary statements and notification of the funding status of their application no later than April 2016.