Cycle 1 2016 Funding Cycle

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

Published February 1, 2016

This PCORI Funding Announcement applies to the funding cycle that closes on June 6, 2016, at 5 p.m. (ET). Application guidelines, templates, and other resources are available at http://www.pcori.org/Cycle-1-2016-methods/.
About PCORI

The Patient-Centered Outcomes Research Institute (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 Congress in 2010 as a nonprofit, nongovernmental organization. PCORI’s purpose, as defined by our authorizing legislation, is to help patients, clinicians, purchasers, and policy makers make better-informed health decisions by “advancing the quality and relevance of evidence about how to prevent, diagnose, treat, monitor, and manage diseases, disorders, and other health conditions.”

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## Overview

**Published**  
February 1, 2016

**Letter of Intent Due**  
March 2, 2016, by 5 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 April 8, 2016. 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**  

**Key Dates**

<table>
<thead>
<tr>
<th>Event</th>
<th>Date</th>
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</thead>
<tbody>
<tr>
<td>Online System Opens</td>
<td>February 1, 2016</td>
</tr>
<tr>
<td>LOI Deadline</td>
<td>March 2, 2016, by 5 p.m. (ET)</td>
</tr>
<tr>
<td>LOI Screening Notification</td>
<td>April 8, 2016</td>
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<tr>
<td>Application Deadline</td>
<td>June 6, 2016, by 5 p.m. (ET)</td>
</tr>
<tr>
<td>Merit Review:</td>
<td>September 2016</td>
</tr>
<tr>
<td>Awards Announced:</td>
<td>November 2016</td>
</tr>
<tr>
<td>Earliest Start Date</td>
<td>January 2017</td>
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</tbody>
</table>

**Maximum Project Budget (Direct Costs)**  
$750,000

**Maximum Research Project Period**  
Three 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 shown clearly. Organizations may submit multiple applications for funding. Individuals are not permitted to apply.

**Review Criteria**

1. Study identifies critical methodological gap(s) in PCOR/CER (Comparative Effectiveness Research)
2. Potential for the study to improve PCOR/CER methods
3. Scientific merit (research design, analysis, and outcomes)
4. Patient-centeredness
5. Patient and stakeholder engagement
New or Revised for the Cycle 1 2016 Funding Cycle:
The Cycle 1 2016 PFA contains a number of changes (described below). First, however, we want to note some significant and substantive changes to the Methods PFA that will be made beginning with the next funding cycle, Cycle 3 2016. (There is no Methods PFA for Cycle 2 2016.)

Beginning with Cycle 3 2016, the Methods PFA will fund only 2–3 Research Areas of Interest (RAIs) in a particular cycle. LOIs or applications that do not address one of the selected RAIs will be deemed nonresponsive for that cycle. The selection of these RAIs will reflect the strategic priorities of PCORI’s Methods Program. The RAIs for Cycle 3 2016 have not yet been finalized.

The revisions for Cycle 1 2016 include:

- **RAI 1: Methods for Patient and Stakeholder Engagement**
  - Removal of subtopic (formerly RAI 1b): Methods of patient and stakeholder engagement to improve representation of populations, settings, and phases of PCOR/CER

- **RAI 2: Methods for Patient-Centered Outcomes (PCOs) and Patient-Reported Outcomes (PROs)**
  - Addition of possible research questions for subtopic RAI 2b: Development and application of core outcome sets that contain PROs
  - Addition of possible research questions in RAI 2c: Stated preference and natural language processing methods related to PROs

- **RAI 3: Research Related to the Ethical Conduct of PCOR/CER**
  - Renamed (formerly “Research Related to Human Subjects Protections’’)
  - Organized into five subtopics, including addition of new subtopic 3c: Research on the ethical issues associated with engaging patients and/or other stakeholders as research partners in PCOR/CER

- **RAI 4: Methods to Improve Study Design**
  - Consolidated former subtopics 4a and 4b into new subtopic 4a: Methods related to pragmatic clinical trials
  - New subtopic 4b: Methods related to non-randomized study designs
New subtopic 4c: Methods related to embedding PCOR/CER studies into existing infrastructure

RAI 5: Methods to Improve Validity and Efficiency of Analyses
- Removed emphasis on former subtopics related to missing data, instrumental variables, and time-varying factors
- Addition of new subtopic 5a: Methods related to complex interventions
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PCORI Cycle 1 2016 Funding Announcement: Improving Methods for Conducting Patient-Centered Outcomes Research
I. Introduction

Summary of Program

In this PCORI Funding Announcement (PFA) for Improving Methods for Conducting Patient-Centered Outcomes Research (PCOR), the Methods Program aims to fund high-priority methodological research topics in PCOR and comparative clinical effectiveness research (CER). Studies should address methodological gaps in PCOR/CER, supporting PCORI’s Methods Strategic Imperative to develop and promote rigorous PCOR methods, standards, and best practices.

Background

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 might apply differently to different 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 conducting PCOR/CER. 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 improve patients’ healthcare outcomes.

Research Areas of Interest

PCORI is interested in supporting research that advances methods relevant to PCOR/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 the PCORI Methodology Standards to develop their research question(s) and Research Plan.

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

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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.
# Methods for Patient and Stakeholder Engagement

The Methods Program is interested primarily 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 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 RAI 1:

<table>
<thead>
<tr>
<th>a)</th>
<th>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</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Development of methods to evaluate impact of engagement</td>
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<tr>
<td></td>
<td>• Development of methods to evaluate uptake of relevant research findings into clinical practice or PCOR/CER</td>
</tr>
<tr>
<td></td>
<td>• Development of methods to discern appropriate engagement at each phase of research, priority population, or health condition</td>
</tr>
<tr>
<td></td>
<td>• Development of methods to collect, analyze, balance, and reconcile input from various patient and stakeholder perspectives in PCOR/CER</td>
</tr>
<tr>
<td></td>
<td>• Development of methods to identify factors outside of patient and stakeholder engagement that have contributed to or hindered the uptake of relevant findings for end-users, such as structural or institutional factors or temporal trends</td>
</tr>
</tbody>
</table>

| b) | Methods of patient and stakeholder engagement to improve recruitment and retention of patients into trials, observational studies, and registries |
|    | • 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) |

Applications 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. Applications examining ways to increase survey and questionnaire response rates will also be considered nonresponsive.

# Methods for Patient-Centered Outcomes (PCOs) and Patient-Reported Outcomes (PROs)

For the purposes of this PFA, the Methods Program is not interested in funding narrowly focused instrument development projects, which would result in products limited to a specific disease, health condition, behavior, therapeutic area, or priority population. Such applications will be considered nonresponsive.

The following topics are considered priorities for RAI 2:
<table>
<thead>
<tr>
<th>a)</th>
<th>Methods related to PRO interpretability, value, and use</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Development of methods to evaluate feasibility and acceptance of PRO into routine clinical care</td>
</tr>
<tr>
<td></td>
<td>• Development of methods to evaluate relationships between PROs and clinical outcomes</td>
</tr>
<tr>
<td></td>
<td>• Development of methods to evaluate PRO score interpretation and longitudinal assessment</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>b)</th>
<th>Methods related to PRO integration into routine clinical care and research</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Development of methods to identify and address barriers and facilitators for incorporating PROs into routine clinical care and research</td>
</tr>
<tr>
<td></td>
<td>• Development of methods to evaluate integration of PROs into electronic health records (EHRs), routine clinical care, care quality assessment, PCOR/CER, clinical data research networks, patient-powered research networks, and other registries</td>
</tr>
<tr>
<td></td>
<td>• Development and application of core outcome sets that contain PROs and represent the minimum that is measured and reported in clinical trials, observational studies, and routine clinical care</td>
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</table>

<table>
<thead>
<tr>
<th>c)</th>
<th>Methods related to PRO variation by mode of administration, platform, setting, and approach</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>• Development of methods to compare and integrate PRO reporting from multiple settings (e.g., clinic-based, home-based, and mobile data collection)</td>
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<tr>
<td></td>
<td>• Development of methods to identify and address concordance/discordance between patient and surrogate reports and other data sources</td>
</tr>
<tr>
<td></td>
<td>• Development of stated preference methods that cross domains and facilitate efforts to characterize and better understand patients' preferences</td>
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<tr>
<td></td>
<td>• Development of natural language processing methods for PRO data</td>
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</tbody>
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<table>
<thead>
<tr>
<th>d)</th>
<th>Methods related to PRO data collection and completeness</th>
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<tbody>
<tr>
<td></td>
<td>• Development of methods to enhance completeness and reduce missing PRO data</td>
</tr>
<tr>
<td></td>
<td>• Development of methods to measure both positive and negative change (e.g., symptoms and function)</td>
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<tr>
<td></td>
<td>• Development of methods to estimate optimal measurement time points</td>
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</table>

### 3. Research Related to the Ethical Conduct of PCOR/CER

The Methods Program is interested in funding projects on the ethical conduct of PCOR/CER. Applications responding to this RAI must include an empirical component. Purely conceptual and theoretical work will be considered nonresponsive.

The following topics are considered priorities for RAI 3:
a) Research on ethical issues arising in the context of PCOR/CER study designs (e.g., cluster randomized trials, adaptive trials, and conventional randomized controlled trials [RCTs])

b) Methods of patient-centered privacy preservation in registries and other data sources used in PCOR/CER

c) Research on the ethical issues associated with engaging patients and/or other stakeholders as research partners in PCOR/CER

d) Research on Institutional Review Board (IRB) approval, monitoring, and review of PCOR/CER

e) Research on novel approaches to recruitment, informed consent, and retention of patients in PCOR/CER

4. Methods to Improve Study Design

The Methods Program is interested in funding projects that foster improvements in study design to address PCOR/CER questions. The following topics are considered priorities for RAI 4:

| a) Methods related to pragmatic clinical studies | • Development of methods to improve the design and conduct of cluster-randomized trials  
| | • Development of methods for adaptive trials, especially those using Bayesian approaches  
| | • Development of methods to manage adaptation of treatment strategies while minimizing threats to the internal validity of studies (e.g., studies of complex interventions) |
| b) Methods related to non-randomized study designs | • Development of methods to improve the design and conduct of PCOR/CER studies in circumstances limiting the use of RCTs |
| c) Methods related to embedding PCOR/CER studies into existing infrastructure | • Development of methods to enable routine, inexpensive nesting of PCOR/CER studies into existing infrastructure (e.g., registries, cohort studies, and data research networks) |

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. Applications responding to this RAI should address critical methodological gaps in existing analytical methods to generate valid estimates of the effects of interventions given particular data sources, hypotheses, and study design(s).

**NOTE:** The Methods Program has funded many 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 overlap significantly with previously funded projects or concurrent applications and that the applications fill a gap in the program’s portfolio.

The following topics are considered priorities for RAI 5:

| a) Methods related to complex interventions | • Development of methods to improve the measurement and analysis of contextual influences and other effect modifiers  
| | • Development of methods to improve the measurement and |
### 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 RAI 6:

<table>
<thead>
<tr>
<th>a) Methods to improve distributed analyses in data research networks</th>
<th>b) Methods to obtain longitudinal and complete data in data research networks</th>
</tr>
</thead>
</table>
| - 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 and propensity scoring in distributed research networks  
- Development of methods to evaluate heterogeneity in claims and EHR data (e.g., process to identify the type of heterogeneity within 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 | - Development of methods to evaluate optimal linkage of multiple data sources, such as 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

Nonresponsiveness

Applications to Improving Methods for Conducting Patient-Centered Outcomes Research PFA that propose the following types of research will be considered nonresponsive:

- **Cost-effectiveness research**
  - Conducts a formal cost-effectiveness analysis
  - Directly compares the costs of care between two or more alternative approaches to providing care

- **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**
  - Develops, refines, and validates disease- or condition-specific measures

Applications may measure and report utilization of any or all health services, but may not employ direct measurements of the costs of two or more alternative clinical approaches.

PCORI does have an interest, however, in studies that address questions about conditions leading to high costs to the individual or to society. This is included in our review criterion on impact of the condition on the health of individuals and populations. Thus, PCORI is 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

With respect to the issue of addressing conditions that lead to high costs, applications that include studies of these issues without using a formal cost-effectiveness analysis or directly measuring and comparing costs of care alternatives will be considered responsive and will be reviewed.

Consistent with PCORI’s [authorizing law](http://www.pcori.org/sites/default/files/PCORI_Authorizing_Legislation.pdf/), PCORI does **not fund** research whose findings will include:

- Creation of clinical practice guidelines or clinical pathways
- Coverage recommendations

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2 Available at http://www.pcori.org/sites/default/files/PCORI_Authorizing_Legislation.pdf/.
• Payment or policy recommendations
• Establishing efficacy for a new clinical strategy
• Pharmacodynamics
• Study of the natural history of disease
• Basic 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 applicants are encouraged to review funded research on PCORI’s website.³

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 CER questions.

Methodological Considerations

Regardless of study design, applications must adhere to all relevant PCORI Methodology Standards.⁴ 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 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 Effects

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

³ Available at http://www.pcori.org/research-results/.
⁴ Available at http://www.pcori.org/research-results/research-methodology/.
Standards for Systematic Reviews

These standards should be considered minimal. Additional best practices, including guidelines for conducting clinical trials developed by other organizations, should be addressed, if applicable, in the application for PCORI funding.

Upcoming New and Revised Methodology Standards

In 2015 the Methodology Committee undertook a process to review the existing Methodology Standards, updating and adding new Standards where indicated. While these proposed revised and new Standards are still under review and not yet benefited from public comment, we encourage you to refer to the potential 2015 revisions. Applicants should continue to adhere to the current Methodology Standards.

Patient and Stakeholder Engagement

Applicants must complete this section of the Research Plan, providing clear and concise justification of the types of patients, caregivers, and stakeholders that will be engaged and noting how those individuals will contribute to the research. To assist applicants, PCORI provides an Engagement Rubric, which can be found in the PCORI Funding Center. PCORI also provides sample Methods Engagement Plans 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, or dissemination of research because of the proposed project’s technical nature, applications should justify why. Highly technical applications should consider whether engaging other stakeholders or end-users (e.g., data architects, clinicians, domain experts, health services researchers with different expertise than that of the research team members, policy makers, etc.) would be of value in the methodological process and in the dissemination and implementation plans.

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 outcomes may be examined in defined subpopulations, otherwise known as HTE. PCORI recognizes that some proposed studies might represent important PCOR opportunities even in the absence of a broadly diverse study population. However, the burden is on the applicant to justify the importance of the study in the absence of diversity and to discuss which subgroups are most important and how they will be analyzed—including whether the study will be powered 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 strategy’s effects might differ across subpopulations. PCORI has developed a list of

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populations of interest to guide our efforts in research and engagement:

- Racial and ethnic minority groups
- Low-income groups
- Women
- Children (age 0–17 years)
- Older adults (age 65 years and older)
- Residents of rural areas
- Individuals with special healthcare needs, including individuals with disabilities
- Individuals with multiple chronic diseases
- Individuals with rare diseases
- Individuals whose genetic makeup affects their medical outcomes
- Patients with low health literacy/numeracy and/or limited English proficiency
- Lesbian, gay, bisexual, and transgender (LGBT) persons
- Veterans and members of the Armed Forces and their families

Protection of Human Subjects

This component (up to five pages) is included in the Research Plan Template. Applicants should describe the protection of human subjects involved in their 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, titled “Human Subjects Research Policy” in the Supplemental Grant Application Instructions for All Competing Applications and Progress Reports, which was 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 including women, minorities, and children. PCORI requires that applicants proposing clinical trials 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). Reviewers’ comments on human subjects research are not reflected in the overall application score, but PCORI staff may use them during potential funding negotiations. Final determinations about adequacy of human subject protections rest with the 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.

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

PCORI requires that all applicants 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 on the NIH website.8

Replication and Reproducibility of Research and Data-Sharing Plan

PCORI is committed to maximizing the utility and usability of data generated and 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 research in other populations. Please propose a method for sharing data and appropriate documentation upon request.

Recruitment (if applicable)

Applications should include information about the size and representativeness of the potential pool of human subjects from which recruitment will occur and the means by which this size estimate was determined. Likewise, applications should provide evidence-based estimates of how many participants are ultimately expected in the study based on anticipated recruitment, application of the study’s inclusion and exclusion criteria, expected acceptance (or refusal) rates, and other factors, such as failure to follow up. Such estimates must be discussed in the applications and specified in the Milestone Schedule. Merit reviewers and PCORI staff will review the estimates, and PCORI will monitor them 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 appropriately interprets the findings in clinical or other decisional contexts. Subject matter experts—individuals with expertise in 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: (1) a 500-word abstract for medical professionals, (2) a standardized summary of the study results for patients and the general public, and (3) 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 an Application

PCORI Online

To submit an application, you must register with PCORI Online9 and submit both a Letter of Intent (LOI) and an application for each cycle in which you are applying. See the PCORI Funding Center10 for applicant resources, including application guidelines and templates.

Letter of Intent

Applicants should download the LOI 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 file. The LOI is limited to three pages, excluding references. Applicants should use in-text citations and follow American Medical Association (AMA) style. 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, because 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 document. 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 the proposed research will advance methods for PCOR/CER and the importance of this research to the relevant stakeholders (e.g., patients, clinicians, and policy makers).

- **Objectives:** Describe the research objective(s) and list the specific aims that will address the identified methodological gap.

- **Methods:** Provide a detailed description of the methodological work that is planned for each of the specific aims and the ways in which it addresses the identified methodological gaps. Include a sufficient description of the following elements to demonstrate the scientific rigor of the proposed research:
  - Study design
  - Study population and sample size (if applicable)
  - Primary data collection methods (if applicable)

9 Available at https://pcori.fluxx.io/.
10 Available at http://www.pcori.org/funding-opportunities/.

PCORI Cycle 1 2016 Funding Announcement: Improving Methods for Conducting Patient-Centered Outcomes Research
Data sources and data sets (if applicable)

Analytic methods

- **Outcomes (projected) and Anticipated Impact**: Identify and explain the specific anticipated contributions and applications of the methodological advancement to PCOR/CER as well as the patients and/or other stakeholders who will benefit from it.

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

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

**Letter of Intent Review**

LOIs are evaluated based on the following:

- 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 PCORI Methodology 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 an LOI significantly overlaps with funded studies or concurrent LOIs.

Only applicants with LOIs deemed **most responsive** to this PFA will be invited to submit a full application. PCORI staff review the LOIs, which are not scored during review. Notification of the request to submit a full application will occur no later than April 8, 2016. 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 (PI)
- Institution

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

**Note**: A PI may only submit one LOI per PFA. However, an individual listed as a PI on one LOI may be
listed as and serve in another role (e.g., co-investigator or consultant) on other LOIs within the same PFA during the same cycle. A PI may submit multiple LOIs to different program PFAs in a cycle, but the PI must ensure that the research topics and projects are not similar. If a PI submits an LOI to multiple program PFAs, LOIs that exhibit scientific overlap or that appear to be duplicate submissions will be disqualified. PCORI will contact the PI and provide him or her with an opportunity to choose which PFA he or she would like to apply to. This applies to single and dual-PI submissions.

Project Budget and Duration

Applications submitted under the Methods research funding stream will not be granted an exception to the research project duration limit of three years (not including peer review) and/or the project budget limit of $750,000 in direct costs. The maximum budget includes all research- and peer-review-related costs. (Please refer to the Application Guidelines for further details.) Refer to Appendix 2 in the Application Guidelines for a list of allowable and unallowable costs. Note that, although subcontractor direct and indirect costs are considered 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-1-2016-methods/

- **PCORI Online System**  
  https://pcori.fluxx.io

- **PCORI Funding Awards**  
  http://www.pcori.org/research-results

IV. Merit Review

PCORI's merit review process is designed to support the following goals:

- To identify applications that have the strongest potential to help patients, caregivers, clinicians, and other stakeholders make informed decisions to improve patient outcomes
- To implement a transparent, fair, objective, and consistent process to identify these applications
- To elicit high-quality feedback that reflects a diversity of perspectives to ensure that the PCORI-funded research reflects the interests and views of patients and those who care for them and that it meets the criteria for scientific rigor
- To fund projects that fill important evidence gaps and have strong implementation potential
- To regularly evaluate and continually improve the merit review process and policies in support of PCORI's mission
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.

**Preliminary Review**

PCORI conducts rigorous merit review of all full applications received. 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 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, patient representatives, and representatives of other stakeholder groups. All panel members receive training during the review cycle to ensure that they 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.

**Criterion 1. Study identifies critical methodological gap(s) in PCOR/CER**

The application should address the following:

- Does the application identify and make a persuasive argument for addressing critical gaps in current PCOR/CER methods as noted in the Methodology Report or in the published scientific literature?

**Criterion 2. Potential for the study to improve PCOR/CER methods**

The application should address the following:

- Does the application clearly articulate how the development, refinement, or comparison of methods, and/or the novel application of methods to PCOR/CER improves the validity, trustworthiness, and usefulness of PCOR/CER findings?
- Are the PCOR/CER methods generated from this study likely to inform best practices or standards for PCOR/CER?

**Criterion 3. Scientific merit (research design, analysis, and outcomes)**

The application should address the following:

- Does the application provide a clear conceptual framework or theoretical model and empirical evidence that inform the study design, key variables or constructs, analytical approach, and relationships being tested or explored?
- Does the application describe methods that reflect state-of-the-art thinking and practice in the
relevant methodological area?

- Are the study scope and timeline realistic, including the completion of specific scientific and engagement milestones?
- Does the research team have complementary and integrated expertise to successfully conduct the study?
- Are the research environment and resources adequate to successfully conduct the study?

Criterion 4. Patient-centeredness

Note: A study can be patient-centered even if the end-user is not the patient, as long as patients will benefit from the study findings (e.g., methods to produce more valid, trustworthy, and useful PCOR/CER findings).

The application should address the following:

- Does the application articulate clearly how the study will improve PCOR/CER methods that address outcomes of interest to patients and their caregivers?

Criterion 5. Patient and stakeholder engagement

The application should address the following:

- Are patients and/or other relevant stakeholders meaningfully engaged in appropriate phases of the research?
- Does the proposed study 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 study, does the application justify why it is not appropriate?

In-Person Review

During preliminary review, all administratively and scientifically compliant applications are evaluated and scored based on PCORI’s merit review criteria, including evaluation of adherence to the PCORI Methodology Standards. After the preliminary review is completed, PCORI program staff members evaluate panel scores and critiques to identify a subset of applications for merit reviewers to discuss at the in-person review meeting. Not all submitted applications move on to in-person review.

During the in-person review, merit reviewers meet to discuss applications, clarify further the merits of the proposed research, and identify areas for improvement. In addition, 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 according to the standards outlined in the PFA.

Post-Panel Review

After the in-person meeting, PCORI program staff evaluate final merit review panel 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 Selection Committee considers
recommendations and works with staff to identify a slate of applications for possible funding based on merit review scores, programmatic balance and fit, and PCORI’s strategic priorities. This slate is then proposed PCORI’s Board for consideration and approval.

Summary Statements and Funding Recommendations

Summary statements are provided to applicants approximately two weeks before funding decisions are announced. If an application progresses to in-person discussion, the applicant will receive a summary statement that includes:

- In-person panel discussion notes
- Final average overall score
- Preliminary reviewer critiques
- Application quartile, which provides information for applicants to understand how they did relative to other discussed applications

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, including adherence to the PCORI Methodology Standards. Programs also consider the funds allotted for the current PFA when deciding which applications to recommend to PCORI’s Board for approval. Applicants to this Cycle 1 2016 Improving Methods for Conducting Patient-Centered Outcomes Research PFA will receive summary statements in October 2016 and notification of the funding status of their applications no later than November 2016.