Cycle 1 2016 Funding Cycle

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

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-options/.
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

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<tr>
<th>Published</th>
<th>February 1, 2016</th>
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<tr>
<td>Letter of Intent Due</td>
<td>March 2, 2016, by 5 p.m. (ET)</td>
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Letters of Intent (LOIs) will be screened for responsiveness to this PCORI Funding Announcement (PFA) and for fit to program goals. Only those selected will be permitted to submit full applications. Notification of request to submit full application will occur no later than April 8, 2016.

### Summary

PCORI is seeking applications for comparative clinical effectiveness research (CER) designed to provide information that would inform critical decisions that face patients and caregivers, clinicians, policy makers, and healthcare system leaders. These decisions must be consequential and be occurring now in the absence of sound evidence about the comparative effectiveness of alternative approaches. There must be substantial potential that patients and caregivers will benefit from the new knowledge in ways that are important to them. The premise of this research is that the new knowledge will inform critical healthcare choices by patients and stakeholders. This knowledge will provide insight about the comparative benefits and harms of the options and provide information about outcomes that are important to patients.

### Applicant Resources


### Key Dates

- **Online System Opens:** February 1, 2016
- **Letter of Intent (LOI) Deadline:** March 2, 2016, by 5 p.m. (ET)
- **LOI Status Notification:** April 8, 2016
- **Application Deadline:** June 6, 2016, by 5 p.m. (ET)
- **Merit Review:** September 2016
- **Awards Announced:** November 2016
- **Earliest Project Start Date:** January 2017

### Maximum Project Budget (Total Direct Costs)

$2 million

Note: If your proposed budget is more than $2 million in direct costs and is a head-to-head comparison of two or more interventions or strategies (and not an evidence synthesis study or a project to develop and evaluate a decision support tool), you may wish to apply under PCORI’s Pragmatic Studies To Evaluate Patient-Centered Outcomes Funding Announcement, which will open on February 1, 2016.

### Maximum Research Project Period

Three years

### Funds Available Up to

$32 million

### Eligibility

Applications may be submitted by any private-sector research organization, including any nonprofit or for-profit organization, and any public-sector research organization, including any university or college hospital or healthcare system, laboratory or manufacturer, or unit of local, state, or federal government. 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

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<td>1.</td>
<td>Potential for the study to fill critical gaps in evidence</td>
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<td>2.</td>
<td>Potential for the study findings to be adopted into clinical practice and to improve delivery of care</td>
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<td>3.</td>
<td>Scientific merit (research design, analysis, and outcomes)</td>
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<td>4.</td>
<td>Patient-centeredness</td>
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<td>5.</td>
<td>Patient and stakeholder engagement</td>
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### Contact Us

For programmatic questions, please email (sciencequestions@pcori.org), phone (202-627-1884), or contact us online (http://www.pcori.org/PFA/inquiry). PCORI will provide a response within three business days. However, PCORI cannot guarantee that all questions will be addressed three business days prior to an LOI or application deadline.

Please email pfa@pcori.org for any administrative, financial, or technical questions. PCORI will provide a response within two business days. Please note that during the week of a deadline, response times may exceed two business days. Applicants may call the Helpdesk (202-627-1885) for technical or administrative support. Applicants are asked to plan accordingly. It is the applicant’s responsibility to submit the application on or before the application deadline.

### Other

Deadlines are at 5 p.m. (ET). If deadlines fall on a weekend or a federal holiday, the deadline will be the following Monday or the next day after the federal holiday.

### New or Revised for the Cycle 1 2016 Funding Cycle:
- Updated Criterion 5 to reflect the new dual-PI plan policy
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PCORI Cycle 1 2016 Funding Announcement: Assessment of Prevention, Diagnosis, and Treatment Options
I. Introduction

About PCORI

PCORI funds patient-centered outcomes research (PCOR), a type of comparative clinical effectiveness research (CER) that focuses on outcomes that matter to patients, their caregivers, and their families. The studies that PCORI funds must include the perspectives of patients and other healthcare stakeholders.

To be considered responsive, applications must describe research that compares at least two alternative approaches. Approaches may address diagnostic methods, screening strategies, interventions for prevention or treatment of disease, or strategies to improve the healthcare system. In general, through its various funding announcements, PCORI is interested in studies of interventions that may include:

- Specific drugs, devices, and procedures
- Medical and assistive devices and technologies
- Psychological therapies
- Organizational models and policies within and across healthcare systems (e.g., patient-centered medical homes, clinical protocols, and pathways)

PCORI is seeking applications designed to provide information to inform critical decisions that face patients and caregivers, clinicians, policy makers, and healthcare system leaders. These decisions must be consequential and occurring now in the absence of sound evidence about the comparative effectiveness of alternative approaches. There must be substantial potential for patients and caregivers to benefit from the new knowledge in ways that are important to them. The premise of this research is that the new knowledge will inform critical choices of patients and stakeholders in health care. This knowledge will provide insight about the comparative benefits and harms of the options and provide information about outcomes that are important to patients.

PCORI is entrusted by the public to fund research that matters to patients, their caregivers, and other stakeholders (defined as clinicians and clinician societies, hospitals and health systems, payers [insurance], purchasers [business], industry, researchers, policy makers, and training institutions). PCORI seeks to change the way in which research is conducted by emphasizing the role of diverse research teams that include varying perspectives. PCORI distinguishes itself by supporting research in which patients, caregivers, practicing clinicians, and the broader stakeholder community are actively engaged in generating research questions, reviewing research applications, conducting research, disseminating research findings, promoting the implementation of research findings, and using the results to understand and address patient and other stakeholder needs.

Research of Interest: Comparative Clinical Effectiveness

Patients, caregivers, and clinicians often lack the appropriate evidence required to make the best choices regarding prevention, screening, diagnosis, monitoring, or treatment. Where therapies or technologies have been approved and marketed, there are often gaps in research comparing their effectiveness with that of other clinical options, and prior research may not have included outcomes that are important to patients and their caregivers. In addition, the existing evidence base may not be
relevant for certain patient populations, such as those at the extremes of age or with multiple comorbid conditions.

For this particular PFA on the Assessment of Prevention, Diagnosis, and Treatment Options, PCORI seeks to fund investigator-initiated research that:

- Compares the effectiveness of two or more strategies for prevention, treatment, screening, diagnosis, or management that are known to be efficacious but have not been adequately compared in previous studies; interventions without sufficient evidence of efficacy will be considered only when they are in reasonably common use. PCORI is particularly interested in studies that are conducted in typical clinical populations and that address the full range of relevant patient-centered outcomes (PCOs)
- Addresses a high-priority evidence gap, as identified by prior systematic reviews, clearly defined gaps in clinical guidelines, or other credible evidence reviews
- Investigates, among compared groups, factors that account for variation in treatment outcomes, with attention paid to demographic, biological, clinical, social, economic, or geographic factors, comorbidities, and other factors that may influence those outcomes; strategies may focus on patient populations with a single condition or involve patients with a range of conditions

For this PCORI Funding Announcement (PFA), proposed projects should address the comparison of specific clinical services or strategies that are clearly defined and can be replicated in other clinical settings with minimal adaptations or changes. PCORI does not encourage projects that have the primary goal of developing and testing decision aids or testing the use of lay personnel who perform ancillary services in healthcare settings.

This funding opportunity is broad-based and is not confined to specific clinical services or patient populations. However, the program’s goal is to expand the evidence base that pertains to clinical services that would be chosen by clinicians, patients, and caregivers in usual clinical delivery settings. The services of interest include:

- Prescription drugs and biologics
- Surgical and other interventional procedures
- Techniques for disease screening
- Vaccinations and other interventions to prevent diseases
- Counseling and behavioral interventions
- Complementary and integrative services
- Rehabilitative services
- Diagnostic tests and procedures
II. Requirements for PCORI Research

This section includes language that is specific to PCORI’s requirements for applications for funding. Applicants should use this section as guidance when preparing their applications.

Research Priorities

To be considered responsive, applications must:

- **Describe comparators.** Regardless of the approach being studied, all proposed research projects must compare at least two alternatives. If the applicant proposes “usual care” as a rational and important comparator in the proposed study, then it must be described in detail, coherent as a clinical alternative, and properly justified as a legitimate comparator (e.g., “usual care” is guidelines-based). Additionally, it must be accompanied by an explanation of how the care given in the usual-care group will be measured in each individual patient and how appropriate inferences will be drawn from its inclusion. “Usual care” must be described as mentioned above to ensure that it accounts for geographic and temporal variations, and to ensure that it has wide interpretability, applicability, and reproducibility.

- **Describe research that compares two or more alternatives, each of which has established efficacy.** PCORI expects that the efficacy or effectiveness of each intervention be known. If the efficacy/evidence base is insufficient, then data need to be provided to document that the intervention is used widely. The application must provide information about efficacy of the interventions that will be compared; pilot data may be appropriate. Projects that aim to develop new or novel interventions that lack evidence of efficacy or effectiveness will be considered out of scope.

- **Describe research that studies the benefits and harms of interventions and strategies delivered in real-world settings.** PCORI is interested in studies that provide practical information that can help patients and other stakeholders make informed decisions about their health care and health outcomes.

- **Describe research that is based on health outcomes that are meaningful to the patient population, their caregivers, and family members under study, and that are likely to guide their decisions.** Applications must demonstrate that patients, caregivers, or family members influenced the choice of outcomes to be measured. These outcomes may be measures of quality of life, symptoms of disease, relevant physiological measurements, treatment-related symptoms (side effects), healthcare utilization, or clinical outcomes.

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.

Patient-Centered Outcome Measures

PCORI encourages investigators to design their research using validated outcome measures. Include
preliminary data that support the use of the proposed measures in the study population. Investigators are encouraged to consider those measures described in the Patient Reported Outcomes Measurement Information System\(^1\) (PROMIS).

Studies in Rare Diseases

PCORI is interested in the investigation of strategies that address care for patients with rare diseases. These types of conditions are defined as life-threatening or chronically debilitating. They are of such low prevalence (conditions that affect fewer than 200,000 in the United States [i.e., less than 1 in 1,500 persons]) that special efforts, such as combining data across large populations, may be needed to address them.

Studies of Cost-Effectiveness

Applications will be considered nonresponsive if the proposed research:

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

Proposals that include studies of these issues may measure and report utilization of any or all health services, but may not employ direct measurements of costs of care. For further information, please reference our cost-effectiveness analysis FAQs.

PCORI does have an interest, however, in studies that address questions about conditions that lead to high costs to the individual or to society. This is included in our review criterion on the 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

Addressing specifically the issue of conditions that lead to high costs, our PFAs say that “proposals that include studies of these issues without utilizing a formal cost-effectiveness analysis or directly measuring and comparing costs of care alternatives will be considered responsive and will be reviewed.”

Categories of Nonresponsiveness

PCORI discourages proposals in the following categories and will likely deem them nonresponsive:

- Instrument development, such as new surveys, scales, etc.
- Developing, testing, and validating new decision aids/tools or clinical prognostication tools
- Pilot studies intended to inform larger efforts

\(^1\) Available at http://www.nihpromis.org/.
• Comparisons of patient characteristics rather than clinical strategy options

• Applies to APDTO (Assessment of Prevention, Diagnosis, and Treatment Options), IHS (Improving Healthcare Systems) program applicants ONLY: Studies comparing interventions for which the primary focus is the role of community health workers or patient navigators

Consistent with PCORI’s authorizing law, PCORI does not fund research whose findings will include:

• Coverage recommendations
• Payment or policy recommendations
• Creation of clinical practice guidelines or clinical pathways
• Establishment of efficacy for a new clinical strategy
• Pharmacodynamics
• Study of the natural history of disease
• Basic science or study of biological mechanisms

Avoiding Redundancy

PCORI encourages potential applicants to review funded research at pcori.org, because PCORI intends to balance its funded portfolio to achieve synergy where possible and to avoid redundancy.

Methodological Considerations

Regardless of study design, proposals must adhere to all relevant PCORI Methodology Standards. These include 47 individual standards that fall into 11 categories. The first five categories are cross-cutting and relevant to most PCOR studies. Researchers should refer to all of these standards when planning and conducting their research projects. These categories are:

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

Six other categories of standards will be applicable to 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. These categories are:

• Standards for Data Registries
• Standards for Data Networks as Research-facilitating Infrastructures

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2 Available at http://www.pcori.org/sites/default/files/PCORI_Authorizing_Legislation.pdf/.
• 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. The methodology standards\(^3\) reflect practices that should be followed in all cases, and all deviations need to be explained and well justified. Additional best practices, including accepted guidelines for the conduct of clinical trials or observational studies, should be addressed, if applicable, in the application for PCORI funding.

Applicants should discuss specifically how the planned study design will measure and adjust for potential confounding factors that may obscure or artificially create differences attributable to the alternatives being compared. Examples include, but are not limited to, baseline differences in disease severity or other risk factors within the study population, or differences in participation, adherence, or follow-up that may affect outcomes independently of the interventions being compared.

**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**

PCORI encourages all applicants to describe clearly patient and stakeholder engagement in their research proposals. PCORI understands that patient and stakeholder engagement in research can take many forms; it is not seeking one particular type or method of engagement. Rather, applicants should communicate how patients (those with lived experience), family members, caregivers, and the organizations that represent them, as well as any other relevant stakeholders, will be involved in study activities. Because this type of engagement in research is a relatively new concept, PCORI has developed the Engagement Rubric\(^4\) to guide both applicants and merit reviewers. This rubric is intended to provide examples of engagement and is not intended to be prescriptive. As noted above, studies are expected to adhere to PCORI’s Methodology Standards Associated with Patient-Centeredness as well as to the PCOR Engagement Principles found within the rubric. These and additional resources are available in PCORI’s Engagement in Research page.

**Populations Studied**

PCORI seeks to fund research that includes populations that are diverse 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 heterogeneity of treatment effect (HTE). PCORI

\(^3\) Available at http://www.pcori.org/research-we-support/the-pcori-methodology-report/.

recognizes that some proposed studies may represent important PCOR opportunities even in the absence of a broadly diverse study population. However, the burden is on the applicant in such cases to justify the importance of the study in the absence of diversity and to discuss which subgroups are most important and how they will be analyzed—including whether 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 effects of the strategy might differ across subpopulations. PCORI has developed a list of populations of interest to guide our efforts in research and engagement (note that the Addressing Disparities program requires that proposed research focus on at least one of the groups indicated by an asterisk below):

- 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. Describe the protection of human subjects involved in your proposed 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,” in the Supplemental Grant Application Instructions for All Competing Applications and Progress Reports, issued by the U.S. Department of Health and Human Services (HHS). 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

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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 Protections⁶). Reviewers’ comments on human subject research are not reflected in the overall application score, but PCORI staff may be use them 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 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 from the NIH website.⁷

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 findings in other populations. Please propose a method for sharing data and appropriate documentation upon request.

Recruitment
Proposals should include information about the size and representativeness of the potential pool of patients from which recruitment will occur and the means by which this size estimate was determined. Likewise, proposals should provide evidence-based estimates of how many participants are ultimately expected in the study, based on expected recruitment, application of the study’s inclusion and exclusion criteria, anticipated acceptance (or refusal) rates, and other factors, such as loss to follow-up. Such estimates must be discussed in the applications, must be specified in the milestones, will be reviewed by merit reviewers and PCORI staff, and will be monitored 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 (Board) 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, and 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

Letter of Intent (LOI)

IMPORTANT: With the Cycle 1 2016 Cycle, the Assessment of Prevention, Diagnosis, and Treatment Options Program will be using a screening LOI. You may submit a full application only if invited to do so based on your LOI. Applicants should download the Letter of Intent Template for the Assessment of Prevention, Diagnosis, and Treatment Options 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 and applicants should use in-text citations. The final references page will not be included in the three-page limit. LOIs that exceed the three-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. Please visit the PCORI Funding Center for additional applicant resources, including the PFA and required templates.

The LOI will be evaluated based on the following characteristics of the proposed study:

- Specific aims
- Condition burden and impact
- Evidence gap analysis
- Study design
- Description of participants and participating study site(s)
- Outcomes
- Power calculations
- Hypothesized effect size for intervention on main patient-centered outcome
- Sample size
• Comparators (listed)
• Description of comparators
• Engagement
• “Real-life” applicability of strategies

The LOI Template includes guidance for each item’s response. Please refer to the Application Guidelines for due dates and information on how to submit your LOI via PCORI Online.

Letter of Intent Review

LOIs are evaluated on the following criteria:

• Importance and relevance of the topics to PCORI priorities, as evidenced by critical gaps identified by clinical guidelines developers and recent relevant systematic reviews
• Clarity and credibility of applicants’ responses to the LOI questions
• Programmatic fit and balance, taking into consideration whether the proposed research overlaps previously funded studies or concurrent applications to a significant degree or, conversely, whether the application fills an important gap in PCORI’s portfolio of projects

Only applicants whose LOIs are deemed most responsive to this PFA will be invited to submit a full application. LOIs are reviewed by a minimum of two PCORI staff and are not scored during review. Applicants will be notified no later than April 8, 2016 whether or not they have been selected to submit full applications. PCORI will accept full applications only from organizations so selected.

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
• 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 can 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.
Budget and Project Duration

The maximum budget for this PFA is $2 million total direct costs. The maximum research period of performance is three years (not including peer review). The maximum budget includes all research and peer-review-related costs. (Please refer to the Application Guidelines for further details.) PCORI will not cover costs for interventions that are being compared in the proposed study. For additional details and a complete list of allowable and unallowable costs, refer to Appendix 2 in the Application Guidelines. This program does not consider exceptions to the budget and period-of-performance limits. If you submit an application that exceeds the $2 million total direct cost cap or the three-year period of research performance, your application will not be reviewed.

Submission Dates

LOIs and applications must be submitted in accordance with the published dates and times listed in the Overview and in the PCORI Funding Center.

PCORI Online System

To submit an application, you must register with PCORI Online and submit both an LOI and an application for each cycle to which you are applying.

Applicant Resources

- PCORI Funding Center: [http://www.pcori.org/Cycle-1-2016-options/](http://www.pcori.org/Cycle-1-2016-options/)
- PCORI Online System: [https://pcori.fluxx.io](https://pcori.fluxx.io)
- PCORI Funding Awards: [http://www.pcori.org/research-results](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 research funded by PCORI 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 award approval.

**Preliminary Review**

PCORI conducts rigorous merit reviews of all of the full 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; is 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, describes research that is not comparative, 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. Potential for the study to fill critical gaps in evidence**

The proposal should address the following questions:

- Does the application convincingly describe the clinical burden?
- Does the application identify a critical gap in current knowledge as noted in systematic reviews, clinical practice guidelines, or previous research prioritizations?
- Does the application identify a critical gap in current knowledge evidenced by inconsistency in clinical practice and decision making?
- Would research findings from the study have the potential to fill these evidence gaps?

**Criterion 2. Potential for the study findings to be adopted into clinical practice and improve delivery of care**

The application should describe how evidence that is generated from this study could be adopted into clinical practice and delivery of care by others. The application should address the following:

- Does the application identify who will make the decision (i.e., the decision maker) or use (i.e., the end-user) the study findings (not the intervention) produced by this study, such as local and national stakeholders?
- Does the application identify potential end-users of study findings, such as local and national stakeholders, and describe strategies to engage these end-users?
- Does the application provide information that supports a demand for this kind of a study from end-users?
Would research findings from this study have the potential to inform decision making for key stakeholders? Provide example(s). How likely is it that positive findings could be reproduced by others, resulting in improvements in practice and patient outcomes? Identify the potential barriers that could hinder adoption of the intervention by others.

Does the application describe a plan for how study findings will be disseminated beyond publication in peer review journals and national conferences?

**Criterion 3. Scientific merit (research design, analysis, and outcomes)**
The application should show sufficient technical merit in the research design to ensure that the study goals will be met.

- Does the proposal describe a clear conceptual framework anchored in background literature which informs the design, key variables, and relationship between interventions and outcomes being tested?
- Does the application provide justification that the outcome measures are validated and appropriate for the population?
- Does the research plan describe rigorous methods that demonstrate adherence to PCORI’s Methodology Standards?
- Is each of the comparators (e.g., active intervention arm and comparator arm) clearly described and well justified? If “usual care” is one of the arms, is it sufficiently justified and will it be sufficiently measured?
- Are the sample sizes and power estimates based on careful evaluations of the anticipated effect size? Is the effect size adequately justified in relation to the size or dose of the intervention and the research design (e.g., cluster randomized design)?
- Is the study plan feasible?
  - Is the project timeline realistic, including specific scientific and engagement milestones?
  - Is the strategy for recruiting participants feasible?
  - Are assumptions about participant attrition realistic, and are plans to address patient or site attrition adequate?

**Criterion 4. Patient-centeredness**
The application should demonstrate that the study focuses on improving patient-centered outcomes and employs a patient-centered research design (i.e., design is informed or endorsed by patients). *(Note: study can be patient-centered even if the end-user is not the patient, as long as patients will benefit from information.)* The proposal should address the following:

- Does the application include a thorough description of which outcomes (both benefits and harms) are important to patients, and are those outcomes included in the study plan?
- Does the application provide information that indicates that closing the evidence gap is important to patients and other stakeholders?
• Are the interventions being compared in the study available to patients now, and are they the best options for comparison (including whether they would be chosen by patients and their healthcare providers for managing the condition being studied)?

Criterion 5. Patient and stakeholder engagement
The proposal should demonstrate the engagement of relevant stakeholders (e.g., patients, caregivers, clinicians, hospitals and health systems, payers [insurance], purchasers [business], industry, researchers, policy makers, and training institutions) in the conduct of the study. Quality of engagement should be evaluated based on the scope, form, and frequency of patient and stakeholder involvement throughout the entire research process. The proposal should address the following:

• Does the application provide a well-justified description of how the research team is interdisciplinary? Does the study include the right individuals (researchers, patients, clinicians, other stakeholders) to ensure that the projects will be carried out successfully?

• Does the application show evidence of active engagement among scientists, patients, and others throughout the entire research process (e.g., formulating questions, identifying outcomes, monitoring study, dissemination, and implementation)? Are the frequency and level of patient and stakeholder involvement sufficient to support the study goals?

• Is the proposed engagement plan appropriate and tailored to the study?

• Are the roles and the decision-making authority of all study partners and investigators clearly described?
  o (Dual-PI Option Only) Does the leadership plan adequately describe and justify roles/areas of responsibility of the PIs?

• Are the organizational structure and resources appropriate to carry out the project?

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 PCORI’s 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 forward to in-person review.

During the in-person review, merit reviewers meet to discuss applications, to clarify further the merits of the proposed research, and to identify areas for improvement. In addition, each application is re-scored based on the content of discussion. The chair and PCORI IMRO 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 of Governors. The Selection Committee considers recommendations and works with staff to identify a slate of applications for possible funding based on merit review scores, programmatic balance and fit, and PCORI’s strategic priorities. This slate is then proposed to PCORI’s Board for its 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 PCORI’s 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 current cycle’s PFA will receive summary statements in October 2016 and notification of the funding status of their applications no later than November 2016.