# Limited PCORI Funding Announcement:

## Patient-Powered Research Network (PPRN) Research Demonstration Project: A Cross-PPRN Opportunity

Published October 26, 2015

This limited PCORI Funding Announcement (PFA), which applies to the Cross-PPRN Research Demonstration Projects, closes on March 28, 2016 at 5 p.m. (ET). Funding announcements, templates, and other resources are available at http://www.pcori.org/PFA-Cross-PPRN-Demo-Project.

**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 in order to enhance its work. PCORI helps people make informed healthcare decisions and improves healthcare delivery and outcomes by producing and promoting high-integrity, evidence-based information that comes from research guided by patients, caregivers, and the broader healthcare community.

PCORI was authorized by the Patient Protection and Affordable Care Act of 2010 as a nonprofit, nongovernmental organization. PCORI's purpose, as defined by the Act, is to help patients, clinicians, purchasers, and policy makers make better-informed health decisions by "advancing the quality and relevance of evidence about how to prevent, diagnose, treat, monitor, and manage diseases, disorders, and other health conditions."

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# Overview

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| Published | October 26, 2015 |
| Summary | Patient-powered research networks (PPRNs) were funded by PCORI with the intent of supporting communities or networks of patients motivated to participate in clinical research through the National Patient-Centered Clinical Research Network (PCORnet) and to develop their capacity to govern the research activities of their networks. |
| | The PPRNs have a unique opportunity, as participating networks in PCORnet, to broaden the scope of their research to include topics that not only are relevant to their individual communities, but are meaningful to all patients. Demonstrating the capacity to conduct research across conditions will enhance research capacity and encourage sustainability. |
| | In this limited funding announcement, PCORI seeks to fund up to one comparative effectiveness research (CER) project that will demonstrate scientific, operational, and logistical capacity to collaborate across PPRNs. This Cross-PPRN research project must include at least three collaborating PPRNs, and address comparative clinical and/or health care services questions that reflect shared information needs and decisional uncertainties commonly faced by the collaborating PPRN communities. |
| | There are three objectives: <br> 1. <u>Relevance:</u> Support research on an important comparative clinical and/or health care services question that was generated and prioritized by the participating PCORnet PPRN communities and that remains unanswered due to insufficient or inconclusive evidence. <br><br> 2. <u>Collaboration:</u> Develop efficient processes that demonstrate collaborative research capacity across PPRN networks. Use, develop, and contribute to PCORnet's shared tools and resources (the PCORnet Commons) to accelerate the conduct of research using PCORnet infrastructure. <br><br> 3. <u>Evaluation:</u> Formally test and evaluate the impact of the research project on PCORnet's capacity to support collaborative research and extend the breadth of the PCORnet Commons. |
| Applicant Resources | http://www.pcori.org/PFA-Cross-PPRN-Demo-Project |
| Key Dates | Online System Opens: October 26, 2015 <br> Letter of Intent Town Hall: November 16, 2015 <br> Letter of Intent Deadline: January 6, 2016 <br> Letter of Intent Notification: January 19, 2016 <br> Applicant Town Hall: February 15, 2016 <br> Application Deadline: March 28, 2016 by 5 p.m. (ET) <br> Merit Review: May 2016 <br> Awards Announced: July 2016 <br> Earliest Project Start Date: August 2016 |
| Maximum Project Budget (Total Costs) | $4 million |
| Funds Available up to | $4 million |
| Maximum Project Period | 3 years |

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| **Eligibility** | For this limited PFA, PCORI is soliciting applications only from PPRNs that are funded by PCORI as part of Phase II of the PCORnet initiative.<br><br>The Internal Revenue Service must recognize all applicant organizations. |
| **Review Criteria** | 1. Potential for study to improve health care and outcomes<br>2. Technical merit<br>3. Patient-centeredness<br>4. Patient and stakeholder engagement |
| **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 before an application deadline.<br><br>Please email (pfa@pcori.org) for any administrative, financial, or technical questions. PCORI will provide a response within two business days. Applicants may also call the helpdesk (202-627-1885) for technical or administrative support. Please note that during the week of the application deadline, response times may exceed two business days. 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, respectively. |

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# I. Introduction

## Summary of Program

To improve our nation's capacity to conduct clinical research efficiently and to answer important questions faced by patients, clinicians, and other key stakeholders, PCORI provided $105 million in 2014 to begin building the infrastructure for PCORnet. This large network includes networks of participants from across the country and is intended to support research to improve health outcomes.

In Phase I of PCORnet, PCORI awarded funds for the development of 11 clinical data research networks (CDRNs), which are based in large health systems; 18 patient-powered research networks (PPRNs), which are operated by patient-led groups; and one coordinating center (www.pcornet.org). In Phase II, PCORI expanded PCORnet to include 13 CDRNs and 20 PPRNs. To create a nimble and efficient national resource, the networks need to be collaborative, well-integrated, and highly adaptable. PCORnet's value will ultimately depend on its ability to facilitate relationships across PPRNs, CDRNs, and other key stakeholders in order to conduct collaborative research supported by tools and resources that have broad utility. This collaborative research may directly address comparative clinical or healthcare services questions that reflect shared information needs and decisional uncertainties commonly faced by collaborating PPRN communities. This funding announcement is directed at supporting cross-cutting research that addresses these pressing evidence gaps.

PCORI will fund up to one collaborative Cross-PPRN research project as part of Phase II. This award will support research that not only is relevant to an individual network, but is meaningful to the larger participant community. Through this limited funding announcement, the PPRN networks will be able to organize and collaborate in a multi-network study to develop efficient scientific, operational, and logistical processes. It is envisioned that this collaborative initiative will demonstrate the transformative nature of research conducted across disease communities, uniting individual networks around a common question. As a complement to the PPRN Individual Research Awards, this Cross-PPRN award intends to broaden the collaborative capacity of PCORnet's data infrastructure and can enhance the breadth of the PCORnet Commons, a repository of shared tools, knowledge, expertise, and infrastructure processes that accelerate the conduct of collaborative research.[1] This demonstration project will support PCORnet sustainability by enhancing the PPRNs' capacity to conduct collaborative research. Being able to respond collaboratively to requests to participate in comparative clinical or healthcare services research relevant to a broad range of participant communities will be important for sustaining the long-term viability of a PPRN.

## Research of Interest

PCORI seeks to fund participant-driven comparative effectiveness research (CER) that answers a question that is meaningful to the PCORnet PPRN community. PCORI is particularly interested in a study that:

- Proposes a cross-cutting research question that is generated and prioritized by the participating

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[1] Fjeldstad, Oystein, Snow, Charles, Miles, Raymond, Lettl, Christopher (June 2012).The Architecture of Collaboration, *Strategic Management Journal*, Volume 33, Issue 6, pages 734–750.

PCORnet PPRN communities. This comparative clinical or healthcare services question should reflect shared information needs and decisional uncertainties commonly faced by the collaborating PPRN communities. Topics of particular interest include, but are not limited to:

    a. Cross-cutting conditions or co-morbidities, such as depression, that may influence treatment outcomes or treatment adherence.

    b. The coordination of care across healthcare settings, including interventions that facilitate access to transitional care services from adolescence to adulthood and improve outcomes that matter to patients and caregivers. The interventions should be scalable across conditions and different forms of transitional care. Outcomes important to patients and their caregivers should be included, such as overall health, survival functional ability, health-related quality of life, stress, severity of symptoms, and unanticipated healthcare utilization.

    c. Services and care delivery strategies that incorporate involvement and support of patients and their families or other caregivers in care for patients with chronic conditions. Studies measuring patient and caregiver outcomes (e.g., health-related quality of life, symptom relief, caregiver stress, caregiver well-being) are of particular interest.

- Provides a clear rationale for the PPRN partnerships selected (and CDRNs, where appropriate) and justifies the collective capacity to address the proposed research question.

- Demonstrates a clear strategy by which the participating networks will collectively support the efficient design and conduct of the collaborative research project by utilizing or developing relevant resources from the PCORnet Commons.

- Identifies critical aspects of the PCORnet research infrastructure that will be tested and describes how the capacity of each participating network, and PCORnet overall, will be enhanced as a result of the collaborative research project proposed. Aspects to be assessed should include, but are not limited to, operational processes between participating networks and the Coordinating Center (CC), governance policies required for multi-network studies, processes related to multi-network contracting and Institutional Review Board (IRB) approval, and integration of stakeholder engagement at the local network and study-wide levels.

- Partners with patients, clinicians, and other key stakeholders throughout the entire research process, from idea generation, through study development and conduct, to dissemination and implementation of findings

Studies that are designed to conduct clinical CER either as observational studies or randomized clinical trials are strongly encouraged. Comparators should be known to be efficacious or in wide clinical use but not yet directly compared in previous high-quality studies; it may be appropriate to include as a comparator a generally accepted practice for which there is insufficient evidence of efficacy or effectiveness. Applications should describe earlier studies in sufficient detail to explain why the evidence from those studies is not adequate.

## Cross-PPRN Research Demonstration Project Objectives

This limited PFA will provide PPRNs the opportunity to test their capacity to conduct collaborative research on behalf of participant communities within their own network and across PPRNs. The Cross-PPRN Research Demonstration Project has three main objectives:

1. **Relevance**: Support research on an important comparative clinical or healthcare services research question that is generated and prioritized by the participating PCORnet PPRN communities and that remains unanswered due to insufficient or inconclusive evidence.

2. **Collaboration**: Develop efficient processes that demonstrate collaborative research capacity across PPRN networks. Use, develop, and contribute to PCORnet's shared tools and resources (the PCORnet Commons) to accelerate the conduct of research using PCORnet infrastructure.

3. **Evaluation**: Formally test and evaluate the impact of the research project on PCORnet's capacity to support collaborative research and extend the breadth of the PCORnet Commons.

Applicants are strongly encouraged to review the lists of funded research on PCORI's website and clinicaltrials.gov to ensure that their proposed research does not duplicate projects already funded.

PCORI expects all awardees to commit to utilizing a centralized or single Institutional Review Board for the research study.

## PPRN Capacity Building

For this limited PFA, PCORI is soliciting applications from PPRNs that are funded by PCORI as part of Phase II of the PCORnet initiative that are collaborating with other PPRNs, CDRNS, the CC, and other key stakeholders in order to enhance the collaborative capacity of PCORnet. The collaborating partners should be selected based on key factors, including the level of interest and current readiness of the network to participate fully in the research study; the comprehensiveness of the data at each participating network to support the collection of necessary data elements to conduct the study; the capacity of each participating network to utilize the Common Data Model (CDM) where appropriate; and the required expertise and knowledge of the partners to collectively address the proposed research question.

To ensure that the most efficient, collaborative research processes are developed as a result of this demonstration, we encourage collaboration between as many PPRNs as appropriate for the proposed research question, with the final application including a minimum of three PPRNs (including the lead PPRN). The collaborations are expected to support both the conduct of research and the development of relevant tools and resources within the PCORnet Commons. While PCORI will only fund up to one Cross-PPRN award, PCORI will accept more than one application for review. A PPRN may be involved in up to two applications (including the one the PPRN may be leading). Only one PPRN or PPRN-affiliated institution can lead the application.

The Awardee Institution is responsible for the study, including oversight and dispersion of funds to any and all necessary subcontracts, including institutions from the CDRNs, PPRNs, and the CC. Additional

details for developing the research plan can be found in the Application Guidelines.

PCORI will initially ask PPRNs to submit a Letter of Intent (LOI; see Section III below) and will then invite selected applicants to prepare a full application.

### Continuation of Project

Funding for Years Two and Three will be contingent upon successful progress towards and completion of deliverables (which will be determined during the contract negotiation phase) and an interim report. The interim report will identify challenges encountered, solutions identified, and enhancements made to the research study during the first year. The deliverables and interim report will need to demonstrate the feasibility of the research plan and redesign, where appropriate.

# II.  Guidance for Proposing Research

The application must include a detailed research plan with a clear collaboration component, an engagement plan, an evaluation plan, a staffing plan, and a budget. Please see the Research Plan Template and Application Guidelines, which can be found in the Funding Center, for more detailed instructions on these elements.

### Guidance on the Research Plan

This section relates to the PFA aims of **relevance** and **collaboration**.

All research plans must include a justification for:

- The research question's importance to the participating PCORnet PPRN communities (evidence that all collaborating PPRNs participated in the generation and prioritization of the research question)

- The need to address the targeted evidence gap

- The choice of study design to answer the research question

- The anticipated impact of the study results on patient health outcomes

- The relevance of the patient-reported outcomes selected

- Key aspects of the collaborative activities, including how the activities will be managed and led by the PPRN collaborators, the key responsibilities for each collaborator, how coordination will be enhanced and conflict mitigated, and relevant training or resources that may be necessary to facilitate the effectiveness of the collaboration and budget allocation (IOM, 2015[2])

- Tools and resources that will be utilized, developed, or enhanced for the project, including but not limited to:
    - o  Data governance policies and procedures

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[2] Available at http://www.nap.edu/catalog/19007/enhancing-the-effectiveness-of-team-science.

- o Network policies
- o Procedures and protocols
- o Data-use agreements
- o Business associate agreements
- o Contracting processes
- o Processes related to IRB submissions
- o Development of computable phenotypes
- o Measures of and procedures for using patient-reported outcomes
- o Training for patients and academic/clinical stakeholders
- o Sharing across PPRNs of staff with specific expertise (e.g., biostatistics)

- A proposal for what tools and resources developed will be made available to the PCORnet community, and a related timeline
- A timeline that includes clear and specific scientific and engagement milestones

Additionally, where relevant, the plan should:

- Describe the data sources, means of data collection, follow-up period, study endpoints (including method by which events will be ascertained), statistical analyses, and anticipated limitations
- Describe how data will be captured for the proposed study, including the extent to which data already collected during Phase I will be leveraged for the research project, where appropriate, and the additional data collection efforts that will be required during Phase II
- Characterize the participants in the proposed study and provide evidence to justify anticipated enrollment
- Identify how data elements from the PCORnet Common Data Model (CDM) Version 3.0 will be used
- List data elements not currently captured by CDM Version 3.0 that will be necessary for the research study and describe how these data elements could be incorporated into future versions of the CDM
- Address confounding and discuss the appropriateness of the analytic models proposed
- Discuss potential limitations to the collaborative study and how the limitations will be addressed
- Provide a detailed plan for data sharing, where appropriate (see below)
- Indicate whether the collaborating PPRNs have an IRB Master Reliance Agreement

The research plan should indicate how the project will:

- Compare at least two clinical interventions or treatments

  o Optimally, the study will compare two or more defined strategies. In general, "usual care" is not an appropriate comparator for CER studies submitted to PCORI for funding consideration. "Usual care" is too often ill-defined, difficult to quantify, and subject to considerable geographic and temporal variations, limiting its interpretability, applicability, and reproducibility. If the applicant proposes "usual care" as a rational and important comparator in the proposed study, then it must be described in detail and be properly justified as a legitimate comparator (e.g., usual care is guidelines-based). In addition, 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.

- Evaluate the benefits and harms of each intervention as delivered in typical clinical or community settings

- Ensure that the health outcomes studied are meaningful to the patient population under study; in selected instances, surrogate physiological measurements may be sufficiently linked to final health outcomes of interest, but they may not be the sole study outcome

## Guidance on the Engagement Plan

PCORI requires all applicants to describe clearly the patient and stakeholder engagement planned for their proposed project. PCORI is not seeking one particular type or method of engagement. In addition, studies are expected to adhere to PCORI's Methodology Standards Associated with Patient-Centeredness and to the PCOR Engagement Principles found within the PCORI Engagement Rubric. These and additional resources are available in PCORI's Funding Center.

The PCORI Engagement Rubric also provides guidance on promising practices to consider when developing an engagement plan.

The engagement plan for this application must:

- Describe how the participating PCORnet PPRN community identified and prioritized the research question proposed and the methods used

- Provide a detailed plan for how stakeholders will partner throughout the research process; the Engagement Rubric provides guidance on promising practices for engagement in the planning, conduct, and dissemination of research

- Describe the mechanisms proposed to disseminate information to the PPRN participant community throughout the study period, including information on data use and sharing, relevant interim results, changes to the initial plan, and final outcomes of the study

- Include an evaluation of the dissemination strategies to ensure their effectiveness from a stakeholder perspective. Characteristics to be assessed include the accessibility, appropriateness, and adequacy of the mechanism by which the information was delivered as well as the content and presentation of the information provided

Applicants are encouraged to budget for engagement activities appropriately, including the cost of meetings, travel, and other necessary expenses. In recognition of the value of their contributions, PCORI strongly encourages financial compensation for patient and stakeholder partners serving on research teams.

## Guidance on the Evaluation Plan

This section relates to the PFA aim of **evaluation**.

A significant aim of the Cross-PPRN demonstration project is to test, evaluate, and report on the readiness of PCORnet's collaborative infrastructure, including scientific, operational, and logistical components. The applicant should develop a plan formally to test and evaluate the impact of the research project on PCORnet's capacity to support collaborative research and extend the breadth of the PCORnet Commons. The applicant will also be expected to report on solutions implemented to resolve technical issues encountered.

The application should include a list of activities and a timeline describing the evaluation process. Results from the evaluation will be described in an interim report to PCORI at the end of the project's first year and summarized at the end of the project in a final report that will be made available to the PCORnet community.

The evaluation plan for this application must:

- Identify key activities to be evaluated that will demonstrate feasibility of the research project during the first year of the award

- List the proposed resources that will be utilized or developed and made available to the PCORnet Commons and describe how their effectiveness will be evaluated

- Describe how the project will assess the impact of the collaborative aspects of the research study (between PPRNs and other stakeholder partnerships) on meeting the technical assistance needs of the PPRN community, enhancing the PCORnet Commons, and strengthening the capacity of PCORnet to conduct research

  - Aspects to be considered for evaluation should include but not be limited to operational processes between participating networks and the CC, governance policies required for multi-network studies, processes related to multi-network contracting and IRB approval, and integration of stakeholder engagement at the local network and study-wide levels.

- Describe how the project will evaluate scalability and accessibility of the resources developed for the research project to the larger PCORnet community. Scalability refers to the adaptability and utility of the tools or resources for other PPRNs within the larger PCORnet community

## Selection of the Principal Investigators

Cross-PPRN proposals must be led by at least two co-Principal Investigators (PIs), one of whom is designated as lead PI and has the requisite qualifications and training for conducting the proposed research consistent with any applicable human subject research laws or other laws and any requirements of the applicable IRB. The lead PI must come from the applicant PPRN (or affiliated

institution); however, additional co-PIs may be from other PPRNs. The PIs for this research demonstration proposal can be different from the PPRN PIs. The two PIs should follow the designations listed below.

**(1) PI representing patients, caregivers, or the community**

At least one PI should have the following expertise or experience:

- Meaningfully representing participant perspectives as a patient, caregiver, or community member

- Working collaboratively with researchers

Given the challenges for patients or caregivers with full-time jobs to commit significant time to a research project of this nature, PCORI will be flexible with the time commitment from the patient PI.

**(2) PI representing researchers or clinicians**

At least one PI should have the following expertise or experience:

- Researching in the content area of the proposal

- Researching in epidemiology or health services

- Working with data from his or her host institution

- Leading research studies collaboratively with patient partners

## Nonresponsiveness

Applications will be considered nonresponsive to this PFA if the proposed research:

- Duplicates questions already present in the research topic database

- Exceeds the limits on budget and project duration (see below)

- Tests efficacy (the ability to produce the intended result) or comparative efficacy within a tightly protocol-controlled research setting (as opposed to a more real-world, clinical setting)

- Conducts a formal cost-effectiveness analysis in the form of dollar-cost per quality-adjusted life year to compare two or more alternatives

- Directly compares the costs of care between two or more alternative approaches

PCORI does have an interest, however, in studies of conditions that lead to high costs to the individual or to society. PCORI is also interested in studies that examine healthcare resources or costs as a determinant of—or barrier to—good outcomes. Examples include ways in which out-of-pocket costs may constitute barriers to care.

Further, PCORI considers it important for applicants to discuss cost-related issues, such as the resources needed to implement, replicate, or disseminate a successful intervention. PCORI is interested in the evaluation of interventions intended to reduce health-system waste or increase health-system efficiency. Proposals that include studies of these issues without using a formal cost-effectiveness analysis or comparing the costs of alternatives are considered responsive.

### Features of Patient-Centered Outcomes Research

Patient-centered outcomes research (PCOR) helps people and their caregivers communicate and make informed healthcare decisions, allowing their voices to be heard in assessing the value of healthcare options. This research:

- Assesses the benefits and harms of preventive, diagnostic, therapeutic, palliative, or health-delivery-system features to inform decision making, highlighting the choices that matter to people
- Includes an individual's preferences, autonomy, and needs, focusing on outcomes that people notice and care about, such as survival, functioning, symptoms, and health-related quality of life
- Incorporates a wide variety of settings and diversity of participants to address individual differences and barriers to implementation and dissemination
- Directly compares clinical interventions that are generally available in settings where people access health care

### Preliminary Data and Use of Accepted Measures

PCORI encourages investigators to design their research using valid patient-centered outcome (PCO) measures and to include preliminary data that supports the proposed measures. Investigators are encouraged to consider those measures described in the Patient-Reported Outcomes Measurement Information System.

### Justification of Assumptions

PCORI specifically seeks studies that are large enough to detect clinically meaningful effects. To that end, applicants must justify the proposed sample sizes by explaining the assumptions used to decide on those numbers. The application should clearly state all the necessary assumptions (i.e., the primary outcome measure, estimated difference in the mean value of this measure between study arms, standard deviation of the measure, type I error rate, and any other assumptions). All such estimates must be justified by referring to prior published research or preliminary data.

### Adherence to Methodology Standards

Regardless of study design, proposals must adhere to all relevant PCORI Methodology Standards. These 47 individual standards fall into 10 categories. The first five categories are cross-cutting and relevant to most PCOR studies. Researchers should refer to the standards in these categories when planning and conducting their research projects. The 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

Five other categories of standards will be applicable to particular study designs and methods and should

be used for guidance when relevant. These categories are:

- 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

These should be considered minimal standards. Relevant additional best practices—including guidelines for the conduct of clinical trials developed by other organizations—should be addressed in the application.

### Recruitment

Proposals should include information about the size 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 and specified in the milestones. These estimates will be reviewed by merit reviewers and PCORI staff and monitored by PCORI in the funded research.

### Protection of Human Subjects

In the Research Plan Template, describe the protection of human subjects involved in your research. Use up to five pages. 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 the Section 5 "Human Subjects Research Policy" from the Supplemental Grant Application Instructions for All Competing Applications and Progress Reports[3] issued by the US Department of Health and Human Services. PCORI does not require that applicants comply with sections of this policy that refer to requirements for federal-wide assurance, or that refer to standards for inclusion of women, minorities, and children.

PCORI does require applicants proposing clinical trials to consider including 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 the protection of human subjects in all applications and may provide comments regarding the plans (see How To Evaluate Human Subjects Protections[4]). Reviewers' comments on human subjects research are not reflected in the overall application score but may be used by PCORI staff during any potential funding negotiations. Final determinations about adequacy of human subject protections rest with the IRB or IRBs that have jurisdiction for the study.

The Awardee Institution or organization, whether domestic or foreign, bears ultimate responsibility for

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[3] See http://grants.nih.gov/grants/funding/424/supplementalinstructions.docx.
[4] See http://www.pcori.org/sites/default/files/PCORI-Checklist-for-Evaluating-Human-Subjects-Protections.pdf.

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 in the application as key personnel. The policy and FAQs are available from the NIH website.[5]

## Replication and Reproducibility of Research and Data-Sharing Plan

PCORI is committed to maximizing the utility and usability of data collected in our funded projects. This is essential to building confidence in the accuracy of these findings. PCORI supports policies to promote sharing of study documentation (e.g., study protocol, programming code, and data definitions) so that other researchers may replicate the findings in other populations. Please propose a method for sharing data and appropriate documentation upon request.

## Peer Review and Release of Research Findings

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

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

PCORI will post the following materials on its website no later than 90 days after the draft final research report is accepted: a 500-word abstract for medical professionals, a standardized summary of the study's results for patients and the general public, and a link to the study record on ClinicalTrials.gov (as applicable). The final research report, along with the 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.

## Budget and Project Duration

The maximum budget for this study in this limited PFA is $4 million in total costs. The maximum 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 consider exceptions to the budget and period of performance limits. If you submit an application that exceeds $4 million in total costs or three years in period of performance, your application will be

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[5] See http://grants.nih.gov/grants/guide/notice-files/NOT-OD-08-054.html.

removed for noncompliance. In the budget justification, the budget for the research activities should be clearly delineated from the budget for the evaluation activities.

# III. How To Submit a Proposal

## Letter of Intent

Applicants are required to submit a Letter of Intent (LOI) for the Cross-PPRN Research Demonstration Project.

Applicants should download the LOI Template from the PCORI Funding Center. They must complete the document and convert it to a PDF with a length limit of four pages. All references must be listed at the end of the LOI. LOIs that exceed the page limit (excluding references) will not be reviewed.

Do not upload additional documents as part of your LOI. Letters of endorsement or support are not required at this stage. Their inclusion will result in rejection of the LOI without review.

Please visit the PCORI Funding Center for additional applicant resources, including required templates.

Please answer all of the questions in the LOI Template and then upload your document into the PCORI Online System. The deadline for LOI submission is January 6, 2016 by 5 p.m. (ET).

## Letter of Intent Review

LOIs will be reviewed by PCORI staff for programmatic fit and responsiveness to the PFA and Application Guidelines. LOIs are evaluated based on the following characteristics of the proposed study:

- Specific aims

- Burden and impact

- Evidence gap analysis

- Study design

- Description of participants and participating study sites

- Description of comparators

- Power and sample size

- Rationale for partnerships identified

- Strength of the engagement approach

- Potential to contribute to the PCORnet Commons through the development of shared tools and resources

- Appropriateness of proposed team to achieve proposed aims

- Programmatic fit and balance

Applicants will be notified no later than January 19, 2016 as to whether they have been selected to submit a full application.

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

- Research question(s)

- Specific aims

- Study design

- Comparators

- Principal Investigator

- Institution

**Note:** LOIs that show scientific overlap or that appear to be duplicate submissions will be removed during the LOI screening process.

### Submission Dates

Applications must be submitted in accordance with the published dates and times listed in the Overview of this PFA and in the PCORI Funding Center.

### PCORI Online System

To submit an application, you must register with PCORI Online.

### Applicant Resources

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| **PCORI Funding Center** | http://www.pcori.org/PFA-PPRN-Demo-Projects |
| **PCORI Online System** | https://pcori.fluxx.io |
| **PCORI Funding Awards** | pcori.org/pfaawards |

# IV. Merit Review

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

- To identify applications that have strongest potential to help patients, caregivers, clinicians, and other stakeholders make informed decisions to improve patient outcomes

- To implement a transparent, fair, objective, 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 merit review processes 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 (expected to be no later than July 2016).

**Preliminary Review**

PCORI conducts rigorous merit review of the full applications it receives. Note that applications may be eliminated from the review process for administrative or scientific reasons (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 all understand the programmatic and organizational goals of review.

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

**Criterion 1. Potential for the study to improve health care and outcomes**

The proposal has the potential to lead to meaningful improvement in the quality and efficiency of care and to improvements in outcomes important to the PPRN participant community. This criterion is assessed through the following questions:

- Does the research question address a critical gap in current knowledge as noted in systematic reviews, guideline development efforts, or previous research prioritizations?

- Was the research question generated and prioritized by the PCORnet PPRN community?

- Does the applicant provide evidence, either from previous studies or from pilot work, that indicates the potential for a sizable benefit of the intervention relative to current practice?

- Does the applicant present a credible plan by which findings could be disseminated and implemented quickly within PCORnet (including at the local hospital or clinic level), resulting in improvements in practice and patient outcomes?

**Criterion 2. Technical merit**

The proposal has sufficient technical merit in the research design to ensure that the study goals will be

met. This criterion is assessed through the following questions:

- Does the research plan describe methods that demonstrate adherence to PCORI's Methodology Standards?

- Are each of the comparators clearly described and well justified? If usual care is one of the arms, is it sufficiently justified and will it be sufficiently measured?

- Does the application provide justification that the outcome measures are validated and appropriate for the population?

- Are the sample sizes and power estimates presented based on realistic and careful evaluations of the anticipated effect size, where appropriate? Is the effect size adequately justified in relation to the size or dose of the intervention and the research design?

- Is there a plan to recruit a representative study population, and has the applicant provided evidence that the recruitment of this population is feasible?

- Does the project include a realistic timeline that includes clear and specific scientific and engagement milestones?

- Does the research team have the necessary expertise to complete the research study successfully, including the collaborative aspects and the evaluation? If not, has the applicant partnered with appropriate organizations or experts to assist with their technical assistance needs?

- Does the applicant provide a clear rationale for the collaborative tools, training, and resources being adapted or developed, as well as compelling evidence that the PPRN partnerships selected will optimize the use of existing resources or enhance the efficiency of the co-design processes proposed?

- Do the collaborative aspects of the research project proposed provide an opportunity to transform PCORnet processes or enhance aspects of the PCORnet infrastructure?

- Does the applicant provide a robust approach to evaluating the contribution and impact of the project on the development of the PCORnet Commons and on PCORnet's capacity to support an increasing volume of research in Phase II and beyond?

**Criterion 3. 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 about 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 4. Patient and stakeholder engagement**

The proposal demonstrates 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 scope, form and frequency of patient and stakeholder involvement throughout 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 project 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 clearly described?

- 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 to be discussed at the in-person review meeting. Not all submitted applications move forward to in-person review.

During the in-person review, panels meet to discuss applications and to clarify further the merits of the proposed research, as well as to identify areas for improvement. Additionally, each application is re-scored based on the content of discussion. The Chair and PCORI MRO lead the in-person panel meeting and ensure that all applications receive a fair and thorough review informed by the standards outlined in the PFA.

## Post-Panel Review

After the in-person panel review, PCORI program staff evaluate merit review scores and comments, identify duplication or synergy among funded projects, and consider the fit of applications within the programmatic vision. Program staff members then recommend projects to a Selection Committee, which includes members of PCORI's Board. The Committee considers recommendations and works with

staff to identify a slate of applications for possible funding based on merit review scores, programmatic balance and fit, and PCORI's strategic priorities. This slate is then proposed to PCORI's Board for its consideration and approval. Up to one award will be proposed to PCORI's Board of Governors for its consideration and final approval.

## Summary Statements and Funding Recommendations

Summary statements are provided to applicants approximately two weeks before funding decisions are announced.

Funding recommendations are made by identifying meritorious applications that fit the programmatic needs and that satisfactorily address the merit review criteria while adhering to PCORI's Methodology Standards. Programs also consider the funds allotted for the current funding announcement when deciding which applications to recommend to PCORI's Board for approval. It is expected that applicants to this current cycle's PFA will receive summary statements in late June 2016 and notification of the funding status of their application no later than July 2016. The awards will be for three years, although funding for Years Two and Three is contingent on the one-year interim report, which must demonstrate the project's feasibility and the ability of its staff to redesign, where necessary.

## Contract Execution and Activation

PCORI will issue a contract to the selected Awardee Institution for the study once it conducts a thorough programmatic and administrative review. The awardee must accept PCORI's contract terms and conditions, which will be based on PCORI's research funding contract terms and conditions with additional provisions appropriate for the use of the PCORnet infrastructure and the specific research project. Among the expected contractual terms is a fully-agreed-upon study plan as evaluated by PCORI. The study will commence only after PCORI and the Awardee Institution execute the applicable contract and agree on the final protocol content.