



## **Cycle 2 2016 Funding Cycle**

### **PCORI Funding Announcement: Comparison of Surgical and Nonsurgical Options for Management of Nonspecific Chronic Low Back Pain**

Published April 4, 2016

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This PCORI Funding Announcement (PFA) applies to the funding cycle that closes on August 8, 2016, at 5 p.m. (ET). Application Guidelines, templates, and other resources are available at <http://www.pcori.org/Cycle-2-2016-low-back-pain>.



## **About PCORI**

The Patient-Centered Outcomes Research Institute (PCORI) is committed to transparency and a rigorous stakeholder-driven process that emphasizes patient engagement. PCORI uses a variety of forums and public comment periods to obtain public input to enhance its work. PCORI helps people make informed healthcare decisions and improves healthcare delivery and outcomes by producing and promoting high-integrity, evidence-based information that comes from research guided by patients, caregivers, and the broader healthcare community.

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

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## Overview

Published	April 4, 2016
Letter of Intent Due	May 4, 2016 by 5:00 p.m. (ET)  Letters of Intent (LOIs) will be screened for responsiveness to this PCORI Funding Announcement (PFA) and fit to program goals. Only those applicants selected will be permitted to submit full applications. Notification of denial or approval to submit a full application will occur no later than June 10, 2016.
Summary	<p>PCORI seeks to fund pragmatic clinical trials that compare surgical and nonsurgical options for management of nonspecific chronic low back pain. The research is expected to examine treatment options, as well as systems-level interventions or those aimed at eliminating health or healthcare disparities.</p> <p>Proposed studies must address clinical and healthcare delivery choices faced by patients, their caregivers, clinicians, or delivery systems. Proposed studies must compare two or more active interventions. They must involve patient populations that represent the U.S. population; be large enough to provide precise estimates of hypothesized effectiveness differences; and be large enough to support evaluation of potential differences in treatment effectiveness in patient subgroups.</p> <p>For this solicitation, applicants should document that they have consulted with patients and other stakeholders to identify the important decisional dilemmas and evidence needs that will drive development of the research questions or reference previously documented decisional dilemmas. Although PCORI does not require that relevant national patient organizations, professional organizations, and payer or purchaser organizations be formally included as partners and active participants prior to contract award, successful applicants may be required to develop such formal arrangements. PCORI may require a project Study Advisory Committee (SAC)<sup>1</sup> that is comprised of national or regional organizations that represent, at a minimum, patients and families with lived experience, relevant clinicians, payers, and health plans. Scientific and methodological experts may also be recommended for this oversight role. The SAC advises and assists the research team with refining the study questions, outcomes, and protocol. PCORI expects applications to follow the randomized controlled trial (RCT) study design specified for the research question. <b>Note that this funding program does not support applications to conduct cost-effectiveness analysis, systematic reviews, or development and evaluation of shared decision making or decision-support tools.</b></p> <p>The proposed studies must address the priority research question identified in the main body of the PFA.</p>
Applicant Resources	See <a href="http://www.pcori.org/Cycle-2-2016-low-back-pain">http://www.pcori.org/Cycle-2-2016-low-back-pain</a>

<sup>1</sup> The intent of the SAC described in the PFA is to ensure that a broad spectrum of stakeholders and patients advise and assist the research team with refining the study questions, outcomes, and protocols. These stakeholders and patients must include national or regional organizations that represent, at a minimum, patients or families with lived experience, relevant clinicians, payers, and health plans. Additional representation may be recommended in collaboration with PCORI, including individual patients with lived experience and other relevant stakeholders, such as scientific and methodological experts. However, PCORI understands that engagement structures and approaches vary widely. Other engagement approaches, such as forming stakeholder groups, panels, task forces, working groups, and other bodies, or involving individual patient and stakeholder partners in various ways are also permissible to employ—either in addition to or instead of—the formation of the SAC. The SAC provision is not meant to require that a separate governance or advisory entity be established beyond the study governance and advisory structure the awardee has planned, if an applicant already has an approach for including the relevant and required stakeholders and patient partners. For clarification in your application materials and merit review purposes, please indicate which body or structure is filling the SAC requirements, including the requirements for in-person meetings at least two times per year, and appropriate budgeting.



Key Dates	<p>Online System Opens: April 4, 2016</p> <p>Applicant Town Hall Session: April 20, 2016, 3:00 p.m. – 4:00 p.m. (ET)</p> <p>LOI Deadline: May 4, 2016, by 5:00 p.m. (ET)</p> <p>Screening Notification: June 10, 2016</p> <p>Application Deadline: August 8, 2016, by 5:00 p.m. (ET)</p> <p>Merit Review Dates: November 2016</p> <p>Awards Announced: January 2017</p> <p>Earliest Project Start Date: March 2017</p>
Maximum Project Budget (Total Direct Costs)	\$15 million
Maximum Project Period	Five years
Funds Available Up To	\$22 million
Eligibility	<p>Applications may be submitted by any private-sector research organization, including any nonprofit or for-profit organization; any public-sector research organization, including any university or college hospital or healthcare system, laboratory, or manufacturer; or any 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.</p>
Review Criteria	<ol style="list-style-type: none"> <li>1. Potential for the study to fill critical gaps and generate actionable evidence</li> <li>2. Potential for the study findings to be adopted into clinical practice and improve delivery of care</li> <li>3. Scientific merit (research design, analysis, and outcomes)</li> <li>4. Patient-centeredness</li> <li>5. Patient and stakeholder engagement</li> </ol>
Contact Us	<p><b>Programmatic Inquiries:</b> Contact the PCORI Helpdesk via email (<a href="mailto:sciencequestions@pcori.org">sciencequestions@pcori.org</a>) or phone (202-627-1884), or complete the Research Inquiry Form (<a href="http://www.pcori.org/content/research-inquiry">http://www.pcori.org/content/research-inquiry</a>). PCORI will provide a response within three business days. However, we cannot guarantee that all questions will be addressed in a timely fashion when the inquiry is made three or fewer business days before an LOI or application deadline.</p> <p><b>Administrative, Financial, or Technical Inquiries:</b> Contact the PCORI Helpdesk at <a href="mailto:pfa@pcori.org">pfa@pcori.org</a>. PCORI will provide a response within two business days. Note that during the week of the application deadline, response times may exceed two business days. One week before an application deadline, applicants may also call the PCORI Helpdesk (202-627-1885). Applicants are asked to plan accordingly. It is the applicant's responsibility to submit the application on or before the application deadline.</p>
Other	*Deadlines are at 5:00 p.m. (ET). If a deadline falls on a weekend or federal holiday, the deadline will be the following Monday or the next day after the federal holiday.

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## I. Introduction

### Summary of Program

The Patient-Centered Outcomes Research Institute (PCORI) is launching this funding initiative to support patient-centered comparative clinical effectiveness research (CER) that addresses important questions about the comparison of surgical and nonsurgical options for managing nonspecific chronic low back pain. Through this PCORI Funding Announcement (PFA), PCORI seeks to fund pragmatic clinical trials with a sufficient sample size to address the research question. This program's goal is to generate valid clinical evidence that is readily generalizable to the broader population of people with chronic nonspecific low back pain. The definition of this condition is low back pain on at least 50 percent of days in the past six months, unaccompanied by pain or neurological symptoms and signs in the lower legs, and without abnormalities on imaging tests other than degenerative disc disease<sup>2</sup>. This population includes those individuals who have progressed from a period of intermittent episodes of low back pain to the state of persistent pain on at least half of the days. Such people often have undergone various types of physical interventions, such as physical therapy, exercise programs, or spinal manipulation. They also may have participated in programs using psychological approaches to pain management. For the purposes of this funding announcement, the population does not include those individuals who have undergone previous surgical procedures to treat low back pain.

Applications must address the priority research question described in this funding announcement. The proposed study should also:

- Include patients with chronic nonspecific low back pain who are representative of the population faced with choosing between the proposed study interventions.
- Take place within typical clinical care sites that perform the compared interventions.
- Have a sufficiently large study sample to estimate precise effect sizes similar to those in past trials.
- Specify variables that could be used to define patient subgroups—such as individuals with differing demographic and socioeconomic characteristics and prior treatment history—who may respond differently to the interventions (Heterogeneity of Treatment Effect, or HTE).
- Compare the effectiveness<sup>3</sup> of the study interventions for improving patient-centered outcomes for chronic low back pain.

### Background

Low back pain is a common clinical condition. As many as one quarter of adults in the United States had

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<sup>2</sup> Deyo, R. A., Dworkin, S. F., Amtmann, D., Andersson, G., Borenstein, D., Carragee, E., Weiner, D. K. (2014). REPORT OF THE NIH TASK FORCE ON RESEARCH STANDARDS FOR CHRONIC LOW BACK PAIN. *The Journal of Pain: Official Journal of the American Pain Society*, 15(6), 569–585. <http://doi.org/10.1016/j.jpain.2014.03.005>

<sup>3</sup> "Effectiveness" is the extent to which an intervention does more good than harm in a broad mix of patients when provided under the usual circumstances of healthcare practice (modified from [ec.europa.eu/enterprise/sectors/healthcare/files/docs/rea\\_principles\\_en.pdf](http://ec.europa.eu/enterprise/sectors/healthcare/files/docs/rea_principles_en.pdf)).

back pain lasting a full day during the prior three months<sup>4</sup>. Although most episodes of low back pain are self-limited, some people have recurrent acute episodes, with periods of only minimal symptoms between these acute episodes. Some individuals then transition to a state of persistent low back pain that does not remit. This condition is known as “chronic low back pain” and is defined as low back pain occurring on at least half of the days in the preceding six months<sup>2</sup>. In the United States, low back pain is the largest contributor to years lived with disability<sup>5</sup>. An estimated 149 million workdays are lost every year in the United States due to low back pain<sup>6</sup>. The total costs related to back pain exceed \$100 billion per year in the United States, but only 5 percent of back pain patients generate 75 percent of these costs<sup>7</sup>.

CER on chronic nonspecific low back pain has been limited by several factors, including (1) a lack of consensus on the most clinically meaningful outcomes to measure; (2) small differences, if any, between most therapies within a given category when compared with one another (e.g., various types of psychological interventions); and (3) a lack of clarity in the extant literature regarding which patients respond to which therapies<sup>8</sup>. Because treatment options for low back pain are aligned with different professional disciplines (e.g., acupuncture, physical therapy, spinal manipulation, and spine surgery), existing referral patterns and access to different treatments could be a barrier to diffusion of best clinical practices (especially those that require combinations of multiple or complementary treatments). Thus, insights provided by new CER could have an important clinical impact.

Surgical intervention, which includes various approaches for excising portions of lumbar intervertebral disks and fusing or fixating lumbar vertebrae, is a mode of treatment that is being used with increasing frequency in the United States to manage chronic low back pain. Some patients have clearly defined anatomic conditions (defined by imaging studies and patterns of symptoms) that make them the most suitable candidates for surgical procedures<sup>9</sup>. Previous multi-center clinical trials have found that such patients attain modest benefits from surgery. However, many other patients who have less well-defined anatomic conditions also receive surgery. Ninety percent of lumbar vertebral fusion surgery is done for chronic nonspecific low back pain. The annual rate of lumbar fusion surgery increased almost threefold from 1988 to 2008<sup>10</sup>. A 2007 systematic review (Mirza and Deyo 2007)<sup>11</sup> summarized four randomized trials comparing lumbar fusion surgery with noninvasive interventions. The pooled effect size was four points on the Oswestry Disability Index (1–100), indicating that the average clinical benefit is small.

<sup>4</sup> Vos, T, Flaxman AD, Naghavi N, Lozano R, et al. et al. Years lived with disability (YLDs) for 1,160 sequelae of 289 diseases and injuries 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet*. 2013; 380:2163–96.

<sup>5</sup> Guo HR, Tanaka S, Halperin WE, Cameron LL. Back pain prevalence in US industry and estimates of lost workdays. *Am J Public Health*. 1999; 89(7):1,029–35.

<sup>6</sup> Dagenais S, Caro J, Haldeman S. A systematic review of low back pain cost of illness studies in the United States and internationally. *The Spine Journal*. 2008; 8:8–20.

<sup>7</sup> Chou R, Qaseem A, Snow V, Casey D, et al. Diagnosis and treatment of low back pain: a joint clinical practice guideline from the American College of Physicians and the American Pain Society. *Ann Intern Med*. 2007; 147:4,780–91.

<sup>8</sup> Chou R, Deyo R, Friedly J, Skelly A, Hashimoto R, Weimer M, Fu R, Dana T, Kraegel P, Griffin J, Grusing S, Brodt E. Noninvasive Treatments for Low Back Pain. Comparative Effectiveness Review No. 169. (Prepared by the Pacific Northwest Evidence-based Practice Center under Contract No. 290-2012-00014-I.) AHRQ Publication No. 16-EHC004-EF. Rockville, MD: Agency for Healthcare Research and Quality; February 2016

<sup>9</sup> Weinstein JN, Tosteson TD, Lurie JD, et al. Surgical Versus Nonoperative Treatment for Lumbar Spinal Stenosis Four-Year Results of the Spine Patient Outcomes Research Trial. *Spine* 2010; 35:1329–1338.

<sup>10</sup> Pumberger, M., Chiu, Y. L., Ma, Y., Girardi, F. P., Mazumdar, M., & Memtsoudis, S. G. (2012). National in-hospital morbidity and mortality trends after lumbar fusion surgery between 1998 and 2008. *Journal of Bone & Joint Surgery, British Volume*, 94(3), 359-364.

<sup>11</sup> Mirza, S. K., and Deyo, R. A. (2007). Systematic review of randomized trials comparing lumbar fusion surgery to nonoperative care for treatment of chronic back pain. *Spine*, 32(7), 816-823.



There is not a well-defined consensus on the optimal clinical strategies for identifying those patients with chronic low back pain who may be most likely to achieve benefit from surgery. There remains the concern that surgery (usually a fusion procedure) is too often recommended just because no other treatment approach is available. Some patients may undergo a procedure in which the harms (surgery complications) outweigh the benefits (improved pain and functioning). Most of the current randomized controlled trials (RCTs) in chronic nonspecific low back pain are small and inconclusive. In the absence of good clinical evidence on this question, there is a need for new research that directly addresses surgical and nonsurgical treatment options for people with chronic low back pain. As of January 2016 the [clinicaltrials.gov](http://clinicaltrials.gov) trial registry lists 122 open studies of interventions for chronic low back pain. None of them are randomized trials comparing lumbar fusion surgery with nonsurgical interventions.

Identifying the appropriate interventions and comparators for a new large-scale comparative effectiveness study should be based on the types of treatments found to be most efficacious or those that are most commonly used. A review of current rates of orthopedic procedures for patients with chronic low back pain indicates that fusion procedures are most commonly used. Under this funding announcement, a proposed study should include fusion surgery as one of the treatment options for comparison.

A recent systematic review commissioned by the Agency for Healthcare Research and Quality (AHRQ) addressed nonsurgical treatment options for managing chronic low back pain<sup>8</sup>. This review examined a wide range of treatment approaches. It found that there is moderately strong evidence of efficacy for several different single-treatment modalities when compared with patients receiving no interventions. These single interventions include exercise, yoga, acupuncture, massage and psychological therapies, including cognitive behavioral approaches. However, there is also moderately strong evidence showing that multidisciplinary interventions for chronic low back pain are superior to monotherapies in this patient population. Under this funding announcement, proposed studies should include a comparison group that receives nonsurgical treatment that is multidisciplinary and justified on the basis of convincing evidence regarding its component interventions, which should be evidence-based or in common use for chronic nonspecific low back pain.

### **Research Topic Prioritization**

PCORI's multi-stakeholder Advisory Panel for the Assessment of Prevention, Diagnosis, and Treatment Options rated chronic nonspecific low back pain as a high-priority topic. PCORI then hosted a multi-stakeholder workgroup to develop research questions focusing on the comparative effectiveness of treatments for this patient population. On June 9, 2015, 16 participants representing patients, clinicians, researchers, payers, and purchasers met for a one-day workshop. The meeting was open to the public via teleconference, with slides and meeting materials posted on the PCORI website. Throughout the day, discussions centered on questions submitted by stakeholders and on defining the study population, interventions, and outcome measures.

Subsequently, PCORI met individually with representatives of five professional organizations that represent clinicians who specialize in spine conditions, including nonspecific chronic low back pain (spine

surgeons, orthopedic surgeons, neurosurgeons, physical therapists, and primary care physicians)<sup>12</sup>. The clinicians consistently described chronic nonspecific low back pain as a heterogeneous condition for which they lacked evidence regarding factors associated with response to treatment. To address this problem, PCORI convened a second multi-stakeholder meeting which took place on January 8, 2016<sup>13</sup>. The meeting focused on identifying clinical characteristics that predict how well chronic nonspecific low back pain patients respond to surgery and nonsurgical interventions. The multi-stakeholder panel suggested a number of predictors of response to treatment for exploration (e.g., obesity, current or past use of chronic opioid therapy and/or history of substance abuse, presence of chronic pain in other sites, mental health conditions, etc.).

### Priority Research Question

Applications should propose RCTs that address the priority research question noted below. The study design should maximize the applicability of the study's results in the settings in which patients typically decide between the interventions that the trial compares. The studies should be conducted in such settings. The studies must be relatively large, in part to be able to demonstrate differences in comparative effectiveness in the study arms as randomized, but also to allow adequate power to detect the potential differences in treatment responses in patient subgroups. Applicants are also encouraged to account for and balance the considerations of the pragmatic-explanatory continuum in trial design<sup>14</sup>.

The priority research question is:

#### **What is the comparative effectiveness of lumbar fusion surgery versus an optimized nonsurgical comprehensive multidisciplinary program for chronic nonspecific low back pain?**

PCORI expects the proposed RCT to be a two-armed study comparing lumbar fusion surgery and optimized multidisciplinary nonsurgical management strategies, with patients recruited from primary care settings. Applicants should carefully address the risk of selection bias that often occurs in such surgical trials and the proposed approach to mitigate such concerns (e.g., all recruited patients complete a defined period of standard protocol-driven rehabilitation care before randomization, etc.). Given the anticipated size and scope of proposed studies submitted under this funding initiative, applications should also carefully consider and provide details supporting how the target sample size will be met across all study sites (e.g., expected eligible patient panels, recruitment capacity, integration of research and clinical workflow, etc.). The PICOTs that would apply to this research question include:

- **Population/Patient Problem:** Adults with chronic nonspecific low back pain (no neurological symptoms or structural abnormalities other than disc degeneration) on at least 50 percent of days during the past six months despite usual care (i.e., nonresponsive to one or multiple nonsurgical treatments).
- **Intervention:** Lumbar fusion surgery (Applicants should designate the range of specific procedures and techniques that will be included.)

<sup>12</sup> Refer to <http://www.pcori.org/events/2015/prioritizing-comparative-effectiveness-research-questions-systems-interventions-improve>.

<sup>13</sup> Refer to <http://www.pcori.org/events/2016/prioritizing-comparative-effectiveness-research-questions-treatment-options-chronic-low>

<sup>14</sup> Thorpe KE, Zwarenstein M, Oxman AD, Treweek S, Furberg CD, Altman DG, Tunis S, Bergel E, Harvey I, Magid DJ, Chalkidou K: A pragmatic-explanatory continuum indicator summary (PRECIS): a tool to help trial designers. *J Clin Epidemiol* 2009, 62:464–475.

- Comparator: A comprehensive multidisciplinary nonsurgical approach to manage chronic low back pain. Components of the multidisciplinary approach must be evidence-based, and the overall package should represent the best alternative to surgery.
- Outcome: The National Institutes of Health (NIH) Low Back Pain Task Force outcome measures (function, pain, sleep, mood, medication use, productivity, and use of opioids); healthcare utilization (ER visits, surgery, and hospital admissions); safety (major medical complications and infections); quality of life; and both validated general and low-back-pain-specific disability measures (e.g., Oswestry Disability Index and Roland Morris Disability Questionnaire<sup>2</sup>).
- Time: Follow-up for two years
- Setting: Community practice

PCORI is interested in receiving applications that propose to conduct direct comparisons of alternative treatment regimens. Applicants should provide a convincing explanation for the relevance of treatment regimens compared in the proposed study, citing evidence gaps that are justified on the basis of up-to-date literature reviews. PCORI is particularly interested in studies in populations with important disparities, important comorbidities, or difficult social conditions.

#### Funds Available

PCORI has allotted up to \$22 million in total costs under this PFA to fund high-impact studies related to treating chronic nonspecific low back pain. The proposed budget for all studies under this chronic nonspecific low back pain initiative may go up to \$22 million in total costs as appropriate, depending on the specific priority research question or questions the study proposes to address. The maximum project period is five years.

For this solicitation, PCORI is not requiring that relevant national patient organizations, professional organizations, and/or payer or purchaser organizations be formally included as partners and active participants prior to contract award. However, applicants should document that they have consulted with patients and other stakeholders to identify the important decisional dilemmas and evidence needs that will drive development of the research questions, or refer to previously documented decisional dilemmas. Successful applicants are required to work in collaboration with PCORI staff upon award of the proposed studies to establish a project Study Advisory Committee (SAC) or other appropriate engagement body, that is comprised of national or regional organizations that represent, at a minimum, patients or families with lived experience, relevant clinicians, payers, and health plans. Other representation may be recommended in collaboration with PCORI, including individual patients with lived experience and other relevant stakeholders, among them scientific and methodological experts. The SAC serves to advise and assist the research team with further refinement of the study questions, outcomes, and protocol.

Given the significant treatment costs associated with some interventions, the applications must specifically address, in the context of the proposed studies, the support from payers, health plans, industry sponsors, or others in covering the study interventions and non-study protocol-related clinical costs and services rendered in the care processes. Of particular concern would be different levels of co-

payment between two arms in a comparative study. Ideally, cost-sharing barriers will be eliminated in the study arms or equalized. If the study design does not allow for either option, the applicant should describe why and should also discuss how differences in co-payment costs will be accounted for in the analysis of the study's findings.

It is expected that project budgets and duration will vary substantially, depending on the topic and approach selected, needs for recruitment or primary data collection, length of follow-up, and analytic complexity. PCORI seeks efficient studies, such as those that take advantage of large populations already under observation, registries, and the supportive involvement of delivery systems or health plans to enhance recruitment, data collection, and coverage of treatment-related costs. A prolonged recruitment period is not an acceptable rationale for longer studies. Funding requests to develop or build on initial collaboration between researchers and patient/stakeholder groups are also not appropriate for this funding announcement.

## II. Guidance for Preparing Applications

### Specific Requirements

The proposed study should strive to meet the following requirements:

- Focus on a comparative effectiveness question that is important to patients and other decision makers.
- Address a research gap that has been substantiated by an existing (recent or updated) rigorously conducted systematic review or emphasized by an official professional society's clinical practice guideline.
- Demonstrate consultation with patients and other stakeholders or their representative groups, or reference previously documented decisional dilemmas to determine if the study is answering a critical question—one that, if adequately answered, would substantially improve decision making.
- Receive endorsement by relevant patient organizations, clinician organizations, payer or purchaser consortia, and life sciences industry representatives as potentially answering a critical question, one that if adequately answered would substantially improve decision making.
- Propose a sample size that is sufficiently large to allow for precise estimation of hypothesized effect sizes. The sample size must also support testing of *a priori* hypotheses related to potential differences in effectiveness among relevant patient subgroups (HTE).
- Examine diverse populations receiving care in real-world settings.
- Have strong interest from and support by host delivery systems and clinical care settings.
- Specify broad and simple eligibility criteria that will allow wide generalization of results, while attending appropriately to any ethical concerns of excess risk in some patient subgroups.
- As applicable, compare interventions that can be implemented in real-world settings and are

known to be efficacious, effective, or in common use.

- Include patient-reported outcomes as primary outcomes, when appropriate.
- Provide preliminary evidence of the potential for efficient recruitment, high participation rates, and appropriate oversight by local or centralized Institutional Review Boards (IRBs), including plans for streamlining or waiving individual informed consent in cases of low-risk interventions. PCORI believes that the intensity of oversight and the complexity of informed consent procedures should be closely related to the degree of risk from study participation. Applicants must address this issue and should present evidence that the study will not encounter significant barriers to recruitment or participation.
- Adhere to all applicable [PCORI Methodology Standards](#).<sup>15</sup> The full application will require the applicant to identify the standards appropriate to the proposed study and describe how the study team plans to address each standard.
- In the case of RCTs, also adhere to current best practices (standardized inclusion or exclusion criteria; proper randomization; techniques to minimize potential for missing data; and appropriate safety monitoring, including establishment of a data and safety monitoring board [DSMB] or indication of why such a board is unnecessary).
- Indicate willingness and include a proposed plan for sharing de-identified data for access by other researchers following study completion.

To carry out pragmatic studies, readily adopt the findings in a real-world setting, and maximize the efficient use of resources, care must be taken to prevent these trials from becoming more complex and onerous than necessary. The applicant is encouraged to be creative and consider the following innovative strategies, as appropriate and feasible:

- Be prepared to identify and engage with major patient and stakeholder organizations that would implement study findings, as well as with existing local communities of patients and care providers to refine the research questions and study protocol, help monitor progress, and disseminate the findings.
- Consult with patients and other stakeholders on their decisional dilemma and evidence needs or reference previously documented decisional dilemmas in preparation for the submission of Letters of Intent (LOIs) and the full applications.
- Carefully describe the pertinent evidence gaps and why the project questions represent decisional dilemmas for patients; caregivers and families; and other stakeholders, including clinicians and policy makers. Similarly, applicants should document why project outcomes are especially relevant to patients, and also document meaningful endpoints for patients and their families. Minimize disruption to participants' daily routines (e.g., minimize participant visits intended solely for study assessment purposes; capture PROs during office visits, electronically or by phone).

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<sup>15</sup> Available at [pcori.org/research-we-support/research-methodology-standards/](http://pcori.org/research-we-support/research-methodology-standards/).

- Minimize disruption to participants' daily routines (e.g., minimize participant visits intended solely for study assessment purposes and capture patient-reported outcomes during office visits, electronically or via phone).
- Design the study so that the conduct can, as seamlessly as possible, be integrated with routine clinic or office operations.
- Use efficient methods to obtain participant consent while still meeting ethical and legal requirements.
- Capitalize on the existing electronic health records and other computerized information to identify and recruit eligible patients, monitor study conduct and patient safety, and collect study outcomes information.
- If data standardization and interoperability across study sites has not already been accomplished, develop methods that will enhance the standardization of data that are accessed from different electronic health record systems.

### Nonresponsiveness

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

- Tests efficacy (or comparative efficacy) within a tight, protocol-controlled research setting (as opposed to more real-world and pragmatic CER)
- Conducts a 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
- Measures the relative costs of care of two or more alternative approaches as the primary criteria for choosing the preferred alternative
- Conducts studies of the natural history of disease, instrument development, pharmacodynamics, and fundamental science of biological mechanisms
- Evaluates new or existing decision-support tools. This includes developing and evaluating a decision-support or shared-decision tool or system for patients, clinicians, or both patients and clinicians
- Develops clinical prediction or prognostication tools

Applications that include studies of these issues may measure and report use of any or all health services, but may not employ direct measurements of care costs.

PCORI does have an interest, however, in studying conditions that lead to high costs to the individual or to society. Thus, PCORI is also interested in studies that do the following:

- 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.

Applications that include studies of these issues without using cost-effectiveness analyses or comparing the costs of alternatives are considered responsive.

Furthermore, PCORI discourages applications in the following categories and is likely to deem them nonresponsive:

- Study of the natural history of disease
- Instrument development
- Pharmacodynamics
- Fundamental science or study of biological mechanisms
- Establishing efficacy for a new clinical strategy
- Pilot studies intended to inform larger efforts
- Comparisons of patient characteristics rather than clinical strategy options

### Features of Patient-Centered Outcomes Research (PCOR)

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, and palliative care to inform decision making, highlighting the choices that matter to people
- Is inclusive of an individual's preferences, autonomy and needs, focusing on outcomes that people notice and care about (including survival, functioning, symptoms, and health-related quality of life)
- Incorporates a wide variety of settings and diversity of participants to address individual differences and barriers to implementation and dissemination
- Directly compares clinical interventions that are generally available in the clinical settings
- Obtains stakeholder perspectives to address the burdens to individuals, availability of services, and requirements for technology and personnel

### 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 and relevant information that may be used to answer important CER questions.

### Preliminary Data and Use of Accepted Measures

PCORI encourages investigators to design their research using valid patient-centered outcomes 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 (PROMIS).*<sup>16</sup>

### **Methodological Considerations**

Regardless of study design, applications must adhere to all relevant **PCORI Methodology Standards**.<sup>17</sup> These include 47 individual standards that fall into 11 categories. The first five categories are cross-cutting and are relevant to most PCOR studies. Researchers should refer to all of these standards when planning and conducting their research projects. These five 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

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

Most of these standards should be considered minimal. Additional best practices, including relevant guidelines for conducting clinical trials developed by other organizations, should be addressed in the application for PCORI funding. To help reviewers quickly identify the adherence to a particular standard, applicants must cite each PCORI Methodology Standard within their applications as the standard is being addressed. For example, when applicants describe the need for their proposed study within the Background section, they should indicate the particular standard for Identify Gaps in Evidence in parentheses, such as “(RQ-1).”

Applicants should specifically discuss their capacity to measure such factors as differential adherence to chosen treatments (or participation in intervention programs) that could create or explain apparent differences in the effectiveness of the alternative interventions being compared in clinical populations.

### **Patient and Stakeholder Engagement**

PCORI strongly supports active engagement of patients and other stakeholders, and is committed to

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<sup>16</sup> Available at <http://nihpromis.org/>.

<sup>17</sup> Available at [pcori.org/research-we-support/the-pcori-methodology-report/](http://pcori.org/research-we-support/the-pcori-methodology-report/).



their meaningful participation in PCORI-funded research. All PCORI funding applicants are expected to consult with patients and other stakeholders on their decisional dilemma and evidence needs, or to reference previously documented decisional dilemmas in preparation for the submission of LOIs and applications. To describe the decisional dilemma, state the specific clinical decision(s) and treatment choice(s) confronted by the decision makers, and explain how the findings from the proposed research will inform those decisions. State why this decision, such as choosing between specific treatment strategies, is important to patients and their caregivers. Document the uncertainty patients, clinicians, and other decision makers face in making this decision. Identify the stakeholders you consulted in determining that the proposed study addresses their evidentiary needs for decision making, and indicate your commitment to continuing to engage them actively in the conduct of the study. Similarly, applicants should document why project outcomes are especially relevant to patients and should be meaningful endpoints for patients and their families.

PCORI has developed the [Engagement Rubric](#)<sup>18</sup> to guide the integration of patients and other stakeholders in the development, oversight, management, and implementation of research studies. In addition, studies are expected to adhere to the [PCORI Methodology Standards](#) associated with patient-centeredness and to the PCOR Engagement Principles found within the rubric. PCORI also has a [compensation framework](#)<sup>19</sup> for guidance on compensating individual patient partners on the research team. These and additional resources are available in the [PCORI Funding Center](#).

PCORI understands that applicants may not have the resources to establish formal partnerships prior to contract award, but expects applicants to discuss in their application their plan to work with PCORI to create partnerships with national and regional patient and other stakeholder groups that will contribute to refining the research questions, outcomes, protocols, and study conduct and dissemination.

Successful applicants are required to collaborate with PCORI staff upon award of the proposed studies to establish a project SAC, or other appropriate engagement body, that is comprised of national or regional organizations that represent, at a minimum, patients or families with lived experience, relevant clinicians, payers, and health plans. Other representation may be recommended in collaboration with PCORI, including individual patients with lived experience and other relevant stakeholders, such as scientific and methodological experts. The SAC advises and assists the research team with refining the study question, outcomes, and protocol. It is expected that the SAC will meet regularly in-person at least two times per year and may use virtual communications at other times. These should be budgeted activities represented in the project milestones.

### Populations Studied

PCORI seeks to fund research that includes diverse populations with respect to age, gender, race, ethnicity, geography or clinical status, so that possible differences in CER may be examined (otherwise known as HTE). PCORI recognizes that some proposed studies may represent important PCOR opportunities, even in the absence of a broadly diverse study population. However, the burden is on the applicant in such cases to justify the study's importance in the absence of diversity and to discuss which subgroups are most important and how they will be analyzed, including whether there will be power to

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<sup>18</sup> Available at <http://www.pcori.org/sites/default/files/Engagement-Rubric.pdf>.

<sup>19</sup> Available at <http://www.pcori.org/sites/default/files/PCORI-Compensation-Framework-for-Engaged-Research-Partners.pdf>.

examine the question of effectiveness in subgroups. PCORI is particularly interested in the inclusion of previously understudied populations for whom effectiveness information is particularly needed, such as hard-to-reach populations or patients with multiple conditions. Thus, comparisons should examine the impact of the strategies in various subpopulations, with attention to the possibility that the effects might differ across subpopulations. PCORI has developed the following list of priority populations to guide our research and engagement efforts:

- 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 or numeracy and/or limited English proficiency
- Lesbian, gay, bisexual, and transgender (LGBT) persons
- Veterans and members of the Armed Forces and their families

#### **Budget and Duration of Project**

Applicants may request up to \$22 million in total costs for a project period not to exceed five years. Note that PCORI will not cover costs for interventions that are being compared in the proposed study. (See Appendix 2 in the [Application Guidelines](#) for details.) Applicants should submit realistic budgets and timelines. For those rare circumstances in which the estimated total costs exceed \$22 million, provide a detailed justification in your LOI that ties the extra expense to the project's success. Not all requests for additional funds will be approved. Any request for a project period longer than five years will be denied. For further information regarding PCORI's policies about allowable and unallowable costs, refer to Appendix 2 of the Application Guidelines.

The funding mechanism for this program is a contract. Total project funding is contingent upon successful programmatic and budget performance (e.g., meeting recruitment targets). Milestones and targets, as well as possible pilot phases for the sole purpose of assessing feasibility of recruitment, should be included in the budget and will be negotiated at the time of the award. Awardees will be expected to provide corroborating evidence to receive continual funding support. Some of the activities that will be considered during negotiations include:

- Developing a study protocol and manual of procedures for the intervention

- Assigning roles and responsibilities of members of the study team for implementing the project
- Obtaining clearances from all institutional and community partners, including IRB approvals
- Establishing a DSMB, or providing a clear description of why a DSMB is not necessary
- Executing all subcontractor agreements
- Agreeing on eligible patient populations for study recruitment
- Identifying barriers to patient recruitment in the study and addressing these barriers effectively
- Demonstrating successful recruitment during a pilot phase (if indicated)

Refer to the [Application Guidelines](#) for a list of additional PFA-specific project milestones.

### Collaboration

PCORI is particularly interested in applications that involve community and commercial organizations that can help researchers design, implement, disseminate, and sustain effective interventions. We encourage applications that include novel collaborations with accreditation organizations, credentialing bodies, educational enterprises, patient advocacy groups, industry, professional societies, and subspecialty societies.

### Protection of Human Subjects

This component (up to five pages) is included in the Research Plan Template. Describe the protection of human subjects involved in your research. PCORI follows the Federal Policy for the Protection of Human Subjects (45 CFR part 46), including the Common Rule. For more detailed information, please see Section 5, which is titled “Human Subjects Research Policy,” from the [Supplemental Grant Application Instructions for All Competing Applications and Progress Reports](#),<sup>20</sup> which is issued by the U.S. Department of Health and Human Services. PCORI does not require that applicants comply with sections of this policy referring to requirements for federal-wide assurance or referring to standards for including women, minorities, and children. PCORI also does not require, but strongly encourages, 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 using 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](#)<sup>21</sup>). 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 safeguarding the rights and welfare of human subjects in PCORI-supported activities.

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<sup>20</sup> See <http://grants.nih.gov/grants/funding/424/supplementalinstructions.docx>.

<sup>21</sup> See <http://www.pcori.org/sites/default/files/PCORI-Checklist-for-Evaluating-Human-Subjects-Protections.pdf>.

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

PCORI requires all applicants to adhere to the NIH policy on education in the protection of human subject participants in the conduct of research. This applies to all individuals listed as key personnel in the application. The policy and FAQs are available on the [NIH website](#).<sup>22</sup>

### 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 study documentation (e.g., study protocol, programming code, and data definitions) so that other researchers can replicate the findings in other populations. 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 (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 research methodology or biostatistics expertise; 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's 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 available to the public 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

Applicants should download the Cycle 2 2016 Low Back Pain [LOI template](#) from the PCORI Funding Center. They must complete the document and convert it to a PDF with a four-page limit. All references should be included as in-text citations using American Medical Association citation style. LOIs that exceed the page limit will not be reviewed. Do not upload additional documents, such as letters of endorsement or support, as part of your LOI because they are not requested at this stage. Their

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<sup>22</sup> See <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-08-054.html>.

inclusion will result in LOI rejection without review. Please visit the PCORI Funding Center for additional applicant resources, including the PFA and required templates.

Please answer all of the questions in the LOI template. This includes the question on brief justification for the proposed cost of the study. Providing the answer, “costs not to exceed \$22 million” is not sufficient. Upload your document to PCORI Online. The deadline for LOI submission is May 4, 2016, by 5:00 p.m. (ET).

### Letter of Intent Review

LOIs are evaluated based on the following criteria:

- Whether the proposed topic addresses the priority research question identified in this funding announcement
- Importance of the specific research question (comparison), as evidenced by critical gaps identified by clinical guidelines developers or recent relevant systematic reviews
- A size or scope sufficient enough to have a significant impact on patient outcomes or healthcare practice
- Clarity and credibility of applicants’ responses to the LOI questions, as well as their justification of the proposed study size, citing published estimates, including effect sizes, standard deviations and the need for rigorous comparative analysis of important subgroups
- Prior relevant experience
- Programmatic fit and balance, considering whether the research study question and study design are compliant with requirements in this funding announcement
- Adherence to the administrative and formatting requirements listed in the Application Guidelines, specifically the four-page limit for the LOI

Only applicants whose LOIs are deemed most responsive to this PFA will be invited to submit a full application. Notification of denial or approval to submit an application will occur no later than June 10, 2016. Please refer to the [Application Guidelines](#) for information on how to submit your LOI via PCORI Online.

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

- Research question(s)
- Specific aims
- Study design
- Comparators
- Principal Investigator (PI) (Contact PI and PI #2)
- Institution

If you need to change any of this information or have any questions, please email [pfa@pcori.org](mailto: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 can 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.

### Submission Dates

LOIs and applications must be submitted in accordance with the published dates and times listed in the Overview section of this PFA and in the [PCORI Funding Center](#).<sup>23</sup>

### PCORI Online System

To submit an application, you must register with [PCORI Online](#)<sup>24</sup> and submit both an LOI and an application for each cycle in which you are applying.

### Applicant Resources

PCORI Funding Center	<a href="http://www.pcori.org/Cycle-2-2016-Low-Back-Pain">http://www.pcori.org/Cycle-2-2016-Low-Back-Pain</a>
PCORI Online System	<a href="http://pcori.fluxx.io">pcori.fluxx.io</a>
PCORI Funding Awards	<a href="http://pcori.org/pfaawards">pcori.org/pfaawards</a>

## 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;

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<sup>23</sup> Available at [pcori.org/apply](http://pcori.org/apply).

<sup>24</sup> Available at [pcori.fluxx.io](http://pcori.fluxx.io).

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 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 fill critical gaps and generate actionable evidence**

The proposal should address the following questions:

- Does the application convincingly describe 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 study identify variations in practice patterns that suggest clinical uncertainty?
- Does the application describe the decisional dilemmas experienced by patients and other stakeholders that this study would address?
- Does the study/application have the potential to fill these evidence gaps and inform decision making for key stakeholders (provide example)?

#### **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 potential end-users of study findings, such as local and national stakeholders, and does it incorporate strategies to engage these end-users in dissemination of outcomes? Does the application provide information that supports a demand for this kind of a study from end-users?



- 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, including generalizability to other health systems or treatment settings, or complexity of the intervention, as applicable.
- Does the application describe a plan for how study findings will be disseminated beyond publication in peer review journals and national conferences?
- Can the study be readily adopted in other settings with minimal adaptations or complexities?

**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 to anchor the background literature and inform 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?
- Are 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?
  - Are planned start-up times realistic, including training of personnel? Have the investigators considered and addressed the potential barriers to study initiation within the targeted clinical setting?
  - 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: a study can be patient-centered even if the end-user is not the patient, as long as patients will benefit from its 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? Are those outcomes included in the study plan?
- 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 describes plans for the engagement of and collaboration with 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. PCORI understands that applicants may not have the resources to establish formal partnerships prior to contract award, but expects applicants to discuss in their application their plans to work with PCORI to create the types of partnerships with national and regional patient and other stakeholder groups that will contribute to refinement of research questions, outcomes, protocols, and study conduct and dissemination.

Successful applicants shall plan to work in collaboration with PCORI staff upon award of the proposed studies to establish a project SAC, or other appropriate engagement body, that is comprised of national or regional organizations that represent, at a minimum, patients and families with lived experience, relevant clinicians, payers, and health plans. Other representation may be recommended in collaboration with PCORI, including individual patients with lived experience and other relevant stakeholders, including scientific and methodological experts. The SAC serves to advise and assist the research team with further refinement of the study questions, outcomes, and protocol. It is expected that the SAC will meet regularly in person at least two times per year and may use virtual communications at other times. These are to be budgeted activities and are to be represented in the project milestones. The proposal should address the following:

- Does the application provide a well-justified and comprehensive description of plans to build an interdisciplinary study team that includes appropriate patient and stakeholder representation?
- Are the plans for a strong partnership among scientists, patients, and others throughout the entire research process (e.g., finalizing questions, identifying outcomes, monitoring study, dissemination, and implementation) appropriate and tailored to the study?
- Are the scope, form, and frequency of patient and stakeholder involvement planned throughout entire research process sufficient to support the study goals?
- Are the roles and the decision-making authority of all study partners clearly described?
  - (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. During the in-person review, merit reviewers meet to discuss the applications, further clarify the merits of the proposed research, and identify areas for improvement. Each application is assigned a score based on the content of that discussion. The chair and a PCORI MRO lead the in-person panel meeting and ensure that all applications receive a fair and thorough review according to the standards outlined in the PFA.

### **Post-Panel Review**

After the in-person meeting, PCORI program staff evaluate final merit review panel scores and comments, identify duplication or synergy among funded projects, and consider the fit of applications within the programmatic vision. Program staff members then recommend projects to a Selection Committee, which is comprised of members of PCORI's Board of Governors. The Committee considers recommendations and works with staff to identify a slate of applications for possible funding based on merit review scores, programmatic balance and fit, and PCORI's strategic priorities. This slate is then proposed to PCORI's Board for its consideration and approval.

### **Summary Statements and Funding Recommendations**

Summary statements are provided to applicants approximately two weeks before funding decisions are announced. The applicant will receive a summary statement inclusive of:

- 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.

Funding recommendations are made by identifying meritorious applications that fit the programmatic needs and that satisfactorily address the merit review criteria while adhering to PCORI's Methodology Standards. Programs also consider the funds allotted for the current funding announcement when deciding which applications to recommend to PCORI's Board for approval. Applicants to this current cycle's PFA will receive summary statements in early January 2017 and notification of the funding status of their application no later than January 2017.

### **Board of Governors Approval**

The PCORI Board will consider the selected applications, factoring in the total available funds allotted for this announcement and programmatic needs. PCORI will inform applicants of the Board's decision no later than January 2017.