



Cycle 1 2019 Funding Cycle

PCORI Funding Announcement: Treatment of Anxiety Disorders in Children, Adolescents, and/or Young Adults

Published January 3, 2019

This PCORI Funding Announcement (PFA) applies to the funding cycle that closes April 24, 2019, at 5 pm (ET). Application Guidelines, templates, and other resources are available at <https://www.pcori.org/funding-opportunities/announcement/treatment-anxiety-children-adolescents-andor-young-adults-cycle-1>.



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 and other stakeholders.

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, caregivers, clinicians, policy makers, and other healthcare system stakeholders 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	January 3, 2019																
Letter of Intent Deadline	<p>January 31, 2019, by 5 pm (ET)</p> <p>Letters of Intent (LOIs) will be screened for responsiveness to this PCORI Funding Announcement (PFA) and for fit to program goals. Only those selected will be permitted to submit full applications. Notification of denial or approval to submit a full application will occur no later than February 26, 2019.</p>																
Summary	<p>The Patient-Centered Outcomes Research Institute (PCORI) has had an ongoing interest in funding high-quality clinical studies that compare the effectiveness of evidence-based clinical strategies to treat anxiety disorders in children, adolescents, and/or young adults. Clinical strategies to be studied may include pharmacological interventions, psychological interventions, or a combination of both. Each proposed comparator must be clearly defined, evidence-based, widely available, and appropriate for the age range and clinical severity of the study population.</p> <p>The proposed study population should include patients with a <i>confirmed</i> clinical diagnosis of a primary anxiety disorder and who are between 7 and 25 years of age. Applicants must clearly define the specific age range to be studied and provide a scientific rationale for the proposed study population and interventions. Applicants should consider several factors when defining their study population, including but not limited to: anxiety severity, type(s) of anxiety disorder(s), exposure to previous treatment(s)/treatment failure, recurrent or relapsed illness, patient co-morbidities and/or subpopulations. Studies should be conducted in well-defined, primary, specialty and/or integrated clinical care settings. If psychological services constitute all or part of the delivered intervention(s), they must be well defined and characterized.</p> <p>Randomized controlled trials that compare the effectiveness of treatments are encouraged. Prospective, observational cohort studies that focus on assessing the heterogeneity of treatment effects and/or the comparative tolerability and safety of drugs may also be proposed. All studies should include outcome measures to assess function, symptoms, acceptability of treatment, and the measurement of adverse effects. Studies with a minimum follow-up period of nine months from baseline are sought, with one year of follow-up preferred. In addition, all studies funded through this initiative must include robust sample sizes of at least 300 participants, with sufficient power demonstrated to conduct the proposed analyses.</p>																
Applicant Resources	See https://www.pcori.org/funding-opportunities/announcement/treatment-anxiety-children-adolescents-andor-young-adults-cycle-1																
Key Dates	<table> <tr> <td>Online System Opens:</td> <td>January 3, 2019</td> </tr> <tr> <td>Town Hall:</td> <td>January 22, 2019; 12:00 - 1:00 pm ET</td> </tr> <tr> <td>LOI Deadline:</td> <td>January 31, 2019, by 5 pm (ET)</td> </tr> <tr> <td>LOI Status Notification:</td> <td>February 26, 2019</td> </tr> <tr> <td>Application Deadline:</td> <td>April 24, 2019, by 5 pm (ET)</td> </tr> <tr> <td>Merit Review:</td> <td>July 2019</td> </tr> <tr> <td>Awards Announced:</td> <td>September 2019</td> </tr> <tr> <td>Earliest Project Start Date:</td> <td>December 2019</td> </tr> </table>	Online System Opens:	January 3, 2019	Town Hall:	January 22, 2019; 12:00 - 1:00 pm ET	LOI Deadline:	January 31, 2019, by 5 pm (ET)	LOI Status Notification:	February 26, 2019	Application Deadline:	April 24, 2019, by 5 pm (ET)	Merit Review:	July 2019	Awards Announced:	September 2019	Earliest Project Start Date:	December 2019
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Maximum Project Budget (Direct Costs)	\$5 million direct costs																



Maximum Research Project Period	3.5 years
Funds Available Up To	\$20 million
Eligibility	Applications may be submitted by any private-sector research organization, including any nonprofit or for-profit organization, and any public-sector research organization, including any university or college hospital or healthcare system; laboratory or manufacturer; or unit of local, state, or federal government. The Internal Revenue Service must recognize all U.S. applicant organizations. Nondomestic components of organizations based in the U.S. and foreign organizations may apply, as long as there is demonstrable benefit to the U.S. healthcare system and U.S. efforts in the area of patient-centered research can be shown clearly. Organizations may submit multiple applications for funding. Individuals are not permitted to apply.
Review Criteria	<ol style="list-style-type: none"> 1. Potential for the study to fill critical gaps in evidence 2. Potential for the study findings to be adopted into clinical practice and improve delivery of care 3. Scientific merit (research design, analysis, and outcomes) 4. Investigator(s) and environment 5. Patient-centeredness 6. Patient and stakeholder engagement
Contact Us	<p>Programmatic Inquires: Please contact the PCORI Helpdesk via email (sciencequestions@pcori.org), phone (202-627-1884), or online (http://www.pcori.org/PFA/inquiry). PCORI will respond within two business days. However, we cannot guarantee that all questions will be addressed in two business days prior to an LOI or application deadline.</p> <p>Administrative, Financial, or Technical Inquiries: Please contact the PCORI Helpdesk at pfa@pcori.org. PCORI will respond within two business days. Please note that during the week of a deadline, response times may exceed two business days. 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 pm (ET). If deadlines fall on a weekend or a federal holiday, the deadline will be the following Monday or the next day after the federal holiday.

New or Revised for the Cycle 1 2019 Funding Cycle:

- The primary research question has been modified.
- Maximum direct costs \$5 million.
- Total duration of study: 3.5 years.
- Added a new Methodology Standard category (Standards for Studies of Complex Interventions)—see page 7
- New language on PCORI’s Policy for Data Management and Data-Sharing—see page 11.
- See the Application Guidelines for updates to the templates and other requirements.



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I. Introduction

Summary of Program

The Patient-Centered Outcomes Research Institute (PCORI) is launching this funding initiative to generate needed scientific evidence to help patients, families, and clinicians in making decisions about treatments for pediatric anxiety. PCORI seeks to fund high-quality clinical studies that compare the effectiveness of evidence-based clinical strategies to treat anxiety disorders in children, adolescents, and/or young adults.

For this PCORI Funding Announcement (PFA), the study population should include patients with a *confirmed* clinical diagnosis of a primary anxiety disorder and who are between 7 and 25 years of age. Applicants will be asked to clearly define the specific age range to be studied, and to provide a scientific rationale justifying the proposed study population and interventions. Applicants should consider several factors when defining their study population, including, but not limited to, anxiety severity, type(s) of anxiety disorder(s), exposure to previous treatment(s)/treatment failure, recurrent or relapsed illness, patient co-morbidities, and/or subpopulations. Studies should be conducted in well-defined, primary, specialty, and/or integrated clinical care settings. If psychological services constitute all or part of the delivered intervention(s), they must be well-defined and characterized.

Each proposed comparator must be clearly defined, evidence based, widely available, and developmentally appropriate for the age range and clinical severity of the suggested study population. Studies must include a minimum follow-up period of nine months from baseline; one year of follow-up from baseline is preferred. In addition, all studies funded through this initiative must include robust sample sizes of **at least** 300 participants, with sufficient power demonstrated to conduct proposed primary analyses and subgroups as appropriate to the proposed population.

Background

Anxiety disorders are one of the most common childhood-onset psychiatric disorders in the United States, with a lifetime prevalence of 31.9 percent among adolescents between the ages of 13 and 18, with 8.3 percent diagnosed as having severe anxiety.¹ Pediatric anxiety disorders typically follow an unremitting course and impede the social, emotional, and academic development of youth.² Early intervention may modify the trajectory of the disorder and prevent significant impairment. These disorders often persist into adulthood and are associated with severe mental health conditions such as depression, substance abuse, functional and occupational impairments, and suicidal behavior.³

According to a 2017 systematic review published by the Agency for Healthcare Research and Quality (AHRQ), the main treatment options for pediatric anxiety disorders include psychological interventions, pharmacotherapy, and combination approaches. The AHRQ review found that, among the various

¹ Merikangas KR, He JP, Burstein M, et al. Lifetime prevalence of mental disorders in US adolescents: results from the National Comorbidity Survey Replication–Adolescent Supplement (NCS-A). *J Am Acad Child Adolesc Psychiatry*. 2010;49(10):980-989.

² Bittner A, Egger HL, Erkanli A, Jane Costello E, Foley DL, Angold A. What do childhood anxiety disorders predict? *J Child Psychol Psychiatry*. 2007;48(12):1174-1183.

³ Connolly SD, Bernstein GA. Practice parameter for the assessment and treatment of children and adolescents with anxiety disorders. *J Am Acad Child Adolesc Psychiatry*. 2007;46(2):267-283.

psychological interventions, cognitive behavioral therapy (CBT) is the most widely studied and has the strongest evidence of effectiveness. Among the pharmacological therapies, selective serotonin reuptake inhibitors (SSRIs) and selective serotonin-norepinephrine reuptake inhibitors (SNRIs) have the strongest evidence of effectiveness in children and adolescents.⁴

Despite the range of available evidence-based treatment options, clinical guidelines offer inconsistent advice regarding the treatment for youth. Most guidelines recommend first-line treatment with CBT, but they differ regarding whether and when to introduce pharmacological treatment options.^{3,5,6} In general, the decision to initiate pharmacotherapy depends on a range of factors, including a patient's level of functional impairment, symptom severity, age, access to psychotherapy services, patient or family preferences, or when psychotherapy inadequately addresses symptoms.^{4,7} The clinical management of these patients is further complicated by the co-occurrence of other co-morbidities, such as attention deficit hyperactivity disorder or depression.^{8,9} The benefits of pharmacotherapy must also be weighed against disadvantages such as possible adverse effects, which include nausea, abdominal pain, headache, dizziness, somnolence, agitation, and disinhibition.¹⁰ These adverse effects can affect function and day-to-day quality of life as well as patients' adherence to medication, which renders the treatment less useful or effective.⁴ Suicidality is a labeled risk for many of the medications used in the treatment of anxiety. The minimal duration of continued pharmacotherapy to prevent relapse of symptoms is unclear, as is the optimal manner of discontinuation. Overall, information is lacking to help guide patients, families, and clinicians in deciding what medications to use as first-, second-, or third-line therapies given a patient's individual characteristics.

To begin addressing these evidence gaps, PCORI released a series of PFAs in 2017. In Cycle 2 2017, PCORI released a Pragmatic Clinical Studies (PCS) PFA with a Special Area of Emphasis on *digital applications of CBT for treatment of mild-to-moderate anxiety in children, adolescents, and/or young adults*. PCORI made a major investment under this PFA, funding a large, five-year study comparing *face-to-face versus digital CBT* in mildly to moderately anxious children and adolescents.

In Cycle 3 2017, PCORI introduced a new PCS priority topic that broadly focused on the treatment of anxiety disorders in children, adolescents, and/or young adults, with an emphasis on the comparative effectiveness of different approaches to treatment initiation, sequencing, monitoring, maintenance, and/or relapse prevention. In Cycle 1 2018, PCORI released a targeted PFA that aimed to complement

⁴ Wang Z, Whiteside S, Sim L, et al. *Anxiety in Children*. Rockville, MD: Agency for Healthcare Research and Quality; August 2017. Comparative Effectiveness Review 192. (Prepared by the Mayo Clinic Evidence-based Practice Center under Contract No. 290-2015-00013-1.) AHRQ publication 17-EHC023-EF. <http://www.effectivehealthcare.ahrq.gov/reports/final.cfm>. <https://doi.org/10.23970/AHRQEPCCER192>.

⁵ National Collaborating Centre for Mental Health. *Social Anxiety Disorder: Recognition, Assessment and Treatment*. London, United Kingdom: National Institute for Health and Care Excellence; 2013. Clinical Guideline CG159. <https://www.nice.org.uk/guidance/cg159/evidence/full-guideline-189895069>

⁶ Guidelines & Protocols Advisory Committee. *Anxiety and Depression in Children and Youth—Diagnosis and Treatment*. Victoria, British Columbia, Canada: Guidelines & Protocols Advisory Committee, British Columbia Medical Services Commission; 2010. <https://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/bc-guidelines>

⁷ Tulisiak AK, Klein JA, Harris E, et al. Antidepressant prescribing by pediatricians: a mixed-methods analysis. *Curr Probl Pediatric Adolesc Health Care*. 2017;47(1):15-24.

⁸ Angold, A., Costello, E. J., & Erkanli, A. (1999). Comorbidity. *Journal of Child Psychology and Psychiatry*, 40, 57–87.

⁹ Kendall PC, Brady EU, Verduin TL. Comorbidity in childhood anxiety disorders and treatment outcome. *J Am Acad Child Adolesc Psychiatry* 2001; 40:787.

¹⁰ Dobson ET, Strawn JR. Pharmacotherapy for pediatric generalized anxiety disorder: a systematic evaluation of efficacy, safety and tolerability. *Pediatr Drugs*. 2016;18(1):45-53.

these funding announcements by addressing a critical evidence gap: head-to-head comparisons of pharmacological therapies, in conjunction with evidence-based psychological therapies for children, adolescents, and/or young adults with moderate to severe anxiety.

This new, targeted funding announcement aims to broaden the scope of the Cycle 1 2018 funding announcement and calls for comparisons of evidence-based clinical strategies to treat pediatric anxiety.

Evidence Gaps

New research has the potential to address several important evidence gaps regarding the comparative effectiveness and safety of treatments for anxiety disorders in youth. The 2017 AHRQ systematic review on treatments for pediatric anxiety disorders called for additional research to assess the most beneficial components and forms of CBT, so that more targeted treatments can be developed. In addition, research needs to better explore the impact of patient age, co-morbidities, family demographics, and stressors on treatment effectiveness to inform more individualized treatment decisions. The evidence base is also limited on the comparative effectiveness of medications, combination therapy, and sequences of treatments. Other important limitations of the evidence base include the long-term safety of medications and the clinical course when treatments are discontinued.

The AHRQ systematic review concluded that both SSRIs and SNRIs demonstrated effectiveness in reducing anxiety symptoms; however, slightly larger effect sizes were reported across studies of SSRIs.¹¹ Given the comparable efficacy of these treatments, medication side effect profile and tolerability play a major role in these drug therapy decisions; however, previous studies that have evaluated the adverse events of these medications have been limited by a lack of standardized reporting of treatment-emergent adverse effects and suicidality, as well as a failure to track side effects related to medication discontinuation.¹⁰ Sufficient evidence to help inform patients, families, and providers about the balance of potential medication effectiveness and harms is lacking.

Regarding combination therapy, only three randomized controlled trials (RCTs) have compared the combination of CBT and a medication with CBT alone and/or with medication alone.⁴ The largest of these trials found that the combination of CBT and sertraline (an SSRI) improved primary anxiety symptoms, function, and clinical response more than either CBT alone or sertraline alone.¹² A secondary analysis of the data from this trial, published in 2017, showed that youth with mild to moderate anxiety at baseline achieved remission with CBT alone, sertraline alone, or combination therapy. In contrast, youth with severe anxiety at baseline needed combination therapy to achieve a significant improvement in the likelihood of remission.¹³ These findings suggest that more studies of head-to-head comparisons

¹¹ Wang Z, Whiteside S, Sim L, et al. *Anxiety in Children*. Rockville, MD: Agency for Healthcare Research and Quality; August 2017. Comparative Effectiveness Review 192. (Prepared by the Mayo Clinic Evidence-based Practice Center under Contract No. 290-2015-00013-1.) AHRQ publication 17-EHC023-EF. <http://www.effectivehealthcare.ahrq.gov/reports/final.cfm>. <https://doi.org/10.23970/AHRQEPCCER192>

¹² Walkup JT, Albano AM, Piacentini J, et al. Cognitive behavioral therapy, sertraline, or a combination in childhood anxiety. *N Engl J Med*. 2008;359(26):2753-2766.

¹³ Taylor JH, Lebowitz ER, Jakubovski E, Coughlin CG, Silverman WK, Bloch MH. Monotherapy insufficient in severe anxiety? predictors and moderators in the child/adolescent anxiety multimodal study. *J Clin Child Adolesc Psychol*. September 30, 2017:1-6.

of medications and combination therapy are needed in specifically circumscribed populations to increase the actionable evidence base for treatment of pediatric anxiety disorders.¹⁴

In addition, evidence on the heterogeneity of treatment effects (for both medications and psychological treatments) is needed, given the clinical complexity of these patients. Well-designed RCTs or rigorous, prospective observational studies¹⁵ with *large* sample sizes may help generate valid and useful information for clinicians, patients, and caregivers in choosing treatments on the basis of a patient's characteristics and circumstances.

Priority Research Question

PCORI seeks to fund high-quality clinical studies that address this PFA's research question:

Based on patient- and family-centered outcomes, what is the comparative clinical effectiveness of two or more evidence-based *clinical* strategies for the treatment of anxiety disorders in children, adolescents, and/or young adults?

PCORI calls for meaningful comparisons that reflect real-world clinical decisional dilemmas where significant uncertainty exists in the choice between two or more treatments for a specific type of patient. This decisional dilemma needs to be clearly supported by the evidence base and what evidence gaps have been identified. The proposed study needs to be feasible in the context of current clinical practice patterns and availability of treatments in primary, integrated, and/or specialty care settings.

All studies funded through this initiative must include robust sample sizes of **at least 300 participants**, with sufficient power demonstrated to conduct proposed primary analyses. Applications that propose sample sizes of fewer than 300 participants will be considered nonresponsive.

Where possible, applicants may propose means to evaluate the comparative effectiveness of different approaches to treatment monitoring, maintenance, and/or relapse prevention following an initial effective course of treatment.

Applicants should consider the following parameters when responding to this PFA:

- **Population:** Children or young adults between the ages of 7 and 25 with a *confirmed* clinical diagnosis of a primary anxiety disorder. Applicants must clearly define the specific age range to be studied and provide a scientific rationale for the proposed study population. The application must address how the study will ensure that recruited participants have a *confirmed* clinical diagnosis of a primary anxiety disorder. Applicants should consider several factors when defining and justifying their study population, including, but not limited to, anxiety severity, type(s) of anxiety disorder(s), patient co-morbidities, exposure to previous treatment(s)/treatment failure, recurrent or relapsed illness, and/or subpopulations. Special populations of interest include underserved populations, such as racial and ethnic minorities, low-income youth, youth living in rural areas, and youth with limited access to mental health

¹⁴ Asarnow JR, Rozenman MS, Carlson GA. Medication and cognitive behavioral therapy for pediatric anxiety disorders: no need for anxiety in treating anxiety. *JAMA Pediatr.* 2017;171(11):1038-1039.

¹⁵ Dreyer NA, Schneeweiss S, McNeil BJ, et al. GRACE principles: recognizing high-quality observational studies of comparative effectiveness. *Am J Manag Care.* 2010;16(6):467-471.

services.

- **Interventions:** Clinical strategies may include pharmacological interventions, psychological interventions, or a combination of both. Each proposed comparator must be clearly defined, evidence based, widely available, and appropriate for the age range and clinical severity of the population. If psychological services are proposed, they must be characterized in conformance with the [PCORI Standards for Studies of Complex Interventions](#). See [Important Safety Considerations](#) below for guidance on the inclusion of appropriate human subjects protections.
- **Outcomes:** Applicants should propose patient- and family-centered outcomes that are well validated, responsive to change where baseline measures are employed, and developmentally appropriate for the proposed study population. Outcomes should include at least the following domains: function (e.g., school attendance, avoidance behavior, engagement in social activities); symptoms (e.g., child, parent, and/or clinician report, as appropriate and scientifically justified); acceptability of treatment (e.g., family burden, medication discontinuation, or dropout from therapy); and the measurement of adverse effects (e.g., behavioral activation, suicidality). When selecting outcome measures, applicants should include a measure that permits the comparison of results across similar studies.
- **Timing:** Applicants should specify the duration of each of the active interventions as well as the duration of any maintenance or booster sessions. Studies must include at least nine months of follow-up from baseline, with one year of follow-up preferred, regardless of treatment duration.
- **Setting:** Studies may take place in well-defined, primary, specialty, and/or integrated clinical care settings. If psychological services constitute all or part of the delivered intervention(s), they must be well defined and characterized.

Applicants should consider the potential for attrition due to normal life changes within the study period for the proposed population, and should propose specific strategies (i.e., retention plans) to mitigate these as appropriate, particularly for studies that target young adults.

Important Safety Considerations

Applicants should consult with the Food and Drug Administration regarding any off-label use of medications in the proposed study and seek approval for an Investigational New Drug application, as required. Awardees must plan to have specific and adequate human subjects protection measures in place (e.g., inclusion of a data safety monitoring board, a risk monitoring plan, and discussion of potential risk and how it will be monitored in the consent process). Appropriate monitoring for serious adverse events such as suicidality should be addressed.

Funds Available

PCORI has allotted up to \$20 million in total costs under this PFA to fund up to three high-quality and high-impact studies related to treating anxiety disorders in children, adolescents, and/or young adults. The proposed budget for studies under this initiative may be up to \$5 million in direct costs. Requested budgets should be appropriately scaled to the actual size and scope of the proposed project. The maximum project period is 3.5 years.

PCORI will not cover costs for study interventions that constitute the procedures, treatments, interventions, or other standard clinical care (“patient care”) that an applicant is proposing for comparison in the research project (“patient care costs”). This includes the costs of the delivery of psychological interventions. The host healthcare delivery system, third-party payer, product manufacturer, intervention developer, or other interested party must cover the patient care costs.

PCORI seeks efficient studies, such as those that take advantage of large populations already under observation; registries; research cooperatives; and the supportive involvement of delivery systems or health plans to enhance recruitment, data collection, and coverage of intervention-related costs. A prolonged recruitment period is not an acceptable rationale for longer studies. Funding requests with the primary purpose of developing or building on initial collaboration between researchers and patient or stakeholder groups are also not appropriate for this PFA.

II. Requirements for PCORI Research

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

Research Priorities

To be considered responsive, applications must:

- *Describe comparators.* Regardless of the approach being studied, all proposed research projects must compare at least two alternatives. If the applicant proposes “usual care” as a rational and important comparator in the proposed study, then it must be described in detail, coherent as a clinical alternative, and properly justified as a legitimate comparator (e.g., “usual care” is guidelines-based). It must also be accompanied by an explanation of how the care given in the “usual care” group will be measured in each patient, and how appropriate inferences will be drawn from its inclusion. “Usual care” must be described as mentioned above to ensure that it accounts for geographic and temporal variations, and it has wide interpretability, applicability, and reproducibility.
- *Describe research that compares two or more alternatives, each of which has established efficacy.* PCORI expects the efficacy or effectiveness of each intervention to be known. If the efficacy or evidence base is insufficient, then data need to be provided to document that the intervention is used widely. The application must provide information about the efficacy of the interventions that will be compared; pilot data might be appropriate. Projects aiming to develop new interventions that lack evidence of efficacy or effectiveness will be considered out of scope.
- *Describe research that studies the benefits and harms of interventions and strategies delivered in real-world settings.* PCORI is interested in studies that provide practical information that can help patients and other stakeholders make informed decisions about their health care and health outcomes.
- *Describe consultation with patients and other stakeholders about how the study is answering a critical question.* Explain the pertinent evidence gaps and why the project questions represent decisional dilemmas for patients, caregivers, clinicians, policy makers, and other healthcare

system stakeholders. Describe why project outcomes are especially relevant and meaningful endpoints to patients and other stakeholders.

Categories of Non-responsiveness

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

- Studies that include the costs of clinical services in the proposed budget
- Instrument development, such as new surveys, scales, etc.
- Developing, testing, and validating new decision aids and tools, or clinical prognostication tools
- Pilot studies intended to inform larger efforts
- Comparing patient characteristics rather than clinical strategy options

Consistent with PCORI's [authorizing law](#),¹⁶ PCORI does not fund research whose findings will include:

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

Studies of Cost-Effectiveness

PCORI will consider an application nonresponsive if the proposed research:

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

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

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

- Examine the effect of costs on patients, such as patients' out-of-pocket costs, hardship or lost opportunity, or costs as a determinant of or barrier to access to care

¹⁶ Available at http://www.pcori.org/sites/default/files/PCORI_Authorizing_Legislation.pdf/.



- 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

Avoiding Redundancy

PCORI encourages potential applicants to review funded research at pcori.org. We intend to balance our funded portfolio to achieve synergy and avoid redundancy where possible.

Methodological Considerations

Regardless of study design, applications must adhere to all relevant [PCORI Methodology Standards](#). These include 54 individual standards that fall into 13 categories. The first five categories are cross-cutting and relevant to most PCOR studies. Researchers should refer to all of these standards when planning and conducting their research projects. These cross-cutting categories are:

1. Standards for Formulating Research Questions
2. Standards Associated with Patient-Centeredness
3. Standards on Data Integrity and Rigorous Analyses
4. Standards for Preventing and Handling Missing Data
5. Standards for Heterogeneity of Treatment Effect (HTE)

In addition to these five sets of standards, the first standard of “Standards for Causal Inference Methods” -(CI-1)- is cross-cutting and applicable to all PCOR studies.

The eight other standards categories will be applicable to particular study designs and methods. Applicants should use the standards in each of these categories as guidance when they are relevant to a study. These categories are:

6. Standards for Data Registries
7. Standards for Data Networks as Research-Facilitating Structures
8. Standards for Causal Inference Methods
9. Standards for Adaptive and Bayesian Trial Designs
10. Standards for Studies of Medical Tests
11. Standards for Systematic Reviews
12. Standards on Research Designs Using Clusters
13. Standards for Studies of Complex Interventions

Most of these standards are minimal. The PCORI Methodology Standards reflect practices that applicants should follow in all cases, and all deviations need to be explained and justified. Applicants should address additional best practices—including relevant guidelines for conducting clinical trials developed by other organizations—in the application for PCORI funding. To help reviewers quickly identify adherence to a particular standard, applicants must cite each relevant [PCORI Methodology](#)



Standard within the [Methodology Standards Checklist](#), following the instruction in the checklist itself and in the [Application Guidelines](#). Program staff use the checklist to evaluate applications.

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-Centered Outcome Measures

PCORI encourages investigators to design their research using validated outcome measures. Include preliminary data that support using the proposed measures in the study population. We encourage investigators to consider those measures described in the [Patient-Reported Outcomes Measurement Information System](#)¹⁷ (PROMIS).

Leveraging Existing Resources

PCORI encourages investigators to propose studies that leverage existing resources, such as adding PCOR to an existing large clinical trial or analyzing existing large databases that contain valuable, relevant information that may be used to answer important CER questions. PCORI is interested in studies that leverage existing research network or consortia, as well as established data resources such as patient outcomes registries especially when such patient outcomes registries can be linked to electronic medical record (EMR) data from healthcare delivery systems or administrative claim data from public or commercial insurers to facilitate the conduct of comparative clinical effectiveness research. PCORI does not intend for this PFA to support the development of new patient registries, but rather to support the effective utilization of established patient registries where comprehensive data on patient characteristics and patient outcomes have been collected and/or can be linked to the EMR data or claims data to evaluate treatment outcomes in the proposed CER studies. In circumstances where randomized control trials are not practical or ethically acceptable, studies leveraging established patient outcomes registries can have meaningful and complementary roles in evaluating patient outcomes.

Patient and Stakeholder Engagement

PCORI encourages all applicants to outline how patients and other stakeholders will participate as partners in various phases of the proposed research. Before completing this section of the Research Strategy, applicants should review the [Engagement Rubric](#)¹⁸, which can be found in the PCORI Funding Center. Applicants should also review the PCORI Methodology Standards Associated with Patient-Centeredness and [PCORI's Sample Engagement Plans](#).¹⁹ The rubric and Sample Engagement Plans are not intended to be comprehensive or prescriptive; instead, they provide a variety of examples to incorporate engagement, where relevant, into the research process.

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 Letters of Intent (LOIs) and applications. To describe the decisional dilemma, state the specific clinical decision(s) or treatment choice(s) confronted by the decision makers and explain how

¹⁷ Available at <http://www.nihpromis.org/>.

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

¹⁹ Available at <http://www.pcori.org/sites/default/files/PCORI-Sample-Engagement-Plans.pdf>

the findings from the proposed research will inform those decisions. State why this decision—such as choosing a specific medication, psychological treatment, or combination therapy is important to patients. Document the uncertainty patients and other stakeholders face in making this decision. Identify the patients and other stakeholders you consulted in determining that the proposed study addresses their evidentiary needs for decision making, and indicate your commitment to continue engaging them actively in the conduct of the study. Similarly, applicants should document how the project outcomes are especially relevant and meaningful endpoints to patients and other stakeholders.

Populations Studied

PCORI seeks to fund research that includes diverse populations with respect to age, gender, race, ethnicity, geography, or clinical status, so that possible differences in outcomes may be examined in defined subpopulations, otherwise known as HTE. PCORI recognizes that some proposed studies might represent important PCOR opportunities, even in the absence of a broadly diverse study population. However, the burden is on the applicant to justify the study's importance in the absence of diversity; to discuss which subgroups are most important; and to discuss how the subgroups will be analyzed, including whether or not the study will be powered to examine the question of effectiveness in subgroups. PCORI is particularly interested in including previously understudied populations for whom effectiveness information is especially needed, such as hard-to-reach populations or patients with multiple conditions. Thus, comparisons should examine the impact of the strategies in various subpopulations, with attention to the possibility that the strategy's effects might differ across subpopulations. PCORI has developed the following list of populations of interest to guide our efforts in research and engagement.

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

Protection of Human Subjects

This component (up to five pages) is included in the Research Plan Template. Describe the protection of human subjects involved in your proposed research. PCORI follows the Federal Policy for the Protection of Human Subjects (45 CFR part 46), including the Common Rule. For more detailed information, please see Section 5, titled “Human Subjects Research Policy,” in the [Supplemental Grant Application Instructions for All Competing Applications and Progress Reports](#),²⁰ which is issued by the U.S. Department of Health and Human Services (HHS). In referencing the HHS Supplemental Grant Application Instructions, note that PCORI does not require that applicants comply with sections of that policy that refer to requirements for federal-wide assurance and the inclusion of women, minorities, and children in the proposed studies. Instead PCORI expects applicants to address diversity in study participants in the research plan, through a focus on subpopulations, as described in the above section on [Populations Studied](#). Awardees must also comply with appropriate state, local, and institutional regulations and guidelines pertaining to the use of human subjects in research.

PCORI requires awardees to ensure that there is a Data and Safety Monitoring Plan, which may include the need to appoint a Data and Safety Monitoring Board, as provided in the [PCORI Policy on Data and Safety Monitoring Plans for PCORI-Funded Research](#).²¹

PCORI merit reviewers will examine plans for protection of human subjects in all applications and may provide comments regarding the plans (see [How To Evaluate Human Subjects Protections](#)²²). Reviewers’ comments on human subject research are not reflected in the overall application score, but PCORI staff might use them during potential funding negotiations. Final determinations about the adequacy of human subject protections rest with the Institutional Review Board or international equivalent that have jurisdiction for the study.

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

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

PCORI requires that all applicants adhere to the National Institutes of Health (NIH) policy on education in the protection of human subject participants in the conduct of research. This applies to all individuals listed as key personnel in the application. The policy and FAQs are available on the [NIH website](#).²³

Data Management and Data-Sharing Plan

PCORI encourages openness in research and making research data available for purposes of replication and reproducibility. As such, if an award is made through this targeted Funding Announcement, the Awardee will be required to adhere to [PCORI’s Policy for Data Management and Data Sharing](#).

The Policy articulates PCORI’s requirement that certain Awardees—specifically those funded through the Pragmatic Clinical Studies (PCS) and all targeted Funding Announcements—make the underlying

²⁰ See <http://grants.nih.gov/sites/default/files/supplementalinstructions.docx>

²¹ See <http://www.pcori.org/sites/default/files/PCORI-Policy-Data-Safety-Monitoring-Plans.pdf>

²² See <http://www.pcori.org/sites/default/files/PCORI-Checklist-for-Evaluating-Human-Subjects-Protections.pdf/>.

²³ See <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-08-054.html>.

data and data documentation (e.g., study protocol, metadata, and analytic code) from their PCORI-funded research projects available to third-party requestors. The Policy includes details about what data certain Awardees will be expected to deposit into a PCORI-designated data repository and when that data would be available for third-party requests.

A full data management and data sharing plan is not required at the time of application. If an award is made, the Awardee will be required to develop and maintain such a plan, which is described in detail in the [PCORI Methodology Standards for Data Integrity and Rigorous Analyses](#), specifically Standard IR-7. This plan must be appropriate for the nature of the research project and the types of research project data, and consistent with applicable privacy, confidentiality, and other legal requirements. Awardees are also strongly encouraged to include, as appropriate, language in the research project's informed consent forms that allows for the de-identification and sharing of study data for secondary research purposes.

As part of the Policy, PCORI intends to cover reasonable costs associated with the time and effort needed for preparing, depositing, and maintaining the Full Data Package in the repository for a period of at least seven (7) years following acceptance by PCORI of the Final Research Report. PCORI will negotiate with Awardees on the specific budget needs associated with this Policy requirement at the time of Award, in addition to the requested research project budget.

The information here is meant for informational purposes only and does not attempt to be an exhaustive representation of the Policy for Data Management and Data Sharing. Please refer to the Policy in its entirety for additional information.

Recruitment

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

Peer Review and Release of Research Findings

PCORI has a legislative mandate to ensure the scientific integrity of the primary research it supports and to make study findings widely available and useful to patients, clinicians, and the general public within a specific timeframe. Accordingly, the PCORI Board of Governors (Board) adopted the [Process for Peer Review of Primary Research and Public Release of Research Findings](#).²⁴

In summary, 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 interprets the findings in clinical or other decisional contexts. Subject matter experts; individuals with expertise in research methodology or biostatistics; and patients, caregivers, and other healthcare stakeholders will review the draft final research report. After Awardee Institutions have responded to reviewers'

²⁴ See <http://www.pcori.org/sites/default/files/PCORI-Peer-Review-and-Release-of-Findings-Process.pdf>.

comments to PCORI's satisfaction, the report will be accepted and considered final. PCORI will then prepare a 500-word standardized 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 500-word standardized abstract summarizing the study results for patients and the general public; (3) a link to the study record on [ClinicalTrials.gov](https://clinicaltrials.gov) (as applicable); and (4) ancillary information, including conflict of interest disclosures. The final research report, along with anonymized reviewer comments, will be made publicly available on the PCORI website no later than 12 months after its acceptance, except by prior mutual agreement with the Awardee Institution.

III. How to Submit an Application

Applying for funding from PCORI is a two-stage process. An LOI must be submitted and an applicant must be invited to submit an application.

Letter of Intent (LOI)

Applicants should download the [LOI Template](#) from the [PCORI Funding Center](#). They must complete the document and convert it to a PDF file. The LOI is limited to three pages, excluding references. PCORI suggests including all references as in-text citations using American Medical Association citation style, but other citation styles are accepted. Do not upload additional documents as part of your LOI, including Letters of Endorsement or Letters of Support, because they are not requested at this stage. Their inclusion will result in LOI rejection without review. Please visit the [PCORI Funding Center](#) for additional applicant resources, including the PFA and required templates.

The LOI for the proposed study should contain the following information:

- Title of the proposed study that preferably captures the comparative nature of the study
- Specific aims (clearly stated)
- How the study will improve the quality and relevance of evidence available to help patients and stakeholders make informed health decisions
- Knowledge gap addressed by research question(s)
- Concise description of study design
- Study population (description of participants and participating study sites)
- Outcomes (identification and description of why they are important to patients)
- Sample size
- Comparators (described and listed clearly, with demonstrated efficacy specified for each and details on how the strategies will be delivered in real-world settings)



- Patient and other stakeholder engagement (involvement through planning, conducting, and disseminating)

The LOI Template provides guidance on responding to each item. Please refer to the [Application Guidelines](#) for due dates and information on how to submit an LOI via [PCORI Online](#). **The deadline for LOI submission is January 31, 2019, by 5 p.m. (ET).**

LOI Review

LOIs are evaluated based on the following:

- Importance and relevance of the topics to PCORI priorities, as evidenced by critical gaps identified by clinical guidelines developers and recent systematic reviews
- Clarity and credibility of responses to the LOI questions
- The investigators' prior relevant experience
- Programmatic fit and balance, considering whether the application overlaps with previously funded studies or concurrent applications to a significant degree or, conversely, whether the application fills a gap in the portfolio with certain characteristics, including disease category, topics, priority population, methodologies, and other variables

Only applicants whose LOIs are deemed most responsive to this PFA will be invited to submit a full application. A minimum of two PCORI staff review the LOIs, which are not scored during review. Notification of the request to submit a full application will occur no later than February 26, 2019.

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

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

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

Note: A PI can only submit one LOI per PFA. However, an individual listed as a PI on one LOI may be listed as and serve in another non-PI 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.



Project Budget and Duration

At the time of contract execution, PCORI sets aside all of the funds associated with an awarded project to be made available throughout the contract’s period of performance. The maximum budget includes all research- and peer-review-related costs. Refer to the [Application Guidelines](#) for additional details. Appendix 2 within the guidelines provides a list of allowable and unallowable costs. This PFA does not consider exceptions to the budget or to period-of-performance limits. PCORI will not review requests exceeding the stated maximum budget or period of performance. Note that although subcontractor indirect costs are included in the prime applicant’s direct-cost budget, subcontractor indirect costs are not factored when determining adherence to the PFA’s direct-cost limit.

Submission Dates

LOIs and applications must be submitted in accordance with the published dates and times listed in the Overview section of this document and in the [PCORI Funding Center](#).

PCORI Online

To submit an application, you must register with [PCORI Online](#) and submit an LOI and an application for each cycle to which you are applying.

Applicant Resources

PCORI Funding Center	https://www.pcori.org/funding-opportunities/announcement/treatment-anxiety-children-adolescents-andor-young-adults-cycle-1
PCORI Online System	https://pcori.force.com/engagement
PCORI Funding Awards	http://www.pcori.org/research-results-home

IV. Merit Review

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

- Identify applications that have the strongest potential to help patients, caregivers, clinicians, policy makers, and other healthcare system stakeholders make informed decisions to improve patient outcomes.
- Implement a transparent, fair, objective, and consistent process to identify these applications.
- Elicit high-quality feedback that reflects a diversity of perspectives to ensure that the PCORI-funded research reflects the interests and views of patients and other stakeholders and those who care for them, and that it meets the criteria for scientific rigor.
- Fund projects that fill important evidence gaps and have strong implementation potential.
- 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; the review panel’s preliminary review of full applications; an in-person panel discussion of a subset of full



applications (identified by PCORI’s Research Priority Area Program staff and based on the preliminary review and program priorities); the Selection Committee’s 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 PCORI may eliminate applications from the review process for administrative or scientific reasons (e.g., non-responsiveness). An application may be administratively withdrawn if it is incomplete; submitted past the stated due date and time; or does not meet the formatting criteria outlined in the [Application Guidelines](#), in the PCORI templates, and in PCORI Online. An application can be scientifically withdrawn if it is not responsive to the guidelines described in this PFA, describes research that is not comparative, includes a cost-effectiveness analysis, or otherwise does not meet PCORI programmatic requirements.

PCORI Merit Review Officers (MROs) recruit each review panel based on the number of invited LOIs and topic areas represented by the invited LOIs. MROs recruit the panel chair, scientist reviewers who are subject matter experts, patient representatives, and representatives of other stakeholder groups. All panel members receive training during the review cycle to ensure that they understand the programmatic and organizational goals of review.

The table below is designed to help applicants understand how the PCORI merit review criteria align with criteria from other funding organizations with which applicants might be familiar (e.g., NIH). Though PCORI’s criteria do map to most NIH criteria, there are areas where we ask for different information (i.e., PCORI does not include a criterion that tracks to NIH’s innovation criterion, but does include criteria evaluating patient-centeredness and engagement) reflecting PCORI’s unique approach.

Crosswalk of PCORI Merit Review Criteria with NIH Criteria	
SIGNIFICANCE	<ol style="list-style-type: none"> 1. Potential for the study to fill critical gaps in evidence 2. Potential for the study findings to be adopted into clinical practice and improve delivery of care
APPROACH	<ol style="list-style-type: none"> 3. Scientific merit (research design, analysis, and outcomes) 4. Investigator(s) and environment
PCORI-only Merit Review Criteria	
PATIENT-CENTEREDNESS/ENGAGEMENT	<ol style="list-style-type: none"> 5. Patient-centeredness 6. Patient and stakeholder engagement

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, and to ensure consistency and fairness in how applications are evaluated.

Criterion 1. Potential for the study to fill critical gaps in evidence:

The application should address the following questions:

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

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

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

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

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

The application should show sufficient technical merit in the research design to ensure that the study goals will be met. The application should also address the following questions:

- Does the application describe a clear conceptual framework anchored in background literature which informs the design, key variables, and relationship between interventions and outcomes being tested?
- Does the Research Plan describe rigorous methods that demonstrate adherence to the PCORI Methodology Standards?
- Is the overall study design justified?
- Are the patient population and study setting appropriate for the proposed research question?

- Does the application provide justification that the outcome measures are validated and appropriate for the population?
- Are each of the comparators (e.g., active intervention arm and comparator arm) described clearly and well-justified? If “usual care” is one of the arms, is it adequately justified, and will it be sufficiently measured?
- Are the sample sizes and power estimates appropriate? Is the study design (e.g., cluster randomized design, randomized controlled trial, or observational study) accounted for and is the anticipated effect size adequately justified?
- Is the study plan feasible? Is the project timeline realistic, including specific scientific and engagement milestones? Is the strategy for recruiting participants feasible? Are assumptions about participant attrition realistic, and are plans to address patient or site attrition adequate?

Criterion 4. Investigator(s) and environment

This criterion should assess the appropriateness (e.g., qualifications and experience) of the investigator(s)/team and the environment’s capacity (e.g., resources, facilities, and equipment) to support the proposed project. It should not be an assessment of the institution’s quality.

The application should also address the following questions:

- How well-qualified are the PIs, collaborators, and other researchers to conduct the proposed activities? Is there evidence of sufficient clinical or statistical expertise (if applicable)?
- Does the investigator or co-investigator have demonstrated experience conducting projects of a similar size, scope, and complexity?
- If the project is collaborative or dual-PI, do the investigators have complementary and integrated expertise? Are the leadership, governance, and organizational structures appropriate for the project?
 - (Dual-PI Option Only) Does the Leadership Plan adequately describe and justify PI roles and areas of responsibility?
- Is the level of effort for each team member appropriate for successfully conducting the proposed work?
- Does the application describe adequate availability of and access to facilities and resources (including patient populations, samples, and collaborative arrangements) to carry out the proposed research?
- Is the institutional support appropriate for the proposed research?

Criterion 5. Patient-centeredness

The application should demonstrate that the study focuses on improving patient-centered outcomes and employs a patient-centered research design (i.e., a design informed or endorsed by patients). (*Note:*

The study can be patient-centered even if the end-user is not the patient, as long as patients will benefit from the information.)

The application should also address the following questions:

- 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 6. Patient and stakeholder engagement

The application should demonstrate the engagement of relevant patients and other stakeholders (e.g., patients, caregivers, clinicians, policy makers, hospital and health system representatives, payers [insurance], purchasers [business], industry, researchers, 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 the research process.

The application should also address the following questions:

- Does the application provide a well-justified description of how the research team incorporates stakeholder involvement? Does the study include the right individuals (e.g., patients, caregivers, clinicians, policy makers, hospital and health system representatives, payers, purchasers, industry, researchers, and training institutions) to ensure that the projects will be carried out successfully?
- Does the application show evidence of active engagement among scientists, patients, and other stakeholders throughout the research process (e.g., formulating questions, identifying outcomes, monitoring the study, disseminating, and implementing)? Is 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 described clearly?
- Are the organizational structure and resources appropriate to engage patients and stakeholders throughout the project?

In-Person Review

During preliminary review, all administratively and scientifically compliant applications are evaluated and scored by panels of external reviewers based on PCORI's merit review criteria, including evaluation of adherence to the PCORI Methodology Standards. After preliminary review, PCORI program staff members evaluate panel scores and critiques to identify a subset of applications for merit reviewers to



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

During the in-person review, merit reviewers meet to discuss applications and to clarify further the merits of the proposed research. They also identify areas for improvement. Each application is re-scored based on the content of discussion. The Panel Chair and PCORI MRO lead the in-person panel meeting and ensure that all applications receive a fair and thorough review according to the standards outlined in the PFA.

Post-Panel Review

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

In addition, PCORI evaluates applicant risk before issuing a PCORI award. Factors considered include financial stability, quality of management systems, audit findings, and past performance on PCORI awards (e.g., compliance with PCORI reporting requirements, conformance to PCORI terms and conditions on previous awards, and timely achievement of milestones). Based on the risk assessment, PCORI may impose special terms and conditions on awardees or withhold contract issuance until such business risks are mitigated. **PCORI will not award new contracts to current awardees with overdue reports (progress, interim, final, etc.) until the overdue reports have been submitted to PCORI.**

Summary Statements and Funding Recommendations

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

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

Summary statements for applications that do not progress to in-person discussion include only the preliminary reviewer critiques.

Funding recommendations are made by identifying meritorious applications that fit the programmatic needs and that satisfactorily address the merit review criteria while adhering to the PCORI Methodology Standards. Programs also consider the funds allotted for the current funding announcement when deciding which applications to recommend to the Board for approval. Applicants to this current cycle's



PFA will receive summary statements and notification of the funding status of their application no later than October 2019.