Cycle 1 2018: Pharmacological Treatment for Anxiety Disorders in Children, Adolescents, and/or Young Adults

Town Hall

January 31, 2018
Agenda

• Welcome and Introductions
• PFA overview
• Patient and Stakeholder Engagement
• Administrative Requirements
• Merit Review
• Resources
• Questions?

Submit questions via the chat function in GoToWebinar.

Ask a question via phone at the end of the presentation.
Today’s Presenters

Geeta Bhat, MPH, PMP
Program Associate
Clinical Effectiveness and Decision Science

Laura Esmail, PhD, MSc
Program Officer
Clinical Effectiveness and Decision Science

Denese Neu, PhD, MS
Engagement Officer
Public and Patient Engagement

Joseph Knight, MS, CRA, PMP
Administrator
Contracts Operations

Roycelynn Mentor-Marcel
PhD, MPH
Merit Review Officer
Program Support & Information Management
PCORI’s Mission

PCORI helps people make informed health care decisions, and improves health care delivery and outcomes, by producing and promoting high integrity, evidence-based information that comes from research guided by patients, caregivers and the broader health care community.

PCORI is particularly interested in research conducted in real-world settings that will facilitate widespread dissemination and implementation of findings.
Pharmacological Treatment for Anxiety Disorders in Children, Adolescents, and/or Young Adults Funding Announcement
Objective of this PFA:

- Fund high-quality clinical studies that compare the effectiveness of two or more pharmacological treatments for moderate-to-severe anxiety in children, adolescents, and/or young adults. Examples:
  - Comparisons of shorter-acting selective serotonin reuptake inhibitors (SSRIs) to longer-acting SSRIs
  - Comparisons of SSRIs to selective serotonin-norepinephrine reuptake inhibitors (SNRIs)

Available Funds and Duration:

- A total of $40 million (direct and indirect)
- Up to $15 million in total direct costs per project
- Projects must be completed within 5 years
Treatment of Pediatric Anxiety Disorders: the need for more evidence

- Patients, caregivers, researchers, and stakeholder organizations have indicated the need for CER that examines the treatment options for pediatric anxiety disorders.
- Evidence is significantly lacking for:
  - Head-to-head comparisons of individual medications
  - Comparisons of CBT versus medications
  - Comparisons of combination therapy (CBT + medication) versus monotherapy
  - Treatment sequencing approaches and the discontinuation of treatment
- Larger trials (>400 participants) with follow-up that exceeds 2-3 years are needed to address these evidence gaps.

To address these evidence gaps, PCORI issued a series of funding announcements.

PCORI released a PCS Special Area of Emphasis topic for Cycle 2 2017:
- Studies that compare the effectiveness of one or more digital applications of CBT to an appropriate active control (e.g., face-to-face CBT) for the treatment of mild-to-moderate anxiety in children, adolescents, and/or young adults (through age 25).

For PCS Cycle 3 2017 and PCS Cycle 1 2018, PCORI issued a priority topic:
- Studies that compare the effectiveness of two or more evidence-based approaches for the treatment of anxiety in children, adolescents, and young adults (through age 25).
- Studies which examine comparisons of different approaches to treatment initiation, sequencing, monitoring, maintenance, and/or relapse prevention following an initial effective course of treatment.
The goal: to generate needed scientific evidence to help patients, families, and clinicians to make decisions about pharmacological treatments for children, adolescents and/or young adults with moderate to severe anxiety.
Design Considerations: Population

- Children, adolescents, and/or young adults diagnosed with an anxiety disorder and exhibiting moderate-to-severe symptomatology
  - PCORI is interested in comparisons that are relevant and applicable to a spectrum of developmental stages represented by patients in the age range of 7 through 25 years old
  - Applicants should clearly define the specific age range to be studied and provide a scientific rationale and specific benefit for the proposed study population
  - Clinical diagnoses including any co-morbidities must be specified
- Robust sample sizes of \textit{at least} 300 participants are required
  - Applications that propose sample sizes of fewer than 300 participants will be considered nonresponsive
Design Considerations: Interventions

• Each proposed comparator must include an evidence-based pharmacological treatment option. Comparisons of interest include, but are not limited to:
  – Comparisons of shorter-acting to longer-acting selective serotonin reuptake inhibitors (SSRIs)
  – Comparisons of SSRIs to selective serotonin norepinephrine reuptake inhibitors (SNRIs)
• Pharmacologic comparators must be delivered in conjunction with CBT or another evidence-based psychological intervention
• Applicants must ensure that all comparators are appropriate for the age range and disorder severity of the study population
Design Considerations: Outcomes

• 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 at least include the following domains:
  – Function (e.g., school attendance, avoidance behavior)
  – Symptoms (child-, parent-, and/or clinician-reported, as scientifically justified)
  – Acceptability of treatment (e.g., family burden, dropout from therapy)
  – Adverse effects
Design Considerations: Timing

• Studies must include at least one year of follow-up from baseline, with two years of follow-up preferred
• Applicants should clearly specify the duration of each of the active interventions as well as the duration of any maintenance or booster sessions
Design Considerations: Setting

• Studies may take place in pediatric primary care or combined primary and specialty care settings, reflective of community-based care

• Models that employ care coordination and integration across settings are encouraged
Safety Considerations

- Applicants must include an adequate and appropriate human subjects protection plan
  - For example: 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
- Applicants who propose off-label use of medications should anticipate the potential need to file an Investigational New Drug (IND) application for Food and Drug Administration (FDA) approval
PCORI Methodology Standards

In any study, methods are critical. PCORI’s Methodology Committee developed Methodology Standards to which patient-centered CER must adhere.

The 48 standards can be grouped into 2 broad categories and 12 topic areas.

**Cross-Cutting Standards**
- Formulating Research Questions
- Patient Centeredness
- Data Integrity & Rigorous Analyses
- Preventing/Handling Missing Data
- Heterogeneity of Treatment Effects

**Design-Specific Standards**
- Data Registries
- Data Networks
- Causal Inference Methods*
- Adaptive & Bayesian Trial Designs
- Studies of Medical Tests
- Systematic Reviews
- Research Designs Using Clusters

*The first standard for Causal Inference Methods (CI-1) is considered cross-cutting and applicable to all PCOR/CER studies.*
Patient and Stakeholder Engagement
Patients and Other Stakeholders

- Patient/Consumer
- Caregiver/Family Member of Patient
- Hospital/Health System
- Training Institution
- Policy Maker
- Industry
- Payer
- Patient/Caregiver Advocacy Org
- Clinician

PCORI Community
Patient-Centeredness vs. Patient Engagement

**Patient-Centeredness**
- Does the LOI mention outcomes (both benefits and harms) important to patients?
- Are the interventions being proposed for comparison available to patients now?

**Patient and Stakeholder engagement**
- Does the LOI mention intent to build an interdisciplinary study team that includes appropriate patient and stakeholder representation in consultation with PCORI?
Evidence of Appropriate Engagement of Relevant Patients and Other Stakeholders

• 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.

• Identify the patients and 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.
The Engagement Rubric

The rubric is intended to provide guidance to applicants, merit reviewers, awardees, and engagement/program officers (for creating milestones and monitoring projects) regarding engagement in the conduct of research. It is divided into three segments:

I. Overarching Concepts

The rubric specifically focuses on patient and family engagement in research to help illustrate promising practices emerging in this relatively new area of engagement in research. The term “patient partner” is intended to include patients (those with lived experience), family members, caregivers, and the organizations that represent them who are representative of the population of interest in a particular study.

Although the rubric is called the patient and family engagement rubric, there is an expectation that engagement of other stakeholders (e.g., clinicians, payers, or hospital administrators that are relevant to a particular study) will also be evaluated.

The rubric is intended to provide guidance to applicants, merit reviewers, awardees, and engagement/program officers (for creating milestones and monitoring projects) regarding patient and family engagement in the conduct of research. It is not intended to be comprehensive or prescriptive. Instead, it provides a variety of options to incorporate engagement, where relevant, into the research process. Applicants can choose to include some, but not all, sections, and can include additional innovative approaches not listed here.

The rubric is based on the promising practices identified in the first three rounds of PCORI awards. It is also consistent with PCORI’s Methodology Standards for patient-centeredness and its PCOR Engagement Principles.

The rubric is structured into four sections: Planning the Study, Conducting the Study, Disseminating the Study Results, and PCOR Engagement Principles.

The rubric provides guidance to help applicants “show their work” when describing the details of how patient and family input will be incorporated throughout the entire research process.

II. Planning the Study

III. Conducting the Study

IV. Disseminating the Study Results
Budgeting

- Financial compensation of partners
- Expenses of partners (transportation, childcare, caregiver)
- Budgeting for program staff dedicated to engagement tasks
- Costs of engagement meetings and events (travel, food, audio visual)
- Additional time and resource to incorporate partner feedback into various project process
Public Posting of Partner Names

- Many members of the patient and stakeholder community have requested that PCORI make the names of partnering individuals and organizations available to credit the contributions of the full research team adequately.
- You should provide PCORI only those names of patient or stakeholder partners for whom you have obtained appropriate permission to disclose their identity to PCORI and for PCORI to use their names in public communications.
- If partners wish to remain anonymous, you may use pseudonyms or categorical descriptors (e.g., caregiver to husband with COPD, breast cancer survivor of 20 years).
- If you are selected for funding, the individuals and organizations you provided (including those described by pseudonym or categorical descriptor) will be listed on the project description page along with the other information about your project (such as abstract and PI).
Engagement Resources

- **PCORI’s “The Engagement Rubric”**

- **Sample Engagement Plans**

- **Compensation Framework**

- **Engagement Budgeting**

- **Engagement in Research website page**
  [http://www.pcori.org/funding-opportunities/what-we-mean-engagement](http://www.pcori.org/funding-opportunities/what-we-mean-engagement)

- **PCORI’s Methodology Standards PC-1 to PC-4**
  [https://www.pcori.org/research-results/about-our-research/research-methodology/pcori-methodology-standards](https://www.pcori.org/research-results/about-our-research/research-methodology/pcori-methodology-standards)
Administrative Requirements
Timeline: Pharmacological Treatment of Anxiety Disorders in Children, Adolescents and/or Young Adults

- **PFA Posted:** January 16, 2018
- **Letter of Intent (LOI) Deadline:** February 13, 2018
- **Application Deadline:** May 16, 2018
- **Merit Review:** August 2018
- **Awards Announced:** November 20, 2018
- **Earliest Start Date:** February 2019
Using the PCORI Online System

- Submit your LOI through PCORI Online: [https://pcori.force.com/engagement](https://pcori.force.com/engagement)
- Register as a New User and create your LOI as soon as possible, if appropriate
- Please note that the PI and AO cannot be the same person
- Enter information into all required fields in the system
- [PCORI Online Training Resources](#)
- [PCORI Online Application Cheat Sheet](#)
Eligibility to Submit a Letter of Intent

• Any private sector (non-profit or for-profit) research organization.

• Any public sector research organization (university or college hospital or healthcare system, laboratory or manufacturer, unit of local, state, or federal government).

• Non-domestic components of organizations based in the US and foreign organizations may apply, as long as there is demonstrable benefit to the US healthcare system and US efforts in the area of patient-centered research can be clearly shown.

• Individuals are not permitted to apply.
Letter of Intent (LOI): Requirements

• An LOI is required and must be submitted prior to the deadline.

• To submit an LOI, download the PFA-specific Letter of Intent Template from the Funding Center to begin your LOI.

• You must answer all questions.

• Do not upload additional documents as part of your LOI. Letters of endorsements or support are not accepted at this stage.

• Only those LOIs deemed most responsive (programmatically and administratively) to this PFA will be invited to submit a full application.
Letter of Intent (LOI)

• Download the **Pediatric Anxiety Letter of Intent Template for this cycle** from the [Funding Center](#) to begin your LOI.

• LOIs must not be more than 3 pages excluding references. PCORI suggests including all references as in-text citations using American Medical Association citation style, but other citation styles are accepted. LOIs that exceed the page limit will not be reviewed.

• You must answer all questions, including the question on brief justification for the cost (“Will not exceed $10 million” is not a sufficient answer!).

• Do not upload additional documents as part of your LOI.

• Letters of endorsements or support are not accepted at this stage.

• You must upload your LOI as a PDF in PCORI Online.
• Include the Principal Investigator’s (PI’s) full name on every page in the top left corner of the page header.

• Use at least half-inch margins and single spacing. (The header may fall within the top margin, but the body text should not begin closer than a half-inch from the edge of the page.)

• Use font size Calibri 11 for the main body of the text.

• Keep the numbering of the LOI questions within the LOI template.
Tips for Success

- Adhere to the Application Guidelines for the appropriate PFA and funding cycle
- Start and submit application early
- Have a copy of your approved LOI readily accessible
- Ensure that all team members can see the application in the system (check during the LOI stage)
- Inform your AO of your intent to submit
- Clearly describe comparators for the study
- Document evidence of efficacy/effectiveness for the intervention and comparator(s) and/or demonstrate that they are in widespread use
- Justify your power calculations based on prior evidence of anticipated effect sizes
- Clearly demonstrate the feasibility of the study
  - Show that have the team to do this and you are the right team
  - Define and support your recruitment and retention plan
  - Document that sites are already committed to participating
  - Include realistic timelines for site start-up, IRB approval, and recruitment
- Submit the completed application on/before the due date by 5:00 PM ET
Application Components & Templates

- As seen in the Application Guidelines
  - Projection Information (Abstracts)
  - Budget and Budget Justification
  - Milestones
  - People and Places
  - Research Plan
  - Letters of Support
Application Components: Budget & Justification

• In PCORI Online, for the Budget tab complete the following sections:
  – Detailed Research Project Budget for Each Year of the Research Project Period
  – Detailed Peer-Review Budget for Peer-Review-Related Costs
  – Budget Summary for Entire Project

• In the Templates and Uploads tab, upload the **Budget Justification Template** for the prime applicant and each subcontracted organization for the entire Research Project Budget and Peer-Review Budget for all research and peer-review-related costs. Include the federally negotiated or independently audited indirect cost rate letter (prime contractor) and fringe benefit rate policy verification document (prime contractor).
Milestones/Deliverables

• Milestones
  – Significant events, deliverables, tasks, and/or outcomes that occur over the course of the project that mark progress toward the project’s overall aims

• Deliverables
  – Measurable and verifiable outcomes or products that a project team must create and deliver according to the contract terms

• See Appendix 1 of the Application Guidelines for examples of milestones.
Application Components: People & Places Template

- Leadership Plan Template (Dual PI Applications only)
  - Describe the governance and organizational structure of the leadership team and the research project;
  - Delineate the administrative, technical, scientific, and engagement responsibilities for each PI and the rationale for submitting a dual-PI application;
  - Discuss communication plans and the process for making decisions on scientific and engagement direction;
  - Describe the procedure for resolving conflicts.
  - Note: If this template is applicable, it should be uploaded as the first section of the People and Places Template
Application Components: People & Places (cont.)

• **Leadership Plan (if applicable):** 5 pages
  — Required for Dual-PI Applications

• **Project/Performance Site(s) and Resources:** 15 pages
  — Provide a description of the facilities that will be used during the project, including capacity, capability, characteristics, proximity, and availability to the project.

• **Professional Profile/Biosketch:** 5 pages per individual

• **Patient/Stakeholder Partner Profile/Biosketch:** 5 pages per individual
Application Components: Research Plan

- **Research Strategy: 15 pages**
  - Provide all the information requested, as outlined in the template:
    - Specific Aims
    - Background
    - Significance
    - Study Design or Approach

- **Research Team & Environment: 2 pages**
  - Describe the research team’s capabilities to accomplish the goals of the proposed research project and the appropriateness of the research environment to conduct the study.

- **Dissemination & Implementation: 1 page**
  - Describe how you will make study results available to study participants after you complete the analyses, and possible barriers to disseminating and implementing the results of this research in other settings.
Application Components: Research Plan (cont.)

• **Consortium Contractual Arrangements: 5 pages**
  – Describe the proposed components of the research project that will be performed by subcontracted organizations.
  – Explain the strengths that these partners bring to the overall project to ensure successful submission of contract deliverables in accordance with the milestone schedule.

• **Appendices: 10 pages**
  – Applicants can include additional materials that they believe are useful, but reviewers are not required to review the appendix materials in evaluating the application.

• **Methodology Standards Checklist: no page limit**
  – Applicants must complete each column of this checklist, as appropriate, and include it with the Research Plan PDF upload.
Letters of support should be addressed to the PI to demonstrate the commitment of key personnel and supporting organizations to the proposed project.

Letters of support should be organized in the following manner:

- Letters of organizational support
- Letters of collaboration
- Letters confirming access to patient populations, data sets, and additional resources
Applicants must follow the administrative requirements stated in PCORI’s Application Guidelines.

Applications may be administratively withdrawn for the following reasons:
• Exceeding budget or time limitations
• Not using PCORI’s required templates
• Submitting incomplete sections or applications
What happens to your application after you submit it?
Merit Review
Programmatic Screening

Applications may be programmatically withdrawn for the following reasons:

- Deviation from the approved LOI
- Inclusion of cost-effectiveness analysis (CEA)
- Inclusion of development and dissemination of clinical practice guidelines (CPG)
- Not responsive in areas listed in the Pediatric Anxiety PFA (see pages 8-9 of PFA)
PCORI Merit Review Cycle

- Start: PCORI Funding Announcement (PFA) Development
- Reviewer Recruitment: Letter of Intent (LOI) Receipt
- Reviewer Recruitment: Full Application Receipt
- Reviewer Recruitment: Application Assignment to Reviewers
- Summary Statement Production: Funding Slates Set by Programs
- Selection Committee Meeting
- Board of Governors Funding Slate Review and Approval
- In-Person Meeting
- Programs Set Discussion Line
- Preliminary Review
Applications are reviewed against six criteria:

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
4. Investigator(s) and environment
5. Patient-centeredness
6. Patient and stakeholder Engagement

- Each application is reviewed by three scientists, one patient, and one other stakeholder
- PCORI’s Board of Governors makes funding decisions based on merit review results and program staff recommendations.
# Merit Review Criteria

## Crosswalk of PCORI Merit Review Criteria with NIH Criteria

| SIGNIFICANCE                                      | 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                                          | 3. Scientific merit (research design, analysis, and outcomes)  
|                                                  | 4. Investigator(s) and environment |

### PCORI-only Merit Review Criteria

<table>
<thead>
<tr>
<th>PATIENT-CENTEREDNESS/ENGAGEMENT</th>
<th>5. Patient-centeredness</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>6. Patient and stakeholder engagement</td>
</tr>
</tbody>
</table>
Merit Review Tips

• Address the bulleted points under each merit review criterion in the PFA
  – We refer reviewers to these bulleted points.
• Include sufficient scientific detail while making understandable to range of reviewer types
Results of Merit Review

- Funding decisions will be announced in November 2018 with PCORI BOG meeting
- Non-Discussed Summary Statement
  - Reviewers’ written critiques
- Discussed Summary Statement
  - Reviewers’ written critiques
  - Summary of in-person discussion
  - Final overall score
Resources
Where can I find help?

Visit pcori.org/apply

- Application Guidelines
- FAQs
- PCORI Online User Manuals
- Sample Engagement Plans

Schedule a Call with a Program Officer

- Submit a request at pcori.org/content/research-inquiry
- Call 202-627-1884 (programmatic inquiries)
- E-mail sciencequestions@pcori.org

Contact our Helpdesk

- E-mail pfa@pcori.org
- Call 202-627-1885 (administrative and technical inquiries)
Q&A

Ask a question via the Q & A function in GOTO Meeting.

Ask a question via phone at the end of the presentation.

If we are unable to address your question during this time, e-mail the Helpdesk at pfa@pcori.org or sciencequestion@pcori.org.
Thank You