Management Strategies for Treatment-Resistant Depression

LOI Applicant Town Hall

October 21, 2015
Agenda

- Welcome
- Introduction to PCORI
- Background for the PFA
- Guidance on Preparing a LOI
- Programmatic and Administrative Requirements
- Resources
- Questions

Submit questions via the chat function in Meeting Bridge.

Ask a question via phone (an operator will stand by to take your questions).
Introductions

David Hickam, MD, MPH
Program Director, Science Clinical Effectiveness Research (CER)

Julie McCormack, MA
Program Officer
Clinical Effectiveness Research (CER)

Geeta Bhat, MPH
Program Associate
Clinical Effectiveness Research (CER)

Susan L. Hildebrandt, MA
Director of Stakeholder Engagement

Maricon Gardner, CRA
Contracts Associate, Pre- Award Contracts Management and Administration
Introduction to this PCORI PFA

Julie McCormack, MA
Program Officer, Clinical Effectiveness Research
PCORI’s Mission

To help people make informed health care decisions and improve 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.
We Fund Comparative Clinical Effectiveness Research

Research that....

• Generates evidence comparing benefits and harms of at least two different methods to manage a clinical condition

• Measures benefits in real-world populations

• Informs a specific clinical or policy decision

Adapted from *Initial National Priorities for Comparative Effectiveness Research*, Institute of Medicine of the National Academies
We Fund Comparative Clinical Effectiveness Research

Research that...

- Describes results in subgroups of people
- Applies appropriate methods and data sources
- Helps consumers, clinicians, purchasers, and policy makers make informed decisions that will improve care for individuals and populations

Note: We do not fund cost-effectiveness research
Need for CER for Treatment-Resistant Depression

Treatment-Resistant Depression (TRD) is a complex illness:

- TRD is defined as not having experienced an adequate clinical response to two or more adequate courses of antidepressant treatment
- As many as one-third of people diagnosed with major depressive disorder are classified as having TRD
Need for CER for Treatment-Resistant Depression

Treatment-Resistant Depression (TRD) is a complex illness:

• Current clinical approaches include a multitude of choices
• Few studies have compared alternative management strategies
PFA Overview: Management Strategies for Treatment-Resistant Depression

Objective of this PFA:
- Examine direct comparisons of different treatment strategies and modalities in patients with treatment-resistant depression

In this PFA we seek to fund:
- Pragmatic clinical trials
- Comparative observational studies

Available Funds and Duration:
- A total of $30 million (direct and indirect)
- Up to $10 million in total direct costs per project
- Projects should be completed within 5 years
What is a Pragmatic CER Trial?

- Answers a practical, real world comparative effectiveness research question
- Assesses whether two or more options differ in effectiveness when administered as they are in real life
- Project is conducted in a clinical setting that is as close as possible to a real world setting
- The methodological approach (including study design, outcome measures, and follow-up) is as simple as possible without sacrificing scientific rigor
For patients with treatment-resistant depression who have failed two adequate trials of antidepressant medications, what is the comparative effectiveness of augmentation strategies versus switching to other treatments?

- Populations of interest: co-morbid mental or medical conditions, post-partum populations, racial/ethnic minorities, low socio-economic status
- Interventions of interest: antidepressant medications, antipsychotic medications, psychotherapeutic treatments and complementary and alternative options
- Outcomes of interest: short- and long-term patient functioning, quality of life, depression symptoms, suicidal ideation or behavior, side effects of treatment
Essential characteristics of studies

- Addresses the priority research question
- Studies that directly compare augmentation versus switching strategies
- Include representative patient population
- Have a sufficiently large study population to enable precise estimates of effect sizes and to support evaluation of potential differences in intervention effectiveness in patient subgroups.
- Conduct the study in typical clinical care and community settings
- Has strong endorsement and participation by stakeholders
“Usual care” is generally not an optimal comparator for CER studies.

- It is ill-defined, difficult to quantify, and subject to considerable geographic and temporal variations, thus limiting interpretability, applicability, and reproducibility.

- If the applicant proposes “usual care” as a comparator, it must be justified as a legitimate comparator (e.g., usual care is guideline-based).

- A proposal for a usual care comparator must be accompanied by an explanation of how the care given in the usual care group will be measured and how appropriate inferences will be made.
Research activities not supported by this PFA

- Studies of decision aids
- Efficacy trials (testing a new intervention)
- Pilot studies intended to inform larger efforts
- Natural history studies
- Clinical prediction tools
- Fundamental science studies or studies of biological mechanisms
- Cost-effectiveness studies, including research that aims to compare the overall costs of care between two or more alternatives and use the results to determine the preferred alternative
PCORI Methodology Standards

Not to be addressed, per se, in LOI, but be aware and prepared!

Methodology Standards: 11 Broad Categories

- Formulating Research Questions
- Patient-Centeredness
- Data Integrity and Rigorous Analyses
- Preventing/Handling Missing Data
- Heterogeneity of Treatment Effects
- Data Networks
- Data Registries
- Adaptive and Bayesian Trial Designs
- Causal Inference
- Studies of Diagnostic Tests
- Systematic Reviews

“Gap analysis and systematic reviews should be used to support the need for a proposed study. If a systematic review is not available, a systematic review should be performed using accepted standards in the field (see standard SR-1), or a strong rationale should be presented for proceeding without a systematic review. In the case where a systematic review is not possible, the methods used to review the literature should be explained and justified.”

What to Include in the LOI

Geeta Bhat, MPH
Program Associate, Clinical Effectiveness Research
What PCORI looks for when reviewing LOIs

An important documented decisional dilemma

- Clinical guidelines based on less than optimal evidence
- Credible reviews calling out a research gap, such as systematic reviews
- CER question stated in your Specific Aims
- Proposed comparators should be viable (realistic) and consistent with the decisional dilemma
What PCORI looks for when reviewing LOIs

A well-thought out, appropriate, defensible research strategy

- Adequate study power/appropriate sample size
- Realistic assumptions
- Appropriate study design
- Realistic recruitment strategy, if applicable

Note: The LOI is only 4 pages, so there is not room for much detail, but you should describe why your proposed design is the best possible approach for generating new evidence.
Responsiveness Review

• Letters of Intent are reviewed based on criteria detailed in each PFA
• Additional screening for
  – Comparative effectiveness research
  – NON Inclusion of cost-effectiveness analysis
  – Administrative Guidelines
• Only responsive LOIs will be invited to submit a full application
Patient and Stakeholder Engagement

Susan L. Hildebrandt, MA
Director of Stakeholder Engagement
Patient-Centeredness vs. Patient and Stakeholder 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 stakeholders and researchers

- Applicants are expected to consult with patients and other stakeholders on their decisional dilemma and evidence needs.
- The LOI should describe key partnerships with clinical organizations that would provide the setting for the study.
- 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.
Engagement Resources

- PCORI’s “Engagement Rubric”

- Sample Engagement Plans

- PCORI Compensation Framework

- Engagement in Research website page
  [http://www.pcori.org/content/engagement-research](http://www.pcori.org/content/engagement-research)

- PCORI’s Methodology Standards PC-1 to PC-4
Administrative Requirements

Mary Gardner, CRA
Contracts Associate, Pre-Award
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
Using the PCORI Online System

- Apply through PCORI Online (https://pcori.fluxx.io)
- Access the website using Chrome or Safari browsers only
- Create a new request and begin the LOI
- Designate the LOI with the following individuals:
  - PI, PI Designee, AO, and Financial Officer
- Enter information into all required fields in the system
- Convert the document to PDF file
- Upload the LOI in the system
- An applicant can save information by clicking the ‘Save and Review’ button.
Complete a Letter of Intent (LOI)

- Refer to the PCORI Online User Manual: Submitting a Letter of Intent
  - Pre-Screen Questionnaire
  - PI and Contact Information
  - Project Information
  - Key Personnel
  - Templates and Uploads
- Refer to the PFA-specific LOI Template to address the program’s areas of interest
  - Please make sure to address all required sections of the LOI template
  - Please refer to the specific PFA as each program has its own unique characteristics and requirements
Letter of Intent (LOI)

• An LOI is required and must be submitted prior to the deadline. To submit an LOI, download the Letter of Intent Template specifically for the MANAGEMENT STRATEGIES FOR TREATMENT RESISTANT DEPRESSION Cycle 3 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.
• Please refer to the PFA, Application Guidelines, and PCORI Online User Manuals in the Funding Center here: http://www.pcori.org/funding-opportunities/announcement/treatment-multiple-sclerosis-cycle-3-2015
Management Strategies for Treatment-Resistant Depression tPFA LOI requirements

- Four page limit – See requirements for font size and type, margins, and line spacing.
  - LOIs that exceed four pages will not be reviewed.
- References should be listed at the end and are not included in the four-page limit.
Formatting

• 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.
• Use size 11 Calibri for the main body of the text. Figures and captions may have smaller type.
• Each page must be numbered consecutively for each PDF upload.
• Keep the numbering of the LOI questions within the LOI template.
• Save the document as, Principal Investigator (PI) Last Name_(last five digits of Request ID)_LOI.pdf. A request ID number will be automatically generated once the LOI has been saved.
Budget and Period Limitations

• In the LOI, provide a realistic estimate of the study’s budget.
• Do not just make statements such as “The budget will be within the $10 million limit.”
• Keep budget estimates reasonable. Do not just propose the maximum amount.
**Submission and Key Dates**

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<thead>
<tr>
<th>What</th>
<th>When</th>
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<tbody>
<tr>
<td>LOI due in PCORI Online</td>
<td>November 12, 2015 by 5:00pm ET</td>
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<tr>
<td>Applicants notified as to whether they have been selected to submit a full application</td>
<td>December 18, 2015 by 5:00pm ET</td>
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<td>Earliest Start Date</td>
<td>September 2016</td>
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Resources
Where to go for 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 chat function in Meeting Bridge.

Ask a question via phone (an operator will standby to take your questions).

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