Clinical Strategies for Managing and Reducing Long-Term Opioid Use for Chronic Pain

Cycle 3 2016

LOI Applicant Town Hall

October 11, 2016 / 12:30pm ET
Introductions

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Agenda

- Welcome
- Introduction to PCORI
- Background of 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 standby to take your questions).
Introduction to PCORI

Layla Lavasani, PhD, MHS
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.
Comparative Effectiveness Research

PCORI funds research that...

• Informs a specific clinical or health services decision
• Compares benefits and harms of at least two different methods to prevent, diagnose, treat, or monitor a clinical condition or to improve care delivery
• Is performed in real-world populations
• Addresses heterogeneity of treatment effects
Overview of the PCORI Funding Announcement
Background

• Chronic pain, defined as pain lasting longer than 3 months, is extremely common, debilitating, and costly
  • Affects more than 100 million Americans
• Opioids are widely used for chronic pain
  • Opioid prescriptions have increased 3-fold over the last 20 years
  • Between 5 million and 8 million Americans use opioids for chronic pain management
• Although there is little evidence regarding the effectiveness of chronic opioid therapy, mounting evidence suggests that it may be associated with important harms
  • In 2013, there were over 16,000 deaths due to prescription opioids
  • Harms include: overdose, abuse, addiction, sedation, impaired cognitive function, depression, constipation, and nausea
Evidence Gaps

A recent systematic review commissioned by AHRQ identified a number of key evidence gaps including:

- Long-term (>1 year) effectiveness of dosing strategies and treatment options:
  - Little available evidence on the effectiveness of tapering protocols, short-/long-acting opioids, and opioid rotation
  - No comparative studies of the effectiveness of adding non-opioid (pharmacological or non-pharmacological) treatments to opioids

- Risk mitigation strategies:
  - No long-term studies evaluating the effectiveness of risk mitigation strategies for improving outcomes related to addiction or misuse
  - No long-term studies examining how harms vary depending on cause of pain and patient comorbidities
Objective of this PFA:

- Support patient-centered CER that addresses important questions regarding clinical strategies for managing pain while reducing chronic opioid use
- PCORI strongly encourages pragmatic clinical trials
  - Well-designed observation studies will be accepted
  - LOIs should address one or more of the two priority research questions.

Available Funds and Duration:

- A total of $19 million (direct and indirect) for this cycle
- Up to $10 million in total direct costs per project
- Projects should be completed within 3-5 years
What is a Pragmatic CER Study?

• 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.
Priority Research Question 1

• Among patients with chronic noncancer pain on *moderate/high-dose long-term opioid therapy, what is the comparative effectiveness of strategies for reducing/eliminating opioid use while managing pain?
  – Treatments that are realistic options faced by patients and stakeholders.
  – Strategies may include pharmacological options and/or nonpharmacological options (such as physical therapy, behavioral therapy, commonly used complementary and alternative medicine approaches, and others).
  – As appropriate and necessary, studies should include risk mitigation strategies across all treatment comparators.
  – Alternative nonopioid interventions may also be proposed.

*Applicants should provide a strong rationale along with supporting evidence for the selection of a particular dosage threshold definition.
Priority Research Question 2

- Among patients on moderate/low-dose long-term opioid therapy, what are the comparative effectiveness and harms of strategies used to limit dose escalation?
  - PCORI is interested in studies that compare alternative strategies for limiting dose escalation among patients on moderate/low-dose chronic opioid therapy.
  - We encourage comparisons that may include combinations of: nonopioid interventions, opioid rotation, dosing strategies, or risk mitigation strategies.
  - Applicants should provide a convincing explanation for the relevance of the clinical options being compared, including efficacy data and/or information indicating that the interventions are commonly used in clinical practice.
Outcomes and Subgroup Analysis

- For both of the priority questions, applicants should consider a broad range of outcomes that are important to patients.
- Studies must be adequately powered to assess the following outcome measures at 12 months: opioid dose, pain control, and function.
- Other key outcomes include: health-related quality of life, opioid misuse, safety, mortality, medical side effects of treatment, depression score, and health services use.
- Applicants should consider a minimum one-year follow-up for primary and secondary outcome measures.
- Subgroup analyses should include important comorbidities such as mental health disorders, past or current substance use disorders, or type of pain.
Essential Characteristics of Studies

- Address at least one of the two priority research questions.
- Consult with patients and other stakeholders on the decisional dilemma in preparation for the submission of the LOI and application.
- Include representative patient populations.
- Conduct the study in typical clinical care and community settings.
- 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.
- Measure health outcomes that are meaningful to the patients.
Considerations in the Selection of Comparators

• Explicitly describe the rationale for why particular interventions or combinations of clinical interventions are selected.
• Clearly document the evidence-base of proposed clinical strategies where multiple intervention components are proposed.
• Proposed interventions should be in relatively common use or readily available to patients.
• Proposed comparisons should be reasonably and measurably distinct.
• For both priority questions, PCORI is interested in ambitious studies that include interventions that directly address the issues of dosing, dose changes, dosage reductions, while managing the pain.
**The Case of Usual Care**

• “Usual care” is typically a suboptimal 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 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).

• Additionally, it should be accompanied by an explanation of how the care given in the usual care group will be measure and how appropriate inferences will be drawn from its inclusion.
Research Activities Not Supported by this PFA

• Efficacy trials (testing a new intervention)
• 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
• Natural history studies
• Instrument development, pharmacodynamics, and fundamental science or study of biological mechanisms
• Studies of decision aids, including development of decision aids
• Clinical prediction tools
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
- Preparing/Handling Missing Data
- Heterogeneity of Treatment Effects
- Data Networks
- Data Registries
- Adaptive and Bayesian Trial Designs
- Causal Inference
- Studies of Diagnostic Tests
- Systematic Reviews

LOI Process

Jana-Lynn Louis, MPH
Program Associate,
Clinical Effectiveness Research
Overview of LOI Purpose and Process

• To identify ideas and proposals that are programmatically responsive.
• To provide feedback to applicants.
• Letters of Intent are reviewed by PCORI staff for each of the items requested.
• LOI is due November 1, 2016 by 5pm ET.
• A decision and feedback will be provided by December 2, 2016.
What PCORI Looks for When Reviewing LOIs

- Cite credible reviews calling out a research gap, such as a systematic review
- Describe a well thought-out, appropriate, defensible research strategy
  - Adequate power/appropriate sample size
  - Realistic assumptions
  - Appropriate study design
  - Realistic recruitment strategy, if applicable

Applicants should:

- Address one of the two priority CER question for this PFA
- State the CER question in your specific aims
- Consult patients and others about the decisional dilemma and evidence needs
- Propose comparators that are viable (realistic) and consistent with the decisional dilemma
Engagement Requirements

Greg Martin
Deputy, Chief Engagement and Dissemination Officer
Patient-Centeredness vs. Patient Engagement

• Patient-Centeredness
  – Research questions and outcomes reflect what is important to patients and caregivers and consider patient preferences.

• Patient Engagement
  – Project includes active engagement among scientists, patients, and stakeholders.
  – Project includes community, patient, and caregiver involvement.
• Applicants should consult with patients and other stakeholders on their decisional dilemma and evidence needs or reference previously documented decisional dilemmas in preparation for the submission of LOIs and applications.
• State the specific clinical decision(s) and/or treatment choice(s) confronted by the decision makers, and explain how the findings from the proposed research will inform those decisions.
• State why this decision, such as choosing between specific treatment strategies, is important to patients and their caregivers.
• Document the uncertainty faced by patients, clinicians, and other decision makers in making this decision.
• Identify the stakeholders you consulted in determining that the proposed study addresses their evidentiary needs for decision making.
• Indicate your commitment to continuing to engage them actively in the conduct of the study.
Addressing Engagement

Several approaches to engagement can succeed. PCORI provides many engagement resources for applicants:

- 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)
Administrative Requirements

Mary Gardner, CRA
Associate, Contracts Operations
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 Clinical Strategies for Managing and Reducing Long-Term Opioid Use for Chronic Pain - Cycle 3 2016 from the Funding Center to begin your LOI.
- You must answer all questions, including the question on brief justification for the cost.
- 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.
Clinical Strategies for Managing and Reducing Long-Term Opioid Use for Chronic Pain 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 will be included within 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. Do not include figures or general tables. Tables can only be used for power calculations.
- 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 Information

- 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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<th>What</th>
<th>When</th>
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<tr>
<td>LOI due in PCORI Online</td>
<td>November 1, 2016 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 2, 2016 by 5:00pm ET</td>
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<td>Earliest Start Date</td>
<td>October 2017</td>
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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 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.
Thank You