Spring 2015 Funding Cycle

PCORI Funding Announcement:
Large Pragmatic Studies to Evaluate Patient-Centered Outcomes

Published April 6, 2015
Updated May 11, 2015

This PCORI Funding Announcement applies to the funding cycle that closes July 31, 2015, at 5:00 p.m. (ET). Application guidelines, templates, and other resources are available at http://www.pcori.org/PFA-2015-spring-pragmatic-studies.
About PCORI

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

PCORI was authorized by the Patient Protection and Affordable Care Act of 2010 as a nonprofit, nongovernmental organization. PCORI’s purpose, as defined by the law, is to help patients, clinicians, purchasers, and policy makers make better-informed health decisions by “advancing the quality and relevance of evidence about how to prevent, diagnose, treat, monitor, and manage diseases, disorders, and other health conditions.”

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### Overview

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<tr>
<th>Published</th>
<th>April 6, 2015</th>
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<tr>
<td>Letter of Intent Due</td>
<td>May 1, 2015, by 5:00 p.m. (ET)</td>
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Letters of Intent will be screened for responsiveness to this PCORI Funding Announcement and fit to program goals. Only those applicants selected will be permitted to submit full applications. Notification of request to submit a full application will occur no later than June 5, 2015.

### Summary

Patient-Centered Outcomes Research Institute (PCORI) seeks to fund pragmatic clinical trials, large simple trials, or large-scale observational studies that compare two or more alternatives for addressing prevention, diagnosis, treatment, or management of a disease or symptom; improving healthcare system-level approaches to managing care; or eliminating health or healthcare disparities.

Proposed studies must address critical clinical choices faced by patients, their caregivers, clinicians, and/or delivery systems. They must involve broadly representative patient populations and be large enough to provide precise estimates of hypothesized effectiveness differences, and to support evaluation of potential differences in treatment effectiveness in patient subgroups.

For this solicitation, PCORI is requiring that relevant patient organizations, professional organizations, and/or payer or purchaser organizations be included as partners and active participants in the study. PCORI expects that most awards will be made for study designs that use randomization, either of individual participants or clusters, to avoid confounding bias. However, we recognize that exceptional opportunities may arise, by virtue of natural experiments and/or the existence of large registries, to address pragmatic questions using observational designs. Please note that this funding program does not support applications to conduct cost-effectiveness analyses, systematic reviews (with or without meta-analyses), or development and/or evaluations of shared decision making or decision support tools.

This announcement is a collaborative effort of PCORI’s Clinical Effectiveness Research, Improving Healthcare Systems, and Addressing Disparities research programs. Thus, applications for pragmatic studies may fit within any of these three priority areas.

### Applicant Resources

See all templates in our Funding Center here: [http://www.pcori.org/PFA-2015-spring-pragmatic-studies](http://www.pcori.org/PFA-2015-spring-pragmatic-studies)

### Key Dates

- **Online System Opens:** April 6, 2015
- **Applicant Town Hall Session:** April 14, 2015, 10:00–11:30 a.m. (ET)
- **Letter of Intent (LOI) Deadline:** May 1, 2015, by 5:00 p.m. (ET)
- **LOI Screening Notification:** June 5, 2015
- **Application Deadline:** July 31, 2015, by 5:00 p.m. (ET)
- **Merit Review Dates:** October/November 2015
- **Awards Announced:** January 2016
- **Earliest Project Start Date:** March 2016

### Maximum Project Budget (Total Direct Costs)

$10 million

### Maximum Project Period

5 years
Funds Available up to $90 million

Eligibility
Applications may be submitted by any private-sector research organization, including any nonprofit or for-profit organization; any public-sector research organization, including any university or college hospital or healthcare system, laboratory, or manufacturer; or unit of local, state, or federal government. All US applicant organizations must be recognized by the Internal Revenue Service. Nondomestic 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. Organizations may submit multiple applications for funding. Individuals are not permitted to apply.

Review Criteria
1. Impact of the condition on the health of individuals and populations
2. Potential for the study to improve health care and outcomes
3. Technical merit
4. Patient-centeredness
5. Patient and stakeholder engagement

Contact Us
Programmatic Inquiries: Please contact the PCORI Helpdesk via email (sciencequestions@pcori.org), phone (202-627-1884), or online (http://www.pcori.org/PFA/inquiry). PCORI will provide a response within three business days; however, we cannot guarantee that all questions will be addressed in a timely fashion when the inquiry is made three or fewer business days before a Letter of Intent or application deadline.

Administrative, Financial, or Technical Inquiries: Please contact the PCORI Helpdesk at pfa@pcori.org. PCORI will provide a response within two business days. Please note that during the week of the application deadline, response times may exceed two business days. Applicants may also call the PCORI Helpdesk at (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.

New or Revised for the Spring 2015 Funding Cycle:
- Applicants are not required to present their proposals in person to PCORI staff.
- The PCORI Priority Research Topics have been updated.
- The Recruitment section has been updated.
- Included, as guidance, is a Methodology Standards Checklist, which program staff members use to evaluate applications.
PCORI Funding Announcement Spring 2015 Cycle: Pragmatic Studies
I. Introduction

Summary of Program
The Patient-Centered Outcomes Research Institute (PCORI) is launching this funding initiative to expand its support of patient-centered clinical comparative effectiveness research (CER). PCORI seeks to fund large pragmatic clinical trials (PCTs), large simple trials (LSTs), or large-scale comparative observational studies that involve representative patient populations; have strong endorsement and study participation by relevant patient organizations, professional organizations, and/or payer or purchaser organizations; take place within typical clinical care and community settings; and have a sample large enough to enable precise estimates of effect sizes and to support evaluation of potential differences in treatment effectiveness in patient subgroups. Funded studies will compare the relative effectiveness1 of two or more alternatives for improving patient-centered outcomes. Proposed studies of comparative efficacy2 will be considered non-responsive.

Background
While traditional randomized controlled trials (RCTs) are widely accepted for assessing the efficacy of medical interventions, RCTs are generally expensive and time consuming. Furthermore, findings from these trials may have limited generalizability for evaluating the comparative effectiveness of interventions already in use because of well-documented factors: (1) the comparisons in the trial often fail to reflect the choices faced by patients and clinicians; (2) the population selected for study tends to be homogeneous, highly motivated, and relatively free of many comorbid conditions; (3) research tends to take place in specialized research settings; (4) research protocols are often rigid and not representative of typical clinical practice; and (5) the trial may use a placebo, rather than an active comparator, as the comparison.

To meet these concerns, trials can be designed to address practical comparative questions faced by patients and clinicians; include broader and more diverse populations; and be conducted in real-world clinical and diverse health-system settings. Such trials are often referred to as PCTs because they are intended to provide information that can be directly adopted by healthcare providers. They tend to be conducted in routine clinical care settings, and, in many cases, they must be relatively large, in part because expected differences in comparative effectiveness may be small, yet important, or diverse trials may be able to address effectiveness in different patient subgroups. In some cases, these trials may be much simpler than traditional RCTs, and such trials would be considered LSTs.

The protocols for these trials are typically less complex and less intrusive to routine clinical practice than are efficacy studies. For more extensive discussion on pragmatic versus traditional explanatory trials, see

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1 Effectiveness is the extent to which an intervention does more good than harm in a broad mix of patients when provided under the usual circumstances of healthcare practice (modified from ec.europa.eu/enterprise/sectors/healthcare/files/docs/rea_principles_en.pdf).
2 Efficacy is the extent to which an intervention does more good than harm in ideal patients under ideal circumstances (modified from ec.europa.eu/enterprise/sectors/healthcare/files/docs/rea_principles_en.pdf).
For those trials that target populations at risk for experiencing disparities (e.g., racial/ethnic minorities, low-income groups), it may be necessary to tailor the interventions that take place in real-world settings to address the specific needs of the population. These trials may require complex, multi-component, multi-level interventions (e.g., targeting the patient, provider, and system), as evidenced by the literature on disparities, and it may be necessary to gather more than a minimal level of outcome data to adequately assess the impact of the intervention.

Examples of Successful Pragmatic Clinical Trials

- **Choudhry and colleagues**\(^5\) enrolled 5,855 patients to test whether elimination of out-of-pocket expenses for medications prescribed after a myocardial infarction would increase the percentage of patients who adhere to medication regimens and would improve clinical outcomes.
- In the **Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT)**, 33,357 participants, 55 years or older, with hypertension and at least one other coronary heart disease risk factor, from 623 North American centers were randomized to chlorthalidone, amlodipine, or lisinopril.\(^6\)
- A **randomized, real-world, open-label comparative clinical effectiveness trial** enrolled patients diagnosed as depressed by primary care practitioners. Patients were randomly assigned to a serotonin reuptake inhibitor or one of two tricyclic antidepressants and followed (passively) for 2 years to evaluate depression symptoms, health-related quality of life, healthcare utilization patterns, and costs.\(^7\)

Features of Patient-Centered Outcomes Research

PCORI funds patient-centered outcomes research (PCOR), which helps patients and their caregivers communicate and make informed healthcare decisions, allowing their voices to be heard in assessing the value of healthcare options. This research:

- Assesses the benefits and harms of preventive, diagnostic, therapeutic, palliative, or health delivery-system features to inform decision making, highlighting the choices that matter to people
- Is inclusive of an individual’s preferences, autonomy, and needs, focusing on outcomes that people notice and care about, such as survival, functioning, symptoms, and health-related

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quality of life

- Incorporates a wide variety of settings and diversity of participants to address individual differences and barriers to implementation and dissemination
- Directly compares clinical and delivery-system interventions that are generally available in the settings where people access health care
- Obtains the perspectives of stakeholders to address the burdens to individuals, access to care, quality of care, and requirements for technology and personnel

Research Characteristics and Objectives

PCORI seeks to fund investigator-initiated research having the following characteristics:

- The research studies the benefits and harms of different interventions and strategies that are delivered in typical clinical and community settings.
- The research compares at least two alternative clinical approaches. Because PCORI’s mission is to develop evidence to inform difficult decisions, PCORI strongly prefers applications that propose to compare well-defined interventions that are already being used in the condition and the population of interest.
- The research examines such interventions as specific drugs, devices, and procedures, as well as medical and assistive devices and technologies, behavioral change, complementary and alternative medicine, and interventions occurring at, or pertaining to, the care delivery systems. Please note that “usual care” generally is not an appropriate comparator for CER studies submitted to PCORI for funding consideration. “Usual care” is too often 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 must be accompanied by an explanation of how the care given in the usual care group will be measured in each individual patient and how appropriate inferences will be drawn from its inclusion.
- The research compares health outcomes that are meaningful to the patient population under study (e.g., morbidity, mortality, symptoms, functional status, quality of life, absenteeism from work or school). In select instances, surrogate physiological measurements may be sufficiently linked to final health outcomes to be of interest, but they may not be the sole study outcome.

PCORI has two objectives in this solicitation. First and most importantly, PCORI seeks to commit adequate funding to address critical clinical and health-related questions faced by patients, their caregivers, and their clinicians. Second, PCORI is interested in testing novel and efficient methodological approaches within real-world environments and expects various randomization schemes to be proposed, including individual or cluster randomization. PCORI has particular interest in funding studies that focus on patient-reported outcomes (PROs) that have not been well studied previously; can be completed relatively quickly because the primary outcomes focus on symptoms or other patient-reported measures; examine interventions and outcomes that cut across specific diagnoses (e.g., studies with primary outcomes focused on symptoms, such as pain); or employ strategies to enhance study
efficiency, such as Bayesian adaptive designs in which trial characteristics (e.g., sample size, randomization proportions, treatment arms, or eligibility criteria) evolve during the trial in response to interim trial data (see PCORI’s Standards for the Design, Conduct, and Evaluation of Adaptive Randomized Clinical Trials). Such studies will help determine not only how these approaches might be employed within real-world settings, but especially how such approaches might be integrated within a dynamic, rapid-learning environment (see Robert Wood Johnson Foundation’s Rapid Learning Project).

**Topic Selection**

PCORI’s multi-stakeholder advisory panels have identified high-priority topics and research questions (see Appendix). During PCORI’s award selection process, PCORI Board members on the Selection Committee, merit reviewers and program staff pay particular attention to applications that address PCORI-identified priority topics and research questions. While other prioritized lists of CER questions are also of interest (e.g., the Institute of Medicine [IOM] Priorities for CER, the Agency for Health Care Research and Quality [AHRQ] Future Research Needs Projects), PCORI will give first consideration to those proposals that directly address one or more of the 24 PCORI-identified priority topics (see Appendix). Note that PCORI is open to receiving and reviewing LOIs for studies on investigator-initiated CER questions. In such cases, applicants must explain convincingly why the proposed research question should be considered a high priority. Regardless of the research questions, applicants are expected to adhere to PCORI Methodology Standard RQ1, which states “gap analysis and systematic reviews should be used to support the need for a proposed study.”

By July 2015, PCORI will have made funding decisions on proposals submitted for three Pragmatic Studies Funding Cycles. PCORI may entertain additional studies within a given research topic if the proposed study is deemed complementary to the funded (or to be funded) studies. Therefore, applicants should be aware that the topic of the application may be a factor in PCORI’s decision to invite a full application. (Note: PCORI does not provide information about pending awards.)

In all cases, PCORI expects that researchers preparing applications have partnered with relevant patient organizations, specialty professional organizations, healthcare systems, insurers, and/or employer purchasers. Involvement of these organizations in finalizing and endorsing the research question and their participation in the proposed study are essential requirements for labeling a research question as high priority. If one or more key stakeholders have declined to endorse the study, PCORI would expect this decision to be explained clearly in the application.

PCORI expects that project budgets and duration will vary substantially, depending on the topic and approach selected, needs for recruitment and or primary data collection, length of follow-up, and

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8 Available at pcori.org/assets/Standards-for-the-Design-Conduct-and-Evaluation-of-Adaptive-Randomized-Clinical-Trials.pdf  
9 Available at rwjf.org/en/grants/grantees/rapid-learning-systems.html  
10 Available at iom.edu/~/media/Files/Report%20Files/2009/ComparativeEffectivenessResearchPriorities/Stand%20Alone%20List%20of%20100%20CER%20Priorities%20for%20web.ashx  
11 Available at effectivehealthcare.ahrq.gov/index.cfm/search-for-guides-reviews-and-reports/?pageaction=displayproduct&productid=521  
12 Available at pcori.org/assets/2013/11/PCORI-Methodology-Report.pdf
analytic complexity. PCORI seeks efficient studies, such as those that take advantage of large populations already under observation and the supportive involvement of delivery systems or health plans to enhance recruitment and data collection. A prolonged recruitment period is not an acceptable rationale for longer studies, except possibly in the case of a rare disease. Funding requests to develop or build on initial collaboration between researchers and patient/stakeholder groups are also not appropriate.

In-kind contributions to a proposed study are welcome, as are opportunities for co-funding between PCORI and another research sponsor. Each of these factors is taken as further evidence of the importance of the research question.

II. Guidance for Preparing Applications

Specific Requirements

The proposed study should strive to meet all of the following requirements:

- Focus on a comparative effectiveness question that is important to patients and other decision makers.
- Address a research gap that has been substantiated either by an existing (recent or updated) rigorously conducted systematic review or specifically emphasized by an official professional society's clinical practice guideline.
- Receive an endorsement by relevant patient organizations, clinician organizations, payer/purchaser consortia, and/or life sciences industry representatives as potentially answering a critical question—one that, if adequately answered, would substantially improve decision making.
- Propose a sample size that is sufficiently large enough to allow for precise estimation of hypothesized effect sizes or for clear demonstration of non-inferiority; in addition, the sample size must support testing of a prior hypotheses related to potential differences in effectiveness in relevant patient subgroups (heterogeneity of treatment effects).
- Examine diverse populations receiving care in real-world settings.
- Have strong interest from and support by host delivery systems and clinical care settings.
- Specify broad and simple eligibility criteria that will allow wide generalization of results, while attending appropriately to any ethical concerns of excess risk in some patient subgroups.
- Compare interventions that are known to be efficacious, effective, or commonly in use, and can be implemented in real-world settings.
- Feature near-term outcomes and PROs as primary outcomes, when appropriate.
- Plan to efficiently collect patient-centered outcomes data periodically during follow-up.
- Provide preliminary evidence of the potential for efficient recruitment, high participation rates, and appropriate oversight by local or centralized Institutional Review Boards (IRBs), including plans for streamlining or waiving individual informed consent in cases of low-risk interventions. PCORI believes that the intensity of oversight and the complexity of informed consent
procedures should be closely related to the degree of risk from study participation. Applicants must address this issue and should present evidence that the study will not encounter significant barriers to recruitment or participation.

• Adhere to all applicable PCORI Methodology Standards.13
• In the case of randomized trials, also adhere to current best practices (standardized inclusion/exclusion criteria; proper randomization; techniques to minimize potential for missing data; appropriate safety monitoring, including establishment of a data and safety monitoring board [DSMB] or indication of why such a board is unnecessary).
• Include a plan for sharing de-identified data.

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

• Identify and engage with major patient and stakeholder organizations that would implement study findings—as well as with existing local communities of patients and care providers—to formulate the research questions, design the study, help monitor progress, and disseminate the findings.
• Minimize disruption to participants’ daily routines (e.g., minimize participant visits intended solely for study-assessment purposes; capture PROs during office visits, electronically, or via phone).
• Design the study so that the conduct can, as seamlessly as possible, integrate with routine clinic or office operations.
• Use efficient methods to obtain participant consent while still meeting ethical and legal requirements.
• Capitalize on the existing electronic health records and other computerized information to identify and recruit eligible patients, monitor study conduct and patient safety, and collect study outcomes information.
• If data standardization and interoperability across study sites has not already been accomplished, develop methods that will enhance the standardization of data that are accessed from different electronic health record systems.

Non-responsiveness
Applications will be considered non-responsive to this PFA if the proposed research:

• Tests efficacy (or comparative efficacy) within a tightly protocol-controlled research setting (as opposed to more real-world, pragmatic CER)
• Conducts a formal cost-effectiveness analysis in the form of dollar-cost per quality-adjusted life-year to compare two or more alternatives
• Compares directly the costs of care between two or more alternative approaches

13 Available at pcori.org/research-we-support/research-methodology-standards/
• Measures the relative costs of care of two or more alternative approaches as the primary criteria for choosing the preferred alternative
• Conducts studies of the natural history of disease, instrument development, pharmacodynamics, and fundamental science or study of biological mechanisms
• Evaluates new or existing decision support tools; this includes development and evaluation of decision support or shared decision tool/system for patients or for clinicians, or for both patients and clinicians
• Develops clinical prediction or prognostication tools
• Establishes efficacy for a new clinical strategy
• Pilots studies intended to inform larger efforts
• Compares patient characteristics rather than clinical strategy options
• Compares interventions for which the primary focus or the sole intervention is examining the role of compensated or volunteer community health workers, including patient navigators

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 costs of care.

PCORI does have an interest, however, in studies that address questions about conditions that lead to high costs to the individual or to society. This is included in our review criterion on impact of the condition on the health of individuals and populations. Thus, PCORI is also 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.
• 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.

Proposals that include studies of these issues without utilizing a formal cost-effectiveness analysis or comparing the costs of alternatives are considered responsive.

Features of Patient-Centered Outcomes Research (PCOR)

PCOR helps people and their caregivers communicate and make informed healthcare decisions, allowing their voices to be heard in assessing the value of healthcare options. This research:

• Assesses the benefits and harms of preventive, diagnostic, therapeutic, or palliative care to inform decision making, highlighting the choices that matter to people
• Is inclusive of an individual’s preferences, autonomy, and needs, focusing on outcomes that people notice and care about, such as survival, functioning, symptoms, and health-related quality of life
• Incorporates a wide variety of settings and diversity of participants to address individual differences in and barriers to implementation and dissemination
• Directly compares clinical interventions that are generally available in the clinical settings
• Obtains the perspectives of stakeholders to address the burdens to individuals, availability of services, and requirements for technology and personnel
**Leveraging Existing Resources**

Investigators are encouraged to propose studies that leverage existing resources, such as adding PCOR to an existing large clinical trial or analyzing existing large databases that contain valuable, relevant information that may be used to answer important CER questions.

**Preliminary Data and Use of Accepted Measures**

PCORI encourages investigators to design their research using valid patient-centered outcomes measures and include preliminary data that support the proposed measures. Investigators are encouraged to consider those measures described in the *Patient Reported Outcomes Measurement Information System.*

**Studies in Rare Diseases**

PCORI is interested in the investigation of strategies that address care for patients with rare conditions. Rare diseases are defined as life-threatening or chronically debilitating diseases that are of such low prevalence in populations that special efforts, such as combining data across large populations, may be needed to address them. The term “low prevalence” is defined as conditions that affect fewer than 200,000 individuals in the US or have a prevalence of less than 1 in 1,500 persons.

**Methodological Considerations**

Regardless of study design, proposals must adhere to all relevant PCORI Methodology Standards. These include 47 individual standards that fall into 11 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 five categories are:

- Standards for Formulating Research Questions
- Standards Associated with Patient-Centeredness
- Standards on Data Integrity and Rigorous Analyses
- Standards for Preventing and Handling Missing Data
- Standards for Heterogeneity of Treatment Effect

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

- Standards for Data Registries
- Standards for Data Networks as Research-Facilitating Infrastructures
- Standards for Causal Inference Methods
- Standards for Adaptive and Bayesian Trial Designs
- Standards for Studies of Diagnostic Tests
- Standards for Systematic Reviews

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14 Available at http://nihpromis.org/
15 Available at pcori.org/research-we-support/the-pcori-methodology-report/
Most of these standards should be considered “minimal” standards. Additional best practices, including relevant guidelines for the conduct of clinical trials developed by other organizations, should be addressed in the application for PCORI funding. To help reviewers quickly identify the adherence to a particular standard, applicants must cite each relevant Methodology Standard within their proposal as the standard is being addressed. For example, when applicants describe the need for their proposed study within the Background section, they should indicate the particular standard to Identify Gaps in Evidence in parenthesis, such as “(RQ-1).” Please reference as guidance the Methodology Standards Checklist, which program staff members use to evaluate applications.

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

**Patient and Stakeholder Engagement**

PCORI encourages all applicants to clearly describe the patient and stakeholder engagement in their research proposals. PCORI understands that patient and stakeholder engagement in research can take many forms; PCORI is not seeking one particular type or method of engagement. Rather, applicants should communicate how patients (those with lived experience), family members, caregivers, and the organizations that represent them, as well as any other relevant stakeholders, will be involved in study activities. Because this type of engagement in research is a relatively new concept, PCORI has developed the Engagement Rubric to guide both applicants and Merit Review Officers (MROs). Additionally, studies are expected to adhere to PCORI’s Methodology Standards Associated with Patient-Centeredness and to the PCOR Engagement Principles found within the rubric. These and additional resources are available in PCORI’s Funding Center.

**Populations Studied**

PCORI seeks to fund research that includes diverse populations with respect to age, gender, race, ethnicity, geography, and clinical status. PCORI recognizes that some proposed studies may represent important PCOR opportunities, even in the absence of a broadly diverse study population. However, the burden is on the applicant in such cases to justify the importance of the study in the absence of diversity. Alternatively, PCORI is interested in the inclusion of previously understudied populations for whom effectiveness information is particularly needed, such as hard-to-reach populations or patients with multiple conditions. Thus, comparisons should examine the impact of strategies in various subpopulations with attention to the possibility that the effects might differ across various populations. Populations of interest include those that are less frequently studied. PCORI has developed the following list of priority populations 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
• Individuals with low health literacy or numeracy and/or limited English proficiency
• Lesbian, gay, bisexual, and transgender persons

Budget and Duration of Project

Applicants may request up to $10 million in total direct costs for a project period not to exceed 5 years. PCORI will not cover costs for interventions that are being compared in the proposed study (see Appendix 3 in Application Guidelines for details). Applicants should submit a realistic budget and timeline reflective of the scope and requirements of the proposed study. In some rare circumstances, the estimated budget may exceed $10 million total direct costs, depending on the nature of the research question, the design and analytical requirements of the proposed study, the expected size of the patient enrollment, and/or the complexity and frequency of the outcomes assessment. PCORI expects these to be very selective cases, which include high-priority topics that are of most interest to PCORI. Applicants who intend to propose such studies must provide succinct justifications in their Letter of Intent (LOI), documenting the budget requirements with respect to the scope of the proposed research and the data collection and analysis efforts. Please note this justification counts toward the LOI five-page limit. Any request for a project period longer than 5 years will be denied.

The funding mechanism for this program is a contract. Milestones and deliverables schedule, as well as specified recruitment targets, should be directly linked to and included in the proposed budget, which will be subjected to negotiation at the time of award. Some of the other activities that will be considered during negotiations include:

• Developing a study protocol and manual of procedures for the intervention
• Assigning roles and responsibilities to members of the study team for implementing the project
• Obtaining clearances from all institutional and community partners, including IRB approvals
• Establishing a DSMB, or providing a clear description of why a DSMB is not considered necessary
• Executing all subcontractor agreements
• Agreeing on eligible patient populations for study recruitment
• Identifying barriers to patient recruitment into the study and addressing these barriers effectively
• Structuring a feasibility phase to demonstrate the potential for successful recruitment

Total project funding is contingent upon successful programmatic and budget performance (e.g., meeting recruitment targets). Awardees will be expected to provide corroborating evidence to receive continual funding support. Specifically, at the conclusion of the Year-1 performance period, PCORI will conduct a formal programmatic assessment of the study progress and specified recruitment targets to determine the viability and sustainability of the study. Only studies that are deemed satisfactory in this assessment will receive continual funding support.
Refer to the Application Guidelines\textsuperscript{16} for a list of additional project milestones specific to the PFA.

**Collaboration**

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

**Protection of Human Subjects**

This component is included in the Research Plan Template and should not exceed five pages. Describe the protection of human subjects involved in your research. PCORI follows the Federal Policy for the Protection of Human Subjects (45 CFR part 46), including the Common Rule. For more detailed information, please see the Section 5 “Human Subjects Research Policy” from the Supplemental Grant Application Instructions for All Competing Applications and Progress Reports,\textsuperscript{17} issued by the US Department of Health and Human Services. PCORI does not require that applicants comply with sections of this policy that refer to requirements for federal-wide assurance or that refer to standards for inclusion of women, minorities, and children. All PCORI applications that involve interventions with human subjects should include a data safety monitoring plan. Depending on the anticipated level of risk associated with the proposed study intervention(s), different approaches and options, including a full external DSMB, may be required. Applicants should provide justification of the proposed option in accordance to the expected risk to human subject research participants. Awardees must also comply with appropriate state, local, and institutional regulations and guidelines pertaining to the use of human subjects in research.

PCORI MROs 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\textsuperscript{18}). Reviewers’ comments on human subject research are not reflected in the overall application score but may be used by PCORI staff during any potential funding negotiations. Final determinations about adequacy of human subject protections rest with the IRB or IRBs that have jurisdiction for the study.

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

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

PCORI requires all applicants to 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 personnel listed in the application as Key Personnel. The policy and FAQs are available from the NIH website.\textsuperscript{19}

\textsuperscript{17} See http://grants.nih.gov/grants/funding/424/supplementalinstructions.docx
\textsuperscript{18} See http://www.pcori.org/sites/default/files/PCORI-Checklist-for-Evaluating-Human-Subjects-Protections.pdf
\textsuperscript{19} See http://grants.nih.gov/grants/guide/notice-files/NOT-OD-08-054.html
Replication and Reproducibility of Research and Data-Sharing Plan

PCORI is committed to maximizing the utility and usability of data collected in our funded projects. This is essential to building confidence in the accuracy of these findings. PCORI supports policies to promote sharing of study documentation (e.g., study protocol, programming code, and data definitions) so that other researchers may replicate the findings in other populations. Please propose a method for sharing data and appropriate documentation upon request.

Recruitment

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

III. How to Submit an Application

Letter of Intent

Applicants should download the Spring 2015 Cycle Pragmatic Studies LOI template from the PCORI Funding Center. They must complete the document and convert it to a PDF with a five-page limit. All references should be included as in-text citations. LOIs that exceed the page limit will not be reviewed. Do not upload additional documents as part of your LOI, such as Letters of Endorsement or Support, as 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 FAQs and required templates.

Please answer all of the questions in the LOI template. This includes the question on brief justification for the proposed cost of the study. Providing an answer “costs not to exceed $10 million” is not sufficient. Then upload your document as a PDF into PCORI Online. The deadline for LOI submission is May 1, 2015, by 5:00 p.m. (ET).

Letter of Intent Review

LOIs are evaluated on the following criteria:

- Whether the topics are related to those on PCORI’s own priority list (see Appendix) versus the IOM/AHRQ lists, versus other topics initiated by investigators themselves
- Importance, as evidenced by critical gaps identified by clinical guidelines developers and/or recent relevant systematic reviews
- A size or scope sufficient to have a significant impact on patient outcomes and/or healthcare practices
• Clarity and credibility of applicants’ responses to the LOI questions, as well as their justification of the need for a large pragmatic study, including rationale for the estimated sample size, citing published estimates including effect sizes and standard deviations and need for rigorous comparative analysis of important subgroups
• Prior relevant experience
• Programmatic fit and balance, taking into consideration whether the application significantly overlap with concurrent applications or previously funded studies or, conversely, whether the application fills a gap in PCORI’s portfolio, considering such characteristics as disease category, topics, priority population, and methodologies
• Adherence to the administrative and formatting requirements listed in the Application Guidelines, specifically the five-page limit for the LOI

LOIs are reviewed qualitatively; they are not scored. Only applicants who’s LOIs are deemed most responsive to this PFA will be invited to submit a full application. Notification of denial or approval to submit a full application will occur no later than June 5, 2015. Please refer to the Application Guidelines in the Funding Center for due dates and information on how to submit your LOI in PCORI Online.
All applicants, including those resubmitting from previous Pragmatic Studies PFA cycles, are required to submit a competitive LOI for review by PCORI staff. This allows PCORI to determine if proposed revisions and changes made to specific aims and/or methodological approaches from the original applications align with PCORI’s evolving strategic priorities.

If you are invited to submit a full application, do not make significant changes to your proposed project without consulting a program officer. For example, you should not revise your major aims and study design. Any significant changes are grounds for removal from the review process.

Note: An individual may only submit one LOI as a Principal Investigator (PI) for a particular PFA in the same cycle. While a PI may submit an LOI to other PFAs, the research topic/project must be distinct. LOIs with scientific overlap or that appear to be duplicate submissions to different funding announcements within the same cycle will be removed during the LOI screening process.

Submission Dates
LOIs and applications must be submitted in accordance with the published dates and times listed in the Overview in this PFA and in the PCORI Funding Center.20

PCORI Online System
To submit a proposal, you must register in PCORI Online21 and submit both an LOI and an application for each cycle you are applying.

Applicant Resources

PCORI Funding Center  http://www.pcori.org/PFA-2015-spring-pragmatic-studies

20 Available at pcori.org/apply
21 Available at pcori.fluxx.io
IV. Merit Review

PCORI Merit Review is a multiphase process that includes:
- Evaluation of LOIs
- Invitation of a subset of LOIs to submit full applications
- Administrative and programmatic review of full applications
- Preliminary review by review panels of full applications that met administrative and programmatic requirements
- In-person review panel discussion of full applications
- Programmatic review of summary statements and topics to identify the most meritorious applications that achieve scientific topic balance within the program portfolios;
- Selection Committee deliberation and recommendation of applications for funding
- Board of Governors award approval (no later than January 2016)

Application Review Criteria

The following five criteria are used by PCORI’s review panels during the preliminary and in-person phases to evaluate all submitted applications. Each application should address the listed questions.

Criterion 1. Impact of the condition on the health of individuals and populations
The proposal addresses the following question: Is the condition or disease associated with a significant burden in the US population, in terms of prevalence, mortality, morbidity, costs to society, individual suffering, or loss of productivity?

Criterion 2. Potential for the study to improve health care and outcomes
The application has the potential to lead to meaningful improvement in the quality and efficiency of care and to improvements in outcomes that are important to patients.
- Does the research question address a critical gap in current knowledge as noted in systematic reviews, guideline-development efforts, or previous research prioritizations?
- Is there strong evidence of support by relevant patient, caregiver, clinician, payer, or purchaser organizations?
- Is the research novel or innovative in its methods or approach, the population being studied, or the intervention being evaluated, in ways that make it likely to improve care?
- Do wide variations in practice patterns suggest current clinical uncertainty?
- Do preliminary studies indicate potential for a sizeable benefit of the intervention relative to current practice?
- How likely is it that positive findings could be disseminated and implemented quickly, resulting
in improvements in practice and patient outcomes?

- Are there adequate plans for sustainability of the successful intervention(s) in the chosen settings, or discussion of implementation of successful intervention(s) into similar care settings?

**Criterion 3. Technical merit**
The application has sufficient technical merit to ensure that the study goals will be met.

- Is there a clear research plan with rigorous methods that adhere to PCORI’s Methodology Standards and prevailing accepted best practices?
- Is there a clear comparison condition that is a realistic option in standard practice? Is the comparator sufficiently described to reasonably compare the two or more conditions in the trial?
- Are the proposed comparative conditions currently in use? Is there prior evidence of efficacy or effectiveness for the interventions being compared?
- Is there evidence that the outcome measures are sufficiently sensitive to identify differences between groups?
- Is the study conducted in a patient population that is relevant to the majority of patients with a condition or to a previously understudied subgroup?
- Are the prespecified subgroups reasonable, given the proposed interventions and condition?
- Are the subgroups sufficiently large to allow a rigorous and valid comparative analysis?
- Is the budget appropriate for the proposed research?
- Is there a clear and adequate justification for the study design choices in the proposed pragmatic trial?
- Is there an adequate plan for protection of human subjects participating in this study?
- Do the applicants provide evidence of study feasibility based on availability of participants and experienced staff for efficient start-up?
- Does the project include a realistic timeline that includes clear and specific scientific and engagement milestones?
- Does the research team have the necessary expertise and prior experience in conducting large-scale multicenter trials as well as an appropriate organizational structure to successfully complete the study?
- Is the research environment, including the delivery systems that will host the study, well resourced and highly supportive of the proposed study?

**Criterion 4. Patient-centeredness**
The proposal demonstrates patient-centeredness at every stage of the research. It addresses the questions:

- Is the research focused on questions that affect outcomes of interest to patients and their caregivers?
- Does the research address one or more of the key questions mentioned in PCORI’s definition of PCOR?
Criterion 5. Patient and stakeholder engagement

The application demonstrates that people representing the population of interest and other relevant stakeholders are engaged in ways that are appropriate and necessary in a given research context.

- Are patients and other stakeholders engaged in:
  - Formulating research questions?
  - Defining essential characteristics of study participants, comparators, and outcomes?
  - Identifying and selecting outcomes that the population of interest notices and cares about (e.g., survival, function, symptoms, health-related quality of life) and that inform decision making relevant to the research topic?
  - Monitoring study conduct and progress?
  - Designing and/or suggesting plans for dissemination and implementation activities?

- Are the roles and the decision-making authority of all research partners clearly stated?

- Does the application demonstrate the principles of reciprocal relationships, co-learning, partnership, trust, transparency, and honesty?

Preliminary Review

PCORI conducts rigorous merit review of all applications. PCORI may eliminate applications from the review process for administrative or programmatic reasons (i.e., non-responsiveness). An application may be eliminated if it is incomplete or submitted past the stated due date and time, or if it does not meet the administrative or formatting criteria outlined in the Application Guidelines, in the PCORI templates, and in PCORI Online. An application may also be withdrawn if it is not responsive to the guidelines described in this PFA, describes research that is not comparative, includes cost-effectiveness analysis, or otherwise fails to meet PCORI programmatic requirements. Per our authorizing legislation, if two proposed research plans overlap, funding preference must be given to applications submitted on behalf of the NIH and AHRQ.

One or more specially convened Merit Review panels will review responsive applications. PCORI MROs recruit each panel. MROs also identify the chair, scientist reviewers who are clinical experts familiar with the clinical content of submitted applications, methodological and statistical experts familiar with pragmatic clinical trials and large database analyses, patient representatives trained in review of scientific applications, and representatives of other stakeholder groups.

In-Person Review

Once preliminary review is complete, before the in-person PCORI Merit Review, a team of five members of the merit review panel will review each application using the five criteria and PCORI’s Methodology Standards.

During the in-person review, the full panels meet to discuss the applications, further clarify the merits of the proposed research, and identify areas for improvement. Each application is assigned a score based on the content of that discussion. The chair and a PCORI MRO lead the in-person panel meeting and

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22 Available at https://pcori.fluxx.io/
ensure that all applications receive a fair and thorough review informed by the standards outlined in the PFA.

**Post-panel Review**

After the in-person panel review, the Selection Committee, which includes members of PCORI’s Board of Governors and Methodology Committee, review meritorious applications. The Selection Committee then works with staff to identify a slate of applications for possible funding based on PCORI Merit Review scores, programmatic balance, PCORI’s strategic priorities, and other considerations. This slate is proposed to PCORI’s Board of Governors for its consideration and approval.

**Board of Governors Approval**

The PCORI Board of Governors will consider the selected applications, factoring in the total available funds allotted for this announcement and programmatic needs. PCORI will inform applicants of the Board’s decision no later than January 2016.
Appendix: Research Topics of Interest to PCORI

PCORI Priority Topics

(Asterisks indicate topics for which full applications have been invited based on LOIs from the previous funding cycle.)

- **Medical versus invasive procedures for asymptomatic carotid artery disease**
  - Compare the effectiveness of aggressive medical treatments with invasive procedures in patients with asymptomatic carotid artery disease in terms of stroke rates and other patient-centered outcomes.

- **Surgical options for hip fracture in the elderly**
  - Compare the effectiveness of different surgical treatments in elderly patients with hip fractures in terms of functionality and other patient-centered outcomes.

- **Pelvic floor mesh implants**
  - Compare the effectiveness of the use versus non-use of surgical mesh in repair of pelvic floor dysfunction in terms of infections, urinary or fecal incontinence, bowel injury, pain, sexual function, and other patient-centered outcomes.
  - Compare the effectiveness of different types of mesh using different surgical techniques in terms of the outcomes mentioned above.

- **Treatment strategies for patients with autism spectrum disorder**
  - Perform a large-scale multi-center, randomized control trial with long-term follow-up comparing the effectiveness of applied behavioral analysis (in children 2 to 5 years old) with other accepted treatments for alleviating externalizing and internalizing behavior and improving social skills, parent-child interactions, family well-being, and other patient-relevant outcomes (e.g., changes in core and associated symptoms). Studies should be sufficiently large to permit rigorous analysis of heterogeneity of treatment effects related to provider, parent, family, child, intervention, and other characteristics.

- **Treatment options for patients with multiple sclerosis**
  - Compare management options: These might include Federal Drug Administration approved disease-modifying agents; behavioral interventions, including exercise and physical therapy; and complementary medicine alternatives.

- **Benefits and harms of continuous ambulatory peritoneal dialysis compared with hemodialysis (daily or intermittent home, or conventional in-center) in patients with end-stage renal disease and in important patient subgroups (e.g., by age, race, ethnicity, cardiovascular risk, other comorbidities)**

- **Multi-component interventions to reduce initiation of tobacco use and promote cessation of tobacco use among high-risk populations with known disparities**
  - Compare the effectiveness of clinical interventions to reduce initiation of use of tobacco and promote tobacco cessation among populations with known tobacco disparities, including high-risk and vulnerable populations.
- **Integration of mental and behavioral health services into the primary care of the general population**
  - Compare the effectiveness of evidence-based approaches to providing accessible mental health care for adults in the workforce through integration with other medical practice or other programs (such as Employee Assistance Programs) to improve patient-centered and workforce outcomes (e.g., morbidity, health-related quality of life, productivity, absenteeism, presenteeism, and return-to-work).

- **Integration of mental and behavioral health services into the primary care of persons at risk for disparities in health care and outcomes**
  - Compare the effectiveness of care models that integrate mental and behavioral health care, including substance abuse treatment, into the primary care provided by community health centers and other relevant settings, with the goal of reducing disparities in care (e.g., access to mental and behavioral health services and the diagnosis and treatment of mental and behavioral health conditions) and improving health outcomes among underserved populations, including racial/ethnic minorities, low-income individuals, and rural populations.

- **Management of breast ductal carcinoma in situ (DCIS)**
  - Compare the effectiveness of standard treatment options for DCIS (lumpectomy with or without radiation therapy; mastectomy; hormonal therapy post-surgery) with non-standard options (hormonal therapy alone; active surveillance) on progression to invasive cancer, recurrence of DCIS, DCIS progression without invasive cancer, quality of life, satisfaction with treatment choice at study completion, decisional conflicts, and other patient-relevant outcomes, such as self-image, sexual activity, or change in marital status.
  - Compare different approaches to informed decision making about management of DCIS. Outcomes to include decisional conflicts; treatments received (e.g., mastectomy, lumpectomy, contralateral mastectomy); satisfaction with decision; match of the chosen treatment with the woman’s strength of preference for having an intact breast; and aforementioned clinical outcomes.

- **Reduction of cardiovascular disease (CVD) risk in underserved populations, such as racial and ethnic minorities and those living in rural communities**
  - Compare the effectiveness of multi-disciplinary, systems-focused, and data-driven interventions to improve efficiency, effectiveness, and reliability of care to reduce CVD disparities in underserved populations. Targets for reducing disparities include improvements in hypertension control, treatment for hyperlipidemia, smoking cessation, and/or appropriate use of aspirin. The studies should examine which components of the interventions are critical for achieving risk reduction and provide details on patient-centered outcomes.
  - Compare the effectiveness of various interventions to support self-management of hypertension, hyperlipidemia, tobacco addiction, and/or appropriate use of aspirin in
underserved populations. The studies should examine which components of the interventions are critical for achieving risk reduction and provide details on patient-centered outcomes.

- In so far as possible, CVD interventions should focus on reducing disparities in care experienced by racial and ethnic minorities, low-income individuals, people with low literacy, and rural populations.

- **Strategies for preventing the progression of episodic acute back pain into chronic back pain**
  - Compare the effect of different combinations of multi-modal approaches to patients with episodic back pain (including self-care with or without over-the-counter medications; movement-based therapies, such as exercise and yoga; manipulation and/or mobilization; complementary medicine alternatives; and cognitive-behavioral therapies) on the transition from episodic acute back pain to chronic back pain, symptom relief, patient satisfaction, quality of life, and functional outcomes. Specific outcomes might also include reduction in pain medication use, reduction in patient visits for low-back pain, increase in quality of life, increased time between low-back pain episodes, and decreased severity of episodes (i.e., decreased pain and increased function).

- **Treatment strategies for adult patients with migraine headache**
  - Compare pharmacologic and nonpharmacologic strategies to prevent the transformation from episodic to chronic migraine.
  - Compare pharmacologic and nonpharmacologic strategies for treatment of individual headache episodes on the incidence of medication-overuse headache in patients with high-frequency episodic or chronic migraine.

- **Treatment strategies for symptomatic osteoarthritis (OA), including joint replacement**
  - Compare methods for deciding when to have surgery for OA; use such outcomes as patient satisfaction, functional status, clinical status, and quality of life.
  - Compare the effectiveness of strategies for engaging early-stage OA patients to adopt behaviors that can prevent OA progression and disability.
  - Compare different nonsurgical therapies (e.g., pharmacotherapy, injections, physical therapy and/or exercise, weight loss alone and in combination with other therapies, complementary medicine alternatives) to prevent OA progression and disability. The studies should seek to identify heterogeneity of treatment response among important subgroups of patients.

- **Treatment options for people with opioid substance abuse**
  - Compare different combinations of treatment options for people with opioid substance abuse, focusing on long-term outcomes. Treatment options might include medication-assisted treatments, psychosocial therapies, and complementary medicine alternatives.

- **Particle beam therapy for patients with lung and prostate cancer**
  - Compare the use of particle beam radiation therapy with other forms of radiation therapies in patients with lung or prostate cancer. Short- and long-term outcomes of
interest might include tumor site-specific toxicities, severity of adverse effects, cancer-specific and overall mortality, quality of life, and functional outcomes.

- **Compare the effectiveness of multi-component systems interventions, such as evidence-based models of perinatal care, aimed at improving outcomes, such as pre-term birth and low birth weight, for mothers and babies at risk for health disparities.**
- **Clinical Interventions to reduce nontraumatic lower extremity amputations in racial/ethnic minorities and low-income populations with diabetes: Does expert protocol-driven, team-based care reduce the risk of nontraumatic lower extremity amputations compared with existing and established guideline-based care for racial/ethnic minorities and low-income populations with diabetes?**
  - Team-based care could include, for example, acute-care teams with patient teams; staff working as a team (triage staff, etc.); use of standing orders, electronic medical records (EMRs), and/or hardcopy templates and reminders; knowledge and use of community resources; EMR registry functionality; empanelment; group visits; and novel outpatient-based interventions with rapid response from outpatient setting.
- **Compare the effectiveness of diverse models of comprehensive support services (e.g., incorporation of wraparound services, alternative providers, and technology) for infants and their families/caregivers after discharge from neonatal intensive care unit**
  - We are particularly interested in studies that would help bridge the gap between acute and post-acute care.
  - Proposed research should plan, justify, and adequately power the study to address prespecified patient subgroups (e.g., urban, rural, socioeconomically challenged).
- **Compare the effectiveness of multidisciplinary rehabilitation programs (e.g., community integrated rehabilitation: neurobehavioral, residential community, comprehensive holistic, and home-based services) for moderate to severe traumatic brain injury in non-military or veteran adults**
  - We are particularly interested in studies that would help bridge the gap between acute and post-acute care, and examine the impact on a patient’s functional status.
  - Proposed research should plan, justify, and adequately power the study to address prespecified patient and clinical subgroups (e.g., severity, injury type, impairment level, social support).
- **Compare the effectiveness of alternative models of coordinated pain management (such as specialized, integrated pain centers, coordinated care models that emphasize cross-provider data- and communication-sharing, or those that include risk triage systems with care coordination) for treatment of chronic nonspecific, musculoskeletal pain on improving functional status and other patient-centered outcomes**
- **Compare the effectiveness of the various alternative delivery models (e.g., primary care, schools, mobile vans) versus the dental office in preventing dental caries in children in medically underserved areas**
- **Compare the effectiveness of various strategies aimed at integrating pharmacists or pharmacy services into patient care (e.g., primary/acute care and pharmacy integration, pharmacist-provided preventive care, pharmacist-provided medication management or reconciliation**
services, other pharmacy-specific collaborative care models) on patient-centered outcomes (e.g., reduction in inappropriate medication use and polypharmacy, access to preventive vaccines, reduction in adverse events and hospital re-admissions, improved disease- or condition-specific outcomes)

• Compare the effectiveness of evidence-based screening and primary prevention approaches, including different modes and settings (e.g., universal screening versus targeting at-risk individuals, virtual versus face-to-face screening, within primary care setting versus school-based), at minimizing suicidality among adolescents and improving other patient-centered outcomes

Institute of Medicine 100 Initial Priority Topics for Comparative Effectiveness Research\(^2^3\) (Note: Decision-support topics within the IOM list are not supported in this funding announcement.)

AHRQ Future Needs Projects\(^2^4\)

\(^{23}\) Available at iom.edu/~/media/Files/Report%20Files/2009/ComparativeEffectivenessResearchPriorities/Stand%20Alone%20List%20of%20IOM%20Priorities%20for%20web.ashx

\(^{24}\) Available at effectivehealthcare.ahrq.gov/index.cfm/search-for-guides-reviews-and-reports/?pageaction=displayproduct&productid=521