Cycle 1 2021 Funding Cycle

PCORI Funding Announcement: Pragmatic Clinical Studies To Evaluate Patient-Centered Outcomes

Published January 5, 2021

This PCORI Funding Announcement (PFA) applies to the funding cycle that closes May 4, 2021, at 5 pm ET. Submission Instructions, templates, and other resources are available at https://www.pcori.org/funding-opportunities/announcement/pragmatic-clinical-studies-cycle-1-2021.
About PCORI

The Patient-Centered Outcomes Research Institute (PCORI) was authorized by Congress in 2010 as a nonprofit, nongovernmental organization. PCORI’s purpose, as defined by our authorizing legislation, is to help patients, caregivers, clinicians, policy makers, and other healthcare system stakeholders make better-informed health decisions by “advancing the quality and relevance of evidence about how to prevent, diagnose, treat, monitor, and manage diseases, disorders, and other health conditions” and by promoting the dissemination and uptake of this evidence.

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

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Follow us on Twitter: @PCORI
**Overview**

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<th>Key Dates</th>
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<tr>
<td><strong>Online System Opens:</strong></td>
<td>January 5, 2021</td>
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<tr>
<td><strong>Town Hall:</strong></td>
<td>January 14, 2021, 11:30 am (ET)</td>
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<td><strong>LOI Deadline:</strong></td>
<td>February 2, 2021, by 5 pm (ET)</td>
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<td><strong>LOI Status Notification:</strong></td>
<td>March 2, 2021</td>
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<td><strong>Application Deadline:</strong></td>
<td>May 4, 2021, by 5 pm (ET)</td>
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<td><strong>Merit Review:</strong></td>
<td>July 2021</td>
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<td><strong>Awards Announced:</strong></td>
<td>November 2021</td>
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<td><strong>Earliest Project Start Date:</strong></td>
<td>March 2022</td>
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<th>Maximum Research Project Period</th>
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<td>Applications may be submitted by any private-sector research organization, including any nonprofit or for-profit organization, and any public-sector research organization, including any university or college hospital or healthcare system; laboratory or manufacturer; or unit of local, state, or federal government. The Internal Revenue Service must recognize all US applicant organizations. Nondomestic components of organizations based in the United States 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 shown clearly. Organizations may submit multiple applications for funding. Individuals are not permitted to apply.</td>
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<td>2. Potential for the study findings to be adopted into clinical practice and improve delivery of care</td>
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<td>3. Scientific merit (research design, analysis, and outcomes)</td>
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<td>5. Patient-centeredness</td>
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<td>6. Patient and stakeholder engagement</td>
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<th>Contact Us</th>
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<tr>
<td><strong>Programmatic Inquiries:</strong> <a href="mailto:sciencequestions@pcori.org">sciencequestions@pcori.org</a>, phone (202-627-1884), or online (<a href="http://www.pcori.org/PFA/inquiry">http://www.pcori.org/PFA/inquiry</a>).</td>
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<tr>
<td><strong>Administrative, Financial, or Technical Inquiries:</strong> <a href="mailto:pfa@pcori.org">pfa@pcori.org</a> or phone (202-627-1885).</td>
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PCORI will respond within two business days; however, we cannot guarantee that all questions will be addressed two business days prior to a Letter of Intent (LOI) or application deadline. Applicants are asked to plan accordingly; it is the applicant’s responsibility to submit the application on or before the application deadline.
Important Considerations Related to COVID-19 and Research Studies

The significant global impact of the COVID-19 pandemic has markedly affected healthcare delivery and research. Substantial uncertainties exist about the nature and duration of its impact on research, including intervention delivery and the collection, analysis, and the interpretation of study data. Research staff may face conflicting local and institutional policies to promote safety and the provision of care for those afflicted with COVID-19. They may also face personal risks of exposure, illness, and incapacity related to the pandemic. PCORI considers the safety and well-being of study participants, research staff, and stakeholders to be paramount and advocates that safety be the foundational principle guiding research decisions.

In light of the risks and uncertainties of COVID-19 on population health, health care, and research, PCORI requests applications to this PFA to include an explicit assessment of potential risks and risk management plans/contingencies for the proposed research as it may be affected by COVID-19. In addition to risk assessment and management related to the planning and conduct of the research itself, applicants should also consider provisions in their leadership and staffing plan to have backup or “understudy” staff who can readily assume key duties and assure study continuity in the event of personnel absences due to quarantine, illness, or the provision of clinical care.

PCORI is receptive to LOIs and applications for pragmatic clinical studies (PCS) responsive to this PFA and that encompass a wide range of investigator-initiated research questions addressing patient-centered outcomes in comparative effectiveness. Such research may potentially include topics related to COVID-19 and its long-term impacts on health. PCORI notes with caution, however, that the size and expected timeframe for PCS studies to generate research results may not readily fit the acute research needs of the COVID-19 pandemic.
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I. Introduction

Summary of Program

PCORI is launching this funding initiative to support large pragmatic studies in patient-centered comparative effectiveness research (CER). Such studies are designed to aid decision makers in choosing between two or more clinical care interventions through the comparison of their effectiveness, safety, and other characteristics that are important to stakeholders. The program goals are to (1) address critically important evidence gaps in decision making where insufficient comparative effectiveness information poses a significant barrier to clinical or healthcare system decision making about two or more healthcare options, and (2) gain insight into the heterogeneity of treatment effects (HTE) for subgroups and individuals through the study of large and diverse populations.

PCORI seeks to fund large pragmatic clinical trials, large simple trials, or large-scale comparative observational studies that involve representative patient populations; have strong endorsement and study participation by relevant patient organizations, professional organizations, 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. Randomized study designs are strongly encouraged but not required. Funded studies will compare the effectiveness of two or more alternatives for improving patient-centered outcomes that are evaluated under real-world conditions of clinical care. Studies to establish the efficacy of novel or unproven interventions are nonresponsive and will not be considered.

Background

Pragmatic clinical trials and studies serve the primary purpose of supporting decision makers in choosing between two or more clinical care interventions. Pragmatic research is typically conducted under conditions that resemble usual clinical practice and are thus relevant, applicable, and generalizable to real-world care populations and settings. In contrast, traditional (or explanatory) controlled trials employ homogeneous populations and highly standardized research conditions intended to assess the efficacy of medical interventions or to answer a narrowly defined research question; they have limited generalizability for evaluating the comparative clinical effectiveness of interventions already in use because of the following factors: (1) the comparisons in the trial often fail to reflect the choices patients, clinicians, or policy makers face; (2) the chosen study population 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 tightly controlled and not representative of typical clinical practice; and (5) the trial may use a placebo, rather than an active comparator, as the comparison.

To overcome the limitations of traditional explanatory research studies, applicants to this funding announcement should propose pragmatic clinical trials or studies designed to address practical comparative questions faced by patients, clinicians, and policy makers. Studies should include broadly diverse populations and be conducted in typical clinical and health system settings to provide information that healthcare decision makers can apply directly. The protocols for these trials are typically less complex, minimally burdensome, and less intrusive to routine clinical practice compared
with traditional controlled trials. Pragmatic clinical studies sought under this funding announcement will generally be large in sample size to evaluate small yet important differences in comparative clinical effectiveness and to permit the evaluation of effectiveness in different patient subgroups. Trials may be much simpler than traditional randomized controlled trials (RCTs) and be considered large simple trials.

In developing a pragmatic approach to study design, conduct, and analysis, applicants are encouraged to review descriptions of the pragmatic-explanatory continuum or PRECIS-2 as articulated by Patsopoulos,1 Thorpe et al.,2 Loudon et al.,3 Nicholls et al.,4 and Zwarenstein et al.5 A statement of the clinical decision(s) to be informed by the trial results should be provided, accompanied by a table summarizing the planned study design features for each domain and the rationale for their applicability, relevance, and importance in addressing the stated clinical decision(s). This tabular summary is preferred over a PRECIS-2 wheel-like diagram. The population, settings, and conduct of the intervention should conform as closely as possible to the expected conditions in which the research findings will be applied. Study design choices should fit the stated decisional purpose of the study rather than seek to be maximally pragmatic.

Pragmatic clinical trials proposed under this funding announcement must adhere to the PCORI Methodology Standards, which establish minimum requirements for patient-centered outcomes research. While no PCORI Methodology Standards are specific to pragmatic trials, the Standards for Studies of Complex Interventions have special relevance to the pragmatic emulation of typical clinical care conditions and their variability. Applying the complex intervention standards to delineate the causal pathway(s), core function(s), and permissible form(s) of interventions will guide investigators to determine what adaptations to the intervention and its delivery can be allowed to optimize the balance of study fidelity, flexibility, and scientific rigor. Although pragmatic studies must often accommodate some degree of flexibility in intervention delivery across multiple study sites, interventions must be sufficiently well defined to be replicable in their dissemination and implementation in US health care. Additional guidance on treatment fidelity, participant adherence, monitoring, and usual care comparators can be found in the PCORI Guidance on the Design and Conduct of Trials in Real-World Settings: Factors to Consider in Pragmatic Patient-Centered Outcomes Research.6

For pragmatic trials targeting populations at risk for experiencing disparities (e.g., racial or ethnic minorities, low-income groups, other vulnerable populations), special considerations may apply. It may

3 Loudon K, et al. The PRECIS-2 tool: designing trials that are fit for purpose. Research Methods & Reporting. 2015;350:h2147. http://www.bmj.com/content/350/bmj.h2147 (Note that this article describes an updated process to assess how closely the proposed study design elements [e.g., delivery of intervention and population of interest] mirror those encountered in usual care, a proxy for pragmatic. The term usual care, as used in this article, differs from how PCORI interprets and uses the term in the context of CER funding announcements—a control comparator.)
be necessary to tailor interventions that take place in real-world settings to address the population’s specific needs using complex, multicomponent, multilevel interventions (e.g., targeting the patient, provider, and system). In these instances, it may be necessary to gather more than the typically minimal level of outcome data collected in pragmatic trials to assess the impact of the intervention adequately. Often, evidence-based interventions have been shown to be effective in the general population but lack evidence for effectiveness in those populations at risk for disparities. The Addressing Disparities priority area is thus interested in funding studies that tailor and test these types of interventions. Applicants may use interventions that have documented efficacy or effectiveness in similar situations with some adaptation if necessary—if the efficacy is well documented (e.g., with prior research or with a systematic review) and based on a sufficiently strong rationale for why the intervention would be expected to be efficacious in the proposed new setting(s) and/or population(s). If an intervention is to be adapted, PCORI expects most of the proposed time and budget to be aimed at assessing comparative effectiveness rather than adapting and validating the interventions.

**Specific Program Requirements**

The proposed study should strive to meet the following requirements:

- Compare interventions that are known to be efficacious, effective, or commonly used and that can be implemented in real-world settings.
- Focus on a comparative clinical effectiveness question that is important to patients and other decision makers.
- Address an evidence gap in decision making among available options; this gap should have been substantiated by an existing (recent or updated), rigorously conducted systematic review or emphasized by an official professional society’s clinical practice guideline.
- Demonstrate consultation with patients and other stakeholders or their representative groups, or reference previously documented decisional dilemmas to determine if the study is answering a critical question—one that, if adequately answered, would substantially improve decision making.
- Propose a sample size that is sufficiently large to allow for precise estimation of hypothesized effect sizes or for clear demonstration of noninferiority. The sample size must also support testing of a priori hypotheses related to potential differences in effectiveness among relevant patient subgroups (HTE).
- Examine diverse populations receiving care in real-world settings.
- For studies aiming to reduce or eliminate health or healthcare disparities, specify one or more of the Addressing Disparities Program target populations (i.e., racial or ethnic minorities; low-income groups; residents of rural areas; individuals with special healthcare needs, including individuals with disabilities; individuals with low health literacy or numeracy or limited English proficiency; and sexual and gender minority individuals) that will be the focus of the study. Studies should test the ability of interventions to improve outcomes (including patient-centered, clinical, and structural outcomes) and reduce disparities for at-risk populations.
- Have strong interest from and support of host delivery systems and clinical care settings.
- Specify broad and simple eligibility criteria that will allow for wide generalization of results while
attending appropriately to ethical concerns of excess risk in some patient subgroups.

- Feature long-term outcomes and patient-reported outcomes (PROs) as primary outcomes, when appropriate.
- Plan to collect patient-centered outcome data efficiently and 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 (if applicable). 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 present evidence that the study will not encounter significant recruitment or participation barriers. The relevant IRBs make the final determination of the adequacy of informed-consent procedures and participant protections.

- Adhere to all applicable PCORI Methodology Standards. The full application will require the applicant to identify the standards applicable to the proposed study and to describe how the study team plans to address each standard.
- In the case of RCTs, adhere to current best practices (i.e., standardized inclusion or exclusion criteria; proper randomization; techniques to minimize potential for missing data; and appropriate safety monitoring, including establishing a Data and Safety Monitoring Board [DSMB] or indicating why such a board is unnecessary).

To carry out studies that allow for adoption of the findings in a real-world setting, and to maximize the efficient use of resources, applicants should take care to prevent these trials from becoming more complex and onerous than necessary. We encourage applicants to be creative and consider the following innovative strategies, as appropriate and feasible:

- Consult with patients and other stakeholders on their decisional dilemma and evidence needs, or reference previously documented decisional dilemmas in preparation for submitting letters of intent (LOIs) and full applications.
- Carefully describe the pertinent evidence gaps and why the research project questions represent decisional dilemmas for patients, caregivers, clinicians, policy makers, and other healthcare system stakeholders. Similarly, applicants should document why project outcomes are especially relevant and meaningful endpoints for patients and their families.
- Minimize disruption to participants’ daily routines (e.g., minimize participant visits intended for study assessment purposes; capture PROs during office visits, electronically, or via phone).
- Design the study so most of its conduct can occur using routine clinic or office operations.
- Use efficient methods to obtain participant consent while still meeting ethical and legal requirements.
- Capitalize on existing electronic health records (EHRs) and other computerized information to identify and recruit eligible patients, monitor study conduct and patient safety, and collect study outcomes information. PCORI specifically encourages applications that use the National Patient-
Centered Clinical Research Network (PCORnet) infrastructure.

- If data standardization and interoperability across study sites have not already been accomplished, develop methods that will enhance the standardization of data that are accessed from different EHR systems.

**Nonresponsiveness**

Applications will be considered nonresponsive to this PCORI Funding Announcement (PFA) if the proposed research does the following:

- Tests efficacy (or comparative efficacy) of interventions that are novel or with limited evidence of efficacy
- Involves studies conducted within tightly controlled research environments instead of in clinical settings reflective of real-world healthcare delivery
- Evaluates the validity or efficacy of (rather than the comparative clinical effectiveness of) new or existing decision support tools (This includes the development and efficacy evaluation of decision support or shared decision tools or systems for patients, clinicians, or both.)
- Develops clinical prediction tools
- Pilots studies intended to inform larger efforts
- 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

**Invited Research Areas**

PCORI invites Pragmatic Clinical Studies (PCS) applications addressing CER questions that meet the scope and intent of this PFA, align with PCORI’s national research priority areas, and adhere to PCORI Methodology Standard RQ1, which states that “gap analysis and systematic reviews should be used to support the need for a proposed study.” For the PCS PFA, PCORI seeks investigator-initiated, patient-centered CER applications aligned with its national priority areas described in the following section.

**Investigator-Initiated Research**

This PFA focuses on three long-established PCORI national priority areas: Addressing Disparities; Assessment of Prevention, Diagnosis, and Treatment Options; and Improving Healthcare Systems. In addition to these three areas, PCORI’s 2019 reauthorizing legislation provided additional direction about national research priorities to include research related to intellectual and developmental disabilities and to maternal mortality.

The **Addressing Disparities** priority area focuses on overcoming barriers that disproportionately affect health outcomes or healthcare delivery, by identifying best practices to reduce disparities and improve health equity in target populations (i.e., racial and ethnic minority groups; low-income groups; residents of rural areas; individuals with special healthcare needs, including individuals with disabilities; patients with low health literacy, low numeracy, or limited English proficiency; and sexual and gender minority individuals). Previous research has identified pervasive disparities in access to high-quality health care...
and worse health outcomes for specific populations across multiple conditions and multiple settings. Disparities in outcomes have been documented based on race or ethnicity, gender, geographic location, socioeconomic status, disability, and other factors. PCORI seeks to fund studies that yield evidence to help guide decisions about how to eliminate disparities in health and health care, as well as how to ensure that people receive care according to their needs and can achieve the best possible health outcomes.

Interventions to reduce persistent disparities are multifactorial, complex, and context specific. Often, evidence-based interventions have been shown to be effective in the general population but lack evidence for effectiveness in those populations at risk for disparities. The Addressing Disparities priority area is thus interested in funding studies that tailor and test these types of interventions. Applicants may use interventions that have documented efficacy or effectiveness in similar situations with some adaptation if necessary—if the efficacy is well documented (e.g., with prior research or with a systematic review) and based on a sufficiently strong rationale for why the intervention would be expected to be efficacious in the proposed new setting(s) and/or population(s). If an intervention is to be adapted, PCORI expects most of the proposed time and budget to aim at establishing comparative effectiveness rather than adapting and validating the interventions.

Assessment of Prevention, Diagnosis, and Treatment Options (APDTO): Many approved and marketed therapies or technologies have evidence gaps about their effectiveness, compared with other clinical options, and about outcomes important to patients and their caregivers. Often the existing evidence base is not relevant for certain patient populations, such as those at the extremes of age or those with multiple comorbid conditions. For the APDTO priority area, PCORI seeks to fund investigator-initiated research that does the following:

- Compares the effectiveness of two or more clinical interventions for the prevention, treatment, screening, diagnosis, or management of clinical conditions; interventions should be known to be efficacious but not adequately compared in previous studies
- Addresses a high-priority evidence gap as identified by authoritative sources, such as prior systematic reviews or clinical practice guidelines
- Documents a need for the proposed new research, based on a compelling need to have better evidence for informing clinical choices
- Investigates, among compared groups, factors that account for variation in treatment outcomes, with attention to demographic, biological, clinical, social, economic, or geographic factors; comorbidities; and other factors that may influence those outcomes

For the APDTO priority area, proposed projects should address the comparison of specific clinical services or clinical strategies that are clearly defined and that can be replicated in other clinical settings with minimal adaptations or changes. The program’s goal is to expand the evidence base that pertains to clinical services that would be chosen by clinicians, patients, and caregivers in usual clinical delivery settings. The services of interest include prescription drugs and biologics, surgical and other interventional procedures, techniques for disease screening, vaccinations, and other interventions to prevent diseases, counseling and behavioral interventions, complementary and integrative services,
rehabilitative services, and diagnostic tests and procedures.

The Improving Healthcare Systems (IHS) priority area invites research on the comparative clinical effectiveness of alternative features of healthcare systems (e.g., innovative technologies, incentive structures, healthcare service delivery designs) that are intended to optimize the quality, outcomes, and efficiency of patient care and that have the greatest potential for sustained impact and replication within and across healthcare systems. Healthcare systems encompass multiple levels (e.g., individual patients, family and social supports, providers and care teams, organizations or practice settings, local community resources, state- and national-level policy environments) and include entities organized to deliver, arrange, purchase, or coordinate health services. Healthcare delivery models (e.g., integrated health systems, patient-centered medical homes) and care settings (e.g., hospitals, physician practices, nursing homes, community health clinics, patients’ homes) also define healthcare system operations. Nontraditional settings, such as schools and public housing units, also may qualify if they provide interventions to improve health and health care. PCORI seeks studies that determine which system features lead to improved patient-centered outcomes, timeliness, safety, and equity, and which provide valuable knowledge to patients, their caregivers, and clinicians, as well as to other key stakeholders, including payers and employers. Studies are encouraged to include adequately powered subgroup analysis and address understudied or underrepresented patient populations in research.

Broad outcomes of interest for research on the effects of system changes are as follows:

- Patients’ access to care, high quality of care, support for self-care, and coordination of care across healthcare settings
- Professional decision making based on patients’ personal values
- Experiences that are important to patients and their caregivers, such as overall health, functional ability, health-related quality of life, stress, severity of symptoms, survival, and unanticipated healthcare utilization, such as hospitalizations or emergency department use
- The efficiency of healthcare delivery, as measured by the amount of ineffective, duplicative, or wasteful care provided to patients

The IHS program values research studies that leverage healthcare system resources to support intervention requirements or studies where healthcare organizations and other stakeholders (e.g., payers, health care system leaders) indicate their intention to adopt an intervention if it is proven effective. Also of interest is research that tests practices that combine evidence-based guidelines (such as Choosing Wisely) with patient, provider, or combined incentives to elicit patient preferences as well as to reduce harms faced by patients.

For the recent priority areas of Intellectual and Developmental Disabilities and Maternal Mortality, stakeholder input and elaboration of specific research needs are underway. Pending their completion, PCORI invites applications to this PFA for trials comparing clinical and/or health system interventions to address adverse consequences and outcomes in these two priority areas, including applications that address disparities in vulnerable populations. Applications may propose to examine treatment or management interventions to maximize function and quality of life for individuals living with intellectual and developmental disabilities, and families and caregivers of individuals with intellectual and
developmental disabilities.

Applications proposing to compare interventions to reduce maternal mortality are also invited. Broadly interpreted, interventions of interest to decrease maternal morbidity and mortality may occur from preconception through the postpartum period. Implementation of interventions may occur through providers; patients; family and care support systems; payers; health systems; and/or local, state, and federal policy.

Project Budget and Duration

Applicants may request up to $10 million in total direct costs. At the time of contract execution, PCORI sets aside all funds associated with an awarded project to be made available throughout the contract’s period of performance. The maximum budget includes all costs related to research and peer review. In addition, for this funding cycle of Pragmatic Clinical Studies, PCORI will pilot consideration of funding support for meritorious applications providing well-supported and justified requests to cover patient care costs defined to include the intervention being studied as well as clinical personnel costs for those providing the care. For additional information on the conditions for such coverage, see the Coverage of Intervention Costs section.

Applicants should submit a realistic budget and timeline reflecting the proposed study’s scope and requirements. Note that, although subcontractor indirect costs are included in the prime applicant’s direct cost budget, subcontractor indirect costs are not factored when determining adherence to the PFA’s direct cost cap.

PCORI expects that project budgets and duration will vary substantially depending on the topic and approach selected, the recruitment or primary data collection needs, the length of follow-up, and the analytic complexity. PCORI seeks efficient studies, such as those taking advantage of large populations already under observation, as well as those with 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 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 research question’s importance.

II. General Requirements for PCORI Research

This section includes language that is specific to PCORI’s requirements for programmatic responsiveness under this funding announcement. Applicants should use this section as guidance when preparing their applications. For information related to administrative and technical requirements for LOI and application submissions, please consult the PCORI Submission Instructions for important instructions on how to use the PCORI Online System and for Applicant Resources pertinent to this announcement.

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 does the following:

- 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 (e.g., survival, functioning, symptoms, health-related quality of life)
- Investigators are encouraged to design their research using validated outcome measures such as those described in the Patient-Reported Outcomes Measurement Information System (PROMIS). Likewise, PCORI encourages the use of core outcome sets, such as those developed by the Core Outcomes Measures in Effectiveness Trials Initiative to facilitate cross-study analysis. See http://www.comet-initiative.org/
- Incorporates a wide variety of settings and diversity of participants to address different forms of healthcare delivery, commonly seen patients, individual differences, and barriers to implementation and dissemination
- Directly compares clinical and delivery system interventions that are currently available or used in the settings where people access health care
- Obtains stakeholder perspectives to address the burdens to individuals, care access, care quality, and technology and personnel requirements

Responsiveness
To be considered responsive, applications must do the following:

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

- **Describe research that studies the benefits and harms of interventions and strategies delivered in real-world settings.** PCORI is interested in studies that provide practical information that can help patients and other stakeholders make informed decisions about their health care and health outcomes.

### Categories of Nonresponsiveness

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

- Instrument development, such as new surveys, scales, etc.
- Developing, testing, and validating new decision aids and tools, or clinical prognostication tools
- Comparing patient characteristics rather than clinical strategy options

Consistent with PCORI’s authorizing law, PCORI does not fund research whose findings will include the following:

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

### Cost Effectiveness and Cost

PCORI’s authorizing law was amended by reauthorization legislation in 2019 to include a new mandate to consider, as appropriate, the full range of clinical and patient-centered outcomes data relevant to patients and stakeholders. The reauthorizing language clarifies that, in addition to the relevant health outcomes and clinical effectiveness, relevant outcomes may include the potential burdens and economic impacts of the utilization of medical treatments, items, and services.

As such, where PCORI previously directed in its past Funding Announcements that proposed studies could not employ direct measurements of cost, PCORI now allows and encourages proposed studies that include collection of data describing these potential burdens and economic impacts when relevant to

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7 Available at http://www.pcori.org/sites/default/files/PCORI_Authorizing_Legislation.pdf/.
patients and caregivers or to other stakeholders, as further described below and in the accompanying FAQs. PCORI’s intention is that funded research captures such burdens and economic impacts to provide the full range of outcomes data relevant to decision makers.

Specifically, applications responding to this PFA may do the following:

- Include data collection on burdens or economic impacts associated with interventions, that are relevant to patients, caregivers, and other stakeholders. PCORI-funded studies have often included impacts on healthcare utilization; data that capture costs of these impacts will now be considered responsive.
- Include data collection on burdens and economic impacts relevant to other stakeholders, such as medical out-of-pocket costs, time costs, other costs patients or caregivers incur in the course of seeking care (e.g., for childcare or transportation), or productivity costs.

However, proposed research may not measure economic impacts as the primary outcome of a proposed study. Proposals that have economic measures as the primary outcome will be considered nonresponsive.

Further, consistent with past Funding Announcements, PCORI will consider an application nonresponsive if the proposed research does the following:

- Conducts a formal cost-effectiveness analysis of alternative approaches to providing care
- Directly compares the costs of care between two or more alternative approaches to providing care or relies on modeling to develop estimates of “total costs of care” designed to enable such comparisons

For further information, please reference PCORI’s cost-effectiveness analysis FAQs.

PCORI has a continued interest in studies addressing questions about conditions that lead to high costs to individuals or society. This interest is reflected in our review criterion on the condition’s impact on the health of individuals and populations. Thus, as addressed in the FAQs, PCORI is interested in studies that do the following:

- 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.

In Fall 2020, PCORI proposed draft principles that will serve as a point of reference for providing guidance to potential applicants on what is included in “the full range of clinical and patient-centered outcomes relevant to, and that meet the needs of, patients, clinicians, purchasers, and policy makers,” consistent with PCORI’s authorizing law. The draft principles will be finalized following review of robust stakeholder input PCORI received during a 60-day public comment period that ended November 13, 2020. These draft principles will inform both PCORI’s expectations for applicants and the corresponding review evaluation of applications submitted in response to this
PCORI Cycle 1 2021 Pragmatic Clinical Studies to Evaluate Patient-Centered Outcomes PFA. Final principles and guidance are expected to be available in Spring 2021.

Coverage of Intervention Costs

Historically, PCORI has not covered the costs for study interventions that constitute the procedures, treatments, interventions, or other standard clinical care (patient care) that are being proposed for comparison in the research project (patient care costs). For the Cycle 1 2021 Pragmatic Clinical Studies PFA, PCORI is piloting consideration of funding support for meritorious applications that provide well-supported and justified requests to cover patient care costs defined to include the intervention being studied as well as clinical personnel costs for those providing the care. See the Submission Instructions.

Investigators seeking coverage of patient care costs should note their requests when submitting Letters of Intent to this PFA. Invited applications should describe and justify proposed patient care costs and provide a full justification addressing the criteria below, as described in the Submission Instructions.

PCORI will apply the following criteria in determining whether to consider funding support for patient care costs:

- Does the study address a strategically important comparative effectiveness question? For example, does it address a comparative effectiveness question identified by a systematic review or related to a national PCORI priority area such as Intellectual and Developmental Disabilities or Maternal Morbidity and Mortality? Would study results have a potentially significant impact on clinical decision making or policy formation due to a major therapeutic advance such as a new medical product, procedure, or care delivery innovation?

- Is there evidence that the absence of coverage of patient care costs will pose a significant barrier to adequate recruitment of participants or to the access or inclusion of key participant groups?

- Is there a high likelihood of sustained uptake of study results in the absence of future cost subsidies as evidenced by commitments of one or more key stakeholders? Have these key stakeholders convincingly demonstrated their support to the future uptake of study results through strong letters of support or via contributions of funding or other resources?

Avoiding Redundancy

PCORI encourages potential applicants to review published research and listings of ongoing funded research at pcori.org and at clinicaltrials.gov. PCORI will balance our funded portfolio to achieve synergy and avoid redundancy where possible. Applicants proposing research that overlaps or is redundant with published or ongoing research must provide a strong justification for why it merits PCORI funding.

Methodological Considerations

The PCORI Methodology Standards represent minimal requirements for the design, conduct, analysis, and reporting of scientifically valid PCOR. Regardless of study design, applications must adhere to all relevant PCORI Methodology Standards, and all deviations need to be justified. Given PCORI’s interest in trials conducted in real-world practices and settings using representative patient populations, the standards for complex interventions may have special relevance.

Applicants should address additional best practices—including relevant guidelines for conducting clinical
Leveraging Existing Resources, Including PCORnet

PCORI encourages applicants to consider the potential merits of using the clinical research infrastructure and data resources of PCORnet. PCORnet® is designed to improve the nation’s capacity to conduct efficient large-scale clinical research, by drawing on a network of clinical research networks capturing the healthcare experiences of millions of Americans. PCORnet includes patients, clinicians, health systems, and health plans across the country interested in supporting research to improve health care and health outcomes. The network currently includes nine clinical research networks, representing more than 100 health systems, two health plan research networks, a coordinating center, and a central office. PCORnet can be used as a source of research-ready clinical sites to enroll participants for feasibility testing of recruitment or for participation in a full-scale trial; it can also be used to provide preparatory data in support of clinical trial design through its large longitudinal data sets that capture clinical outcomes and details of specific procedures, treatments, disease severity, and comorbid illnesses.

PCORnet offers the following:

- Clinical research networks able to participate as clinical sites in randomized research trials
- Actively engaged patients
- Preexisting, standardized, curated, and research-ready clinical data to inform clinical trial design, conduct, and operations

Outside of participation as clinical sites, PCORnet data resources may inform aspects of clinical trial design, feasibility assessment, effect sizes, and potential study power. Examples include, but are not limited to, the following:

- Providing background to the research question or feasibility of study
- Documenting the importance of the research question
- Estimating the size of the potentially eligible population
- Determining the range of current treatment practices and sequencing
- Assessing the duration of continuous treatment, care, and follow-up

Studies in Rare Diseases

PCORI is interested in the investigation of strategies addressing care for patients with rare diseases. These conditions are defined as life-threatening or chronically debilitating. They are of such low prevalence (i.e., affecting fewer than 200,000 in the United States, or less than one in 1,500 persons) that special efforts—such as combining data across large populations—might be needed to address them.

Patient and Stakeholder Engagement

In PCORI-funded research, patients and other healthcare stakeholders are viewed as research partners.
who leverage their lived experience and/or professional expertise to ensure that research is more patient-centered, relevant, and feasible to conduct in real-world settings. When developing an engagement strategy, PCORI encourages applicants to consider the time and resources needed to identify, confirm, and prepare stakeholders for collaborating; the infrastructure needed to manage stakeholder engagement activities; and the specific decision points that will draw on the expertise of stakeholder partners. Research partners must include representatives of the populations most impacted by the condition or issue addressed by the study. Applicants’ use of multiple approaches that are along a continuum of engagement from input to shared leadership are allowable and encouraged. For example, study teams may find it useful to solicit input from a large group of stakeholders using quick-turnaround methods (e.g., focus groups, surveys, crowd-sourcing, virtual or in-person roundtables and community forums) in addition to engaging stakeholders via ongoing consultative groups (e.g., advisory committees, working groups), collaborative arrangements, and leadership positions (e.g., co-investigators, multidisciplinary steering committees) that are sustained over the course of the study.

For this PFA, applicants should provide a basic outline of an engagement approach that includes (1) a proposed list of patient and other healthcare research partners (include names and affiliations, if available), the perspectives they will represent, and justification for their inclusion; (2) the goals for working with stakeholders, which may include affecting the acceptability, feasibility, rigor, and/or relevance of the study; (3) a description of how the team will collaborate with and/or gather input from stakeholders at key decision points throughout the study; and (4) proposed ideas for how stakeholder advisory committees and/or governance committees that include stakeholders will be structured and their purpose. Advisory committees, or other appropriately justified governance structures, should meet regularly throughout the study or, at a minimum, three times per year. Following review, PCORI may offer suggestions of additional stakeholder representatives (e.g., scientific and methodological experts, providers with clinical or intervention delivery expertise) to serve on committees or governance structures. PCORI’s Engagement Rubric, and other engagement resources available on PCORI’s website, can be a helpful resource to guide applicants on engagement approaches to consider in different phases of a research study.

Populations Studied and Recruited

PCORI seeks to fund research that includes diverse populations with respect to age, gender, race, ethnicity, geography, or clinical status, so that possible differences in outcomes may be examined in defined subpopulations. PCORI recognizes that some proposed studies might represent important PCOR opportunities, even in the absence of a broadly diverse study population. However, the burden is on the applicant to justify the study’s importance in the absence of diversity; to describe which subgroups are most important; and to discuss how the subgroups will be analyzed, including whether the study will be powered to examine the question of effectiveness in subgroups.

PCORI is particularly interested in including previously understudied populations for whom effectiveness information is especially needed, such as hard-to-reach populations or patients with multiple conditions. Thus, comparisons should examine the impact of the strategies in various subpopulations, with

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attention to the possibility that the strategy’s effects might differ across subpopulations. PCORI has
developed the following list of populations of interest to guide our efforts in research and engagement.
(Note that Addressing Disparities Priority Area studies require the proposed research to focus on at least
one of the groups indicated by an asterisk below.)

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

Regardless of the population studied, investigators are expected to provide evidence-based estimates
regarding the representativeness of the potential pool of participants from which recruitment will occur;
the target sample size; and recruitment and retention rates, reflecting the study’s inclusion and
exclusion criteria as well as factors that may impact the final sample size (e.g., loss to follow-up).

Protection of Human Subjects

PCORI follows the Federal Policy for the Protection of Human Subjects (45 CFR part 46), including the
Common Rule. For more detailed information, see Section 5, “Human Subjects Research Policy,” in the
Supplemental Grant Application Instructions for All Competing Applications and Progress Reports,10
issued by the US Department of Health and Human Services (HHS). In referencing the HHS Supplemental
Grant Application Instructions, note that PCORI does not require applicants to comply with sections of
the policy that refer to requirements for federal-wide assurance and the inclusion of women, minorities,
and children in the proposed studies. Instead, PCORI expects applicants to address diversity in study
participants in the research plan, through a focus on subpopulations, as described in the above section
on Populations Studied and Recruited. Awardees must also comply with appropriate state, local, and
institutional regulations and guidelines pertaining to the use of human subjects in research.

PCORI requires awardees to ensure that there is a Data and Safety Monitoring Plan, which may include

the need to appoint a DSMB, as described in the PCORI Policy on Data and Safety Monitoring Plans for PCORI-Funded Research.11

PCORI merit reviewers will examine plans for protection of human subjects in all applications and may provide comments regarding the plans (see How to Evaluate Human Subjects Protections12). Reviewers’ comments on human subject research are not reflected in the overall application score, but PCORI staff might use them during potential funding negotiations. Final determinations about the adequacy of human subject protections rest with the IRB or the international equivalent that has jurisdiction for the study.

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

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

PCORI requires that all applicants adhere to the National Institutes of Health (NIH) policy on education in the protection of human subject participants in the conduct of research. This applies to all individuals listed as key personnel in the application. The policy and FAQs are available on the NIH website.13

### III. LOI Review

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

LOIs are evaluated based on the following:

- Compliance with PFA requirements for proposals to conduct a large pragmatic clinical trial or study of significant potential impact on patient outcomes or healthcare practices
- Importance and relevance of the topics to PCORI priorities, as evidenced by critical gaps identified by clinical guidelines developers and recent systematic reviews
- Clarity and credibility of applicants’ responses to the LOI questions
- The investigators’ prior relevant experience
- Programmatic fit and balance, considering whether the LOI overlaps with previously funded studies or concurrent LOIs and/or applications to a significant degree or, conversely, whether the application fills a gap in PCORI’s funded portfolio with certain characteristics, including disease category, topics, priority populations, methodologies, and other variables

Only applicants whose LOIs are deemed most responsive to this PFA will be invited to submit a full application. A minimum of two PCORI staff members review the LOIs, which are not scored during review.

The LOI Template provides guidance on responding to each item. Please refer to the Submission

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Instructions for information on how to submit an LOI via PCORI Online.

IV. Merit Review
PCORI’s merit review process is designed to support the following goals:

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

PCORI merit review is a multiphase process that includes the review panel’s preliminary review of full applications and an in-person panel discussion of a subset of applications (identified by PCORI’s program staff and based on the preliminary review and program priorities). After merit review, key steps include post-panel review of the application by PCORI staff; the PCORI Selection Committee’s recommendation of applications for funding; and, finally, Board of Governors (Board) award approval.

Preliminary Review
PCORI conducts rigorous merit review of the full applications it receives. Note that PCORI may eliminate applications from the review process for administrative or scientific reasons. An application may be administratively withdrawn if it is incomplete; is submitted past the stated due date and time; or does not meet the formatting criteria outlined in the Submission Instructions, in the PCORI templates, and in PCORI Online. An application may be scientifically withdrawn if it is not responsive to the guidelines described in this PFA, describes research that is not comparative, includes a cost-effectiveness analysis, or otherwise does not meet PCORI programmatic requirements.

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

Below are PCORI’s merit review criteria for PCS applications. PCORI’s merit review panel will use these criteria during the preliminary and in-person review phases to evaluate and score all submitted applications and to ensure consistency and fairness in how applications are evaluated.

Criterion 1. Potential for the study to fill important gaps in evidence
The application should clearly justify the importance of the clinical or care delivery problems that the
study will address and whether the proposed approach is appropriately conceptualized. The application should also address the following questions:

- Is this an important research question where the results will inform key stakeholders (e.g., patients, clinicians, health systems, payers, policy makers) in making an important decision? Is there compelling evidence that the research question addresses an important health decision?
- Does the application identify a critical gap in current knowledge as noted in systematic reviews, guideline development efforts, authoritative recommendations by stakeholder organizations, or with evidence of inconsistency in clinical practice and decision making?
- Would research findings from the study have the potential to fill a well-documented evidence gap(s)?
- Does the importance of the research question justify the scope and magnitude of the proposed study?
- Does the application convincingly describe the clinical burden?
- Will the findings remain relevant and valuable given the proposed timeline to achieve them?

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

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

- Does the application identify end-users, such as local and national stakeholders who have expressed their interest in applying study findings?
- Would the study’s findings inform decision making for these key stakeholders?
- What is the likelihood that others could reproduce positive findings, resulting in improvements in practice and patient outcomes?
- Does the application identify potential barriers to intervention adoption and strategies to address such barriers?
- Does the application identify resources or factors that would promote adoption of the intervention?

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

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

- Does the application describe a clear causal framework anchored in background literature that informs the design, key variables, pragmatic elements, and relationship between interventions and outcomes being tested?
- Does the research plan describe rigorous methods that adhere to the PCORI Methodology Standards?
- Is the overall study design justified?
- Are the patient population and study setting appropriate for the proposed research question?
- Does the application provide justification that the outcome measures are validated and appropriate for the population?
- Are each of the comparators (e.g., active intervention arm and comparator arm) described clearly and well justified? Does the application describe the strength of evidence supporting their efficacy and/or widespread use? If usual care is one of the arms, is it adequately justified, and will it be sufficiently measured?
- Are the sample sizes and power estimates well justified and appropriate for the proposed study design as well as the specific research question? Is the anticipated effect size adequately justified?
- Is the overall study plan well justified and coherent?
- Are the project timeline and milestones realistic?
- Is the strategy for recruiting participants feasible? Are assumptions about participant attrition realistic, and are plans to address patient or site attrition adequate?

**Criterion 4. Investigator(s) and environment**

The application should demonstrate the appropriateness (i.e., qualifications and experience) of the investigator(s)/team and the environment’s capacity (e.g., resources, facilities, equipment) to support the proposed project. Assessment of this criterion should not focus on the institution’s reputation, but rather on the breadth and depth of its available personnel and resources. The application should also address the following questions:

- How well qualified are the Principal Investigators (PIs), collaborators, and other researchers to conduct the proposed activities? Does the application present evidence of sufficient clinical, statistical, and study management expertise?
- Does the investigative team have adequate experience in conducting projects of a similar size, scope, and complexity?
- Are the leadership, governance, and organizational structures adequate for the scope of the project?
- If the project is collaborative or dual-PI:
  - Do the investigators have complementary and integrated expertise?
  - Does the Leadership Plan clearly describe and justify investigator roles and areas of responsibility? Does the plan support efficient and high-quality research?
- Do the personnel who will manage engagement activities have appropriate experience, resources, and time commitments to carry out the proposed engagement of patients and stakeholders in research?
- Does the application describe adequate availability of and access to facilities and resources for the proposed research?
- Is the institutional support appropriate for the proposed research?

**Criterion 5. Patient-centeredness**

The application should demonstrate that the study focuses on improving patient-centered outcomes and employs a patient-centered research design—that is, a design informed or endorsed by patients. (NOTE: The study can be patient centered even if the end-user is not the patient, as long as patients will benefit from the information.) The application should also address the following questions:
• Does the application include a thorough description about which outcomes (both benefits and harms) are important to patients, and are those outcomes included in the study plan?
• Does the application provide information that indicates that closing the evidence gap is important to patients and other stakeholders?
• Do the comparators represent challenging choices that patients confront?
• What evidence is presented or planned to assess patients’ willingness to accept the proposed comparators in light of the potential benefits, risks, and burdens of time, inconvenience, out-of-pocket costs, and other factors?

Criterion 6. Patient and stakeholder engagement

The application should demonstrate the engagement of relevant patients and other stakeholders (e.g., patients, caregivers, clinicians, policy makers, hospital and health system representatives, payers [insurance], purchasers [business], industry, researchers, training institutions) in the conduct of the study. Quality of engagement will be evaluated based on scope, form, and frequency of patient and stakeholder involvement throughout the research process. The application should also address the following questions:

• Is the proposed engagement approach appropriate and tailored to the study? Is the frequency and level of involvement of patients, providers, health system partners, scientists, policy makers, and other stakeholders appropriate to support the study goals?
• Are the proposed stakeholders fully representative of the groups most likely to be impacted by the study question? Does the study plan include adequate representation of appropriate stakeholder groups, and from the populations most impacted by the condition to ensure diverse perspectives throughout the research process?
• Are planned engagement activities and resources adequate to assist in determining the acceptability (e.g., the time, resource demands, or other burdens) of the comparators, randomization, and requirements of study conduct and participation for providers and participants?
• Are clear descriptions included of the roles and contributions of all study collaborators in decision making throughout the study?

In-Person Review

During preliminary review, all administratively and scientifically compliant applications are evaluated and scored by panels of external reviewers based on PCORI’s merit review criteria, including adherence to the PCORI Methodology Standards. After preliminary review, PCORI program staff members evaluate panel scores and critiques to identify a subset of applications for merit reviewers to discuss at the in-person review meeting. Not all submitted applications move forward to in-person review.

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

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

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

Summary Statements and Funding Recommendations

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

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

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

Funding recommendations are made by identifying meritorious applications that fit the programmatic needs and that satisfactorily address the merit review criteria while adhering to the PCORI Methodology Standards. Programs also consider the funds allotted for the current funding announcement when deciding which applications to recommend to the Board for approval. Applicants to this current cycle’s PFA will receive summary statements and notification of the funding status of their application no later than November 2021.

V. **PCORI Policies that Govern Awardees Related to Data Access, Privacy, and Public Reporting**

Applicants should be aware that all PCORI awardees are required to comply with the following requirements:
Registering Research Projects

PIs are required to use the naming convention “PCORI-PCORI application number” (i.e., PCORI-XXXX-XXXX). Clinical trials must be registered before enrollment of the first patient. All trials that meet the definition on the NIH database\(^\text{14}\) (see Data Element Definitions) are required to register, if funded.

Funded clinical trials or observational outcomes studies must be registered at ClinicalTrials.gov.

Funded evidence-synthesis studies must be registered at PROSPERO.\(^\text{15}\) Funded patient registries must be registered at https://patientregistry.ahrq.gov/.

PCORI Public Access Policy

PCORI requires all awardees to adhere strictly to PCORI’s publication policies, which will be shared with awardees within the research contract.

Standards for Privacy of Individually Identifiable Health Information

On August 14, 2002, HHS issued a final modification to the Standards for Privacy of Individually Identifiable Health Information, the “Privacy Rule.” The Privacy Rule is a federal regulation under the Health Insurance Portability and Accountability Act (HIPAA) of 1996 that governs the protection of individually identifiable health information and is administered and enforced by the HHS Office for Civil Rights.

Decisions about the applicability and implementation of the Privacy Rule reside with the researcher and his or her institution. The Office for Civil Rights\(^\text{16}\) provides information on the Privacy Rule, including a complete Regulation Text and a set of decision tools related to “Am I a covered entity?” Information on the impact of the HIPAA Privacy Rule on NIH processes involving the review, funding and progress monitoring of grants, cooperative agreements, and research contracts is available from NIH.\(^\text{17}\)

Data Management and Data-Sharing Plan

In accordance with its authorizing legislation, PCORI is committed to publishing and disseminating all information and materials developed using PCORI funding. All recipients of PCORI contracts must agree to these principles and take steps to facilitate data availability.

PCORI encourages openness in research and making research data available for purposes of replication and reproducibility. As such, if an award is made, the awardee will be expected to adhere to PCORI’s Policy for Data Management and Data Sharing. The policy articulates PCORI’s requirement that certain awardees make the underlying data and data documentation (e.g., study protocol, metadata, analytic code) from their PCORI-funded research projects available to third-party requestors.

A full data management and data-sharing plan is not required at the time of application. If an award is made, the awardee is required to develop and maintain such a plan, which is described in detail in the PCORI Methodology Standards for Data Integrity and Rigorous Analyses, specifically Standard IR-7. This plan must be appropriate for the nature of the research project and the types of research project data,

\(^\text{14}\) Available at https://prsinfo.clinicaltrials.gov/.
\(^\text{15}\) Available at http://www.crd.york.ac.uk/prospero/.
\(^\text{16}\) Available at http://www.hhs.gov/ocr/.
and it must be consistent with applicable privacy, confidentiality, and other legal requirements. The policy includes details about what data certain awardees will be expected to deposit into a PCORI-designated data repository and when that data would be available for third-party requests.

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

**Peer Review and Release of Research Findings**

PCORI has a legislative mandate to ensure the scientific integrity of the primary research it supports and to make study findings widely available and useful to patients, clinicians, and the general public within a specific timeframe. Accordingly, the PCORI Board adopted the Process for Peer Review of Primary Research and Public Release of Research Findings.¹⁸

In summary, awardee institutions are required to submit to PCORI for peer review a draft final research report that provides the methodological details, describes the main study results, and interprets the findings in clinical or other decisional contexts. After awardee institutions have responded to reviewers’ comments to PCORI’s satisfaction, the report will be accepted and considered final. PCORI will then prepare two 500-word standardized abstracts summarizing the study results (as detailed below), which the awardee institution will review and approve.

No later than 90 days after the draft final research report is accepted, PCORI will post the following materials on its website: (1) a 500-word abstract for medical professionals; (2) a 500-word standardized abstract summarizing the study results for patients and the general public; (3) a link to the study record on ClinicalTrials.gov (as applicable); and (4) ancillary information, including conflict of interest disclosures. The final research report, along with anonymized reviewer comments, will be made publicly available on the PCORI website no later than 12 months after its acceptance, except by prior mutual agreement with the awardee institution.

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