



## Cycle 3 2020 Funding Cycle

### PCORI Funding Announcement: **Phased Large Awards in Comparative Effectiveness Research (PLACER)**

Published June 9, 2020

Updated August 4, 2020

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This PCORI Funding Announcement (PFA) applies to the funding cycle that closes January 12, 2021, at 5 pm ET. Submission Instructions, templates, and other resources are available at <https://www.pcori.org/funding-opportunities/announcement/phased-large-awards-comparative-effectiveness-research-cycle-3-2020>.

## **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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## Overview

Published	June 9, 2020
Summary	<p>This PFA invites applications for high-quality comparative effectiveness research (CER) projects that will examine a critical patient-centered research question that is also relevant to decision makers and other stakeholders. For this PFA, investigators should propose an individual-level or cluster randomized controlled trial of significant scale and scope, requiring funding in excess of \$10 million in direct costs. The proposed trials should address important decisional dilemmas that require new evidence about the comparative effectiveness of available interventions. Studies must 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.</p> <p>This funding announcement anticipates that the proposed research projects will require an initial feasibility phase with funding support for study refinement, feasibility testing, stakeholder engagement, and infrastructure establishment. Continued funding of the second phase to carry out the full-scale study will be contingent upon the achievement of specific milestones and deliverables in the feasibility phase. In light of the scale, complexity, and scope of studies being solicited under this PFA, PCORI requires that funded trials include a data coordinating center (DCC) with an independent scientific leadership role to advise on and undertake the analytical, statistical, and data management aspects of both study phases.</p> <p>For this solicitation, applicants are not required to demonstrate that patients and other stakeholders are already engaged as research team members at the time an application is submitted, but experienced leadership of engagement activities should be included. Applicants should outline how patients and other stakeholders will participate as partners in various phases of the proposed research, once awarded. Applicants should describe their plan to form a study advisory committee (SAC),<sup>1</sup> or other appropriate engagement body, to ensure that a broad spectrum of patients and other stakeholders advises and assists the research team with refining the study questions, outcomes, and protocols. These patients and other stakeholders must include national or regional organizations that represent—at a minimum—patients, caregivers, clinicians, policy makers, and other healthcare system stakeholders. PCORI may recommend additional representation in collaboration with the applicant, including individual patients with lived experience and other relevant stakeholders, such as scientific and methodological experts.</p>

<sup>1</sup> The intent of the SAC described in the PFA is to ensure that a broad spectrum of patients and other stakeholders advises and assists the research team with refining the study questions, outcomes, and protocols. These patients and other stakeholders must include national or regional organizations that represent—at a minimum—patients, caregivers, clinicians, policy makers, and other healthcare system stakeholders. PCORI may recommend additional representation in collaboration with the applicant, including individual patients with lived experience and other relevant stakeholders, such as scientific and methodological experts. However, PCORI understands that engagement structures and approaches vary widely. Other engagement approaches, such as forming stakeholder groups, panels, task forces, working groups, and other bodies, or those involving individual patient and other stakeholder partners in various ways are also permissible to employ either in addition to or instead of the formation of the SAC. The SAC provision is not meant to require that a separate governance or advisory entity be established beyond the study governance and advisory structure the awardee has planned, if an applicant already has an approach for including the relevant and required patient and other stakeholder partners. For clarification in your application materials and for merit review purposes, please indicate which body or structure is filling the SAC requirements, including the requirements for in-person meetings at least two times per year and appropriate budgeting.

Key Dates	<p>Online System Opens: June 9, 2020</p> <p>Town Hall: July 14, 2020, 12 pm ET</p> <p>LOI Deadline: September 29, 2020, by 5 pm ET</p> <p>LOI Status Notification: October 27, 2020</p> <p>Application Deadline: January 12, 2021, by 5 pm ET</p> <p>Merit Review: April 2021</p> <p>Awards Announced: July 2021</p> <p>Earliest Project Start Date: November 2021*</p>
Maximum Project Budget (Direct Costs)	<p>\$22 million (Feasibility phase maximum: \$2 million; Full-scale study phase: \$20 million)</p> <p>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 research- and peer-review-related costs. This PFA does not consider exceptions to the budget. PCORI will not review submissions exceeding the stated maximum budget.</p>
Maximum Research Project Period	<p>6.5 years (Feasibility phase: 1.5 years; Full-scale study phase: 5 years)</p> <p>This PFA does not consider exceptions to period-of-performance limits. PCORI will not review submissions exceeding the stated period of performance.</p>
Funds Available Up To	\$150 million
Eligibility	<p>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.</p>
Review Criteria	<ol style="list-style-type: none"> <li>1. Potential for the study to fill critical gaps in evidence</li> <li>2. Potential for the study findings to be adopted into clinical practice and improve delivery of care</li> <li>3. Scientific merit (research design, analysis, and outcomes)</li> <li>4. Investigator(s) and environment</li> <li>5. Patient-centeredness</li> <li>6. Patient and stakeholder engagement</li> </ol>
Contact Us	<p><b>Programmatic Inquires:</b> <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>).</p> <p><b>Administrative, Financial, or Technical Inquiries:</b> <a href="mailto:pfa@pcori.org">pfa@pcori.org</a> or phone (202-627-1885).</p> <p>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.</p>

*\*Updated on August 4, 2020: Corrected the Earliest Start Date from July to November 2021.*

## **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 to PLACER encompassing a wide range of investigator-initiated research supporting comparative effectiveness. Such research may potentially include research related to COVID-19 and its impact on health. PCORI notes with caution, however, that the size and expected timeframe for PLACER studies to generate research results does not readily fit the urgent exploration of efficacious solutions to the COVID-19 pandemic.

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## I. Introduction

### Background

The goal of the Phased Large Awards for Comparative Effectiveness Research (PLACER) PCORI funding announcement (PFA) is to support large-scale, high-impact randomized trials in comparative effectiveness research (CER) with risks in achieving their research aims and which therefore merit an initial period of testing and refinement to: (1) determine their feasibility and viability, and (2) maximize the likelihood of full-scale trial success. Federal funders, such as the National Institutes of Health (NIH), commonly employ phased research awards for their largest studies to allow innovation along with appropriate risk management for large research investments. Multiple PCORI advisory and governance bodies endorsed initiation of a large-scale, phased funding opportunity to increase the diversity of PCORI-funded research projects making direct comparisons of clinical treatment options and to enlarge the field of qualified investigators interested in applying to PCORI. An initial feasibility phase can enable robust and diverse stakeholder input and engagement to assess equipoise among study participants (such as health systems, clinicians, and patients) and to maximize their willingness to participate in the research study. Phased research conduct permits refinement of the research question and outcomes; testing of recruitment assumptions and the feasibility of study conduct; refinement of data collection methods and instruments; and the opportunity to detect and address unanticipated challenges to study execution prior to full-scale study implementation. Statistical rigor and power are likewise strengthened by using the feasibility phase to work collaboratively with the expertise of a Data Coordinating Center (DCC) to test and refine the final study size, design, and statistical analyses.

### Program Requirements

PCORI seeks proposals for large randomized trials in clinical CER that are structured into two well-integrated phases: an initial feasibility and testing phase (to establish the trial design, operations, infrastructure, and analysis) followed by a second phase in which conduct of the full-scale clinical trial proceeds based on successful accomplishment of groundwork completed in the feasibility phase. Studies funded under the PLACER PFA must propose an individual-level or cluster randomized controlled trial (RCT) of significant scale and scope with an initial feasibility phase up to 18 months in duration. Continuation to full-scale trial conduct will occur contingent upon the successful demonstration of its feasibility and viability based on review by PCORI and an External Advisory Panel (EAP) using milestones and criteria for the feasibility phase. The full-scale study phase may be up to five years in duration following the feasibility phase. All phases of the proposed research must involve ongoing collaboration with a DCC, which will provide expertise in research design, data collection/management, and statistical analysis.

Applicants to the PLACER PFA should propose a well-developed and formulated RCT addressing a critical gap in comparative effectiveness. Proposed feasibility phase activities should support the trial's refinement and full-scale implementation within 18 months of initiation. In light of PCORI's interest in representative and generalizable studies done in real-world clinical care conditions, populations, and settings, diverse stakeholder engagement is encouraged to aid identification of research activities and processes that are acceptable and achievable by all study participants under the proposed study conditions. Major elements of the full-scale trial should be well planned at the time of application, with

the feasibility phase used to refine, test, and adapt them as necessary. The feasibility phase is neither for de novo study planning nor for the determination of intervention(s) efficacy.

### *Feasibility Phase*

The initial feasibility phase should support all necessary preparatory activities to permit the rapid and efficient conduct of the full-scale trial at the conclusion of the feasibility phase. The feasibility phase may include, but is not limited to, the development and initiation of a robust stakeholder engagement plan, protocol development, piloting of data collection methods, refinement of recruitment methods and estimated enrollment, and establishment of study sites.

The applicant should propose specific milestones and deliverables to be achieved in the feasibility phase using the suggested milestones found in the Milestones Template. The applicant may modify the milestone schedule, as needed, to fit the anticipated duration and timing needs of the feasibility phase, which cannot exceed 18 months. If an award is made, final milestones will be negotiated in conjunction with PCORI and will be used in the evaluation of whether the full-scale study may continue with PCORI support.

PCORI will maintain close oversight of feasibility phase activities, milestones, deliverables, and progress and will initiate its review for potential continuation several months in advance of the feasibility phase concluding date. PCORI will be assisted in its review and oversight of study progress and the decision whether to continue research to full-scale study execution by an EAP; EAP members will possess relevant experience and expertise on the clinical condition(s), research methodology, clinical trial design and statistical analysis, and perspectives of patients, providers, and key stakeholders.

Milestones and deliverables of the feasibility phase will assess the awardee's ability to:

- Establish and/or further develop patient and stakeholder engagement and an engagement plan in support of study design, acceptability to participants, conduct, analysis, and dissemination of findings.
- Provide assurance of recruitment feasibility with defensible estimates of eligible participants and evidence-based projections of the percentages of participants enrolled, randomized, retained, and discontinuing or lost to follow-up.
- Establish subcontracting agreements with the DCC and sub-award sites.
- Finalize the scope of work and study protocol for the full-scale study.
- Develop and finalize the statistical analysis plan for the full-scale study.
- Develop detailed plans for site onboarding, research conduct, and data collection/reporting.
- Finalize clinically relevant and patient-centered outcome measures.
- Test data collection instruments and reporting methods for outcomes assessment.
- Develop and submit plans for all aspects of ethical and regulatory oversight and protection of human subjects.
- Develop detailed plans for data management and quality control.
- Refine a comprehensive stakeholder engagement plan.
- Carry out additional specific tasks appropriate to the proposed research.

At the conclusion of the feasibility phase and irrespective of PCORI's decision to continue funding of the full-scale trial, all awardees must provide a detailed report outlining all feasibility phase findings, including activities related to stakeholder engagement, study design decisions, analytical plan development, protocol development, recruitment planning and estimation, site selection and readiness, and other factors outlined in the research plan.

### *Data Coordinating Center (DCC)*

Due to the scale, complexity, and scope of studies being solicited under this PFA, PCORI requires applicants to include a DCC with an independent scientific leadership role in study decision making about the analytical, statistical, and data management aspects of both study phases. For potential applicants to this PFA, a Letter of Intent (LOI) may be submitted without a DCC being in place—with the proviso that invited applicants include a DCC as part of their application submission. Applications that do not include a DCC will be considered nonresponsive and removed from further review consideration.

The DCC is expected to make a substantive contribution to refining the final trial design and protocol, data collection and management, and the statistical analysis plan. During the full-scale study phase, the DCC is expected to manage data reporting, monitor study enrollment and retention, assure data quality and completeness, prepare reports for the Data Safety and Monitoring Board (DSMB), carry out all necessary statistical analyses of study findings, and ensure a high level of data integrity, security, and protection.

PCORI requirements and expectations for DCC are as follows:

- PCORI recommends that the PI of the DCC be named as a dual-PI to promote DCC parity, scientific independence, and autonomy in study decisions. If other arrangements are proposed, applicants must provide strong evidence that an alternative arrangement will ensure the independent voice of the DCC in its oversight functions.
- Applicants must certify or otherwise document the existence of adequate policies, procedures, and standards to ensure independence, autonomy, absence of conflicts, and firewalls between clinical care and study data.
- PCORI advocates separation and independence of clinical and data/statistical leadership of the study and strongly discourages the use of a combined DCC and clinical coordinating center (CCC). If such an arrangement is proposed, it must provide evidence of distinct lines of institutional reporting, accountability, and financing between the DCC and CCC.
- If the DCC is not the prime applicant but a subcontractor, the prime applicant/awardee institution bears responsibility for ensuring that all relevant regulatory and certification requirements of the data coordinating centers are met to guarantee data integrity, safety, confidentiality, etc.

### *Full-Scale Study*

Proximate to the planned initiation of the full-scale study, PCORI and the EAP will evaluate feasibility phase progress and determine whether the accomplishments and findings indicate a strong likelihood that the planned full-scale study remains feasible with a good chance of success. If the full-scale trial goes forward, PCORI will modify the original contract; the full-scale study milestones may be revised

based on feasibility phase findings.

### **Invited Research Areas**

PCORI invites PLACER 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 PLACER PFA, PCORI seeks either investigator-initiated or patient-centered CER applications aligned with its national priority areas described in the following section. Following them are five exemplars of research topics that address one or more of these priority areas. PCORI is including these examples to illustrate the desired scale and scope being sought in PLACER applications; they manifest a high degree of complexity and a significant burden on the US population by virtue of their prevalence and associated loss of productivity and/or individual experience. These research topics are not explicit PCORI priority topics for this PFA.

### ***Investigator-Initiated Research***

This PFA focuses on three long-established national priority areas of PCORI: Addressing Disparities; Assessment of Prevention, Diagnosis, and Treatment Options; and Improving Healthcare Systems. In addition to these three, PCORI's 2019 reauthorizing legislation provided additional direction about national research priorities to include research with respect 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, numeracy, or limited English proficiency; and sexual and gender minorities persons). 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 remaining 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 defined clearly 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, and 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 and patient-centered medical homes) and care settings (e.g., hospitals, physician practices, nursing homes, community health clinics, patients' homes) also define healthcare system operations. 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 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

IHS values research studies that leverage healthcare system resources to support intervention requirements or studies where healthcare organizations and other stakeholders (e.g., payers) 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 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 systems interventions to address adverse consequences and outcomes in these two priority areas. 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. For both priority areas, applications that address disparities in vulnerable populations are welcome.

### *Exemplar Topics*

PCORI seeks to fund trials that compare two or more alternatives which represent a critical choice for patients, caregivers, clinicians, and other healthcare stakeholders as evidenced by gaps identified in clinical practice guidelines, systematic reviews, and prioritization exercises. Research topics selected for this funding announcement should be appropriately complex and represent a significant burden on the US population in terms of prevalence, loss of productivity, and/or individual experience. Example topics for studies that could potentially meet the size and scope requirements for this funding mechanism appear below; however, these are not explicit PCORI priorities.

#### **Osteoporotic Fracture Prevention**

Osteoporosis, or porous bone, is a disease characterized by low bone mass and structural deterioration

of bone tissue, leading to bone fragility and an increased risk of fractures of the hip, spine, and wrist.<sup>2</sup> Approximately two million US adults experience an osteoporotic or other low-or no-trauma fracture each year, a number that is projected to increase with the aging population.<sup>3</sup> Fractures are associated with pain, loss of mobility and self-care, and impaired quality of life.<sup>4</sup>

Clinical practice guidelines and systematic reviews have identified many important unanswered questions related to the use of drug therapies in osteoporotic fracture prevention.<sup>5,6,7,8</sup> For example, what is the comparative effectiveness of different durations of drug therapy with or without drug holiday on outcomes such as major osteoporotic fracture, functional status, hospitalization, nursing home placement, and others? Do certain patients derive greater benefit or greater harm of different long-term treatment strategies, including use of drug holidays?

### Migraine Prophylaxis in Adults

Migraine is a common disorder, characterized by recurrent attacks of headache and other symptoms, including sensitivity to light and noise, visual disturbances, and nausea. Episodic and chronic migraine affects roughly 12 percent of the population in the United States and is more prevalent in women than in men.<sup>9</sup> The disorder is a major cause of disability<sup>10</sup>, and is associated with low health-related quality of life and high economic burden.<sup>11</sup>

Clinical practice guidelines and systematic reviews have identified many important evidence gaps

<sup>2</sup> NIH Consensus Development Panel on Osteoporosis Prevention, Diagnosis, and Therapy. Osteoporosis prevention, diagnosis, and therapy. *JAMA*. February 14, 2001;285(6):785-95. Review.

<sup>3</sup> Burge R, Dawson-Hughes B, Solomon DH, Wong JB, King A, Tosteson A. Incidence and economic burden of osteoporosis-related fractures in the United States, 2005-2025. *J Bone Miner Res*. March 2007;22(3):465-75.

<sup>4</sup> Borhan S, Papaioannou A, Gajic-Veljanoski O, Kennedy C, Ioannidis G, Berger C, Goltzman D, Josse R, Kovacs CS, Hanley DA, Prior JC, Morin SN, Kaiser SM, Cheung AM, Thabane L, Adachi J; CaMos Research Group. Incident Fragility Fractures Have a Long-Term Negative Impact on Health-Related Quality of Life of Older People: The Canadian Multicentre Osteoporosis Study. *J Bone Miner Res*. May 2019;34(5):838-848.

<sup>5</sup> Camacho PM, Petak SM, Binkley N, Clarke BL, Harris ST, Hurley DL, Kleerekoper M, Lewiecki EM, Miller PD, Narula HS, Pessah-Pollack R, Tangpricha V, Wimalawansa SJ, Watts NB. AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS AND AMERICAN COLLEGE OF ENDOCRINOLOGY CLINICAL PRACTICE GUIDELINES FOR THE DIAGNOSIS AND TREATMENT OF POSTMENOPAUSAL OSTEOPOROSIS - 2016—EXECUTIVE SUMMARY. *Endocr Pract*. September 2016;22(9):1111-8. doi: 10.4158/EP161435.ESGL. Erratum in: *Endocr Pract*. March 2017;23(3):383.

<sup>6</sup> Compston J, Cooper A, Cooper C, Gittoes N, Gregson C, Harvey N, Hope S, Kanis JA, McCloskey EV, Poole KES, Reid DM, Selby P, Thompson F, Thurston A, Vine N; National Osteoporosis Guideline Group (NOGG). UK clinical guideline for the prevention and treatment of osteoporosis. *Arch Osteoporos*. December 2017;12(1):43. doi: 10.1007/s11657-017-0324-5. Epub 2017 Apr 19.

<sup>7</sup> Fink HA, MacDonald R, Forte ML, Rosebush CE, Ensrud KE, Schousboe JT, Nelson VA, Ullman K, Butler M, Olson CM, Taylor BC, Brasure M, Wilt TJ. Long-Term Drug Therapy and Drug Holidays for Osteoporosis Fracture Prevention: A Systematic Review. Comparative Effectiveness Review No. 218. (Prepared by the Minnesota Evidence-based Practice Center under Contract No. 290-2015-00008-I) AHRQ Publication No. 19-EHC016-EF. Rockville, MD: Agency for Healthcare Research and Quality; April 2019. Posted final reports are located on the Effective Health Care Program search page. DOI: <https://doi.org/10.23970/AHRQEPCCER218> Link to Exit Disclaimer.

<sup>8</sup> Siu A, Allore H, Brown D, et al. National Institutes of Health Pathways to Prevention Workshop: Research Gaps for Long-Term Drug Therapies for Osteoporotic Fracture Prevention. *Ann Intern Med*. 2019;171:51–57. [Epub ahead of print April 23, 2019]. doi: <https://doi.org/10.7326/M19-0961>

<sup>9</sup> Lipton RB, Bigal ME, Diamond M, Freitag F, Reed ML, Stewart WF; AMPP Advisory Group. Migraine prevalence, disease burden, and the need for preventive therapy. *Neurology*. January 30, 2007;68(5):343-9.

<sup>10</sup> Mokdad, Ali H., et al. "The state of US health, 1990-2016: burden of diseases, injuries, and risk factors among US states." *JAMA* 319.14 (2018): 1444-1472.

<sup>11</sup> Blumenfeld A, Varon S, Wilcox TK et al. Disability, HRQoL and resource use among chronic and episodic migraineurs: results from the International Burden of Migraine Study (IBMS). *Cephalalgia* 2011;31:301–15.

related to drug and device treatments for migraine prophylaxis.<sup>12,13,14,15,16,17</sup> For example, what are the comparative benefits and harms of treatments for the prevention of episodic or chronic migraine, including newly available pharmacologic treatments and devices, on reduction in frequency of migraine, loss of working days, and use of abortive therapies or opioids? How does the effectiveness of these strategies vary based on patient characteristics, such as age, sex, comorbidities, and prior treatment response?

### Improving Outcomes in Maternal Morbidity and Mortality

Rates of severe maternal morbidity and pregnancy-related deaths have been increasing over the past few decades in the United States,<sup>18,19</sup> and significant disparities persist for racial and ethnic minorities and rural populations. Sixty percent of maternal deaths are considered preventable, and research shows that black, indigenous, and rural women receive fewer prenatal care visits than white and urban women<sup>20</sup>, and the quality of care for these women is often lower.<sup>19</sup>

There are several important questions related to health services to improve maternal outcomes, including increasing access and improving the quality of care that women receive.<sup>21,22,23,24</sup> For example, what is the comparative effectiveness of culturally tailored care models (e.g., different models of comprehensive reproductive health care, including services such as care coordination, home visits, patient navigators, doula care, teledelivery of care components, and case management) to increase patient access, continuity of care, adherence, patient experience of care, and reduce disparities,

<sup>12</sup> Scottish Intercollegiate Guidelines Network (SIGN). Pharmacological management of migraine. Edinburgh: SIGN; 2018. (SIGN publication no. 155). [February 2018]. Available from URL: <http://www.sign.ac.uk>

<sup>13</sup> Shamiyan, TA, Kane RL, and Taylor FR. "Migraine in Adults: Preventive Pharmacologic Treatments [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US); 2013. (AHRQ Comparative Effectiveness Reviews)."

<sup>14</sup> Jackson JL, Cogbill E, Santana-Davila R, Eldredge C, Collier W, Gradall A, Sehgal N, Kuester J. A Comparative Effectiveness Meta-Analysis of Drugs for the Prophylaxis of Migraine Headache. *PLoS One*. July 14, 2015;10(7):e0130733. doi: 10.1371/journal.pone.0130733. eCollection 2015.

<sup>15</sup> Herd et al (2018), Botulinum toxins for the prevention of migraine in adults. *Cochrane Database of Systematic Reviews* 2018, Issue 6. Art. No.: CD011616. DOI: 10.1002/14651858.CD011616.pub2.

<sup>16</sup> Institute for Clinical and Economic Review (ICER). "Calcitonin Gene-Related Peptide (CGRP) Inhibitors as Preventive Treatments for Patients with Episodic or Chronic Migraine: Effectiveness and Value." Final Evidence Report. July 2018.

<sup>17</sup> Ibekwe et al. Canadian Agency for Drugs and Technologies in Health (CADTH) Issues in Emerging Health Technologies. "Monoclonal Antibodies to Prevent Migraine Headaches." February 2018.

<sup>18</sup> "Severe Maternal Morbidity in the United States." *Centers for Disease Control and Prevention*, January 31, 2020, [www.cdc.gov/reproductivehealth/MaternalInfantHealth/SevereMaternalMorbidity.html](http://www.cdc.gov/reproductivehealth/MaternalInfantHealth/SevereMaternalMorbidity.html). Accessed March 25, 2020.

<sup>19</sup> "Pregnancy Mortality Surveillance System." *Centers for Disease Control and Prevention*, 4 Feb. 2020, [www.cdc.gov/reproductivehealth/maternal-mortality/pregnancy-mortality-surveillance-system.htm?CDC\\_AA\\_refVal=https://www.cdc.gov/reproductivehealth/maternalinfanthealth/pregnancy-mortality-surveillance-system.htm#trends](http://www.cdc.gov/reproductivehealth/maternal-mortality/pregnancy-mortality-surveillance-system.htm?CDC_AA_refVal=https://www.cdc.gov/reproductivehealth/maternalinfanthealth/pregnancy-mortality-surveillance-system.htm#trends).

<sup>20</sup> Gadson A, A.E., Mehta P, *Exploring the social determinants of racial ethnic disparities in prenatal care utilization and maternal outcome. Semin Perinatol*, 2017(41): p. 308-317.

<sup>21</sup> National Research Council. 2000. *The Consequences of Maternal Morbidity and Maternal Mortality: Report of a Workshop*. Washington, DC: The National Academies Press. <https://doi.org/10.17226/9800>.

<sup>22</sup> National Academies of Sciences, Engineering, and Medicine. 2020. *Birth Settings in America: Outcomes, Quality, Access, and Choice*. Washington, DC: The National Academies Press. <https://doi.org/10.17226/25636>.

<sup>23</sup> Implementing Telehealth in Practice: ACOG Committee Opinion Summary, Number 798. *Obstet Gynecol*. February 2020;135(2):493-494. doi: 10.1097/AOG.0000000000003672.

<sup>24</sup> Dennis CL, Dowswell T, Dennis CL, Dowswell T. Psychosocial and psychological interventions for preventing postpartum depression. *Cochrane Database of Systematic Reviews* 2013, Issue 2. Art. No.: CD001134.

morbidity and mortality?

### Prevention of Suicide among Youth (ages 15-24)

Suicide rates have increased by 35 percent since 1999,<sup>25</sup> and suicide was the second leading cause of death<sup>26</sup> among youth ages 15 to 24 in 2017. Although the rate of suicide attempts is twice as high for adolescent girls, adolescent boys are more likely to die by suicide.<sup>27</sup> Lesbian, gay, bisexual, transsexual, and queer (LGBTQ) populations<sup>28</sup> have increased suicide rates, with the highest rates for transgender people, and the racial/ethnic categories with the highest rates of suicide are American Indian/Alaskan Native youth,<sup>29</sup> followed by non-Hispanic whites. In addition, although suicide rates have historically been lower among black individuals compared to whites, recent studies have found alarming increases in suicide attempts and deaths among black youth;<sup>30,31</sup> this rate has been increasing faster than any other racial/ethnic group.<sup>32</sup>

Clinical practice guidelines,<sup>33,34</sup> systematic reviews,<sup>35,36</sup> and task force reports<sup>37</sup> have identified many important questions regarding the most effective approaches to youth suicide prevention. For example, what is the comparative effectiveness of various brief interventions, psychological treatments, and follow-up strategies for youth with suicidal ideation on engagement in care, suicidal ideation, or self-harm? Do approaches tailored to specific subpopulations (e.g., LGBTQ, black, Hispanic, American Native/Alaskan Native) improve outcomes for these populations? What is the comparative effectiveness

<sup>25</sup> Hedegaard, Curtin, & Warner. Increase in Suicide Mortality in the United States, 1999-2018. Centers for Disease Control and Prevention. NCHS Data Brief, No. 362. April 2020.

<sup>26</sup> Curtin & Heron. Death Rates Due to Suicide and Homicide Among Persons Aged 10-24: United States, 2000-2017. Centers for Disease Control and Prevention. NCHS Data Brief, No. 352. October 2019.

<sup>27</sup> Shain B & AAP Committee on Adolescence. Suicide and Suicide Attempts in Adolescents. *Pediatrics*. July 2016;138(1). pii: e20161420. doi: 10.1542/peds.2016-1420.

<sup>28</sup> di Giacomo E, Krausz M, Colmegna F, et al. Estimating the Risk of Attempted Suicide Among Sexual Minority Youths: A Systematic Review and Meta-analysis. *JAMA Pediatr*. December 1, 2018;172(12):1145-1152. doi: 10.1001/jamapediatrics.2018.2731.

<sup>29</sup> Cwik MF, Tingey L, Lee A, et al. Development and piloting of a brief intervention for suicidal American Indian adolescents. *Am Indian Alsk Native Ment Health Res*. 2016;23(1):105-124. doi: 10.5820/aian.2301.2016.105.

<sup>30</sup> Bridge JA, Horowitz LM, Fontanella CA, et al. Age-Related Racial Disparity in Suicide Rates Among US Youths From 2001 Through 2015. *JAMA Pediatr*. July 1, 2018;172(7):697-699. doi: 10.1001/jamapediatrics.2018.0399.

<sup>31</sup> Lindsey MA, Sheftall AH, Xiao Y, Joe S. Trends of Suicidal Behaviors Among High School Students in the United States: 1991–2017. *Pediatrics*. November 2019;144(5). pii: e20191187. doi: 10.1542/peds.2019-1187. Epub 2019 October 14.

<sup>32</sup> Ring the Alarm: The Crisis of Black Youth Suicide in America. A Report to Congress from the Congressional Black Caucus Emergency Taskforce on Black Youth Suicide and Mental Health. 2019. [https://watsoncoleman.house.gov/uploadedfiles/full\\_taskforce\\_report.pdf](https://watsoncoleman.house.gov/uploadedfiles/full_taskforce_report.pdf). Accessed April 16, 2020.

<sup>33</sup> Department of Veterans Affairs and Department of Defense. VA/DoD Clinical Practice Guideline for the Assessment and Management of Patients at Risk for Suicide. Version 2.0, May 2019. <https://www.healthquality.va.gov/guidelines/MH/srb/VADoDSuicideRiskFullCPGFinal5088212019.pdf>.

<sup>34</sup> Wasserman D, Rihmer Z, Rujescu D, et al. The European Psychiatric Association (EPA) Guidance on Suicide Treatment and Prevention. *Eur Psychiatry*. 2012; 27(2):129–41. [PubMed: 22137775]

<sup>35</sup> Morken IS, Dahlgren A, Lunde I, Toven S. The Effects of Interventions Preventing Self-harm and Suicide in Children and Adolescents: An Overview of Systematic Reviews. Version 2. *F1000Res*. 2019 June 20, 019 [revised February 18, 2020];8:890. doi: 10.12688/f1000research.19506.2. eCollection 2019.

<sup>36</sup> Robinson J, Bailey E, Witt K et al. What Works in Youth Suicide Prevention? A Systematic Review and Meta-Analysis. *EClinicalMedicine*. October 28, 2018;4-5:52-91. doi: 10.1016/j.eclinm.2018.10.004. eCollection October–November 2018.

<sup>37</sup> National Action Alliance for Suicide Prevention: Research Prioritization Task Force. 2014. *A Prioritized Research Agenda for Suicide Prevention: An Action Plan to Save Lives*. Rockville, MD: National Institute of Mental Health and the Research Prioritization Task Force. [https://theactionalliance.org/sites/default/files/agenda.pdf\\_](https://theactionalliance.org/sites/default/files/agenda.pdf_)

of telehealth approaches employed during the COVID-19 pandemic?

### Optimal Systolic Blood Pressure Target in Older Adults

Hypertension, defined as abnormally high arterial blood pressure, is very common and a modifiable risk factor for cardiovascular disease. Hypertension affects 65 percent of adults over 60 years of age, and 76.5 percent of adults over 80 years of age in the United States.<sup>38</sup> Two-thirds of elderly adults with hypertension have multiple comorbidities such as diabetes, heart failure, and/or history of stroke.<sup>39</sup>

Clinical practice guidelines<sup>40,41,42</sup> and systematic reviews<sup>43,44</sup> have identified many important unanswered questions related to the treatment of hypertension in older individuals, including those with comorbidities, living in long-term-care facilities, or of different racial and ethnic backgrounds. For example, what are the comparative benefits and/or harms for different systolic blood pressure targets in older adults with hypertension and frailty, diabetes, kidney disease, or dementia on outcomes such as cardiovascular and other adverse events, and cognitive impairment?

### Project Budget and Duration

Applicants may request up to \$2 million in total direct costs for the initial feasibility phase and up to \$20 million for carrying out the full-scale trial. The feasibility phase should be completed no later than 18 months after contract initiation, and the subsequent phase involving full-scale study conduct should not exceed five years (excluding PCORI peer review). 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. (Please refer to the [Submission Instructions](#) for further details.)

In general, PCORI will not cover costs for interventions that are being compared in the proposed study. (See Appendix 2: Allowable and Unallowable Costs in the [Submission Instructions](#) for details.) 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,

<sup>38</sup> Mozaffarian D, Benjamin EJ, Go AS, et al. Heart disease and stroke statistics--2015 update: a report from the American Heart Association [published correction appears in *Circulation*. 2015 Jun 16;131(24):e535] [published correction appears in *Circulation*. February 23, 2016;133(8):e417]. *Circulation*. 2015;131(4):e29-e322.

<sup>39</sup> Bisognano JD, Townsend KA, Skyles AJ, Samuels KM. Prevalence of comorbidities and their influence on blood pressure goal attainment in geriatric patients. *Am J Geriatr Cardiol*. 2007;16(1):24-29.

<sup>40</sup> Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APHA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines [published correction appears in *Hypertension*. June 2018;71(6):e140-e144]. *Hypertension*. 2018;71(6):e13-e115.

<sup>41</sup> Hypertension in adults: diagnosis and management NICE guideline [NG136] Published date: August 28, 2019

<sup>42</sup> Williams B, Mancia G, Spiering W, et al. 2018 ESC/ESH Guidelines for the management of arterial hypertension: The Task Force for the management of arterial hypertension of the European Society of Cardiology and the European Society of Hypertension: The Task Force for the management of arterial hypertension of the European Society of Cardiology and the European Society of Hypertension [published correction appears in *J Hypertens*. January 2019;37(1):226]. *J Hypertens*. 2018;36(10):1953-2041.

<sup>43</sup> Garrison SR, Kolber MR, Korownyk CS, McCracken RK, Heran BS, Allan GM. Blood pressure targets for hypertension in older adults. *Cochrane Database of Systematic Reviews* 2017, Issue 8. Art. No.: CD011575

<sup>44</sup> Kirk JK, Allsbrook J, Hansell M, Mann EM. A systematic review of hypertension outcomes and treatment strategies in older adults. *Arch Gerontol Geriatr*. 2017;73:160-168.

subcontractor indirect costs are not factored when determining adherence to the PFA's direct-cost cap. .

A contract is the funding mechanism for this program. A milestones and deliverables schedule, as well as specified recruitment targets, should be linked directly to and included in the proposed budget that will be subject to negotiation at the time of award. Activities captured in milestones include, but are not limited to, the following:

- Developing a study protocol and procedure manual for the intervention
- Assigning roles and responsibilities to study team members for project implementation
- Forming a SAC or other appropriate engagement body
- Providing a detailed task-based budget with level of effort for project staff, specified by task
- Obtaining clearances from all institutional and community partners, including Institutional Review Board (IRB) approvals
- Establishing a DSMB or providing a clear description of why one is unnecessary
- Executing all subcontractor agreements
- Agreeing on eligible patient populations for study recruitment
- Identifying barriers to patient recruitment in 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 throughout both study phases. As previously stated, to receive continuous funding support for the second phase of full-scale trial operations, awardees must provide evidence of adequate progress and achievements during the feasibility phase. Starting approximately six months before the planned conclusion of the feasibility phase, PCORI and an EAP will begin to examine information from the awardee to assess the full-scale study's viability and sustainability. Only studies that are deemed satisfactory in this assessment will receive continuous funding support.

## 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:

- Assesses the benefits and harms of preventive, diagnostic, therapeutic, palliative, and health information communication or dissemination strategies, 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 (including survival, functioning, symptoms, and health-related

quality of life)

- Investigators are encouraged to design their research using validated outcome measures such as the measures 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

### Research Priorities

To be considered responsive, applications must:

- Describe information from patients and other stakeholders about how the study is answering a critical question. Explain the pertinent evidence gaps and why the project questions represent decisional dilemmas for patients, caregivers, clinicians, policy makers, and other healthcare system stakeholders. 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 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 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:

- Observational studies without randomization
- 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,<sup>45</sup> PCORI does not fund research whose findings will include:

- 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

### Studies of Cost-Effectiveness

PCORI will consider an application nonresponsive if the proposed research:

- 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

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 care costs. For further information, please reference our [cost-effectiveness analysis FAQs](#).

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

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<sup>45</sup> Available at [http://www.pcori.org/sites/default/files/PCORI\\_Authorizing\\_Legislation.pdf/](http://www.pcori.org/sites/default/files/PCORI_Authorizing_Legislation.pdf/).

- Evaluate interventions to reduce health system waste or increase health system efficiency

### Coverage of Intervention Costs

In general, PCORI will not cover 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”).

### Avoiding Redundancy

PCORI encourages potential applicants to review published research and listings of ongoing funded research at [pcori.org](http://pcori.org) and at [clinicaltrials.gov](http://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 trials developed by other organizations—in the application for PCORI funding. An additional resource for applicants using pragmatic design features is PCORI’s [Guidance on the Design and Conduct of Trials in Real-World Settings](#).

### Leveraging Existing Resources, Including PCORnet

PCORI encourages applicants to consider the potential merits of using the clinical research infrastructure and data resources of PCORnet, the National Patient Centered Clinical Research Network. PCORnet is designed to improve the nation’s capacity to conduct efficient large-scale clinical research, by drawing upon 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 (CRNs), representing more than 100 health systems, two health plan research networks (HPRNs), a coordinating center, and a central office. PCORnet can be 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:

- 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 (affecting fewer than 200,000 in the US [i.e., less than 1 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 partners who leverage their lived experience and/or professional expertise to influence research to be more patient centered, relevant, and useful. Engagement approaches and practices vary from project to project based on the patient population, the setting, and the needs of a study. PCORI encourages study teams to be creative in their methods for engaging with research partners. Effective involvement of patients and other stakeholders requires a well-thought-out engagement plan that includes the goals for engagement and information on who will be involved, what preparation will be provided, the points and intensity of involvement, and the decision-making process. Engagement extended to study participants, including clinicians and healthcare providers, may prove particularly valuable if sought during the feasibility phase of proposed PLACER trials.

### **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 discuss 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 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.

- 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
- Patients with low health literacy, 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](#),<sup>46</sup> which is 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 that applicants comply with sections of that 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 provided in the [PCORI Policy on Data and Safety Monitoring Plans for PCORI-Funded Research](#).<sup>47</sup>

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<sup>46</sup> See <http://grants.nih.gov/sites/default/files/supplementalinstructions.docx>.

<sup>47</sup> See <http://www.pcori.org/sites/default/files/PCORI-Policy-Data-Safety-Monitoring-Plans.pdf>.

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 Protections](#)<sup>48</sup>). 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 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](#).<sup>49</sup>

## **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, phased randomized trial 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 the portfolio with certain characteristics, including disease category, topics, priority population, methodologies, and other variables

**IMPORTANT NOTE:** For potential applicants to this PFA, an LOI may be submitted without including a DCC—with the proviso that applicants invited to submit a full application must include a DCC as part of their submission.

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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<sup>48</sup> See <http://www.pcori.org/sites/default/files/PCORI-Checklist-for-Evaluating-Human-Subjects-Protections.pdf/>.

<sup>49</sup> See <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-08-054.html>.

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 application by PCORI staff; the 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 (e.g., nonresponsiveness, such as failure to include a DCC). 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.

The table below is designed to help applicants understand how the PCORI merit review criteria align with criteria from other funding organizations with which applicants might be familiar (e.g., NIH). Although PCORI's criteria do map to most NIH criteria, there are areas where we ask for different information reflecting PCORI's unique approach (e.g., PCORI does not include a criterion that tracks to NIH's innovation criterion but does include criteria evaluating patient-centeredness and engagement).

Crosswalk of PCORI Merit Review Criteria with NIH Criteria	
SIGNIFICANCE	<ol style="list-style-type: none"> <li>1. Potential for the study to fill critical gaps in evidence</li> <li>2. Potential for the study findings to be adopted into clinical practice and improve delivery of care</li> </ol>
APPROACH	<ol style="list-style-type: none"> <li>3. Scientific merit (research design, analysis, and outcomes)</li> <li>4. Investigator(s) and environment</li> </ol>
PCORI-only Merit Review Criteria	
PATIENT-CENTEREDNESS/ENGAGEMENT	<ol style="list-style-type: none"> <li>5. Patient-centeredness</li> <li>6. Patient and stakeholder engagement</li> </ol>

Below are PCORI’s merit review criteria for PLACER 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.

- Is this an important research question for which the answers will help decision makers (e.g., patients, clinicians, health systems, payers, policy makers)? 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 the demonstrated evidence gaps?
- Does the importance of the research question justify the scope and magnitude of the proposed study?
- 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?
- Has the applicant identified potential barriers to intervention adoption and strategies to address such barriers?
- Has the applicant identified 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, 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 are they well justified? What is 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 (e.g., cluster randomized design, RCT) as well as the specific research question? Is the anticipated effect size adequately justified?
- Is the overall study plan for both phases well justified and coherent? Are the project timeline and milestones realistic?

For the proposed DCC:

- Are appropriate plans in place for DCC involvement in development of the final trial design and protocol, the study power and analytical approach, the statistical analysis plan, and the conduct of all proposed analyses?
- Are there adequate plans for data collection/reporting and its quality monitoring for errors, omissions, and completeness?
- Is there a well-justified plan for managing the functions of the DSMB?

For the feasibility phase:

- How likely will the major activities to be accomplished in the feasibility phase prepare for the successful execution of the full-scale trial?
- Is the scope and duration of the feasibility phase appropriate and realistic for what is proposed?
- Does the application adequately plan a defensible and realistic estimate of enrollment considering the available eligible population, acceptance of randomization by providers and participants, burden(s) of participation, attrition, and other factors influencing study entry?
- Is contingency planning adequate for potential obstacles or challenges?

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

This criterion should assess 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. It should not be an assessment of the institution’s reputation, but rather of 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? Is there evidence of sufficient clinical, statistical, and study management expertise?
  - If the project is collaborative or dual-PI, do the investigators have complementary and integrated expertise? If the leader of the DCC is not designated a dual-PI, does the application provide strong justification why this arrangement is not needed?
- Does the investigative team have adequate experience in conducting projects of a similar size, scope, and complexity, including phased studies?
- Are the leadership, governance, and organizational structures adequate for the scope of the project? 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 (including the DCC) appropriate for the proposed research?

For the proposed DCC:

- Are the experience and capabilities of the DCC and the DCC leadership appropriate to the proposed study?
- Does the application clearly describe the DCC’s role and functions?
- Does the application reference the prime institution’s policies and practices to ensure DCC independence and compliance with all applicable data management and security requirements?

#### Criterion 5. Patient-centeredness

The application should demonstrate that the study focuses on improving patient-centered outcomes and employs a patient-centered research design (i.e., 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?
- Do the comparators represent challenging choices that patients confront?
- What evidence is presented or planned to assess patients’ willingness to accept the proposed comparators considering their 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, and training institutions) in the conduct of the study. Quality of engagement should 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, 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 from the list above, to ensure diverse perspectives throughout the research process?
- Are planned engagement activities 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 there clear descriptions of the roles and contributions of all study collaborators in decision making?

#### **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 July 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-XXXXX). Clinical trials must be registered before enrollment of the first patient. All trials that meet the definition on the [NIH database](#)<sup>50</sup> (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](#).<sup>51</sup> Funded patient registries must be

<sup>50</sup> Available at <https://prsinfo.clinicaltrials.gov/>.

<sup>51</sup> Available at <http://www.crd.york.ac.uk/prospéro/>.

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](#)<sup>52</sup> 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](#).<sup>53</sup>

### 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, 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.

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<sup>52</sup> Available at <http://www.hhs.gov/ocr/>.

<sup>53</sup> Available at <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-03-025.html>.

## 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](#).<sup>54</sup>

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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<sup>54</sup> See <http://www.pcori.org/sites/default/files/PCORI-Peer-Review-and-Release-of-Findings-Process.pdf>.