



PATIENT-CENTERED OUTCOMES RESEARCH INSTITUTE

## Reviewer Manual

**Funding Program:**      **Addressing Disparities**

**Review Cycle:**          **Cycle 1, 2017**

**Relevant Dates:**

- **June 9<sup>th</sup>, 2017:** One complete written critique (for one application) is due in PCORI Online.
- **July 7<sup>th</sup>, 2017:** Written critiques and scores for all assigned applications are due in PCORI Online.
- **August 7<sup>th</sup> – 8<sup>th</sup> Washington DC metro area:** In-person Merit Review Panel Meeting
- **November 2017:** Funding decisions are announced.

## Table of Contents

Chapter 1. Setting the Stage .....	4
PCORI's Mission and Strategic Goals .....	4
Comparative Clinical Effectiveness Research .....	4
Effectiveness versus Efficacy.....	5
Evidence Gap.....	5
Usual Care .....	6
Dissemination Goals.....	6
Categories of Research PCORI Does Not Fund.....	6
Overview of PCORI's Merit Review Cycle .....	8
Chapter 2. Broad PFA National Priority: Addressing Disparities.....	9
Addressing Disparities Priority Areas.....	10
Knowledge Check.....	10
Methodology Standards.....	11
Application Responsiveness.....	11
Chapter 3. Merit Review Overview.....	12
Merit Review Goals.....	12
Preliminary Review Overview .....	12
Reviewers as Readers .....	12
Merit Review Criteria .....	13
Understanding Patient-Centeredness vs. Patient Engagement.....	17
Human Subjects Protections.....	19
Evaluating Resubmissions.....	20
Evaluating Budgets.....	21
Chapter 4. Writing Critiques .....	22
Overview .....	22
Offline Critique Template .....	22
Guidelines for Writing Strengths and Weaknesses.....	22
Major and Minor Strengths and Weaknesses.....	23
Examples: Writing Strengths.....	24
Examples: Writing Weaknesses .....	25
Merit Review Scores .....	26



Knowledge Check .....	27
Writing an Overall Narrative .....	29
Assigning an Overall Score .....	30
Revising and Resubmitting a Critique .....	30
Chapter 5. In-person Panel Meeting.....	31
Overview .....	31
Preparing for the In-Person Panel Review .....	31
Panel and Reviewer Roles.....	32
Inside the In-Person Panel Review.....	33
Preparing In-Person Panel Presentations .....	33
Panel Review Discussion Tips.....	33
Appendix 1. COI/Expertise .....	36
Appendix 2. Methodology Standards .....	41
Appendix 3. Engagement Rubric.....	54
Appendix 4. Human Subjects Checklist.....	59



## Chapter 1. Setting the Stage

---

### PCORI's Mission and Strategic Goals

PCORI helps people make informed healthcare decisions, and improves healthcare delivery and outcomes, by producing and promoting high-integrity, evidence-based information that comes from research guided by patients, caregivers, and the broader healthcare community.

#### **PCORI's Strategic Goals:**

- *Increase quantity, quality, and timeliness of useful, trustworthy research information available to support health decisions*
- *Speed the implementation and use of patient-centered outcomes research evidence*
- *Influence research funded by others to be more patient-centered*

PCORI seeks to fund studies that will produce information that allows patients to weigh the benefits and risks of clinical alternatives. This will ensure that people receive care according to their needs and have the opportunity to achieve the best possible health outcomes.

### Comparative Clinical Effectiveness Research

Per its authorizing legislation, PCORI funds research that supports comparative clinical effectiveness research (CER)—comparing health outcomes and the clinical effectiveness, risks, and benefits of two or more approaches to healthcare.

For example: Which option works better to improve patient outcomes for low back pain—medication management or surgery?

#### ***CER research answers patient-centered questions, such as:***

- Given my personal characteristics, conditions, and preferences, what should I expect will happen to me?
- What are my options, and what are the potential benefits and harms of those options?
- What can I do to improve outcomes that are most important to me?
- How can clinicians and the care delivery systems they work in help me make the best decisions about my health and health care?



## Effectiveness versus Efficacy

PCORI is interested in **Comparative Effectiveness Research**—not studies on efficacy.

- *Effectiveness is the extent to which an intervention does more good than harm across a broad mix of patients in a range of clinical settings.*

PCORI seeks to fund studies that compare different treatment options in real-world environments. These real-world environments are more likely to include different medical care settings and patient characteristics. Comparative effectiveness research includes studies where two readily available treatments or interventions are compared with one another, rather than with a placebo or no treatment. These types of studies require a much broader patient population to be able to account for differences among patients and settings, and for the smaller differences researchers are likely to find when comparing two or more active treatments. Effectiveness trials should include comorbidities, variable adherence rates, and the presence of other medication.

- *In contrast, efficacy is the extent to which an intervention does more good than harm in ideal patients under ideal circumstances.*

Efficacy studies show results in an ideal, controlled setting, typically compared to placebo or no active treatment. PCORI is not interested in funding efficacy research because the results from efficacy trials have limited generalizability beyond the trial settings and conditions. Challenges associated with the everyday care of patients and the healthcare choices they make tend to affect how well the treatments perform under real-world conditions.

## Evidence Gap

The applicant should support the importance of the research topic or question by demonstrating an *evidence gap*.

**Evidence gap** – an area of missing information that would help patients and other stakeholders make better decisions about health care. Evidence gaps are usually identified through systematic research reviews that demonstrate unclear or incomplete guidelines. Another way a principal investigator may indicate that their proposed research addresses an evidence gap is by documenting that their topic is a high priority as recommended by research, clinical, and/or stakeholder (i.e., decision-maker) groups (such as the Institute of Medicine or Agency for Healthcare Research and Quality), including specific recommendations for CER.

## Usual Care

PCORI funds research that compares at least two alternative treatments or interventions, both of which must be available in the real world. Sometimes one of these approaches is labeled “usual care.” If the researchers are proposing “usual care” they should first justify that choice as the best comparison for the particular condition or intervention. Further, usual care needs to be carefully described and measured in the study, and be a realistic choice faced by patients and other stakeholders. The clinical characteristics of usual care must be specified, and applicants must provide a persuasive reason for using it a comparator.

## Dissemination Goals

Dissemination and implementation refer to the processes of enhancing the awareness of new research evidence, and speeding the integration of this evidence into practice.

PCORI is interested in robust research findings that can be rapidly disseminated and implemented in clinical and community practice, thus facilitating improvements in healthcare decision making for patients and other stakeholders.

Applicants should describe the potential of research results for dissemination and implementation. We encourage applicants to think creatively about how to disseminate findings.

Traditional dissemination, through research articles or scientific presentations, are unlikely to reach the range of stakeholders who are faced with making clinical decisions.

## Categories of Research PCORI Does Not Fund

### Cost-Effectiveness Analysis (CEA)

CEA examines both the costs and health outcomes of alternative intervention strategies, and the results typically are presented in the form of costs per particular health outcomes or life years saved, etc.

Per its founding legislation, PCORI does not fund studies that:

- Include formal cost-effectiveness analysis (CEA) or
- Directly compare the costs of care between two or more alternative approaches to providing care.

Any applications that propose to conduct CEA are deemed nonresponsive and are not reviewed.



*Please alert your Merit Review Officer if you encounter cost-effectiveness analysis in your application review.*

PCORI does have an interest in studies that address questions about conditions that lead to high costs to the individual or to society. This includes studies that:

- Examine the effect of costs on patients, such as out-of-pocket costs, hardship or lost opportunity, or costs as a determinant of or barrier to access to care.
- Address cost-related issues, such as the resources needed to replicate or disseminate a successful intervention.
- Evaluate interventions to reduce health system waste or increase health system efficiency.

### Development of Decision Aids

Decision aids are tools that are meant to help patients and their caregivers facing complex decisions. Aids do not replace providers, but function to support a team approach to decision-making between the patients and their healthcare providers. These tools help prepare the patient for consultations with their providers by increasing the patient's health literacy. The tools also help clinicians limit decision conflict.

Examples of decision aids could include:

- Brochures
- Audiovisual materials
- Educational sessions
- Websites
- Counseling sessions
- Computer programs

PCORI is not currently interested in funding the development or testing of decision aids. If the application describes how their research could be used in decision making or later guideline development, however, that is acceptable.

### Other Categories of Research PCORI Does Not Fund

PCORI does not fund research whose findings will include:

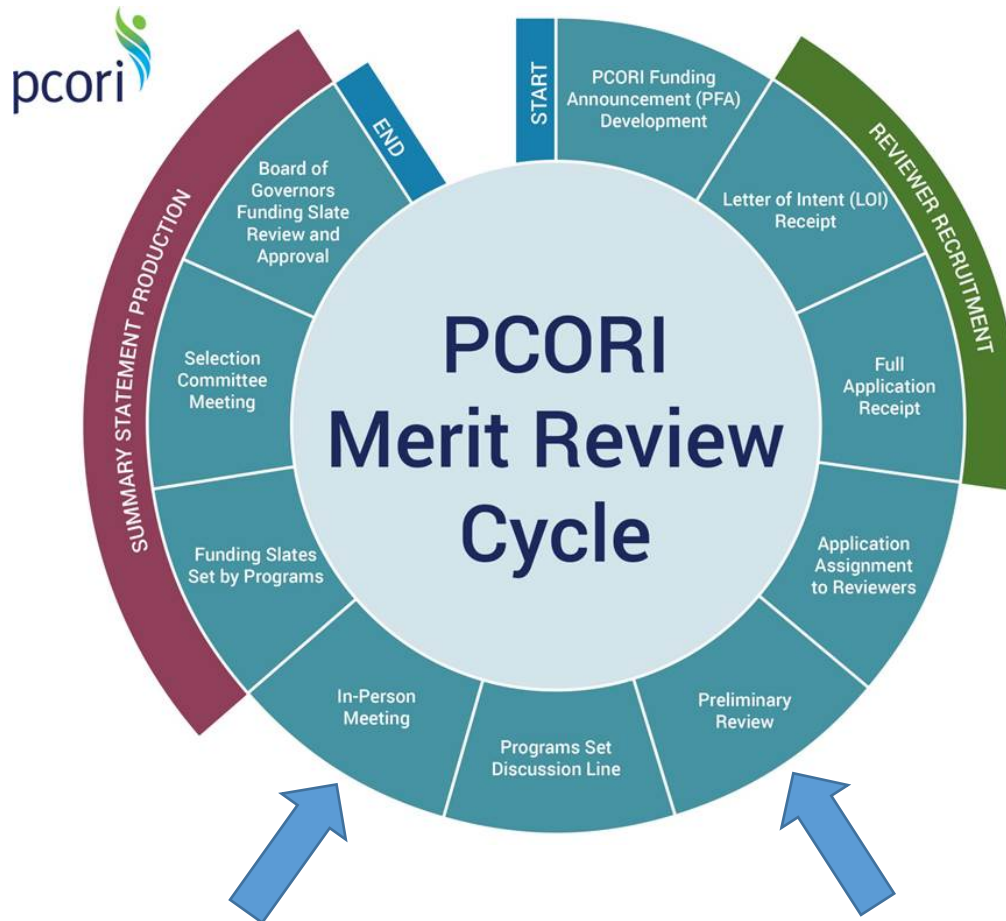
- Creation of clinical practice guidelines or instruments to measure outcomes
- Insurance coverage recommendations
- Payment or policy recommendations
- Establishing efficacy for a new clinical strategy or in a tightly controlled environment
- Pharmacodynamics (studies that focus purely on the effects of drugs and the mechanism of their action)
- Study of the natural history of disease or comparison of patient characteristics rather than treatment strategies
- Fundamental science or study of biological mechanisms, or how medications work in the body



*Please alert your Merit Review Officer if you encounter these topics as aims in the applications you review.*

## Overview of PCORI's Merit Review Cycle

PCORI Merit Reviewers play an important role in helping PCORI to fund the highest quality research with the strongest potential to improve patient outcomes. Reviewers participate in two phases of the merit review cycle: Preliminary Review and the In-Person Meeting. This manual will go into more detail about each of these phases.





## Chapter 2. Broad PFA National Priority: Addressing Disparities

---

PCORI informs the research community of opportunities to apply for research contracts via PCORI Funding Announcements (PFAs). Reading your assigned PFA will help provide context for the applications that you review.

The Addressing Disparities (AD) PFA seeks applications for clinical comparative effectiveness research designed to evaluate and compare interventions intended to reduce or eliminate disparities in health and health care. Applications must compare evidence-based interventions to improve health outcomes and reduce disparities for target populations. Studies should focus on overcoming barriers that may disproportionately affect health outcomes or focus on identifying best practices for reducing disparities in target populations (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 and/or limited English proficiency; and lesbian, gay, bisexual, and transgender (LGBT) persons).

Through the Addressing Disparities PFA, PCORI seeks to fund research that:

- Compares evidence-based interventions to reduce or eliminate disparities in patient-centered outcomes (PCOs), including health, health care, and patient-reported outcomes
  - For example, by accounting for possible differences at the patient, provider, or systems level, the research determines which interventions can be most effective for eliminating disparities in outcomes
- Compares benefits and risks of treatment, diagnostic, prevention, or service options, with a focus on eliminating disparities
- Compares and identifies best practices for tailoring evidence-based interventions to patient populations at risk for disparities

Research applications submitted to the AD program must focus on one or more of these target populations:

- 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 and/or limited English proficiency
- Lesbian, gay, bisexual and transgender (LGBT) persons

[Please click here to access the Addressing Disparities funding announcement.](#)

## Addressing Disparities Priority Areas

The AD Program is interested in funding comparative effectiveness studies that focus on:

- Interventions to address disparities in human immunodeficiency virus (HIV) prevention and treatment
- Interventions to reduce sleep disorder disparities among racial and ethnic minorities
- Pharmacologic and non-pharmacologic treatments for Alzheimer's disease and other forms of dementia
- Interventions to improve communication between clinicians and people with disabilities

## Knowledge Check

Instructions: After reading over your PFA, select the correct answer.

*Which research question would NOT be funded under the Addressing Disparities PFA?*

- A. Does intervention A work better than intervention B to improve clinician communication with LGBT patients regarding health questions they care about?*
- B. How does the staffing at top-performing hospitals serving inner-city ethnic minorities compare to those at lower-performing hospitals serving similar populations? Do these differences lead to better patient-centered and clinical outcomes?*
- C. Do ethnic minorities with limited English proficiency experience disparities in patient-centered outcomes relative to those who speak English fluently?*
- D. Which of three interventions works best to enhance social support for rural lung cancer patients?*

**Answer: The correct answer is C.** This research question focuses on describing disparities rather than identifying the best method to reduce existing disparities, and focuses on patient characteristics rather than clinical strategies.

The AD program is not interested in:

- Instrument development
- Studies that develop, test, and validate new decision aids/tools or clinical prognostication tools
- Pilot studies intended to inform larger efforts
- Comparisons of patient characteristics rather than clinical strategy options

## Methodology Standards

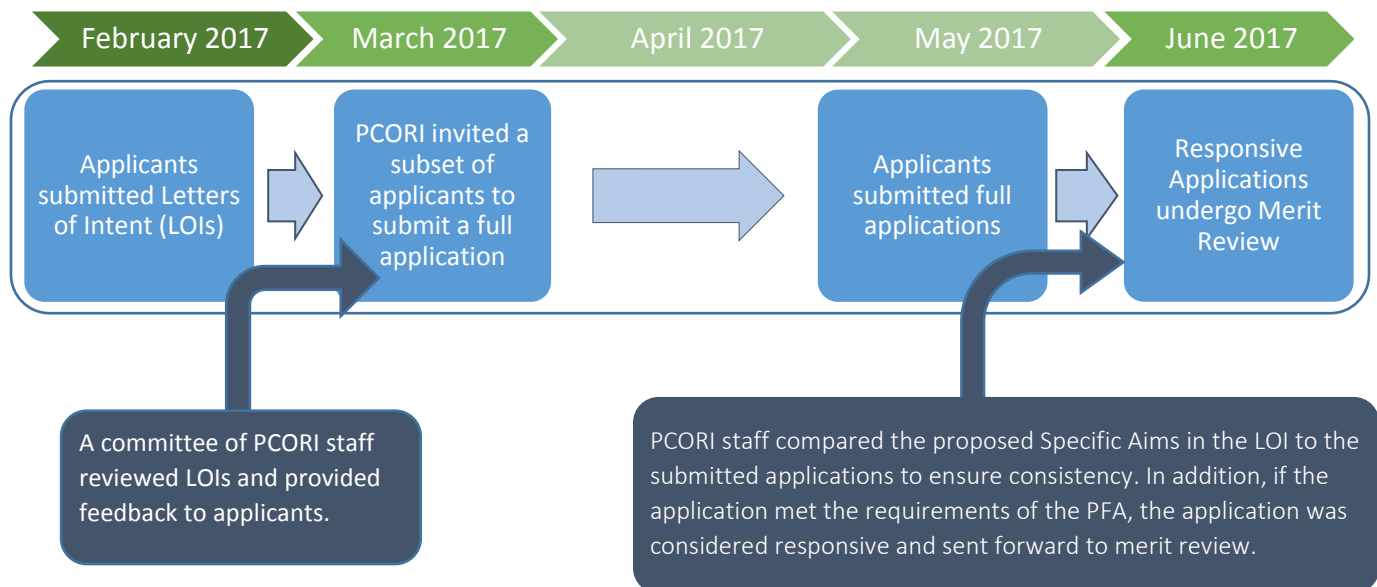
Your PFA includes a section on Methodological Considerations. The PCORI Methodology Committee was tasked with setting standards that describe scientifically sound methods to be used by all PCORI awardees, which resulted in the PCORI Methodology Standards. Please see Appendix 2 for more information on Methodology Standards.

Why do methods matter to PCORI?

- Rigorous methods ensure that studies produce trustworthy information that can be used to improve healthcare outcomes.
- Methods describe how researchers collect data, administer interventions, and analyze results.

## Application Responsiveness

The figure below describes the process by which applications are reviewed by PCORI Merit Review and Science Program Staff to ensure that the applications are responsive to the PFA. The applications that you have been assigned to review have been judged to be programmatically responsive and ready for your review.



## Chapter 3. Merit Review Overview

---

### Merit Review Goals

PCORI's Merit Review process is designed to support the following goals:

- To identify applications that have the strongest potential to help patients, caregivers, clinicians and other stakeholders make informed decisions to improve patient outcomes;
- To implement a transparent, fair, objective, and consistent process to identify these applications;
- To elicit high-quality feedback that reflects a diversity of perspectives to ensure that the research funded by PCORI reflects the interests and views of patients and those who care for them and that it meets the criteria for scientific rigor;
- To fund projects that fill important evidence gaps and have strong implementation potential;
- To regularly evaluate and continually improve the merit review process and policies in support of PCORI's mission.

### Preliminary Review Overview

All reviewers should begin the Preliminary Review by reading the full PCORI Funding Announcement (PFA) for the applications they are reviewing, to make sure they understand PCORI's programmatic and organizational goals. They then carefully evaluate their assigned applications according to PCORI's Merit Review criteria.

For each of their assigned applications, reviewers will:

- Write a critique highlighting the application's strengths and weaknesses
- Assign scores for each of the criteria that align with their written critiques
- Write a summary evaluating the application as a whole
- Provide an overall score for the application



Returning reviewers should bear in mind that PFAs are revised often, so they should thoroughly read the PFA for the applications they are reviewing.

### Reviewers as Readers

In addition to writing a critique for each assigned application, each reviewer will serve as a Reader and be asked to pay especially close attention to a small subset of the applications to be discussed at the in-person panel meeting. As a Reader, you do not need to provide any written comments. Instead, we ask that you raise key application strengths and weaknesses during panel discussion. Your merit review officer will provide further guidance.

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>

In your critique, evaluate the application's adherence to the themes indicated by the bulleted questions under each of the criteria described below.

### Criterion 1. Potential for the study to fill critical gaps in evidence

The proposal addresses the following questions:

- Does the application convincingly describe the clinical burden?
  - Does the application identify a critical gap in current knowledge as noted in systematic reviews, guideline development efforts, or previous research prioritizations?
  - Does the application identify a critical gap in current knowledge, evidenced by inconsistency in clinical practice and decision making?
  - Would research findings from the study have the potential to fill these evidence gaps?
- The key considerations are whether or not the applicants make the case that the question they are addressing is one that is of interest to stakeholders in the real world. Is there a gap in the available research evidence that needs to be filled?

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

The application should describe how evidence that is generated from this study could be adopted into clinical practice and delivery of care by others. The application should address the following questions:

- Does the application identify who will make the decision (i.e., the decision maker) or use (i.e., the end-user) the study findings (not the intervention) this study produces, such as local and national stakeholders?
- Does the application identify potential end-users of study findings—such as local and national stakeholders—and describe strategies to engage these end-users?
- Does the application provide information that supports a demand for this kind of a study from end-users?
- Would this study's research findings have the potential to inform decision making for key stakeholders? If so, provide an example. How likely is it that positive findings could be

reproduced by others, resulting in improvements in practice and patient outcomes? Identify the potential barriers that could hinder adoption of the intervention by others.

- Does the application describe a plan for how study findings will be disseminated beyond publication in peer-review journals and at national conferences?

➤ When reviewing your applications for dissemination potential, remember that applicants:

- are asked to describe the potential for dissemination and implementation of their research findings, but
- are not expected to disseminate and implement findings during the research period covered by PCORI funding.

*For research that produces important findings, subsequent applications to support dissemination and implementation efforts may be submitted for consideration for funding under separate funding announcements.*

### 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 conceptual framework anchored in background literature which informs the design, key variables, and relationship between interventions and outcomes being tested?
  - Does the Research Plan describe rigorous methods that demonstrate adherence to PCORI Methodology Standards?
  - Is the overall study design justified?
  - Are the patient population and study setting appropriate for the proposed research question?
  - Does the application provide justification that the outcome measures are validated and appropriate for the population?
  - Are each of the comparators (e.g., active intervention arm and comparator arm) described clearly and well-justified? 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 appropriate? Is the study design (e.g., cluster randomized design, randomized controlled trial, or observational study) accounted for and is the anticipated effect size adequately justified?
  - Is the study plan feasible? Is the project timeline realistic, including specific scientific and engagement milestones? Is the strategy for recruiting participants feasible? Are assumptions about participant attrition realistic, and are plans to address patient or site attrition adequate?
- Address each set of bulleted questions, taking special care to consider whether weaknesses are easily fixable, and whether the research design adequately addresses the study aims.

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

This criterion should assess the appropriateness (e.g., qualifications and experience) of the investigator(s)/team and the environment's capacity (e.g., resources, facilities, and equipment) to support the proposed project. It should not be an assessment of the institution's quality. The application should also address the following questions:

- How well-qualified are the PIs, collaborators, and other researchers to conduct the proposed activities? Is there evidence of sufficient clinical or statistical expertise (if applicable)?
- Does the investigator or co-investigator have demonstrated experience conducting projects of a similar size, scope, and complexity?
- If the project is collaborative or dual-PI, do the investigators have complementary and integrated expertise? Are the leadership, governance, and organizational structures appropriate for the project?
  - (Dual-PI Option Only) Does the Leadership Plan adequately describe and justify PI roles and areas of responsibility?
- Is the level of effort for each team member appropriate for successfully conducting the proposed work?
- Does the application describe adequate availability of and access to facilities and resources (including patient populations, samples, and collaborative arrangements) to carry out the proposed research?
- Is the institutional support appropriate for the proposed research?



Applications with dual principal investigators will submit a leadership plan in the People and Places section of the application. If you are assigned a dual-PI application, evaluate the leadership plan under Criterion 4.

#### 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 information.)* The proposal should also address the following questions:

- Does the application include a thorough description about which outcomes (both benefits and harms) are important to patients, and are those outcomes included in the study plan?
  - Does the application provide information that indicates that closing the evidence gap is important to patients and other stakeholders?
  - Are the interventions being compared in the study available to patients now, and are they the best options for comparison (including whether they would be chosen by patients and their healthcare providers for managing the condition being studied)?
- Please note that the measurement of patient-reported outcomes does not necessarily equate to “patient-centered”. Please also note that the project can be patient-centered even if the outcomes are not patient-reported, or if the interventions are not delivered directly to patients. “Patient-centered” means that the outcomes are considered important by a target population, as related by members of the target population. For instance, an application may compare different lengths of time providers have to spend with patients in two clinic structures. The outcomes could include

provider visit time and provider satisfaction. However, the research question may stem from patient complaints that they do not have enough time to talk to their providers during visits. Thus, the application might still be patient-centered.

#### 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, hospitals and health systems, 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:

- Does the application provide a well-justified description of how the research team incorporates stakeholder involvement? Does the study include the right individuals (e.g., researchers, patients, caregivers, clinicians, policy makers, and other healthcare system stakeholders) to ensure that the projects will be carried out successfully?
- Does the application show evidence of active engagement among scientists, patients, and other stakeholders throughout the research process (e.g., formulating questions, identifying outcomes, monitoring the study, disseminating, and implementing)? Is the frequency and level of patient and stakeholder involvement sufficient to support the study goals?
- Is the proposed Engagement Plan appropriate and tailored to the study?
- Are the roles and the decision-making authority of all study partners described clearly?
- Are the organizational structure and resources appropriate to engage patients and stakeholders throughout the project?



## Understanding Patient-Centeredness vs. Patient Engagement

When evaluating Criteria 5 and 6, it is important to distinguish between patient-centeredness and patient and stakeholder engagement.

- ***“Patient-centeredness” means:***
  - *The project aims to answer questions or examine outcomes that matter to patients within the context of patient preferences.*
  - *The application employs a patient-centered research design – one that is informed or endorsed by patients.*
  - *Research questions and outcomes should reflect what is important to patients and caregivers.*

Patient-centered research should strive to answer the following questions patients frequently ask when making health decisions:

1. “Given my personal characteristics, conditions, and preferences, what should I expect will happen to me?”
2. “What are my options, and what are the potential benefits and harms of those options?”
3. “What can I do to improve the outcomes that are most important to me?”
4. “How can clinicians and the care delivery systems they work in help me make the best decisions about my health and health care?”



A study can be patient-centered even if the end-user is not the patient, as long as patients will benefit from its information.

- ***“Patient and stakeholder engagement” means:***
  - *Patients are partners in research, not just “subjects” or tokens without active collaborative roles.*
  - *Active and meaningful engagement between scientists, patients, and other healthcare stakeholders.*
  - *Community, patient, and caregiver involvement already in existence or a well-conceived plan.*

*Patient-centeredness focuses on the importance of the research questions and outcomes to patients, while patient and stakeholder engagement focuses on how patients and other stakeholders are involved in the research, from design to implementation and dissemination.*

## Where to find good examples of Patient and Stakeholder Engagement

To help explain what the phrase “engagement in research” means, PCORI worked with its Advisory Panel on Patient Engagement to develop the [Engagement Rubric](#). The rubric was created using promising engagement practices from previous funding cycles, and is meant to be a tool for applicants to formulate their Engagement Plans, *not as a scoring rubric for reviewers to evaluate applications*. Reviewers should not expect all applications to match the illustrated examples in the rubric.

## About the Rubric

- Provides some real examples from PCORI-funded projects of options—not strict guidelines—for incorporating engagement into the research process
- Is not intended to be prescriptive and comprehensive

## Elements of the Rubric

- **Planning the Study:** How might patients be involved in formulating the research question to be studied or in designing various elements of the study? Potential activities include:
  - Developing the research question and relevant outcomes to be studied, to ensure that the project and its results will be useful and important to patient and stakeholder communities.
  - Defining the characteristics of study participants, to minimize the risk that certain patients will be included or excluded due to criteria that are not relevant.
  - Designing the study to minimize disruption to patient and stakeholder study participants, thereby promote retention of study participants.
- **Conducting the Study:** What are the ways patients and other stakeholders could participate in and monitor the conduct of the project? Potential activities include:
  - Drafting or revising study materials and protocols, to ensure feasibility for clinicians and patient participants.
  - Participating in recruitment of study participants, to increase and sustain recruitment and ensure viability of the study.
  - Participating in data collection and data analysis, to lend unique and varied perspectives on interpretation of the data.
  - Participating in the evaluation of patient and stakeholder engagement, to ensure authenticity and value of engagement.
  - Serving as a patient representative on a data safety monitoring board, to make the DSMB composition more robust and patient-centered.
- **Disseminating the Study Results:** How might patients and other stakeholders help plan for and participate in dissemination? Potential activities include:
  - Identifying partner organizations for dissemination, to ensure meaningful and direct connections with end-users.
  - Planning dissemination efforts, shaping study design and protocol from the very beginning to be focused on the final product.
  - Participating in dissemination efforts, such as authoring manuscripts and presenting study findings, to offer the patient and stakeholder perspective and to reach new and different audiences.



- Identifying opportunities to present or share information about the study, even as it is in progress, to move away from traditional models of dissemination and think more creatively about how to get information into the hands of those who need it.

The rubric also defines the six PCOR Engagement Principles: *reciprocal relationships, co-learning, partnership, trust, transparency, and honesty*.

- **Reciprocal Relationships:** This principle is demonstrated when the roles and decision-making authority of all research partners, including the patient and other stakeholder partners, are defined collaboratively and clearly stated.
- **Co-Learning:** This principle is demonstrated when the goal is not to turn patients or other stakeholder partners into researchers, but to help them understand the research process; likewise, the research team will learn about patient-centeredness and patient/other stakeholder engagement, and will incorporate patient and other stakeholder partners into the research process.
- **Partnerships:** This principle is demonstrated when time and contributions of patient and other stakeholder partners are valued and demonstrated in fair financial compensation, as well as in reasonable and thoughtful requests for time commitment by patient and other stakeholder partners. When projects include priority populations, the research team is committed to diversity across all project activities and demonstrates cultural competency, including disability accommodations, when appropriate.
- **Transparency, Honesty, and Trust:** These principles are demonstrated when major decisions are made inclusively and information is shared readily with all research partners. Patients, other stakeholders, and researchers are committed to open and honest communication with one another.

It is important to distinguish “patient partners” from patient subjects. Patient partners are patients (those with lived experience), family members, caregivers, and organizations that are representative of the population of interest in a particular study. Patient partners are valuable members of the research team and involved in the planning, conduct, and dissemination of the research, whereas patient subjects are those individuals enrolled as study participants. In a similar capacity, stakeholder partners who are members of constituencies based on professional, rather than personal experience, can serve as members of the research team as well.

See Appendix 3 for the complete Engagement Rubric.

### Human Subjects Protections

After you have evaluated all six Merit Review criteria, please evaluate the adequacy of human subjects protections in your assigned applications.

- PCORI requires that research involving human subjects include adequate safeguards.
- Institutional Review Boards selected by awardees have authority for ensuring the protection of human subjects.
- PCORI seeks your assistance in identifying issues with protection of human subjects that PCORI staff should review with potential funding awardees.

- Concerns about protections for human subjects *should not be factored into the application's score.*
- Flag these concerns for PCORI staff by checking the appropriate box and providing your comments in PCORI Online.

See Appendix 4 for detailed guidance for evaluating Human Subjects Protections.

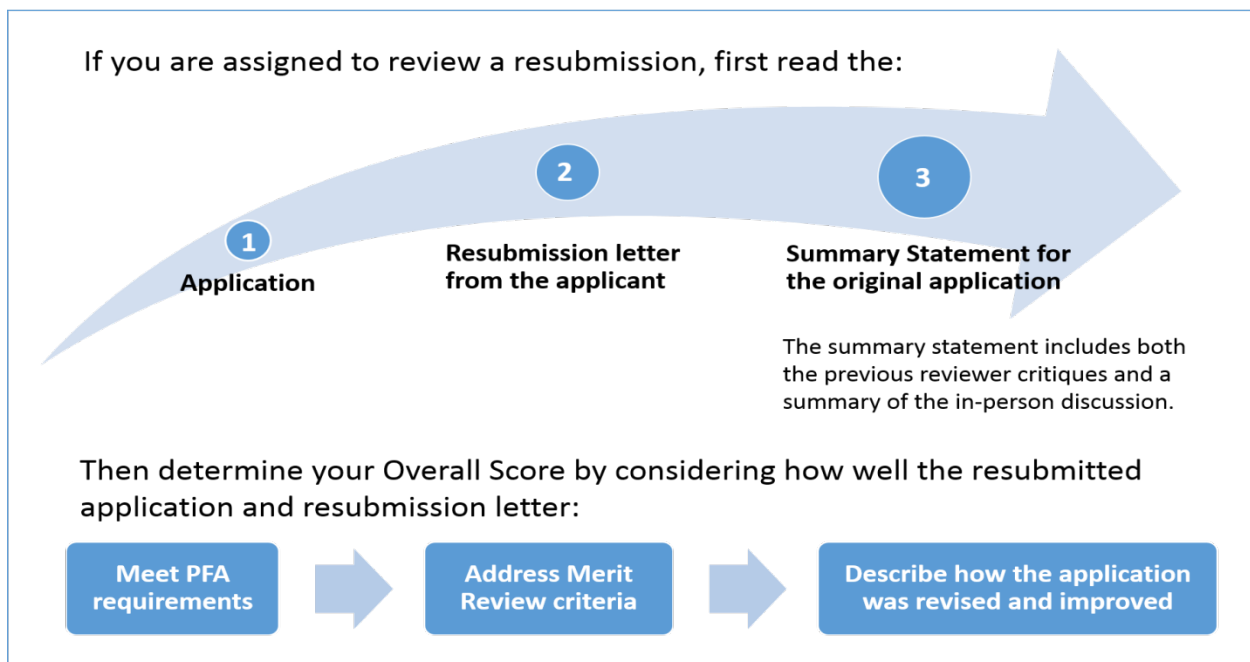
## Evaluating Resubmissions

### What is PCORI's resubmission policy?

An applicant may resubmit an application that was not funded. An application is considered a resubmission if it has previously completed PCORI's merit review process, including receipt of the summary statement.

When resubmitting an application, applicants include a resubmission letter with their revised application.

The resubmission letter is an opportunity for applicants to provide an overview of how the application has been strengthened in its scientific merit and responsiveness to the current PFA. **Simply responding to previous reviewers' concerns is not sufficient;** the application must be programmatically responsive and demonstrate methodological rigor and patient-centeredness.



**TIP:** Review the resubmission statement letter *after* reading the application to better understand the changes the investigators made to their original application.

## Evaluating Budgets

All applicants submit a detailed budget and justification for the duration of the proposed study. The budget reflects the work outlined in the application and must support all objectives.

If a project is awarded, the applicant moves into the post-award phase. Budgets are carefully scrutinized to ensure that the proposed budget is appropriate for the size and scope of the study and does not have any unallowable costs (e.g., costs that are not directly related to the research activity at hand). Since PCORI awards contracts, not grants, negotiations between the awarded organization and PCORI can work out issues in the budget or projected project milestones.

*Reviewers do not need to comment or closely analyze the budgets.* However, as you look over the application, please flag any issues with the proposed budget in your critiques.

- Provide specific information on any budgetary issues that are not sufficiently described, considered, or justified. Insofar as these issues may affect the impact of the study, you may include these comments under Criterion 2.
- Look for appropriate budgeting for costs related to engagement, such as financial compensation of patient and other stakeholder partners, costs of meetings, and other facilitators of patient and stakeholder partner participation in research (include these comments under Criterion 5).



*If you identify a concern in the budget, do not factor it into your score for the application unless it affects the likelihood of study success.*

## Chapter 4. Writing Critiques

### Overview

Written critiques will be included in the final summary statements and will be used by several audiences during the Merit Review process:

- By applicants to inform possible resubmissions
- By you to prepare your oral presentation of your critique at the In-Person Panel Review
- By other In-Person Panel Review Members to help prepare for their participation in the In-Person Panel discussion
- By PCORI staff as they build funding slates and manage projects

The goal of the critique is to ensure that applicants, other reviewers, and PCORI staff understand the strengths and weaknesses of each application, based on the merit review criteria. This helps PCORI identify the most meritorious applications and helps applicants understand the strengths and weaknesses of their application, which can inform how they strengthen subsequent submissions.

### Offline Critique Template

PCORI provides a critique template to all reviewers each cycle to ensure that guidance is consistent and incorporates any changes for that cycle. This document is a helpful tool that you should use to write your critiques. Each criterion will have its own section where perceived strengths and weaknesses can be organized, and scores can be provided.

#### Guidelines for Writing Strengths and Weaknesses

##### **Write critiques, not summaries**

- ✓ A critique provides a detailed analysis and assessment of the application, not a summary of the content of the application.

##### **Provide details**

- ✓ Provide an explanation of why a specific point is a weakness or a strength.
- ✓ Provide constructive criticism and be specific.
- ✓ Do not use direct quotes from the application, but provide page numbers when referring to specific sections.

##### **Be objective**

- ✓ Refrain from discussing your own personal experiences. Generalize your experiences to other patients with different conditions and experiences.
- ✓ Write your critique from the perspective of your specific stake in the healthcare process.

##### **Judge on application's merit**

- ✓ Evaluate each application as submitted. Your score and critique should be based on the application as-is, not the application's potential.
- ✓ Do not make assumptions about the principal investigator's intent. If information seems to be left out of an application, consider whether or not that is a weakness.

- ✓ Applications should not be compared to one another. You might be assigned two applications focused on the same disease or condition, and you should be careful to not let the review of one affect the review of the other.

## Major and Minor Strengths and Weaknesses

Using modifiers—major, moderate, and minor—to describe strengths and weaknesses of your assigned applications can help you determine scores for each Merit Review criterion. The modifiers also help others who read your critiques to understand which points are more important to you and drove your score.

**Major Strength:** An attribute that is likely to lead to improvements in healthcare and/or outcomes

**Moderate Strength:** An attribute that would probably lead to improvements in healthcare and/or outcomes

**Minor Strength:** An attribute that could lead to improvements in healthcare and/or outcomes

**Minor Weakness:** An easily addressable weakness that does not substantially lessen the impact of the study's results on healthcare and/or outcomes

**Moderate Weakness:** A weakness that would lessen the impact of the study's results on healthcare and/or outcomes

**Major Weakness:** A weakness that would seriously limit the impact of the study's results on healthcare and/or outcomes

- ✓ The scoring chart below provides additional guidance and characteristics to help you determine a score for each criterion based on major and minor strengths and weaknesses.
- ✓ Feel free to copy/paste our wording for these modifiers in your critiques. For example, "The limited role of patient partners **would seriously limit the impact of the study's results on healthcare and/or outcomes** because \_\_\_\_\_."

## Examples: Writing Strengths

Below are sample strengths for Criterion 2: Potential for the study findings to be adopted into clinical practice and improve delivery of care, written from a stakeholder's perspective.

Review each critique excerpt and decide which one best aligns with PCORI's guidelines for writing strengths and weaknesses.

### Sample Critique 1

Strengths:

- This study proposes to use biological pre-treatment indicators to study the effectiveness of consuming chicken soup for alleviating cold symptoms.
- One of my patients has struggled with a sore throat for many years and she hates taking medicine. I would be happy if I could give this patient chicken soup instead.

### Sample Critique 2

Strengths:

- Currently there are no biological pre-treatment indicators to predict cold symptom response to chicken soup. This study of biological measures to predict the success of chicken soup will provide caregivers with the information they need to know when to cook chicken soup rather than giving cold medicine to their sick family members. (Major)
- There is a large variability in response to treatment of the common cold. The use of biological measures to predict chicken soup outcomes has the potential to reduce some of that variability for clinicians and may have an impact on the community as a whole. (Moderate)
- The applicants have clearly identified local and national stakeholders who have expressed a need for better understanding of the benefits of chicken soup for the common cold. (Moderate)
- The applicants describe a clear plan for disseminating the results of this study via television cooking programs featuring chicken soup recipes, which will reach a broad general audience. (Major)

**Answer: The correct answer is Sample Critique 2.**

**Sample Critique 1** is not appropriate because it is vague and personal and omits modifiers. The first point summarizes the aim of the research, but does not follow up by describing WHY it is a major, moderate or minor strength. The second point expresses a personal opinion rather than an objective description.

**Sample Critique 2** is appropriate because it directly addresses Criterion 2: Potential for the study to improve healthcare and outcomes findings to be adopted into clinical practice and improve delivery of care. It is objective in tone, and it also mentions the magnitude of the strength.



## Examples: Writing Weaknesses

Below are sample weaknesses for Criterion 6: Patient and Stakeholder Engagement, written from a patient's perspective. Take a moment to review each of the critiques and decide which one best aligns with PCORI's guidelines for writing strengths and weaknesses.

### Sample Critique 1

Weaknesses:

- Patients and caregivers were not formally engaged in the formulation of the research questions. The application needs to include more details about if and how influenza survivors requested the interventions outlined and, further, if they were interested in the difference between the treatments offered. (Major)
- A more detailed and specific plan is needed describing how patients will be involved in monitoring the conduct and progress of the study, particularly in light of the trust issues between the patient communities and healthcare providers identified in the application. (Moderate)

### Sample Critique 2

Weaknesses:

- No engagement plan. Is this feasible?
- Have you asked influenza survivors what kind of outcomes they would like to see?
- I have worked with this population of patients, and the project is just not going to work if doctors get to call all the shots in monitoring the project.

**Answer: The correct answer is Sample Critique 1.**

**Sample Critique 1** is appropriate because it directly addresses Criterion 6. People representing the population of interest and other relevant stakeholders are engaged in ways that are appropriate and necessary in the given research context. This critique provides details about what could be improved, and makes clear suggestions for improvement.

**Sample Critique 2** is not appropriate because it conveys an inflammatory and personal tone.

## Merit Review Scores

Once you have finished describing the strengths and weaknesses for each criterion, you will provide a score for that criterion. The scoring range for the overall application and for the individual criteria consists of a nine-point scale, with lower numbers indicating higher quality. Numerically low scores (such as 1-3) reflect applications that have major strengths in a criterion area, while numerically higher scores (such as scores of 7-9) are associated with applications that are very weak in that criterion area.

The number and magnitude of strengths and weaknesses for each criterion should reflect the criterion score. For example, a score of 1 would correlate with an exceptionally strong application with essentially no weaknesses. An application with an overall score of 4 might have a mix of moderate strengths and moderate weaknesses, with strengths outweighing weaknesses. A score of 7 or 8 might indicate major weaknesses and minor strengths. The scores will depend on the individual reviewer.

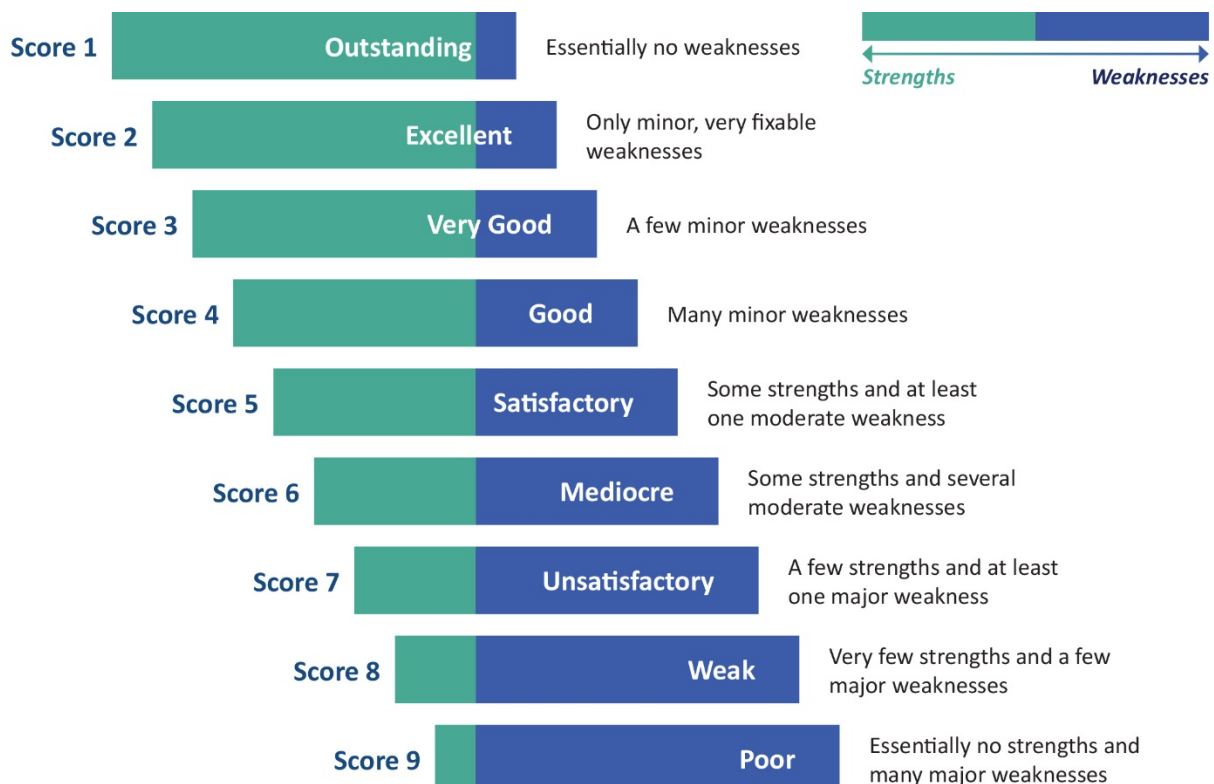
### Align scores to critiques

- If you assign a poor score, be clear about the weaknesses of the application (and vice versa).
- Text and score alignment will help other reviewers, staff, and the applicant understand your perspective when they read your reviews.
- The use of modifiers like major, moderate, and minor to describe strengths and weaknesses helps the reader understand what drove your scores.



The modifiers (major, moderate, minor) should help you determine a score for each criterion. When determining your score, consider how many strengths versus weaknesses you've identified. Also consider how the gravity of those strengths or weaknesses balance each other.

### Merit Review Scoring Chart: Criterion Scores



## Knowledge Check

- 1) **Instructions:** Take a moment to read the sample critique below and decide which score best aligns with the written critique. Select the best answer.

### Sample Critique:

#### **Criterion 6: Patient and Stakeholder Engagement**

##### *Strengths:*

- *The research team will assemble often to reformulate study questions and assess progress. There will be an internet listserv to facilitate discussion. Procedures are in place to make changes if needed based on the opinions of the designated individual stakeholders. This is a moderate strength.*

##### *Weaknesses:*

- *There is an extensive list of stakeholders with advanced degrees engaged in all aspects of the study; however, there is an absence of patient or caregiver input. For example, patients/caregivers with the common cold were not consulted on the design or implementation of the study nor are they involved in monitoring its progress. Also if patients/caregivers were involved in the design of the study we would have a better idea if the technique of sending letters to invite patients to participate in the study would be their preferred method of engagement. The exclusion of these very important stakeholders in the study design is a major weakness of this study.*
- *More specific details and commitments and/or plans for dissemination by stakeholders other than the PI/research team are needed to strengthen evidence of stakeholder engagement.*
- *There is no plan for patient/caregiver/advocate dissemination of the results. This is a major weakness of the study because patients with the common cold are characteristically disengaged and may not be reached through the medical community. Plans to engage and disseminate into the patient community by outreach measures would strengthen this study.*

**A. Score 3 – Very good, a few minor weaknesses**

**B. Score 8 – Weak, very few strengths and a few major weaknesses**

**Answer: The correct answer is B.** A criterion score of 8 would best align with the sample written critique because there are several major weaknesses listed, but only a few strengths. A score of 3 would not align with the written critique because there are too many major weaknesses listed for this application to be scored as excellent for this criterion.

- 2) **Instructions:** Take a moment to read the sample critique below and decide which score best aligns with the written critique. Select the best answer.

**Sample Critique:**

**Criterion 6: Patient and Stakeholder Engagement**

*Strengths:*

- *A major strength is that multiple stakeholder and patient groups are proposed to assist with the conduct of the study.*
- *Specific dissemination groups are discussed, including regional stakeholders and national dissemination advisers. This is a major strength.*
- *Moderate strength: Patients and stakeholders were identified through interest and their involvement with the ABC Patient Advisory Council.*

*Weaknesses:*

- *The initial formulation of research questions relied on national leaders, and less on regional stakeholders and patients, a minor weakness.*

**A. Score 7 – Unsatisfactory, a few strengths and at least one major weakness**

**B. Score 2 – Excellent, only minor, very fixable weaknesses**

**Answer: The correct answer is B.** A criterion score of 2 would best align with the sample written critique because there are several solid strengths listed and only one minor weakness. A criterion score of 7 would not align with the written critique because the reviewer has only listed one minor weakness (the formulation of research questions did involve stakeholder input, just not at the regional level). The applicant has worked with a patient advisory council and lists specific groups that will collaborate on dissemination; these are solid strengths.

## Writing an Overall Narrative

The overall narrative should provide a high-level summary of the strengths and weaknesses of the application as a whole. The overall summary should be in paragraph format, instead of in a bulleted list, and should describe the likelihood that the research would exert a sustained, powerful influence on healthcare and patient-centered outcomes.

The overall narrative is a great place to give general feedback to the applicant. Keep in mind that your comments under each criterion should not simply be repeated in this section, because this would not be useful for the applicant. We want reviewers to provide a narrative about how the various strengths and weaknesses affect their overall evaluation of the application.



Consider the overall narrative as an “elevator brief.” If you had to describe the most salient points on the merits of the application to someone in the time it would take to ride an elevator 10 floors, what would you say?

### Example of a well-written Overall Narrative:

#### **Overall Summary Score = 5**

#### **Please provide your overall comments:**

There is a need to improve the delivery of depression care in primary care settings. Most individuals with depression are initially treated in primary care, but identification of depression, referrals, and even medical treatment within the primary care setting are not consistent and usually not evidence based. This project provides an opportunity to identify the optimal model for primary care delivery of depression care. While this is an important and innovative project, the application does have one major and several much more minor weaknesses. The major weakness is the absence of broad input from nurses, physician assistants, and other care providers in primary care offices. Physicians are not the only stakeholders in how primary care offices are organized. More minor weaknesses involve the measures that are used to identify depression, and limited dissemination plan. These weaknesses are easily fixed, but more thought should be given to the engagement of stakeholders.

## Assigning an Overall Score

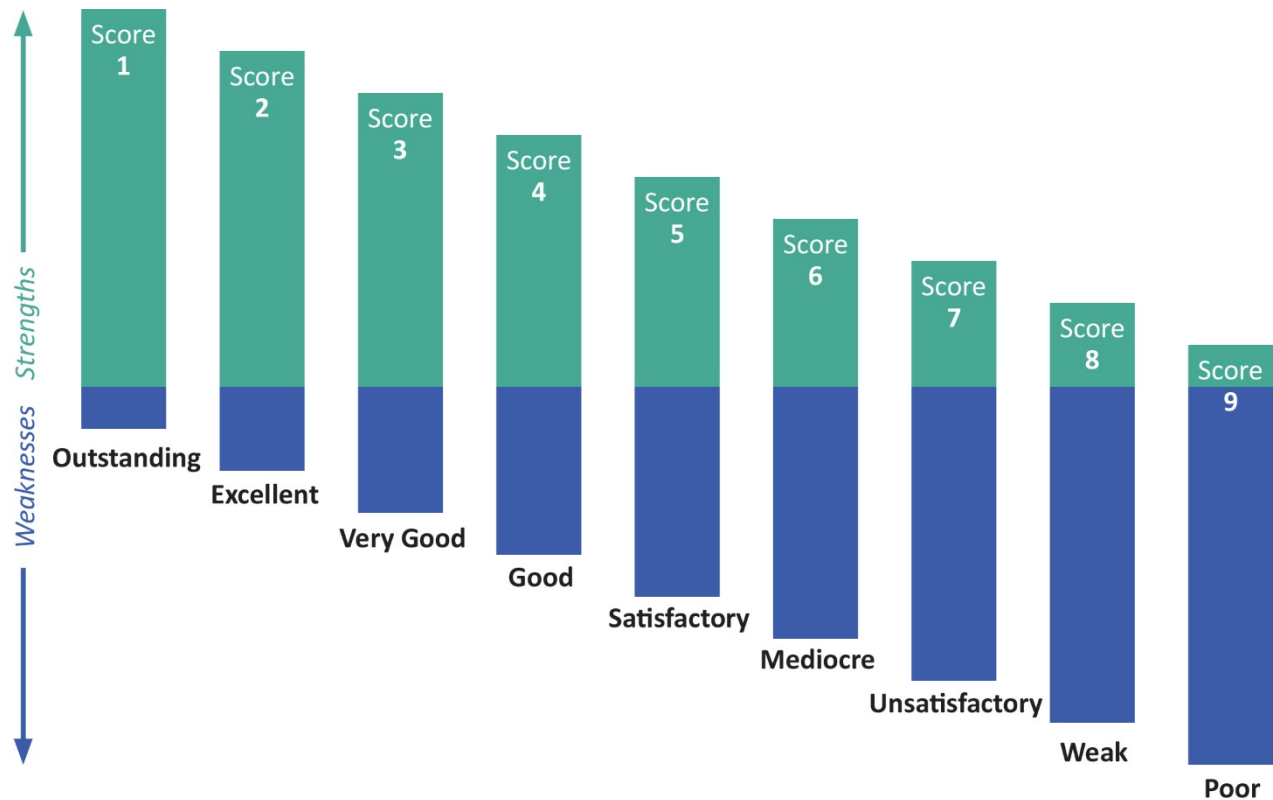
The overall score:

- Takes into consideration the entire application's strengths and weaknesses
- Accounts for all of the criteria you considered but is not an average of individual criterion scores
- Should not fall outside of the range of scores given for each criterion (for example, if you rated the criteria 3-8, do not assign an overall score of 9)



To assign an overall score, use the same 1 to 9 scale you used to score each individual criterion where 1 is the best possible score, and 9 is the worst possible score.

## Merit Review Scoring Chart: Overall Score



## Revising and Resubmitting a Critique

Almost every reviewer, no matter how experienced, will receive feedback from their Merit Review Officer for how to clarify comments in his or her critiques, especially for the first critique.

When revising and resubmitting a critique, please ensure that you:

- Thoroughly review the feedback provided by your MRO
- Pay close attention to all feedback to ensure that you address all questions and concerns
- Ask questions to ensure that you have a clear understanding of the specific areas of needed improvement

Prior to the In-Person Panel Review, MROs will review all critiques. This is a critical step in our review process.

## Chapter 5. In-person Panel Meeting

---

### Overview

The In-Person Panel Review provides an opportunity for reviewers to discuss the strengths and weaknesses of the applications selected for discussion after the Preliminary Review phase. The full panel has an opportunity to ask questions and fully discuss each application, with facilitation by the Chair. This discussion helps reviewers provide scores for the applications that they were not assigned to review.

- Reviewers receive a brief orientation to the panel process and group rules.
- The Panel Chair introduces each application.
- Reviewers assigned to each application make individual oral presentations, describing the strengths and weaknesses that drove their scores of the application.
- Members of the full panel ask questions and discuss the application.
- The Chair records an oral summary of the panel discussion.
- Each panel reviewer provides a final overall score for the application.

### Preparing for the In-Person Panel Review

#### Before the In-Person Panel Review:

- ☐ Review the list of applications that will be discussed at the In-Person Panel Review. Your Merit Review Officer will send you this list in discussion order before the panel meeting.
- ☐ Review all of the written critiques and preliminary scores for all of your assigned applications, including those for which you have been assigned as Reader.
- ☐ Prepare your brief oral presentation using main strengths and weaknesses from your written critique.
- ☐ If you have time, review the abstracts and written critiques for the other applications on the discussion list.



Becoming familiar with all of the applications and their critiques will help you understand and score these applications after participating in the discussion.



## Panel and Reviewer Roles

The following people will be in the room during the In-Person Panel Review

<b>Panel Reviewers</b> (not PCORI Staff members) <ul style="list-style-type: none"><li>About two-thirds of the panel reviewers will be scientists and the other third will be patients and stakeholders</li></ul>
<b>Merit Reviewer Officer (MRO)</b> (PCORI staff member) <ul style="list-style-type: none"><li>Serves as main PCORI point of contact for reviewers</li><li>Provides guidance to reviewers on PCORI process and policy</li><li>Presents brief orientation to panel proceedings</li><li>Answers panel members' questions about PCORI and the review process</li><li>Records notes of the panel discussion, which are also incorporated into the final summary statement</li></ul>
<b>Panel Manager</b> (PCORI staff member) <ul style="list-style-type: none"><li>Serves as administrative point of contact for reviewers</li><li>Provides support for reviewers in the online scoring system and other technical needs</li></ul>
<b>Panel Chair</b> (not a PCORI staff member; usually an experienced senior-level scientist) <ul style="list-style-type: none"><li>Introduces and facilitates discussion of each application<ul style="list-style-type: none"><li>Helps clarify key strengths and weaknesses of applications</li><li>Ensures that scores and verbal critiques align</li><li>Clarifies points of scoring disparities among reviewers</li></ul></li><li>Records an oral summary of the discussion of each application</li></ul>
<b>Observers</b> <ul style="list-style-type: none"><li>PCORI program staff members often attend the in-person meeting so they can better understand the projects they will recommend for funding</li><li>Mentors are available on-site to provide support for patient and other stakeholder reviewers if needed.</li></ul>



## Inside the In-Person Panel Review

Click [HERE](#) or below on the embedded video to watch a simulation of an in-person panel review:



## Preparing In-Person Panel Presentations

Panel discussion gives reviewers an opportunity to participate in a thoughtful discussion about the strengths and weaknesses of the selected applications. Reviewers should familiarize themselves with all applications on the discussion list in advance, even if they were not assigned to review them. Your presentation should cover the main strengths and weaknesses of the applications you reviewed.

- Start by thinking about what other reviewers will need to know about the strengths and weaknesses of each application, based on your evaluation, in order to score the application.
- Review the written critiques that were submitted by the other three reviewers on your assigned applications. This will help you identify topics that are likely to be discussed in the panel.

Remember, you have about **two (2) minutes** to present. Be clear and to the point. Do not summarize the application, but you can add key details that the Chair may not have covered in his or her introduction or that have not been provided by the reviewers who have already presented.

## Panel Review Discussion Tips

Making sure that the In-Person Panel is a welcoming, safe, and open environment requires more than coming prepared to discuss your critique—it also requires being a thoughtful, respectful, and engaged participant. Here are some tips that can help you manifest these qualities in this stage of the process.



### **Avoid Repetition**

Avoid repetition of points made by previous reviewers. This will keep the discussion moving and allow adequate time to review each application on the schedule.

- If you agree with a reviewer's perspective, you can summarize why you agree:
  - "I agree with the previous reviewer about..."
- If you disagree with the reviewer's viewpoint, be sure to voice your views and disagree with the idea, not the person:
  - "I view this differently because..."
  - "I would like to add these important strengths/weaknesses that haven't been mentioned..."

### **Maintain a Productive Discussion**

A critical part of the In-Person Panel Review is a productive discussion. As a panel reviewer, you can help maintain a productive discussion by:

- Respecting all viewpoints
- Engaging in active listening
- Asking good questions
- Using words such as good, bad, better, or worse to describe scores, instead of high or low; this is to avoid confusion since low numerical scores indicate high quality
- Minimizing the use of acronyms and jargon
- Being culturally aware/sensitive

### **Respect all Viewpoints**

Although you may not agree with what other panel reviewers say, it is important that you:

- Listen to what others have to say before expressing your viewpoint
- Refrain from insulting, name-calling, criticizing, or putting down a panel member
- Build on one another's comments
- Work towards shared understanding
- Be mindful of cultural differences and the needs of different patient populations
- Be respectful of the different constituencies around the table; each person brings a valuable viewpoint that helps PCORI find the best research to improve patient outcomes

### **Practice Active Listening**

A successful panel member uses active listening in order to check assumptions, clarify his or her thoughts, and understand others.

Here are a few active listening strategies that you can use during the In-Person Panel Review:

- Mentally commit to listening
- Avoid distractions
  - Turn off mobile devices
  - Avoid answering email and visiting web sites not related to the applications
  - Refrain from side conversations
- Take notes while you listen
- Jot down questions that you would like to ask



- Face the person who is speaking

### Ask Good Questions

Good questions are the key to a productive discussion. Questions can be used to probe for deeper analysis, get clarifications or examples, explore implications, or respectfully challenge opinions or ideas.

Examples of common In-Person Panel Review questions include:

- Can you tell me more about the engagement plan?
- Would patient advocacy groups be willing to disseminate the findings of the research?
- Can a clinician or clinical administrator in the room talk about how well this intervention could be implemented in clinical practice if this research were to find it effective?

### Use Strength and Weakness Modifiers

Communicating the magnitude of the strengths and weaknesses you found in an application will provide useful context to the discussion. Use the major-moderate-minor modifiers from your critiques to indicate whether weaknesses, in particular, are fixable or not.

For example:

- There is no evidence that patients were consulted during the design of the study, which is a major weakness.
- School nurses were not included in the original stakeholder advisory committee, but this is a minor weakness that is fixable.



## Appendix 1. COI/Expertise

---

### **INFORMATION FOR PCORI MERIT REVIEWERS ON CONFIDENTIALITY, CONFLICT OF INTEREST, AND RATING EXPERTISE**

(February 2, 2015)

[Click here to access PCORI's guidance on conflict of interest and rating expertise online.](#)

The Patient-Centered Outcomes Research Institute (PCORI) welcomes a broad array of stakeholder reviewers to participate in the evaluation of research applications ("Reviewers"). Reviewers are essential to helping PCORI fulfill its mission and to fund research that is both scientifically rigorous and truly patient centered. Given the important role of Reviewers in PCORI's application selection process, PCORI requires Reviewers to abide by a number of policies and commitments that support a fair and objective merit review process. This document provides information about three important obligations of any Reviewers participating in PCORI's merit review process: A) Confidentiality and Non-Disclosure; B) Conflict of Interest; and C) Rating Expertise.

#### **A. CONFIDENTIALITY AND NONDISCLOSURE**

Maintenance of confidentiality is a critical component of merit review. All Reviewers are required to agree to the terms of a PCORI Non-Disclosure Agreement ("NDA") before they participate in merit review activities. By agreeing to the NDA, Reviewers confirm that they will preserve and not disclose confidential information and that they will not use any confidential information except as required to perform the responsibilities of merit review.

In the context of preserving the confidentiality of the merit review, it is important that materials reviewed before or during the merit review meeting as well as discussion content of the merit review meeting not be disclosed to anyone at any time before, during, or after the merit review meeting except as part of the application evaluations during the actual meeting. Confidential information includes any information that has not been made public, such as information about applications, number of applications discussed, research topics, negative or positive outcomes of the meeting, and any personal information about other reviewers disclosed as part of the merit review process.

In order to maintain the integrity of the review process, Reviewers must not contact any applicants for whom they have access to application material. Merit assessments of applications must be completed using only the information provided by the applicant at the time of submission. Reviewers must not request additional information from applicants once the application has been submitted. If Reviewers need assistance in reviewing applications, he or she may contact their Merit Review Officer (MRO) for help or clarification.

Reviewers must not use social media or other electronic media tools during merit review panel discussions or activities. Reviewers must not discuss the review with other reviewers absenting themselves from the room for conflict of interest (COI) reasons, or with reviewers of any other panel. If a Reviewer is asked to disclose information about the contents of an application or about the nature of review discussions, he or she must inform the person making the request that merit review participants may not disclose such information and must inform the panel MRO that he or she has been contacted directly.

It is the responsibility of each Reviewer to safeguard the confidentiality of review material while it is in his or her possession, not to share the material with other persons, and to properly dispose of both hard copy and electronic materials at the conclusion of the panel meeting or when directed to do so.

The actions outlined above are among the steps that a Reviewer should take to fulfill his/her obligations under the Non-Disclosure Agreement.

## **B. CONFLICT OF INTEREST (COI)**

PCORI's Board of Governors has adopted a Conflict of Interest Policy that applies to all PCORI activities, including merit review of applications for research funding. A copy of the PCORI Conflict of Interest Policy is provided to all Reviewers and is available on PCORI's website. The information here is intended to help Reviewers understand how PCORI implements and interprets the Conflict of Interest Policy in the context of merit review activities, including how conflicts of interest should be disclosed and addressed.

PCORI requires each Reviewer to disclose conflicts of interest as a condition of participating (or being considered for participation) in merit review. PCORI relies on the professionalism and integrity of each Reviewer to identify any financial or personal associations that have the potential to bias or have the appearance of biasing the Reviewer's activities and decisions in merit review. The *appearance or perception* of bias can be enough to undermine the public trust. All efforts should be made to identify all associations that may give rise to a conflict of interest. **It is important that each Reviewer submit COI disclosures by the requested deadline so that application assignments can be made to the full panel in a timely manner.**

A COI in merit review exists when a Reviewer or a close relative or professional associate of the Reviewer has a financial or personal association related to an application, including the applicant and investigators, which may bias the evaluation of the application or create the perception of bias. The term "close relative" includes a parent, spouse, domestic partner, or child. Depending upon factors like financial dependency, cohabitation, and family history, sometimes other relatives could also be considered "close relatives." Reviewers should use their best judgment in determining when a familial relationship is close enough that the relative's associations could bias or appear to bias their decision making.

Financial associations often involve relationships or interests that may cause a Reviewer to have a financial stake in whether certain applications are selected for PCORI funding. Regardless of the level of financial involvement or other interest, if a Reviewer feels, or may be perceived as being, unable to provide an objective evaluation, he or she may not participate in the review of the application. Personal associations can be either professional or non-professional relationships with the applicant, the investigator(s), or a person or organization whose interests would be affected by the project under review.

For COI purposes, applicant and investigators include the roles listed below.

- **Applicant:** Principal Investigator (PI) listed in the application
- **Investigator:** All active participants (PI, co-PI, research partner, collaborator, consultant, subcontractor, and other senior/key personnel) listed in the application



Based on the nature of the COI, it may be handled at either the PFA or application level. Please review the following examples of COI and how to handle them at each level. While the following are provided as general examples, PCORI reserves the right to address conflicts of interest on a case-by-case basis.

### **1. PCORI Funding Announcement (PFA) Level COI**

Certain conflicts of interest can be viewed as involving such powerful influences or deeply-felt relationships that they have the potential to bias (or appear to bias) a Reviewer's evaluation of *all of the applications* submitted in response to a PFA. For example, a Reviewer might hold so large a financial interest in one application that it would not reasonably appear the Reviewer could impartially evaluate competing applications that have been submitted in response to the same PFA.

If any of the following types of conditions apply, the Reviewer cannot serve on panel reviewing applications received in response to a particular PFA.

- The Reviewer is an investigator in an application on a PFA reviewed by the panel.
- The Reviewer has a close relative who is an investigator on an application reviewed by the panel.

There may be other circumstances, in addition to those identified above, in which a Reviewer feels unable to serve impartially on a panel evaluating applications submitted in response to a specific PFA, or in which it might appear that the Reviewer cannot do so. The Reviewer should report such conflicts to the panel's MRO or the Associate Director, Merit Review and self-recuse from participating on the panel for applications related to the specific PFA.

### **2. Application Level COI**

In contrast to PFA-level conflicts of interest, the potential for bias created by other types of conflicts may be confined to the review of a particular application. If any of the following types of conditions apply, the Reviewer can serve on the panel but must recuse himself or herself from the discussion and scoring of the application. The Reviewer will not have access to that application or participate in the discussion or scoring of the application, and the recusal will be documented.

- The Reviewer or his/her close relative currently receives, or within the past 12 months has received, medical care from the applicant entity, principal investigator, or other individuals identified in the application as key personnel.
- The Reviewer or his/her close relative currently has a significant personal or professional relationship with the applicant entity, principal investigator, or other key personnel. (Note that sometimes negative relationships – for example, a professional rivalry – can be a significant personal or professional relationship.)
- The Reviewer or his/her close relative provides, or within the past 12 months has provided, technical assistance to the applicant entity, principal investigator, or other key personnel in any of the following ways:
  - Assistance with preparing or submitting the application.
  - Providing the applicant entity, principal investigator, or other key personnel with resources for the application that are not freely available to others in the research community -- e.g., specialized data analysis, service, or confidential material.

Note that providing resources that are freely available to anyone in the scientific community (e.g., letter of support, service, equipment, data, or other material) would not be considered a conflict of interest.

- The Reviewer or his/her close relative is employed at the applicant entity.
  - For multi-campus State institutions, a Reviewer who is primarily employed at one campus of the institution is not considered to have a conflict of interest with respect to an application submitted by another campus of the same institution provided that the reviewer has no institutional responsibilities that would significantly affect the other campus.
  - For private institutions and affiliates, a Reviewer who is primarily employed at one affiliate of the institution is not considered to have a conflict of interest with respect to an application submitted by another affiliate of the same institution provided that the reviewer does not have institutional responsibilities that would significantly affect the other affiliate.
- The Reviewer or his/her close relative is actively negotiating, or has an agreement about future employment at the applicant entity.
- The Reviewer or his/her close relative has a professional relationship other than employment with an applicant entity – e.g., consulting or other vendor contract, service on board of directors, service on advisory committee.
- The Reviewer or his/her close relative could receive professional gain or advancement (e.g., publications, scientific prizes, or academic appointments) as the direct result of the application funding decision.
- The Reviewer or his/her close relative could receive a financial benefit exceeding \$10,000 per year from individuals or companies that own or manufacture medical treatments, services, or items that the application proposes to study.

### **C. RATING EXPERTISE**

PCORI merit review is designed to incorporate the perspective of scientists, patients, and other healthcare stakeholders, including having merit review panels that incorporate appropriate areas and levels of expertise. To support appropriate composition of merit review panels, Reviewers will be notified when application abstracts and lists of key personnel are available and accessible in PCORI Online. When reading the application title and abstracts, Reviewers should indicate for each application whether their expertise matches with the content of the application and whether that content match is *high, medium, low, or none*.

For Scientific reviewers, PCORI expects reviewer rating of expertise for specific applications to be made on the basis of the individual's research expertise and science training. Please note that expertise is an indication of the extent of the reviewer's subject-matter expertise and is not a reflection of his or her willingness to review an application.

It is not necessary for any patient or stakeholder reviewer to indicate high, medium, or low expertise on applications. Patients and stakeholders provide critical and important perspectives during the review process, independent of technical expertise. If patient or stakeholder reviewers do have specific disease expertise, however, it is appropriate to indicate this in the system. Please also note that the ratings are used to match applications to reviewers and are not a reflection of the relative importance of any reviewer on the panel.

Please use the following descriptors to indicate Rating Expertise:



<b>Rating</b>	<b>Description For Scientists</b>
<b><i>High</i></b>	The Reviewer is able to evaluate the application with little or no need to make use of background material or the relevant literature. The Reviewer has likely published in areas closely related to the science presented in the application.
<b><i>Medium</i></b>	The Reviewer has most of the knowledge to evaluate the application but will require some review of relevant literature to fill in details or increase familiarity with the system employed. The Reviewer may employ similar methodologies in his or her own work but may need to review the literature for recent data relevant to the application.
<b><i>Low</i></b>	The Reviewer understands the broad concepts but is unfamiliar with the specific methodology or other details, and reviewing the application would require considerable preparation.
<b><i>None</i></b>	The Reviewer has only superficial or no familiarity with the concepts and methodology described in the application.

**It is important that each Reviewer submit the expertise information by the requested deadline so that application assignments can be made to the full panel in a timely manner.**

#### **D. ENFORCEMENT AND CONCLUSION**

If a Reviewer violates his or her obligations as a reviewer, including relating to Confidentiality, Conflicts of Interest, or Rating Expertise, PCORI may implement sanctions or corrective measures, as appropriate. These sanctions may include: removing the Reviewer from the panel; notifying other panel members of the violation; initiating an internal investigation of the Reviewer's conduct and its consequences; and disqualifying the Reviewer, indefinitely or for a specified period, from participating as a PCORI reviewer.

If any Reviewer has any questions about the information outlined in this document on Confidentiality and Non-Disclosure, Conflicts of Interest, or Rating Expertise, please contact your panel's MRO.

PCORI is grateful for the important contributions that Reviewers make to PCORI's application selection process.



## Appendix 2. Methodology Standards

---

### PCORI Methodology Standards

Updated: October 13, 2015

Published: February 4, 2014

#### Cross-Cutting Standards for PCOR

##### 1: Standards for Formulating Research Questions

###### **RQ-1: Identify gaps in evidence**

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

###### **RQ-2: Develop a formal study protocol**

Studies should include a formal protocol specifying at least one purpose for which the data were collected (e.g., effectiveness, safety, natural history of disease, quality improvement); data sources and linkage plans, if any; data feasibility and quality, measure(s) of effect; and use of any standardized data dictionaries (nationally or internationally accepted).

###### **RQ-3: Identify specific populations and health decision(s) affected by the research**

To produce information that is meaningful and useful to people when making specific health decisions, research proposals and protocols should describe: 1) the specific health decision the research is intended to inform; 2) the specific population for whom the health decision is pertinent; and 3) how study results will inform the health decision.

###### **RQ-4: Identify and assess participant subgroups**

In designing studies, researchers should identify participant subgroups of interest and, where feasible, design the study with adequate precision and power to reach conclusions specific to these subgroups. In addition, subgroup information should be reported for later systematic reviews.

###### **RQ-5: Select appropriate interventions and comparators**

When evaluating an intervention, the comparator treatment(s) must be chosen to enable accurate evaluation of effectiveness or safety compared to other viable options for similar patients. Researchers should make explicit what the comparators are and how they were selected, focusing on clearly describing how the chosen comparator(s) define the causal question, reduce the potential for biases, and allow direct comparisons. Generally, non-use (or no specific treatment) comparator groups should be avoided unless no specific treatment is a likely option in standard care.

###### **RQ-6: Measure outcomes that people representing the population of interest notice and care about**

Identify and include outcomes the population of interest notices and cares about (e.g., survival,

function, symptoms, health-related quality of life) and that inform an identified health decision. Define outcomes clearly, especially for complex conditions or outcomes that may not have established clinical criteria. Provide information that supports the selection of outcomes as meeting the criteria of “patient-centered” and “relevant to decision makers,” such as patient and decision-maker input from meetings, surveys, or published studies. Select outcomes based on input directly elicited from patient informants and people representative of the population of interest, either in previous studies or in the proposed research.

## 2: Standards Associated with Patient-Centeredness

### **PC-1: Engage people representing the population of interest and other relevant stakeholders in ways that are appropriate and necessary in a given research context**

People representing the population of interest include individuals who have the condition or who are at risk of the condition and, as relevant, their surrogates or caregivers. Other relevant stakeholders may include clinicians, administrators, policy makers, or others involved in healthcare decision making. Stakeholders can be engaged in the processes of:

- Formulating research questions;
  - Defining essential characteristics of study participants, comparators, and outcomes;
  - Identifying and selecting outcomes that the population of interest notices and cares about (e.g., survival, function, symptoms, health-related quality of life) and that inform decision making relevant to the research topic;
  - Monitoring study conduct and progress; and
  - Designing/suggesting plans for dissemination and implementation activities.
- When applicable, research proposals should describe how these stakeholders will be identified, recruited, and retained. If engagement is not necessary or appropriate in these processes, explain why.

### **PC-2: Identify, select, recruit, and retain study participants representative of the spectrum of the population of interest and ensure that data are collected thoroughly and systematically from all study participants**

Research proposals and subsequent study reports should describe: 1) the plan to ensure representativeness of participants; 2) how participants are identified, selected, recruited, enrolled, and retained in the study to reduce or address the potential impact of selection bias; 3) efforts employed to maximize adherence to agreed-on enrollment practices; and 4) methods used to ensure unbiased and systematic data collection from all participants.

If the population of interest includes people who are more difficult to identify, recruit, and/or retain than other study populations (for example, individuals historically underrepresented in healthcare research such as those with multiple disease conditions, low literacy, low socioeconomic status, or poor healthcare access, as well as racial and ethnic minority groups and people living in rural areas), then specify plans to address population-unique issues for participant identification, recruitment, and retention.

### **PC-3: Use patient-reported outcomes when patients or people at risk of a condition are the best source of information**

When patients or people at risk of a condition are the best source of information regarding outcomes of interest, then the study should employ patient-reported outcome (PRO) measures in lieu of, or in addition to, measures derived from other sources. Proposals should describe:

1. the concept(s) underlying each PRO measure (e.g., symptom or impairment) and how it is meaningful to, and noticed by, patients in the population of interest;
2. how the concept relates to the health decisions the study is designed to inform;
3. how the PRO measure was developed, including how patients were involved in the development; and
4. evidence of measurement properties including content validity, construct validity, reliability, responsiveness to change over time, and score interpretability, including meaningfulness of score changes in the population of interest with consideration of important subgroups.

If these measurement properties are not known, a plan for establishing the properties must be provided. Caregiver reports may be appropriate if the patient cannot self-report the outcomes of interest. If PROs are not planned for use in the study, justification must be provided.

#### **PC-4: Support dissemination and implementation of study results**

Support dissemination and implementation of study results by suggesting strategies, indicating clinical and policy implications, and working with patients or organizations to report results in a manner understandable to each target audience.

### **3: Standards for Data Integrity and Rigorous Analyses**

#### **IR-1: Assess data source adequacy**

In selecting variables for confounding adjustment, researchers should assess the suitability of the data source in terms of its ability to assure robust capture of needed covariates.

#### **IR-2: Describe data linkage plans, if applicable**

For studies involving linkage of patient data from two or more sources (including registries, data networks, and others), describe:

1. each data source and its appropriateness, value, and limitations for addressing specific research aims;
2. any additional requirements that may influence successful linkage, such as information needed to match patients, selection of data elements, and definitions used; and
3. the procedures and algorithm(s) employed in matching patients, including the success, limitations, and any validation of the matching algorithm.

#### **IR-3: A priori, specify plans for data analysis that correspond to major aims**

Researchers should describe the analytic approaches that will be used to address the major research aims prior to data collection. These include definitions of key exposures, endpoints, and covariates. Also identify patient subgroups of interest, plans (if any) for how new subgroups of interest will be identified or how analysis plans may be adapted based on changing needs and scientific advances, and plans for how missing data will be handled.

**IR-4: Document validated scales and tests**

Studies should include documentation of the name of the scales and tests selected, reference(s), characteristics of the scale, and psychometric properties.

**IR-5: Use sensitivity analyses to determine the impact of key assumptions**

The results of these sensitivity analyses should be reflected in the interpretation of results.

**IR-6: Provide sufficient information in reports to allow for assessments of the study's internal and external validity**

Reporting guidelines for specific designs can be found at the [EQUATOR Network website](#). This website has brought together all reporting guidelines that have been developed using formal approaches, many of which have been adopted by journals, such as CONSORT (for randomized clinical trials), STARD (for diagnostic tests), and STROBE (for observational studies).

## 4: Standards for Preventing and Handling Missing Data

**MD-1: Describe methods to prevent and monitor missing data**

Investigators should explicitly anticipate potential problems of missing data. The study protocol should contain a section that addresses missing data issues and steps taken in study design and conduct to monitor and limit the impact of missing data. Missingness can occur from patient dropout, failure to provide data, and/or administrative or data management issues. As relevant, the protocol should include the anticipated amount of and reasons for missing data, as well as plans to follow up with participants. This standard applies to all study designs for any type of research question.

**MD-2: Describe statistical methods to handle missing data**

Statistical methods for handling missing data should be pre-specified in study protocols. The reasons for missing data should be considered in the analysis. The plausibility of the assumptions associated with the approach should be assessed. A discussion of the potential ramifications of the approach to missing data on the results should be provided. This standard applies to all study designs for any type of research question.

**MD-3: Use validated methods to deal with missing data that properly account for statistical uncertainty due to missingness**

Statistical inference of intervention effects or measures of association should account for statistical uncertainty attributable to missing data. This means that methods used for imputing missing data should have valid Type I error rates and that confidence intervals should have the nominal coverage properties. This standard applies to all study designs for any type of research question. Bayesian methods and methods such as multiple imputation satisfy this condition, along with various likelihood-based and other validated methods. Single imputation methods like last observation carried forward and baseline observation carried forward are discouraged as the primary approach for handling missing data in the analysis. If investigators do use single-based imputation methods, they must provide a compelling scientific rationale as to why the method is appropriate.

**MD-4: Record and report all reasons for dropout and missing data, and account for all patients in reports**

Whenever a participant drops out of a research study, the investigator should document the following:

1. the specific reason for dropout, in as much detail as possible;
2. who decided that the participant would drop out; and
3. whether the dropout involves some or all types of participation.

Investigators should attempt to continue to collect information on key outcomes for participants unless consent is withdrawn. This standard applies to all prospective study designs that aim to assess intervention effectiveness. All participants included in the study should be accounted for in the report, whether or not they are included in the analysis. Describe and justify any planned reasons for excluding participants from analysis.

#### **MD-5: Examine sensitivity of inferences to missing data methods and assumptions, and incorporate into interpretation**

Examining sensitivity to the assumptions about the missing data mechanism (i.e., sensitivity analysis) should be a mandatory component of the study protocol, analysis, and reporting. This standard applies to all study designs for any type of research question. Statistical summaries should be used to describe missing data in studies, including a comparison of baseline characteristics of units (e.g., patients, questions, or clinics) with and without missing data. These quantitative results should be incorporated into the interpretation of the study and reflected in the discussion section and possibly the abstract.

## **5: Standards for Heterogeneity of Treatment Effects**

### **HT-1: State the goals of HTE analyses**

State the inferential goal of each HTE analysis, specifying how it is related to the topic of the research, translate this into an analytic approach, and highlight the linkages between the two. Identify analyses as hypothesis driven (sometimes denoted confirmatory), or hypothesis generating (sometimes denoted exploratory).

### **HT-2: For all HTE analyses, pre-specify the analysis plan; for hypothesis-driven HTE analyses, pre-specify hypotheses and supporting evidence base**

The study protocol should unambiguously pre-specify planned HTE analyses. Pre-specification of hypothesis-driven HTE analyses should include a clear statement of the hypotheses the study will evaluate, including how groups will be defined (e.g., by multivariate score or stratification) and outcome measures, and the direction of the expected treatment effects. The pre-specified hypotheses should be based on prior evidence, which should be described clearly in the study protocol and published paper.

### **HT-3: All HTE claims must be based on appropriate statistical contrasts among groups being compared, such as interaction tests or estimates of differences in treatment effect**

A common error in HTE analyses is to claim differences in treatment effect when one group shows a statistically significant treatment effect and another does not. To claim differences in treatment effect among subgroups, appropriate statistical methods must be used to directly contrast them. Such contrasts include, but are not limited to, interaction tests, differences in treatment effect estimates with standard errors, or a variety of approaches to adjusting the estimated subgroup effect, such as Bayesian shrinkage estimates. Within each subgroup level, studies should present the treatment effect estimates and measures of variability.

**HT-4: For any HTE analysis, report all pre-specified analyses and, at minimum, the number of post hoc analyses, including all subgroups and outcomes analyzed**

Protocols and study reports must report the exact procedures used to explore HTE, including data mining or any automatic regression approaches. HTE analyses should clearly report the procedures by which subgroups were defined (e.g., by categorical predictors or continuous risk scores) and the effective number of subgroups and outcomes examined. If a non-prespecified stratum or subgroup is claimed to show a treatment effect that is different from others, methods should be used that account for the number of contrasts examined. These methods include, but are not limited to, p-value adjustment, false discovery rates, Bayesian shrinkage estimates, adjusted confidence intervals, and validation methods (internal or external).

## Standards for Specific Study Designs and Methods

### 6: Standards for Data Registries

**DR-1: Requirements for the design and features of registries**

Registries established for conducting PCOR must have the following characteristics to facilitate the collection and aggregation of usable data, to ensure appropriate privacy and confidentiality, to document changes to the registry protocol, and to guide robust analyses that include important confounders.

- **Patient Follow-up** - The objective(s) of the registry should determine the type, extent, and length of patient follow-up. Describe what triggers the follow-up, the follow-up measures, and the last contact with the patient. Ensure that the planned follow-up time is adequate to address the main objective and that planned patient-retention efforts are suitable to the target population and anticipated challenges. Describe expected loss to follow-up and potential effect on the results, including possible biases resulting from differential loss.
- **Data Safety and Security** - Registry custodians should provide transparency for institutional review boards by describing data use agreements, informed consent, data security, and approaches to protecting security including risk of re-identification of patients. If using previously collected data, describe how these address the risk of re-identification of patients and the actual use of data compared with the originally designed and consented use of the data.
- **Data Quality Assurance** - A quality assurance plan for registries should address: 1) structured training tools for data abstractors; 2) use of data quality checks for ranges and logical consistency for key exposure and outcome variables and covariates; and 3) data review and verification procedures, including source data verification plans and validation statistics focused on the key exposure and outcome variables and covariates for which sites may be especially challenged. A risk-based approach to quality assurance is advisable, focused on variables of greatest importance.
- **Document and Explain Any Modifications to the Protocol** - Modifications to a registry protocol may be necessary for a variety of reasons. When modifications are necessary, they should be explained, documented, and made available to anyone planning to use the registry data.

- **Consistent Data Collection** - Clear, operational definitions of data elements should be provided. Create and distribute standard instructions to data collectors. Use standardized data element definitions and/or data dictionaries whenever possible. When creating a new registry, published literature should be reviewed to identify existing, widely used definitions before drafting new definitions.
- **Systematic Patient Enrollment and Follow-up** - Enroll patients systematically and follow them in as unbiased a manner as possible, using similar procedures at all participating sites. Describe how patients and providers were recruited into the study to allow the impact of selection bias to be clearly understood; for example, by explaining whether the sampling was population-based or otherwise and any efforts employed to confirm the quality of adherence to agreed-on enrollment practices.
- **Monitor and Minimize Loss to Follow-up** - Monitor loss to follow-up to ensure that follow-up is reasonably complete for the main objective. Minimizing loss to follow-up requires having a target and advance planning for what actions will be employed in the event that this target is in jeopardy. At the outset of the registry, develop a patient retention plan that documents when a patient will be considered lost to follow-up and what actions will be taken to minimize such loss. At the enrollment visit, consider collecting multiple types of contact information (e.g., telephone, mailing address, and email address) for the patient, as well as collecting contact information for an alternate contact if the patient cannot be reached directly verify contact information at each subsequent visit and update as needed. When a patient misses a visit, contact the patient following a standard protocol (e.g., phone call one day after missed visit, email one week after missed visit). If the patient withdraws from the registry, attempt to document the reason for withdrawal so that issues can be identified and addressed (e.g., overly burdensome patient-reported outcome measures). Efforts at minimizing loss to follow-up should be tempered by considerations and sensitivity to repeated intrusions on patients and to the health conditions and interventions under study. Consider collecting enough information to permit accurate linkage with other data sources, such as the National Death Index, for long-term follow-up.
- **Collect Data to Address Confounding** - Registries should identify important potential confounders during the planning phase and collect reasonably sufficient data on these potential confounders to facilitate the use of appropriate statistical techniques during the analysis phase.

## **DR-2: Selection and use of registries**

Researchers planning PCOR studies relying on registries must ensure that these meet the requirements contained in Standard DR-1 and must document each required feature of the registry(s) to be used (e.g., in an appendix to the funding application or study protocol). Deviations from the requirements should be justified by explaining why a required feature is not feasible or not necessary to achieve the overall goals of Standard DR-1.

## **DR-3: Robust analysis of confounding factors**

In studies that use registries to evaluate the comparative effectiveness or safety of interventions, investigators should select an approach for adjusting for known and measured confounders, such as multivariable regression analysis or propensity scores to create matched comparison groups, or an



instrumental variable analysis if a valid instrument is available. It is also desirable to examine the robustness of the results through sensitivity analyses focused on testing key assumptions and evaluating the likely impact of unmeasured confounders. The rationale for using selected techniques, any assumptions made, and the strengths and limitations of the techniques should be described in reports of the study findings to allow for informed interpretation of the results.

## 7: Standards for Data Networks as Research-Facilitating Structures

### DN-1: Requirements for the design and features of data networks

Data networks established for conducting PCOR must have the following characteristics to facilitate valid, useable data and to ensure appropriate privacy, confidentiality, and intellectual property protections:

- **Data Integration Strategy**—In order for equivalent data elements from different sources to be harmonized (treated as equivalent), processes should be created and documented that either 1) transform and standardize data elements prior to analysis or 2) make transformation logic available that can be executed when data are extracted. The selected approach should be based on an understanding of the research domain of interest.
- **Risk Assessment Strategy**—Data custodians should measure the risk of re-identification of data and apply algorithms to ensure that the desired level of confidentiality is achieved to meet the need of the particular PCOR application.
- **Identity Management and Authentication of Individual Researchers**—Develop reliable processes for verifying credentials of researchers who are granted access to a distributed research network and for authenticating them.
- **Intellectual Property Policies**—A research network should develop policies for the handling and dissemination of intellectual property (IP); networks should also have an ongoing process for reviewing and refreshing those policies. IP can include data, research databases, papers, reports, patents, and/or products resulting from research using the network. Guidelines should balance 1) minimizing impediments to innovation in research processes and 2) making the results of research widely accessible, particularly to the people who need them the most.
- **Standardized Terminology Encoding of Data Content**—The data contents should be represented with standardized terminology systems to ensure that their meaning is unambiguously and consistently understood by parties using the data.
- **Metadata Annotation of Data Content**—Semantic and administrative aspects of data contents should be annotated with a set of metadata items. Metadata annotation helps to correctly identify the intended meaning of a data element and facilitates an automated compatibility check among data elements.
- **Common Data Model**—Individual data items should be assembled into a contextual environment that shows close or distant association among data. A common data model (CDM) specifies necessary data items that need to be collected and shared across participating



institutes, clearly represents these associations and relationships among data elements, and promotes correct interpretation of the data content.

#### **DN-2: Selection and use of data networks**

Researchers planning PCOR studies relying on data networks must ensure that these networks meet the requirements contained in Standard DN-1, and they must document each required feature of the data network(s) to be used (e.g., in an appendix to the funding application or study protocol). Deviations from the requirements should be justified by explaining why a required feature is not feasible or not necessary to achieve the overall goals of standard DN-1.

## **8: Standards for Causal Inference Methods**

#### **CI-1: Define analysis population using covariate histories**

Decisions about whether patients are included in an analysis should be based on information available at each patient's time of study entry in prospective studies or on information from a defined time period prior to the exposure in retrospective studies. For time-varying treatment or exposure regimes, specific time points should be clearly specified and the covariates history up to and not beyond those time points should be used as population descriptors.

#### **CI-2: Describe population that gave rise to the effect estimate(s)**

When conducting analyses that in some way exclude patients from the original study population, researchers should describe the final analysis population that gave rise to the effect estimate(s).

#### **CI-3: Precisely define the timing of the outcome assessment relative to the initiation and duration of exposure**

To ensure that an estimate of an exposure or intervention effect corresponds to the question that researchers seek to answer, the researchers must precisely define the timing of the outcome assessment relative to the initiation and duration of the exposure.

#### **CI-4: Measure confounders before start of exposure and report data on confounders with study results.**

In general, variables for use in confounding adjustment (either in the design or analysis) should be ascertained and measured prior to the first exposure to the therapy (or therapies) under study. If confounders are time varying, specific time points for the analysis of the exposure effect should be clearly specified and the confounder history up to and not beyond those time points should be used in that analysis.

#### **CI-5: Report the assumptions underlying the construction of propensity scores and the comparability of the resulting groups in terms of the balance of covariates and overlap**

When conducting analyses that use propensity scores to balance covariate distributions across intervention groups, researchers should assess the overlap and balance achieved across compared groups with respect to potential confounding variables.

#### **CI-6: Assess the validity of the instrumental variable (i.e., how the assumptions are met) and report the balance of covariates in the groups created by the instrumental variable for all instrumental**

### **variable analyses**

When an instrumental variable (IV) approach is used, empirical evidence should be presented describing how the variable chosen as an IV satisfies the three key properties of a valid instrument:

1. the IV influences choice of the intervention or is associated with a particular intervention because both have a common cause;
2. the IV is unrelated to patient characteristics that are associated with the outcome; and
3. the IV is not otherwise related to the outcome under study (i.e., it does not have a direct effect on the outcome apart from its effect through exposure).

## **9: Standards for Adaptive and Bayesian Trial Designs**

### **AT-1: Specify planned adaptations and primary analysis**

The adaptive clinical trial design should be prospectively planned and the design clearly documented, including:

- potential adaptations, including
- results and populations that be in determining adaptation;
- models to be used; and
- Planned analysis of the primary

The description of the design should be sufficiently detailed that it could be implemented from the description of procedures. The specification of the design should be completed and documented in the trial protocol before enrollment begins. This specification should include, in all but the simplest designs, a statistical analysis plan (SAP) that is separate from the trial protocol in which all necessary detail is provided regarding planned interim and final analyses. Prior specification is a prerequisite for valid and meaningful evaluation of an adaptive design.

### **AT-2: Evaluate statistical properties of adaptive design**

While not necessary for simple designs, the statistical properties of complex adaptive clinical trial designs should be thoroughly investigated over the relevant range of important parameters or clinical scenarios (e.g., treatment effects, accrual rates, delays in the availability of outcome data, dropout rates, missing data, drift in participant characteristics over time, subgroup-treatment interactions, or violations of distributional assumptions). Statistical properties to be evaluated should include Type I error, power, and sample size distributions, as well as the precision and bias in the estimation of treatment effects.

Additional performance metrics may also be evaluated (e.g., the frequency with which specific adaptations occur, the likelihood of substantial covariate imbalance, the likely adequacy of final data for subgroup and safety analyses). The programming code used to create the simulations should be retained with version control. The programming code and software used should be made available to stakeholders who have a need to know, including reviewing agencies.

### **AT-3: Specify structure and analysis plan for Bayesian adaptive randomized clinical trial designs**

If a Bayesian adaptive design is proposed, the Bayesian structure and analysis plan for the trial must be clearly and completely specified. This should include any statistical models used either during the

conduct of the trial or for the final analysis, prior probability distributions and their basis, utility functions associated with the trial's goals, and assumptions regarding exchangeability (of participants, of trials, and of other levels). Specific details should be provided as to how the prior distribution was determined and if an informative or non-informative prior was chosen. When an informative prior is used, the source of the information should be described. If the prior used during the design phase is different from the one used in the final analysis, then the rationale for this approach should be indicated. Utility functions, if employed, should be defined, and their source should be described. Computational issues, such as the choice of software, the creation and testing of custom software, and software validation, should be addressed as well. Software used for Bayesian calculations during trial design, trial execution, and final analysis must be functionally equivalent. When feasible, software or programs should be made available to relevant stakeholders for evaluation and validation.

**AT-4: Ensure clinical trial Infrastructure is adequate to support planned adaptation(s)**

The clinical trial infrastructure, including centralized randomization, data collection related to the assessment and recording of key outcomes, data transmission procedures, and processes for implementing the adaptation (e.g., centralized, web-based randomization), must be able to support the planned trial. In simple adaptive trials, qualitative verification of the capabilities of the proposed trial infrastructure may be adequate. Trials with more complicated requirements, such as frequent interim analyses, require thorough testing prior to trial initiation. Such testing should involve the trial's data collection and data management procedures, the implementation of the adaptive algorithm, and methods for implementing the resulting adaptation(s). The impact on the trial's operating characteristics of delays in collecting and analyzing available outcome data should be assessed. The study plan should clarify who will perform the analyses to inform adaptation while the study is ongoing and who will have access to the results. The interim analyses should be performed and reviewed by an analytical group that is independent from the investigators who are conducting the trial. Trial investigators should remain blinded to changes in treatment allocation rates as this information provides data regarding treatment success.

**AT-5: Use the CONSORT statement, with modifications, to report adaptive randomized clinical trials**

The following sections of the CONSORT statement can be used to report key dimensions of adaptation:

- Adaptation of randomization probabilities (sections 8b and 13a);
- Dropping or adding study arms (sections 7b and 13a);
- Interim stopping for futility and superiority (sections 7b and 14b);
- Sample size re-estimation (sections 7a and 7b);
- Transitioning of stages (e.g., seamless Phase II/III designs) ( sections 3a, 7a, 7b, and 16); and
- Modification of inclusion and exclusion criterion (sections 4a and 13a).

CONSORT sections 16, 20, and 21 may also be expanded to report additional aspects of an adaptive trial.

If the trial incorporates adaptations other than those listed above, the authors should use their judgment as to where in the CONSORT structure to include both design details and the associated results. All possible adaptations included in the prospective design, even if they did not occur, should be included in the report.

## 10: Standards for Studies of Diagnostic Tests

### **DT-1: Specify clinical context and key elements of diagnostic test study design**

A comparative evaluation of diagnostic tests should specify each of the following items and provide rationale in support of the particular choices:

1. the intended use of the test and the corresponding clinical context, including referral for additional testing, referral for additional treatments, and modification of current treatment and target populations;
2. the goal of the comparison;
3. the technical specifications of the tests as implemented in the study;
4. the approach to test interpretation;
5. the sources and process for obtaining reference standard information, when applicable; and
6. the procedures for obtaining follow-up information and determining patient outcomes, when applicable.

These items ought to be specified for all designs, including observational designs (e.g., those using medical records or registries). If these items are not available directly, validated approaches to approximating these study elements from available data should be used.

### **DT-2: Study design should be informed by investigations of the clinical context of testing**

Design of comparative effectiveness studies should outline clinical pathways involving the tests and the anticipated implications of test use on downstream processes of care and patient outcomes. In the written research methods and study protocol, investigators should give examples of clinical pathways to demonstrate thorough understanding of the clinical context.

### **DT-3: Assess the effect of factors known to affect diagnostic performance and outcomes**

Studies of diagnostic tests should include an assessment of the effect of important factors known to affect test performance and outcomes, including the threshold for declaring a “positive” test result, the technical characteristics of the test and the interpreter, and the setting of care.

### **DT-4: Structured reporting of diagnostic comparative effectiveness study results**

Broadly accepted checklists for reporting studies and assessing study quality, such as CONSORT, STARD, and QUADAS, should be consulted and utilized. Consult the CONSORT 2010 checklist for reporting randomized controlled trials. Consult the STARD checklist for reporting diagnostic accuracy studies.

Consult the QUADAS-2 (updated in 2011) for additional guidance on reporting information that would be more useful to systematic reviews of diagnostic accuracy studies.

### **DT-5: Focus studies of diagnostic tests on patient-centered outcomes, using rigorous study designs with preference for randomized controlled trials**

Studies of clinical outcomes after diagnostic testing should use a prospective randomized study design when possible. If a non-randomized design is proposed, the reason for using an observational study (or modeling and simulation) should be addressed and efforts to minimize confounding documented.

## 11: Standards for Systematic Reviews

### **SR-1: Adopt the Institute of Medicine (IOM) standards for systematic reviews of comparative effectiveness research, with some qualifications**

Systematic reviews are used to answer questions based on comprehensive consideration of all the pertinent evidence, and can also identify the gaps in evidence and how they might be resolved. Standards for systematic reviews are currently in use, but credible authorities, such as Cochrane and the Agency for Healthcare Research and Quality (AHRQ), vary somewhat in their recommended standards. The IOM recently issued standards that draw broadly from available sources. The PCORI Methodology Committee endorses these standards but recognizes that there can be flexibility in the application of some standards without compromising the validity of the review, specifically:

- Searches for studies reported in languages other than English are not routinely recommended, but may be appropriate to some topics
- Dual screening and data abstraction are desirable, but fact-checking may be sufficient. Quality control procedures are more important than dual review per se; and
- Independent librarian peer review of the search strategy is not required; internal review by experienced researchers is sufficient.

## Appendix 3. Engagement Rubric

---

### Engagement Rubric for Applicants

Updated: June 6, 2016

Published: February 4, 2014

[Click here to access PCORI's Engagement Rubric online.](#)

#### General Guidance

- The Engagement Rubric illustrates how input from patient and stakeholder partners can be incorporated throughout the entire research process. For additional context, consult the “Why Engage?” website landing page and PCORI’s Conceptual Framework.
- The Engagement Rubric is intended to provide guidance to those planning or conducting research, merit reviewers, awardees, engagement/program officers (for creating milestones and monitoring projects), and interested patients, caregivers, patient/caregiver organizations and other stakeholders, regarding engagement in the conduct of research.
- The rubric is not intended to be comprehensive or prescriptive. Instead, it provides a variety of options to incorporate engagement, where relevant, into the research process. Applicants using the rubric can choose to include some, but not all, activities and are encouraged to include additional innovative approaches not listed here.
- This guidance is based on the promising practices identified in studies from the PCORI portfolio. It is also consistent with PCORI’s Methodology Standards for patient-centeredness and Patient-Centered Outcomes Research (PCOR) Engagement Principles explained below.

#### PCORI Engagement Principles

As you use the rubric and fill out your Engagement Plan, demonstrate how you espouse the six PCORI Engagement Principles in your work. They are:

- **Reciprocal Relationships:** This principle is demonstrated when the roles and decision-making authority of all research partners, including the patient and other stakeholder partners, are defined collaboratively and clearly stated.
- **Co-Learning:** This principle is demonstrated when the goal is not to turn patients or other stakeholder partners into researchers, but to help them understand the research process; likewise, the research team will learn about patient-centeredness and patient/other stakeholder engagement, and will incorporate patient and other stakeholder partners into the research process.
- **Partnerships:** This principle is demonstrated when time and contributions of patient and other stakeholder partners are valued and demonstrated in fair financial compensation, as well as in reasonable and thoughtful requests for time commitment by patient and other stakeholder partners. When projects include priority populations, the research team is committed to diversity across all project activities and demonstrates cultural competency, including disability accommodations, when appropriate.

- Transparency, Honesty, and Trust: These principles are demonstrated when major decisions are made inclusively and information is shared readily with all research partners. Patients, other stakeholders, and researchers are committed to open and honest communication with one another.

## Definitions

- “Patient partners” is intended to include patients (those with lived experience), family members, caregivers, and the organizations that are representative of the population of interest in a particular study.
- It is important that patient partners are not confused with patient subjects; patient partners are members of the research team and involved in the planning, conduct, and dissemination of the research, whereas patient subjects are those individuals actually enrolled into the study as participants.
- “Stakeholder partners” may include members of constituencies based on professional, rather than personal, experience. For example, these constituencies can include: clinicians, purchasers, payers, industry, hospitals and health systems, policy makers, and training institutions. Some individuals may fit into several categories.

## Key Considerations for Planning, Conducting, and Disseminating Engaged Research:

- For the proposed intervention, think through the project from original concept to implementation, and identify the various stakeholders and patients who would need to be included in order for the project to be as successful as possible.
- Think about the budget for your engagement, including compensation for patient and stakeholder partners as well as costs of meetings, IT, and other facilitators of multi-disciplinary work. For additional guidance, PCORI’s [Compensation Framework](#) provides guidance about how best to compensate patient partners serving on research teams. Additionally, PCORI’s [Budgeting for Engagement Activities](#) document provides guidance on how to budget for engagement activities.
- Avoid relying entirely on patient partners who have dual roles on the project (e.g., relying on stakeholders or researchers who also happen to be patients). Including at least one patient partner who has no other role on the project is important.
- There are myriad ways to discuss and demonstrate engagement in a research proposal including asking partners to provide letters of support, bio-sketches thoroughly describing the roles and decision-making authority of all partners, and clear inclusion of engagement activities and compensation in your budget.

## Guidance for Applicants Completing a PCORI Funding Announcement (PFA) Engagement Plan

The Engagement Rubric is divided into three sections; planning, conduct, and dissemination. Each section includes descriptions of the types of activities likely to take place within each phase of research and examples of engagement from PCORI-funded projects. Each numbered section below corresponds to a numbered section in the engagement plan that accompanies each PFA.

**1. PLANNING THE STUDY:** Describe how patient and stakeholder partners will participate in study planning and design. (As you fill out Section 1 of your Engagement Plan, refer to the information below.)

Potential activities include:

- Developing the research question and relevant outcomes to be studied, to ensure that the project and its results will be useful and important to patient and stakeholder communities.
- Defining the characteristics of study participants, to minimize the risk that certain patients will be included or excluded due to criteria that are not relevant.
- Designing the study to minimize disruption to patient and stakeholder study participants, thereby promote retention of study participants.

Real-World Examples:

- Mental health study: Patient partners and community members helped craft the study name and materials to reduce the potential for stigma and to reframe the goal of the study as a movement toward emotional well-being rather than away from a mental health challenge. The anticipated benefit of this input is improved recruitment of study participants and greater acceptance of the study by the community in which it is occurring.
- Large pragmatic study comparing surgery to antibiotics: Over 800 patients were surveyed about their preferences for these treatment options and that input was used to shape the proposal. In this same study, significant clinician input changed the study inclusion criteria, study logistics, and criteria for “failure” for one of the arms.
- Diabetes study: Clinicians who reviewed the initial study design indicated that clinical practice is quite variable and suggested that a three-arm approach would be more appropriate for the study. The study design was revised accordingly and those changes aim to make the study more reflective of real clinical settings.
- Study on use of prescription drug for stroke patients: stroke survivors serving as patient partners on the study identified “home-time” or the number of days when a patient is living at home, not hospitalized or in another institution as an important new outcome. This input from patients was vital in directing the study toward an outcome that they truly cared about.
- Chronic pain study: The initial survey tool was lengthy and to be administered over the phone. Patient partners, feeling that a lengthy phone survey would create a barrier for chronic pain patients, shortened and redesigned the tool to be self-reported and -paced, facilitating greater ease of participation.
- Post-discharge care study: Clinicians have been actively involved in the analysis of initial data runs and have asked key questions that have helped refine the study’s analytic plan. The study is now looking more closely at variations in patterns of care and outcomes.

**2. CONDUCTING THE STUDY:** Describe how patient and stakeholder partners will participate in the study conduct. (As you fill out Section 2 of your Engagement Plan, refer to the information below.)



Potential activities include:

- Drafting or revising study materials and protocols, to ensure feasibility for clinicians and patient participants.
- Participating in recruitment of study participants, to increase and sustain recruitment and ensure viability of the study.
- Participating in data collection and data analysis, to lend unique and varied perspectives on interpretation of the data.
- Participating in the evaluation of patient and stakeholder engagement, to ensure authenticity and value of engagement.
- Serving as a patient representative on a data safety monitoring board, to make the DSMB composition more robust and patient-centered.

Real-World Examples:

- Chronic pain study: The informed consent document is developed with patient partners to make it understandable to study participants. This involvement is anticipated to improve recruitment because potential participants will feel more informed and comfortable.
- Large pragmatic study about chronic pain: Patient partners will assess the patient-centeredness of the care delivered in the study by following (with their consent) the participant through all aspects of study. The observations of the patient partners will be used to improve study processes and make them more patient-centered.
- Asthma study: Clinicians and patients both provided guidance on who should deliver the intervention, when it should be provided during the process of care, and how it should be delivered. These suggestions are intended to make the study more streamlined into the usual provision of care for both patients and clinicians.
- Falls prevention study: A caregiver of aging parents who have experienced falls is serving as a patient/caregiver representative on the project's data safety monitoring board. A patient/caregiver representative serving in that capacity can offer interpretations of benefit, risk, and data analysis from a lived-experience perspective.
- Pediatric surgery study: Parent partners shared that, were they being approached to participate in the study, they'd feel more comfortable if the person discussing the risks and benefits of surgery (and involvement in the study) was a surgeon. When that adjustment was made to the protocol, rates of recruitment increased.

**3. DISSEMINATING THE STUDY RESULTS:** Describe how patient and stakeholder partners will be involved in plans to disseminate study findings and to ensure that findings are communicated in understandable, usable ways. (As you fill out Section 3 of your Engagement Plan, refer to the information below.)

Potential activities include:

- Identifying partner organizations for dissemination, to ensure meaningful and direct connections with end-users.

- Planning dissemination efforts, shaping study design and protocol from the very beginning to be focused on the final product.
- Participating in dissemination efforts, such as authoring manuscripts and presenting study findings, to offer the patient and stakeholder perspective and to reach new and different audiences.
- Identifying opportunities to present or share information about the study, even as it is in progress, to move away from traditional models of dissemination and think more creatively about how to get information into the hands of those who need it.

#### Real-World Examples:

- Trauma study: The research team will convene a policy summit with relevant professional societies during the third year of the study to focus on identifying ways to speed the implementation of findings into practice.
- Care planning study: A national investing and financial planning firm is expanding their educational services to seniors, families, and their own financial planners. This firm will link to the study's website from its national website, and will disseminate the tool through their newsletters, financial planning conferences, and directly to high-impact planners.
- Large pragmatic study comparing surgery to antibiotics: Seven payers, three policymakers, and four large employers provided letters of support for the study and have agreed to disseminate findings to their networks when results are available. This involvement will ensure broad-based and diverse dissemination.
- Neurology study: The research team presented at a neurology patient advocacy conference to inform the community that this research was ongoing and to stay tuned for future results.
- Large pragmatic study about chronic pain: Physical therapists partnering in the study will design a Continuing Education (CE) program that will be delivered as part of the intervention. Patient partners will contribute by providing feedback on what kind of therapy and communication techniques will be more or less likely to be effective during an acute pain episode. Though also used during the course of the study, this CE can be an important dissemination tool upon study conclusion.

## Appendix 4. Human Subjects Checklist

---

### How to Evaluate Human Subjects Protections

January, 2015

[Click here to access detailed guidance for evaluating Human Subjects Protections online.](#)

PCORI requires that research involving human subjects include adequate safeguards. Institutional Review Boards selected by awardees have authority for ensuring the protection of human subjects. PCORI asks merit reviewers to assist with identifying any issues with protection of human subjects that PCORI staff should review with potential funding awardees.

Human subjects protections concerns should not be factored into the application's score, but they should be flagged for PCORI staff by checking the appropriate box and providing written comments in PCORI Online.

The four bullets below provide guidelines that may be helpful to merit reviewers in identifying concerns that PCORI staff should be aware of for any potential awardee. Please note any concerns regarding human subjects protections in your review.

- **Risks to Human Subjects**

Does the application adequately describe human subjects involvement, characteristics, and design; sources of material; and potential risk, including:

- Description and justification for the proposed involvement of human subjects
- Characteristics of subject population (number, age range, and health status, e.g., physical and cognitive functioning)
- Inclusion/exclusion criteria
- Rationale for involvement of vulnerable populations (e.g., fetuses, pregnant women, children, prisoners, institutionalized individuals)
- Role of collaborating sites where research will be performed
- Description and justification of research procedures (including dosage and frequency of intervention)
- Description of what research material, data, and information will be collected
- Access to personally identifiable information collected and retained
- Management and protection of materials and information
- All potential risks to subjects (e.g., physical, psychological, financial, legal) including likelihood and seriousness
- Any alternative treatments or procedures available to subjects in lieu of participation

- **Adequacy of Protection against Risks**

Does the application adequately describe recruitment, informed consent, and protections against risk, including:

- How subjects will be recruited
- Description of informed consent and parental permission and assent
- Waiver for any elements of consent



- How risks described previously, including privacy and confidentiality, will be minimized
  - Additional protections for vulnerable populations
  - Ensuring necessary medical/professional intervention for adverse events
- **Potential Benefits of the Proposed Research to Human Subjects and Others**
  - Does the application adequately describe how potential risks to subjects appear reasonable in relation to anticipated benefits?
- **Importance of the Knowledge to Be Gained**
  - Does the application adequately describe how potential risks to subjects appear reasonable in relation to the importance of the knowledge that may result from the study?