Extended DFRR Instructions

ORGANIZATION OF COMPARATIVE EFFECTIVENESS RESEARCH REPORTS

The following instructions apply to all projects that focus on a comparative effectiveness research (CER) question. The contents of the Methods and Results sections may differ from projects that have non-CER aims, such as qualitative research or instrument development. The DFRR must include all the sections listed below.

- **ABSTRACT**
  - Start on a new page.
  - Prepare an abstract of up to 1000 words that describes for readers the main results of the study and provides the background, methodological details, study limitations, and conclusions.
  - Use language appropriate for general scientific audiences. Spell out all acronyms at first use.
  - Structure the abstract as follows:
    - **Background:** Describe the research question and the methodological gap(s) addressed by the research. Do not put references in the abstract.
    - **Objectives:** State the specific aims of the research.
    - **Methods**: Describe the study population, the research design (i.e., the approach used to address the objectives), interventions, data sources or data sets (as applicable), study outcomes, and methods of analysis and evaluation. Identify the primary outcome(s).
    - **Results:** Report the main results in a format appropriate to the type of research, starting with a description of the study population, followed by the primary outcome. Include numerical results, including 95 percent confidence intervals (95% CI), for at least the primary outcome measure(s). Do not use tables or figures in the abstract.
    - **Conclusions**: State the main conclusions based on the results of the research in one to two sentences. Be sure that they align with the content of the Conclusions section at the end of the report.
    - **Limitations**: Summarize the major study limitations.

- **BACKGROUND**
  - Start on a new page.
  - Provide a concise review of research related to the target condition or problem with healthcare delivery. Cite the principal past studies or a systematic review. Identify the main evidence gaps and explain what would be required to address them (e.g., larger study, multiple sites).
  - State the main research question(s) and the significance and potential impacts of the research as envisioned at the time of the award.
  - Conclude the background with an overview of the study goals and list the specific aims. If these aims have hypotheses, please list them here. Please use consistent language for the aims and hypotheses throughout the report.

- **PATIENT AND STAKEHOLDER ENGAGEMENT**

The Patient and Stakeholder Engagement section starts on a new page.

- Describe how stakeholders were identified, recruited, and retained; the types and number of stakeholders involved; and the engagement activities that occurred or are ongoing related to this research project.
- Describe and provide examples of how patient and stakeholder feedback was obtained and considered, and how it influenced elements of your study (such as developing the research question, designing the study, implementing the study, and disseminating the research results).

Note: PCORI defines patient and stakeholder engagement as partnership in the research enterprise. Your description should not include activities of study participants who might have engaged in focus groups or other activities described in the study protocol. Please describe these activities in the Methods and Results sections.

You may list the names of your patient and stakeholder partners (i.e., co-investigators, consultants, advisors) in the DFRR, along with their roles and expertise to show the diversity of the partnerships andacknowledge their involvement. However, all partners need to be informed if their names will be listed and should acknowledge their consent through some written communication before their names are listed. This is also true for any individuals that you list as part of your Acknowledgments.

- **METHODS**

Provide a detailed account of the elements in this section in the order listed here. If the project has more than one aim and the aims have distinct methods and results, consider organizing the Methods and Results sections of the study by aim rather than including methods for all aims in one section, followed by all results. You may find that some items on the following list of headings are not pertinent to a specific aim. It is up to you to decide when to include or exclude specific headings. For instance, "Study Setting" may be relevant only for prospective studies based in real-world settings, rather than for large database studies. Also, if you organize by study aim, please include a brief descriptive title for the study aim in the section containing methods or results for the study aim.

Study Overview:

- Describe the big picture to orient the reader before you get into the details of your study.
- Provide a brief paragraph to restate for the reader the study aims and the methods planned to achieve those aims, including the overall study design.
- Consider including a figure that illustrates the study flow, especially if there are multiple overlapping aims.

Study Setting:

- Describe the study setting(s) and the reasons for choosing it/them. This section could apply to the choice of a data set or registry for an observational study but may not be applicable for some types of studies.

Participants:

- Describe how study participants were identified, selected, recruited, enrolled, and assigned to the intervention and comparison groups to minimize potential impacts of selection bias.
- Describe the methods for generating random allocation sequences and any steps taken to conceal allocation.
- If cluster randomization was used, describe the eligibility criteria for the study clusters and procedures for stratifying or matching clusters.
- Among eligible individuals, describe how reasons for declining participation were determined.

- List the complete inclusion and exclusion criteria.
- If the study design is *retrospective*, describe the database, cohort, or registry and why you chose it.

Interventions and Comparators or Controls:

- Describe how the chosen comparators represent appropriate interventions in the context of the relevant study framework, reduce the potential for biases, and allow direct comparisons.
- If the comparator is "usual care" or "treatment as usual," describe how it represents a legitimate and coherent clinical option.
- Describe the duration of the intervention and comparator conditions and how the use of the intervention by individual participants is measured.
- If the study is a cluster randomized trial, indicate whether the interventions are directed at the cluster level or the individual participant level, or both.
- If the interventions are performed according to a specific sequence of tasks and events, include a table or figure illustrating the order of tasks in the intervention, with brief descriptions of each task. For instance, the table for a group-based psychosocial intervention could list the meeting topics with one to two sentences describing what happens at each meeting.

Study Outcomes: Describe the study outcomes, listing primary and secondary outcomes separately, and identify patient-reported outcomes.

- Explain why you selected these outcomes and how they are relevant for patients and clinicians. Identify outcome measurement instruments by their full name, explain why they were chosen, and cite references that describe their reliability and validity.
- Provide the minimal clinically important difference (MCID) for primary outcomes when available, explain how it was determined, and provide a reference.

Covariates: Describe the sources of other measures used in the study, including any measures of baseline characteristics or subgroups.

Sample Size Calculations and Power: State the target sample size and discuss how you calculated it based on the MCID of your primary outcome and estimates of effect size and their variance.

- For cluster randomized studies, describe your process for determining the number and size of clusters and methods used to reflect dependence.
- For observational studies, describe how you decided on the study size.

Time Frame for the Study: Describe the length of the intervention period and the follow-up schedule and why you chose it. A figure such as a Gantt chart may be helpful here.

Data Collection and Sources: If applicable, describe your processes for making follow-up contact with each patient, your efforts to maximize the follow-up rate, and the protocol for making contact before declaring a participant to be lost to follow-up. Describe how you ascertained the reasons given by participants who withdrew from the study or became lost to follow-up. If the study is retrospective, describe the origin of each database, cohort, or registry and any problems with missing data (and the likely causes).

Analytical and Statistical Approaches: This section should contain detail sufficient to inform someone who wants to replicate your study. Provide detailed analytic plans for each of your hypotheses. Please explain any differences between the study population as randomized and the study population on which you based your analyses. Clearly label your primary analysis (intent-to-treat, complete case, etc.). Describe key assumptions of the analytic methods and whether the study satisfied them. If there is considerable loss to follow-up of study participants, be sure to describe in detail how you handled missing data (e.g., multiple imputation, maximum likelihood analyses, sensitivity analyses), including your rationale, if any, for assuming missingness at

random, as appropriate.

- As applicable, describe methods for identifying heterogeneity of treatment effect in subgroups (univariate analyses versus risk-stratification models).
- For observational studies, describe how you dealt with confounding (e.g., propensity score, instrumental variables, and sensitivity analyses [e.g., E-value]).
- Link your prespecified statistical plans to each study aim or outcome to which they apply, being clear when you used different statistical methods for different aims or outcomes. Identify any preplanned sensitivity analyses or post-hoc, exploratory analyses (i.e., not originally proposed but planned after learning the main study results).

Changes to the Original Study Protocol: Describe any important study modifications from the protocol as originally approved. Based on the CONSERVE 2021 statement, important modifications are those that "could have a potentially meaningful effect on the study's objectives or research question; ethical acceptability, including benefits and harms to participants; internal validity and generalizability; feasibility; or analytical methos and statistical power." Confirm PCORI and/or IRB approval and explain the reasons for any IRB-required or otherwise necessary protocol modifications.

- **RESULTS**

Present the key findings as they relate to the research questions and specific aims of the project, supported by the relevant tables and figures. The presentation of the study findings should adhere to the appropriate reporting guidelines and expectations for the type of methodological research conducted (check the EQUATOR Network for a variety of study designs).

Some reports may need to follow more than one reporting guideline because the aims differ in their study designs (e.g., aim 1, Systematic Reviews (PRISMA); aim 2, Prognostic and Prediction Studies (TRIPOD), etc.). Other reports may need to follow one of the extensions. This article provides a comprehensive review of the most common reporting guidelines for clinical trials (e.g., Consolidated Standards of Reporting Trials [CONSORT]). Like the study methods, the study results may be presented by study aim if the aims are sufficiently distinct that the narrative would be clearer. Either way, please present the results in the order specified below:

- Begin the results with an overview of participant flow through the study interventions, indicating the number of participants who were "lost to follow-up." Include here a participant flow diagram that shows the study population at different times in the study:
  - Employ a CONSORT diagram for randomized trials and a similar flow diagram or a table for observational studies. These figures should show the number of people potentially eligible, those examined for eligibility, those confirmed as eligible, those who agreed to participate, those randomly assigned to each intervention/comparator, those who completed follow-up, and those analyzed.
- List the reasons for ineligibility, unwillingness to participate, failure to complete follow-up, and other exclusions from the analytic data set, and provide the numbers of patients for each reason.
- If the study population differs for any aim or research question, provide a separate flow diagram if this information cannot be accommodated in the main flow diagram. In the text of the overview, please indicate the lost-to-follow-up rate for the primary outcome for each study arm.
- Include a table that describes the rates of the baseline characteristics of the total sample and the study arms, and any analyses used to determine group differences at baseline. The use of *P* values to determine whether differences in baseline characteristics are important is not appropriate in randomized trials. Present standardized differences in baseline characteristics by

treatment group to allow the reader to compare the magnitude of differences between groups.

- Organize the presentation of outcomes by the order in which the research questions or specific aims were listed earlier in the report. Be sure to include results for all outcomes and analyses that were part of your PCORI award. As with the Methods section, when you use headings like "Aim 1", please include a short title. When providing data on the outcomes, please provide absolute values and 95% CI for each outcome for each study arm in addition to effect estimates (ratios, differences, or difference-in-differences and their respective 95% CI). Give the exact *P* value (e.g., *P* = .03 instead of *P* < .05).
- Present study results in the following order:
  - Primary outcome analyses
  - Secondary outcome analyses
  - Heterogeneity of treatment effects or subgroup analyses
  - Sensitivity analyses (may be summarized in the text and presented in detail in one or more appendices)
  - *Post-hoc* or exploratory analyses
- For qualitative study aims (e.g., interviews with participants or staff), refer to the section below on qualitative study descriptions.

- **DISCUSSION**

Start the discussion with a succinct recap of the main results for the study. Describe the place of the results within the body of evidence in the existing literature. Discuss the potential for the results to help stakeholders make healthcare decisions. Discuss the relationship between primary and secondary outcomes and give your judgment about the effectiveness of the intervention, if applicable.

Consider the lessons learned that can help others prepare similar research or implement the interventions discussed in this report. Discuss, as applicable, the potential for generalizability of the study results. As required by the authorizing law, include a section on "considerations specific to certain sub-populations, risk factors, and co-morbidities, as appropriate." Similarly, give a critical appraisal of the strengths and limitations of the research. Finally, provide concise, targeted recommendations for future research.

Use the following headings as appropriate:

- Summary of Results
- Results in Context
- Potential to Impact Healthcare Decision-Making
- Lessons Learned
- Generalizability
- Subgroup Analyses or Heterogeneity of Treatment Effects
- Study Limitations
- Future Research

- **CONCLUSIONS**

Provide a high-level summary of the principal aim of the research, the primary outcome findings, and the study implications. Consider the strength of the evidence supporting your conclusions, taking into account the internal validity (strengths and limitations of the study) and external validity (relevance to other populations) of the results. If the study is negative for the primary outcome, be conservative in interpreting positive secondary results.

- **REFERENCES**
  - Authors are responsible for ensuring the accuracy of citations. Check for any duplicate or incomplete references before finalizing the reference list. If changes are necessary, recheck the numbering in the text itself.
  - Format citations and references according to AMA Manual of Style. Number the references in the order of their appearance in the text.
- **ACKNOWLEDGMENTS**
  - If applicable, please acknowledge any specific patients, stakeholders, or study staff who made a special contribution to the study. Be sure to inform anyone you acknowledge that their name will appear in the report and obtain their written consent to be listed.
  - Please limit acknowledgments to one page, except under unusual circumstances.
- **RELATED PUBLICATIONS**
  - List all journal publications (identified as submitted, in press, or published) resulting from the research supported by this PCORI award.
- **SHARING DATA SETS AND DATA DOCUMENTATION**
  - If applicable, please describe your data sharing plans per the policy, including where you will be depositing the data, the expected makeup of the data sets, and the approximate date of deposit.

ORGANIZATION OF METHODS PROGRAM RESEARCH REPORTS

DFRRs for PCORI Methods projects are organized differently because they typically are not experimental in design. Therefore, many of the requirements for most PCORI-funded DFRRs do not apply.The DFRR must contain the following sections.

- **ABSTRACT**
  - Start on a new page.
  - Prepare an abstract of up to 1000 words that describes for readers the main results of the study and provides the background, methodological details, and conclusions needed to interpret the results.
  - Use language appropriate for general scientific audiences. Spell out all acronyms at first use.
  - Structure the abstract as follows:
    - **Background:** Describe the research question and the methodological gap(s) addressed by the research. Do not put references in the abstract.
    - **Objectives:** State the specific aims of the research.
    - **Methods:** Describe the research design (i.e., the approach used to address the objectives), data sources or data sets (as applicable), study outcomes, and methods of analysis and evaluation. Identify the primary outcome.
    - **Results:** Report the main results in a format appropriate to the type of research. Include numerical results for at least the primary outcome measure.
    - **Conclusions:** State the main conclusions based on the results of the research.
    - **Limitations:** Include a summary of the major study limitations.

- **BACKGROUND**
  - Start on a new page.
  - Provide a concise introduction to the methodological gap(s) in patient-centered outcomes research/comparative effectiveness research (PCOR/CER) addressed by the research. At the end of the section, state the goals of the proposed research, including the specific aims and the potential impact of the research as envisioned at the time of the award.

- **PATIENT AND STAKEHOLDER ENGAGEMENT**
  - Start on a new page.
  - Consult PCORI Methodology Standard PC-1 to describe the involvement of patients and other stakeholders as partners in this study.
  - Describe how stakeholders were identified, recruited, and retained; the types and number of stakeholders involved; and the engagement activities that occurred or are ongoing related to this research project.
  - Describe and provide examples of how patient and stakeholder feedback was obtained and considered, and how it influenced elements of your study (such as developing the research question, designing the study, implementing the study, and disseminating the research results).

Note: PCORI defines patient and stakeholder engagement as partnership in the research enterprise. Your description should not include activities of study participants who might have engaged in focus groups or other activities described in the study protocol. Please describe these activities in the Methods and Results sections.

For research that did not involve patient and/or other stakeholder engagement, please explain the reasons that engagement with patients and/or other stakeholders was not considered for this study.

You may list the names of your patient and stakeholder partners (i.e., co-investigators, consultants, advisors) in the DFRR, along with their roles and expertise to show the diversity of the partnerships andacknowledge their involvement. However, all partners need to be informed if their names will be listed and should acknowledge their consent through some written communication before their names are listed. This is also true for any individuals that you list as part of your Acknowledgments.

- **METHODS**

Describe the research strategy for addressing the identified methodological gaps. Describe the following elements sufficiently to allow readers to understand and assess the research as it was conducted.

- **Research Design** (e.g., theory development, simulation studies, primary data collection, secondary data analyses)
- **Data Sources and Data Sets** (as applicable), including justification for the selection of a particular source or data collection method
- **Analytical and Evaluative Approach** (i.e., how the methods were evaluated), including outcome measures and investigation of underlying assumptions
- **Changes to the Original Study Protocol:** Describe any important study modifications from the protocol as originally approved. Based on the CONSERVE 2021 statement, important modifications are those that "could have a potentially meaningful effect on the study's objectives or research question; ethical acceptability, including benefits and harms to participants; internal validity and generalizability; feasibility; or analytical methos and statistical power." Confirm PCORI and/or IRB approval and explain the reasons for any IRB-required or otherwise necessary protocol modifications.

- **RESULTS**

Present the key findings as they relate to the research questions and specific aims of the project, supported by the relevant tables and figures. The presentation of the study findings should adhere to the appropriate reporting guidelines and expectations for the type of methodological research conducted (check the EQUATOR Network for a variety of study designs). Some reports may need to follow more than one reporting guideline because the aims differ in their study designs (e.g., aim 1, Systematic Reviews [PRISMA]; aim 2, Prognostic and Prediction Studies [TRIPOD], etc.). Other reports may need to follow one of the extensions. Like the study methods, the study results may be presented by study aim if the aims are sufficiently distinct that the narrative would be clearer. Either way, please present the results in the order specified below. The most common types of study designs that PCORI funds include the following:

- Clinical trials (CONSORT)
- Observational studies (STROBE and RECORD)
- Systematic reviews (PRISMA)
- Diagnostic studies (STARD)
- Prognostic and prediction studies (TRIPOD)

- Qualitative/mixed-methods (SRQR and COREQ)

As applicable, when providing data on the study outcomes, please provide the relevant units and absolute values for each outcome, as well as 95% CIs for the key statistic and the exact *P* value (e.g., *P* = .03 instead of *P* < .05).

- **DISCUSSION**

Describe the key findings within the existing scientific literature, discussing the potential for the results to advance methods for PCOR/CER and to improve the validity, trustworthiness, and usefulness of PCOR/CER findings. This discussion should include a critical appraisal of the strengths and limitations of the research. As required by the authorizing law, discuss "considerations specific to certain sub-populations, risk factors, and co-morbidities, as appropriate." Finally, provide concise, targeted recommendations for further research, if appropriate.

Use the following headings as appropriate:

- Summary of Results
- Results in Context
- Potential to Impact Healthcare Decision-Making (if applicable)
- Lessons Learned
- Generalizability
- Subgroup Analyses or Heterogeneity of Treatment Effects (if applicable)
- Study limitations
- Future research

- **CONCLUSIONS**

Briefly summarize the results and supporting evidence, including any threats to the reliability and validity of the findings attributable to limitations of the research. Describe the significance of these findings to the relevant PCOR/CER stakeholders.

- **REFERENCES**
  - Authors are responsible for ensuring the accuracy of citations. Check for any duplicate or incomplete references before finalizing the reference list.
  - Format citations and references according to AMA Manual of Style. Number the references in the order of their appearance in the text.

- **ACKNOWLEDGMENTS**
  - If applicable, please acknowledge any specific patients, stakeholders, or study staff who made a special contribution to this study. Be sure to inform anyone you acknowledge that their name will appear in the report and obtain their written consent to be listed.
  - Please limit acknowledgments to one page, except under unusual circumstances.

- **RELATED PUBLICATIONS**
  - List all journal publications (identified as submitted, in press, or published), preprints, or software packages resulting from the research supported by this PCORI award.

REPORTING QUALITATIVE METHODS AND RESULTS IN THE DFRR

Many PCORI-funded research projects include multiple or mixed methods (i.e., qualitative and quantitative). In such cases, investigators need to incorporate a description of the qualitative methods and results into the DFRR structure described above. Describing the qualitative elements often means adding subsections to the Methods and Results sections of the report. Please use well-researched and recommended standards for reporting these details. The EQUATOR Network has several relevant standards for reporting qualitative data. Another resource is the Standards for Reporting Qualitative Research.

The following elements should be included when writing the Methods and Results for qualitative research:

- **METHODS**
  - **Study Design:** Please describe the methodological congruence of the elements of the study design. The purpose, questions, and methods of research are all interconnected and interrelated; being clear about the relationships helps ensure that the study appears as a cohesive whole rather than fragmented isolated parts. Be clear if the study design is a multi-method design (for instance, if you conducted qualitative interviews that informed your comparative effectiveness trial) or if it is a mixed-methods design (i.e., qualitative and quantitative components combined for one aim). If mixed methods, please describe when the data were integrated and why the mixed methods were necessary. Report the qualitative approach, research paradigm, or guiding theory (e.g., phenomenological, grounded theory, case study).
  - **Sampling Strategy:** Please specify, for example, whether sampling was purposive, stratified purposive, snowball, convenience, or maximum variation. Give the inclusion and exclusion criteria and describe how the sample size was determined.
  - **Data Collection Methods:** Please describe approaches such as focus groups, one-on-one interviews, and observations, and explain the relationship of the method(s) to the research question(s). Describe how the data collection tool (e.g., the guide for interviews or focus groups) was developed. Explain how (if needed) it was modified during the data collection process and give the rationale for refinements in the context of the research question(s). Provide information on data collection, such as audio recording, transcribing, and field notes.
  - **Data Analysis:** Please describe the coding scheme and the iterative process used to create it, the number of coders and brief description of their training, assessment of inter-rater reliability, analytic software used, data management, and verification of data integrity. Describe thematic saturation, including the iterative process of data collection and analysis to arrive at this point. Discuss the final sample size based on this process.

- **RESULTS**
  - **Synthesis and Interpretation:** Please cover these points in the main findings, including those

contributing to the development of a theory or model.
    - Empirical data, specifically quotes, text excerpts, and field notes

- **DISCUSSION**
    - Summarize the qualitative findings.
    - Describe how the qualitative findings relate to the CER results.
    - Include qualitative methods and results in discussions of study strengths, limitations, futureresearch, and conclusions, as appropriate.

Investigators should use their best judgment in deciding whether to include additional information about the qualitative parts of their research projects in the DFRR. The goals are to include enough information so that readers can fully understand the study procedures and outcomes and that otherscan replicate the procedures in another study. Investigators may consider putting longer illustrative quotes, field notes, and interview guides into an appendix.