Methods Consultation Panel for Pragmatic Clinical Studies: Evaluation and Recommendations

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Overview

- Evaluation Rationale and Methods
- Evaluation Findings – Spring 2014 PCS
- Evaluation Update – Fall 2014 PCS
- Recommendations
Purpose of Merit Review and Methods Consultation

**Merit Review**

- Identify applications with potential to help patients and other stakeholders make informed decisions to improve health outcomes
- Elicit high-quality feedback from diverse perspectives to ensure that funded research:
  - meets the criteria for scientific rigor, and
  - reflects the interests of patients and those who care for them

**Methods Consultation Panel (MCP)**

- Additional, focused assessment of methods
- Identify strengths, weaknesses, and recommended solutions for weaknesses
- Rate criticality of weaknesses and feasibility of solutions
- Inform funding decisions and PIR (PCORI information requests)
Spring 2014 PCS Review: Guidance on Assessing Project Methods

Merit Review
Criterion 3: Technical Merit

The proposal has sufficient technical merit to ensure that the study goals will be met. It includes:

- A clear research plan with rigorous methods that adhere to PCORI’s Methodology Standards and prevailing accepted best practices
- A clear and adequate justification for the study design choices in the proposed pragmatic trial
- A realistic timeline that includes specific scientific and engagement milestones
- A research team with the necessary expertise and an appropriate organizational structure
- A research environment, including the delivery systems that will host the study, that is well-resourced and highly supportive of the proposed study

Methods Consultation
Written Assessment Form

1. Study Design
   - Participants, interventions, outcomes, sample size, treatment assignment, blinding

2. Study Conduct and Analyses
   - Data and safety monitoring, data management, missing data, HTE, causal inference

3. Overall Assessment of Application’s Proposed Methods
   - Is design adequate for study purpose?
   - Does healthcare decision that the study will inform match proposed design?
   - Are there any design dimensions that, if modified, would help the design better address the question proposed?
Evaluation Approach: Quantitative and Qualitative Information

• **Tracking Applications in Review Processes:**
  • # projects sent for Methods Consultation
  • # projects funded conditionally or not funded based on Methods Consultation

• **Written Reviewer Assessments:**
  • # and type of changes recommended (e.g., sample size, outcome measures)
  • Uniqueness relative to the Merit Review
  • Method Consultation Panelists’ rating of the importance and feasibility of recommended changes

• **Staff and Methods Consultation Panelist Debriefs:**
  • Procedural feedback
  • Perceptions of the impact of the consultation
  • Incorporating recommendations from consultation with applicants
Methods: Qualitative Analysis (Spring 2014)

• Sampled 10 of 22 applications based on funding status and Merit Review scores

• Data Extraction (Strengths & Weaknesses)
  • Methods Consultation: comments from Section 1 (Design) and Section 2 (Study Conduct and Analyses)
  • Merit Review: comments from the Technical Merit Criterion section for the three Scientific Reviewers

• Data Coding (Weaknesses)
  • Created a predetermined list of weakness categories from Methods Consultation written assessment template
  • Compared Merit Review and Methods Consultation weakness comments for uniqueness
Number of Strengths & Weaknesses Identified by Scientist Reviewers in Merit Review and Methods Consultation (Spring 2014)

N= 10 sampled applications

Criteria 1-5 from Merit Review (3 Scientific Reviewers)
Methods Consultation (1 Scientific Reviewer)
Categorizing Comments on Methodological Weaknesses (Spring 2014)

Design
- Participants
- Interventions
- Outcomes
- Sample size
- Treatment assignment
- Blinding
- Design- Other

Study Conduct & Analyses
- Data and safety monitoring
- Data management
- Missing data
- Heterogeneity of Treatment Effect
- Causal inference
- Study Conduct & Analyses- Other

# of Comments

N= 10 sampled applications

PATIENT-CENTERED OUTCOMES RESEARCH INSTITUTE
Methods Consultation Weaknesses that Duplicated Merit Review Weaknesses

84% of the weaknesses from the Methods Consultation were unique from the Merit Review

N= 22 Duplicative Weaknesses

PATIENT-CENTERED OUTCOMES RESEARCH INSTITUTE
Methods Consultants’ Rating of Importance of Weaknesses

- **Minor**: the validity of the study result is unlikely to materially change
- **Moderate**: the validity of the study result could be materially affected
- **Major**: the validity of the study result is seriously threatened; the study probably should not be done if this isn’t addressed

*N= 167 Weakness Comments*
Methods Consultation: Recommendations

Recommendations were provided for 98 (59%) of the weaknesses identified.

Panelists’ Ratings of Difficulty to Implement Recommendations

- Low: 30%
- Moderate: 41%
- High Difficulty: 20%
- Unrated: 9%

N= 98 Recommendations
Use of Feedback from Methods Consultations

Process:
- Incorporated into PCORI Information Requests (PIR)
- Conversations between program staff and PI
- Option of additional consultation with methods consultants

Outcomes reported by PCORI staff:
- Opportunity to carefully consider and discuss rationale for decisions
- Increased communication between PCORI staff and PIs
- Higher confidence in methods decisions
- In some cases, changes to study design
Feedback from the Methods Consultation Panelists

- More guidance needed regarding the scope of their review
- Requests to receive all application materials and appendices
- Most reviewers liked receiving the Merit Review critiques and saw value in identifying new issues or validating their own views
- Recommendations for Merit Review
  - More statistical expertise on review panels
  - More space in applications to describe study design
Feedback from PCORI Staff – 1

• Consultation yielded high-quality critiques and additional useful information about study methods

• Consultation didn’t find any fatal flaws that changed funding decisions

• Recommended solutions have the potential to be a major value added

• Importance of getting strong methodological reviewers in the merit review
Feedback from PCORI Staff – 2

• Clarity needed regarding the purpose and scope

• Obtain consultation for a targeted set of applications with specific methodological questions/concerns

• Merit Review critiques should be used to steer the Methods Consultation
  o Goal is not an “independent” second review

• Need more time to consider which applications need Methods Consultation
Recommendations: Consider a Phased Approach

- Methods Consultation can adapt as Merit Review process is refined
Fall 2014 PCS

Understanding differences compared to Spring 2014
Fall 2014 PCS: Technical Merit Criterion

• Is there a clear research plan with rigorous methods that adhere to PCORI’s Methodology Standards and prevailing accepted best practices?
• Is there a clear comparison condition that is a realistic option in standard practice? Is the comparator sufficiently described to reasonably compare the two or more conditions in the trial?
• Are the proposed comparative conditions currently in use? Is there prior evidence of efficacy or effectiveness for the interventions being compared?
• Is there evidence that the outcome measures are sufficiently sensitive to identify differences between groups?
• Is the study conducted in a patient population that is relevant to the majority of patients with a condition or to a previously understudied subgroup?
• Are the pre-specified subgroups reasonable given the proposed interventions and condition?
• Are the subgroups sufficiently large to allow a rigorous and valid comparative analysis?
• Is the budget appropriate for the proposed research?
• Is there a clear and adequate justification for the study design choices in the proposed pragmatic trial?
• Is there an adequate plan for protection of human subjects participating in this study?
• Do the applicants provide evidence of study feasibility based on availability of participants and experienced staff for efficient start-up?
• Does the project include a realistic timeline that includes clear and specific scientific and engagement milestones?
• Does the research team have the necessary expertise and prior experience conducting large-scale multicenter trials and an appropriate organizational structure to successfully complete the study?
• Is the research environment, including the delivery systems that will host the study, well-resourced and highly supportive of the proposed study?
Methods: Qualitative Analysis (Fall 2014)

- **Sampled 10 of 16 applications** based on funding status and Merit Review scores

- **Data Extraction (Strengths and Weaknesses)**
  - Methods Consultation: comments from Section 1 (Design) and Section 2 (Study Conduct and Analyses)
  - Merit Review: comments from the Technical Merit Criterion section for the three Scientific Reviewers

- **Data Coding (Strengths and Weaknesses)**
  - Identified comments from Spring and Fall 2014 Merit Review Critiques on
    - Heterogeneity of Treatment Effect (subgroup analyses)
    - Data and Safety Monitoring
Strengths & Weaknesses Identified by Scientist Reviewers in Merit Review and Methods Consultation By Review Cycle

- **N= 10 sampled applications**
- **Criteria 1-5 from Merit Review (3 Scientific Reviewers)**
- **Methods Consultation (1 Scientific Reviewer)**

**Criteria**
- Criterion 1
- Criterion 2
- Criterion 3
- Criterion 4
- Criterion 5
- Methods Consultation

**Strengths**
- **Criteria 1**: 79 (Sp14), 68 (Fa14), 33, 17
- **Criterion 2**: 95 (Sp14), 48, 58
- **Criterion 3**: 123 (Sp14), 169 (Fa14), 120
- **Criterion 4**: 76 (Sp14), 66 (Fa14), 28, 32
- **Criterion 5**: 74 (Sp14), 84 (Fa14), 16, 36
- **Methods Consultation**: 70 (Sp14), 84 (Fa14), 167, 164

**Weaknesses**
- **Criterion 1**: 16
- **Criterion 2**: 17
- **Criterion 3**: 16
- **Criterion 4**: 16
- **Criterion 5**: 16
- **Methods Consultation**: 16

**Institute**
- **Patient-Centered Outcomes Research Institute**
Summary of Findings:

• Methods Consultation identified additional methodological weaknesses and provided value for PCORI program staff

• More clarity on the scope and purpose needed
  • Focus on projects likely to be funded and opportunities for enhancement of project methods
  • Opportunity to address specific concerns from Merit Review or PCORI staff

• Indications that modifications to Merit Review can enhance review of proposal methods
Recommendations: Methods Consultation

• Be clear with staff, merit reviewers, and methods consultants about the purpose and scope of Merit Review and Methods Consultation, including how the information will be used.

• Use Methods Consultation for targeted consultation on methodological issues and solutions for specific concerns or questions identified in Merit Review or by PCORI program staff.

• Allow time for Program Staff to thoughtfully identify applications for Methods Consultation.

• Provide Methods Consultants with the Merit Review critiques (all reviewers, including patient/stakeholders) and summary statements to provide full context for methodological questions/concerns.
Other Implications

• What do we **ask for** in our Merit Review? Do we get it?

• What do we **want** from our Merit Review? Is this what we ask for?

• Revisiting guidance to applicants—are we clear in our expectations regarding methodological rigor and study design?
Appendix
## Coding Taxonomy: Study Design

<table>
<thead>
<tr>
<th>Category</th>
<th>Examples</th>
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</thead>
<tbody>
<tr>
<td><strong>Participants</strong></td>
<td>Study eligibility criteria, enrollment issues, recruitment settings</td>
</tr>
<tr>
<td><strong>Interventions</strong></td>
<td>Comparator intervention, timeline for implementing intervention, treatment leakage (<em>exposure to multiple interventions</em>), treatment fidelity, intervention feasibility</td>
</tr>
<tr>
<td><strong>Outcomes</strong></td>
<td>Outcome ascertainment (<em>follow-up methods, lag time</em>), determination of baseline characteristics, detection bias</td>
</tr>
<tr>
<td><strong>Sample size</strong></td>
<td>Power analysis, detection of effect</td>
</tr>
<tr>
<td><strong>Treatment assignment</strong></td>
<td>Randomization, stratification variables</td>
</tr>
<tr>
<td><strong>Blinding</strong></td>
<td>Allocation concealment</td>
</tr>
<tr>
<td><strong>Design - other</strong></td>
<td>External validity/generalizability, study complexity, lack of clarity or rationale for design decisions, challenges for implementation, incentives</td>
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</tbody>
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# Coding Taxonomy: Study Conduct & Analyses

<table>
<thead>
<tr>
<th>Category</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Data and safety monitoring</strong></td>
<td>DSMB expertise (<em>particularly biostatistics</em>), procedures for safety monitoring</td>
</tr>
<tr>
<td><strong>Data management</strong></td>
<td>Logistical data collection issues, <em>data</em> cleaning, use of technology (<em>electronic medical records</em>), data management team expertise</td>
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<td><strong>Statistics: missing data</strong></td>
<td>Loss to follow-up, analytic methods for handling missing data</td>
</tr>
<tr>
<td><strong>Statistics: heterogeneity of treatment effect</strong></td>
<td>Treatment heterogeneity, subgroup analyses</td>
</tr>
<tr>
<td><strong>Statistics: causal inference</strong></td>
<td>Confounding, Type I &amp; Type II error</td>
</tr>
<tr>
<td><strong>Study conduct &amp; analyses - other</strong></td>
<td>Lack of information for analysis plan and statistical methods, specific proposed statistical methods</td>
</tr>
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