Developing a CER Question and Submitting a Letter of Intent

Diane Bild, MD, MPH
Senior Program Officer
Clinical Effectiveness Research

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PATIENT-CENTERED OUTCOMES RESEARCH INSTITUTE

In This Session

- What PCORI is seeking in Comparative Effectiveness Research (CER)
- Developing a CER question
- Elements of the Letter of Intent (LOI)
- Pitfalls and tips for the LOI
- Questions and answers!

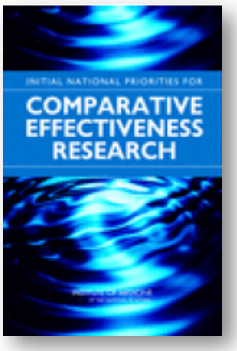
Why the LOI is So Important

- Allows PCORI to convey what we are seeking, concisely
- Enables investigators to concisely convey the CER question to PCORI
- Minimizes wasting time writing and reviewing long proposals

Comparative Effectiveness Research (CER)

Why We Need CER

" . . . for want of appropriate studies, innumerable practical decisions facing patients and doctors every day do not rest on a solid foundation of knowledge about what constitutes the best choice of care."

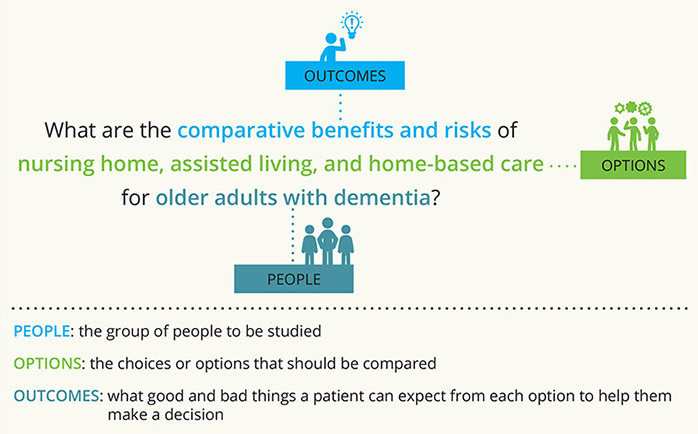


Institute of Medicine Report June 2009

Developing a CER Question

- Base it on well-documented evidence gaps as well as input from patient and other stakeholder groups.
- Propose to compare strategies or interventions.
- Include patient-centered outcomes, including, as appropriate, patient-reported outcomes.

How to Write a Practical & Useful Research Question

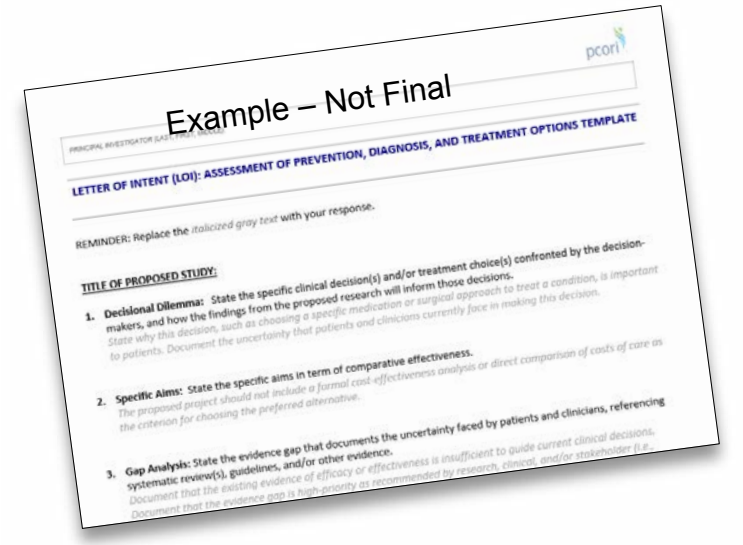


http://www.pcori.org/get-involved/suggest-patient-centered-research-question/how-write-practical-useful-research-question

Elements of the Letter of Intent

- Sections shown in the following slides are representative only

LOI: Find Template at PCORI Funding Center Corresponding to the Program of Interest



LOI Sections: Specific Aims

- State the specific aims in term of comparative effectiveness.

  - *Clearly state the main purpose of the study.*
  - *Do not include a formal cost-effectiveness analysis or direct comparison of costs of care as the criterion for choosing the preferred alternative.*

LOI Sections: Decision Dilemma

- State the specific clinical decision and/or treatment choices confronted by the decision-makers.

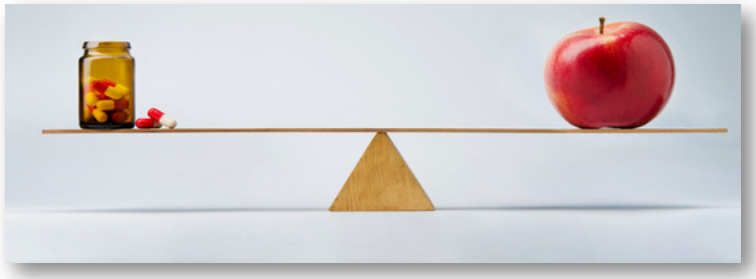
  - *State why this decision is important to patients.*
  - *Make it clear how this research will provide valuable information.*

LOI Sections: Gap Analysis

- State the evidence gap that underlies the uncertainty faced by patients, clinicians, and other decision makers
  - *Document the lack of existing evidence*
  - *Cite relevant systematic reviews, guideline gaps, or recommendations for CER from groups such as the Institute of Medicine and AHRQ*

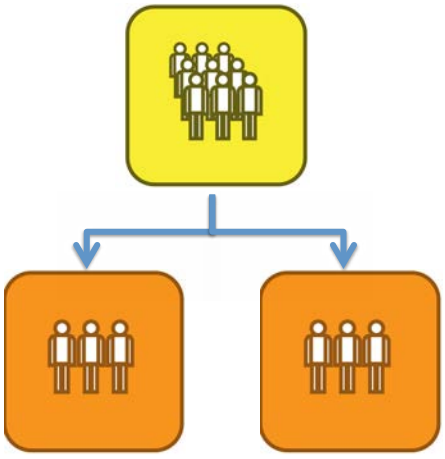
LOI Sections: Comparators

- List the options or clinical strategies being compared. Note that all options must be in current clinical use.
  1. Medication A
  2. Medication B
  3. Physical therapy



LOI Sections: Study Design

- Briefly describe the study design
  - *Describe how selection bias and confounding will be mitigated in nonrandomized designs*



LOI Sections: Study Population and Setting

- Specify the study population and the settings.

LOI Sections: Sample Size and Power

- Provide the total sample size for the main CER analysis and the number per arm.
  - *State the study's power and provide the hypothesized effect size and other assumptions used to estimate power.*
  - *Provide support for the hypothesized effect size of the interventions being assessed.*
  - *As a general guide, <100 per arm will be considered too low, unless the condition is rare.*

LOI Sections: Outcomes

- Describe the study outcomes and why the outcomes are important to patients.
  - *Clearly defined*
  - *Patient-centered*
  - *Measurable*
  - *Valid*

LOI Sections: Engagement

- Briefly state how patients and stakeholders are involved in all aspects of the research and list specific organizations involved.
  - *Make clear how patients, family members, caregivers, and the organizations that represent them will be involved in planning the study, conducting the study, and potential dissemination of study results.*

Appendices to the LOI

LOI Sections: Real-Life Applicability

- State how the intervention will be delivered and received in real-life clinical settings and inform decisions about health care and outcomes.

Pitfalls and Tips

Common Pitfalls in Developing CER Questions #1

Novel Strategies

- Strategies being compared should each have known efficacy and/or be used in clinical practice.

Example of Pitfall #1

PRINCIPAL INVESTIGATOR (BLOW, JOSEPH):

LETTER OF INTENT (LOI): ASSESSMENT OF PREVENTION, DIAGNOSIS, AND TREATMENT OPTIONS TEMPLATE

TITLE OF PROPOSED STUDY: Reducing Falls in the Elderly.

1. **Specific Aims:** State the specific aims of this study.
    1. To compare our falls intervention, Safe and Healthy Lifestyles for the Elderly Program (SHLEP) to a CDC educational program in terms of prevention of falls, hip fracture, quality of life, and mortality.
    2. To disseminate SHLEP for implementation in other settings.

Our goal is to identify effective patient-centered strategies to reduced falls, fall related injuries, and related morbidity and mortality in older populations. We will use compare an established education program developed by the CDC to the SHLEP developed at the University of Podunk. We recently published a study of 20 patients showing the acceptability of the intervention. . . .

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No estimate of current use of SHLEP in clinical practice

Common Pitfalls in Developing CER Questions #1a

Novel Strategies – now offered on line!

- Strategies being compared should each have known efficacy and/or be used in clinical practice.

Common Pitfalls in Developing CER Questions #2

No clearly defined gap

- Document that there is a significant gap and that the field has been reviewed
- Cite credible, respected sources, including systematic reviews and guideline gaps

Example of Pitfall #2

4. **Gap Analysis:** Add a statement describing the evidence gap; be sure to include references, such as systematic review(s), guidelines, and other evidence.

There is inadequate attention paid to risk of falls in the elderly. Compounding the problem are comorbid conditions, d… …e the risk of falls. Inappropriate use of medic… …al screening tools and interventions. … and we believe will have a significant im… …roblems and mortality.

It is widely acknowledged that … …reduce the risk of falls in the elderly. In addi… …ne to fully address the risk of falls in their pati… …f-administered or administered by a …

No references to systematic reviews or guidelines based on suboptimal evidence

Common Pitfalls in Developing CER Questions #3

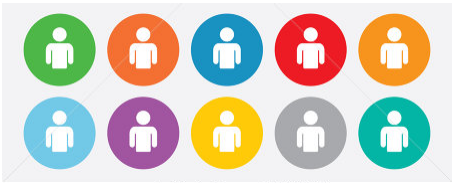
"Usual care" as a comparator

- Use caution when proposing usual care as a comparator
- Usual care is often ill-defined and difficult to quantify
- Consider how the findings will be interpreted, applied, and reproduced
- Usual care must be well-described, if proposed

Common Pitfalls in Developing CER Questions #4

Lack of support for proposed sample size

- State clearly what the effect size is and what it is based on (clinically meaningful and realistic).
- State power, alpha level.
- Account for drop-out.
- Discuss subgroups and heterogeneity of treatment effects.



Example of Pitfall #4

8. Power Calculations: State the power of the proposed study to detect the hypothesized effect, including support for all assumptions, (e.g., type-1 error level, standard deviation in outcome measure, underlying event rate). Note power for important subgroups, if applicable.

We will randomize 50 patients per arm. With this number, we estimate that we will have 80% power to detect a 50% reduction in falls. We believe the intervention will reduce the risk of falls by 50% over 6 months. . . .

Effect size unrealistically high

No evidence cited to support the proposed effect size

No accounting for drop-out

More Tips

- Incorporate appropriate **patient-centered outcomes**; assure measures are valid
- Identify **experienced research partners**
- Include **patient advocacy and professional organizations** to formulate the research and a dissemination and implementation plan

Questions?

- ". . . she's got gaps, I got gaps, together we fill gaps."

—Rocky

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