Ensuring value by building on what is known

Use of systematic reviews to support proposals for new research at PCORI

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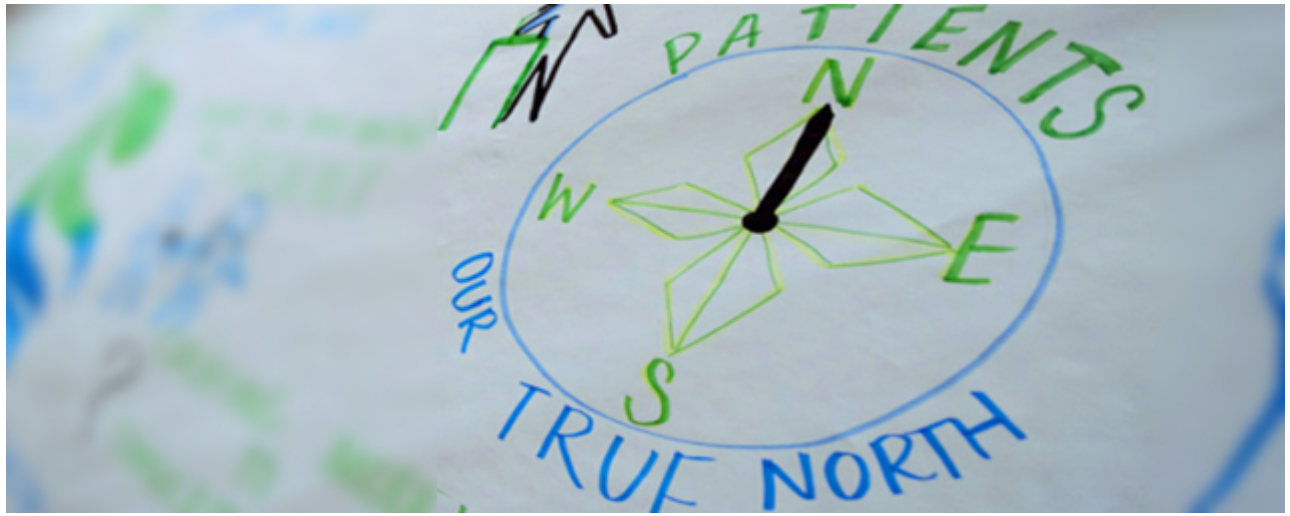
1.

Who PCORI Is and What We Do

About PCORI



- An independent research institute authorized by Congress in 2010 and governed by a 21-member Board of Governors representing the entire healthcare community
- Funds comparative clinical effectiveness research (CER) that engages patients and other stakeholders throughout the research process
- Seeks answers to real-world questions about what works best for patients based on their circumstances and concerns

Our Broad and Complex Mandate

"The purpose of the Institute is to **assist patients, clinicians, purchasers, and policy-makers in making informed health decisions** by advancing the quality and relevance of evidence concerning the manner in which diseases, disorders, and other health conditions can effectively and appropriately be prevented, diagnosed, treated, monitored, and **managed through research and evidence synthesis…**

… and the dissemination of research findings with respect to the relative health outcomes, clinical effectiveness, and appropriateness of the medical treatments, services…"

—from PCORI's authorizing legislation

Authorizing legislation mandated creation of Methodology Committee and Standards

- Legislation established a Methodology Committee to "**develop and improve the science and methods of comparative clinical effectiveness research**."
  - Charged with providing "specific criteria for internal validity, generalizability, feasibility, and timeliness of research and for health outcomes measures, risk adjustment, and other relevant aspects of research and assessment with respect to the design of research."

Methodology Standards: 13 Broad Categories

- Formulating Research Questions
- Data Networks
- Patient-Centeredness
- Causal Inference
- Data Integrity and Rigorous Analyses
- Adaptive and Bayesian Trial Designs
- Preventing/Handling Missing Data
- Studies of Medical Tests
- Heterogeneity of Treatment Effects
- Systematic Reviews
- Data Registries
- Research Designs Using Clusters
- Complex Interventions

2.

Background and Objective

Background

In 2009, thought leaders estimated that **85% of biomedical research is avoidably wasted** [Chalmers and Glasziou, Lancet 2009]

- Series of papers followed in the Lancet in 2014 which included 17 recommendations across all stages of research production
  - Included **recommendation for reducing waste when what is already known is ignored** [Chalmers, Bracken et al, Lancet 2014]

    "Research funders and regulators should demand that proposals for additional primary research are justified by systematic reviews showing what is already known, and increase funding for the required syntheses of existing evidence."

- Ensuring Value in Research (EViR) Funders' Forum Guiding Principle 2:

  "Research should only be funded if set in the context of one or more existing systematic reviews of what is already known or an otherwise robust demonstration of a research gap."

Current requirements by funders

- In 2017, Nasser et al examined the policies of 12 health research funders and found that PCORI and NIHR are the only funders that require applicants to reference systematic reviews in funding applications
  - Meeting presentation by Nasser et al , "What do funders do to increase value and reduce waste in research?," World Conference on Research Integrity, May 30, 2017, Amsterdam

- PCORI addresses this at two points:
  1. Methodology Standard RQ-1 requires applicants to cite gaps in evidence identified in a current systematic review to justify the need for a study
  2. Merit Review Criterion 1 addresses the potential for the study to fill critical gaps in evidence
     - *Applicants must describe burden, critical gap in current knowledge as noted in systematic reviews, guideline development efforts, or previous research prioritizations or as by inconsistency in clinical practice and decision making*

Objective

- To assess PCORI's performance on Methodology Standard RQ-1 and Guiding Principle 2 within a key subset of applications for large clinical studies (Pragmatic Clinical Studies (PCS) applications)

3.

Assessment of Current Practice

Building on Previous Work:
Assessment of Practice at NIHR

- **Bhurke et al results:** Found that **94%** (76 of 81) trials referenced a systematic review (SR) in application. **All 5 trials that did not cite a SR** had justifiable reasons

Bhurke *et al. BMC Medical Research Methodology* (2015) 15:108
DOI 10.1186/s12874-015-0102-2

BMC Medical Research Methodology

RESEARCH ARTICLE Open Access

Using systematic reviews to inform NIHR HTA trial planning and design: a retrospective cohort

Sheetal Bhurke[1,2*], Andrew Cook[2,3], Anna Tallant[2], Amanda Young[1,2], Elaine Williams[2] and James Raftery[1,2,3]

Bhurke et al vs PCORI Methods

Bhurke et al. Methods	PCORI Methods
Reviewed 81 funded trials	Reviewed 99 submitted PCS applications (funded + unfunded)
Defined SR as one or more of following: a) Reviews with "systematic review" in title and with SR methodology b) Cochrane review c) NICE TA	Defined SR as one or more of following: a) Title of citation included the words "systematic review" b) Cochrane review c) NICE TA d) Research plan identified citation as a SR in the text and a subsequent review of the abstract confirmed that it was a SR e) AHRQ publication (CER Review, Future Research Needs, Evidence Report, etc.)
If a trial didn't cite a SR, documented why	If a trial didn't cite a SR, documented what was cited instead
Assessed whether SR informed trial design and which trial design component(s) it informed: • Treatment comparison • Frequency, dose • Outcome selection	Categorized how SR was used: • Background/Significance • Evidence Gap • Study Design

Results:
Overall

The **majority** (95%, 94 of 99) **of PCS research applications cited at least one SR**

Table 1. Citation of systematic reviews for any reason in PCS applications

	WINTER 2015 (n=19)	SPRING 2015 (n=26)	CYCLE 3 2015 (n=11)	CYCLE 2 2016 (n=15)	CYCLE 3 2016 (n=28)	TOTAL PCS (n=99)
Cited a SR	16 (84%)	24 (92%)	11 (100%)	15 (100%)	28 (100%)	**94 (95%)**
Did Not Cite a SR	3 (16%)	2 (8%)	0 (0%)	0 (0%)	0 (0%)	**5 (5%)**

All 5 of the applications that did not cite a SR instead cited one or more IOM CER or PCORI priority topics, clinical practice guidelines, independent panel reports, or research prioritizations

Results:
Adherence to Methodology Standard RQ-1

- Among 91 analyzable PCS applications, **74%** (67 of 91) **cited a SR for the purpose of justifying an evidence gap, at a minimum**

- There was **no apparent difference between funded and unfunded PCS applications** in terms of the proportion of applications that cited a SR for any reason or to justify an evidence gap

Summary
Limitations and Next Steps

- We may have missed SR citations. Our process was systematic but may have not been complete
- We did not confirm that every citation with “systematic review” in the title also used appropriate SR methodology
- We did not evaluate the SRs to evaluate the relevance or appropriateness of their citation in the research plan
- Results may not represent other types of applications
- Discussion of deepening or broadening the audit is ongoing with our Methodology Committee

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Thank You!