Pragmatic Clinical Studies
PCORI Investigators’ Experience

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NIH Collaboratory
Steering Committee Webinar
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Patient Centered Outcomes Research Institute (PCORI)

• **An independent, non-profit research institute** to support informed health decisions of **diverse stakeholders** via research & dissemination activities

• Funds **comparative clinical effectiveness research (CER) of >2 head-to-head options** to care for a clinical condition or to improve health care delivery

  • More than 770 research and research-related awards
  
  • Funding to-date in excess of $2.6 billion

  • Special interests in subgroup differences, disparities, vulnerable populations, and research methodologies
PCORI Research Investments

**BY THE NUMBERS**

**Research Projects By Area**

- **METHODOLOGY** $144 Million (6%)
- **INFRASTRUCTURE** (Including PCORnet) $387 Million (16%)
- **CER** $2 Billion (78%)

**Most Studied Conditions**

- Mental/Behavioral Health 136
- Cancer 91
- Neurological Disorders 77
- Cardiovascular Diseases 72
- Multiple Chronic Conditions 60

**Most Studied Populations of Interest**

- Racial/Ethnic Minorities 320
- Low Socioeconomic Status 213
- Women 172
- Older Adults 149
- Individuals with Multiple Chronic Conditions 122

*Number of projects (out of a total of 493). A project may study more than one condition or population of interest.*
All PCORI-funded research projects include at least 3 pragmatic elements

- Primary outcomes relevant to multiple stakeholders as well as patients
- Broad eligibility criteria
- Real-world settings

Stakeholder engagement & participation is critical

Compliance required with PCORI Methodology Standards
PCORI Pragmatic Clinical Studies Portfolio (N=42)

- Large studies, up to 5y duration, $10 million direct costs
- Less complex protocols, minimal intrusion on routine practice encouraged
- Pragmatism is not required to be maximized
- Focus on generalizable results for rapid dissemination & implementation

Informed by

- Guidance on the Design and Conduct of Trials in Real-World Settings: Factors to Consider in Pragmatic Patient-Centered Outcomes Research
- Relevant Methodology Standards i.e. for Complex Interventions, Cluster Designs, etc.
Needs Assessment* of Pragmatic Clinical Study (PCS) Investigators

Done to identify opportunities to support, improve, and potentially foster collaborative learning opportunities of funded investigators

Feedback elicited July – September 2019

- In-depth interviews: Awardees & PCORI stakeholders (N=8)
- Awardee web survey:
  - Included all PIs and lead Project Manager/Coordinators (N=89)
  - RR= 84% with only 1 study unrepresented
- In-person meeting of PIs/designees: ~80% of studies represented

*Contracted through Westat
Study Implementation Phase of PCS Portfolio (N=41)

Survey Responses
August 2019

- Contract negotiation phase: 12%
- Startup/onboarding phase: 31%
- Active recruitment at one or more sites: 57%
- Recruitment closed: ongoing follow-up & data collection: 15%
- Data analysis phase: 9%
- Reporting of results: 5%
Challenges Volunteered by Survey Respondents

When asked for brief descriptions of any current study challenge(s), 57 of 89 respondents reported at least one.

Three leading themes were identified among survey respondents:

1. Flexibility and real-world implementation
2. Patient recruitment, enrollment, and retention
3. Study site startup and onboarding

In-person meeting probed attendees on the 3 top survey themes.

#1 for PIs
#1 for PMs
At least half of attendees endorsed this being a challenge, noting

- “Pragmatic” is poorly understood & widely interpreted by study sites & clinicians
  - Some believe ‘anything goes’, that ‘it’s ok to be sloppy’ including not delivering the intervention or to ‘improve’ IT with QI
- Ground rules, a taxonomy, or “guardrails” are needed to set boundaries around the required degree of fidelity and allowable flexibility of interventions
- One PI provided sites with lists of clinical practice and data collection activities allowed flexibility and which required rigorous implementation
- Writing a protocol to accommodate flexibility is difficult
- Guidance or methods are needed to assess adherence of clinicians (and patients) and remain pragmatic
Recruitment and Enrollment: Challenges of Pragmatic Studies

- Distinctive to pragmatic studies is the no/low research experience of “real-world” clinical sites with fewer resources (personnel, space, infrastructure, time) to handle research & trial operations
- Informed consent
  - Distinctive to PCORI CER studies: Needing consent when interventions are currently delivered in normal care without informed consent
- Differences across interventions in reimbursement, insurance, or patient out of pocket costs
Study Site Startup and Onboarding: Main Sources of Challenges

• Subcontracting and IRB approval(s) take time
• Start-up, onboarding, and training are complicated
  • Reimbursement/incentives/disincentives for sites to enroll, carry out research-related interventions, data collection, and patient follow up
  • Turnover of clinical staff, leadership, data systems (e.g. EHR upgrades) or policy changes
• Implementing a common protocol across sites with varying clinical care processes, staffing, community factors, and patient populations
• Highly experienced research settings are confused by pragmatic elements foreign to explanatory or industry-sponsored trials
Patients were cited most often as important stakeholders and study contributors

- Contribute perspective, understanding of obstacles, and language/framing suggestions
- Help with recruitment & enrollment
- Help in understanding/overcoming obstacles or barriers
- Input to make study design relevant

PCORI is assessing the evidence on the potential benefits of patient and other stakeholder engagement
Next Steps for PCORI

Continue to engage all PCORI investigators on challenges and potential solutions to research done in real world populations & care settings

Apply knowledge of substantial upfront planning needs for large pragmatic studies

- Experience is informing funding opportunity to be opened in June 2020: Phased Large Awards in Comparative Effectiveness Research
- Will use an initial feasibility phase for study refinement, feasibility testing, stakeholder engagement, and infrastructure establishment
- Second phase of full-study execution contingent on meeting feasibility phase criteria and milestones
Nine domains scored as low, medium, or high in readiness

Highlighting seven highly relevant to external and clinical stakeholders in comparative effectiveness study design

• Evidence base for efficacy
• Feasibility to implement under existing conditions and resources
• Effort needed to capture outcomes
• Perceived economic viability of intervention
• Acceptability of intervention to providers in feasibility and need
• Priority of study to external stakeholders
• Impact or usefulness of results to stakeholders

PCORI is hearing of many disruptions to ongoing research in order to safeguard public health, patient, and research staff safety

- Varying degrees of research suspension at study sites except for coronavirus research
  - New enrollment suspended at many sites
- Patient contact halted or constrained to virtual encounters
- PCORI accepting all institutional directives
- Where research activities remain allowed, PCORI is reviewing proposed modifications on a case-by-case basis with an open & flexible approach
PCORI is rapidly initiating new funding initiatives addressing COVID-19

- **HERO Study** has opened a registry of HCW & RCT of HCQ prophylaxis
- Funding Opportunity for COVID-19-Related Enhancements to Existing PCORI Awards in
  - Research
  - Engagement
  - Dissemination & Implementation
- Additional opportunities anticipated soon: See [COVID-19 Targeted Funding Preannouncement](#)