Pragmatic Clinical Studies

PCORI Investigators' Experience

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NIH Collaboratory

Steering Committee Webinar

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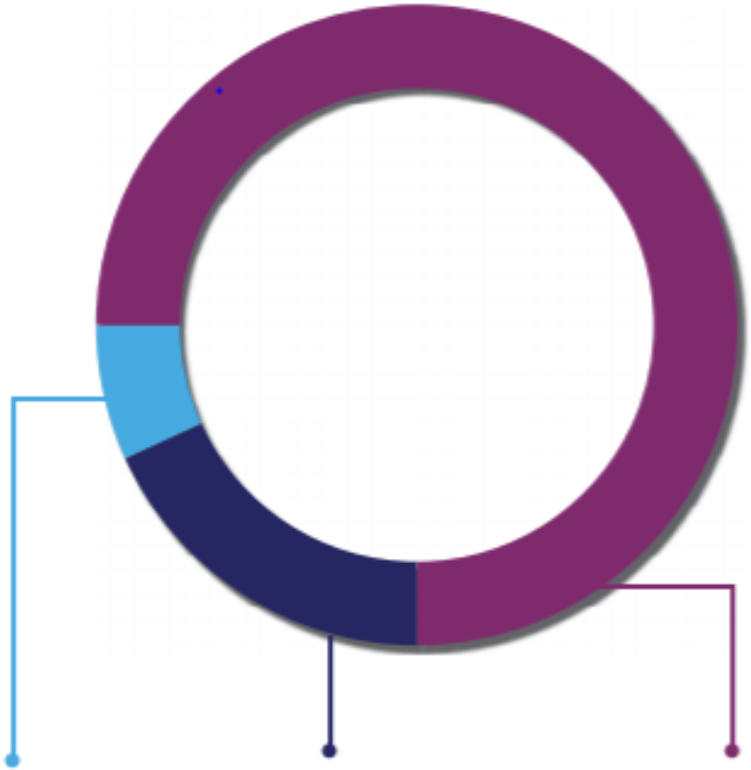
Patient Centered Outcomes Research Institute (PCORI)

- 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.*

PCORI Research Projects & Pragmatism

- **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 Research Projects & Pragmatism

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

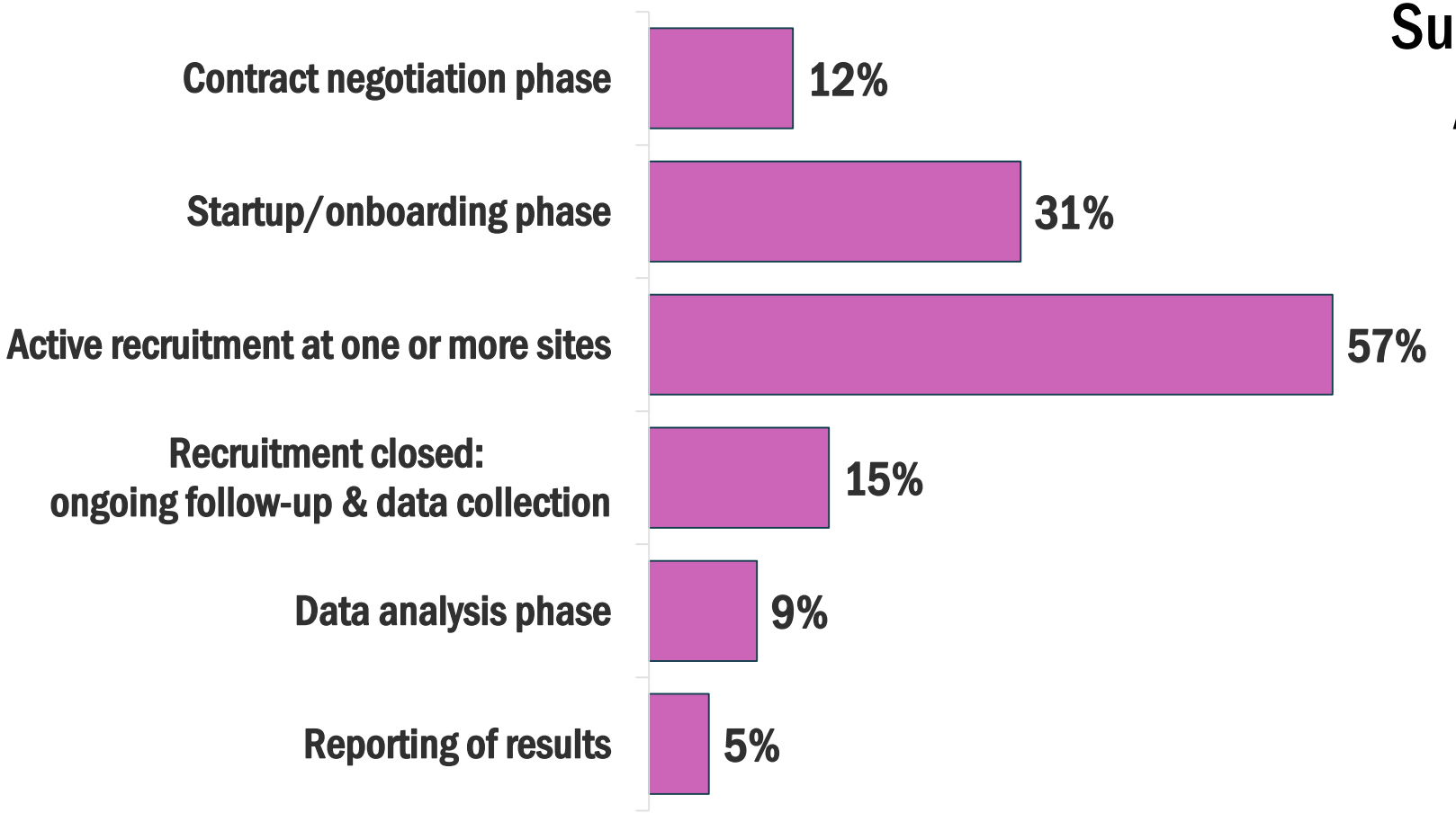
Done to identify opportunities to support, improve, and potentially foster collaborative learning opportunities of funded investigators

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

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 ← #1 for PIs
2. Patient recruitment, enrollment, and retention
3. Study site startup and onboarding ← #1 for PMs

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

Flexibility and Real-World Implementation

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

An Upside to Challenges: Stakeholder Engagement

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

Feasibility Assessment Tool: Readiness Assessment of Pragmatic Trials (RAPT)

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

Baier et al. *BMC Research Methodology* (2019) 19:156 https://doi.org/10.1186/s12874-019-0794-9

Research Impacts of SARS-CoV-2Research

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

SARS-CoV-2 & Research Operations

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

Thank you & Questions

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