PCORI Experience with Pragmatic Clinical Trials

Anne Trontell, MD, MPH

Associate Director, Clinical Effectiveness and Decision Sciences

NIH Collaboratory Meeting

May 15, 2018

pcori

PATIENT-CENTERED OUTCOMES RESEARCH INSTITUTE

PCORI

- An independent, non-profit research institute authorized in 2010 with a mandate to **support informed health decisions by a broad array stakeholders** via research and dissemination activities
- Funds comparative clinical effectiveness research (CER) of ≥2 options to care for a clinical condition or to improve health care delivery
- **Focus on patient-centered outcomes** of benefits, harms, and burdens
- Research **done in real-world populations and settings** with attention to subgroup differences
- Strategic Research Priorities
  - Assessment, Prevention, Diagnosis, and Treatment Options
  - Improving Healthcare Systems
  - Communication and Dissemination
  - Disparities
  - Methods

Extensive PCORI Investment in RWE

Total PCORI funding of $1.73 billion for 548 *studies*

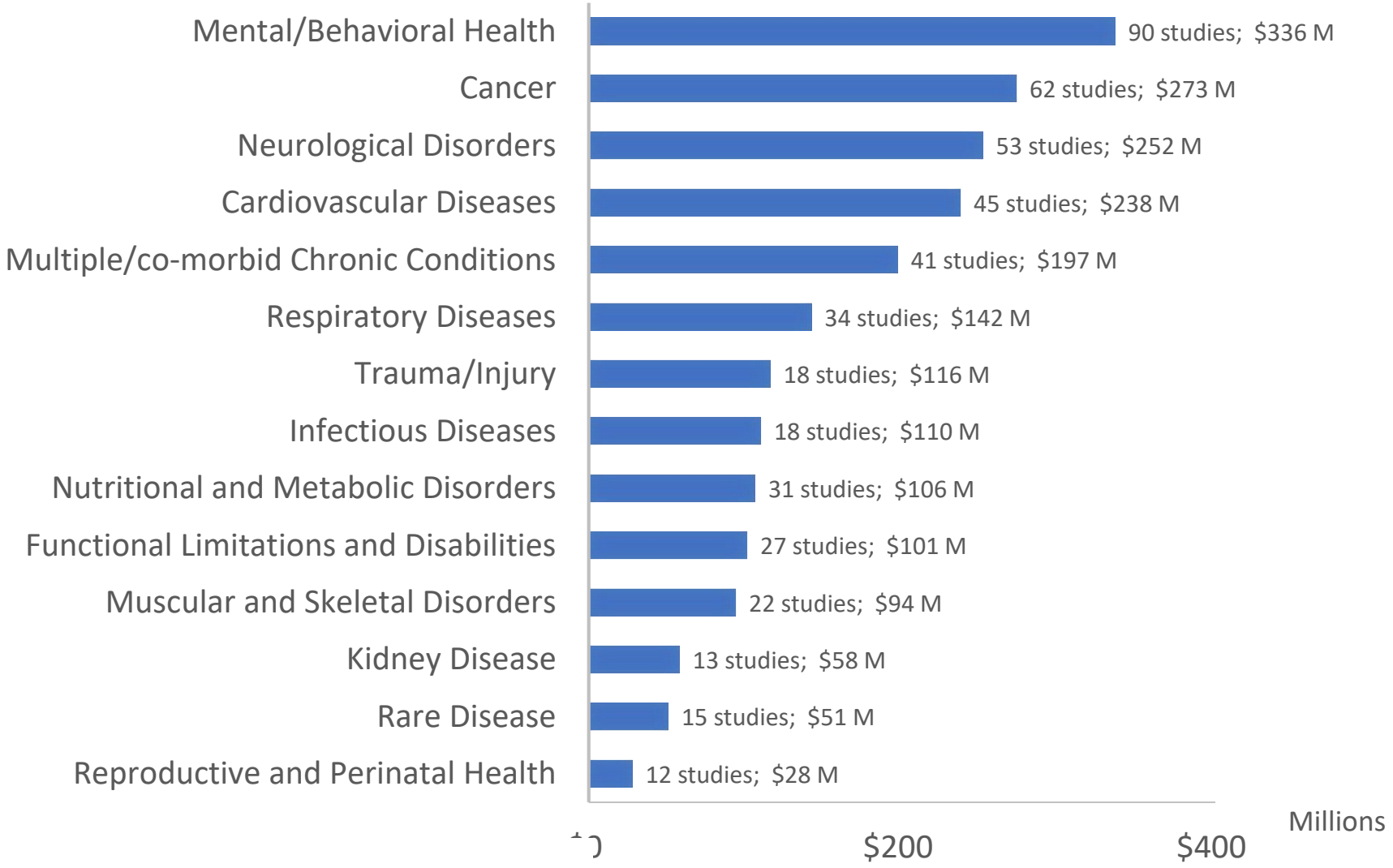
- 224 studies address the 16 highest cost conditions in the U.S

Randomized trials with pragmatic focus: 310 trials ($1.3 billion)

- 151 compare A vs. B options for individual patients
  - 61 trials with a prescription drug in one arm ($310 million)
- 159 trials in Healthcare Delivery and Disparities Research ($657 million)
- Design types & size
  - 61 trials using cluster designs ($367 million)
  - 81 trials to enroll ≥ 1000 participants
  - 51 larger trials with > $8 million total costs

PCORI's PCT Research Portfolio

Total CER funding awarded by condition category



A project may be counted across more than one condition category; chart shows top 14 funded categories. The PCORI Clinical Trial CER portfolio includes 310 projects.

Emerging Lessons

- Challenges of real-world populations & conditions
  - Health systems – Institutional buy-in, flexibility, coordination, data system/technology barriers
  - A vs. B comparisons –Limited clinician & patient time; treatment option availability or coverage
  - Unexpected changes arise frequently
- Case examples that engagement helps accrual and retention
- Quantitative analyses now beginning as first studies reach completion

Lessons Learned

- Study design and conduct must be “fit for purpose” of answering the study question
  - NOT necessarily better with more pragmatic features
- Real world variations in pragmatic trials require judicious planning, management, and measurement
  - NOT laissez-faire conduct
- Internal validity must be preserved
  - NOT sacrificed in the name of external validity or generalizability

Lessons Learned: Investigator Survey

- PIs with large ($>10M) pragmatic studies underway (N=40 invited, 28 responses, 70% response rate)
- Pick list of 13 items asking re questions, concerns, or challenges with their study
  - ~90% respondents picked $\geq$ 1 (max 8)
  - Median 4, mean 3.6
- Dominant struggles encountered
  - Fidelity/flexibility allowed in treatment arms
  - Unexpected events/sources of variation after protocol finalized
  - Treatment adherence by participants and providers

Lessons Learned: Investigator Comments

- Complexities of protocol, trial conduct, or interventions often not fully manifest until underway
- How to monitor intervention fidelity & patient adherence without undue interference with real-world conditions
- How to engage busy clinicians and elicit cooperation

Summary

- PCORI and Collaboratory have complementary PCT experience
- Contributions of PCORI PCT experience
  - Purposeful patient and stakeholder engagement
  - Many trials for case examples & aggregate analysis
    - Individual randomization
    - A vs. B comparisons & fidelity/adherence issues
- Fertile opportunity for learning about clinical trial design and conduct

Thank You

Anne Trontell, MD, MPH

atrontell@pcori.org

www.pcori.org

info@pcori.org

twitter

YouTube

pcori

PATIENT-CENTERED OUTCOMES RESEARCH INSTITUTE

Back up slides

PI Survey Response Distribution

Balancing fidelity/ flexibility of interventions	13
Implementation after protocol finalized	13
Dealing with participant adherence	8
Ease of measuring primary outcome	7
Practitioner adherence to protocol	7
Practitioner training in interventions	7

PI Survey Response Distribution

Balancing inclusion and exclusion criteria	6
Adequacy of defining the interventions	6
Appropriate follow-up intensity	6
Other	8

PCORI's Mandate

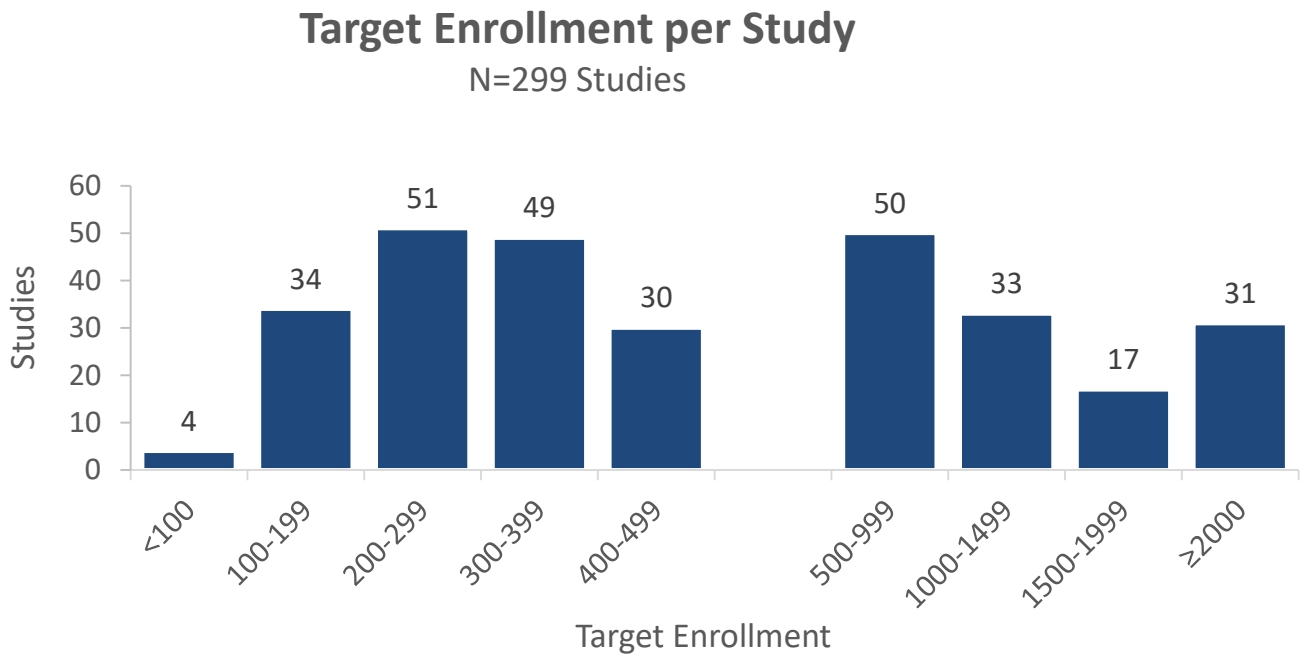
"The purpose of the Institute is to **assist patients, clinicians, purchasers, and policy-makers in making informed health decisions** by advancing the quality and relevance of evidence concerning the manner in which diseases, disorders, and other health conditions can effectively and appropriately be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

PCORI RCTs: Target Enrollment

Among randomized trials that enroll individuals* (N=299)



Among PCORI Trials:

- 44% plan to enroll ≥ 500 participants
- 27% plan to enroll ≥ 1000 participants

PATIENT-CENTERED OUTCOMES RESEARCH INSTITUTE

*An additional 11 RCTs plan to enroll sites, but do not plan to enroll individuals