MEETING SUMMARY

Advisory Panel on Clinical Trials Meeting Summary

November 6, 2020

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Overview

On November 6, 2020, the PCORI Advisory Panel on Clinical Trials (CTAP) held its 16th meeting virtually.

CTAP's 15 members include patient representatives and experts in clinical trials, biostatistics, epidemiology, and ethics. Two members of PCORI's Methodology Committee serve ex officio on CTAP. The meeting was open to the public via webinar, and meeting materials were posted to the PCORI website.

During this meeting, members listened to an overview of CTAP's charge, process for selecting members, and accomplishments to date. They received an update on the principles that PCORI has proposed to address the requirement in PCORI's 2019 reauthorization legislation to capture, as appropriate, the full range of outcomes data in its research studies. These data include economic and cost data related to the utilization of healthcare services as well as outcomes and measures of costs and burdens that are important to patients. Another session focused on the strategic plan that PCORI's Board of Governors is preparing for the next 10 years and the feedback on this plan that PCORI has solicited and continues to solicit from a broad range of stakeholders. CTAP then discussed ways for PCORI to address two new priority topics identified by Congress in PCORI's reauthorizing legislation: intellectual and developmental disabilities (IDD) and maternal morbidity and mortality (MMM). The final meeting session addressed PCORI's response to the changes to PCORI-funded clinical trials in response to COVID-19–related research interruptions.

CTAP Overview

Allie Rabinowitz, MPH, Senior Program Associate in the Comparative Effectiveness and Decision Science program at PCORI, explained that CTAP was established in the legislation that authorized PCORI. Its charge is to advise PCORI on clinical trial selection, design, implementation, and technical issues for patient-centered outcomes research. PCORI solicits applications for new CTAP members each year, and PCORI's Board of Governors approves all CTAP members. CTAP typically meets twice a year in person, but CTAP members and subcommittee sometimes provide ad hoc advice on methodological and design issues related to PCORI clinical trials.

Examples of CTAP accomplishments to date include input to the Methodology Standards to address clinical trial recruitment, accrual, and retention; advice on the ADAPTABLE trial of aspirin for cardioprotection in people with cardiovascular disease; and involvement in the development and implementation of several PCORI policies and programs.

PCORI's Proposed Principles for the Consideration of the Full Range of Outcomes

Andrew Hu, MPP, Director of Public Policy and Government Relations at PCORI, explained that the 2019 legislation to reauthorize PCORI directs the institute to capture, as appropriate, the full range of outcomes data in its research studies. These data include economic and cost data related to the utilization of healthcare services as well as outcomes and measures of costs and burdens that are important to patients.

PCORI has developed draft principles for meeting its statutory mandate to consider the full range of outcomes data in PCORI-funded research. PCORI has asked the public to comment on these draft principles by November 13. PCORI will use this public comment, as well as input from other stakeholders, to update the principles and issue the final version for approval by the PCORI Board of Governors in March 2021. In the meantime, PCORI is developing initial guidance for applicants, and the Methodology Committee will update the Methodology Standards to reflect the principles.

So far, stakeholders have expressed broad support for consideration of costs and economic impact data in PCORI research. They also emphasized the need to use a patient-centered, holistic approach to the consideration of costs; consider cost burdens and impacts at societal and community levels; and capture implementation or program costs.

CTAP suggestions for PCORI were to:

- Use the economic data to study the impact of costs on health disparities.
- Identify types of studies for which collection of cost and economic data would and would not be appropriate.
- Develop new methodology standards for collecting implementation and program cost data.
- Establish a central repository for the cost data collected by PCORI-funded studies.
- Include experts in review panels who can appropriately assess proposals for studies that collect economic data.

Strategic Planning: Identifying National Priorities

Michele Orza, ScD, Chief of Staff in PCORI's Office of the Executive Director, explained that the Board of Governors has launched a process to prepare a strategic plan for the next 10 years. The national priorities that guided PCORI's research during its first 10 years are likely to be reframed as long-term goals for the nation's health. The two new priority topics, IDD and MMM, will also be part of PCORI's research agenda.

Dr. Orza listed the five original national priorities for research and feedback on each priority received from stakeholders:

- Addressing disparities: This priority is more important than ever and needs to be strengthened (e.g., to eliminate and not simply address disparities).
- Assessment of prevention, diagnosis, and treatment options: PCORI should address the link between prevention and broader public health, incorporate environmental factors and public health efforts into this priority, and maintain its focus on comparative trials of drugs, devices, surgical techniques, and other interventions.
- Communication and dissemination research: PCORI should not simply study communication and research but should actually engage in communication and conduct research. Community engagement can facilitate strong dissemination.
- Improving healthcare systems: PCORI research should reflect the intersection between this priority and the broader public health ecosystem (e.g., through research on the social determinants of health).
- Accelerating patient-centered outcomes research and methodological research: The data infrastructure ecosystem could lead to efforts that complement PCORI's work, and the human component of the infrastructure (e.g., capacity building to include diverse participants in research and development of a patient-centered outcomes research pipeline) needs to be emphasized.

Suggestions for PCORI from CTAP members included the following:

- Ensure that investigators recruit diverse participants successfully by communicating in lay terms the lessons learned from clinical trials and why this information is important.
- Provide funding for studies to hire community members who have experience recruiting special populations and communicating the value of research, as well as the risks and potential benefits of participation.
- Fund research on patient-centered strategies to address gaps in the diagnostic testing system.

2019 Research Priorities: MMM and IDD

Elisabeth Houtsmuller, PhD, Associate Director of PCORI's Healthcare Delivery and Disparities Research program, reported that PCORI plans to address MMM throughout the continuum from preconception to one year after delivery. PCORI has started to engage various organizations in discussions of the most suitable approach to research on MMM for PCORI.

Kelly Dunham, MPP, Senior Manager of Strategic Initiatives at PCORI, defined IDD as disorders that are usually present at birth and that negatively affect the trajectory of the individual's physical, intellectual, and/or emotional development. As with MMM, PCORI reviewed the literature and talked to stakeholders to identify IDD research questions to address.

CTAP suggestions were as follows:

For MMM:

- Consider broader environmental and systemic issues, such as maternity or paternity leave.
- For engagement efforts, reach out to:
  - The Special Supplemental Nutrition Program for Women, Infants, and Children
  - State perinatal quality collaboratives
  - The education community
- Fund studies of risk factor assessments for newly married couples or sexually active young adults.
- Include structural racism as a topic in its MMM framework.

For IDD:

- In addition to health status, study quality of life in people with IDD.
- Fund research to develop better tools to measure quality of life in people with IDD.
- For engagement efforts, reach out to:
  - Schools
  - Organizations that focus on hearing and other types of sensory differences that could influence IDD risk

COVID-19 Disruptions to Research

Jason Gerson, PhD, Senior Program Officer for the Clinical Effectiveness and Decision Science program at PCORI, described types of disruptions experienced by almost all PCORI-funded clinical research because of the COVID-19 pandemic. For example, studies have been suspended at some or all sites, recruitment and informed consent approaches have been altered, and some studies have changed their primary research question or how they deliver their intervention.

When PCORI considers proposed adaptations to studies needed because of COVID-19–related disruptions, it determines whether the adaptations change the nature of the research question and whether the adapted research would still address an important evidence gap. When an adaptation involves delivering the intervention virtually instead of in person, PCORI considers whether sufficient evidence demonstrates the efficacy of this mode of delivery.

A PCORI survey of pragmatic clinical study investigators found that about 60% had already made changes to their studies, a third were still experiencing operational suspension at some sites, and 28% were pilot testing modifications to their original plans. Only 11% had experienced no disruptions. Challenges listed included replacing in-person with virtual delivery of interventions and collecting data remotely or via individuals who are not clinicians. Some investigators were not sure whether remote assessments were feasible for their study.

Dr. Gerson described two scenarios for CTAP to discuss:

- Scenario 1: A study is comparing two in-person, outpatient behavioral interventions to treat a common mental health condition. Because of COVID-19, sites now plan to deliver the intervention virtually. If the virtual delivery option is not used, the study must be paused until in-person delivery can resume.
- Scenario 2: A study originally included in-person physical assessments and measurements by a certified assessor, but it can no longer conduct research on site. The principal investigator proposes to have patients collect measurements under virtual observation by research staff. This change would let the study move forward, but whether virtual collection of certain data has been validated is not clear.

During the discussion, Dr. Gerson and Anne Trontell, PhD, MPH, Associate Director of the Clinical Effectiveness and Decision Science program, clarified that when awardees know that they will be unable to meet their recruitment targets, PCORI reviews the proposed modifications, taking into consideration the variations in the course of the pandemic and how the institution in question is responding to the pandemic. Some studies might simply need additional time to meet their recruitment targets. If PCORI decides that the study can proceed with changes, it makes the needed funds and other resources (including additional time) available. When study personnel are unable to perform their usual duties, PCORI suggests that these individuals work on data cleaning, literature searching, and other tasks that might otherwise be performed later in the study.

CTAP comments on the two scenarios included the following:

- Most healthcare visits in the future are likely to be virtual, and the pandemic could accelerate this shift. If studies conducted now do not use virtual platforms, their findings might become irrelevant in a few years.
- Participants in studies that use virtual interventions and assessments might need not only Internet access but also support in using virtual platforms, especially if they are not familiar with this type of technology.
- PCORI has an opportunity to compare the effectiveness of in-person and virtual care delivery models.
- Changing the delivery mode in an ongoing study from in person to virtual complicates the outcomes analyses.
- Person-reported outcomes captured remotely will be platform dependent. Investigators should therefore conduct confirmatory factor analyses and other measures to ensure consistent measurement.
- When a study, such as the one in Scenario 2, needs to shift from in-person to remote delivery of an assessment, it should first pilot the remote assessment in a smaller sample.
- When changes such as those described in the two scenarios are considered, PCORI should gather input from study participants on these changes.