Advisory Panel on Clinical Trials Summer 2021 Meeting

August 10th, 2021

1:00 PM – 5:00 PM ET

United States (Toll-free): +1 877 309 2074
Access code: 996-130-092 (muted)

Webinar URL: https://global.gotowebinar.com/join/7467579926704871438/751640640
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- Meeting is available to the public and is being recorded.
- Members of the public are invited to listen in, and the recording will be made publicly available after the event on PCORI's website.

GoToWebinar Housekeeping

- Remember to mute your microphone if you are not speaking.
- If possible, please turn on your video camera when speaking.
- If you have poor connection, make sure to dial in through phone (not computer).
- If you are experiencing technical difficulties, contact “PCORI AV” via the chat function.
- To queue to speak, submit your name through the chat to “Organizers Only”.
  - Feel free to use your camera when speaking.
- If you would like to send a comment to the entire group, select “All Attendees” in the chat function.

COI Statement

Welcome to the CTAP Summer 2021 Virtual Meeting. I want to remind everyone that disclosures of conflicts of interest of members of CTAP are publicly available on PCORI's website and are required to be updated annually. Members of the CTAP are also reminded to update your conflict of interest disclosures if the information has changed. You can do this by contacting your staff representative, Jess Robb.

If the CTAP will deliberate or take action on a matter that presents a conflict of interest for you, please inform the Chair so we can discuss how to address the issue. If you have questions about conflict of interest disclosures or recusals relating to you or others, please contact your staff representative, Jess Robb.

Welcome and Goals for the Day

Catherine Crespi, PhD, MS (Chair)
Professor of Biostatistics,
UCLA Fielding School of Public Health

Anne Trontell, MD, MPH
Associate Director,
Clinical Effectiveness and Decision Science, PCORI

Today's Agenda

Tues, August 10th		
Time	**Agenda Item**	**Presenter**
1:10	Welcome and Goals for the Day	Catherine Crespi Anne Trontell
1:20	Overview of PCORI Strategic Priorities	Laura Lyman Rodriguez
2:20	COVID-19 Impact to Research Insights on PCORI Response: COVID Adaptations	Jason Gerson Jess Robb
3:20	Break	
3:30	PCORI's use of PCORnet: Insights from ADAPTABLE	Claudia Grossmann
4:20	Farewells to panelists	Anne Trontell
5:00	Adjourn	

Strategic Planning: Proposed National Priorities for Health

Laura Lyman Rodriguez, PhD

Interim Chief Program Support Officer &
Senior Advisor to Executive Director

Purpose of Today's Conversations

Purpose

- Update on strategic planning process
- Opportunity to engage with the proposed National Priorities for Health and to gather perspectives

Goal

- Identify synergies among the National Priorities and consider what those may mean for the Research Agenda
- Identify critical needs and areas to address through the Research Agenda

Scope of Strategic Planning Activities

- **National Priorities**
- Research Agenda
- PCORnet® strategic vision for PCORI's next phase
- Methodology Committee focus for PCORI's next phase
- Commitment Planning and strategies to increase funding
- Scenario Planning based on the changes in landscape and environment
- Priorities from reauthorizing legislation
    - Maternal morbidity and mortality
    - Intellectual and developmental disabilities
    - Full range of outcomes data

Revised Strategic Framework
Evolving to National Priorities for Health

National Priorities As Part of Process

National Priorities

- Broad areas that include the patient-centered comparative effectiveness research (CER) PCORI supports
- Reflect priorities of patients, stakeholders, and the broader healthcare system
- Transparently demonstrate rationale for PCORI investments

Research Agenda

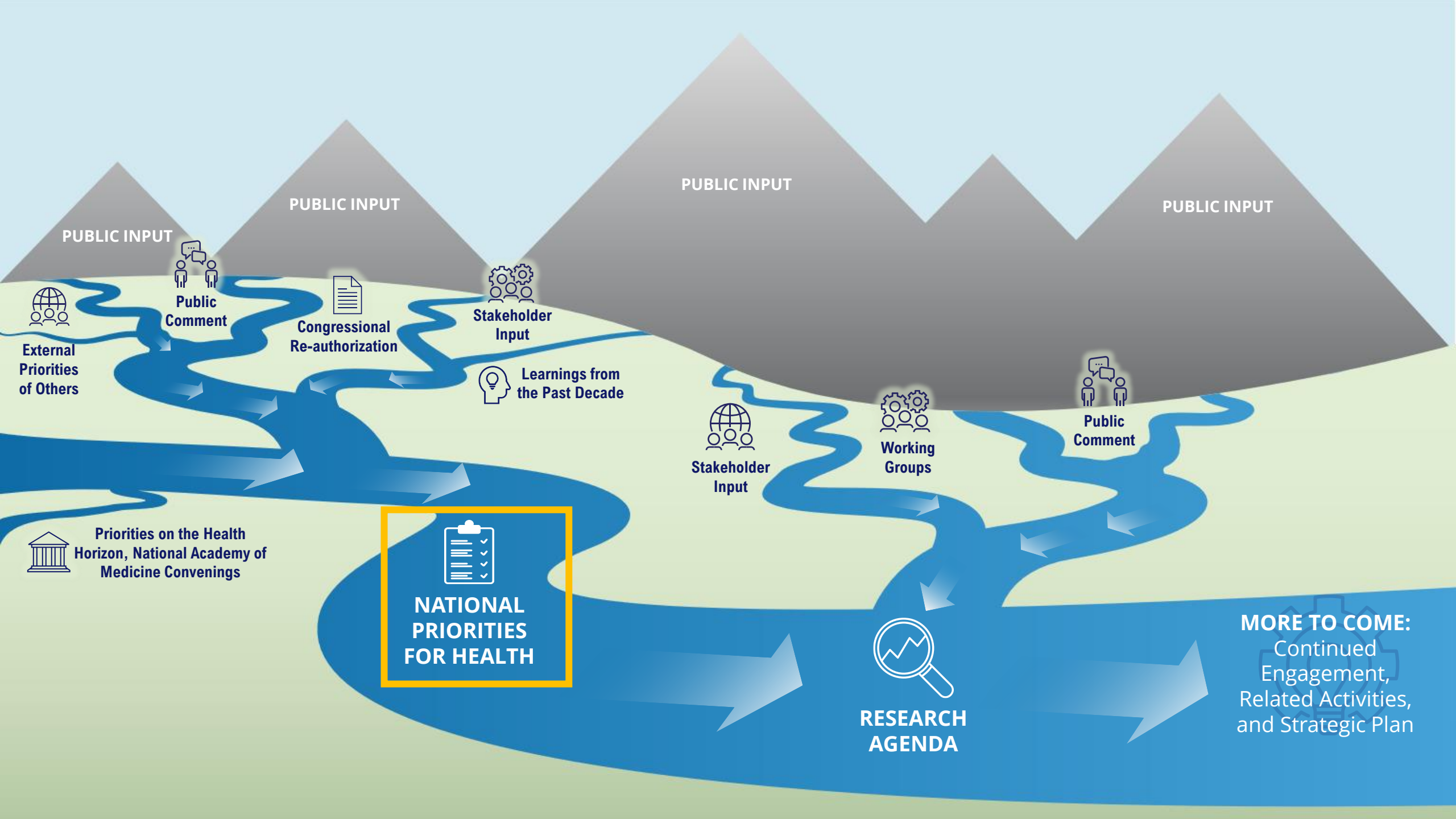
- Establishes research framework through which PCORI achieves progress on National Priorities
- Articulates and reflects evolving evidence needs of patients, stakeholders, and the broader healthcare system

Topic Development

- Process of ongoing cultivation and refinement of specific topics and/or sub-topics
- Questions refined with input from patient and stakeholder partners
- Articulates focused areas for funding

Picking Up From When We Last Spoke

- In November 2020, the CTAP considered the revised strategic framework and what the reframing meant for National Priorities.
- What we heard from the panel:
  - Support infrastructure (e.g., health systems) necessary to enable coordinated care/ easy navigation for patients within diverse populations
  - Support patient-centered strategies to address gaps across the care continuum (e.g., diagnostic testing system)
  - Consider strategies (engagement, technology, etc.) for recruiting diverse populations to participate in clinical trials
- This was reinforced and complemented by input from other convenings, meetings, and discussions.


PUBLIC INPUT
PUBLIC INPUT
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PUBLIC INPUT
External Priorities of Others
Public Comment
Congressional Re-authorization
Stakeholder Input
Learnings from the Past Decade
Priorities on the Health Horizon, National Academy of Medicine Convenings
NATIONAL PRIORITIES FOR HEALTH
Stakeholder Input
Working Groups
Public Comment
RESEARCH AGENDA
MORE TO COME: Continued Engagement, Related Activities, and Strategic Plan

Developing National Priorities for Health

- The themes below resulted from across the inputs
- At its April 2021, meeting, PCORI Board of Governors supported developing and further shaping these themes for National Priorities for Health

Health Equity

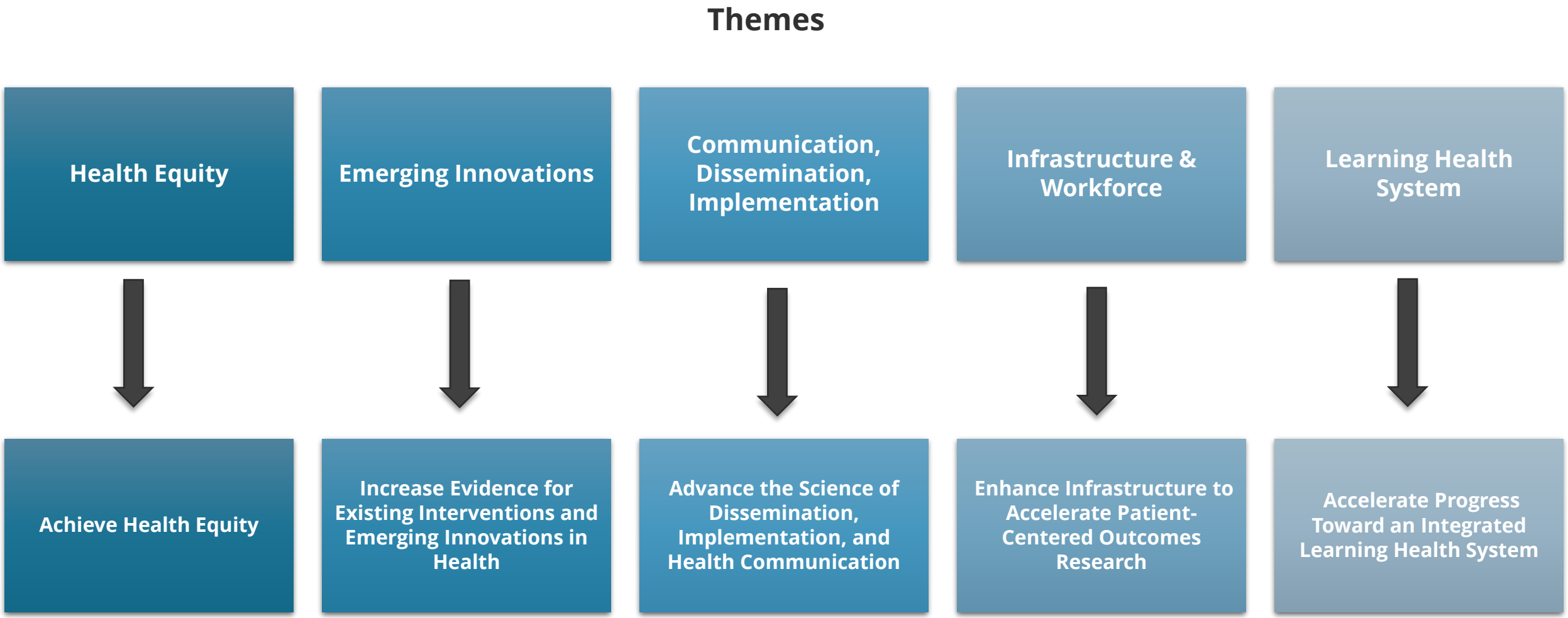
Emerging Innovations

Communication, Dissemination, Implementation

Infrastructure & Workforce

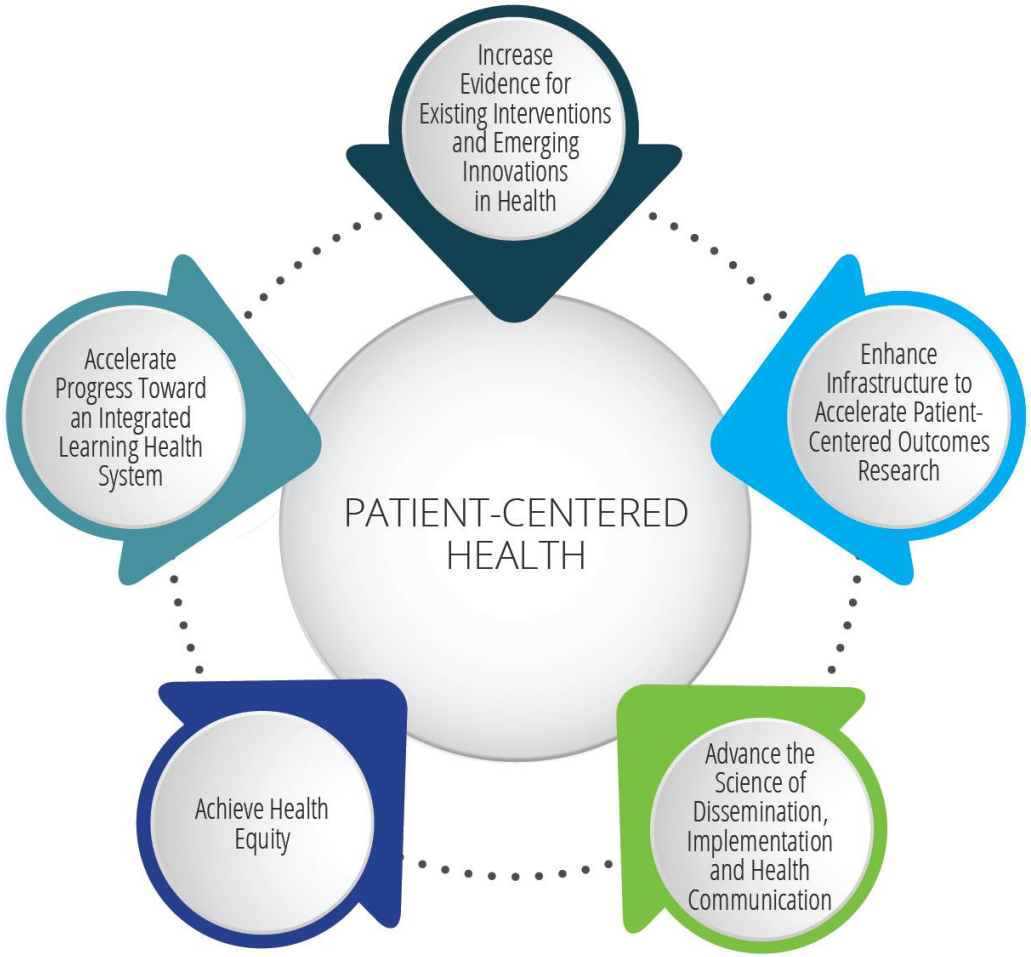
Learning Health System

Going from Themes to National Priorities



Proposed National Priorities for Health
Creating Synergistic Opportunities for Progress

At its June 2021, meeting, PCORI Board of Governors approved the National Priorities for Health to be posted for public comment (June 28 – August 27, 2021).



Looking Forward to Hearing From You
Previewing Questions

- What are critical needs and areas to address through the National Priorities?
  - How can clinical trial design and conduct be supportive of these Priorities?

- What synergies exist among the National Priorities? What might those mean for the Research Agenda?

- Imagine 5 years in the future, what potential impacts could these National Priorities for Health have on comparative clinical effectiveness research? Are there specific areas that PCORI could make a real impact on in this timeframe?

Proposed National Priorities for Health

Increase Evidence for Existing Interventions and Emerging Innovations in Health

Strengthen and expand ongoing comparative clinical effectiveness research focused on both existing interventions and emerging innovations to improve healthcare practice, health outcomes, and health equity

Strategies to address this priority include:

- monitor the research landscape for potentially high impact innovations
- evaluate existing and emerging innovations in clinical care interventions, systems changes, healthcare delivery, technologies, public health, and social determinants of health
- study unintended consequences, adverse events, barriers to care, burdens and economic impacts, and widened disparities in care outcomes associated with existing and emerging innovations
- expand scope of stakeholders engaged in PCORI's work from topic inception through implementation of the results
- emphasize inclusion of populations who are underserved, under-represented, and disadvantaged in CER research
- support CER of evidence gaps in diverse populations, geographic areas, and settings to foster equitable uptake practices

Proposed National Priorities for Health

Enhance Infrastructure to Accelerate Patient-Centered Outcomes Research

Enhance the infrastructure that facilitates patient-centered outcomes research to drive lasting improvements in health and transformation of both the research enterprise and care delivery

Strategies to address this priority include:

- develop and expand the universe of engaged patients and communities and representative leadership, research workforce, and clinician partners
- advance the accessibility and utilization of real-world data
- build synergies and leverage current work within health systems and by stakeholders
- integrate patient-centered outcomes research findings into learning health systems

Proposed National Priorities for Health

Advance the Science of Dissemination, Implementation, and Health Communication

Advance the scientific evidence for and the practice of dissemination, implementation, and health communication to accelerate the movement of comparative clinical effectiveness research results into practice

Strategies to address this priority include:

- fund CER studies of delivery or implementation strategies
- communicate research findings effectively and in ways tailored to diverse audiences
- actively deliver information to targeted audiences to use to inform healthcare discussions and decisions
- promote the uptake of research findings into practice, to contribute to improved healthcare and health
- engage stakeholders and communities in strategic partnerships across diverse settings to improve the uptake of evidence

Proposed National Priorities for Health

Achieve Health Equity

Expand stakeholder engagement, research, and dissemination approaches that lead to continued progress towards achieving health equity in the United States

Strategies to address this priority include:

- fund CER to improve health outcomes for individuals of all backgrounds
- strengthen efforts to support inclusive and diverse stakeholder engagement
- disseminate and implement research findings with the intention of informing broader health equity strategies
- collaborate with health, research, advocacy, social service, educational, and other organizations to reduce health inequities
- identify and fund novel ways to support the professional development and increase the engagement of investigators of color, investigators with disabilities, and populations who are historically under-represented in research endeavors

Proposed National Priorities for Health

Accelerate Progress Toward an Integrated Learning Health System

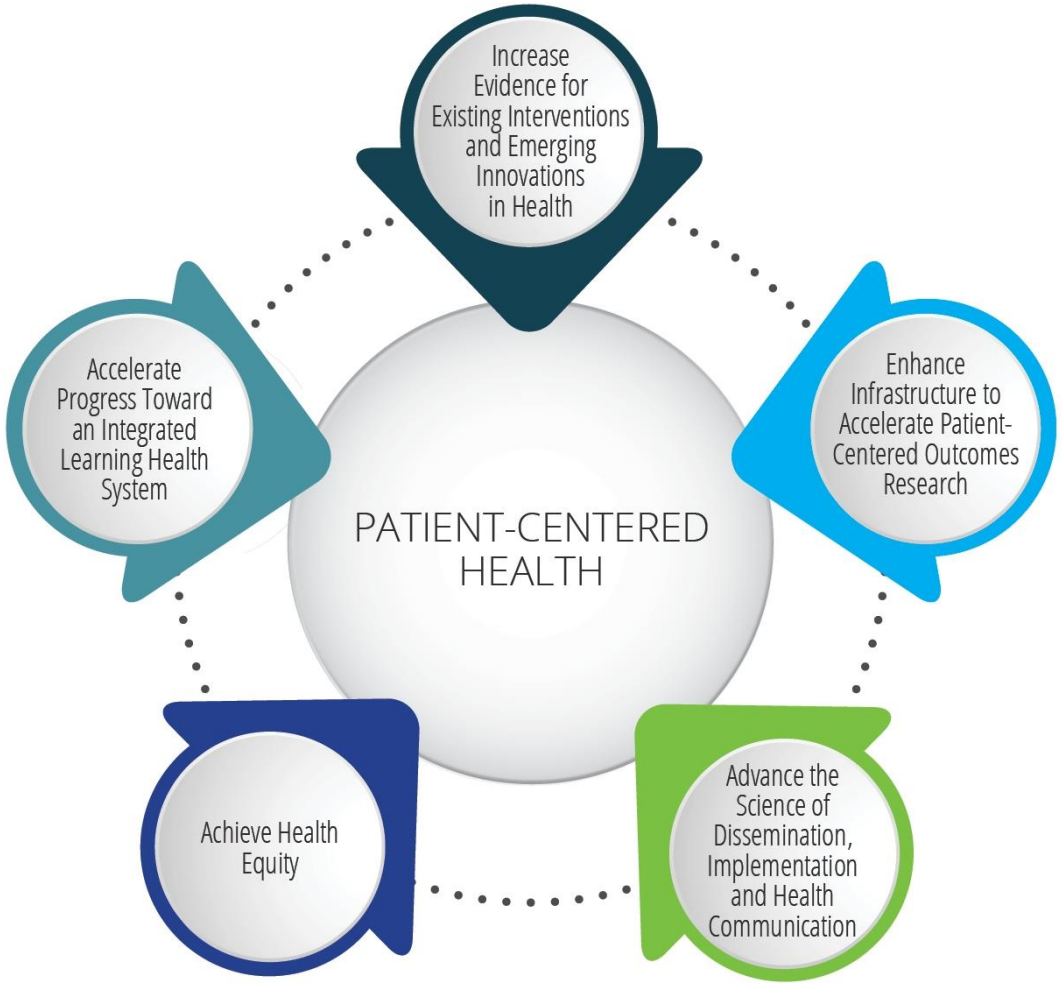
Foster actionable, timely, place-based, and transformative improvements in patient-centered experiences, care provision, and ultimately improved health outcomes through collaborative, multisectoral research to support a health system that serves the needs and preferences of individuals

Strategies to address this priority include:

- fund multi-sector interventional CER focused on health outcomes and grounded in the context of specific settings, communities, and needs
- implement research on precision and personalized medicine and whole-person health into practice
- incorporate the full range of outcomes to influence value that encompasses diverse outcomes and perspectives among patients, families, caregivers, and providers
- formalize partnerships to ensure an integrated learning health system that meets the needs of patients and caregivers
- use data analytic and informatic tools to inform and enable real-time decision making

Looking Forward to Hearing From You

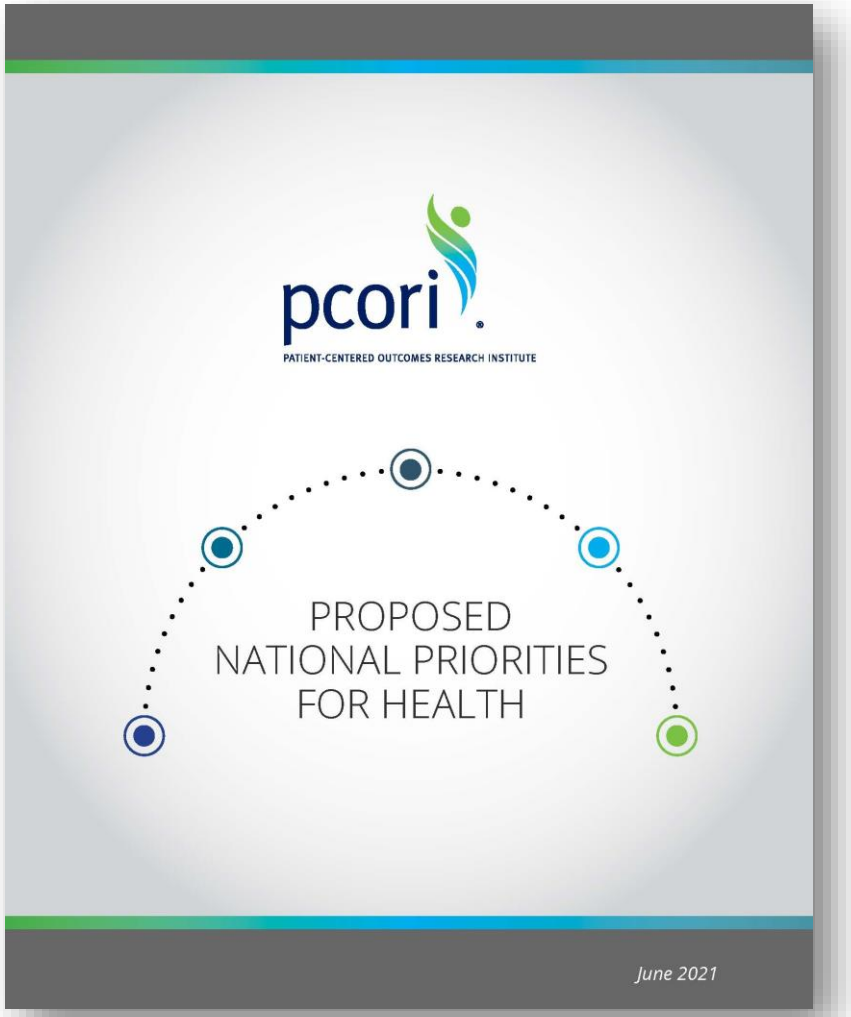
- What are critical needs and areas to address through the National Priorities?
  - How can clinical trial design and conduct be supportive of these Priorities?
- What synergies exist among the National Priorities? What might those mean for the Research Agenda?
- Imagine 5 years in the future, what potential impacts could these National Priorities for Health have on comparative clinical effectiveness research? Are there specific areas that PCORI could make a real impact on in this timeframe?



Public Comment Period
Proposed National Priorities for Health

- Submit comments during PCORI's 60-Day Public Comment Period **(June 28 – August 27)**

- pcori.org/nationalprioritiesforhealth



Thank You!

PCORI's COVID-19 Activities

Jason Gerson, PhD
Senior Program Officer, CEDS

Jess Robb, MPH
Senior Program Associate, CEDS

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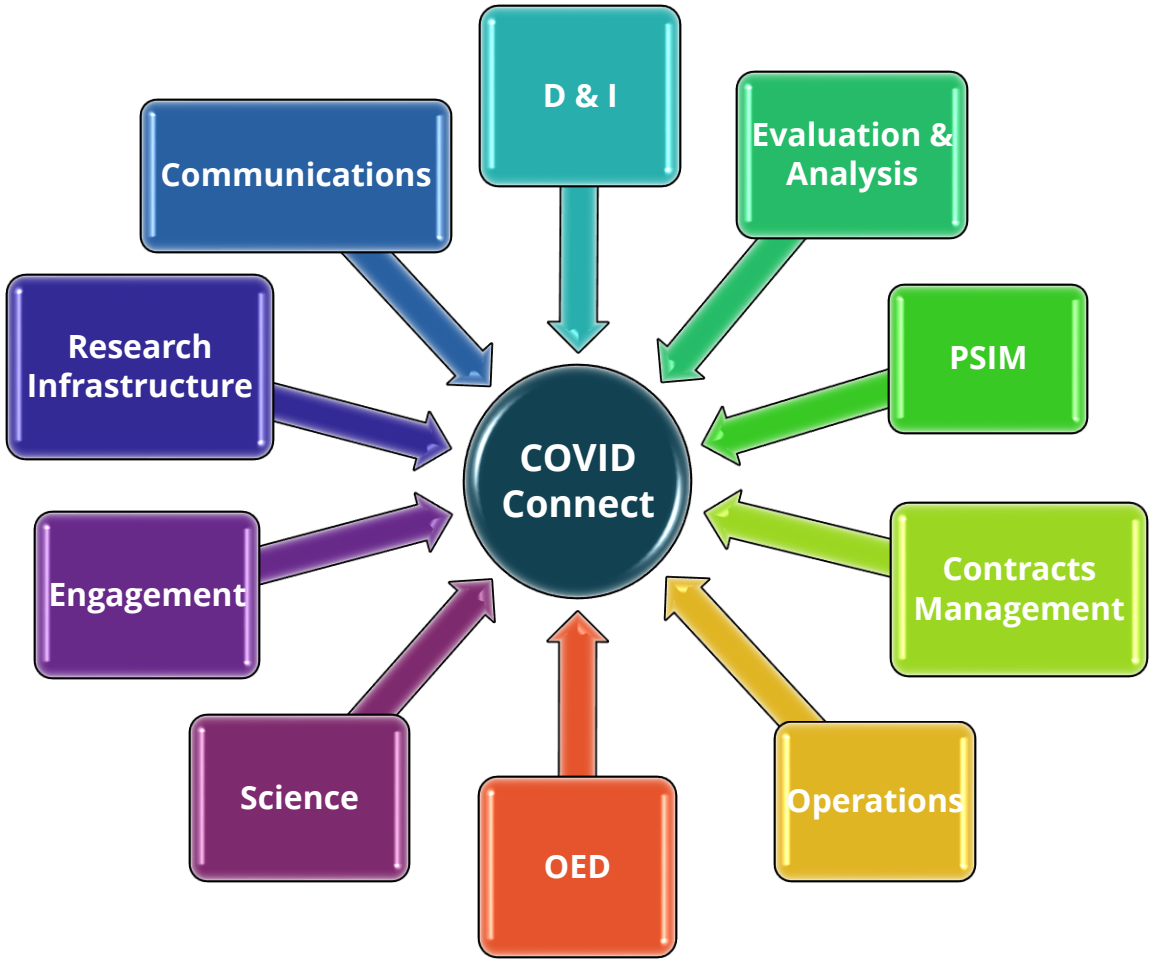
Topics Covered

- COVID Connect
- COVID-related Research Efforts
- COVID-related Engagement Efforts
- COVID-related Dissemination & Implementation Efforts

COVID Connect: Coordinating PCORI's COVID Response

- Goal: develop a **mission-aligned strategy** for PCORI's rapid response to the COVID-19 pandemic informed by relevant staff, stakeholder, and portfolio input.
- COVID Connect is a **cross-departmental** team with representation across PCORI.
- Subgroups: Topic Development, Stakeholder Engagement, Portfolio Analysis and Synthesis
- Membership **evolves** based on various stages of work and need of the organization



PCORI's COVID-19 Portfolio:

122 Enhancements, 9 Targeted Research Studies, and 25 Special Cycle Engagement Awards

122 Enhancements Awarded, *$34.8 million*

53

Engagement Award Enhancements
$7 million

13

D&I Enhancements
$5.8 million

47

Research Enhancements
$19.2 million

8

Methods Enhancements
$2.3 million

1

PCORnet Enhancement
$526,020

36 New Awards in Research & Engagement, $44.5 *million*

25

Engagement Award Special Cycle
$3.7 million

11

Targeted Research Studies (COVID tPFAs)
$40.8 million

Research

Enhancements

COVID-19 Targeted Research PFAs

Special Areas of Emphasis

COVID Enhancements to Existing Research Projects

- Support enhancements to existing research awards that could be initiated quickly to influence the outcome of the pandemic and that have some relationship to the original award, using existing teams that are currently funded by PCORI.
- Enhancement results will be posted alongside, and in some cases before, the results for the main project.

COVID Enhancements to Existing Research Projects

PCORI funded **Fifty Enhancements to Research Awards** totaling $21.7 million

Focus of 41 CER enhancements

13 enhancements about COVID-19 as a condition

28 enhancements about providing care during a pandemic

Themes from 8 Methods Enhancements

2 Developing clinical prediction models

2 Informing COVID-19 care

Other themes: data visualization, machine learning

Note: studies may include more than one theme

One PCORnet Enhancement

"optimize and rigorously validate key COVID-19 data elements related to the treatment and outcomes associated with **COVID-19 coagulopathy**"

Key statistics about CER Enhancements:

Condition Categories

	# of studies*
Mental & Behavioral Health	14
Nutritional & Metabolic	7
Neurological	6
Cancer	6
Cardiovascular	6

Priority Populations

	# of studies*
Black, Indigenous, and People of Color	18
Low Income	12
Women	9
Older adults	9

Telehealth

18 enhancements include telehealth components

*Studies may include more than one condition or population

COVID-19 Targeted PFA

- PFA developed and posted on accelerated timeline in response to the urgency of the pandemic; accelerated Merit Review and programmatic review to ensure timely decision-making
- Priority Areas:
  - Adaptations to healthcare delivery
  - Impact of COVID-19 on disproportionately affected populations
  - Impact of COVID-19 on healthcare workforce well-being, management, and training
- PFA posted in May 2020; 9 awards announced in August 2020
- Studies up to 2 years in duration; actionable findings within first 12 months
- Small Studies: up to $2,500,000; Large Studies: up to $5,000,000

COVID Targeted PFA Research Projects

PCORI funded **9 Targeted COVID-19 Research Awards** totaling $29.8 million

Focus of Awards

5 awards focus on COVID-19 as a condition

4 awards focus on ways to provide care during a pandemic

Themes

3 targeted awards are relevant to nursing homes or other **congregate living settings**

Key statistics about targeted studies:

Primary Condition	# of studies*
COVID-19	5
Mental/Behavioral Health	3
Non-Disease Specific	1

*Studies may include more than one condition

Priority Populations	# of studies*
Low Income	6
Black, Indigenous, and People of Color	5
People with MCC	3

Telehealth

5 targeted awards include telehealth components

Increasing Vaccine Confidence among Long-Term Care Workers PFA

- What interventions are effective in increasing COVID-19 vaccine confidence and uptake among LTC workers?
- 2 awards announced in July 2021
  - **CONFIDENT: A Randomized Trial to Increase COVID-19 Vaccine Confidence in Long-Term Care Workers**
  - **ENSPIRE Study: Engaging Staff to Improve COVID-19 Vaccination Rates at Long-Term Care Facilities**

Broad PFA Special Area of Emphasis: Post-acute COVID-19

Cycle 1 2021

- Management and survivorship of post-acute COVID-19
- Impact of COVID-19 on disproportionately affected populations
- Impact of COVID-19-related social isolation and loneliness on health outcomes

Cycle 2 2021

- Treatment and survivorship of post-acute COVID-19
- Health system and healthcare delivery management of post-acute COVID-19
- Strategies to improve outcomes of COVID-19 for disproportionately affected populations
- Impact of COVID-19-related social isolation and loneliness on health outcomes

PCORnet

HERO Program

CDC Surveillance Partnership

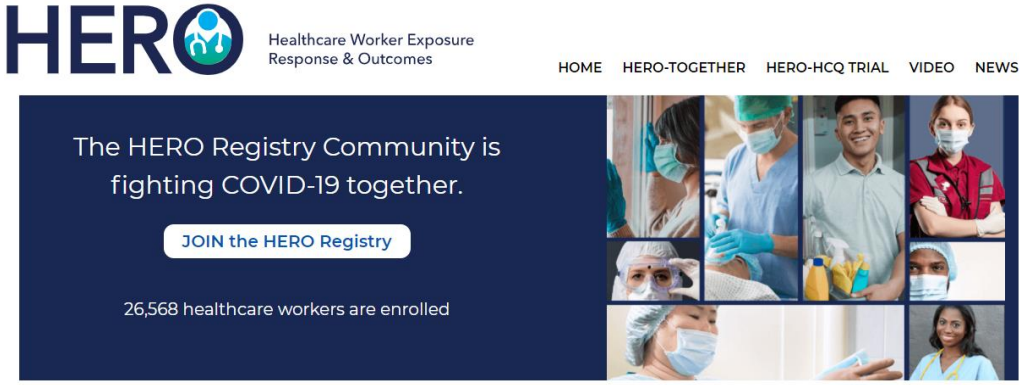
ACTIV 6

PCORnet-NCATs Vaccine Collaboration

HERO Program

- HERO Health Care Worker Registry
  - >40,000 HCW enrolled as of August 2021
  - Addition of family members
  - HERO Together- Pfizer-funded study on long term vaccine side effects

- Hydroxychloroquine Trial
  - Completed Feb 2021
  - 1,363 enrolled
  - Manuscript under review



PCORnet and CDC Partnership on COVID-19 Surveillance

- CDC funding 43 PCORnet sites for continued COVID-19 surveillance
- Biweekly refreshes and surveillance queries of COVID-specific subset of PCORnet Common Data Model
- Recent focus on Long COVID and incidence of high priority diagnoses up to 150 days post positive test

ACTIV-6

- ACTIV-6 is a randomized, blinded, and placebo-controlled Phase III platform trial to test the efficacy of repurposed medications to treat COVID-19 in the outpatient setting.
  - 5-8 arms determined by existing ACTIV medication prioritization committee
  - Conducted under an IND
- PCORnet is leading ACTIV-6, serving as the Clinical Coordinating Center, Data Coordinating Center, and contributing approximately 40 vanguard sites.
  - Leverage HERO-HCQ experience
  - Enhance patient-centeredness
- Goal is to enroll 15,000 patients across estimated 80+ sites

PCORnet-NCATs Vaccine Collaboration

Unique PCORnet Capabilities

- PCORI and NIH leadership (with support from the FDA) have been co-developing a collaborative approach with the goal of leveraging data infrastructures to investigate research topics related to vaccine breakthrough (e.g., computable phenotype for breakthrough that would facilitate cohort identification for future research).
- The PCORnet Common Data Model (CDM) is the only CDM with a distinct immunization table that includes data on administered and self-reported vaccines.
- The PCORnet data infrastructure is uniquely capable of engaging participants in a prospective research study.

PCORI Response to Adaptations due to COVID

Review: Background

The ongoing COVID-19 pandemic is disrupting the conduct of clinical research, impacting almost all PCORI-funded clinical research projects.

Disruptions include:

Operational

- Study suspension at all/some sites
- Alteration of recruitment mechanisms
- Alteration of consent approaches
- IRB review for proposed/ necessary changes
- Maintaining stakeholder engagement

Scientific

- Altered primary research question or causal model
- Modified intervention delivery (e.g., in-person to virtual)
- Non-randomized choice/use of modified intervention by clinicians or patients (e.g., choice of in-person vs. virtual delivery)
- Remote/nonclinical collection of assessments/outcomes
- Potential impacts on study precision/power

Transition to Long-Term Management of Research Change Requests due to COVID

Internal "Adaptation Review Team" (ART) tracks and triages all change requests to assess their scientific, methodologic, and engagement impacts

- Track need for time/additional funds, and minor protocol changes
  - Input from investigator and PCORI program staff
- Moderate/major protocol changes receive in-depth review
  - Population, intervention/comparator, outcomes, timing, setting (PICOTS)
  - Mode of delivery or data collection (e.g. in-person to remote)
  - Implications to research question
  - Strength of evidence of efficacy
  - Acceptability of the change by participants
  - Feasibility of carrying out change across all participating sites/staff

Protocol Changes: Framework from Methodology Standard for Complex Interventions

- Pragmatic trials are complex interventions in having multiple, interacting components of behaviors, activities, personnel, and contexts

- PCORI Methodology Standard for Complex Interventions requires a causal model be specified describing
  - **Core function(s)** of intervention (e.g. education)
  - Allowable **forms** to achieve the core function (e.g. verbal or written information-sharing)
  - Planned or permissible **ADAPTATIONS** to **the form** (e.g. video or online information)
  - Process measurements and planned evaluation

Types of Adaptations – What Affects Their Potential Use in Findings?

- Remote consent
- Remote intervention delivery
  - Use of audio only vs. cell phone vs. tablet/laptop
  - Group vs. individual sessions
  - Behavioral interventions (counseling, training/coaching)
  - Hands on or whole-body assessment (yoga, rehabilitation, physical therapy, exercise)
- Outcome assessment by self-report vs. clinical observation (6 min walk, blood pressure, body weight)
- Findings and impact of mixing in-person and remote delivery across and within patients and sites

Key Questions in ART Review

Does the proposed adaptation change the research question/PICOTs?

- Do the adaptations have evidence of efficacy?
- Do the changes affect the trial population or effect size?
- Is remote data collection valid and reliable?
- Will the adaptation vary in implementation across time, sites, or participants?
- Has there been input or endorsement of acceptability/feasibility from patients and stakeholders?

Summary of Adaptation Experience to Date

- Most reviews ultimately result in an approval, but may need additional information and modification
  - Methods or subject matter expert consultation
  - Interim feasibility/acceptability pilot testing frequently recommended
- Benefits of PCORI process
  - Standardized review
  - Use of complex intervention framework
  - Contributions of already-engaged patients and stakeholders
  - Ability to evaluate and learn from experience
- Continuous and iterative quality improvement process!

Discussion

Questions

- Are there analytic considerations for investigators to keep in mind?
  - Considerations for specific study designs, e.g. cluster RCTs, stepped wedge?
- If ART proposes a feasibility/acceptability assessment of adaptation, what parameters should be set or requested? What justification is needed?
  - Timing and information needed? % of sample, # of sample?
  - Should the pilot sample be a part of the larger parent study, or a separate sub-sample?

Questions

- Considerations for peer review: reporting modifications due to COVID interruptions (note: recent CONSERVE 2021 guidance)
  - *"If modifications were informed by trial data, describe how the interim data were used, including whether they were examined by study group, and whether the individuals reviewing the data were blinded to the treatment allocation"*
  - Implications for ART review and recommendations?

- Are there other considerations that ART should keep in mind regarding how to review proposed adaptations?

Orkin AM, Gill PJ, Ghersi D, et al. Guidelines for Reporting Trial Protocols and Completed Trials Modified Due to COVID-19 Pandemic and Other Extenuating Circumstances: The CONSERVE 2021 Statement. JAMA. 2021;326(3):257-265.

Thank You!

Break (10 min)

Feel free to turn off camera and mute your line.

Please remain logged into the webinar

PCORI's use of PCORnet

Insights from ADAPTABLE

Claudia Grossmann, PhD
Senior Program Officer,
Research Infrastructure

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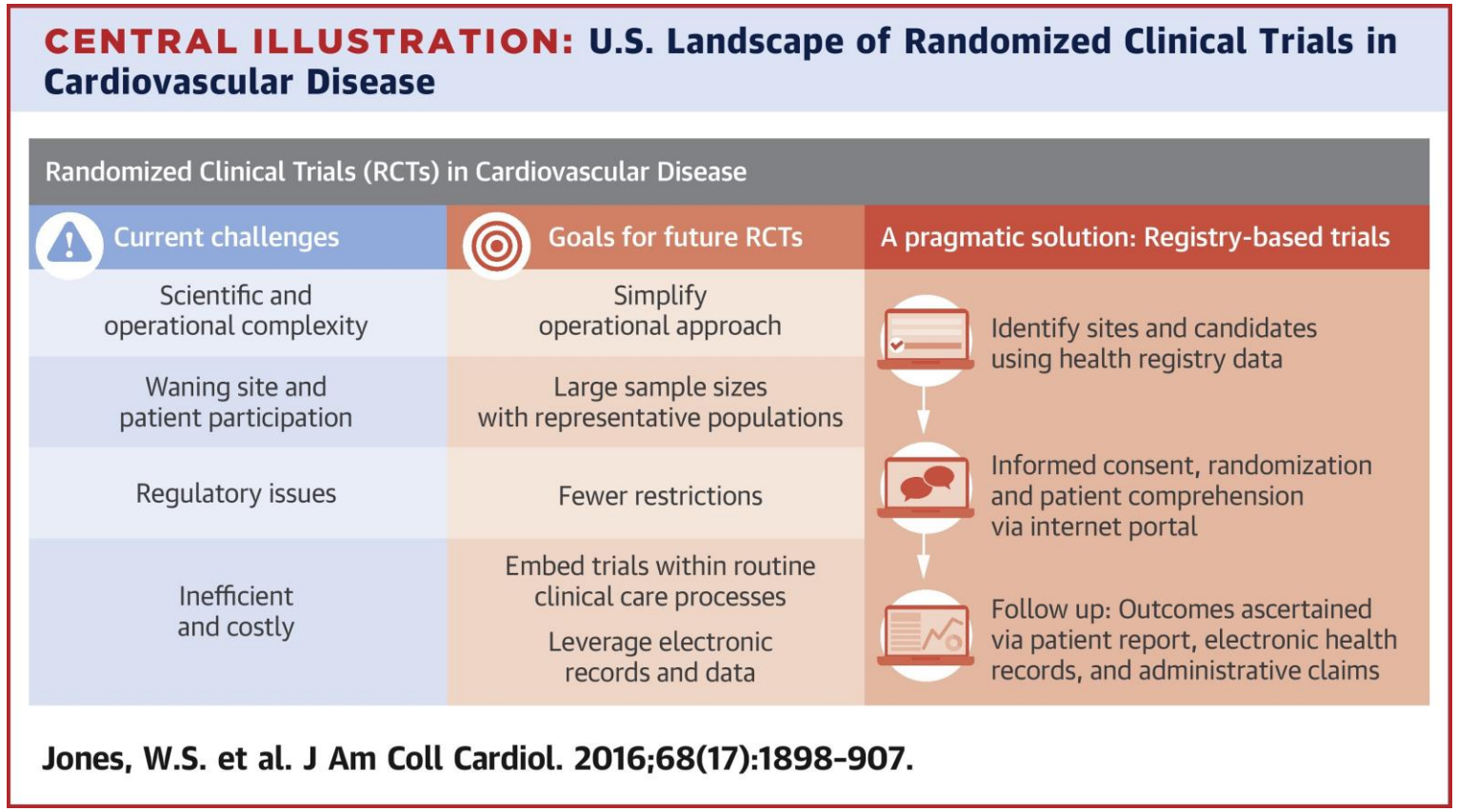
Learning about Aspirin Dosing & PCORnet for PCTs

- In 2014, U.S. patients with heart disease reflected significant, unexplained dosing variation
    - 60% daily dose of 325 mg
    - Unmet need important to patients and clinicians, but unanswered

- In 2015, as the first PCORnet Demonstration Project, **PCORI funded ADAPTABLE to provide an answer + understand capabilities**

Evolution of Clinical Trials

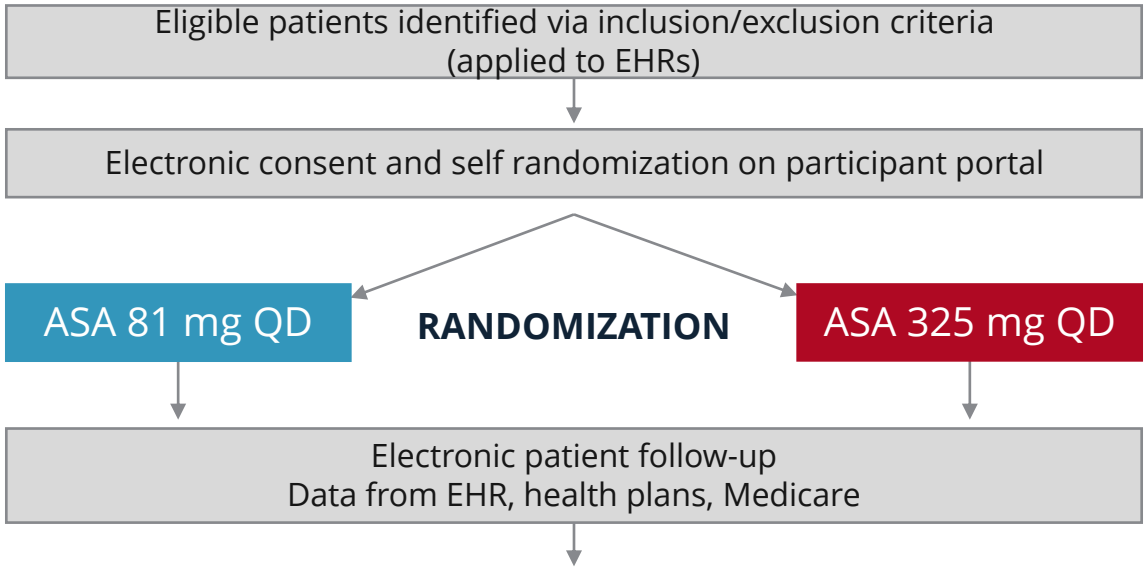


Can you leverage PCORnet to…

- Identify tens of thousands of people
- Engage
- Recruit
- eConsent
- Randomize @ home
- Remotely follow-up

Pragmatic Study Design

15,000 patients with known ASCVD + ≥ 1 “enrichment factor”



Primary Endpoint:
Composite of all-cause mortality, hospitalization for MI, or hospitalization for stroke

Primary Safety Endpoint:
Hospitalization for major bleeding

Adaptable

ClinicalTrials.gov: NCT02697916

Endpoint Confirmation

- Data sources:
  - Participant report via simple online portal
    - Call center backup
  - EHR data from PCORnet CDM
  - Claims data
    - Private insurance, CMS

- Nonfatal endpoints defined by *ICD-10* algorithms
- All-cause death captured by EHR, health insurance claims, or proxy

Adaptable

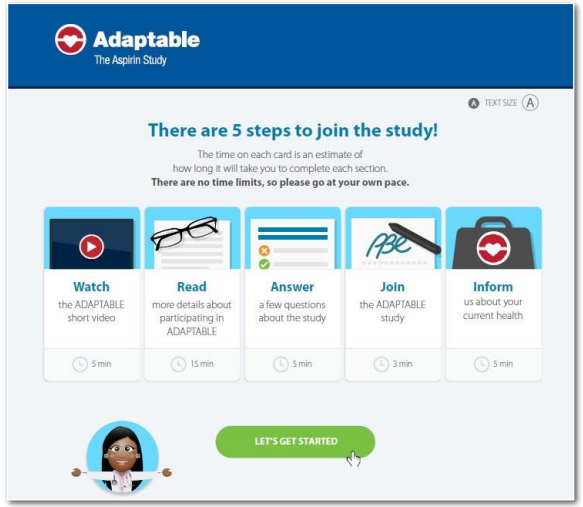
Patients Guided the Study

THE ADAPTORS

FACEBOOK LIVE

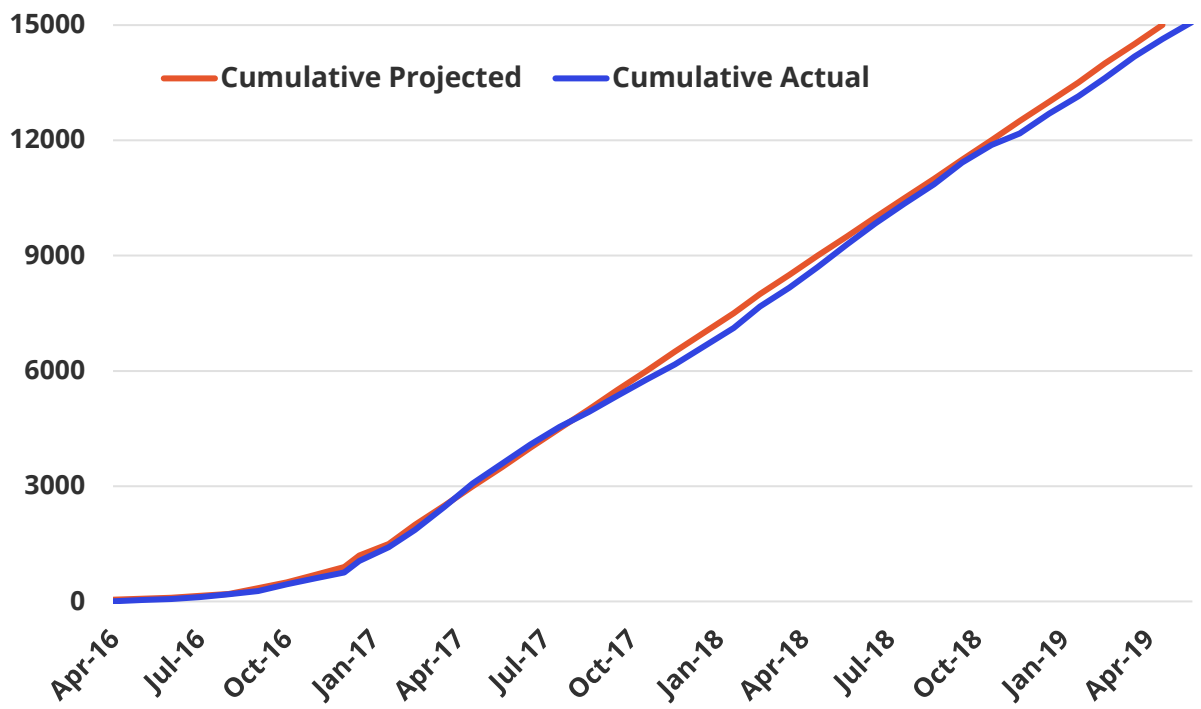
PATIENT ENGAGEMENT PAVILION

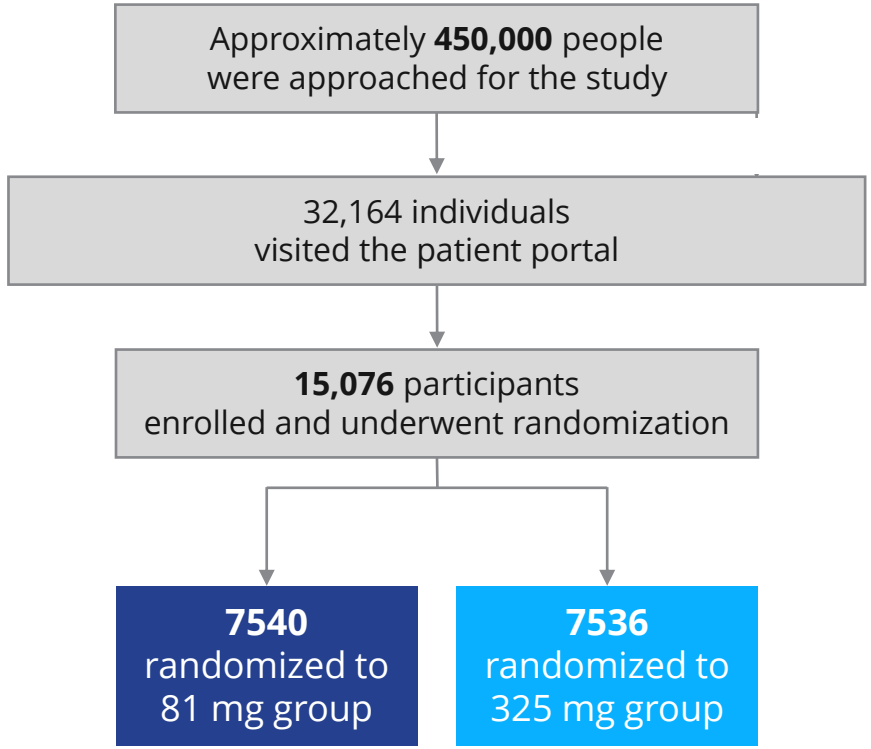
PATIENT INFORMED RECRUITMENT



Adaptable

Over 15,000 Enrolled in 3 Years at 40 sites





Adaptable

Baseline Characteristics

	81 mg group	325 mg group
Age, median, (25th, 75th), years	67.7 (60.7, 73.6)	67.5 (60.7, 73.5)
Female sex, no. (%)	2307 (30.6%)	2417 (32.1%)
Race, Black or African American, no. (%)	664 (8.8%)	647 (8.6%)
Race, White, no. (%)	6014 (79.8%)	5976 (79.3%)
Hispanic ethnicity, no. (%)	249 (3.3%)	232 (3.1%)
Weight, median (25th, 75th), kg	90.0 (78.6, 103.6)	90.0 (78.2, 104.1)
Current Tobacco use, no. (%)	696 (9.2%)	686 (9.1%)
Aspirin use before study		
81 mg	5823/6850 (85.0%)	5724/6687 (85.6%)
162 mg	168/6850 (2.5%)	142/6687 (2.1%)
325 mg	845/6850 (12.3%)	812/6687 (12.1%)
Dual antiplatelet use at baseline	1570 (22.5%)	1511 (22.1%)

Effectiveness and Safety Outcomes

	81 mg group N=7434	325 mg group N=7330	HR (95% CI)
Primary endpoint	590 (7.28%)	569 (7.51%)	**1.02 (0.91 - 1.14)**
All-cause death	315 (3.80%)	357 (4.43%)	**0.87 (0.75 - 1.01)**
Non-fatal MI	228 (2.99%)	213 (2.87%)	**1.06 (0.88 - 1.27)**
Non-fatal stroke	102 (1.23%)	92 (1.27%)	**1.09 (0.82 - 1.45)**
PCI or CABG	471 (6.05%)	446 (5.96%)	**1.04 (0.92 - 1.19)**
Transient Ischemic Attack	20 (0.23%)	25 (0.35%)	**0.79 (0.44 - 1.42)**

Study Medication in ADAPTABLE

	Overall	81 mg	325 mg
Dose switching, % *	24.2%	7.1%	41.6%
Aspirin discontinuation, % **	9.1%	7.0%	11.1%
Median days of exposure, assigned aspirin dose	551 days (139 - 737)	650 days (415 – 922)	434 days (139 – 737)
Median days of exposure, any aspirin dose	658 days (426 - 932)	670 days (439 – 944)	646 days (412 – 922)

**Defined as at least one dose change*

***Reasons for aspirin discontinuation:*
25% participant did not want to continue
75% doctor's decision or medical condition (e.g., atrial fibrillation, dyspepsia)

Trial Conclusions

- No observed difference in death / MI / stroke in patients assigned to 81 mg vs. 325 mg
- There was a difference in fidelity to the study dose/intervention (more dose switching in 325 mg group)
    - Potential reasons that patients did not stay on the 325 mg dose
        - Tolerability
        - Medical reasons
        - Participant preferences
        - Clinician practices

What Did We Learn about PCORnet?

- ✓ Identify tens of thousands of people
- ✓ Engage people
- ✓ Recruit
- ✓ E-consent
- ✓ Randomize at home
- ✓ Remotely follow-up

- – Administrative efficiencies still require attention
- – Site performance variable
- – E-Recruitment is not that simple
- – EHR data latency and completeness
- – Clinician/patient engagement critical

Competing Approaches to Recruitment

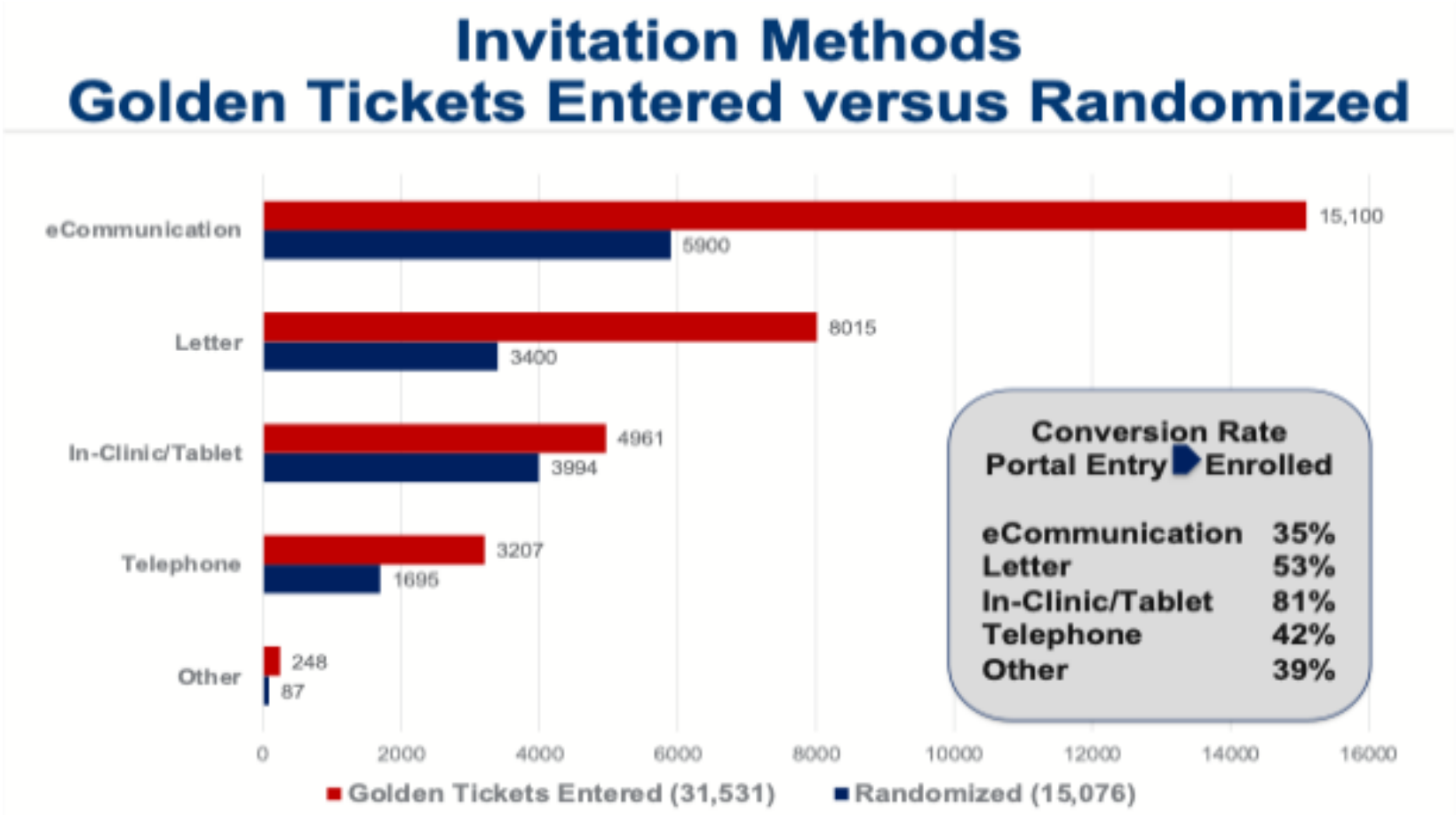
"Pragmatic"

- Broad-based outreach to large pool of eligible patients (email, mail, social media, etc.)
- Lower labor/time intensity
- Lower cost
- Faster pace of contact eligible patients

"Personalized"

- Traditional outreach involving personal, one-on-one interface (in-clinic, via phone, etc.)
- Higher labor/time intensity
- Higher cost
- Slower pace of contacting eligible patients

E-Recruitment Was Not Sufficient



Matrix of Data Sources Required Due to Variable Outcomes & Data Latency

	Data sources available			
Scenario	Self-report	EHR	Claims (CMS or Private)	N
1	X			39
2	X	X		8591
3	X		X	275
4	X	X	X	4456
5		X		1402
6			X	84
7		X	X	212
8				17
Overall				15076

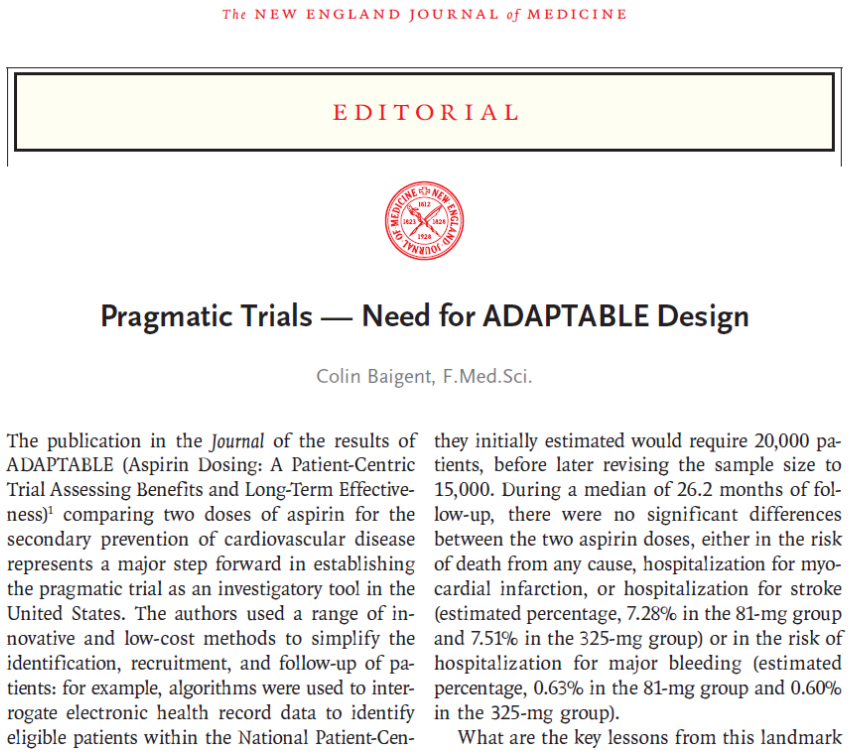
Engaged Patients Are Essential

- ADAPTORS were engaged throughout
- Required dedicated effort from the CC and the patient partners
- Patient engagement is especially important with virtual trials

Lesson Learned

- Successful sites connect clinical, informatics, and trial leaders – data are necessary but not sufficient
- Leverage the PCORnet Master Data Sharing Agreement and Single IRB
  (these were not in place when ADAPTABLE began)
- Establish benchmarks and track site performance
- Establish early lessons learned and address performance
- Plan for hybrid approaches to recruitment that benefit from local resources
- Hybridize data (Baseline – EHR; Outcomes depending on question)
- Engage patients early, often and throughout!

ADAPTABLE as proof of concept



The NEW ENGLAND JOURNAL of MEDICINE

EDITORIAL

Pragmatic Trials — Need for ADAPTABLE Design

Colin Baigent, F.Med.Sci.

The publication in the *Journal* of the results of ADAPTABLE (Aspirin Dosing: A Patient-Centric Trial Assessing Benefits and Long-Term Effectiveness)[1] comparing two doses of aspirin for the secondary prevention of cardiovascular disease represents a major step forward in establishing the pragmatic trial as an investigatory tool in the United States. The authors used a range of innovative and low-cost methods to simplify the identification, recruitment, and follow-up of patients: for example, algorithms were used to interrogate electronic health record data to identify eligible patients within the National Patient-Centhey initially estimated would require 20,000 patients, before later revising the sample size to 15,000. During a median of 26.2 months of follow-up, there were no significant differences between the two aspirin doses, either in the risk of death from any cause, hospitalization for myocardial infarction, or hospitalization for stroke (estimated percentage, 7.28% in the 81-mg group and 7.51% in the 325-mg group) or in the risk of hospitalization for major bleeding (estimated percentage, 0.63% in the 81-mg group and 0.60% in the 325-mg group).

What are the key lessons from this landmark

The publication in the Journal of the results of ADAPTABLE…represents a major step forward in establishing the pragmatic trial as an investigatory tool in the United States. The authors used a range of innovative and low-cost methods to simplify the identification, recruitment, and follow-up of patients."

"[T]he method can now be adapted and used more widely. This should allow many more clinical questions to be answered, with obvious benefits to health care consumers." *-- Colin Baigent, F.Med.Sci., Editorial: Need for ADAPTABLE Design, N Engl J Med, May 27, 2020*

Discussion

- What opportunities and directions do you see for PCORnet in light of ADAPTABLE and its multiple uses in COVID research?
- Other suggestions?

Thank You!

Learn more at **www.theaspirinstudy.org**

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The National Patient-Centered Clinical Research Network

Adaptable

Farewell to Panelists

Anne Trontell, MD, MPH
Associate Director,
Clinical Effectiveness and Decision Science, PCORI

Farewell to our Panelists!

- Catherine (Kate) Crespi - Chair
- Nancy Dreyer
- Elisa Hurley
- Jane Perlmutter
- Henry Sacks

Wrap Up and Next Steps

Catherine Crespi, PhD, MS (Chair)
Professor of Biostatistics,
UCLA Fielding School of Public Health

Anne Trontell, MD, MPH
Associate Director,
Clinical Effectiveness and Decision Science, PCORI

Potential Topics for Future CTAP Discussion

- More on any of today's topics?
- Platform and adaptive clinical trials
- Recruitment, enrollment, and retention of diverse participants in trials

Thank you!

Additional Resources

Engagement-related COVID-19 Activities

Engagement Award Enhancements
COVID-19 Targeted Engagement PFAs
D&I Award Enhancements

Engagement Award COVID Enhancements

53 Enhancements to Engagement Awards ($7 million) to

37	10	4	2
Capacity Building *$4.9 million*	Dissemination Initiative *$1.4 million*	PPRN Limited Competition *$540,625*	Conference Support *$93,515*

Race and COVID 19: Outcomes that Matter to the Black Community

Project Objectives

- Identify research questions, shaped by beliefs, values, and preferences, that address patient-centered outcomes that are most important to Black Americans.

Project Activities

- Through town halls, PCOR training workshops, and focus groups, the project team will convene its longstanding community partners, including patients, caregivers, community-based organizations, faith and civic organizations, and beauty industry leaders to co-create a network of community members and academicians trained in PCOR research methods.
- This network will be prepared and activated to collaborate in PCOR and CER, addressing priorities, values, and preferences related to COVID-19 outcomes that matter to the Black community.
- Establish guidelines and processes for disseminating relevant COVID-19 health information, PCOR outcomes, and priorities to the broader community.

Outcomes

- The outcomes of this process will lead to PCOR priorities developed by the Black community, guidelines for information dissemination through trusted and reliable community outlets, and community-academic partnerships trained and prepared to engage in PCOR research based on the priorities derived from the Black community.

Nadine J. Barrett, PhD, MS, MA
Duke University
Durham, NC
Project Period 2020-2021

Engagement Award COVID-19 Targeted PFAs

Summer 2020

25 Special Cycle COVID-19 awards ($3.7 million awarded)

- Up to 12 months (completed in June 2021)
- Up to $150,000 total costs
- Focused on methods of engagement to build capacity for PCOR/CER in the context of COVID-19

Fall 2021

- Up to 18 months
- Up to $200,000 total costs
- Focus on building capacity for stakeholder engagement in PCOR/CER specifically related to:
  - Long-term effects of post-acute COVID-19;
  - Impact of COVID-19 on disproportionately affected populations;
  - Impact of COVID-19 on social isolation and loneliness
  - Engaging, educating, and promoting informed decision making around COVID-19 vaccines

Dissemination and Implementation

COVID Enhancements

13 Enhancements to D&I Awards ($6.1 million) will adapt interventions for remote delivery, update materials, and increase reach

8 D&I enhancements have added new remote interventions – or remote delivery of interventions – including via an EHR system or patient portal.

7 D&I enhancements are adding new content for patients, including educational and support materials addressing challenges associated with COVID.

>40k

9 D&I enhancements are increasing their reach, delivering interventions to more than 40,000 additional patients and caregivers.

D&I Award COVID Enhancement Example: Adapting Antibiotic Stewardship Program for Remote Delivery

Enhancement Activities

- Pediatric outpatient settings have seen a dramatic shift to telehealth. Evidence suggests that antibiotic stewardship is less effective in telemedicine than during in-person visits.

- This enhancement will adapt educational content for clinicians, audit-and-feedback reports, and practice facilitation to address appropriate antibiotic prescribing for acute respiratory illnesses (ARTIs) during telemedicine visits.

Antibiotics are the most commonly prescribed medication for children, primarily in outpatient settings for treatment of acute respiratory tract infections (ARTIs). Contrary to current guidelines, many children are prescribed broad-spectrum rather than narrow-spectrum antibiotics as first-line treatment.

The original D&I project adapts and implements a tested antibiotic stewardship program to improve outpatient prescribing at 350,000 ARTI visits in diverse practice settings across 5 health systems.

Jeffrey Gerber, MD, PhD
Children's Hospital of Philadelphia

Implementation of PCORI's Major Research Investments
Awarded November 2019