

Board of Governors Meeting

via Teleconference/Webinar

May 5, 2020

11:00 AM – 2:30 PM

Welcome and Introductions

Christine Goertz, DC, PhD

Chairperson, Board of Governors

With Deep Appreciation



*For your exceptional leadership,
your tireless dedication,
and commitment*

Josephine P. Briggs , MD

PCORI's New Executive Director



Nakela L. Cook, MD, MPH



- Dr. Cook is a cardiologist with a long and distinguished career as a researcher and advocate for engaging patients, clinicians, and other stakeholders in key research initiatives
- She joined PCORI on April 15th, 2020. Please join us in welcoming Dr. Cook!

Agenda



11:00 AM

Call to Order and Welcome

11:10-11:20

Consider for Approval:

- Minutes of March 2, 2020 and April 1, 2020 Board Meetings
- Proposed Amendments to Bylaws

11:20-12:00

Executive Director's Report

12:00-12:30

COVID-19 Response Update

- Progress on COVID-19 Targeted PFA
- Consider for Approval: Alternative Review and Approval Framework for Awards Under this PFA

1:00-1:40

- PCORnet HERO Registry and Trial

1:40-1:50

- Enhancements of Existing Awards

1:50-2:00

- Monitoring & Evaluating the Impact of the Pandemic on Our Work

2:00-2:30

Public Comment

2:30

Wrap-up and Adjournment

Board Vote

Call for a Motion to:

- **Approve** the minutes of the March 2, 2020 and the April 1, 2020 Board of Governors meetings

Call for the Motion to be Seconded:

- **Second** the Motion
- If further discussion, may propose an **Amendment** to the Motion or an **Alternative** Motion

Voice Vote:

- Vote to **Approve** the **Final** Motion
- Ask for votes in favor, opposed, and abstentions

Proposed Amendments to PCORI Bylaws to Conform Bylaws with Reauthorizing Legislation

Sharon Levine, MD

Chair, Governance Committee

Mary Hennessey, Esq.

General Counsel

Proposed Bylaws Amendments



- Proposed Bylaws amendments are to conform Bylaws with Reauthorizing Legislation:
 - Clarifies language about preserving evenly staggered terms of Board and about filling vacancies created by Board members who leave Board prematurely
 - Revises appointment authority for Methodology Committee members from the Comptroller General to PCORI's Board of Governors
 - Updates citation to authorizing law to reflect reauthorizing legislation
 - Clarifies existing language to confirm that committees, working groups, and ad hoc committees shall not exercise the power of the Board except as authorized by the Board

Amendments to the Bylaws require a vote of 2/3 of the Board members present at a Board meeting at which a quorum is established.

Board Vote

Call for a Motion to:

- **Approve** the Amended Bylaws

Call for the Motion to be Seconded:

- **Second** the Motion
- If further discussion, may propose an **Amendment** to the Motion or an **Alternative** Motion

Roll Call Vote:

- Vote to **Approve** the **Final** Motion
- Ask for votes in favor, opposed, and abstentions

Executive Director's Report

Nakela L. Cook, MD, MPH

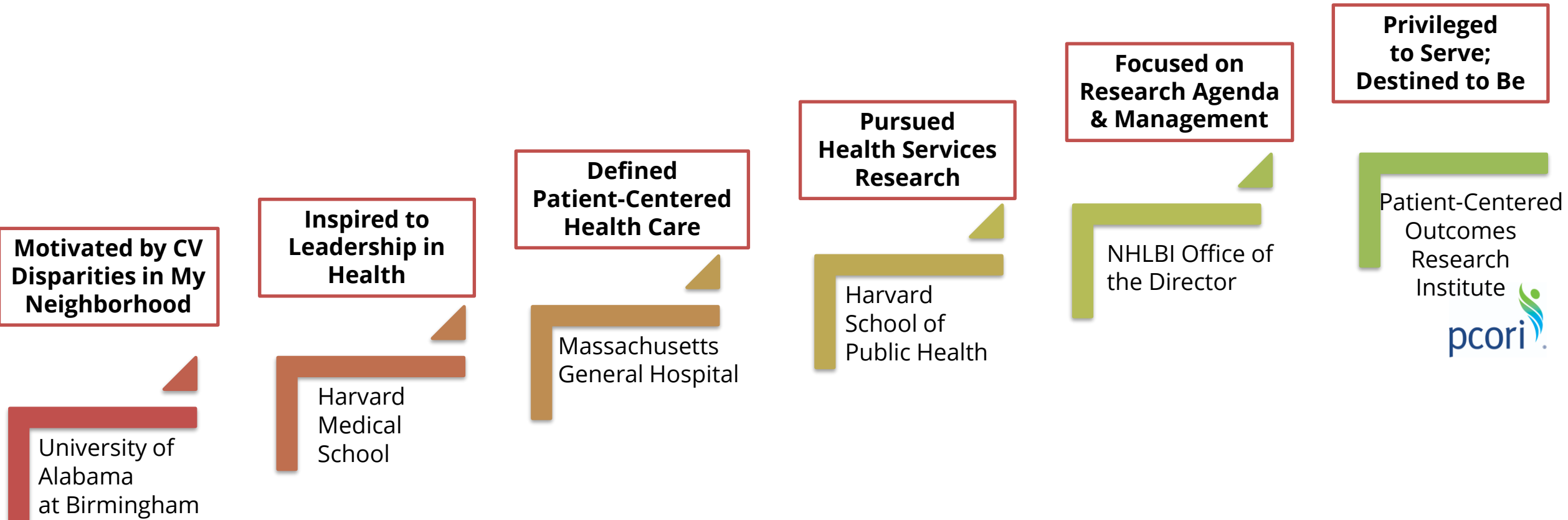
Executive Director

Navigating Our Course



- **My First Few Weeks**
 - My Path to PCORI
 - Early Onboarding
 - Passionate and Mission-Driven PCORI Staff and Board
- **Envisioning PCORI 2.0**
 - Opportunities for the Future
 - Learning in a Public Health Crisis
- **Our Course Together**
 - Year 1 Priorities
- **PCORI's Response to the COVID-19 Pandemic**

My Path to PCORI: Influenced by My Life Experiences



Outstanding, Resilient Staff and Mission-Driven Board at the Heart of PCORI



- **Overcoming Challenges in Pursuit of the Mission**

“Courage is simply doing whatever is needed in pursuit of the vision”

— Peter M. Senge, *The Fifth Discipline: The Art & Practice of The Learning Organization*

- **Dedicated and Mission-Driven**

- Remarkable achievements to celebrate
- Rallied to usher through reauthorization

A true testament to your efforts



Overcoming the Challenges of Our Current Environment

- **Confronting health concerns**
 - Dynamic efforts of cross-functional health emergency planning team for COVID-19
- **Remote working**
 - Stepped up to maintain PCORI's operations and identify how we can make a difference
 - PCORI uniquely poised to ask and answer meaningful research questions in health care delivery



Building Upon a PCORI Legacy

Research Done Differently

Mission: Help people make informed health care decisions and improve health care delivery and outcomes by *producing and promoting high integrity, evidence-based information that comes from research* guided by patients, caregivers and the broader health care community.



Established mission, vision, values that resonate with stakeholders

Transformed research culture with patient-centered approach

Delivered research results & platforms poised for implementation

Staffed to operationalize app to award process and D&I for impact

Established highly effective engagement process

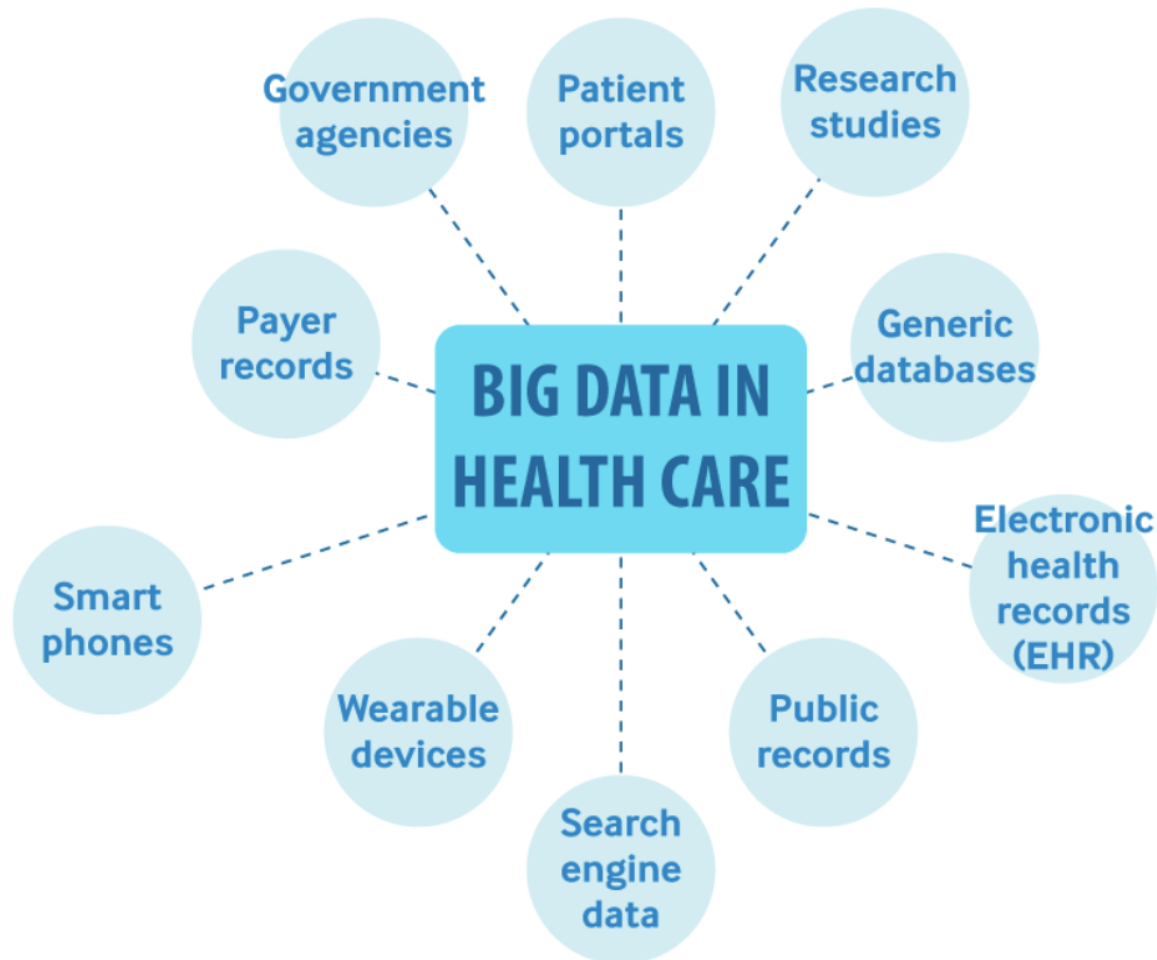
Navigating Our Course



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Evolving Healthcare and Research Landscape in a Big Data Era

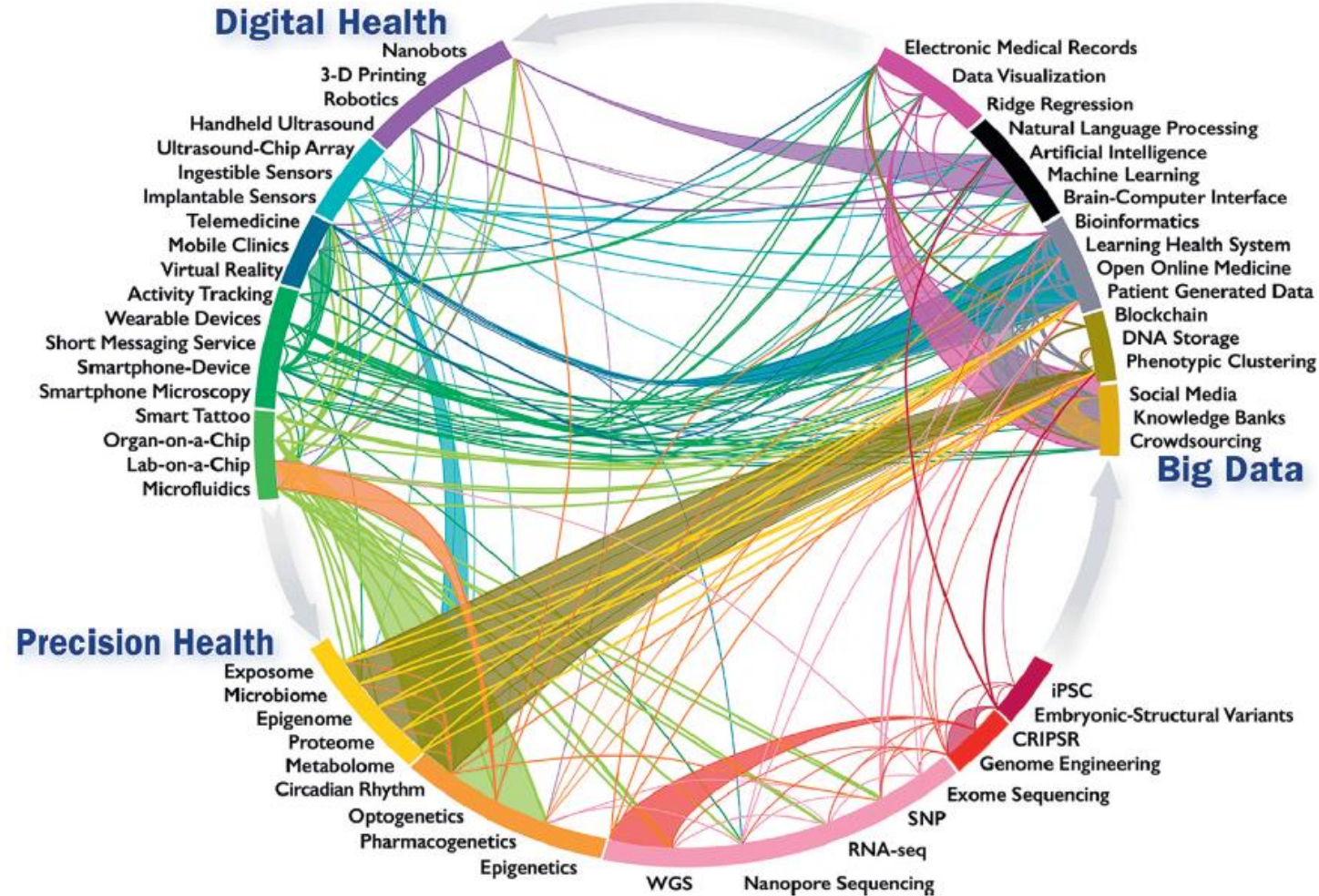
Sources of Big Data in Healthcare



Applications for Big Data in Healthcare

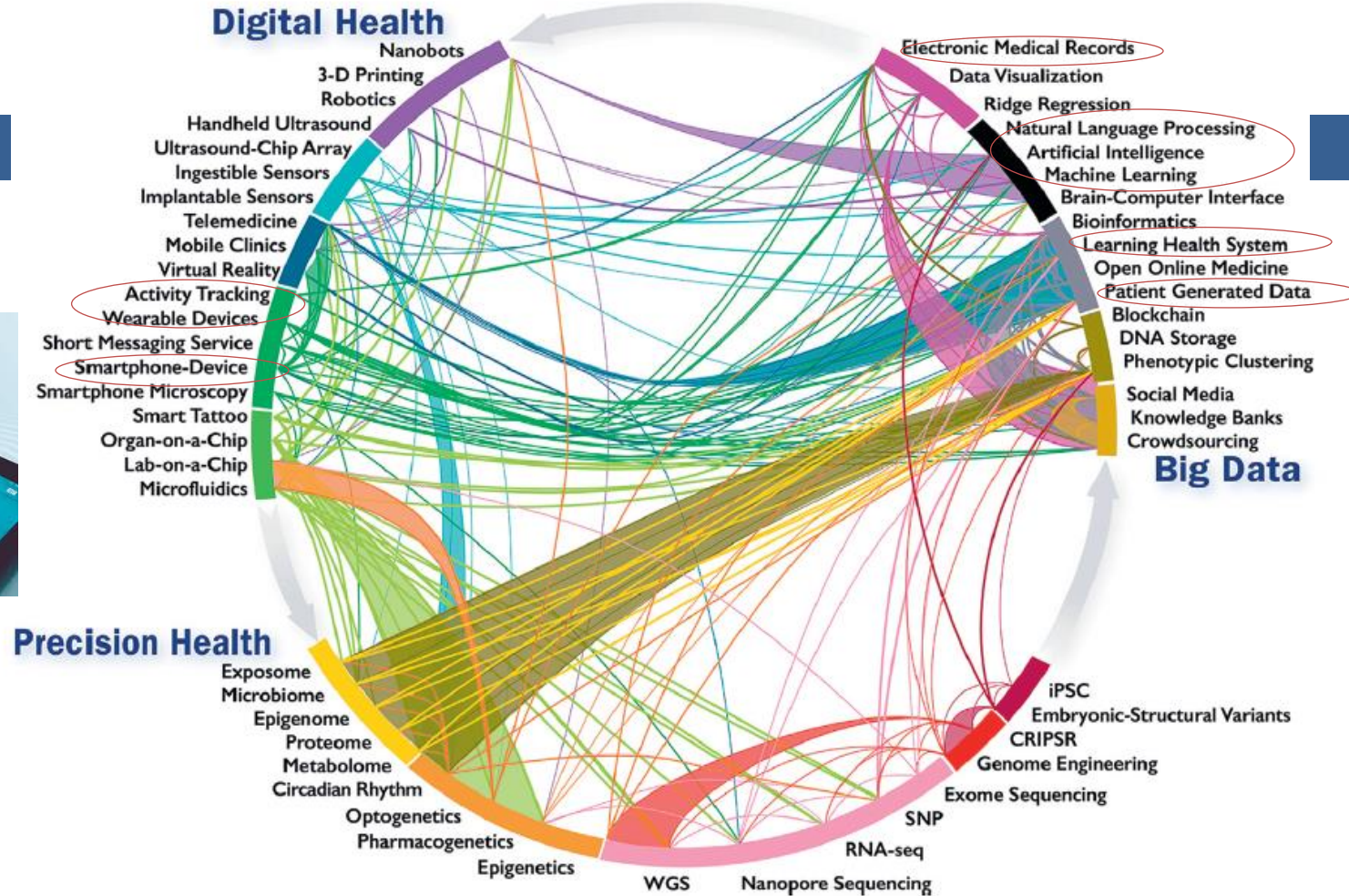


Leveraging Innovations in Healthcare to Promote the Science of Delivery for Improved Outcomes



Leveraging Innovations in Healthcare to Promote the Science of Delivery for Improved Outcomes

Patient-Centered



Community-Centered



Despite Marked Improvements in Health, Disparities and Variation in Care Still Remain

This Issue Views **90,724** | Citations **22** | Altmetric **4322**

Special Communication

November 26, 2019

Life Expectancy and Mortality Rates in the United States, 1959-2017

Steven H. Woolf, MD, MPH¹; Heidi Schoomaker, MAEd^{2,3}

» Author Affiliations

JAMA. 2019;322(20):1996-2016. doi:10.1001/jama.2019.16932

<https://jamanetwork.com/journals/jama/article-abstract/2756187>

Black curve indicates age-adjusted mortality for all US adults aged 25 to 64 years; bolded data points indicate joinpoint years, when the linear trend (slope) changed significantly based on joinpoint analysis. The lowest mortality rates per 100 000 (and the years they were achieved) are listed first in parentheses; mortality rates for 2017 listed second. Source: CDC WONDER.

Copyright 2019 American Medical Association. All Rights Reserved. Date of download: 4/28/20

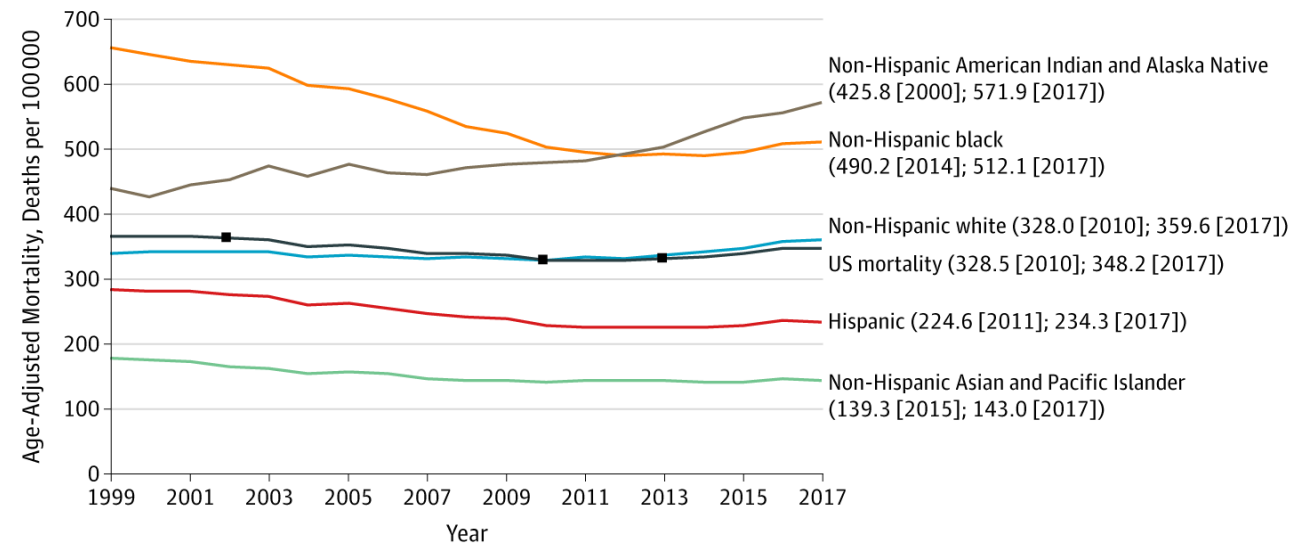


The analysis documents a host of health disparities by geography, sex, and race... The authors also consider how poverty, income inequality, unstable employment, psychological distress, and divergent state policy choices could explain these outcomes, especially for vulnerable populations.

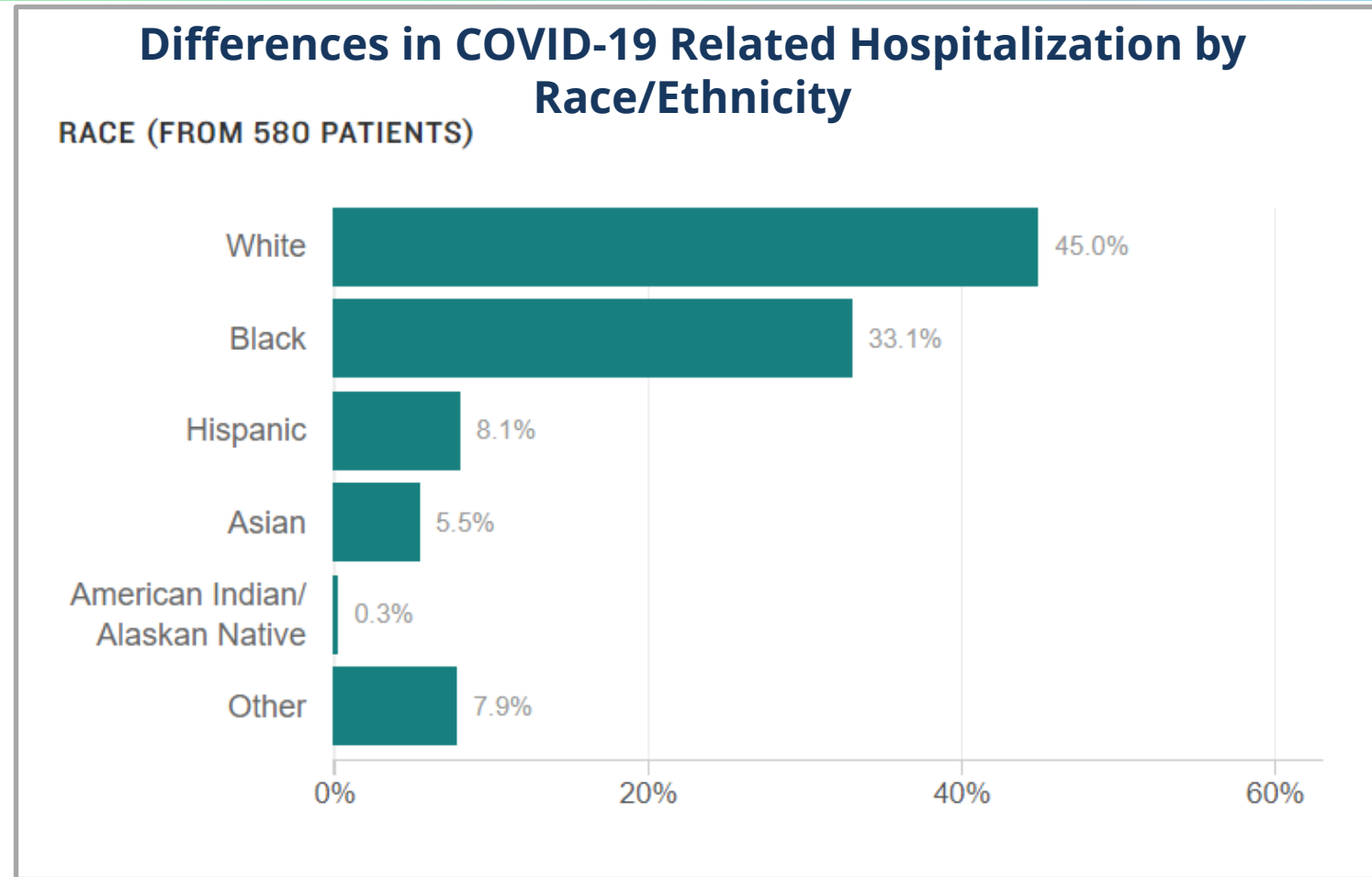
Quote from Associated Editorial

Koh HK, et al. Confronting the Rise and Fall of US Life Expectancy. JAMA. Nov 2019. <https://jamanetwork.com/journals/jama/fullarticle/2756159>

Age-Adjusted Mortality Rates, US Adults Aged 25-64 Years, by Race/Ethnicity, 1999-2017

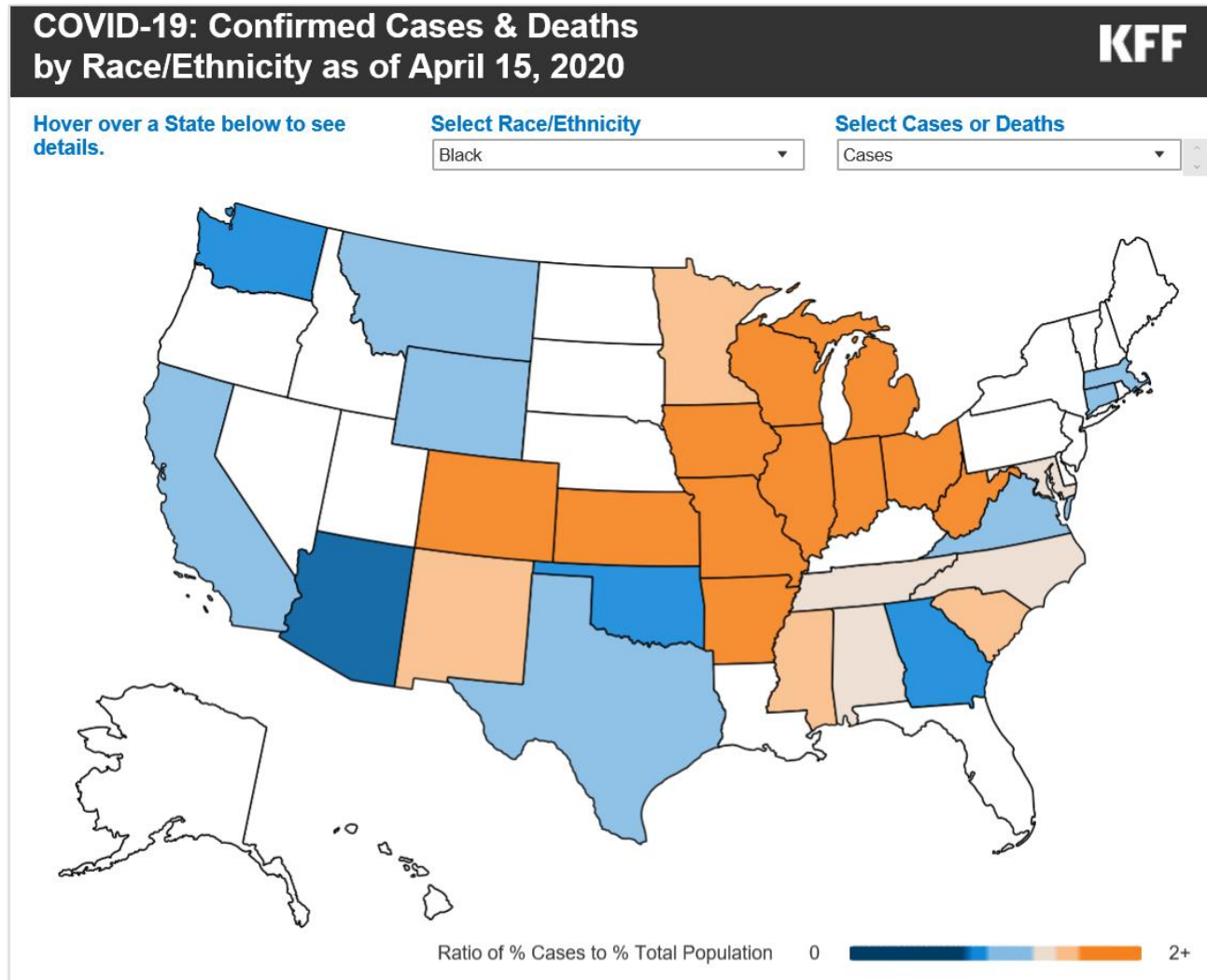


COVID-19 Outcomes Clearly Elucidate the Challenge of Health Disparities



Source: Aubrey A, Neel J. CDC Hospital Data Point To Racial Disparity In COVID-19 Cases. April 8, 2020. ([link](#))
Data from Centers for Disease Control and Prevention ([link](#)); Figure credit: Stephanie Adeline/NPR

Emerging Data: Unmasking the Interplay Between Race/Ethnicity and COVID-19



Illinois

Reporting Race/Ethnicity Data: Yes
Race/Ethnicity: **Black**

% Cases 26%
% Deaths 41%
% Total Population 14%

Kansas

Reporting Race/Ethnicity Data: Yes
Race/Ethnicity: **Black**

% Cases 17%
% Deaths 33%
% Total Population 5%

South Carolina

Reporting Race/Ethnicity Data: Yes
Race/Ethnicity: **Black**

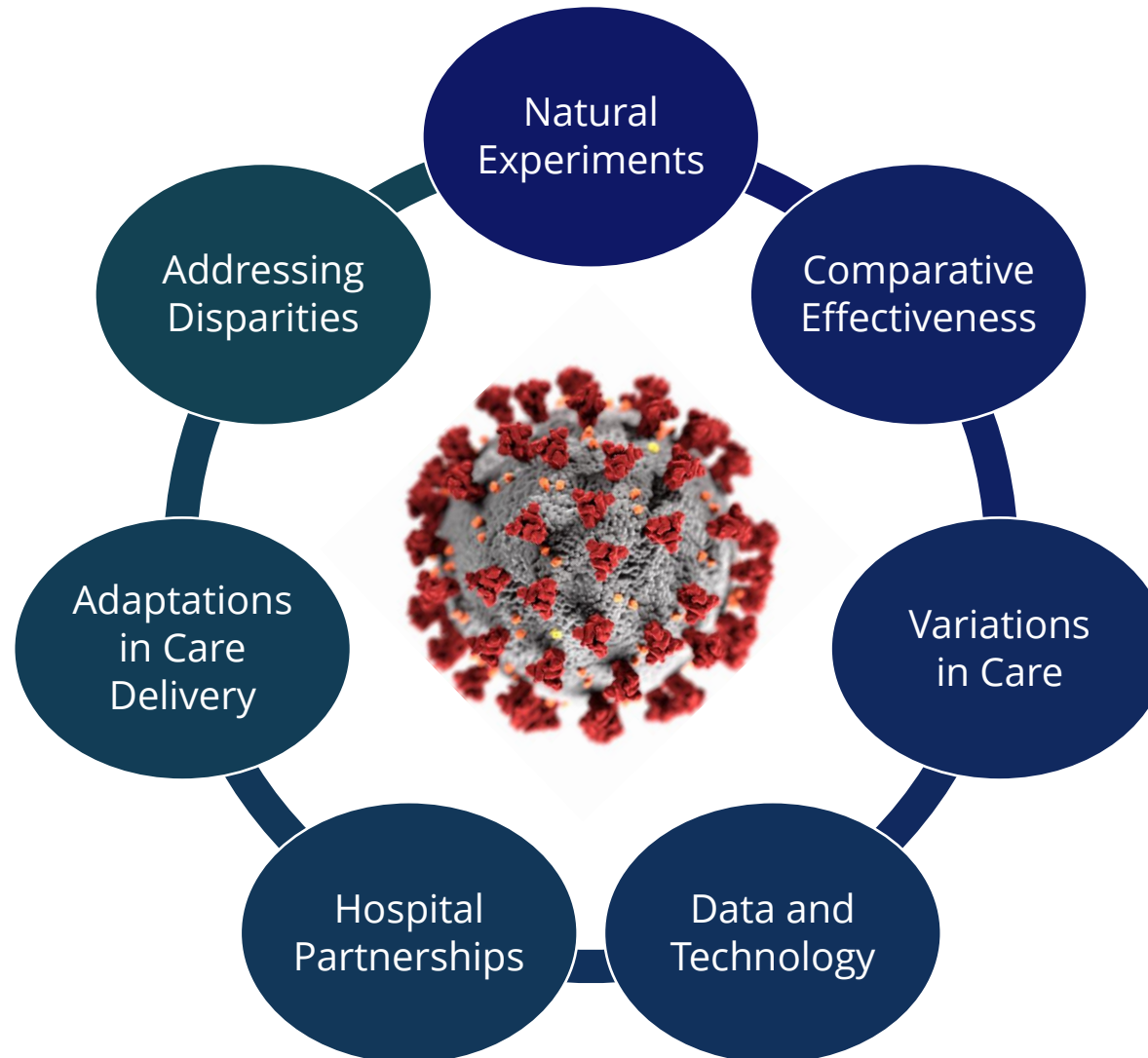
% Cases 41%
% Deaths 50%
% Total Population 26%

Source: Kaiser Family Foundation. [COVID-19: Confirmed Cases & Deaths by Race/Ethnicity as of April 15, 2020](#). Distribution of Cases/Deaths by Race/Ethnicity based on KFF analysis of publicly available state websites. Total State Population Distribution by Race/Ethnicity based on KFF analysis of 2018 American Community Survey. Accessed 4/28/20

COVID-19 Pandemic – Not Only a Stress Test, But Also a Learning Opportunity

Advancing PCORI 2.0

A Learning Organization
Nimbly Embracing
Opportunities in a Crisis for
Short and Long-term
Impact



PCORI 2.0: Opportunities to Accelerate Impact on Care Delivery and Patient Health Outcomes



Engagement

- New and sustained partnerships
- Diverse stakeholder inclusion
- Bipartisan congressional support

Impact:

- *Patients, payers, systems as partners for dissemination & uptake*
- *Evidence to implementation*
- *PCORI integral in research ecosystem*

Innovation

- Patient-centered learning healthcare
- Rapid cycle of evidence to implementation
- Pragmatic approaches to ↓ disparities

Impact:

- *“Real-time” implementation of findings*
- *Uptake into guidelines & care*
- *Reduced variation in care & disparities in conditions/pops*

Operations

- Creative funding approaches
- Efficient & effective processes

Impact:

- *Nimble and adaptable methods to speed innovation to results to patients*
- *Robust pool of outstanding research (built capacity)*

PCORI 2.0: Opportunities to Accelerate Impact on Care Delivery and Patient Health Outcomes



Engagement

- New and sustained partnerships
- Diverse stakeholder inclusion
- Bipartisan congressional support

Impact in Post COVID-19 Era:

- *Hospitals and healthcare systems working together*
- *Gaps in evidence for decision-making driving research*
- *PCORI essential*

Innovation

- Patient-centered learning healthcare
- Rapid cycle of evidence to implementation
- Pragmatic approaches to ↓ disparities

Impact in Post COVID-19 Era:

- *"Real-time" queries, output, and implementation*
- *Accelerated uptake*
- *Acute focus on variation in care & disparities*

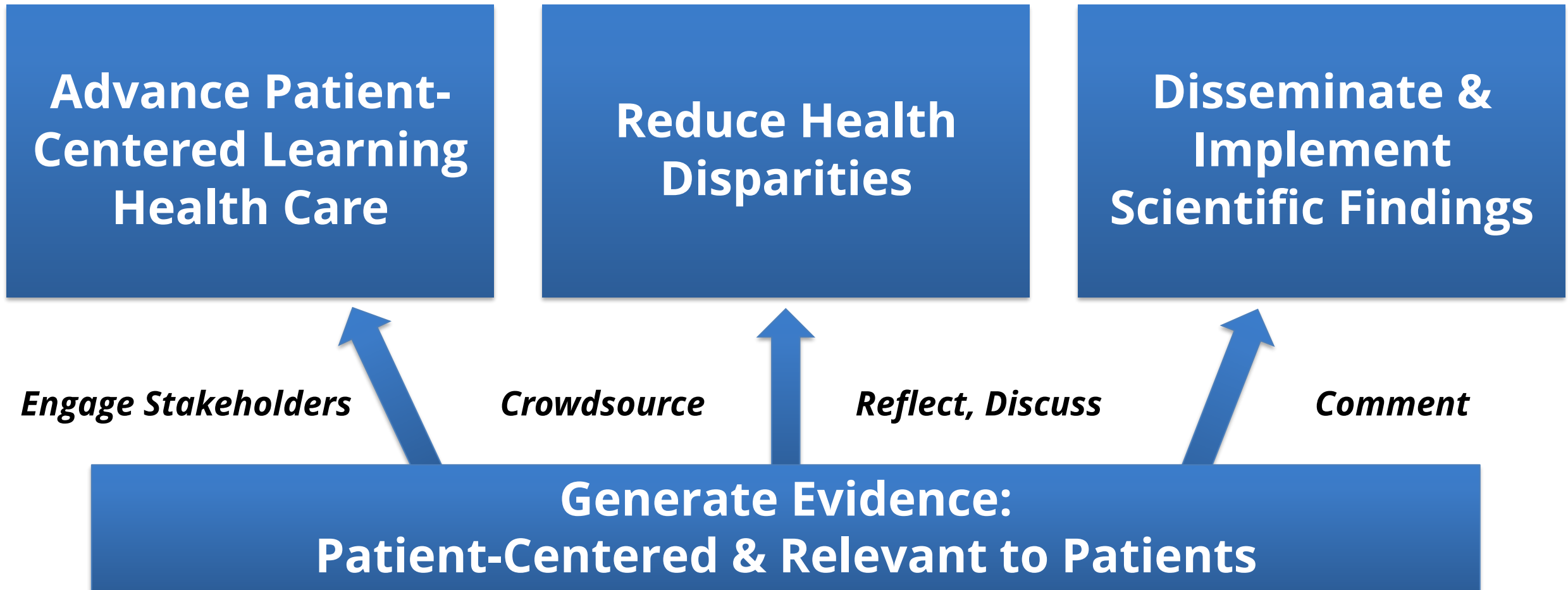
Operations

- Creative funding approaches
- Efficient & effective processes

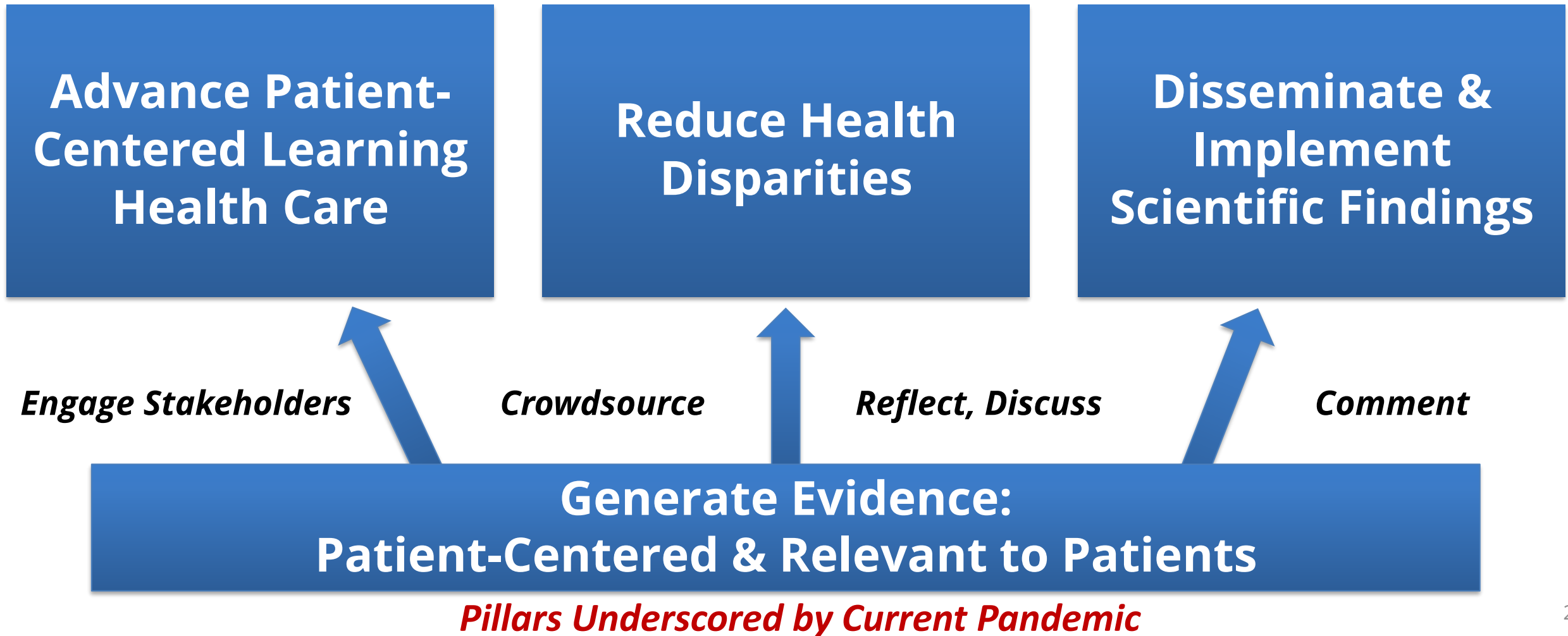
Impact in Post COVID-19 Era:

- *Nimble and adaptable processes, research*
- *Clearer approach to leveraging data, technology, infrastructure*
- *Expanded research pool*

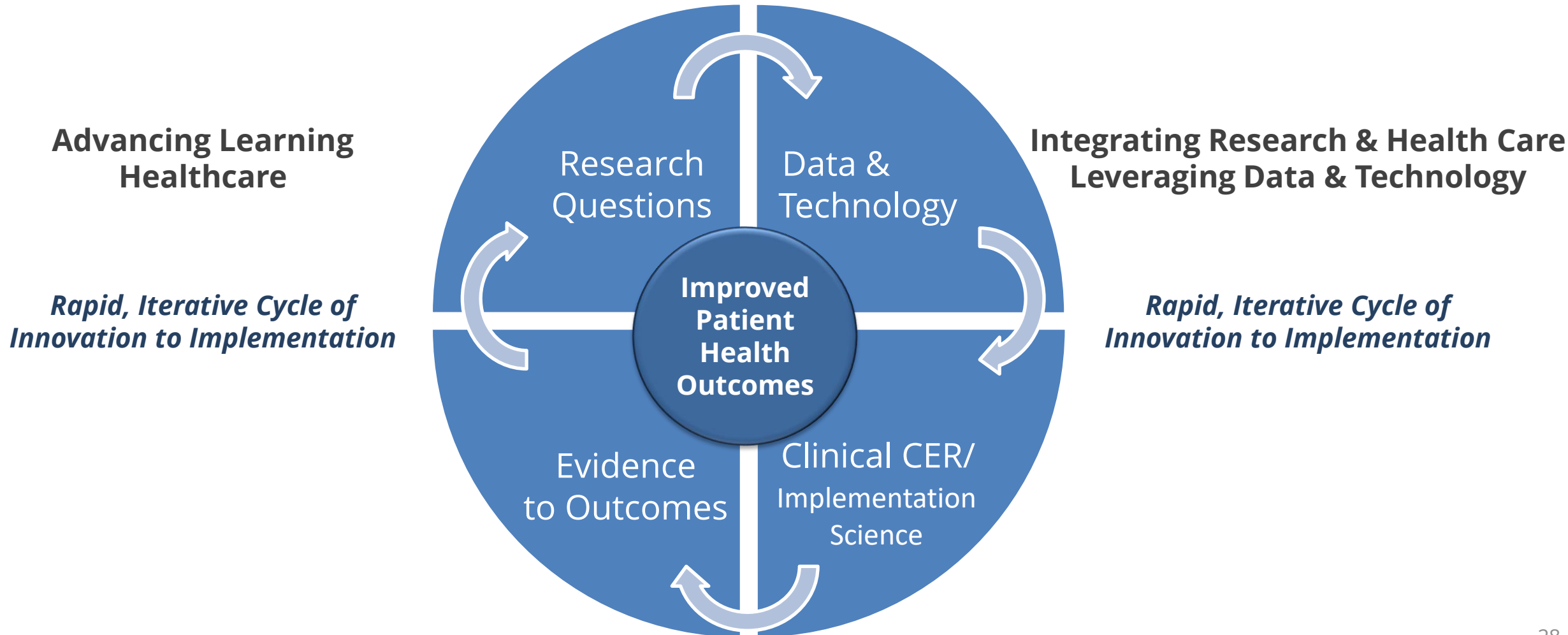
Envisioning PCORI 2.0



Envisioning PCORI 2.0



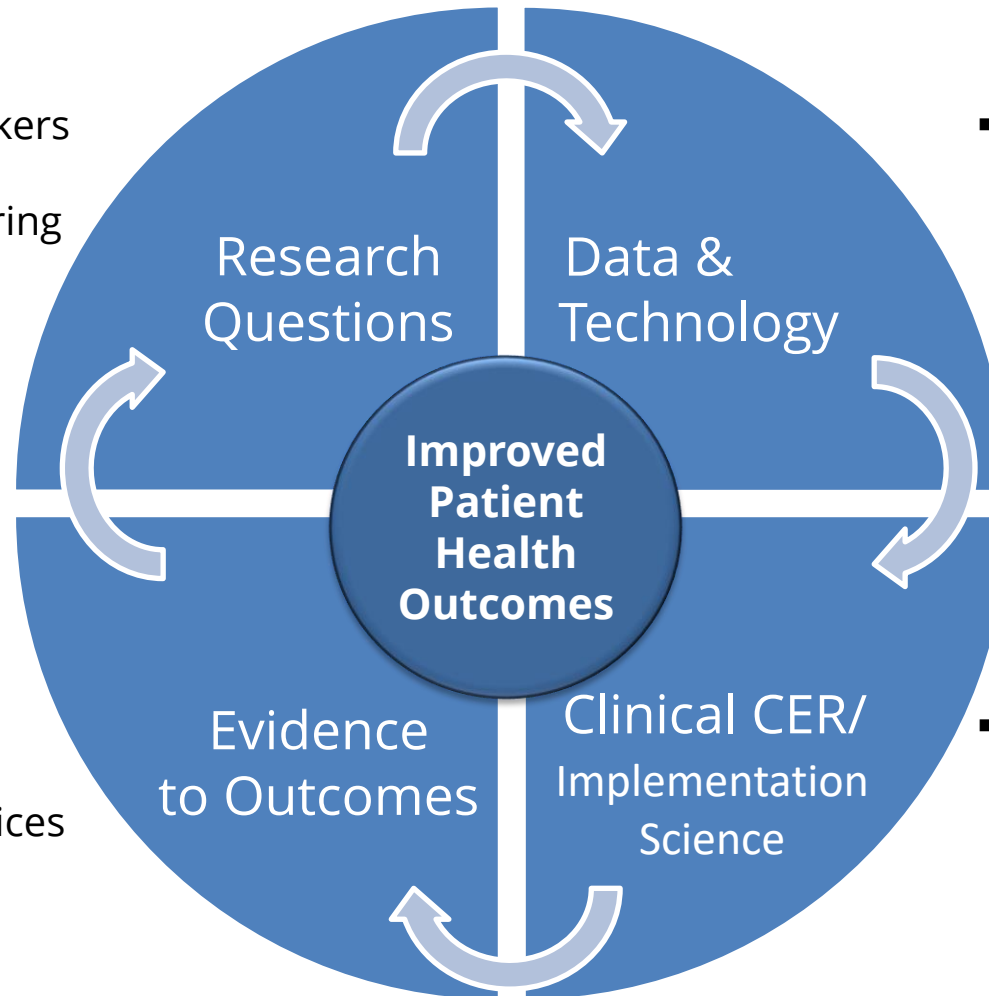
PCORI 2.0: A Virtuous Cycle of Evidence to Implementation



PCORI 2.0: A Virtuous Cycle of Evidence to Implementation

- Relevant to patients & decision-makers
- Driven by research findings
- Informed by surveillance & monitoring

- Context-specific D&I in specific populations & settings
- Risk stratification & therapeutic choices



- Monitor, risk stratify, target/intervene
 - EHRs
 - Data science platforms and tools
 - Training & capacity-building

- Evidence that
 - Targets conditions, populations, health disparities
 - Influences guidelines

Navigating Our Course



- **My First Few Weeks**
 - My Path to PCORI
 - Early Onboarding
 - Passionate and Mission-Driven PCORI Staff and Board
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- **Our Course Together**
 - Year 1 Priorities
- **PCORI's Response to the COVID-19 Pandemic**

Navigating Our Course

First Year Focus

- Shared Principles
- Onboarding and Assessments
- PCORI's Response to the COVID-19 Pandemic
- National Priority Setting and Development of Research Agenda and Strategic Plan
- Other Priorities Stemming from Legislation (e.g., Maternal Mortality, Intellectual and Developmental Disabilities, Cost Outcomes, and Methodology Committee)



Collaborative Strategy to Advance a Vision for PCORI 2.0

Refreshing National Priorities, Research Agenda, and Strategic Plan

Garner diverse input to guide scientific directions

*Patients, Clinicians, Researchers, Purchasers, Payers, Industry,
Hospitals & Health Systems, Policy Makers, Training Institutions*

Listening Tour
Board & Staff

Conduct portfolio analyses & evaluate research programs

Refine priority research areas

Develop implementation plans

Align resources with research priorities

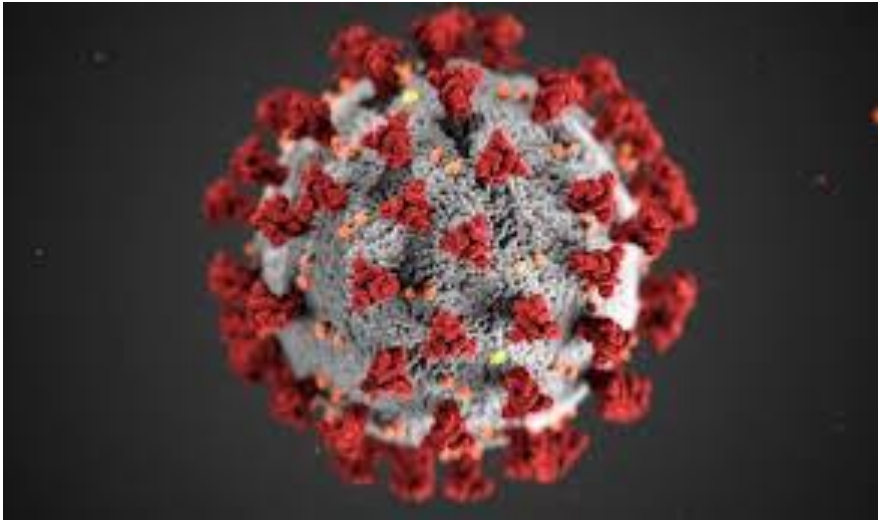
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A Pandemic of Unprecedented Scale and Consequences

**Cumulative Confirmed Cases
of COVID-19:**
>3 million worldwide



Source: COVID-19 Dashboard by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU). <https://coronavirus.jhu.edu/map.html> Accessed 4/28/20.

A Multi-Pronged Approach in Response to the COVID-19 Health Crisis

In our efforts to inform the current pandemic and learn for the future, PCORI has identified **three priority areas**:

**Health Care
Delivery**

**Vulnerable
Populations**

**Health Care
Workers**

Many approaches to supporting critical work in these three areas and more:

Awards

- Enhancements of existing awards
- Solicitation of new awards, e.g., natural experiments
- Health care worker registry and trial

Information Sharing

- Webinars
- Collaboration with other funders

Adapting for Awardees and Applicants

- Adaptations to existing projects
- Extending application timelines

Open Opportunities

Applicant and Awardee FAQs Related to COVID-19: PCORI is working to assist applicants and awardees in finding solutions that may help address issues related to disruptions associated with COVID-19, including general guidance and information about funding application deadline extensions.



Confronting COVID-19: Finding Hospital Capacity and Improving Patient Flow

A Webinar Series Hosted by PCORI for Hospitals and Health Systems

PCORI – Always Relevant

Meaningful research questions in health care delivery



Does pre-exposure prophylaxis with HCQ reduce rates of COVID-19 among healthcare workers?

What are the most effective practices for telehealth? Can this natural experiment shed light on whether telehealth can deliver similar outcomes for patient care and management?

What are the predictors of poor outcomes in COVID-19 infection and can we systematize predictive algorithms to determine who is likely to need intensive care?

What approaches are effective in eliminating health and health care disparities in COVID-19 outcomes and how are they generalizable to disparities more broadly?

Updates on PCORI's COVID-19 Response



COVID-19 Targeted PFA Update

Jason Gerson, PhD



Enhancements of Existing Awards: Enabling Existing Projects to Address COVID-19

Steve Clauser, PhD, MPA



HERO Registry and Randomized Clinical Trial Program

Josephine Briggs, MD

Guest presenters:

- Chris Forrest, MD, PhD
- Susanna Naggie, MD



Monitoring & Evaluating the Impact of the Pandemic on Our Work

Laura Forsythe, PhD, MPH

Questions?

COVID-19 Response Update

Nakela Cook, MD, MPH

Executive Director

Jason Gerson, PhD

Senior Program Officer
Clinical Effectiveness and Decision Science

Update: COVID-19 Targeted PCORI Funding Announcement (PFA)

Jason Gerson, PhD

Senior Program Officer
Clinical Effectiveness and Decision Science

Overview of COVID-19 Targeted PFA



- On April 1, 2020 the PCORI Board of Governors approved \$30M for funding new research studies, dissemination and implementation projects, engagement projects, and projects using PCORnet
- A targeted research solicitation is forthcoming with three priority areas:
 - 1. Adaptations to healthcare delivery**
 - 2. Impact of COVID-19 on vulnerable populations**
 - 3. Impact of COVID-19 on healthcare workforce well-being, management, and training**

(Other topics are allowable but these three will be given preference)
- Total costs: 2 tiers - up to \$2.5M, up to \$5M
- Maximum project period: 2 years, primary outcomes reported within 12 months
- Preannouncement posted on April 21; PFA opens on May 5

Rationale: Adaptations to Healthcare Delivery



COVID-19 related restrictions of in-person care delivery, loosened regulations on telehealth, and COVID-19 surge planning have led to:

- Many services now being delivered via telehealth; 50% increase in March vs. Feb (Kaiser Health News, 2020)
- Several million Americans could require hospitalization or intensive care over the next six months due to the pandemic (Arora, Fried, Health Affairs Blog, 2020)
- Steep decreases in in-person primary care visits, resulting in 42% of primary care offices needing to layoff or furlough staff (Primary Care Collaborative, 2020)

Examples: Adaptations to Healthcare Delivery

Potential questions include:

- What is the impact on patient-centered outcomes of alternative healthcare delivery models (e.g., telehealth, hospital at home) implemented due to COVID-19?
- What has been learned about barriers and facilitators to their effective implementation?

Rationale: Impact of COVID-19 on Vulnerable Populations



Early analyses have shown evidence of significant disparities in access and outcomes. (Yancy, 2020)

- Black Chicago residents are dying at nearly 6 times the rate of white residents (Reyes et al., 2020); in NYC, the fatalities of Hispanics and African Americans exceeds their representation in the population (34% vs. 29% and 28% vs. 22% of the populations, respectively) (New York State Department of Health)
- Cases of COVID-19 among Native Americans cared for by the Indian Health Service (IHS) are approaching the number of available IHS hospital beds, which are often geographically distant (Van Dorn, Cooney, & Sabin, 2020)
- Adults with intellectual and developmental disabilities often rely daily on the help of others for basic needs. Social distancing risks loss of food, transportation, hygiene assistance, and critical emotional support (Sigafoos, 2020)

Examples: Impact of COVID-19 on Vulnerable Populations

Potential questions include:

- What are effective clinical pathways to improve outcomes for vulnerable & high-risk patients?
- Which system- or organizational-level responses can prevent or mitigate differential impact of COVID-19 in low-income and low-resource settings?

Rationale: Impact of COVID-19 on Healthcare Workforce Well-being, Management, and Training



The focus on the well-being of the healthcare workforce complements PCORI's COVID-19 related investments, namely funding the Healthcare Worker Exposure Response and Outcomes (HERO) registry, which will engage healthcare workers and help identify important topics to the workforce.

- Reported rates of healthcare worker infection are as high as 20%, with actual rates unknown and thought to be significantly higher (Jewett & Szabo, 2020)
- Limited availability of appropriate personal protective equipment (PPE) and shortages of medical resources are forcing life-or-death decisions, resulting in depression, anxiety, insomnia, and distress among healthcare workers (HCW) (Gold, 2020)

Examples: Impact of COVID-19 on Healthcare Workforce Well-being, Management, and Training



Potential questions include:

- What policies, practices, or programs are effective to expedite health systems to shift human resources, redeploy and/or train current and new HCW to fill healthcare delivery needs?
- What are effective strategies to protect the physical and/or mental well-being of the health care workforce?

Vote: Alternative Review and Approval Framework for Awards under COVID-19 Targeted PCORI Funding Announcement

Nakela Cook, MD, MPH

Executive Director

Alternative Review and Approval Framework for COVID-19 Targeted PCORI Funding Announcement (PFA)



Details and tentative dates:

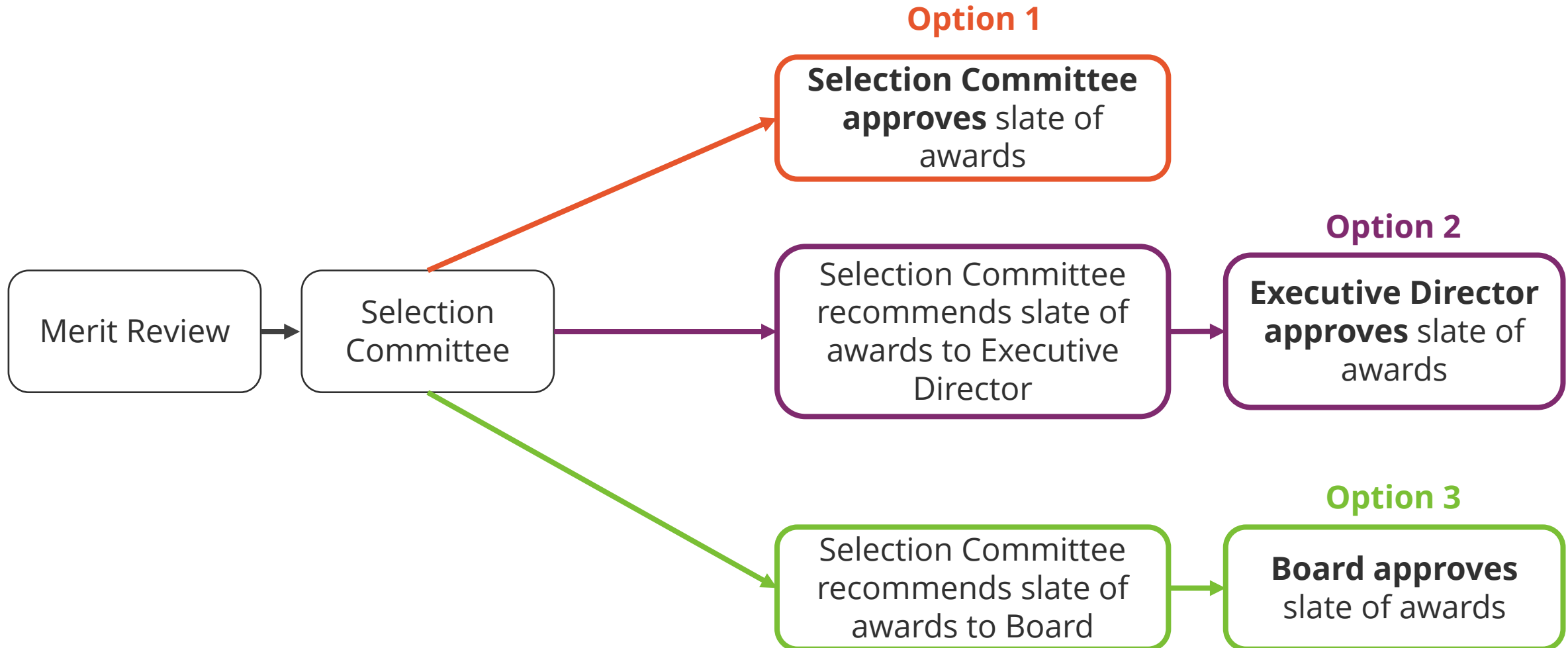
- PFA opens **May 5**
- Applications due **May 26**
- Merit review **June 23**
- Selection Committee meeting **June 30**
- If needed, Board meeting **early July**
(would need to be scheduled)

Distinct features:

1. No LOI requirement
2. Expedited programmatic screening
3. Expedited merit review

Further discussion about approval requirements.

Approval Process Options for COVID-19 Targeted PFA



	Approval	Process	Pros	Cons
1	Selection Committee Approval	Selection Committee reviews and approves projects. Approved projects will be reported to the full Board at its next public meeting. Action: Board will need to vote to delegate approval authority to Selection Committee for FY20 projects from the COVID-19 PFA.	• Maintains input of SC in application vetting process • Acknowledges urgency of the need • Expedites approvals as compared to usual processes	• No public Board meeting to approve slate of awards • Limits opportunity for broader input on slate of awards from Board members
2	Selection Committee Recommends Slate for Executive Director Approval	Selection Committee recommends slate of awards to Executive Director. Executive Director approves slate of awards. Approved projects will be reported to the full Board at its next public meeting. Action: Board will need to vote to delegate approval authority to Executive Director for FY20 projects from the COVID-19 PFA.	• Maintains input of SC in application vetting process • Expedites approvals as compared to usual processes • Consistent with approval authority granted by Board to Executive Director for other COVID-19 related funding (e.g., HERO and enhancements)	• No public Board meeting to approve slate of awards • Limits opportunity for broader input on slate of awards from Board members
3	Selection Committee Recommends Slate for Board Approval	No change in usual approval processes, though could expedite scheduling of Board meetings following Selection Committee meetings. Action: None.	• Maintains routine application vetting and approval processes • Preserves input from Board members on recommended slate of awards	• Will need to schedule additional Board meetings on short timeline • Less expedited compared to other options

Proposed Motions Corresponding to Options for COVID-19 Targeted PFA Approval Process



- Motion for Option 1:
 - That the Selection Committee be authorized to approve slate of awards for funding in FY20 from the COVID-19 PFA, consistent with the Board-approved funding commitment relating to COVID-19 projects
- Motion for Option 2:
 - That the Executive Director be authorized to approve slate of awards in FY20 recommended for funding by the Selection Committee from the COVID-19 PFA, consistent with the Board-approved funding commitment relating to COVID-19 projects
- Motion for Option 3:
 - That there be no change to the existing authority held by the Board in FY20 to approve slate of awards recommended for funding by the Selection Committee from the COVID-19 PFA

Board Vote

Call for a Motion to:

- **Approve** [Motion as appropriate]:
 - **Motion for Option 1:** That the Selection Committee be authorized to approve slate of awards for funding in FY20 from the COVID-19 PFA, consistent with the Board-approved funding commitment relating to COVID-19 projects
 - **Motion for Option 2:** That the Executive Director be authorized to approve slate of awards in FY20 recommended for funding by the Selection Committee from the COVID-19 PFA, consistent with the Board-approved funding commitment relating to COVID-19 projects
 - **Motion for Option 3:** That there be no change to the existing authority held by the Board in FY20 to approve slate of awards recommended for funding by the Selection Committee from the COVID-19 PFA

Call for the Motion to be Seconded:

- **Second** the Motion
 - If further discussion, may propose an **Amendment** to the Motion or an **Alternative** Motion

Roll Call Vote:

- Vote to **Approve** the **Final** Motion
 - Ask for votes in favor, opposed, and abstentions

BREAK

We will return at 1:00 PM ET



Join the conversation on Twitter via
@PCORI

Welcome Back

Christine Goertz, DC, PhD

Chairperson, Board of Governors



Healthcare Worker Exposure Response and Outcomes (HERO) Registry and Hydroxychloroquine (HERO-HCQ) Trial Program

Josephine Briggs, MD

Acting Chief Science Officer

HERO Registry and HERO-HCQ Trial Program Award



On April 1, 2020 the Board approved:

- Use of the mechanism of a PCORI-issued invitation to submit a proposal for funding of the **Healthcare Worker Exposure Response and Outcomes (HERO) Registry and HERO-HCQ Trial** research program to be conducted using **PCORnet**
- Review, negotiation, and approval of the invited proposal and funding commitment under the authority of the **Executive Director**
- A funding commitment up to \$50M total costs for funding the research

HERO Registry and HERO-HCQ Trial Registry and Trial Leadership



- **Principal Investigator and Awardee Institution (Sponsor)**
 - Adrian Hernandez, MD, MHS, Duke University
- **Co-Principal Investigators:**
 - Hero Registry PI, Emily O'Brien, PhD, Duke Clinical Research Institute (DCRI)
 - HERO-HCQ Trial, Susanna Naggie, MD, DCRI
- **HERO Research Program Steering Committee:**
 - Co-chairs external to Duke University and DCRI
 - Judith Currier, MD, MSc, University of California, Los Angeles
 - Russell Rothman, MD, MPP, Vanderbilt University Medical Center
 - 1-2 representatives per PCORnet Clinical Research Network including Healthcare worker representatives
 - Registry Subcommittee
 - Chaired by Chris Forrest, MD, PhD, Children's Hospital of Philadelphia
 - Ancillary Studies and Publications Subcommittee
 - Co-chaired by Betsy Shenkman, PhD, University of Florida and Susanna Naggie, MD, DCRI
 - Healthcare Worker Stakeholder Subcommittee

PCORI HERO Program Advisory Panel



- The principle charge of the **Advisory Panel** is to provide advice to PCORI's Executive Director (ED) about overall funding and monitoring questions and issues related to the HERO Program.
- The **Advisory Panel** provides guidance, as requested, on topics relating to PCORI's funding and monitoring of the Research Project.
- The Panel does not serve the function of a Data and Safety Monitoring Board. Establishing and overseeing the DSMB is the responsibility of Duke University, the Awardee Institution, which is the sponsor.
- The Panel has met twice, on April 1 and April 22, and will meet as needed, at least monthly, throughout PCORI's funding of the HERO Program.

PCORI Advisory Panel Members



- **Panel Chair**
 - Mike Lauer, MD (Current Methodology Committee Member)
 - Deputy Director for Extramural Research, National Institutes of Health
- **Panel Members**
 - David DeMets, PhD
 - Professor Emeritus, School of Medicine and Public Health at University of Wisconsin-Madison
 - Maureen Fagan, MHA, DNP (Current Advisory Panel on Patient Engagement Member)
 - Chief Experience Officer, University of Miami Health
 - Alicia Fernandez, MD (Current Board Member)
 - Professor of Clinical Medicine, University of California San Francisco
 - Elisa Hurley, PhD (Current Advisory Panel on Clinical Trials Member)
 - Executive Director, Public Responsibility in Medicine and Research
 - Dan Kurtizkes, MD
 - Chief, Division of Infectious Diseases, Brigham and Women's Hospital
 - Professor, Harvard Medical School
 - Vlado Perkovic, PhD
 - Dean of Medicine, University of New South Wales

The Role of the HERO Registry in the COVID-19 Response



- The HERO Registry facilitates the participation of **Health Care Workers (HCWs)** as partners to facilitate research on COVID-19 issues.
- Studies of novel therapies such as unapproved drugs and vaccines are outside PCORI's legislative mandate.
- **HCWs** are recognized as valuable partners for studies such as vaccine trials which are outside PCORI's mandate, but partnership with other funders and collaborators on such studies is part of the Registry mandate.
- Leaders of the Registry report extensive discussions about potential partnerships with possible Federal sponsors, such as partnership with the NIH ACTIV consortium.

HERO REGISTRY

Chris Forrest, MD, PhD
Children's Hospital of Philadelphia

Emily O'Brien, PhD
Duke Clinical Research Institute



Healthcare Worker Exposure
Response & Outcomes

HERO Registry

May 5, 2020

Christopher B. Forrest, MD, PhD
Professor of Pediatrics
Children's Hospital of Philadelphia
Director, PEDSnet (a PCORnet Clinical Research Network)
Chair, HERO Registry Sub-Committee

Objectives

1. **Community:** build a community of healthcare workers organized to better understand effects of the pandemic on them.
2. **Research:** offer participants opportunities to participate in research that can improve their health and lives. (Elicit their priorities)
3. **Return results:** return results to all participants as a group and personalized to each individual.

Enrollment Criteria

- At least 18 years of age
- Work in a facility that provides healthcare services
- Can read English or Spanish

That's it – just three.

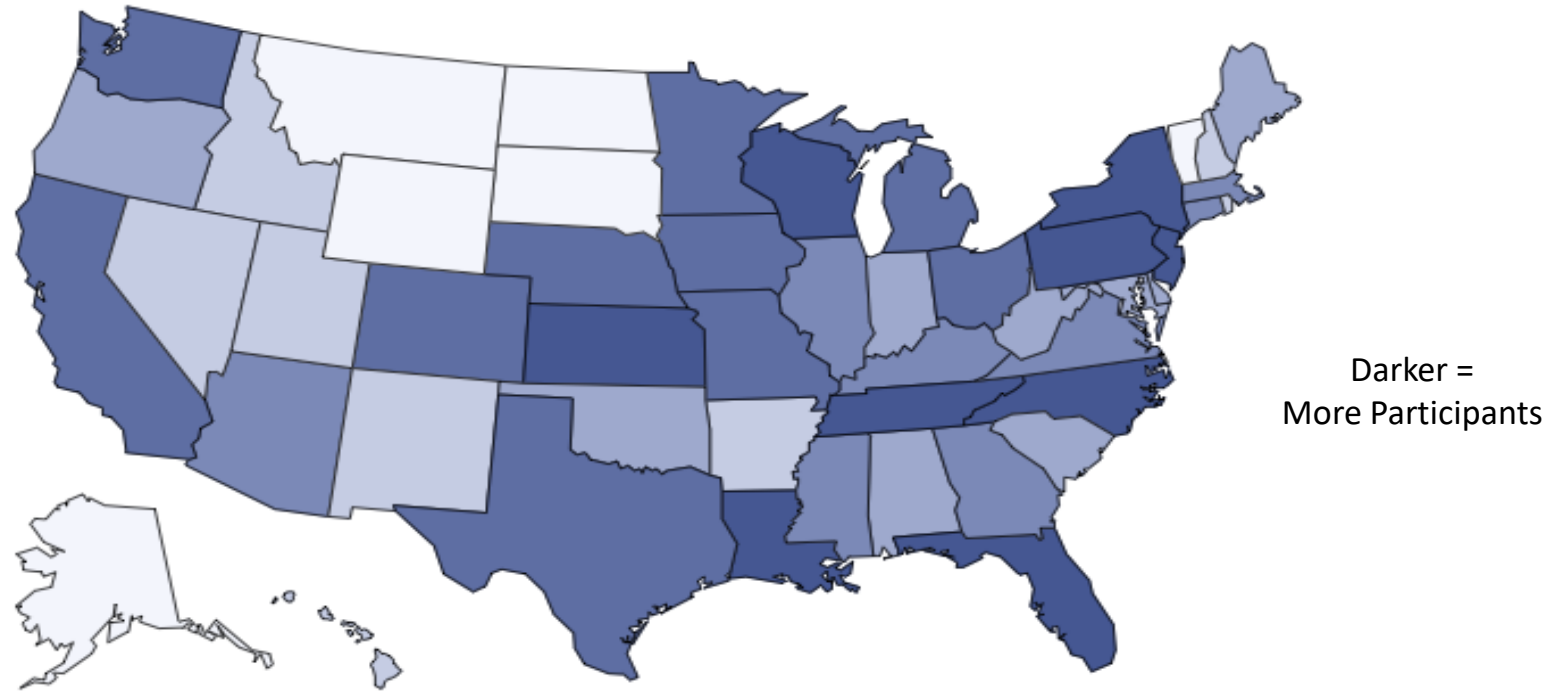
We aspire to form a **community of 100,000** or more healthcare workers.

Creative strategies for enrollment and widespread leadership are needed.

Value Proposition for HCWs

- Contribute to our knowledge on the impact of the pandemic on the health and lives of HCWs
- Gain access to trials, tools, and technologies that may improve their health (e.g., HCQ trial)
- Return of results: at the group and individual level

Enrollment (5/1/2020 = 9,440)



- Enrollment from all 50 states
- Will increase as new sites activate
- Additional methods needed

Core Registry Content

- Demographics
- Profession and place of work
- HCQ trial enrollment criteria
- COVID-19 exposures and illness
- Access to personal protective equipment
- Health: sleep, emotional distress (anxiety and depression), fatigue, stress, general health/well-being
- Concerns
- Burnout

Preliminary Results - Demographics (n=7,945)

- Age: 41y (interquartile range: 33-50y)
- Female: 75%
- Race: 85% white, 5% Black/AA
- Ethnicity: 3% Hispanic
- Place of work: 80% hospital
- Primary role: 31% nurse, 21% physician

COVID-19 Exposures and Illness and Trial Interest (n=7,945)

- Exposure: 40% at work, 4% community, 56% none
- Testing: 12% have been tested
 - Of those tested, 16% positive (2% of total)
- Interested in HCQ Trial: 63% yes (~5,000)

Access to PPE (n=4,811)

- 96% wearing masks
- Access to following is a “small/big problem”
 - N95 masks: 29%
 - Face shield/goggles: 20%
 - Surgical masks: 19%
 - Gloves: 4%
 - Soap: 3%

Impact on Health (n=7,945)

- Had a lot of the day yesterday:

- Tired: 54%
- Stress: 53%
- Trouble sleeping: 44%
- Worry: 41%
- Sad: 24%
- Pain: 19%
- Angry: 16%

Healthcare Worker Concerns (n=794)

Topic Category	Topics	N (%)
Antibody testing and immunity	• Interpretation of antibody testing results • Availability of antibody testing • Immunity in asymptomatic individuals • Degree and duration of immunity	198 (27)
Personal Protective Equipment (PPE)	• Adequate access to PPE • Effectiveness of PPE • Standard guidelines for use of PPE	197 (27)
Transmission and risk	• Personal risk of exposure • Risk of exposure by healthcare and community settings • Risk of exposure to family • How virus is transmitted	143 (19)

Engagement

- Returning aggregate results through email, website, and an interactive Town Hall event
- Healthcare workers are on all HERO committees
- Prioritizing HCW concerns that participants report for future Registry surveys
- Exploring ways to co-design future studies



HERO
Healthcare Worker Exposure
Response & Outcomes

HERO Registry: What We Are Learning So Far, April 29, 2020

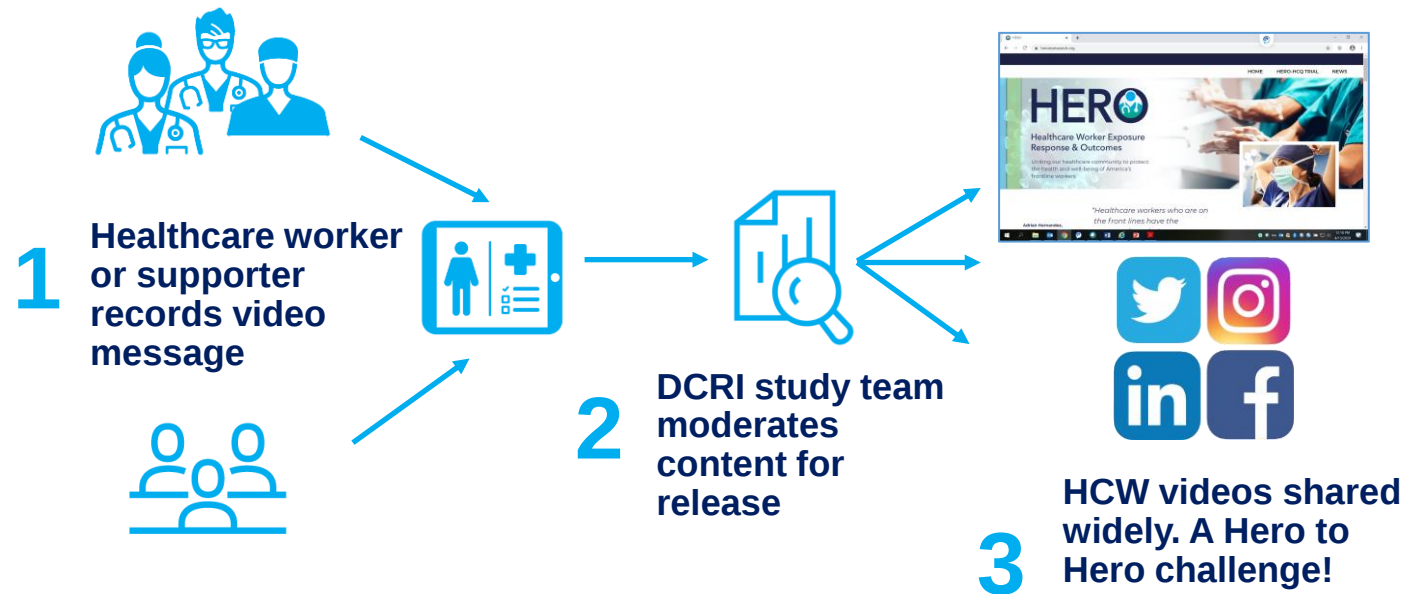
Posted on [April 30, 2020](#) by [Patty McAdams](#)

Emily O'Brien, PhD, FAHA, Duke Population Health Science
Principal Investigator, HERO Registry

Christopher B. Forrest, MD, PhD, Children's Hospital of Philadelphia
Chair, HERO Registry Sub-Committee

The HERO Registry is off to a fantastic start! As of April 29th, 2020, 8,688 healthcare workers have joined the HERO community from all 50 states. Members of the HERO community work in all types of healthcare facilities from hospitals to hospices, skilled nursing facilities, primary care practices, radiology units, dialysis

HERO Stories to build and unite our research community...



HERO-HCQ Randomized Clinical Trial

Hydroxychloroquine Dose

- Hydroxychloroquine is being used extensively for treatment in patients with COVID-19 and in individuals exposed to the virus to prevent disease.
- Study drug and Placebo were donated by Sandoz, and do not come from the commercial pharmacy supply line.

A Surge in Prescriptions

This slide contained a line chart from an April 25 *New York Times* article entitled [Prescriptions Surged as Trump Praised Drugs in Coronavirus Fight](#). The chart showed a weekday average of first-time prescriptions for chloroquine and hydroxychloroquine rose from 683.6 to more than 31,000 after the administration discussed the drugs at a White House briefing. The average decreased to about 3,200 several days later.

Why Study of HCQ Remains a Priority

- Extensive use but no definitive evidence for benefit.
 - There are potential biological mechanisms supported by in vitro evidence, but the clinical evidence is of low quality and contradictory.
- From the NIAID guidelines published on April 20:
 - **“There are insufficient clinical data to recommend either for or against using chloroquine of hydroxychloroquine for the treatment of COVID-19.”**
- As noted by the FDA in a statement on April 24, concern has arisen about its safety for treatment in COVID-19 patients, particularly when used in combination with azithromycin.
- The combination of extensive use, weak evidence and safety concerns creates an urgent public health need for definitive studies.

HERO-HCQ Randomized Clinical Trial

Susanna Naggie, MD

Duke Clinical Research Institute

Adrian Hernandez, MD, MHS

Duke Clinical Research Institute

Hydroxychloroquine Background

- In the 1600s powder from the cinchona tree brought to Spain from Peru (reportedly after the Viceroy of Peru's wife acquired malaria and improved dramatically with treatment)
- 1800s Quinine isolated from the bark by French chemists
- 1939 Bayer synthesizes a series of quinine-related compounds for treatment of malaria for troops fighting in the Pacific in WWII, including Chloroquine (which was initially dismissed as too toxic for humans)
- 1945 after extensive clinical trials Chloroquine approved and recognized as the superior agent
- In 1959 a modification to the compound via hydroxylation led to the development of Hydroxychloroquine, which has remained in use unchanged until today
- In the early 1950s it started being used for treatment of Lupus, and then for treatment of other rheumatologic diseases

Solitto, Abigail & MacKeigan, Jeffrey. (2015) Leaving the Lysosome behind: Novel developments in Autophagy inhibition. Future Medicinal Chemistry.

Hydroxychloroquine Today

- 128th most prescribed drug in the US, with over **5 million** prescriptions in 2017
- Classified as a WHO essential medicine
- Used for prophylaxis and treatment of uncomplicated malaria (in regions without high rates of Chloroquine resistance) and treatment of numerous rheumatologic conditions including: lupus, rheumatoid arthritis, Sjorgens and porphyria cutanea tarda
- Safety data has mostly been generated from patients treated for malaria and lupus (different treatment doses and durations than CoVID-19)

Kane SP. The Top 300 of 2020, ClinCalc DrugStats Database, Version 20.0. ClinCalc: <https://clincalc.com/DrugStats/Top300Drugs.aspx>. Updated December 23, 2019
World Health Organization Model List of Essential Medicines, 21st List, 2019. Geneva: World Health Organization; 2019.

Hydroxychloroquine Safety

- No large-scale studies comparing hydroxychloroquine to other DMARDs, but observational studies suggest it is generally safe and well-tolerated
- All AE listed for chloroquine are less common with HCQ
- American College of Rheumatology (ACR) identifies HCQ as DMARD with least contraindications (only Child-Pugh C)
- For initiation of HCQ for long term use, ACR recommends baseline CBC, liver transaminases, creatinine
 - No additional monitoring required after baseline
 - No baseline ECG recommended
- ACR recommends an ophthalmologic exam within the first year
- Most common AE with HCQ are
 - GI side effects (nausea) – primarily with high dose
 - Rash
 - Retinopathy (prolonged therapy)

Alpay-Kanitez, Cemal MD et al. Favorable retention rates and safety of conventional anti-rheumatic drugs in older patients with rheumatoid arthritis, Medicine: April 2020 - Volume 99 - Issue 16.; C. Ponticelli & G. Moroni (2017) Hydroxychloroquine in systemic lupus erythematosus (SLE), Expert Opinion on Drug Safety, 16:3, 411-419.

Hydroxychloroquine: QTc prolongation

Reports when used as anti-malarial or for SLE/rheumatoid arthritis are most relevant to a prophylaxis study

- ECG analysis in 85 patients with connective tissue disease – no difference from normal
- Pre-print large observational study comparing HCQ to other DMARDs +/- azithromycin or amoxicillin
 - No increased SAE with HCQ or HCQ + amoxicillin or other DMARDs
 - Increased risk of cardiovascular events and mortality when HCQ was combined with azithromycin

Risk factors for cardiac toxicity

- Underlying cardiac damage related to COVID-19
- Concomitant medications that prolong QTc
 - Azithromycin (currently NOT recommended in combination by NIH) – Doxycycline recommended if atypical coverage indicated⁷
- Existing cardiac conditions: cardiac disease, history of ventricular arrhythmia, bradycardia (<50 beats per minute)
- Hypokalemia and/or hypomagnesemia
- Drug-drug interactions increasing HCQ concentrations

Molina JM, et al. Médecine et Maladies Infectieuses **2020**; Chorin E et al. medRxiv **2020**; Morgan ND et al. J Clin Rheumatol **2013**; 19(5): 286-8; Chen CY et al. Clin Toxicol (Phila) **2006**; 44(2): 173-5.; Yelve K et al. BMJ Case Rep **2012**; 2012; Stas P et al. Int J Cardiol **2008**; 127(2): e80-2; <https://covid19treatmentguidelines.nih.gov/> ; Available at <https://www.acc.org/latest-in-cardiology/articles/2020/03/27/14/00/ventricular-arrhythmia-risk-due-to-hydroxychloroquine-azithromycin-treatment-for-covid-19>; Giudicessi et al. Mayo Clin Proceedings. 2020, <https://doi.org/10.1016/j.mayocp.2020.03.024>; Lane et al. Safety of hydroxychloroquine, alone and in combination with azithromycin, in light of rapid widespread use for COVID-19: a multinational, network cohort and self-controlled case series study.

What do we know so far about Hydroxychloroquine and COVID?

- Reports to date are specific to use of HCQ with/without azithromycin to treat inpatients with COVID
- Six studies are public that report on efficacy of HCQ for COVID
 - 1 case series
 - 2 retrospective
 - 3 randomized (small size)
- The quality of the majority is poor
- The majority suggest a lack of benefit of HCQ to treat COVID
- The 2 retrospective studies suggest higher AE but these were unable to control for clinical decision to treat with HCQ, which may occur in sicker patients
- 15 treatment studies in ClinTrials.gov and many more globally
- No information yet on the safety or efficacy of HCQ for prevention of COVID
- The primary proposed mechanism of action for HCQ is as a modest antiviral
- The most likely opportunity for benefit is in prevention or in early disease
- 19 prevention studies in ClinTrials.gov
- U Minn HCW PEP study DSMB recently lowered the sample size due to high rate of COVID in control arm (enrollment ~800 and ongoing)
- Large adaptive multi-armed treatment trial RECOVERY has enrolled >8000 participants and ongoing

<https://www.medrxiv.org/content/10.1101/2020.04.16.20065920v1>; Tang . HCQ open-label RCT. medRxiv.

<https://www.medrxiv.org/content/10.1101/2020.04.10.20060558v1>; Mahevas et al-

<https://www.medrxiv.org/content/10.1101/2020.04.10.20060699v1>; Chen, Hu et al. 2020; Chen, Liu et al. 2020; Gautret, Lagier et al. 2020

What are we doing to ensure safety of Healthcare Workers in the HERO-HCQ Trial?

- The HERO-HCQ Trial is being conducted under an **IND with FDA oversight**
- The HERO-HCQ protocol **excludes any HCW at high risk for HCQ toxicity** including HCW at high risk for QT prolongation, severe skin reactions, retinopathy, severe heart disease, or medications that can interact with HCQ
- HERO-HCQ has a **Data Safety and Monitoring Board** that will meet frequently (weekly at present) to review safety events and to ensure severe unexpected events are identified and reported to the FDA
- The FDA has stressed the importance of only using unproven medications for COVID, like HCQ, as part of a clinical trial like HERO-HCQ

I am a HCW, why would I join HERO-HCQ?

- Healthcare workers are at high risk for COVID infection
 - MMWR reported 19% of COVID infections in HCW on the subset of patients with data on role as HCW
- It is critical to protect the health and safety of our essential workforce
- Until a vaccine is developed, we need additional preventative measures beyond PPE
- HCQ has antiviral activity versus SARS-CoV-2
- Antivirals are more likely to have efficacy in prevention of infection or disease and in treatment of early disease
- HCQ has been used for treatment and prevention of malaria and for treatment of chronic autoimmune conditions for ~70 years
- Recent concerns for safety of HCQ are in COVID and primarily when combined with azithromycin or other QTc prolonging agents
- The HERO Clinical Trial will exclude HCW at risk of AEs and is being conducted with FDA oversight to ensure safety of all participants



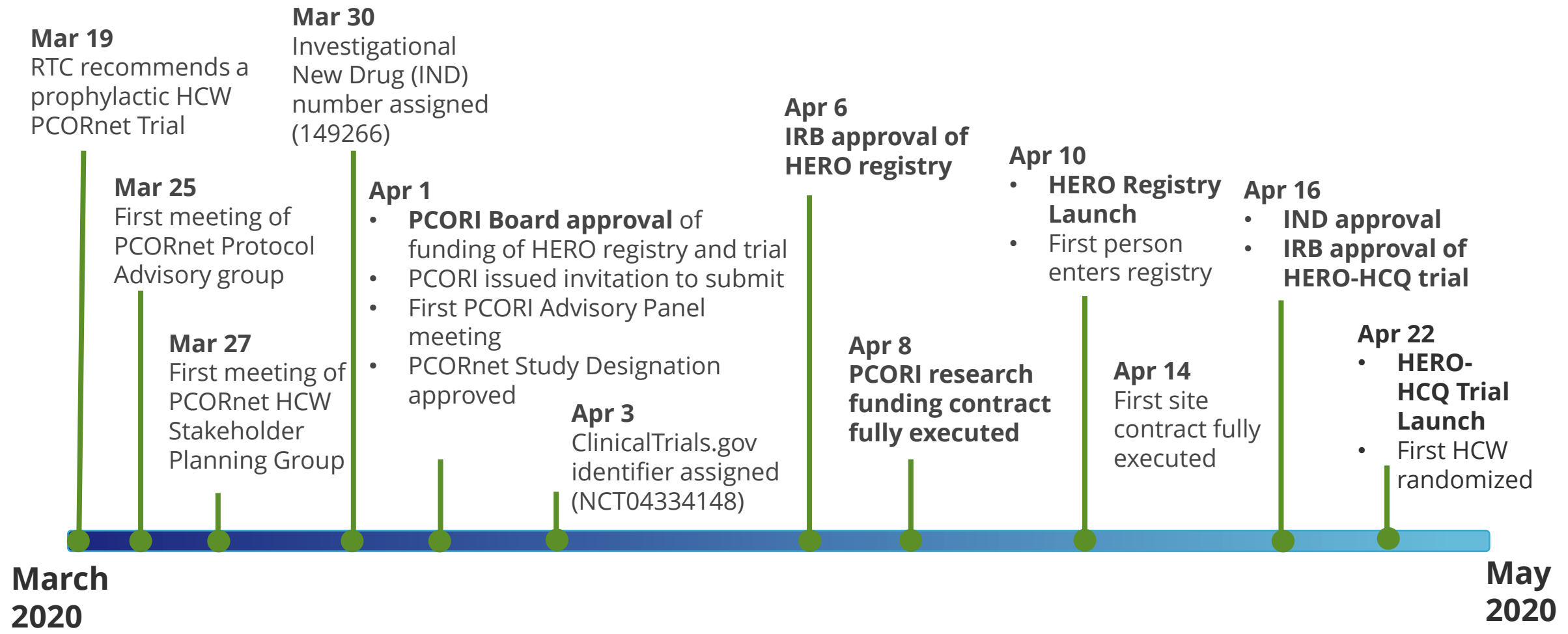
Healthcare Worker Exposure
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Discussion

Oversight of the HERO-HCQ RCT

- The **HERO-HCQ** trial oversight mechanisms include the following:
 - Trial conducted under Investigational New Drug Safety FDA requirements
 - Data Safety and Monitoring Board established by DCRI, the sponsor
 - Trial subject to Institutional Review Board (IRB) review
- Monitoring processes assure safety or futility issues will be addressed promptly.
- Consistent with best practices for RCT oversight, early termination is possible if indicated by either safety or futility.
- PCORI contractual mechanism and processes reduce financial impact of early termination.

Rapid Timeline



PCORI's vision for PCORnet is a national infrastructure designed to find a faster more powerful way to conduct CER to improve the nation's health and health care

Discussion

Enhancements of PCORI- Funded Awards: Enabling Existing Projects to Address COVID-19

Steven Clauser, PhD, MPA

Program Director

Healthcare Delivery and Disparities Research

PCORI: Rapidly Responding to COVID-19 Public Health Emergency



- PCORI is seeking ways to play a leading and meaningful role in national research response to current threat of COVID-19
 - Board approved up to \$20M in funding allocation enabling the adaptation of currently funded research and other projects
- On April 10, PCORI posted three funding opportunities to seek investigator-initiated proposals to address the COVID-19 public health crisis for **current awardees in the form of enhancements**
- Expect to receive proposals that offer exciting ways to transform existing funded awards that serve the award's original aims and result in findings related to COVID-19
- Anticipate high volume of enhancement proposals due to expressed enthusiasm from awarded investigators

Enhancements Funding Opportunity

- Enhancements opportunity applies to all active awards under the Research, Engagement Awards, and D&I mechanisms
- Can include modest additions to existing aims and/or be an adjunct project that addresses COVID-19
 - Enhancement must be related to the original award
- Review will include internal department review, as well as cross-departmental input, to expedite review and approval of these enhancements
 - Executive Director makes the final approval for all funding decisions following input and recommendations at the cross-departmental level
- Anticipated start date of enhancements: Mid-May

Monitoring & Evaluating the Impact of the Pandemic on Our Work

Laura Forsythe, PhD, MPH

Director, Evaluation and Analysis

The Pandemic is Affecting the Entire Research Enterprise Including PCORI



- Factors affecting research during the pandemic
 - Limitations on in-person interactions
 - Institutional restrictions on research activities
 - Competing demands for healthcare staff
- These are having an impact on projects' ability to
 - Enroll new participants in the same way or at all
 - Deliver interventions through planned mode
 - Collect new data

We Are Monitoring and Evaluating the Impact of the Pandemic on All Aspects of Our Work



Metrics directly related to the pandemic

- Changes to protocols
- Changes to engagement plans
- Project delays, suspensions, & terminations
- Responses to targeted funding opportunities for COVID-19
- Dollars invested for COVID-19 - suspensions, adaptations, enhancements, targeted studies
- Expected impact of COVID-19 studies

Routine metrics likely to be affected by the pandemic

- Responses to funding opportunities & funds committed
- Operational expenses
- Project performance & recruitment success
- Publication of results
- Speed of Peer Review
- Use of PCORnet
- Uptake and impact of findings

PCORI is a Learning Organization



- We are adapting many of our existing processes and piloting new ones in order to respond rapidly to the pandemic
- Thus the pandemic offers opportunities to learn how to be a more effective funder, for example
 - Responding rapidly to emerging research priorities
 - Expediting organizational processes
- ***What other information about our COVID-19 portfolio and the effects of the pandemic on all of our work would be helpful for future decision-making?***
- ***What other learning opportunities do you see?***

Public Comment Period

Kristin Carman, MA, PhD

Director, Public & Patient Engagement

Closing Remarks

Wrap Up and Adjournment

 202.827.7700

 info@pcori.org

 www.pcori.org

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