



Healthcare Worker Exposure
Response & Outcomes

The HERO Program: PCORnet® at Work to Create a Healthcare Worker Community for Rapid Cycle Evidence

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Emily O'Brien, PhD, PI, HERO-Registry, Duke University

Russell Rothman, MD, MPP, Chair, HERO Steering Committee, Vanderbilt University

Chris Forrest, MD, PhD, Chair, HERO Registry, Children's Hospital of Pennsylvania

PCORI Background



- PCORI was established to fund comparative effectiveness research to help patients and those who care for them make better-informed decisions.
- With the dramatic demands on our health and our health care system caused by the COVID-19 pandemic, the US health care system faces an unprecedented stress test to adapt to meet new demands.
- For PCORI's COVID-19 response, three broad focus areas have emerged:
 - Emphasis on the adaptations in how health care is delivered,
 - Emphasis on vulnerable populations,
 - Emphasis on the well-being of the health care worker.



PCORI Response to COVID-19



On April 1, 2020 the PCORI Board of Governors voted to approve a major funding allocation on COVID-related research:

- 1) Enhancements/adaptations to existing projects
Learn more at <https://www.pcori.org/funding-opportunities/announcement/covid-19-related-enhancements-research-awards>
- 2) New research studies, dissemination and implementation projects, engagement projects, and projects using PCORnet
More information coming soon; monitor PCORI website or sign up for newsletter
- 3) Funding a large PCORnet based research project on health care workers:
Part 1: a registry study of healthcare workers
Part 2: randomized trial addressing hydroxychloroquine (HCQ) for prophylaxis

PCORI Resources



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PCORI's NEW Executive Director



**Nakela Cook, MD, MPH,
FACC**

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.





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HERO Program: Overview

**Uniting our healthcare community to protect the
health and well-being of America's frontline workers**

Stories from the front line...

“It is hard to think that by doing my daily job, not only can I get sick, but I can infect those that I love the most. This is the time to be proactive, to develop ways to stay safe on the front lines. I encourage everyone to be a part of HERO—and part of the solution.”

Jorge Lascano

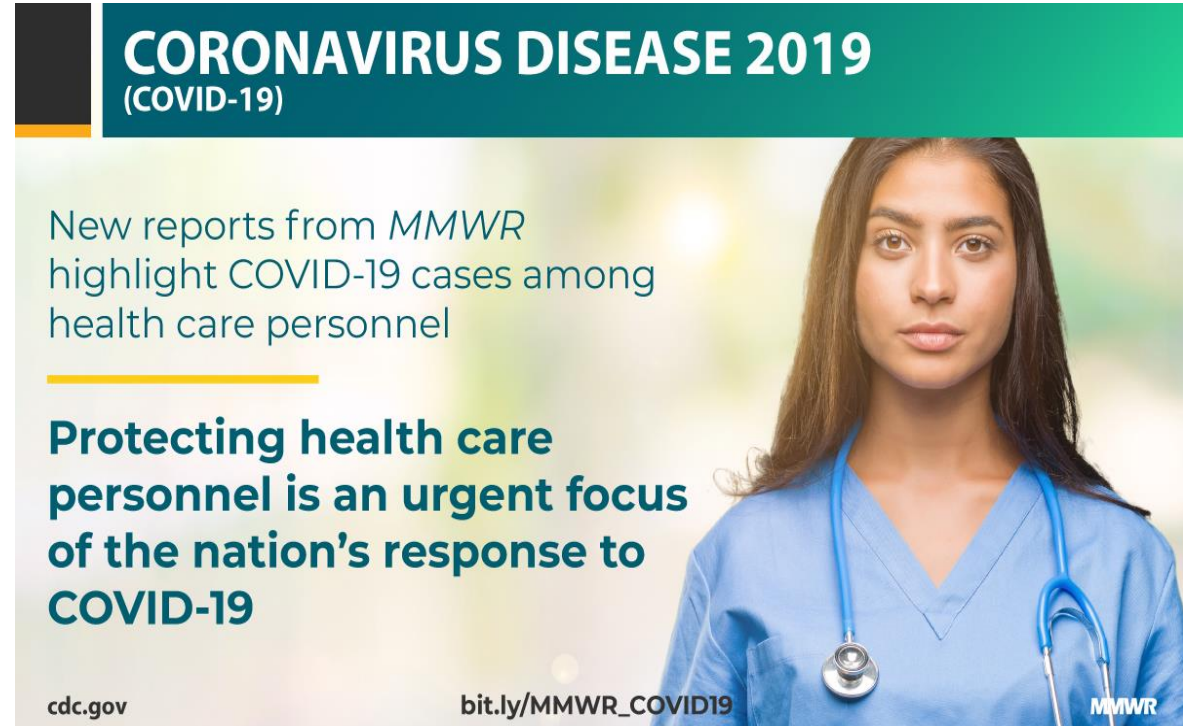
Physician, University of Florida



Visit: https://youtu.be/ys_cjqj332U

We Need to Protect our Healthcare Workers

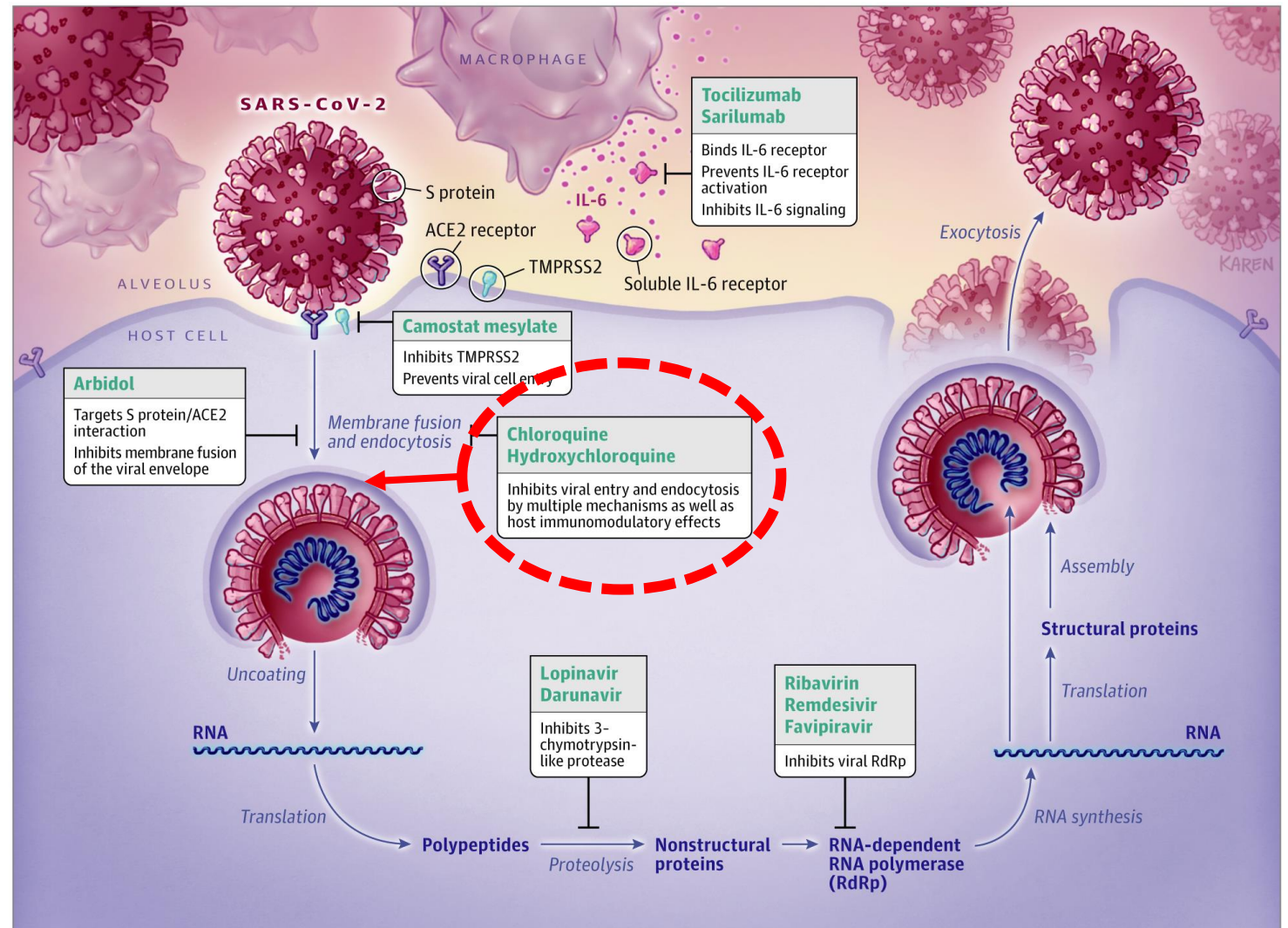
- Ongoing international concerns of risks to Health Care Workers (HCW)
- Reported rates of HCW conversion to COVID-19 positive status reported (~20%)
- >9000 healthcare workers infected in US
- Need to protect frontline HCW from clinical infection or becoming transmission vectors
- High risk individuals in ICU, ER, EMS, SNFs – but other groups may be at risk as well
- No existing – proven – prophylactic therapy
 - Therapies could help, but could also harm
- Stress and burnout are serious concerns, as is the lack of personal protective equipment



Characteristics of Health Care Personnel with COVID-19 — United States, February 12–April 9, 2020. MMWR Morb Mortal Wkly Rep 2020;69:477–481.

Chloroquine or Hydroxychloroquine as a potential prophylaxis

- Multiple, small studies reporting or ongoing
- Variety of results
- Remdesivir and Chloroquine effectively inhibit the novel coronavirus (2019-nCoV) in vitro. Cell Research (2020) 30:269–271; <https://doi.org/10.1038/s41422-020-0282-0>
- In-Press Article on review of single center RCT show some possible benefit of chloroquine for treatment. A. Cortegiani, G. Ingoglia, M. Ippolito, et al., A systematic review on the efficacy and safety of chloroquine for the treatment of COVID-19, Journal of Critical Care, <https://doi.org/10.1016/j.jcrc.2020.03.005>



Questions and Answers Needed for Hydroxychloroquine in COVID-19 ERA: Prophylaxis work?

• Benefits

- Decades of experience
- First approved 04/18/1955
- In a class of medications that was first used to prevent and treat malaria.
- Primary use in high risk inflammatory diseases (SLE, RA)
- Preferred agent in pregnancy with SLE
- Anti-viral activity
 - In-vitro viral suppression
 - Small studies with viral suppression

• Risks

- Serious side effects are rare and associated with longer exposure.
- Most common: nausea and diarrhea
- Less common: rash, hair changes, and muscle weakness.
- Rarely anemia
- Small studies with QT prolongation typically in setting of multiple agents and higher risk individuals

Urgent Questions Need Ready Collaborations...

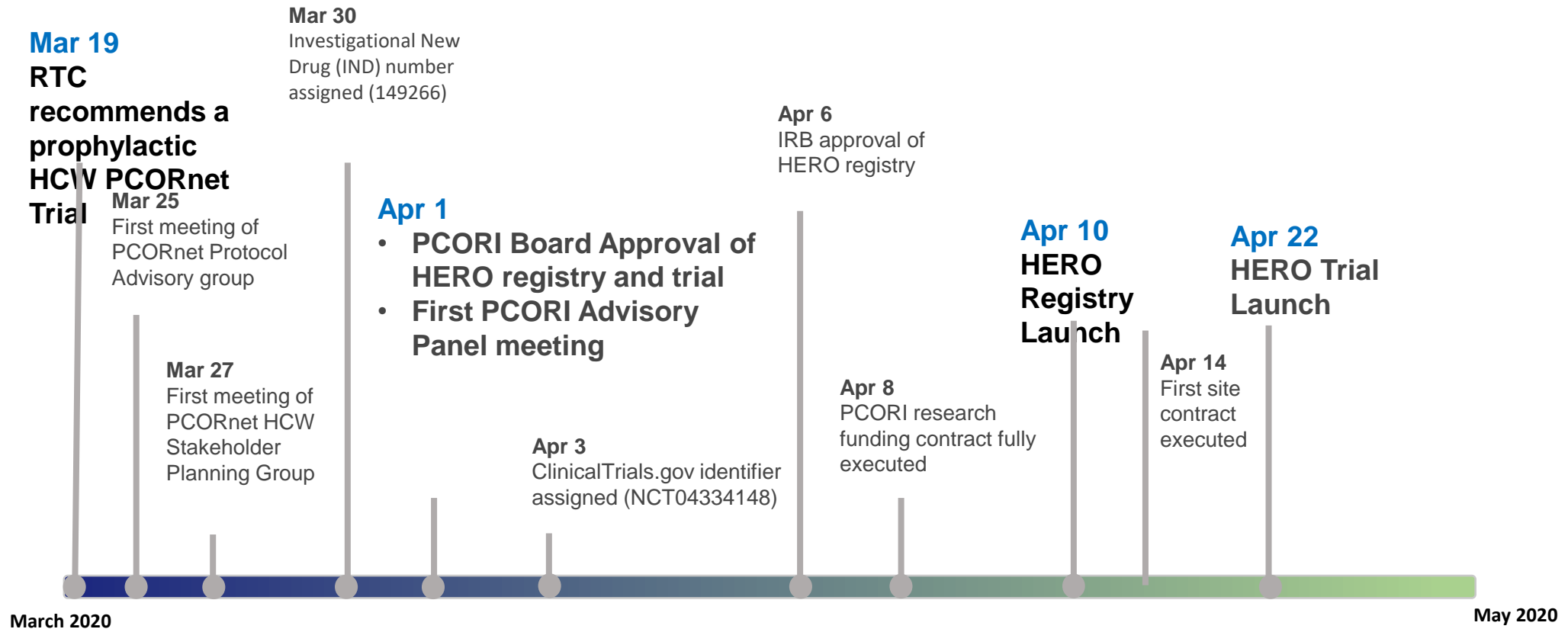
- The Patient-Centered Outcomes Research Institute (PCORI) has long invested in PCORnet,[®] the National Patient-Centered Clinical Research Network to be research ready
- Thus with PCORI funding and PCORnet infrastructure, the Healthcare Worker Exposure Response & Outcomes (HERO) program quickly organized to help



HERO 

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Research Timelines Change in a Pandemic



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

The HERO Program

- **Designed and to be conducted with multiple stakeholders**
 - Healthcare workers –front-line workers
 - Professional Societies
 - Federal Agencies
 - Health systems
- **Will enroll thousands of Healthcare Workers into a living registry**
 - To understand the impact of COVID 19 on HCW health, well-being, stress, PPE availability, and other to-be-defined modules
 - To build a community to support and engage HCW
 - To answer questions – related to COVID19 and not – important to HCWs
 - To understand preferences about participation in future trials
- **Will randomize 15,000 at-risk HCWs into a trial to determine if hydroxychloroquine can prevent COVID19 infection**



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HERO Registry: Rationale and Approach

**Uniting our healthcare community to protect the
health and well-being of America's frontline workers**



IS HERE TO HELP

Join the HERO mission

It's a difficult time for healthcare workers on the COVID-19 front lines.

**Caring for
patients in
uncertain times** + **Protecting
themselves
and their families**

In response, we invite healthcare workers to unite in a mission – the HERO Registry.

Be part of a national response to address the problems our healthcare heroes face in real time—and over time.

What is the HERO Registry?

HERO will engage healthcare workers in a research community to understand their experiences and interests.

We will track critical health outcomes associated with caring for patients with COVID-19, such as emotional distress, burnout, and well-being.

We will help speed clinical studies that address unmet needs for healthcare workers, such as an upcoming study of hydroxychloroquine's effectiveness in preventing coronavirus infections

Together, healthcare workers can ENGAGE to help find the answers that will PROTECT and IMPROVE the health and well-being of America's front line.

Why a community of healthcare workers?

- Healthcare workers are on the front lines of the COVID-19 pandemic
- Their duty is to protect and treat us all
- But on the front lines, they are more at risk, both physically and mentally, to the toll the pandemic poses
 - Personally
 - And with their families
- We need evidence to keep healthcare workers and their families safe and healthy, which ultimately will help protect us all

“By taking care of our healthcare teams, we can take better care of our patients.”

Dawn Hawley

ER Nurse, Vanderbilt University
Medical Center

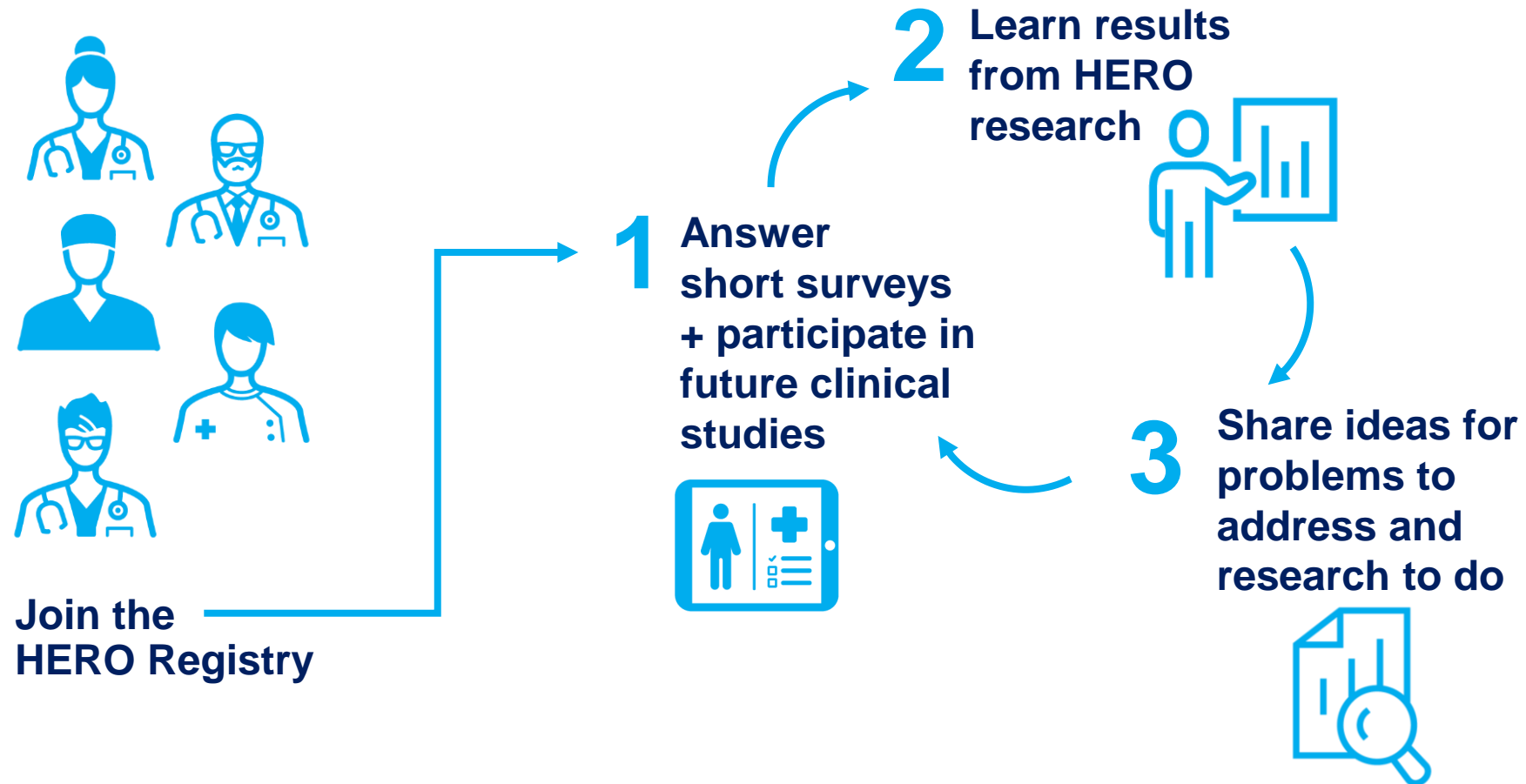
About the HERO Registry

- The HERO Registry invites healthcare workers across the nation to join together to share their experiences and needs to address the COVID-19 pandemic
- By understanding their concerns and interests, we can rapidly generate much needed evidence to help protect them—their health and well-being
- The HERO Registry is *at the ready* to engage participants in rapid research for potential protective therapies (e.g. hydroxychloroquine, vaccines, etc.)
- The Registry will also be poised to address other emerging research priorities and serve as a research community for HCWs

“We’re calling on all healthcare workers to share their perspectives so that we can understand and provide answers to the problems they face in real time – and over time.”

Emily O’Brien
HERO Registry Team Lead

*Together, healthcare workers can **ENGAGE** to help find answers that will **PROTECT** and **IMPROVE** the health and well-being of America's frontline*



Who should join?

- Anyone who works in a setting where people receive health care – nurses, therapists, physicians, emergency responders, food service workers, environmental services workers, interpreters, transporters, etc.
- To join, HERO Registry participants must be:
 - A U.S. healthcare worker of any profession
 - ≥ 18 years old
- Enrollment is free and takes only a few minutes
- Healthcare workers can participate as much or as little as they like





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HERO Registry: Key Elements

**Uniting our healthcare community to protect the
health and well-being of America's frontline workers**

Design Features

- Rapid, large registry of engaged healthcare workers (HCW)
 - “HCW” defined as any individual who is currently employed in a setting where individuals receive healthcare
- All participants complete a basic profile of key characteristics and indicating interest in future trial participation
- Questionnaires related to:
 - Health status
 - Anxiety
 - Burnout
 - COVID-19-related symptoms, testing, diagnosis and healthcare utilization
 - PPE availability
 - Problems the HCW is facing
- Biweekly web-based follow-up

Objectives

1. Create a community of HCWs who may be at risk of COVID-19 infection
2. Identify HCWs interested in engaging in upcoming clinical trials related to COVID-19 and obtain preferences and willingness regarding participation
3. Create a dataset of basic clinical and environmental COVID-19 risk factors and clinical and emotional outcomes for analysis

Eligibility Criteria

INCLUSION

- Individual currently works in a setting where individuals receive healthcare (“healthcare worker”) in the U.S.
- Age ≥ 18
- Able to speak and read English or Spanish

EXCLUSION

- No specific exclusion criteria

Baseline Profile

- Demographics
- Past COVID-19 testing and diagnosis
- COVID-19 Risk factors
 - Brief medical history
 - Smoking status
 - Care delivery setting (emergency department, ICU, respiratory services, other)
 - Known COVID-19 exposure
- Healthcare system where employed

Questionnaires

Current

- PROMIS Global Health Measures (physical and mental SF)
- Daily impact index (stress, anger, sleep, pain, fatigue, anxiety)
- PPE access and use
- Free-text question to identify issues of greatest importance to participants

Future

- More questionnaires adding in ongoing manner in response to HCW-identified priorities (examples: life satisfaction, burnout, depression, moral injury)
- Weekly check-ins to remind participants about available questionnaires, to ask about new symptoms, testing, or hospitalizations

Analyses (Examples)

- Number and percent of participants who enroll in the HERO Registry Study by geographic region, age, COVID-19 risk factors, and past COVID-19 diagnosis
- Distribution of COVID-19 risk factors by participant characteristics
- Distribution of PPE use and availability by characteristics
- Proportion of participants undergoing changes in health status (e.g. new diagnosis of COVID-19, ER visits, hospitalization)
- Proportion of all participants enrolled in the HERO Registry who participate in an ancillary research study

Ancillary studies anticipated to address additional questions.

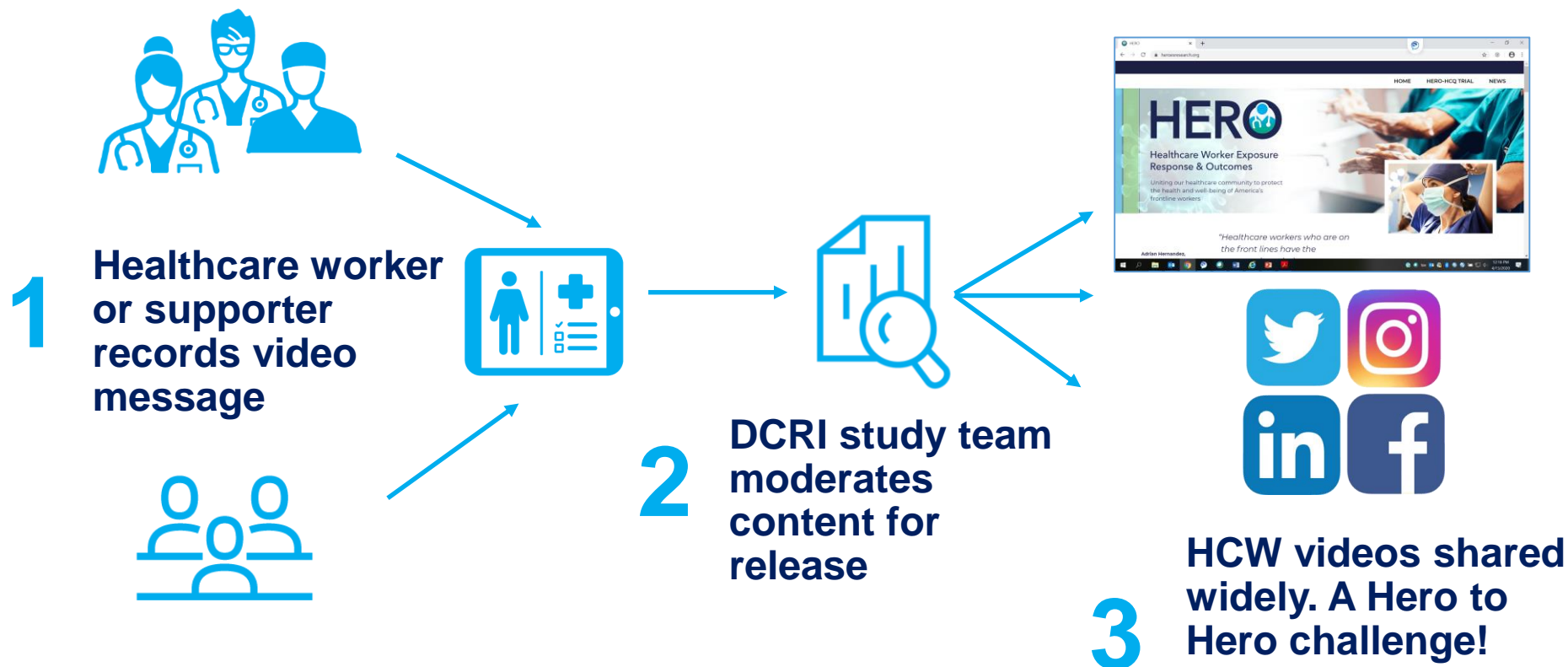
Recruitment and Consent

- Recruitment methods
 - IRB-approved advertisements
 - Social & conventional media
 - Care provider recommendation
 - Peer recommendation
- Consent
 - E-consent to cover baseline and follow-up data capture
 - **HCQ Trial (and potentially other studies) will require additional consent**

Healthcare Work Engagement is Key

- Seat on HERO Steering Committee
- Dedicated Healthcare Worker Subcommittee
- Seat on DSMB
- Specific outreach plans, including the HERO to HERO video challenge

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





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HERO-HCQ Trial: Key Elements

**Does hydroxychloroquine prevent
COVID-19 infections among healthcare
workers?**

Design and Operational Features

- Rapid, large registry of healthcare workers – enrollment open to all
 - To understand healthcare worker burnout, stress, and other experiences
 - To facilitate enrollment in HERO-HCQ and future trials and understand preferences for participation
- Healthcare workers eligible for the HERO-HCQ trial will work at one of the 40 PCORnet sites participating in the trial
 - Pre-screened within the registry, and referred to their local participating site
 - Site will confirm healthcare worker status, randomize onsite, and provide month supply of study drug
 - Complete enrollment within 4-6 weeks/site (10 total for trial)
- Trial participants will have weekly web-based check-ins for symptoms, side effects, exposure history, quality of life, through week 8. Call center rescue for missed check-ins.
- Baseline and end of study swab-checks for viral shedding
- Baseline and end of study serum for future testing for sero-conversion

Aims

Primary:

- To evaluate the efficacy of HCQ to prevent COVID-19 clinical infection in healthcare workers (HCWs)

Secondary:

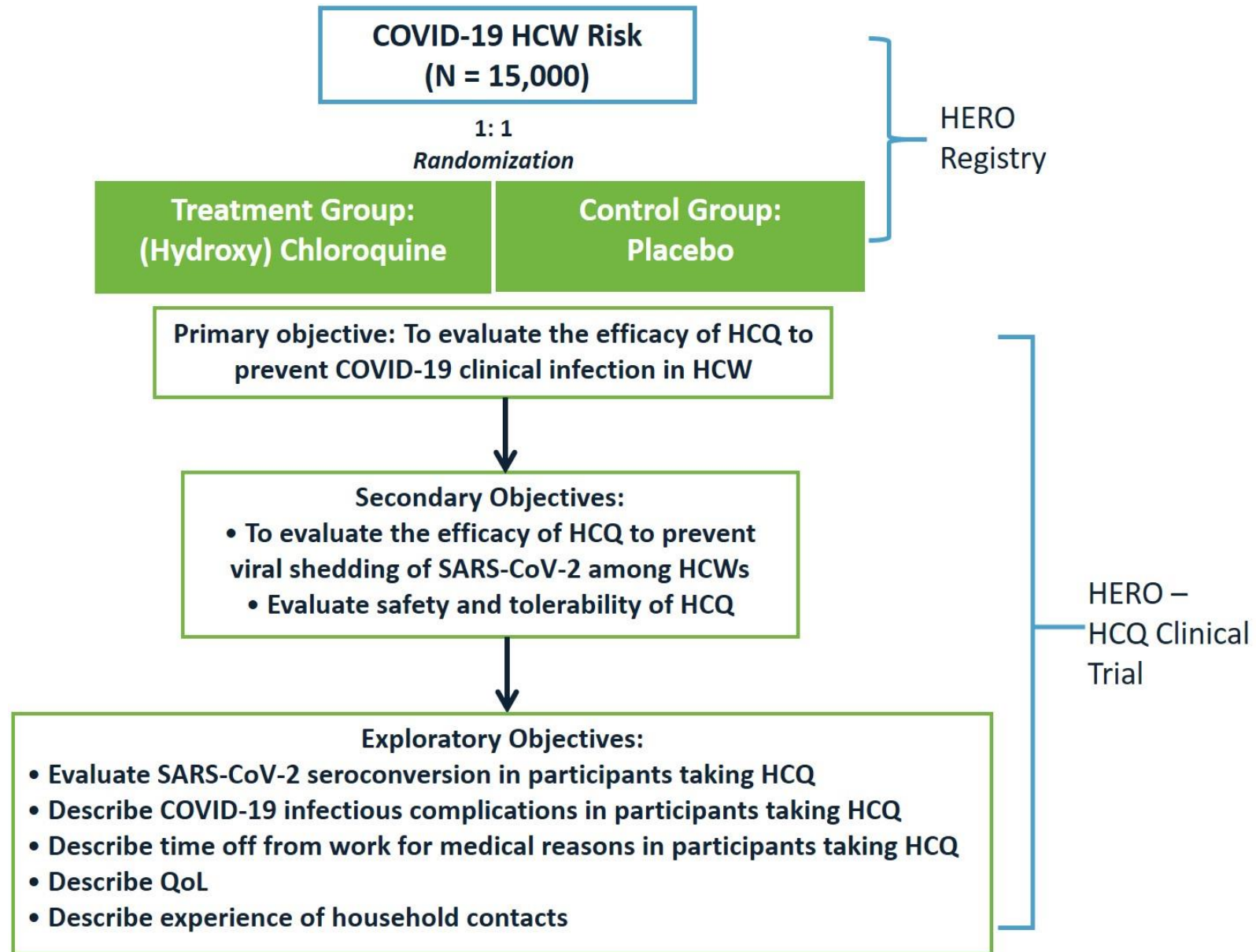
- To evaluate the efficacy of HCQ to prevent viral shedding of SARS-CoV-2 among HCWs
- Evaluate safety and tolerability of HCQ

Aims

Exploratory:

- Evaluate SARS-CoV-2 seroconversion in participants taking HCQ
- Describe COVID-19 infectious complications in participants taking HCQ
- Describe time off from work for medical reasons in participants taking HCQ
- Describe Quality of Life (QoL)
- Describe experience of household contacts

Design



Key Eligibility Criteria

INCLUSION

- Healthcare worker >18 years old
- At risk for COVID-19 infection through work exposure:
 - in the Intensive care unit, **or**
 - in the Emergency department, **or**
 - in Emergency services, **or**
 - in a COVID-19 hospital unit/ward, **or**
 - in respiratory services, **or**
 - in COVID-19 testing location
 - in inpatient hospital unit/area with potential COVID-19 cases
 - in long-term care, assisted living or skilled nursing facilities

EXCLUSION

- Prior diagnosis of COVID-19 infection
- Respiratory illness with new-onset fever (Temperature > 100°F) or ongoing cough or dyspnea within 14 days
- Congenital prolonged QT syndrome
- Current or planned use of QT prolonging drugs (e.g. procainamide, disopyramide, mexiletine, flecainide, propafenone, amiodarone, sotalol, cimetidine, dronedarone, dofetilide, levofloxacin, ciprofloxacin, moxifloxacin)
- End stage renal disease
- Pre-existing retinopathy
- Cirrhosis
- Ventricular arrhythmias requiring medical treatment
- Severe coronary artery disease or heart failure/cardiomyopathy with ongoing symptoms
- Current or planned use of use of anti-seizure drugs

Dose

- Hydroxychloroquine 600 mg BID loading dose of study drug for the first day, followed by 400 mg QD for 29 days.
- Study drug will be supplied as 200 mg tablets.
- Matching placebo
- Rationale
 - current *in vitro* studies report a wide range of EC50 for SARS-CoV-2,
 - variability of absorption and of tissue distribution into the lung,
 - due to a lack of phase 1b data for this drug in SARS-CoV-2 infection, the optimal pharmacokinetic/pharmacodynamic target is unknown.

Regulatory

- Will be under an IND w/FDA
- Regulatory relevant indication
 - Example:
 - “PLAQUENIL is indicated for the suppressive treatment and treatment of acute attacks of malaria due to Plasmodium vivax, P. malariae, P. ovale, and susceptible strains of P. falciparum.”
 - Safety profile will be important for healthcare workers

Ethics and Safety Oversight

- Use of central IRB (WIRB) or rapid review at site
- Streamlined safety reporting
 - No individual SAE reporting
 - Aggregate SAE reporting to FDA if there is a marked imbalance with HCQ over placebo
- Data and safety monitoring board to meet frequently
 - Chair reviews aggregate SAE data
 - DSMB meeting bi-weekly
 - End early for efficacy or safety or futility



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heroesresearch.org

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