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

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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.
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

Chloroquine or Hydroxychloroquine as a potential prophylaxis

- Multiple, small studies reporting or ongoing
- Variety of results

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
    o In-vitro viral suppression
    o 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
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
HERO Registry:
Rationale and Approach
Uniting our healthcare community to protect the health and well-being of America’s frontline workers
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 workers.

1. Join the HERO Registry

2. Answer short surveys + participate in future clinical studies

3. Share ideas for problems to address and research to do

2. Learn results from HERO research
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
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)
  o “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:
  o Health status
  o Anxiety
  o Burnout
  o COVID-19-related symptoms, testing, diagnosis and healthcare utilization
  o PPE availability
  o 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 $\geq 18$
• 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 Sub-committee
• Seat on DSMB
• Specific outreach plans, including the HERO to HERO video challenge
HERO Stories to build and unite our research community…

1. Healthcare worker or supporter records video message

2. DCRI study team moderates content for release

3. HCW videos shared widely. A Hero to Hero challenge!
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
  o To understand healthcare worker burnout, stress, and other experiences
  o 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
  o Pre-screened within the registry, and referred to their local participating site
  o Site will confirm healthcare worker status, randomize onsite, and provide month supply of study drug
  o 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

COVID-19 HCW Risk (N = 15,000)

1:1 Randomization

Treatment Group: (Hydroxy) Chloroquine
Control Group: Placebo

Primary objective: To evaluate the efficacy of HCQ to prevent COVID-19 clinical infection in HCW

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

Exploratory Objectives:
- 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 QoL
- Describe experience of household contacts

HERO Registry

HERO – HCQ Clinical Trial
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:
    o “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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