

The HERO (Healthcare Worker Exposure Response & Outcomes) Program: An Online Community to Support Observational Studies, Randomized Trials, and Long-Term Safety Surveillance



Emily O'Brien, PhD
Associate Professor
Department of Population Health Sciences
Duke Clinical Research Institute

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Russell Rothman, MD, MPP
Professor
Internal Medicine, Pediatrics, & Health Policy
Senior Vice President for Population and Public Health
Director, Institute for Medicine and Public Health
Vanderbilt University Medical Center

Funding and Disclosures

- The HERO Registry is funded through a Patient-Centered Outcomes Research Institute Award (COVID-19-2020-001). The program is coordinated by the Duke Clinical Research Institute and leverages PCORnet®, the National Patient-Centered Clinical Research Network
- HERO-Together is funded by Pfizer, Inc. (New York, NY, USA), is currently ongoing, therefore the final outcomes of this study may differ from outcomes described in this summary.
- HERO-Together is coordinated by the Duke Clinical Research Institute

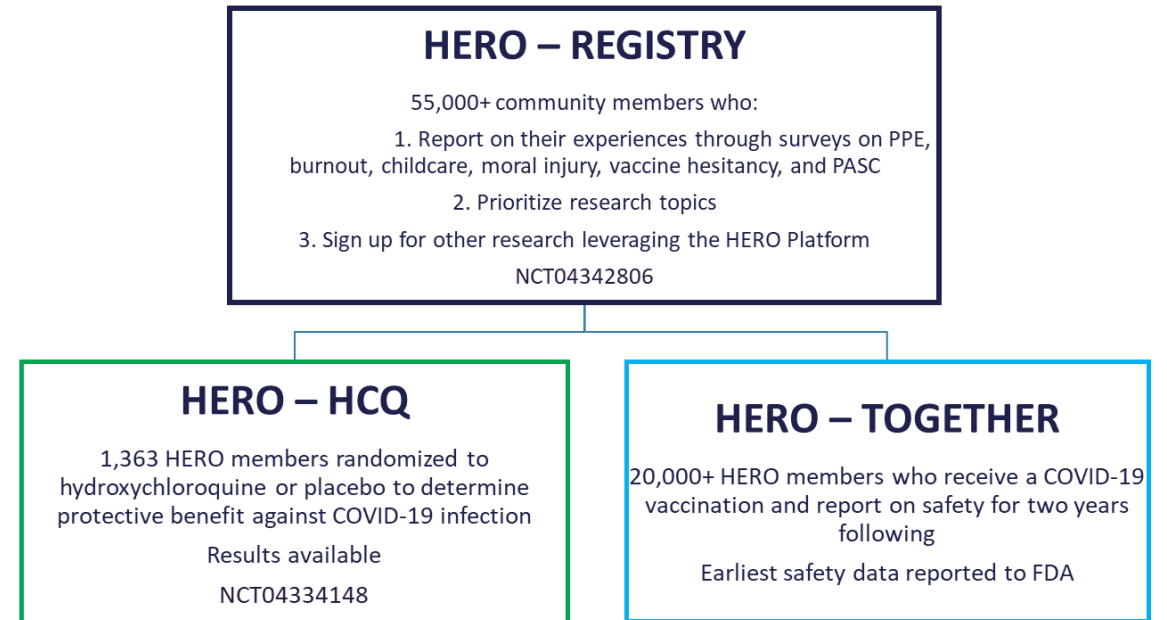
Outline

- HERO Program Overview
- HERO Registry
- HERO-HCQ
- HERO-Together
- Lessons Learned

March 2020

Urgent Questions Need Ready Collaborations...

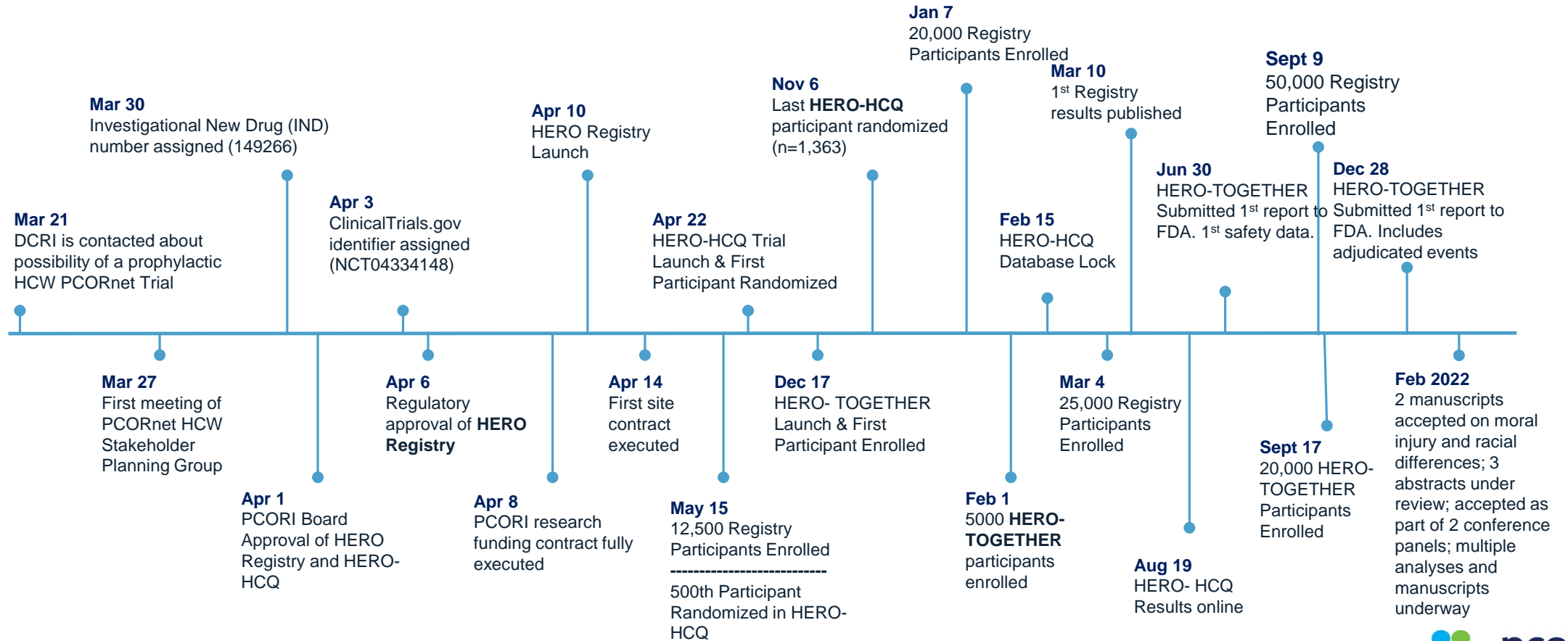
- The Patient-Centered Outcomes Research Institute (PCORI) invested in PCORnet,[®] the National Patient-Centered Clinical Research Network to be a fast, efficient, responsive network for patient-centered research.
- PCORI funded the Healthcare Worker Exposure Response & Outcomes (HERO) program quickly to help address unanswered questions related to COVID-19 and its impact on individuals working in, and affiliated with, healthcare
- HERO Together enabled a safety study to launch within a week of Pfizer-BNT vaccine approval



HERO Timeline

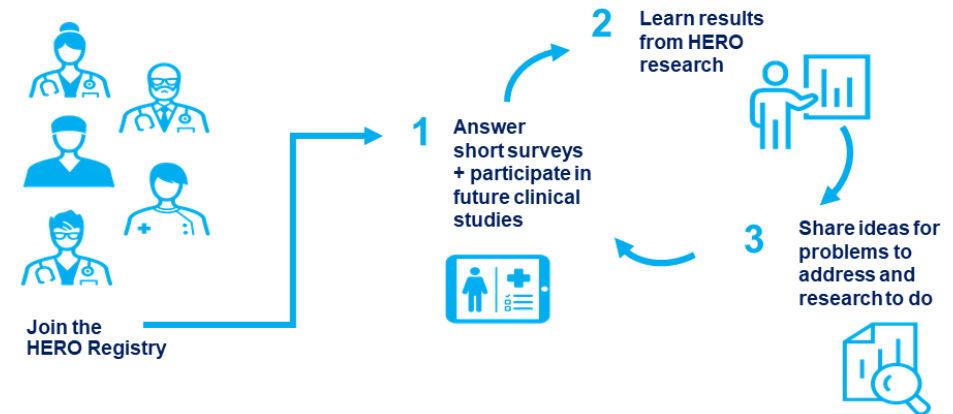
March 2020

March 2022



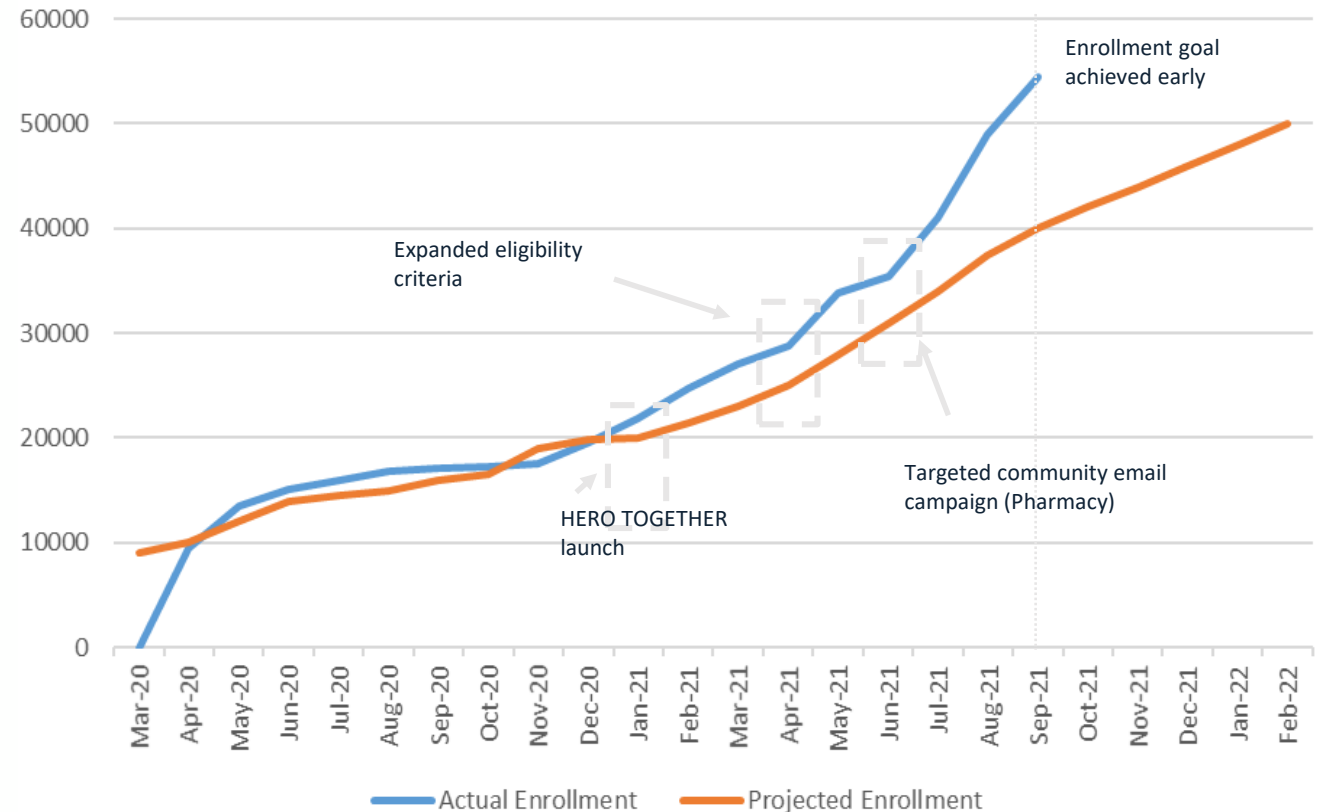
HERO Registry Objectives

- Create a **virtual community** of diverse adult healthcare workers and their surrounding family and community members;
- Establish an engaged and research-ready community of individuals interested in **engaging in upcoming research studies**, including those related to COVID-19;
- Create a **dataset of health-related measurements**, risk factors, and outcomes for analysis and decision-making;
- **Share information about the healthcare worker experience** during the COVID-19 initial, second, and any subsequent waves of infection.



Using multiple recruitment strategies...

- PCORnet site navigators
- Social media
- Pharmacy referrals
- Marketing campaigns
 - Targeted campaigns in cities with high ratio of healthcare workers and diverse population
- Partnerships with national associations, unions, and well-known public figures



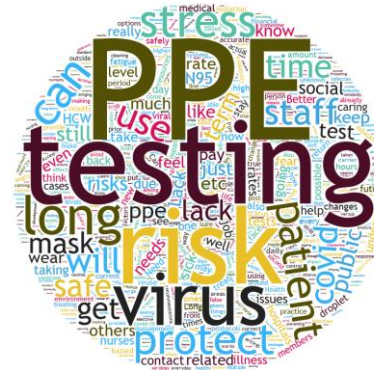
....even some rapping.



Measuring priorities

The HERO Baseline Survey asked: “What are the most pressing or important issues today that you feel need to be better understood related to healthcare workers and COVID-19?”

Spring 2020



Summer 2020



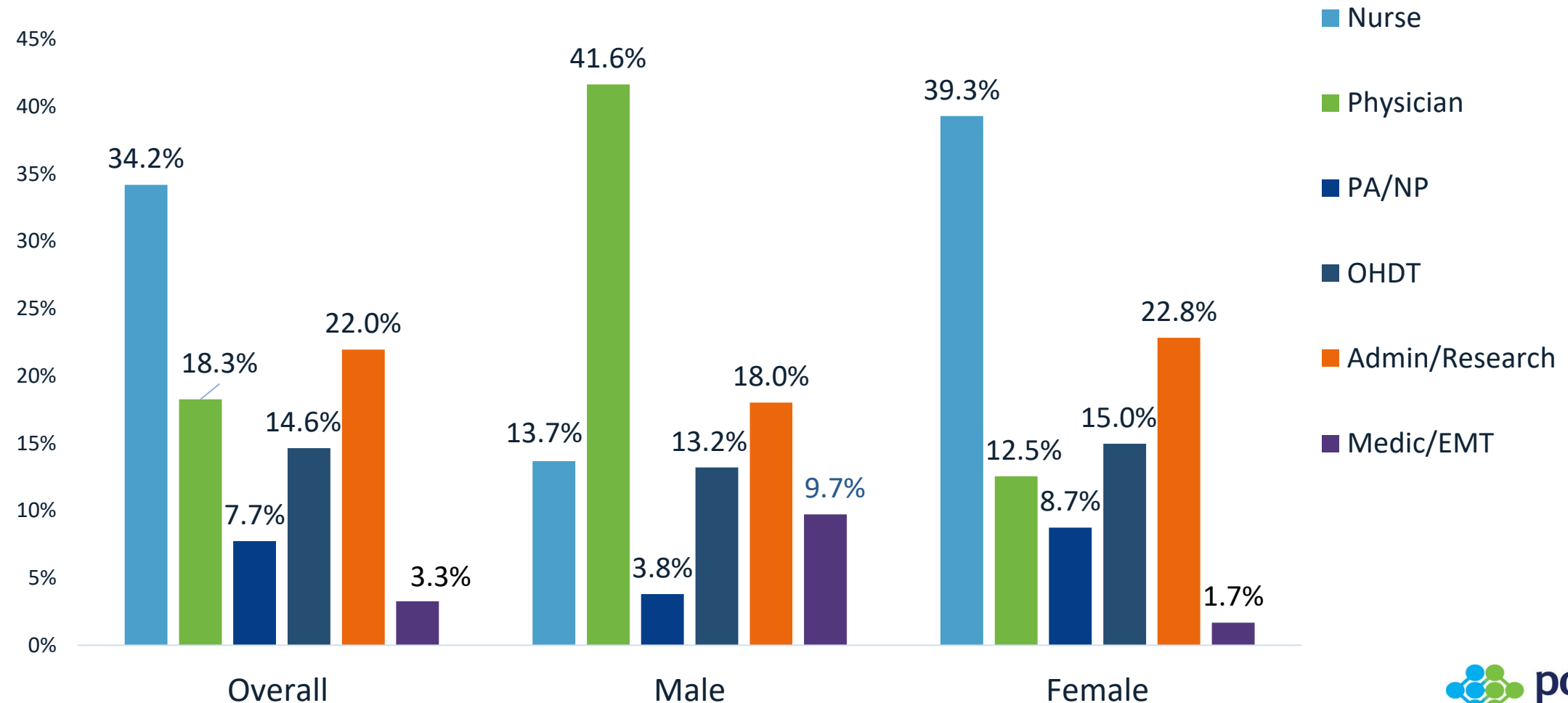
Fall 2020



Winter 2020

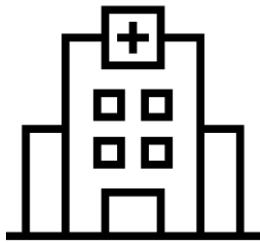


HCW Professional Role



Hot Topics

HERO Registry Monthly Polls



Workplace topics

- Moral injury
- Leaving healthcare
- Mental health resource availability
- Employer vaccine requirements
- Feelings of anger



Vaccine topics

- Willingness to be vaccinated
- Access to vaccine
- Vaccines in children
- Booster receipt

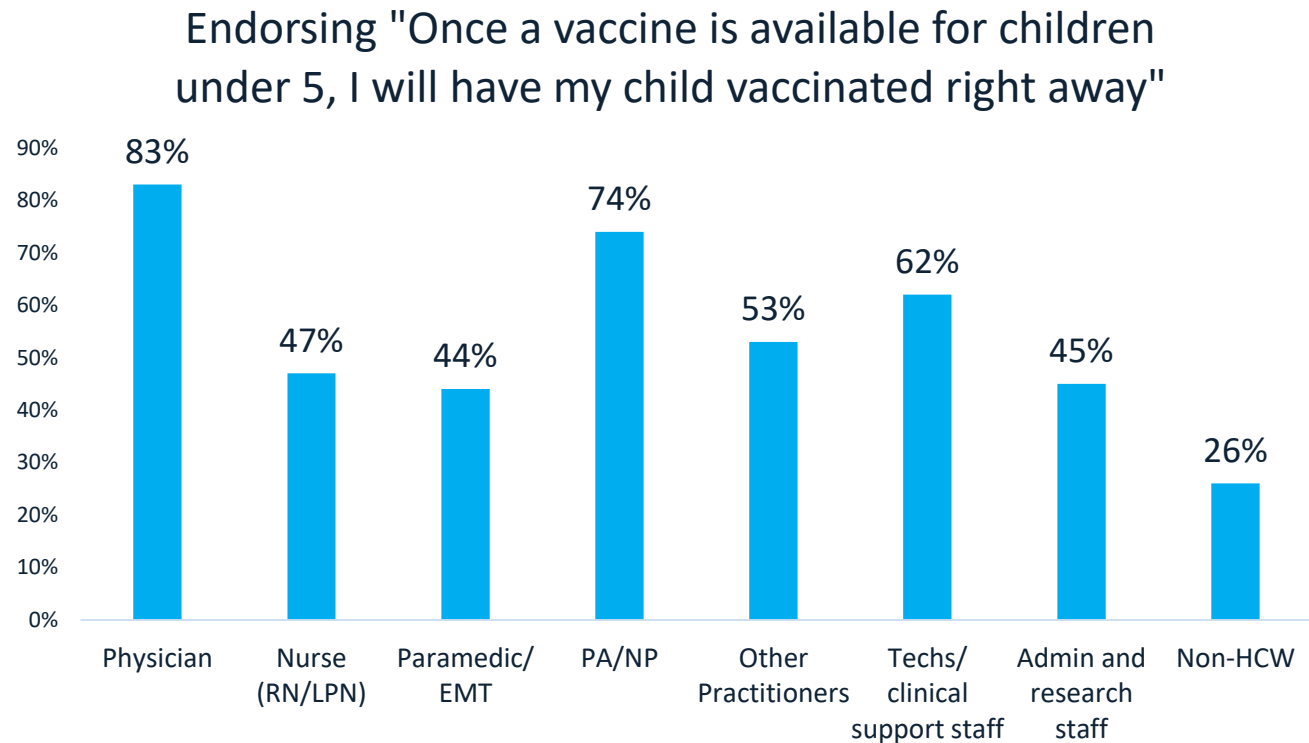


Home life

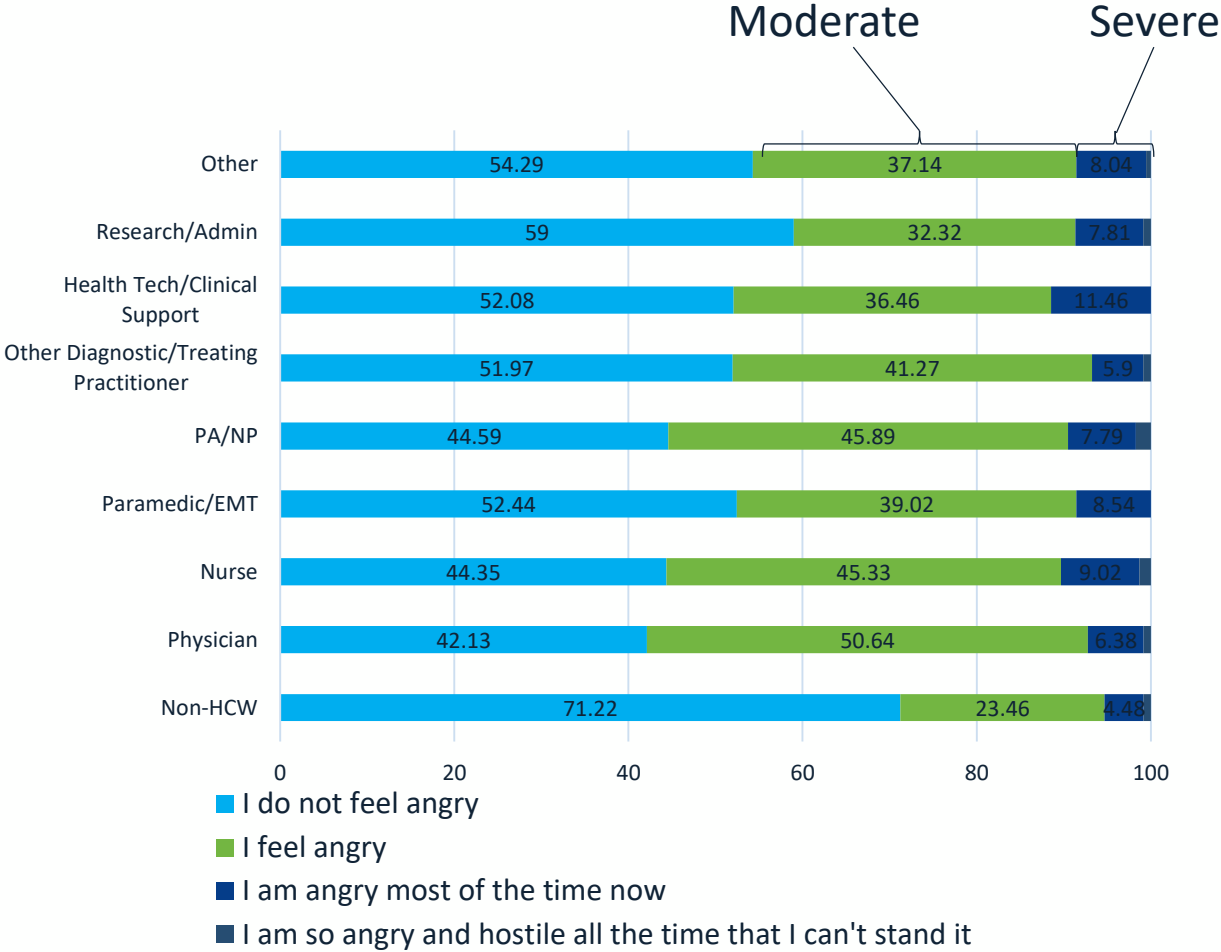
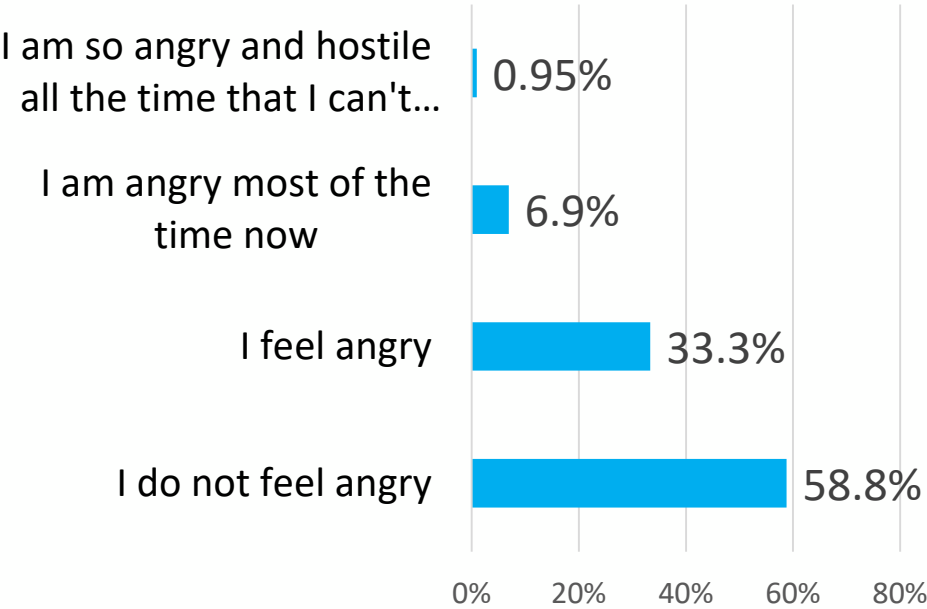
- Ability to work impacted by changes in school or childcare
- Financial burden of pandemic
- Return to School

Vaccines in Children Hot Topic Results

- 80% of HCW parents of 12-18 year olds said their kids were already vaccinated vs 68% of non-HCW parents
- Among parents of kids under 5, HCWs much more likely to vaccinate their kids right away than non-HCWs (57% vs. 26%)
- Women more likely than men to say they will wait and see for kids under 5

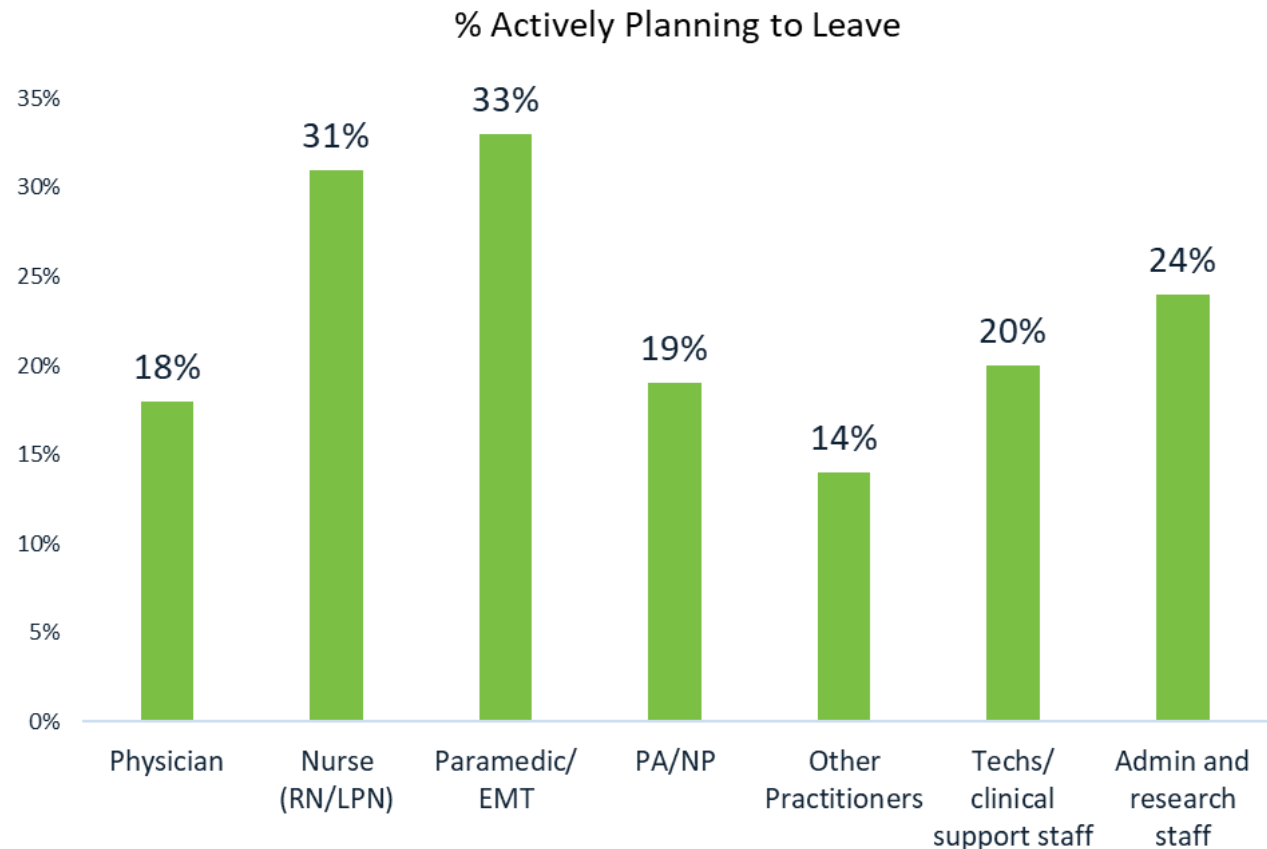


Anger Hot Topic Results



Intent to Leave Healthcare Hot Topic Results

- Increased % considering to leave or had already left
 - 57% in December 2021 vs 45% in May 2021
- In December 2021, over 2/3 of nurses and half of physicians considering/planning to leave or had already left
- Major drivers:
 - Burnout (74%)
 - Lack of appreciation from employer (50%)
 - Lack of mental/emotional support from employer (36%)





Selected Papers



Patterns of Potential Moral Injury in Post-9/11 Combat Veterans and COVID-19 Healthcare Workers



Jason A. Nieuwsma, PhD^{1,2,3} , Emily C. O'Brien, PhD⁴, Haolin Xu, MS⁴,
Melissa A. Smigelsky, PhD^{1,3} , VISN 6 MIRECC Workgroup, HERO Research Program, and
Keith G. Meador, MD, ThM, MPH^{1,3,5}

¹Integrative Mental Health, Department of Veterans Affairs, Durham, NC, USA; ²Department of Psychiatry and Behavioral Sciences, Duke University Medical Center, Durham, NC, USA; ³VA Mid-Atlantic Mental Illness Research, Education and Clinical Center, Durham, NC, USA; ⁴Duke Clinical Research Institute, Durham, NC, USA; ⁵Department of Psychiatry and Preventative Medicine, Center for Biomedical Ethics and Society, & Graduate Department of Religion, Vanderbilt University, Nashville, TN, USA.



Design of the Healthcare Worker Exposure Response and Outcomes (HERO) research platform

Anne Friedland^a, Adrian F. Hernandez^a, Kevin J. Anstrom^a, Mei Lin Chen-Lim^b,
Lauren W. Cohen^a, Judith S. Currier^c, Christopher B. Forrest^b, Ryan Fraser^a, Elizabeth Fraulo^a,
Anoop George^d, Eileen Handberg^e, Jennifer Jackman^a, Jayne Koellhoffer^f, Daryl Lawrence^g,
Renee Leverty^a, Patty McAdams^a, Brian McCourt^a, Brenda Mickley^a, Syed Hasan Naqvi^h,
Emily C. O'Brien^a, Rachel Olson^a, Clyde Praterⁱ, Russell L. Rothman^g, Elizabeth Shenkman^f,
Jack Shostak^a, Kisha Batey Turner^g, Laura Webb^a, Chris Woods^a, Susanna Naggie^{a,*}, on behalf
of the HERO Research Program

^a Duke Clinical Research Institute, Duke University, Durham, NC, United States of America

^b Children's Hospital of Philadelphia, Philadelphia, PA, United States of America

^c University of California Los Angeles, Los Angeles, CA, United States of America

^d Temple University Hospital, Philadelphia, PA, United States of America

^e University of Florida, Gainesville, FL, United States of America

^f Doylestown Health, Doylestown, PA, United States of America

^g Vanderbilt University Medical Center, Nashville, TN, United States of America

^h University of Missouri, Columbia, MO, United States of America

ⁱ Williamson Medical Center, Franklin, TN, United States of America

eClinicalMedicine

Part of THE LANCET Discovery Science

Racial/Ethnic Disparities in Healthcare Worker Experiences During the COVID-19 Pandemic: An Analysis of the HERO Registry

Jay B. Lusk^{a,b,*}, Haolin Xu^c, Laine E. Thomas^c, Lauren W. Cohen^c, Adrian F. Hernandez^c, Christopher B. Forrest^d, Henry J. Michtalik^e,
Kisha Batey Turner^f, Emily C. O'Brien^c, and Nadine J. Barrett^g, on behalf of the HERO Research Program

^aDuke University School of Medicine, Durham, NC, USA

^bDuke University Fuqua School of Business, Durham, NC, USA

^cDuke Clinical Research Institute, Duke University, Durham, NC, USA

^dDepartment of Pediatrics, Children's Hospital of Philadelphia, Philadelphia, PA, USA

^eDepartment of Medicine, Johns Hopkins University, Baltimore, MD, USA

^fVanderbilt University Medical Center, Nashville, TN, USA

^gDepartment of Family Medicine and Community Health, Duke University, Durham, NC, USA



Impact of the Early Phase of the COVID-19 Pandemic on US Healthcare Workers: Results from the HERO Registry



Christopher B. Forrest, MD, PhD¹ , Haolin Xu, MS², Laine E. Thomas, PhD²,
Laura E. Webb, BS², Lauren W. Cohen, MA², Timothy S. Carey, MD, MPH³,
Cynthia H. Chuang, MD, MSc⁴, Nancy M. Daraiseh, PhD⁵, Rainu Kaushal, MD⁶,
James C. McClay, MD, MS⁷, François Modave, PhD⁸, Elizabeth Nauman, MPH, PhD⁹,
Jonathan V. Todd, PhD, MSPH¹⁰, Amisha Wallia, MD, MS¹¹, Courtney Bruno, MSW¹,
Adrian F. Hernandez, MD, MHS², and Emily C. O'Brien, PhD² for the HERO Registry
Research Group

¹Applied Clinical Research Center, Children's Hospital of Philadelphia, Philadelphia, PA, USA; ²Duke Clinical Research Institute, Duke University School of Medicine, Durham, NC, USA; ³Department of Medicine, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA; ⁴Department of Medicine, Penn State College of Medicine, Hershey, PA, USA; ⁵Cincinnati Children's Hospital, University of Cincinnati, Cincinnati, OH, USA;

⁶Department of Population Health Sciences, Weill Cornell Medicine, New York, NY, USA; ⁷University of Nebraska Medical Center, Omaha, NE, USA;

⁸Department of Health Outcomes and Biomedical Informatics, College of Medicine, University of Florida, Gainesville, FL, USA; ⁹Louisiana Public Health Institute, New Orleans, LA, USA; ¹⁰OCI-HIN, Inc., Portland, OR, USA; ¹¹Division of Endocrinology, Metabolism and Molecular Medicine,

Department of Medicine and the Institute for Public Health and Medicine, Northwestern University Feinberg School of Medicine, Chicago, IL, USA.



HERO-HCQ

- March 2020
 - Popular support for potentially effective – but untested and unproven treatment to protect against COVID-19
 - In vitro studies suggested possible effect
 - Established safety profile
 - Healthcare workers at high-risk amid shortages of PPE and surging infection



Liu et al. *Cell Discovery* (2020)6:16
<https://doi.org/10.1038/s41421-020-0156-0>

Cell Discovery
www.nature.com/celldisc

CORRESPONDENCE

Open Access

Hydroxychloroquine, a less toxic derivative of chloroquine, is effective in inhibiting SARS-CoV-2 infection in vitro

Jia Liu¹, Ruiyuan Cao², Mingyue Xu^{1,3}, Xi Wang¹, Huanyu Zhang^{1,3}, Hengrui Hu^{1,3}, Yufeng Li^{1,3}, Zhihong Hu¹, Wu Zhong² and Manli Wang¹



HERO-HCQ Design

Primary:

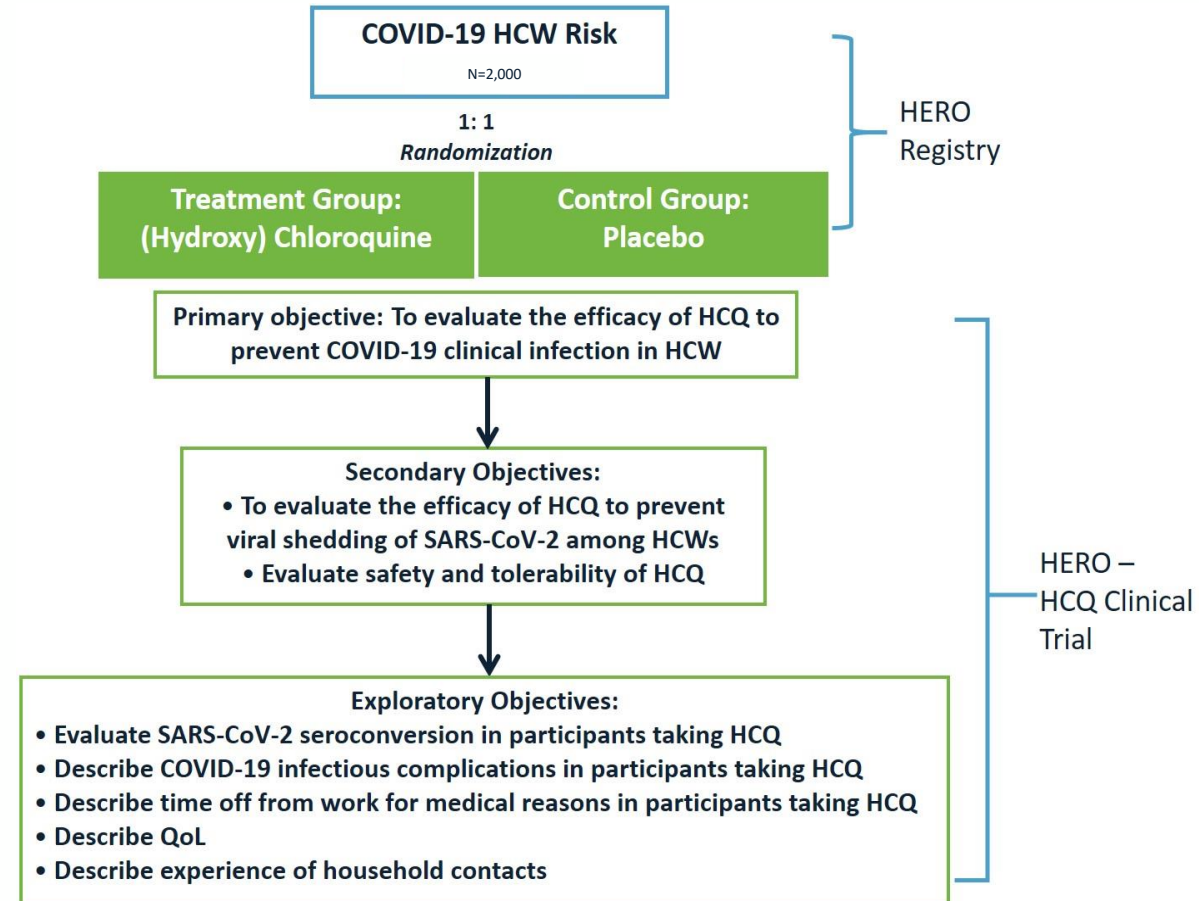
- To evaluate the efficacy of hydroxychloroquine (HCQ) to prevent COVID-19 infection in healthcare workers
 - Intervention: Hydroxychloroquine 600 mg BID loading dose on the first day, followed by 400 mg QD for 29 days, versus matched placebo

Secondary:

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

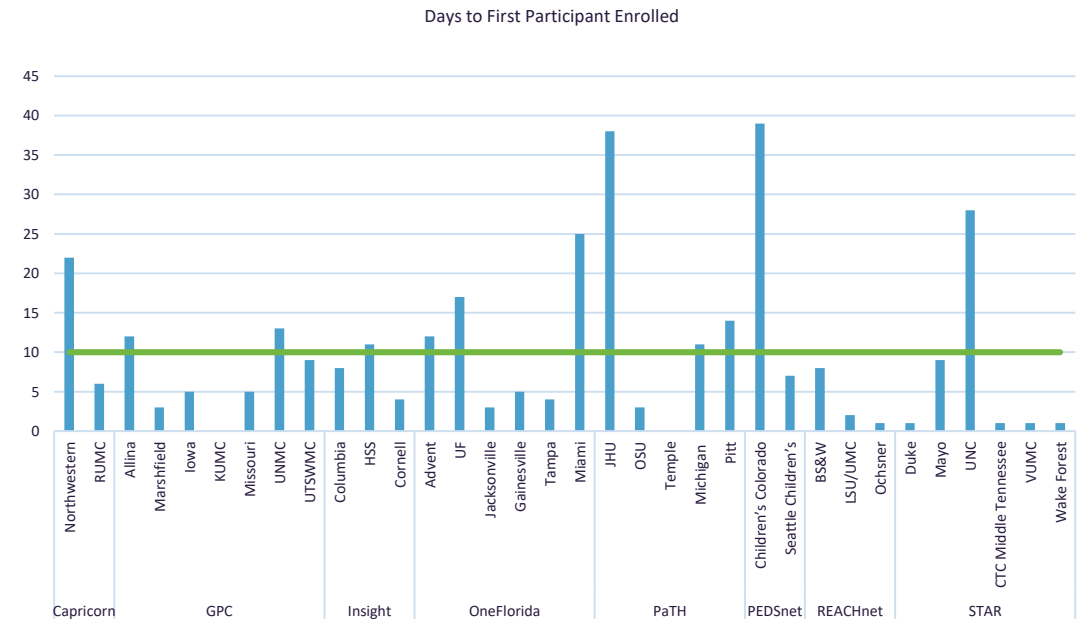
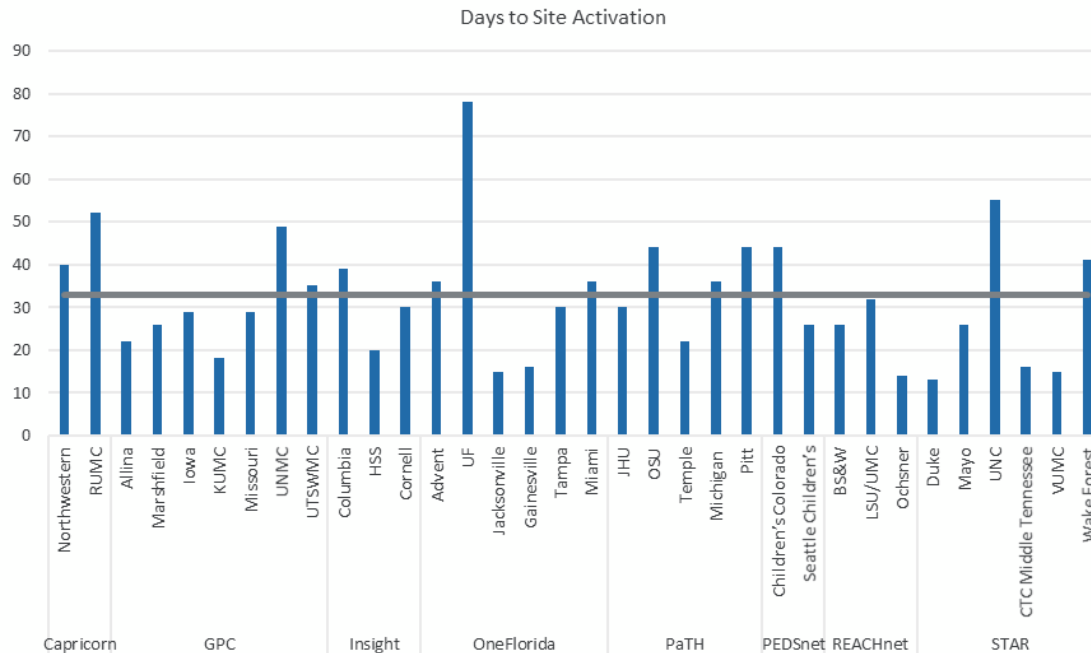
Design:

- Largely remote trial using HERO Registry. In-person visit 0 and 30 days for PCR and serology testing



HERO-HCQ Start-Up and Enrollment

- 34 PCORnet sites enrolled 1,363 participants between April – November 2020



- Long-standing partnerships, existing processes for site identification and communication, transparent reporting and lessons learned achieved:
 - Average: **30 days** to site activation | **10 days** first participant enrolled

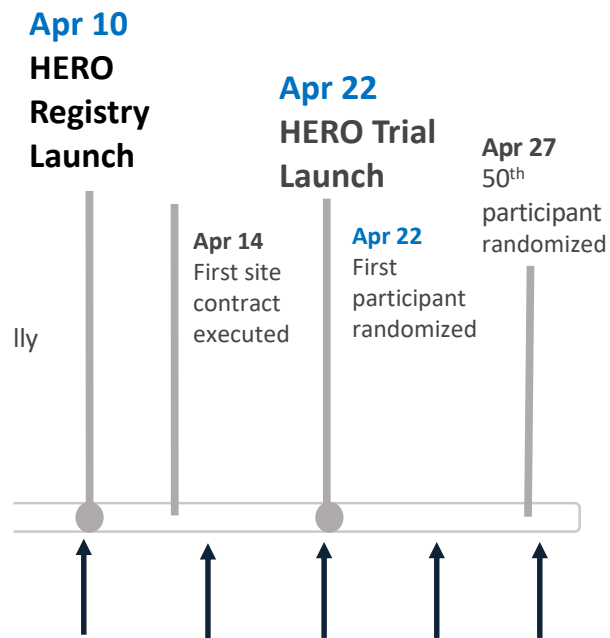
HERO-HCQ Results

- Powered for 2,000 participants, enrollment stopped at 1,363

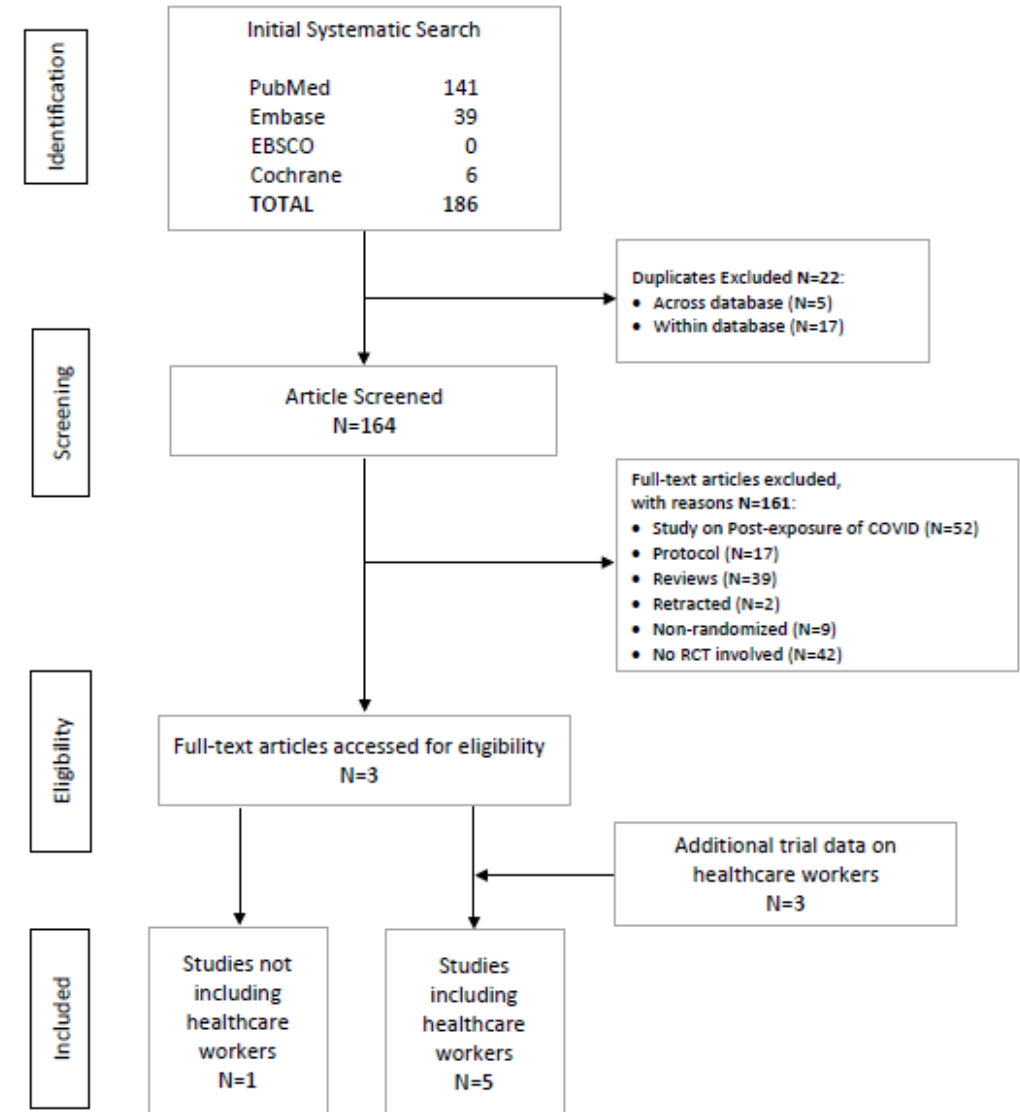
	Overall (n=1359)	HCQ (n=683)	Placebo (n=676)	Estimate (95% CI)	p-value
Primary					
Clinical infection by day 30	94 (6.9%)	41 (6.0%)	53 (7.8%)	-1.84 (-4.60, 0.87)	0.20
Confirmed: New onset fever, cough, or dyspnea AND confirmed PCR test	9 (0.7%)	3 (0.4%)	6 (0.9%)	-0.45 (-1.65, 0.50)	0.34
Suspected: Fever, cough, or dyspnea wo confirmed PCR test	85 (6.3%)	38 (5.6%)	47 (7.0%)	-1.39 (-4.03, 1.21)	0.31
Secondary					
SARS COV2 detection at day 30 Covance PCR test	4 (0.3%)	2 (0.3%)	2 (0.3%)	-0.00 (-0.87, 0.86)	1.0

HCQ Meta-Analysis

- A number of other studies were also underpowered to detect a significant effect due to enrollment challenges

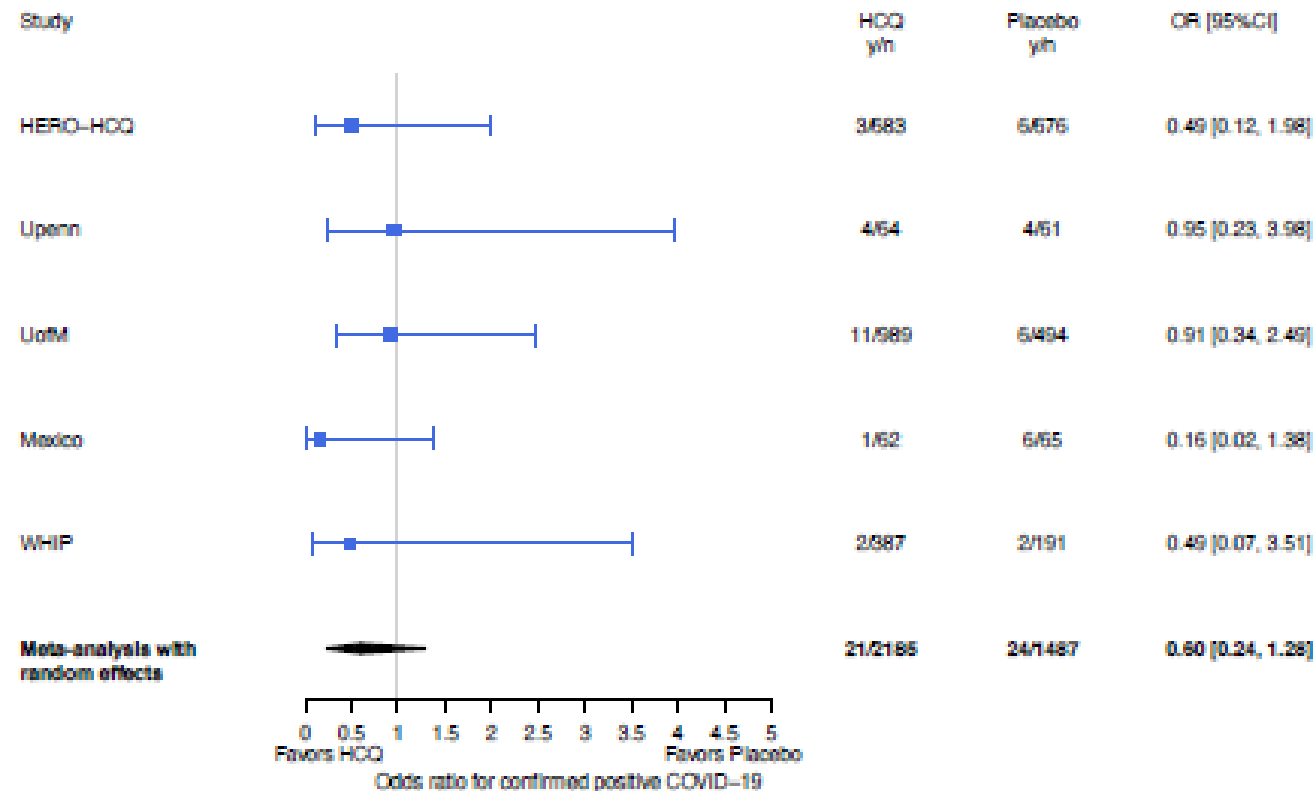


Pre-prints, study data leaks, tweets, FDA warning



HCQ Meta-Analysis Results

- Confirmed results of HERO-HCQ



Key Takeaways

- The HERO program rapidly created a novel and reusable trial infrastructure and referral system
- PCORnet sites were poised to randomize participants into a trial in <30 days
- Sometimes media can help research efforts ...sometimes it can hurt our ability to collect definitive evidence

Siteless Vaccine Safety Surveillance

Primary objective: Estimate the real-world incidence of safety events of interest and other clinically significant events among vaccinated individuals.

Secondary objective: Evaluate whether the vaccine recipients experience increased risk of events. Estimate the rates of events among subcohorts (e.g., pregnant women, immunocompromised, and stratified by age).



Post-marketing surveillance: an important contributor to safety-related label changes

Annals of Internal Medicine

ORIGINAL RESEARCH

Postmarketing Safety of Vaccines Approved by the U.S. Food and Drug Administration

A Cohort Study

Noam Tau, MD; Dafna Yahav, MD; and Daniel Shepshelovich, MD

Background: Vaccines are one of the greatest achievements in public health. Prevalence and clinical significance of emerging postapproval, vaccine-related safety issues have not been systematically studied.

Objective: To explore postmarketing safety modifications in U.S. Food and Drug Administration (FDA)-approved vaccine labels.

Design: Retrospective cohort study.

Setting: United States.

Participants: Initial and subsequent labels of all vaccines that were FDA-approved between 1 January 1996 and 31 December 2015.

Measurements: The primary aim was a descriptive analysis of the prevalence and characteristics of postapproval, safety-related label changes. The secondary aim was to describe the distribution of data sources triggering these modifications.

Results: The study cohort comprised 57 FDA-approved vaccines. Initial approval for 53 (93%) of the vaccines was supported by randomized controlled trials, with a median cohort size of 4161 participants (interquartile range, 2204 to 8634 partici-

pants). There were 58 postapproval, safety-related label modifications associated with 25 vaccines (49 warnings and precautions, 8 contraindications, and 1 safety-related withdrawal). The initial approval trial characteristics were similar in vaccines with and without postmarketing, safety-related label modifications. The most common safety issue triggering label modifications was expansion of population restrictions ($n = 21$ [36%]), followed by allergies ($n = 13$ [22%]). The most common source of safety data was postmarketing surveillance ($n = 28$ of 58 [48%]).

Limitation: The data source of the initial signal triggering safety-related label changes may not necessarily represent all safety data received and processed by the FDA.

Conclusion: Over a 20-year period, vaccines were found to be remarkably safe. A large proportion of safety issues were identified through existing postmarketing surveillance programs and were of limited clinical significance. These findings confirm the robustness of the vaccine approval system and postmarketing surveillance.

Primary Funding Source: None.

Ann Intern Med. 2020;173:445-449. doi:10.7326/M20-2726

For author, article, and disclosure information, see end of text.

This article was published at Annals.org on 28 July 2020.

Annals.org

- Over a 20-year period, vaccines were found to be remarkably safe
- A large proportion of safety issues were identified through post-marketing surveillance programs

Tau N, et al. *Ann Intern Med.* 2020; 173(6):445-449.

Rationale for studying the post-vaccine experience

Healthcare workers will be early SARS-CoV-2 vaccine recipients



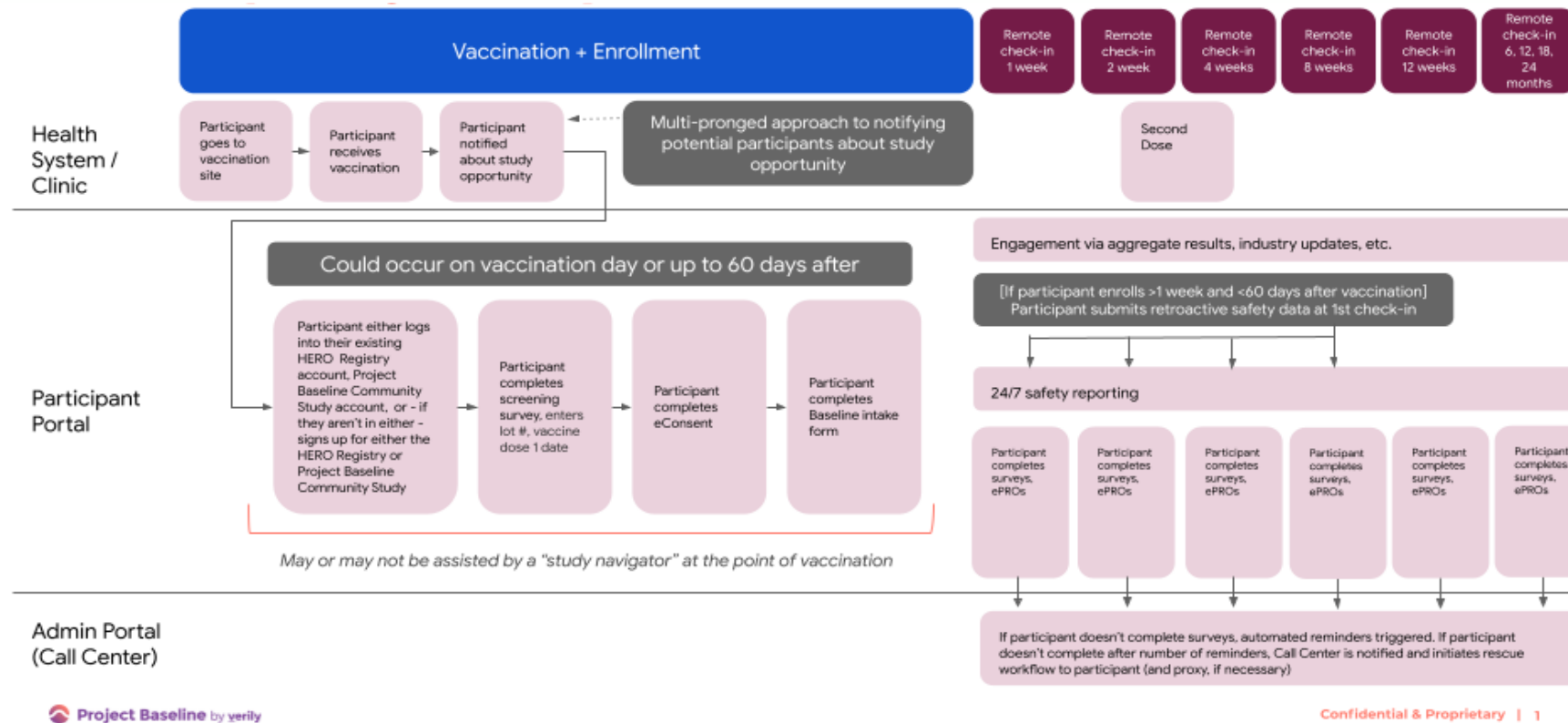
Emergency use-authorization will be based on limited follow-up data



There is a need for long-term safety surveillance for SARS-CoV-2 vaccines

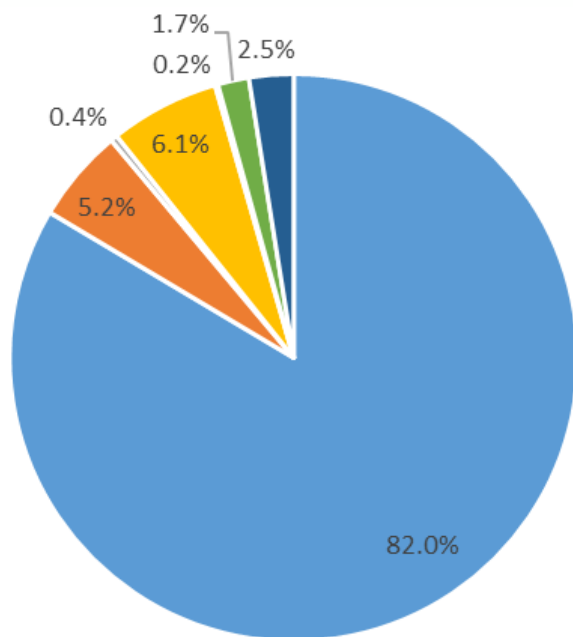


Participant Journey



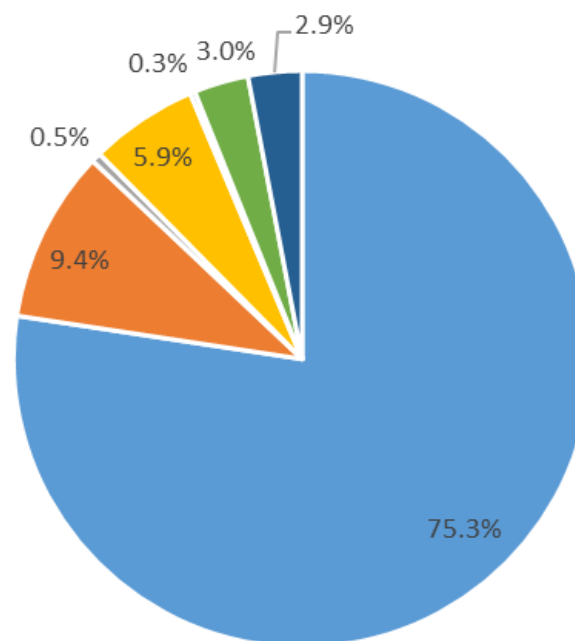
Community Pharmacy Partnership

Pre-campaign



8% Hispanic, Latino/a

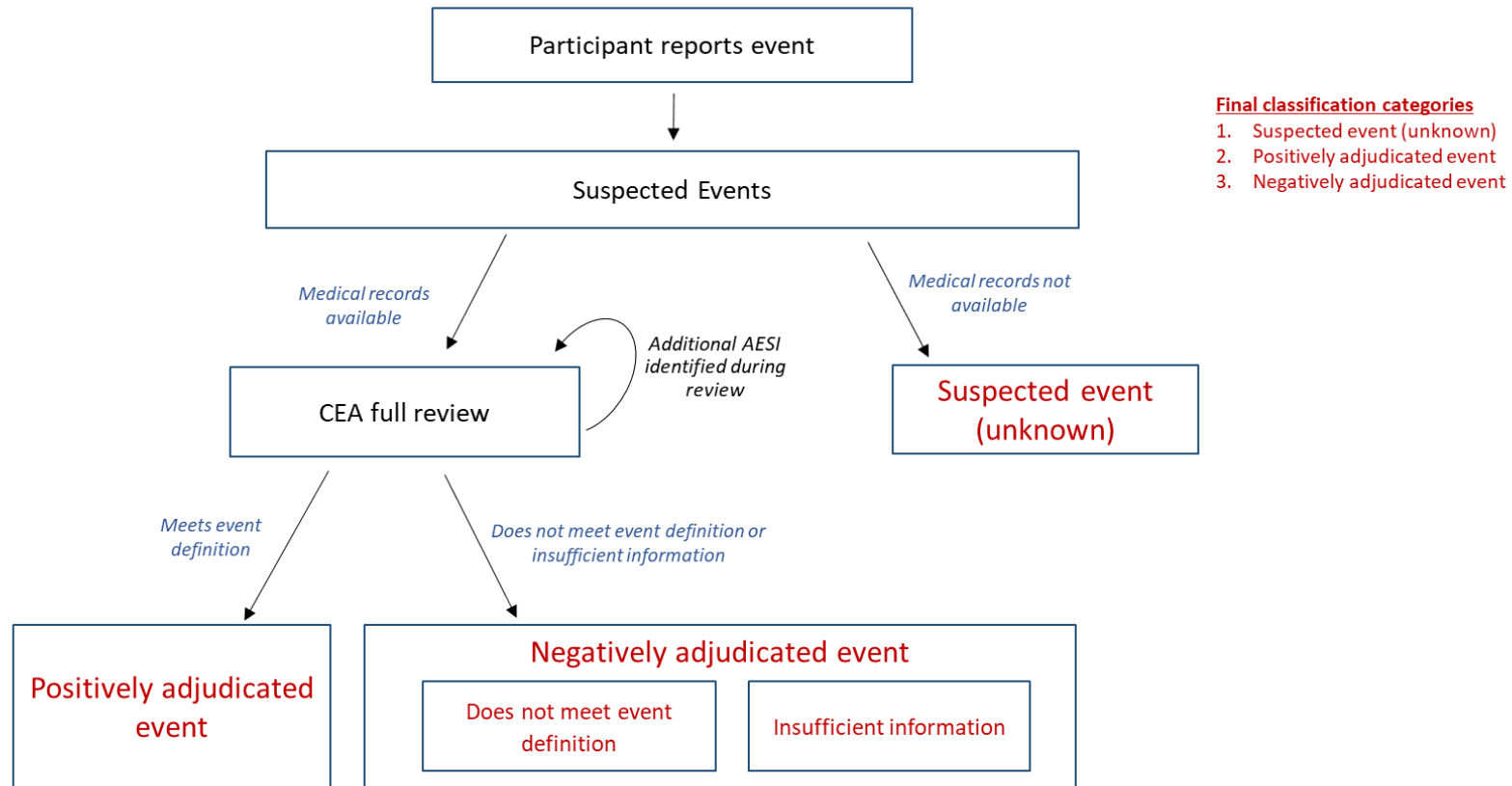
Post-campaign



12% Hispanic, Latino/a

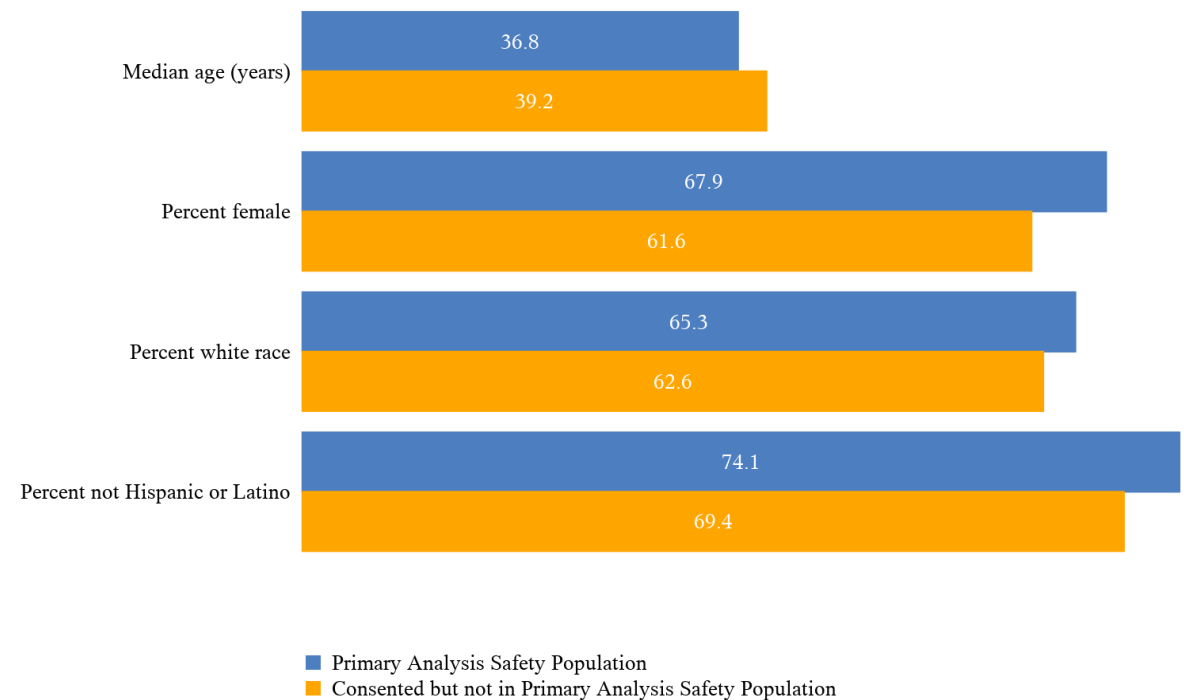
- White
- Black
- American Indian or Alaska Native
- Asian
- Native Hawaiian or Other Pacific Islanders
- Other
- Multi-race

Event Adjudication

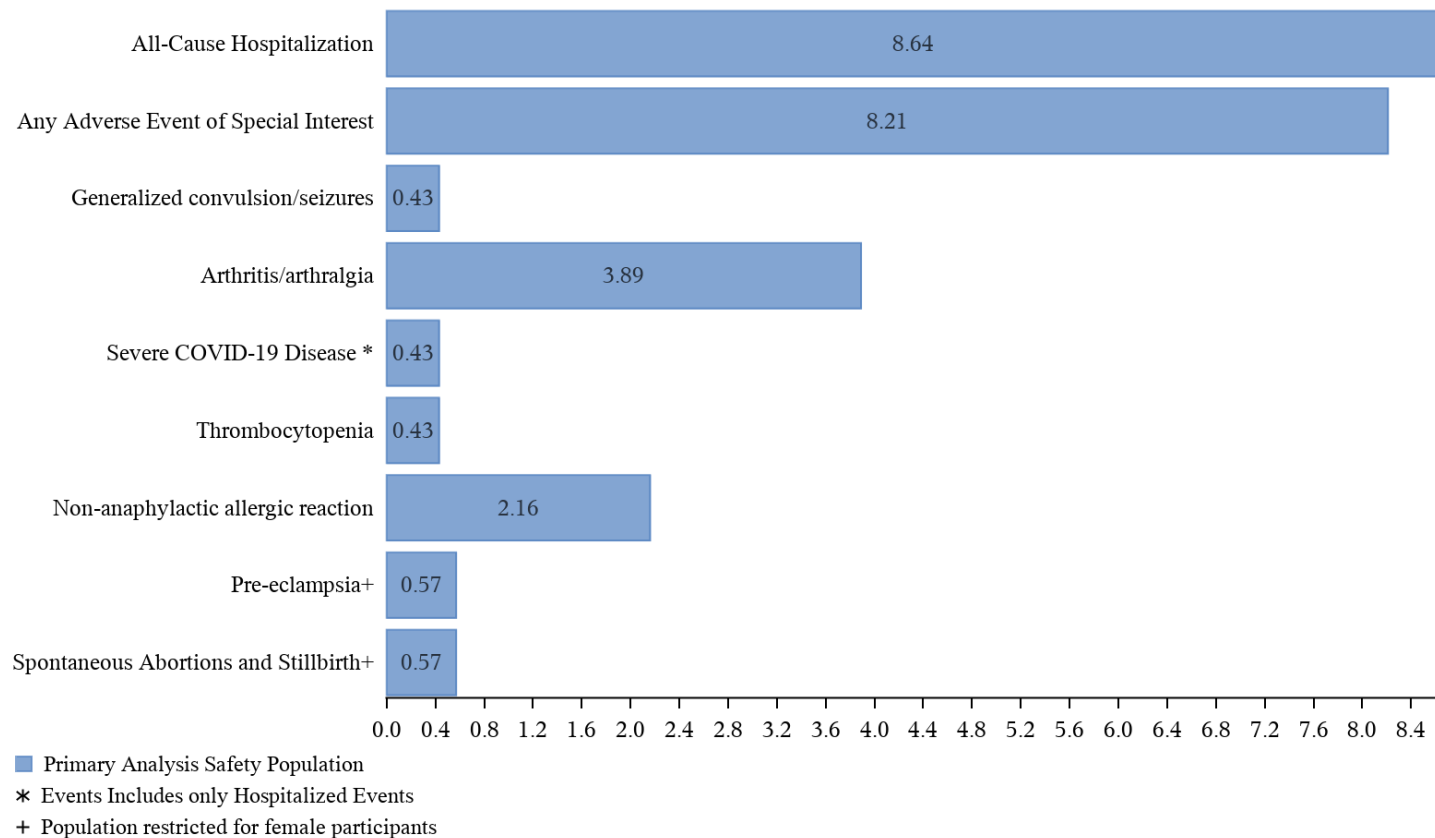


Final HERO Together Study Population

- Total consented population:
N=20660
- Primary analytic population:
N=9410 (receipt of Pfizer vaccine
within past 10 days)
- Median days since first vaccine
dose at enrollment: 3 days



Adjudicated Event Rates (per 1000 p-years)



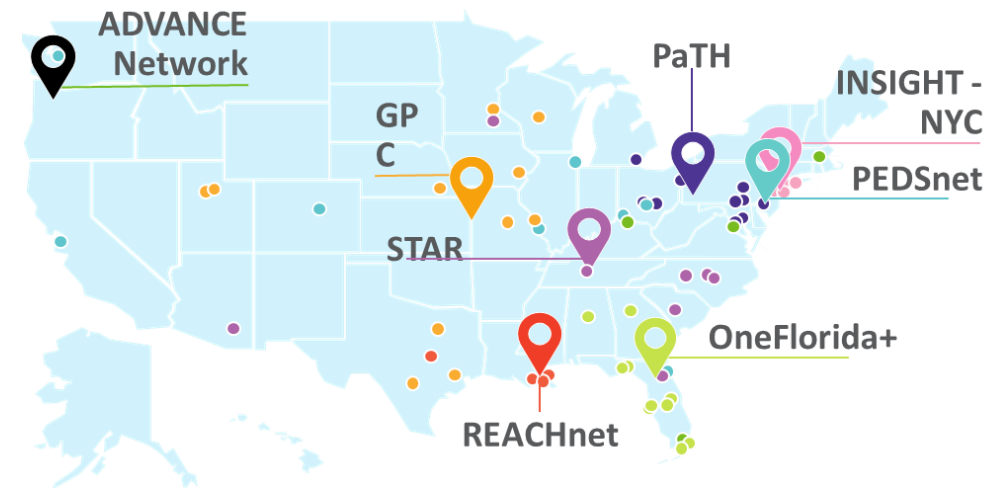
HERO-Together Conclusions

- The final HERO-Together study population was primarily white, female, and had low comorbidity burden
- The incidence proportions of reported hospitalizations were numerically similar for the PASP and the ACP
- The most common adjudicated safety events in the PASP included non-hospitalized arthritis/arthralgia and non-hospitalized non-anaphylactic allergic reaction
- These proportions were generally consistent with those in the ACP

Lesson Learned #1: The Power of Research Networks

PCORnet enabled rapid start-up through:

- Leveraging an existing coordinating center
- Use of a common data model
- Existing connections with local research teams



Lesson Learned #2: Good engagement strategies evolve with stakeholder needs



HeroesResearch

@HeroesResearch

The **#HERORegistry** is open to all **#healthcareworkers**, their friends and family members to help understand what it's like to live and work during the **#COVID19 #pandemic**. | Learn more: heroesresearch.org

HERO
Healthcare Worker Exposure
Response & Outcomes



Jul 11, 2022

HERO Registry Data Finds Racial/Ethnic Disparities Among Healthcare Workers

March 22, 2022

A recent study published by The Lancet eClinicalMedicine using HERO Registry data found racial and ethnic disparities experienced by healthcare workers during the COVID-19 pandemic. This observational cohort study, funded by the Patient-Centered Outcomes Research Institute (PCORI), surveyed over 24,000 U.S. healthcare workers enrolled in the HERO Registry between April 2020 and June 2021. Study healthcare workers shared their experiences with COVID-19 testing, diagnosis, workplace burnout, emotional struggles, and thoughts on ...

Thank you, Participants!

Enrollment is now closed. Thanks to the more than 20K participants who are helping us understand experiences with COVID-19 vaccines.



COVID-19 Research Opportunity

Learn more about the outpatient [ACTIV-6 study](#) for people with mild-to-moderate COVID-19.



ACTIV-6

WORKING TOGETHER TO HELP PEOPLE
WITH COVID-19 FEEL BETTER FASTER.

activ6study.org [#feelbetterfaster](#)

Lessons Learned: #3 – Novel Recruitment Strategies can Enhance Diversity

Bringing research to people means thinking outside the box.



Lesson Learned #4: Robust siteless research is possible!



Intentional
engagement



Working with mission-
driven partners



Balancing pros and cons
of different data streams

Thank You

Questions?

Supplemental Slides