

Leveraging PCORnet® to Respond to Emerging Concerns during the COVID-19 Pandemic

Background

At the onset of the COVID-19 pandemic, the Patient-Centered Outcomes Research Institute (PCORI) rapidly developed and funded initiatives to answer emerging COVID-19-related questions. Additionally, PCORI worked collaboratively with federal agencies to coordinate ongoing efforts to rapidly address evolving needs of patients, healthcare workers, and other stakeholders.

PCORI's investment in PCORnet®, the National Patient-Centered Clinical Research Network, a federated research infrastructure to enable faster and more efficient comparative clinical effectiveness research, contributed substantively to its ability to act nimbly and swiftly to address critical research needs related to the pandemic.

PCORnet is a “network of networks” composed of Clinical Research Networks (CRNs) that span diverse geographic areas of the United States, patient partners, and a Coordinating Center that provides technical and logistical support to the Network Partners. PCORnet infrastructure resources include access to electronic health record data from more than 66 million patients across over 60 health systems nationwide and access to 30 million patients for clinical trial recruitment. PCORnet Network Partners have also developed a strong foundation of trust among participating health systems and the public, supporting the network's robust, patient-centered research efforts and enabling its rapid response to the COVID-19 pandemic.

The pandemic presented an urgent need for collaboration between PCORI and federal partners and reliance on complementary skills, knowledge, and experience. PCORnet served as the nexus of many of the resulting initiatives.



Healthcare Worker Exposure Response and Outcomes (HERO) Program

At the start of the pandemic, federal members of PCORI's governing board from the National Institutes of Health (NIH) and the Food and Drug Administration (FDA) recognized the potential value of PCORnet in supporting large-scale trials to examine the effectiveness of drugs for the prevention or treatment of COVID-19. Working in concert with these two federal agencies, PCORI funded the HERO Research Program, consisting of a registry of healthcare workers, a population that was particularly vulnerable to COVID-19 exposure, and a clinical trial examining the effectiveness of hydroxychloroquine (HCQ) to prevent COVID-19 infection among healthcare workers.

The development of the HERO program followed by the funding decision and study start-up were accomplished on a highly accelerated timeline. In April 2020, less than one month after the PCORI Board of Governors approved

funding for the program, both the HERO Registry and Trial were launched. The trial was conducted under an Investigational New Drug Application with FDA oversight and concluded in February 2021 after enrolling 1,363 HERO members with a manuscript inclusive of trial results forthcoming.

The HERO Registry was used as a foundation for rapid research studies such as the HCQ trial, and to engage healthcare workers in understanding the impact of COVID-19 on their lives. The registry united healthcare workers as members of the research community, helped them share their experiences and interests, and tracked critical health outcomes associated with caring for patients with COVID-19, such as stress and burnout. As of June 2021, nearly 34,600 healthcare workers and their family members have enrolled into the registry, encompassing every state in the United States.

The HERO Research Program is powered by critical stakeholders such as healthcare workers, their families, and community members, who collectively guide research priorities and participate in the program's governance. Research with stakeholder engagement at the core is aligned with the fundamental foundation of both PCORnet and PCORI.

The strong partnerships and trust established among the PCORnet Network Partners enabled the rapid launch of the HERO program, allowing PCORI to respond quickly to this unprecedented crisis.

HERO-Together

Building on the foundation of the HERO Registry, Pfizer funded a vaccine safety study, HERO-Together. The goal of this observational study is to examine the short- and long-term safety of covid-19 vaccines among people vaccinated outside of clinical trials under emergency use authorization. The HERO-Together vaccine surveillance program demonstrates the value of having high-quality registries, like the HERO Registry, to support public health efforts.

The study aims to enroll approximately 20,000 healthcare workers after they receive the COVID-19 vaccine and follow them for two years. Information regarding their health and any unexpected medical care will be collected to assess their experience with the vaccine. This study was launched in December 2020 and, as of July 2021, has enrolled just over 13,000 HERO members.

Collaboration with the CDC

Given the need for reliable information on the characteristics of people infected with COVID-19 and the implications on public health, the Centers for Disease Control and Prevention (CDC) partnered with the Public Health Informatics Institute and Harvard Pilgrim Health Care to leverage data collected by PCORnet Network Partners for ongoing surveillance.

The CDC has funded 43 PCORnet sites for continued COVID-19 surveillance. Queries distributed across these sites have revealed insights including trends on the use of different medications for the treatment of COVID-19 and the presence of racial disparities in infection versus hospitalization rates. This collaboration was made possible through the efforts of PCORnet Network Partners rapidly adapting the PCORnet Common Data Model to capture and standardize biweekly data updates on patients with a diagnosis of COVID-19, a positive SARS-CoV-2 test, or other respiratory conditions. To date, aggregate data stripped of any personal identifying information related to nearly half a million patients with a COVID-19 diagnosis or positive SARS-CoV-2 test result have been shared with CDC.

This surveillance initiative is unique in comparison to the Vaccine Safety Datalink (VSD) project led by CDC. The health records that comprise the PCORnet infrastructure include both ambulatory and inpatient encounters, offering much more depth and detail as opposed to VSD data comprising only inpatient encounters. These records allow for a deeper understanding and broader insight into patient characteristics and predictors of disease, as well as long-term monitoring.

CDC continues to work with PCORnet leaders to determine how to best leverage data from a large network of healthcare organizations to support CDC's COVID-19 response. The biweekly queries enable the initiative to be agile and address questions arising from the evolving challenges of the pandemic. Recent areas of focus have included long COVID and the incidence of high priority diagnoses up to 150 days after a positive test.

Collaboration with the NIH (ACTIV-6)

Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV), directed by the Foundation for the National Institutes of Health (FNIH), is a public-private partnership focused on COVID-19. The goal of the ACTIV initiative is to prioritize and speed the development of the most promising COVID vaccines and therapeutics.

ACTIV-6, a subset of the ACTIV initiative, is a randomized, blinded, and placebo-controlled phase III platform trial to test the efficacy of repurposed medications to treat COVID-19 in the outpatient setting. It aims to provide definitive evidence for patients and their clinicians seeking safe, effective ways to manage COVID-19 and avoid progressing to more severe illness needing hospitalization.

ACTIV-6 will leverage PCORnet resources to rapidly access 40 vanguard sites, streamline study start-up timelines, and enroll participants. The Duke Clinical Research Institute, the co-lead of the PCORnet Coordinating Center, will serve as the clinical coordinating center for ACTIV-6 and Vanderbilt University, the lead site of the PCORnet STAR Clinical Research Network, will serve as the data coordinating center for ACTIV-6, placing PCORnet Network Partners at the forefront of this initiative.

ACTIV-6 adds a critical new component to our understanding of how best to deploy PCORnet resources to help most effectively lessen the severity of COVID-19

PCORI COVID-19 Enhancement and Targeted Funding Awards

In addition to the collaborations with federal agencies, PCORI built on its *rapid response to the COVID-19 health crisis* by approving funding for research addressing questions about how best to manage COVID-19 and effects of the pandemic. Funding included enhancements to existing projects that enable researchers to adapt their work to address COVID-19 as well as new projects under a targeted COVID-19 funding opportunity.

Many of these studies benefited from the utilization of the PCORnet infrastructure, allowing fast and efficient responses to vital public health questions. These PCORnet-enabled research studies addressed a range of important COVID-19-related research areas, including

among people who have contracted the disease. Rapid, robust research, like this initiative facilitated by PCORnet, provides vital information to support the practice of evidence-based medicine even in times of public health crises. ACTIV-6 is the first ACTIV trial in which patients and stakeholders are engaged as essential partners.

Collaboration with the FDA

Real-world data can help advance our nation's ability to respond to the COVID-19 global pandemic by significantly informing and safely speeding diagnostic and therapeutic processes. At FDA's request, the Reagan-Udall Foundation for the FDA, in collaboration with Friends of Cancer Research, launched the COVID-19 Evidence Accelerator. PCORnet Network Partners, with enhancement funding from PCORI, have been engaged in the work of the Evidence Accelerator to help design and execute parallel analyses for several use cases, including the use of remdesivir in hospitalized COVID-19 patients and understanding the natural history of coagulopathy in COVID-19 patients. These efforts are allowing the community to rapidly obtain insights from real-world data.

the development of prediction models to improve COVID-19 health outcomes, effects of telehealth on the well-being of older patients with multiple chronic health conditions, the impact of telemedicine on patient-centered outcomes and disparities in outcomes for patients with chronic disease, analyzing COVID-19 risk for patients taking blood pressure medication, as well as the impacts of COVID-19-related policy decisions on people's health and financial status.

The use of PCORnet resources to facilitate PCORI-funded COVID-19 research initiatives as well as collaborative partnerships with federal agencies like NIH, CDC, and FDA have supported PCORI in implementing a comprehensive and efficient response to the COVID-19 pandemic.

References

▶ PCORnet-enabled COVID-19 research

- <https://www.pcori.org/research-results/2016/methods-identify-and-predict-which-patients-will-have-high-healthcare-needs>
- <https://www.pcori.org/research-results/2016/examining-effectiveness-case-management-programs-preventing-hospital-stays>
- <https://www.pcori.org/research-results/2018/comparing-ways-patients-and-clinics-improve-blood-pressure-control>
- <https://www.pcori.org/research-results/2020/comparing-patient-reported-impact-covid-19-shelter-place-policies-and-access>
- <https://www.pcori.org/research-results/2020/evaluating-comparative-effectiveness-telemedicine-primary-care-learning-covid>

▶ PCORI Blog—<https://www.pcori.org/blog>

- <https://www.pcori.org/news-release/statement-role-pcornet-supporting-activ-6-trial-medications-use-treating-covid-19>

▶ PCORnet Website Newsroom—<https://pcornet.org/all-news/>

- <https://pcornet.org/news/cdc-uses-pcornet-resources-to-shape-national-understanding-of-covid-19/>
- <https://pcornet.org/news/pcornet-enabled-hero-registry-tops-20k-participants-as-pfizer-partners-for-vaccine-safety-study/>
- <https://pcornet.org/news/pcornet-enabled-hero-registry-launched-unites-frontline-healthcare-workers-to-fight-covid-19/>