## Predictors of COVID-19 Seropositivity Among Healthcare Workers: An Important Piece of an Incomplete Puzzle

Gregory W Ruhnke, MD, MS, MPH,<sup>1\*</sup> Aaron Richterman, MD, MPH<sup>2</sup>

<sup>1</sup>Section of Hospital Medicine, Department of Medicine, University of Chicago, Chicago, Illinois; <sup>2</sup>Division of Infectious Diseases, Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania.

ARS-CoV-2 seroprevalence studies of healthcare workers (HCWs) provide valuable insights into the excess risk of infection in this population and indirect evidence supporting the value of personal protective equipment (PPE) use. Seroprevalence estimates are composite measures of exposure risk and transmission mitigation both in the healthcare and community environments. The challenge of interpreting these studies arises from the diversity of HCW vocational roles and work settings in juxtaposition to heterogeneous community exposure risks. In this issue, two studies untangle some of these competing factors.

Investigators from Kashmir, India, assessed the relationship between seropositivity and specific HCW roles and work sites.<sup>1</sup> They found a lower seroprevalence among HCWs at hospitals dedicated to COVID patients, relative to non-COVID hospitals. This seemingly paradoxical finding likely results from a combination of vigilant PPE adherence enforced through a buddy system, restrictive visitation policies, HCW residential dormitories reducing community exposure, and a spillover effect of careful in-hospital exposure avoidance practices on out-of-hospital behavior. A similar spillover effect has been hypothesized for low HCW seroprevalence relative to the surrounding community in California.<sup>2</sup>

In complement, researchers at a large New York City (NYC) hospital found higher overall HCW seropositivity rates compared with the community, though estimates were strikingly variable after detailed stratification by job function and location.<sup>3</sup> The gradient of seroprevalence showed the highest risk among nurses and those in nonclinical, low-wage jobs (eg, patient transport, housekeeping), a finding also seen in another US study prior to adjustment for demographic and community factors.<sup>4</sup> This finding highlights the association between socioeconomic status, structural community exposure risk factors such as multiple essential workers living within multigenerational households, and the challenges of sickness absenteeism. High seroprevalence among nurses and emergency department HCWs (who expeditiously evaluate many undifferentiated patients) may reflect both greater aggregate duration of exposure to infected patients and increased frequency of PPE donning and doffing, resulting in fatigue and diminished vigilance.<sup>5</sup>

A NYC-based study similarly showed high HCW seroprevalence, although no consistent associations with job function (albeit measured with less granularity) or community-based exposures were identified.<sup>6</sup> Several studies comparing HCW to local community

\*Corresponding Author: Gregory W Ruhnke, MD, MS, MPH; Email: gruhnke@ medicine.bsd.uchicago.edu; Telephone: 773-834-8350.

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seropositivity rates have reached disparate conclusions.<sup>27</sup> These contrasting data may result from variability in vigilance of PPE use, mask use in work rooms or during meals/breaktimes, sick leave policies driven by staffing demands, and neighborhood factors. In addition, selection biases and timing of blood sampling relative to viral transmission peaks (with differing degrees of temporal antibody waning) may contribute to the apparent discordance. In particular, comparative community-based samples vary greatly in their inclusion of asymptomatic patients, which can substantially affect such estimates by changing the denominator population.

We draw three conclusions: (1) Evidence for HCW exposure often tracks with community infection rates, suggesting that nonworkplace exposures are a dominant source of HCW seropositivity; (2) vigilant PPE use and assertively implemented protective measures unrelated to patient encounters can dramatically reduce infection risk, even among those with frequent exposures; and (3) HCW infection risk during future peaks can be effectively restrained with adequate resources and support, even in the presence of variants for which no effective vaccination or preventive pharmacotherapy exists. Given the divergent seroprevalence rates found in these studies after detailed stratification by job function and location, it is important for future studies to evaluate their relationship with infectious risk. Accurately quantifying the excess risks borne by HCWs may remain an elusive objective, but experiential knowledge offers numerous strategies worthy of proactive implementation to preserve HCW safety and well-being.

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