

Concerns with and recommendations for COVID-19 research related to asymptomatic infection and mask wearing

Kevin Escandón, MD MSc¹, Angela K. Ulrich, PhD^{2,3}, Roger Chou, MD⁴

¹ School of Medicine, Universidad del Valle, Cali, Colombia

ORCID 0000-0002-7173-7486

² Center for Infectious Disease Research and Policy, University of Minnesota, Minneapolis, MN, USA

ORCID 0000-0002-4360-9719

³ Division of Environmental Health Sciences, School of Public Health, University of Minnesota, Minneapolis, MN, USA

⁴ Oregon Health & Science University, Portland, OR, USA

Correspondence: Kevin Escandón, MD, MSc, Universidad del Valle, 760043 Cali, Colombia (kevin.escandonvargas@gmail.com).

Alternate correspondence: Angela K. Ulrich, PhD, Center for Infectious Disease Research and Policy, University of Minnesota, Minneapolis, MN, USA (ulric063@umn.edu)

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TO THE EDITOR—We read with interest the recent study by Sims et al. [1]. The authors of this serological study of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) among 20,614 healthcare workers (HCWs) in Michigan, US concluded that employees wearing an N95 filtering facepiece respirator (FFR) or a powered air-purifying respirator (PAPR) had a significantly higher asymptomatic SARS-CoV-2 infection (ASI) proportion relative to those wearing a surgical mask or “other mask”. Herein we highlight some pressing concerns with this manuscript.

First, the methods used likely resulted in misclassification of ASI status. Symptom status was based on self-report within a 30-day window prior to blood collection between April 13 and May 28, 2020. Since seropositivity reflects cumulative exposure, persons who were infected more than 30 days prior would have been classified as ASI, regardless of whether they had symptoms at the time of infection. In addition, reliance on serology excluded employees with recent infection who had not yet seroconverted; the time to seroconversion and antibody kinetics may vary with symptom status [2,3]. For a more accurate assessment of ASI status, we suggest a sensitivity analysis that excludes all participants who reported a COVID-19 diagnosis 30 days or more before the study-associated blood draw and SARS-CoV-2-positive participants with symptoms within 2 weeks of the blood draw.

In assessing ASI, future studies should provide comprehensive case definitions, granular symptom assessment via standardized questionnaires, follow-up of symptom status, and polymerase chain reaction testing results if available [4,5], to avoid much of the potential misclassification of presymptomatic, paucisymptomatic, and postsymptomatic individuals as asymptomatic.

Second, we are concerned that the text states the proportion of ASI was 58.7% among HCWs involved in direct patient care compared to 46.0% of those not involved in patient care, but the supplemental figures suggest the opposite. If HCWs involved in direct patient care were less likely to develop ASI as the figures suggest, the crude odds ratio should support a negative association (<1), rather than a positive one.

Third, there is potential misclassification of the type of mask use. An individual may wear various types of masks (or none at all) in different healthcare settings, and interactions not only related to patient care but also between HCWs not wearing personal protective equipment can lead to transmission [6–8]. Additional potential confounders include SARS-CoV-2 testing, interventions other than mask wearing, consistency and appropriateness of mask wearing, host risk factors for COVID-19 severity, and pre-existing immunity [9,10]. Furthermore, in a community with widespread transmission, it is difficult to link an infection to occupational exposure. All these limitations make it inherently challenging to conclude whether exposure was occupational and to determine the type of mask (if any) was used during the relevant exposure. The conclusions related to ASI and mask wearing should therefore be cautiously interpreted.

Potential conflicts of interest

All authors declare no conflicts of interest and have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest.

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