

# Masks Reduce Viral Inoculum of SARS-CoV2



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Thank you for allowing us to respond to the important points made by Dr. Bhargava on our paper published in the *J Gen Intern Med*. To respond to the first point, we completely agree that the interplay between pathogen and host is a complicated one that depends on many features of both the virus and the host, including co-morbidities, age, immune status, and nutritional status of the latter. We were trying to bring in one more factor that could be related to the severity of COVID-19 disease, which is that of the viral inoculum, but that is not in any way meant to detract from the important host factors already known and well-described in the literature to date to influence the severity of COVID-19 disease. There have been many excellent descriptions of the risk factors that could predispose to severe COVID-19 disease, including the possibility of vitamin D deficiency as raised by the author. However, our paper joins a number of others at this point<sup>1–6</sup> to describe one factor—which is the effect of the viral inoculum—on severity of COVID-19 outcomes, which was the sole purpose of the commentary.

In terms of the second point, there was no implication of our commentary that people should be deliberately infected with SARS-CoV-2. In fact, as practicing infectious diseases physicians, we feel very strongly, that—given the case-fatality rate of the infection—challenge trials should not be performed for SARS-CoV-2. Our article discusses the hypothesis that viral inoculum may be one factor that contributes to the severity of disease for COVID-19, as it does for a number of viral infections in both animals and humans, but there is no implication of performing challenge trials in this article.

Finally, the mechanism by which a high viral inoculum may lead to more severe disease is via a dysregulated and overwhelmed innate immune response to a higher viral dose for infections in which immunopathology plays a role in viral pathogenesis<sup>7</sup>, such as COVID-19. Indeed, the imbalanced host response and cytokine storm described by the author is one of the reasons by which dexamethasone helps decrease the mortality of COVID-19 patients in those with severe infection.

We think that viral inoculum may be one of the factors contributing to this dysregulated immune response but agree with the author that co-morbidities and other factors in the host (including age) play important roles in disease outcomes. Therefore, we agree with the author that facial masking, along with other important COVID-19 mitigation public health strategies, such as social distancing, testing in nursing homes and good infection control, and hand hygiene, are all important. Our commentary was focused on a single factor that could contribute to disease severity that had not been raised much in the literature, but the excellent work done to date to define other risk factors is acknowledged and appreciated.

Thank you again for the opportunity to respond to the important points raised in this letter—*M. Gandhi, C. Beyrer, E. Goosby*

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## **Compliance with Ethical Standards:**

**Conflicts of Interest:** *The authors declare that they have no conflict of interest.*

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