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Reliance on the highest-quality studies of Long Covid is appropriate and not evidence of bias

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We want to thank Dr. Fanshawe for his letter.[1] We believe we share the common goal of enhancing understanding of Long Covid so we can better estimate the burden, appropriately allocate healthcare provisions and improve patient care.

To respond to his points in order, historical studies that employed a change in seropositivity status to distinguish infected cases from controls[2 3] are expected to be more accurate than those relying on antigen or PCR test positivity alone. Studies using serology status minimise the bias created by misclassifying cases with mild or no symptoms as 'uninfected controls.' The studies cited in our paper[4 2 3] that used serology were well-designed. They did not find a significant difference in prevalence of Long Covid between cases and controls, highlighting the very low risk of persistent symptoms after infection.

The UK Office of National Statistics survey, while appearing relatively well-matched, is expected to have suffered to some extent from the same biases as other studies that did not use serological confirmation: namely, systematically excluding those with mild or asymptomatic cases because they are less likely to be tested. Even without serological confirmation, a more recent Norwegian study[5] of non-hospitalised adults aged 30–70 years found a reassuring Long Covid incident diagnoses rate of 0.4% of infected adults, with prevalence declining to 0.1% (or 1/1000) of the adult population at 6–12 months post-infection during the omicron period. Notably, one of the strongest risk factors for developing Long Covid was pre-existing psychological diagnoses, indicating—even in this study with reassuringly low incidence—that the number of the Long Covid diagnoses may have been overestimated due to misclassification.

We maintain that the highest-quality studies provide Long Covid prevalence estimates that are more reassuring than what is typically communicated to the public, and that symptoms, which appear after SARS-CoV-2 infection, tend to promptly resolve after acute infection.[6–8]

The review Dr. Fanshawe cites[9] as evidence Long Covid is 'multifactorial' and 'debilitating' is unreliable for multiple reasons. First, it indicates 10%–30% of people who are *not* hospitalised with COVID-19 suffer from Long Covid. We can see this statistic is unrealistic prima facie now that most of the population has been infected at least once and 10%–30% of people do not suffer from Long Covid. The recent Norwegian study[5] suggests it is two orders of magnitude lower (and may be less common with proper classification). Second, the review[9] he cites relies on, among other data, a highly-problematic US Centers for Disease Control and Prevention (CDC) study[10] of people who received a diagnosis of COVID-19 documented in their electronic medical record and compared their likelihood of a subsequent incident diagnosis (related or unrelated to COVID-19) to those who had not had a documented COVID-19 diagnosis. First, this study is at risk of misclassification bias because they included any new condition that developed after COVID-19 as Long Covid and, although it may be debilitating and involve multiple organs, may have nothing to do with the SARS-CoV-2 infection. Second, those who receive a COVID-19 diagnosis in a medical chart are expected to differ from those who test at home or whose infections are undiagnosed; those that seek care are more likely to have underlying health conditions and/or more severe COVID-19 cases. These could introduce confounding and sampling bias, respectively.

Including multiple studies that are similarly biased to overestimate Long Covid prevalence in a systematic review of Long Covid would only serve to hyperbolise risk when combined.[11] This was clearly evidenced in systematic reviews falsely claiming that 80% of adults[12] and 25% of children[13] suffer from Long Covid after acute infection.

Improving accuracy in Long Covid research and acknowledging the limitations and biases of existing studies will hopefully lead to both 1. An improved societal understanding of post-COVID-19 sequela and 2. Evidence-based diagnostics and treatments so patients can receive effective treatment and support.

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