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## Brain Behavior and Immunity

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## Response to the letter by Lin et al.

As mentioned by Lin et al. in their letter, addressing vaccine hesitancy as a possible source of bias in research on the consequences of breakthrough COVID-19 infections is an important issue. This has been largely ignored by previous studies on this topic (Al-Aly et al., 2022; Antonelli et al., 2021; Kuodi et al., 2022). In our study, we sought to partially address this issue by restricting the control cohort to patients who had received at least one influenza vaccine prior to their COVID-19 infection (Taquet et al., 2022). While imperfect, this approach at least excludes those with the most enduring forms of vaccine hesitancy. We specified in our paper that “people with specific hesitancy towards COVID-19 vaccine but not other vaccines would still be included in this cohort” and this is important to keep in mind when interpreting the findings.

Regarding the moderation of analysis by number of vaccine doses, our data indeed show that having received two doses of the vaccine prior to COVID-19 infection was associated with even lower risks of several (but not all) acute and post-acute sequelae. In our analyses, while we stratified cohorts by age group and number of vaccine doses separately, we did not conduct an analysis in which each age group was further stratified by number of vaccine doses. This would have been a substantial undertaking. Moreover, 70% of the cohort with breakthrough COVID-19 infection had received 2 doses of the vaccine (vs. 30% who had received one dose). It is therefore likely that the results are primarily driven by people who were fully vaccinated against COVID-19. Moreover, a recently published study based on US veterans (mean age 62.8 years) and restricted to patients fully vaccinated broadly showed incomplete protection against post-acute COVID sequelae (Al-Aly et al., 2022). Further studies are needed to elucidate the moderation of the effect of vaccine by age group and number of vaccine doses. In

particular, little is known about the effect of ‘booster’ doses on post-COVID outcomes.

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Maxime Taquet<sup>a,b,\*</sup>, Quentin Dercon<sup>a,c</sup>, Paul J Harrison<sup>a,b</sup>

<sup>a</sup> Department of Psychiatry, University of Oxford, Oxford, UK

<sup>b</sup> Oxford Health NHS Foundation Trust, Oxford, UK

<sup>c</sup> MRC Cognition & Brain Sciences Unit, University of Cambridge, UK

\* Corresponding author at: Department of Psychiatry, University of Oxford, Oxford, UK.

E-mail address: [maxime.taquet@medsci.ox.ac.uk](mailto:maxime.taquet@medsci.ox.ac.uk) (M. Taquet).

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