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Letter to the Editor

# Vaccine effectiveness of ChAdOx1 nCoV-19 against COVID-19 in a socially vulnerable community in Rio de Janeiro, Brazil: author's response

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# To the editor

We appreciate the interest in our publication [1,2]. First, we would like to highlight that our study followed a pre-specified protocol, which was based on other protocols for evaluation of COVID-19 vaccine effectiveness applying case-control, test-negative study design conducted in Brazil and in accordance with the World Health Organization (WHO) recommendations [3,4].

Regarding the decrease in effectiveness following the first dose, the change overtime for the first dose is shown in Table 1 of the original article [2]. We did not evaluate change overtime for the second dose because we had not sample size/power to conduct this analysis. As stated in our discussion, the observed decrease overtime for the first dose can be attributed to some reasons. For instance, waning, which is the natural decline of protection, as well as the surge of the Delta variant. Because we do not have data on sequencing, we cannot disentangle this issue further, as well as we cannot obtain an estimate for protection against Gamma and Delta variants. We agree that evaluation of effectiveness by age is important [3], but we pre-specified that we would conduct this analysis by the median age. Subgroup analysis could lead to spurious findings if not pre-specified. We have very few elderlies recruited in the study because of the age distribution of the analysed population in "Complexo da Maré." Finally, our study population comprises only adults, and children were not even receiving COVID-19 vaccines at the time of study, therefore it would be impossible to estimate direct vaccine effectiveness in children.

Regarding potential confounding factors, we excluded previous infected individuals (eFigure 3, supplementary material of the original article [2]). We agree that personal behaviour could affect the risk of infection, and if this behaviour is different between vaccinated individuals compared to unvaccinated individuals, we could have residual confounding, as acknowledged in the article [2]. However, as also discussed in the manuscript, our indicator bias did not indicate any remarkable bias, under the assumption of a case-control, test-negative design [5]. We agree cross-protection could influence on vaccine effectiveness estimates if those tested negative individuals were symptomatic by some virus with cross-protection, however this is still a hypothesis for COVID-19 vaccines.

We would like to highlight that our vaccine estimates were in accordance to previous literature and robust to several sensitivity analyses, as shown in the supplementary material of the original article [2].

## Transparency declaration

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# Author contributions

OTR and FAB equally contributed to this study.

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