Authors' Reply

Bell, Samira; Campbell, Jacqueline; Lambourg, Emilie; Mark, Patrick

Published in:
Journal of the American Society of Nephrology

DOI:
10.1681/ASN.2022030382

Publication date:
2022

Document Version
Peer reviewed version

We thank Ashby for his interest in our study. Our data clearly demonstrate a two dose COVID-19 vaccination regimen is insufficient protection for patients either on dialysis or with a kidney transplant which is entirely in keeping with other emergent data demonstrating higher COVID-19 mortality in double vaccinated patients with kidney failure when compared to other clinically vulnerable patients[1-3]. There are differences in vaccine efficacy between studies in patients with kidney failure depending on population studied, degree of immunosuppression, vaccination regimen, mechanism of reporting of positive COVID-19 infection and infectivity of the prevalent variant of SARS-Cov-2. However, the totality of evidence supports that whilst two dose vaccination may improve outcomes to some degree, there is still an unacceptably high proportion of double vaccinated patients with kidney failure dying or being hospitalized withing 28-30 days of a positive COVID-19 test reported at 9% and 34% respectively up until September 21, 2021 in our study[1] and 9.5% and 30% in Canada, albeit with a follow up only until June 30, 2021[2]. To date, there are still comparatively few reports of the effect of COVID-19 vaccination on clinical outcomes rather than serological markers of response in this population.

We acknowledge the lack of consideration of time at risk in our study as a potential problem. Whilst we note the merits of this approach, it does pose challenges when implementing in a highly vaccinated population. We do not feel that including person time would significantly affect the analyses as the follow-up period is short (March- October) and patients are classed as fully vaccinated 2 weeks following their 2nd dose. We have used 1st March 2021 as the date when we included both vaccinated and unvaccinated patients for our vaccine effectiveness calculation as this was the point when all patients would have had the opportunity to be vaccinated. With regards to the suggestion that by not accounting for person time exposed, we are underestimating vaccine efficacy. If this is the case, as the population progressively transitions to double vaccinated status, it is likely that the double-vaccinated will be slightly less exposed to Covid than the unvaccinated and so vaccinated individuals have slightly less follow-up time thereby slightly overestimating vaccine effectiveness (if at all) in our study. 814 infections were the total number of infections from the

beginning of pandemic March 2020 (apologies for a typographic error in one listing of the date in the paper for which we have submitted a correction). 357 infections were in those who had 2 doses, 25 not vaccinated and the partially vaccinated were excluded. In terms of the second point with regards to defining groups as of 19th of September, we have repeated the analyses according to the suggested permutations. Vaccine effectiveness was slightly lower rather than under-estimated. We have clearly described the limitations of the methodology we employed and presented the accompanying confidence intervals as a measure of precision. We feel that our paper reinforces a very important message that outcomes following two doses of COVID-19 vaccine in patients receiving kidney replacement therapy provides insufficient protection and so patients should be encouraged to take up additional vaccine doses and other preventive measures should continue to be implemented.

References

1. Bell S, Campbell J, Lambourg E, Watters C, O'Neil M, Almond A, et al.: The Impact of Vaccination on Incidence and Outcomes of SARS-CoV-2 Infection in Patients with Kidney Failure in Scotland. *J Am Soc Nephrol*, 2022 10.1681/ASN.2022010046
2. Oliver MJ, Thomas D, Balamchi S, Ip J, Naylor K, Dixon SN, et al.: Vaccine Effectiveness Against SARS-CoV-2 Infection and Severe Outcomes in the Maintenance Dialysis Population in Ontario, Canada. *Journal of the American Society of Nephrology***:** ASN.2021091262, 2022 10.1681/asn.2021091262
3. Andrews N, Tessier E, Stowe J, Gower C, Kirsebom F, Simmons R, et al.: Duration of Protection against Mild and Severe Disease by Covid-19 Vaccines. *New England Journal of Medicine,* 386**:** 340-350, 2022 10.1056/NEJMoa2115481