

Article details: 2021-0044	
Title	SARS-CoV-2 antibodies in Ontario healthcare workers during and following the first wave of the pandemic: a cohort study
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Reviewer 1	Dr. Steven Drews
Institution	ProvLab Alberta
General comments	<p>Thank you for allowing me to review this manuscript. I have some further comments below.</p> <p>Major-</p> <p>Page 7/22- lines 7-14- it was unclear to me if the demographics (e.g. employment type) mentioned are for the 1062, 1001 or 355 and whether they stay stable as the numbers of HCW drop over 0,6 and 12 week periods. Please clarify this further; related to this, the methods sound like this was a rolling recruitment strategy over first wave but I am not completely clear if this was the case; could this be clarified</p> <p>page 7/22 lines 44-58- It is not clear to me how appropriate PPE was defined. I am assuming that this was task-based but it is not evident until the Discussion that this may be the case; although it is still not clear. Given that this is an important risk factor, it would be nice if you could briefly describe early on.</p> <p>Page 10 lines 1-21 and related to Figures 3 a-c- I think that one key limitation identified is that the results in Figures 3 a-c are the product of an EIA and that "quantification" or interpretations of dropping signals may not actually represent dropping antibody titers.</p> <p>Minor-</p> <p>Page 4/22 line 22- Even with an S antigen based EIA, the literature does suggest that we can expect to see waning at 90-120 days post onset of symptoms; this might be a good point to identify here</p> <p>Page 6/22 lines 52-53- Add "Vienna, Austria" or company location to R core info</p> <p>Page 10/22 lines 17-22- would suggest that another reason for false negative would be if the HCW had a waned Immune response prior to recruitment</p> <p>Tables 2 and 3 - has some odd font changes vs Table 1 and rest of text</p> <p>References- please provide dois of www for refs 4, 14, 20, 22, 25, 27, 40</p>
Reviewer 2	Fred Yoichi Aoki
Institution	Department of Clinical Pharmacology, University of Manitoba, Winnipeg, Man.
General comments	<p>Summary</p> <p>Science and colleagues report some of the results of a study looking at the</p>

prevalence of SARS-CoV-2 antibody in serum samples from 1062 Healthcare Workers (HCW) recruited from The Hospital for Sick Children, a tertiary care pediatric hospital in Toronto (N = 376), two combined adult-pediatric hospitals in London, ON (LHSC; N = 349) and a community hospital in Markham, ON (N = 337), in blood samples collected at 0, 6 and 12 weeks during the first wave of the COVID-19 pandemic April 1 to September 23, 2020.

They then sought associations of antibody-positivity with demographic, occupational and non-hospital risk factors (symptomatic household contacts and identification of SARS-CoV-2 positive household members as identified by public health), using logistic regression analysis.

Results are presented of antibody tests for 100% of samples at time 0 (N = 1062), 94% at 6 weeks (N = 1001) and 32% at 12 weeks (N = 344). The reason for the smaller sample at 12 weeks was that only samples obtained before September 24, 2020 were utilized for this report.

53 HCW were seropositive, of whom 48 were seropositive at entry and 5 seroconverted during the study. These data were then used for regression analysis that demonstrated that seropositivity was significantly correlated with a known unprotected exposure to a patient with COVID-19 disease, contact by a public health nurse because of a non-hospital exposure and infection prior to enrollment.

Working on a unit with a COVID-19 outbreak was not associated with seropositivity. In multivariate analysis, presence of symptomatic contacts in the household was the strongest predictor of seropositivity (adjusted odd ratio [aOR] 7.61; $p < 0.001$).

Among those who tested seropositive at 6 or 12 weeks (and were not positive at baseline), presence of symptomatic household contacts remained a strong predictor (a OR 8.17) and younger age and non-white race were also predictive. Of note, providing direct care to patients with COVID-19 was associated with a reduced chance of infection (a OR 0.34)

Comments to Authors

In ignoring 24% of serum test results (61 at 6 weeks and 718 at 12 weeks of a total of 3,186 sera (1062 x 3), you have omitted data on SARS-CoV-2 seroprevalence at 12 weeks [and seroincidence over 12 weeks] that may have markedly underestimated the actual prevalence of SARS-CoV-2 seropositivity and its determinants in these volunteers.

If the seroprevalence data (53 total seropositive individuals consisting of 48 who were positive at enrollment and 5 who became seropositive at 6 or 12 weeks) are indeed different from the actual prevalence rate, then it follows that the regression analyses would also be incorrect. Accordingly, it seems to this reviewer that calculations not including antibody results from 779 samples [0, 61 and 718 samples at 0, 6 and 12 weeks = 779; 24% of the total of 3,186 (1062 x 3 sample times)], are premature. That is, this analysis should not yet be undertaken and certainly not submitted for publication as definitive. This reviewer recommends that this manuscript be withdrawn and resubmitted when all the data are available.

At the time of analysis of the complete data set, could I suggest the following:

- Describe what change in anti-SARS-CoV-2 IgG immunoassay is consistent with a significant rise or fall. This is important in assisting readers to understand what change constitutes a significant rise or decline over time or no change (durability).
- In Table 3, please consider how brackets are placed. In Table 3 brackets indicate both number of subjects (n = 53) and seemingly, % e.g. "Symptomatic contacts in the household 7/49 (14)".

	<p>In the rows, please check what the denominator is in each row.</p> <p>iii. Specify the start and end dates of the ‘first wave’ of COVID-19 disease to provide context for serosurvey study period (April 1 – September 23, 2020).</p> <p>iv. Consider providing evidence of the incidence of SARS-CoV-2 infection during the 12 week study period for subjects.</p>
Author response	The comments were very helpful and we believe our paper has benefited from the revisions made.