PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	SARS-CoV-2 seroprevalence among Vancouver public school staff in British Columbia, Canada: A cross-sectional study
AUTHORS	Goldfarb, David; Mâsse, Louise; Watts, Allison W.; Hutchison, Sarah M.; Muttucomaroe, Lauren; Bosman, Else S.; Barakauskas, Vilte E.; Choi, Alexandra; Dhillon, Nalin; Irvine, Mike A.; Reicherz, Frederic; O'Reilly, Collette; Sediqi, Sadaf; Xu, Rui Yang; Razzaghian, Hamid R.; Sadarangani, Manish; Coombs, Daniel; O'Brien, Sheila F; Lavoie, Pascal

VERSION 1 – REVIEW

REVIEWER	Malekzadeh, Reza Tehran University of Medical Sciences, Digestive Oncology Research Center
REVIEW RETURNED	28-Oct-2021

GENERAL COMMENTS	Interesting study.

REVIEWER	Kadkhoda, Kamran Cleveland Clinic
REVIEW RETURNED	10-Nov-2021

GENERAL COMMENTS	1. Fair study however their final message has to be carefully written as it may be misinterpreted as vaccination and NPI are not needed. 2. Authors need to know that a large proportion of peds don't develop Abs and if they do, they lose them fast. 3. They also need to use a neuralization assay or at the very least an orthogonal approach for testing instead of just one assay and merely rely on IFU claims. Common CoVs are common among peds especially in Fall and Winter months. Here's one good example to follow: https://wwwnc.cdc.gov/eid/article/27/2/20-4088_article 4. This study was entirely done pre-Delta and may not be easily applicable to what we see now. Overall these sero-surveys have very limited and at times misleading messages for public health decision-making. By the advent of vaccination for 5-11 these studies may further lose their usability.

REVIEWER	Ulyte, Agne University of Zurich, EBPI
REVIEW RETURNED	15-Nov-2021

GENERAL COMMENTS	Thank you for the opportunity to review this study. It is reporting the prevalence of SARS-CoV-2 infection in school staff based on 3 sources – official statistics, self-reported diagnosed cases, and serology. Further, it compares the estimates to those of general

	population (official statistics and blood donor serology) and children (official statistics). The study reports a remarkably low seroprevalence (2-3%) both in staff and general population in February-May 2021, when 10-25% and higher seroprevalence has been observed in similar time in other countries in Europe and North America. It is also remarkable that under-diagnosis of cases seems very small (i.e., few seropositive staff were not tested positive before). I would like to draw authors' attention to some major comments: - the seroprevalence reported is very low in comparison to European countries and US at the same period. It is not clear from the article whether this (internationally) surprising result was expected due to some circumstances of British Columbia. Please reflect in the Discussion and Abstract conclusion. - A key result is also the proportion of not-diagnosed seropositive cases among staff. Please discuss, also including relevant comparison with other countries/settings. - Introduction could be improved by motivating this study and its research question more. The authors introduce the setting and context, but only hint in half a sentence that data is lacking from 2021. Please provide the context of what questions were/are open by the time the study was conducted, by referring to relevant literature (e.g., difference between staff and population infections in setting with open schools not known) and how it aimed to answer them. - the questionnaire setting and timeline for staff and donors was not entirely clear for me as described now. Was the same questionnaire used, with identical questions? If not, what were differences – and how they impact comparison? What is the time difference between questionnaire and serological test in both groups? - Authors report a rather wide range of test accuracy parameters in the Methods, including rather different estimates for the different tests used. However, in the models, only single sensitivity and specificity value is used for adjustment. If I understand correctly, the tests used on donor and staff samples were not the same (and those used on vaccinated staff samples). Thus, using a single accuracy value in all scenarios does not seem justified. Also, specificity of 100% seems rather unlikely for any diagnostic test (indeed, authors report themselves that one PCR-positive participant was negative for S, and several negative for N – which should mean specificity was not 100%; a specificity of 100% probably just means that the validation study was too little, it is much more likely to be 99.9% at most). Perhaps this is the reason why adjusted seroprevalence CI is practically the same as unadjusted. Due to (always) imperfect test, I would expect CI to be larger when adjusted. It is possible to incorporate the uncertainty in test accuracy parameters with Bayesian approaches, e.g., as implemented in R package bootComb. Please detail how the uncertainty of test accuracy was approached, and discuss the limitation that accuracy is likely overestimated by the official commercial test providers due to spectrum bias and small validation studies, if you believe this is relevant for the tests you applied. - Please provide a short motivation for using N results for vaccinated persons, for readers not familiar with different serological responses to vaccination and infection. It would be great if you could mention how the sensitivity of N and S test changes over time too (e.g., how recent were the infections in the sample where 100% sensitivity was reported). - I found the terminology used in the article around incidence

	somewhat not consistent. Perhaps you could confirm to use cumulative incidence or period incidence as relevant, rathe than just "incidence". Also, please make clear when you are referring to diagnosed COVID-19 cases, diagnosed SARS-CoV-2 infections, and detected SARS-CoV-2 positive serology, as the interpretation would be quite different. - Please revise results to first provide some basic descriptives of the study population (e.g., N of schools or staff tested), before diving into the serological or incidence results. - Please provide more details on how you were able to confirm which self-reported cases were linked to infections in schools. Is that self-report? Based on PCR sequencing? - Thank you for detailing the weights for blood donor seroprevalence adjustment in the supplement. Perhaps you could mention just the variables used for weighting, and the reference population used, in the main text too. - The conclusion that "seroprevalence among staff was low after widespread community transmission" seems contradictory. 2.3% seroprevalence in blood donors does not seems to hint to "widespread community transmission"; after more than a year of pandemic, much higher seroprevalence would be expected. Also, staff seroprevalence is not "low" compared to donors, it is very similar. Further, please consider these minor comments: P2, lines 11 and 16: not clear why different dates are provided. Please unify or explain in the abstract what specifically is meant with these different dates. P2, line 27: "viral testing" – please specify (PCR testing for SARS-CoV-2? Also including rapid antigen testing? Self-reported?) P2, line 27: adjusted – for what? Please specify here briefly. P2, line 43: "reference data" is only for PCR detected cases, not seroprevalence, based on results in main text. Please revise the sentence to clarify this. The sentence also claims "possibility to assess selection bias", however, the article does not "assess" selection bias, only reports that it is expected to be low. Please add the actual assessment or revise this statement. P2, line 49: by "unlikely based on comparison" authors seem to imply that similar seroprevalence in donors and staff means no selection. I would not agree – such similarity could also be observed in case staff actually had different seroprevalence but selection lead to similar estimates. Please revise. P3, lines 20-22: it is not clear for me how this reported cumulative incidence is different from the one presented in Results. In case this is indeed Results, no need to mention in Introduction. In case these data are openly available already, they might not be justified to be presented as original results. Please clarify. The timeline is also unclear – why these dates chosen? Why sometimes reported as from specific day (June 1) and sometimes just month (February)? Lines 24-25: perhaps mention that/if these breaks were regular/scheduled? Line 38: "data obtained from blood donors" – the way it is formulated now, not clear if you only use questionnaire or also serology data from the donors. P4, line 3: please use 2020/2021 or 2020/21 consistently. Line 32: exposure to student cases – do you mean that reported student cases were calculated from September 8? Please revise to clarify (the incidence of what?) Line 37: not clear for me, and thus might be perhaps also for some

	other readers, what is meant by “metro Vancouver”. Metropolitan area? Metro stations? (I am sorry if this sounds like a naïve question to Canadians!) P5, line 48: “access to screener” – do you mean, this many individual IP addresses opened the website? It is not entirely clear for me what is reported here. Line 54: perhaps you could actually report the data that is “not shown”, since it is simply two proportions? (i.e., % of staff in elementary and secondary schools in the District). Line 50: sentence seems incomplete P6, line 7: incidence rate – do you mean secondary attack rate among school staff? Overall – please revise dates throughout to always use consistent format (e.g., October – May 2021 is not clear, is this October 2020?) Table 1: perhaps better to report % of participants in whose family there was at least one essential worker? Median of 0 is not telling a lot, and probably only very few will report more than 1 additional working adult in the household (?). Table 2 – please revise to explain all abbreviations (e.g., CITF) Table 3 – perhaps adding a column for total would be useful (rather than having to divide frequency by percent by the reader) Figure 1 – please add a legend to the graph. Use of two different y-axis is discouraged – I find it rather confusing. Please consider a separate graph – especially since the lines show unrelated numbers (dotted and solid line are somewhat in parallel, tracking the pandemic, while dashed line represents study design/recruitment process). SFigure 1: please add N to every cell and revise the diagram so that the cells represent participant groups rather than criteria, and that the criteria are marked on arrows (rather than “no” or “yes” – to an implicit question only). Currently, I read that “Participant was vaccinated n=35” there were 35 vaccinated participants, and it is not clear how many you considered positive, and how many switched to be tested with N. Of interest would be to read from this figure, N of S reactive participants, N vaccinated and not vaccinated among them, N of double negatives/discordant results, etc. SFigure 2: removing schools with 0 cases is somewhat misleading in my opinion. Also, it might not be necessary to show incidence in each school (please also revise: is it rather cumulative incidence? Over what period?). I would suggest to reformat into a histogram of binned incidence (including zero), with N of schools within incidence bins on Y-axis. It is not clear for me, why staff incidence available only in selected schools and almost always bigger than student incidence? Please also make clear which data source is reflected here (public or questionnaires?) SFigure 3: I find it confusing that maps do not show exactly the same area (B is zoomed in). Is there a reason? Please explain or unify. Please also specify the legends: Number of participants – staff who filled questionnaire? Provided blood for serology? Frequency – of what? Blood donors among the total population? Per capita population? It is currently not clear for me how to interpret the maps, and what should be the conclusion (that sampling is roughly from similar areas?)

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Prof. Reza Malekzadeh, Tehran University of Medical Sciences Comments to the Author:
Interesting study

→ Thank you

Reviewer: 2
Dr. Kamran Kadkhoda, Cleveland Clinic
Comments to the Author:
1. Fair study however their final message has to be carefully written as it may be misinterpreted as vaccination and NPI are not needed.

→ We agree that vaccination and other mitigation measures are crucial to safely allow for schools to remain open and mention the importance of these mitigation mention the importance of mitigation measures that were in place during the period of the study (e.g. line XX "Mitigation strategies employed in BC schools have been shown elsewhere to minimize risk in educators to a level comparable to the risk in the community…". Given that the focus on the article is not to send any negative message about vaccination, and that most jurisdictions are well through their student vaccination programs we hope that the reviewer may not be as concerned with this specific issue lately.

2. Authors need to know that a large proportion of peds don't develop Abs and if they do, they lose them fast.

→ Although it is still of debate as to whether children are less or more likely to develop antibody responses following SARS-CoV-2 infection when compared with adults, we feel this is not relevant to this manuscript as we did not conduct serology testing in children, only adults.

3. They also need to use a neuralization assay or at the very least an orthogonal approach for testing instead of just one assay and merely rely on IFU claims. Common CoVs are common among peds especially in Fall and Winter months. Here's one good example to follow: https://wwwnc.cdc.gov/eid/article/27/2/20-4088_article

→ Thank you for this feedback. We utilized well-described in vitro diagnostic electrochemiluminescence immunoassays in our study. Both assays have regulatory approval as IVDs (e.g. with Health Canada, FDA) and have been extensively evaluated with numerous industry independent peer-reviewed publications demonstrating their excellent diagnostic sensitivity and specificity, including by our own group (as referenced - https://pubmed.ncbi.nlm.nih.gov/34304088/). Neutralizing antibody assays are generally less useful for diagnostic purposes (which was the primary aim within the context of our study) but rather are used to assess function of a humoral immune response. In several studies they have in fact been shown to have very poor sensitivity (e.g. https://www.nature.com/articles/s41467-021-22958-8). Similar to the referenced EID article, we also did apply a testing algorithm with modified orthogonal approach with testing with the Roche nucleocapsid assay when there was a borderline signal/cut-off ratio detected with the primary Ortho Spike protein based assay in order to help achieve maximum sensitivity and specificity. This is described in the appendix. Regarding endemic coronaviruses in children, again we did not conduct serology testing in children so this concern should not apply.

4. This study was entirely done pre-Delta and may not be easily applicable to what we see now. Overall these sero-surveys have very limited and at times misleading messages for public health decision-making. By the advent of vaccination for 5-11 these studies may further lose their usability.

→ We agree this study was conducted pre-Delta variant and discuss this limitation of the study. Now with Omicron we also modified the corresponding paragraph in the discussion to include this one too.

Reviewer: 3
Dr. Agne Ulyte, University of Zurich
Comments to the Author:
Thank you for the opportunity to review this study. It is reporting the prevalence of SARS-CoV-2 infection in school staff based on 3 sources – official statistics, self-reported diagnosed cases, and serology. Further, it compares the estimates to those of general population (official statistics and

blood donor serology) and children (official statistics). The study reports a remarkably low seroprevalence (2-3%) both in staff and general population in February-May 2021, when 10-25% and higher seroprevalence has been observed in similar time in other countries in Europe and North America. It is also remarkable that under-diagnosis of cases seems very small (i.e., few seropositive staff were not tested positive before).
I would like to draw authors' attention to some major comments:
- the seroprevalence reported is very low in comparison to European countries and US at the same period. It is not clear from the article whether this (internationally) surprising result was expected due to some circumstances of British Columbia. Please reflect in the Discussion and Abstract conclusion.

→ Thank you for suggesting we add additional information regarding the context in British Columbia. We have expanded sections of the introduction and discussion explaining that Canada and British Columbia in particular had relatively low SARS-CoV-2 infection incidence in the global context. With this in mind, the low seroprevalence in school staff may not be too surprising. Of note, the contact tracing data we reviewed in BC, and have access to in Canada, suggest that most school COVID cases come from outside the school in, rather than "inside-out". We believe these data are consistent with other places in the world, and would suggest that school cases, and infection in the school staff reflect community transmission rates. If this is true, it could be plausible that the seroprevalence in school staff remain comparable to the community in other settings.

- A key result is also the proportion of not-diagnosed seropositive cases among staff. Please discuss, also including relevant comparison with other countries/settings.

→ In the discussion we do highlight that 60% of those who tested positive with serology, already had a prior positive PCR result that was obtained through routine clinical testing in the community. We have added reference to the ratio of seropositivity rate to cumulative incidence rates across seroprevalence studies done globally (average ratio is 18) (ref. https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0252617). "

- Introduction could be improved by motivating this study and its research question more. The authors introduce the setting and context, but only hint in half a sentence that data is lacking from 2021. Please provide the context of what questions were/are open by the time the study was conducted, by referring to relevant literature (e.g., difference between staff and population infections in setting with open schools not known) and how it aimed to answer them.

→ We have attempted to address this comment by adding further context to the introduction, but the space is extremely limited. Our main question was about finding out what was going to be the seroprevalence in teachers in the setting of schools. As the reviewer can imagine we had no idea how the pandemic was going to evolve, if schools were going to close, etc. when we designed the study. Much of this, unfortunately, was designed a posteriori and the intro as it stands now highlight the new knowledge we have been able to gain with the data and setting we have available.

- the questionnaire setting and timeline for staff and donors was not entirely clear for me as described now. Was the same questionnaire used, with identical questions? If not, what were differences – and how they impact comparison? What is the time difference between questionnaire and serological test in both groups?

→ The questionnaires were only administered to the school staff participating in the study. The Canadian Blood Services blood donors only had questions administered as part of the routine donation process. We have specified the data that was collected regarding the blood donors in the methodology section. "For blood donors, we only had access to age, sex, postal code of residence and COVID-19 vaccination status at the time of blood donation using questionnaires administered by Canadian Blood Services as part of the routine donation process". (period-matched data from blood donors were used).

- Authors report a rather wide range of test accuracy parameters in the Methods, including rather different estimates for the different tests used. However, in the models, only single sensitivity and specificity value is used for adjustment. If I understand correctly, the tests used on donor and staff samples were not the same (and those used on vaccinated staff samples). Thus, using a single accuracy value in all scenarios does not seem justified. Also, specificity of 100% seems rather

unlikely for any diagnostic test (indeed, authors report themselves that one PCR-positive participant was negative for S, and several negative for N – which should mean specificity was not 100%; a specificity of 100% probably just means that the validation study was too little, it is much more likely to be 99.9% at most). Perhaps this is the reason why adjusted seroprevalence CI is practically the same as unadjusted. Due to (always) imperfect test, I would expect CI to be larger when adjusted. It is possible to incorporate the uncertainty in test accuracy parameters with Bayesian approaches, e.g., as implemented in R package bootComb. Please detail how the uncertainty of test accuracy was approached, and discuss the limitation that accuracy is likely overestimated by the official commercial test providers due to spectrum bias and small validation studies, if you believe this is relevant for the tests you applied.

→ We used a Bayesian approach to compute 95%CI accounting for the uncertainty of the specificity and sensitivity of the serology test, and the 95%CI marginally changed from 2.30% (95% CrI: 1.62% - 3.08%) to 2.34% (95% CrI: 1.54% - 3.20%) so we believe this difference is negligeable and can be omit from the article (to simplify). We have added to the methods: "Uncertainty of the serology tests was approached incorporating the uncertainty in test parameters using a Bayesian approach with no meaningful changes to 95% confidence intervals [2.30% (95% CrI: 1.62% - 3.08%) vs. 2.34% (95% CrI: 1.54% - 3.20%)]."

In terms of the potential overestimation by the official commercial test for the blood donors, for the Roche S assay that was used for the blood donor samples there are now published studies describing sensitivity/specificity (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8393518/) so we don't need to rely on the manufacturer's claims, and the values we inferred from in the article remain valid.

- Please provide a short motivation for using N results for vaccinated persons, for readers not familiar with different serological responses to vaccination and infection. It would be great if you could mention how the sensitivity of N and S test changes over time too (e.g., how recent were the infections in the sample where 100% sensitivity was reported).

→ We have now added a statement in the methods explaining the rationale for using a nucleocapsid based serology assay for determining infection status in vaccinated participants. "Vaccines used in Canada elicit a spike (S) antibody response, whereas natural infection elicits both an S and a nucleocapsid (N) response. Thus N responses can be used to determine if a participant has had prior infection regardless of vaccination status."

Also we have added a reference (https://journals.asm.org/doi/10.1128/JCM.00487-21) for the nucleocapsid assay that we have used that shows that the sensitivity of the assay is maintained over time until at least until 1 year post infection (as was also demonstrated in our study with the participants with PCR test confirmed infections).

- I found the terminology used in the article around incidence somewhat not consistent. Perhaps you could confirm to use cumulative incidence or period incidence as relevant, rathe than just "incidence". Also, please make clear when you are referring to diagnosed COVID-19 cases, diagnosed SARS-CoV-2 infections, and detected SARS-CoV-2 positive serology, as the interpretation would be quite different.

→ We have sought to clarify this in the revised version

- Please revise results to first provide some basic descriptives of the study population (e.g., N of schools or staff tested), before diving into the serological or incidence results.

→ We have made major changes to the result section to write it in a more question-driven way, describing the populations first, then the results. The N of schools is also presented in the Setting section of the methods. Of note, we also now include new data showing that the serology sampling was equally distributed among high / low COVID incident schools and the sampled group was representative of the entire District population. Finally, we added at the end of the Result section Bayesian analyses showing that the seroprevalence estimates in the school staff would not change even if we post-stratify for the small differences between school staff sample and entire District.

- Please provide more details on how you were able to confirm which self-reported cases were linked to infections in schools. Is that self-report? Based on PCR sequencing?

→ This was solely based on report by the participant. Participants were asked: if they ever got tested for COVID-19 by nasal swab, saliva or equivalent, how many times, what were the result of each test and what dates each test was done. They were very few missing data. All cases who tested positive by viral OR serology testing were contacted individually by our research staff to confirm the viral testing result.

- Thank you for detailing the weights for blood donor seroprevalence adjustment in the supplement. Perhaps you could mention just the variables used for weighting, and the reference population used, in the main text too.

→ We have now added the details regarding the weighting strategy in the Methods section

- The conclusion that "seroprevalence among staff was low after widespread community transmission" seems contradictory. 2.3% seroprevalence in blood donors does not seems to hint to "widespread community transmission"; after more than a year of pandemic, much higher seroprevalence would be expected. Also, staff seroprevalence is not "low" compared to donors, it is very similar.

→ We have now removed the term "widespread" in the Title and used the term "comparable" in reference to the seroprevalence in school staff versus blood donors in the Abstract.

Further, please consider these minor comments:
P2, lines 11 and 16: not clear why different dates are provided. Please unify or explain in the abstract what specifically is meant with these different dates.

→ The dates provided in this section of the abstract refer to the dates that serum samples were collected for the seroprevalence determination in school staff. This has been adjusted for clarification.

Could change to: "… with an embedded cross-sectional serosurvey among school staff with serum sampled from February 10 to May 15, 2021, comparing to period, age, sex and geographic location-weighted data from blood donors…"

→ Change made in the abstract

P2, line 27: "viral testing" – please specify (PCR testing for SARS-CoV-2? Also including rapid antigen testing? Self-reported?) P2, line 27: adjusted – for what? Please specify here briefly.

→ We have now specified that this was PCR testing for SARS-CoV-2 that was self-reported. The "adjusted seroprevalence" refers to the adjustment that was done for sensitivity/specificity as is further described in the method section.

P2, line 43: "reference data" is only for PCR detected cases, not seroprevalence, based on results in main text. Please revise the sentence to clarify this. The sentence also claims "possibility to assess selection bias", however, the article does not "assess" selection bias, only reports that it is expected to be low. Please add the actual assessment or revise this statement.

→ The reference data includes COVID-19 cases reported to public health during the entire pandemic. We did assess for a key potential selection bias – a possible under or over selection of participants with a known prior history of SARS-CoV-2 infection (see https://link.springer.com/article/10.1007/s10654-021-00727-7). In particular we were able to assess for this possible volunteer bias by determining the overall cumulative incidence (based on PCR testing) in the entire school staff population and we found that this was very similar to the PCR based cumulative incidence in the sample of participants who participated in the study. This is explained in the limitation section of the discussion. **We also added a new (large) section in the methods detailing measures that were taken to limit recruitment bias.**

P2, line 49: by “unlikely based on comparison” authors seem to imply that similar seroprevalence in donors and staff means no selection. I would not agree – such similarity could also be observed in case staff actually had different seroprevalence but selection lead to similar estimates. Please revise.

→ This statement was referring to the selection bias of school staff amongst the entire school staff population. As outlined above we were able to determine the PCR confirmed infection rate for the entire population and therefore we do feel this risk for volunteer bias was reduced. We have now clarified this statement. **We now include new data showing that the study sample was representative of the entire District population.**

Statement has been changed to: “Non-random participant selection amongst the school staff population implies a potential volunteer bias. However, the similar incidence of COVID-19 cases based on self-report (1.4%) compared to the entire District (1.3%) suggests that we did not under-sample those who are in direct contact with students.”

P3, lines 20-22: it is not clear for me how this reported cumulative incidence is different from the one presented in Results. In case this is indeed Results, no need to mention in Introduction. In case these data are openly available already, they might not be justified to be presented as original results. Please clarify. The timeline is also unclear – why these dates chosen? Why sometimes reported as from specific day (June 1) and sometimes just month (February)?

→ These figures are publicly available from the BC Centre for Disease Control and are now appropriately referenced with specific dates applied.

Lines 24-25: perhaps mention that/if these breaks were regular/scheduled?

→ Now mentioned as regularly scheduled.

Line 38: “data obtained from blood donors” – the way it is formulated now, not clear if you only use questionnaire or also serology data from the donors.

→ As mentioned above, the data from the blood donors are captured as part of routine data collection at blood donation and this has been clarified in the text.

P4, line 3: please use 2020/2021 or 2020/21 consistently.

→ We have reviewed this carefully

Line 32: exposure to student cases – do you mean that reported student cases were calculated from September 8? Please revise to clarify (the incidence of what?)

→ As specified in the “Study setting” section of the Methods, schools were open to students in the in the winter and also late spring of 2020 and therefore we did include this period in the determination of potential school exposures. Therefore student cases were included from January 15, 2020 (start of pandemic in BC) to March 4th (so long as they were attending school).

Line 37: not clear for me, and thus might be perhaps also for some other readers, what is meant by “metro Vancouver”. Metropolitan area? Metro stations? (I am sorry if this sounds like a naïve question to Canadians!)

→ We have now sought to clarify this and actually changed this to Vancouver as all the collections did happen in Vancouver.

P5, line 48: “access to screener” – do you mean, this many individual IP addresses opened the website? It is not entirely clear for me what is reported here.

→ Have now clarified this to “… 2162 accessed the initial study screening website…”

Line 54: perhaps you could actually report the data that is “not shown”, since it is simply two proportions? (i.e., % of staff in elementary and secondary schools in the District).

→ This data is now reported in the sentence

Line 50: sentence seems incomplete

→ We have now revised the sentence: “The characteristics of 1689 staff who completed the questionnaire are shown in Table 1. This corresponds to 23.9% of all eligible staff.”

P6, line 7: incidence rate – do you mean secondary attack rate among school staff?

→ Incidence rate is the incorrect term but rather this reflects the cumulative incidence of PCR-confirmed infections amongst the participating school staff. This has now been corrected. “…only 24 self-reported having had COVID-19 cased on nucleic acid amplification tests, for a cumulative incidence of 1.4% of school staff…”

Overall – please revise dates throughout to always use consistent format (e.g., October – May 2021 is not clear, is this October 2020?)

→ Done

Table 1: perhaps better to report % of participants in whose family there was at least one essential worker? Median of 0 is not telling a lot, and probably only very few will report more than 1 additional working adult in the household (?).

→ Done

Table 2 – please revise to explain all abbreviations (e.g., CITF)

→ Done, we have expanded to COVID-19 Immunity Task Force

Table 3 – perhaps adding a column for total would be useful (rather than having to divide frequency by percent by the reader)

→ Done

Figure 1 – please add a legend to the graph. Use of two different y-axis is discouraged – I find it rather confusing. Please consider a separate graph – especially since the lines show unrelated numbers (dotted and solid line are somewhat in parallel, tracking the pandemic, while dashed line represents study design/recruitment process).

→ We felt it was helpful to have the various relevant elements of the pandemic (total cases, school open dates, school related cases) on the same graph in order to provided a clearer visual representation of the dynamics of the pandemic in the city. We have now though sought to further clarify this figure by adding legends explain the two y axis as well as a colour reference.

Figure 1: please add N to every cell and revise the diagram so that the cells represent participant groups rather than criteria, and that the criteria are marked on arrows (rather than “no” or “yes” – to an implicit question only). Currently, I read that “Participant was vaccinated n=35” there were 35 vaccinated participants, and it is not clear how many you considered positive, and how many switched to be tested with N. Of interest would be to read from this figure, N of S reactive participants, N vaccinated and not vaccinated among them, N of double negatives/discordant results, etc.

→ This figure has been updated for clarity as suggested

Figure 2: removing schools with 0 cases is somewhat misleading in my opinion. Also, it might not be necessary to show incidence in each school (please also revise: is it rather cumulative incidence? Over what period?). I would suggest to reformat into a histogram of binned incidence (including zero), with N of schools within incidence bins on Y-axis. It is not clear for me, why staff incidence available

only in selected schools and almost always bigger than student incidence? Please also make clear which data source is reflected here (public or questionnaires?)

→ We have changed this supplemental Figure 2 to illustrate the seroprevalence sampling across high versus low incidence schools, including now schools with zero cases.

Figure 3: I find it confusing that maps do not show exactly the same area (B is zoomed in). Is there a reason? Please explain or unify. Please also specify the legends: Number of participants – staff who filled questionnaire? Provided blood for serology? Frequency – of what? Blood donors among the total population? Per capita population? It is currently not clear for me how to interpret the maps, and what should be the conclusion (that sampling is roughly from similar areas?)

→ these maps reflect only numbers (frequency) of school staff and blood donors who had serological testing done and reflect the geographical representation of these two groups. We have clarified this in the title and also we have made sure that two maps have the same scale/coverage (see attached)

VERSION 2 – REVIEW

REVIEWER	Ulyte, Agne University of Zurich, EBPI
REVIEW RETURNED	01-Feb-2022

GENERAL COMMENTS	Thank you for your careful and detailed revision of the mauscript. All comments have been addressed.