PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Acceptability of OP/Na swabbing for SARS-CoV-2: A prospective observational cohort surveillance study in Western Australian schools
AUTHORS	Thomas, Hannah; Mullane, Marianne; Ang, Sherlynn; Barrow, Tina; Leahy, Adele; Whelan, Alexandra; Lombardi, Karen; Cooper, Matthew; Stevenson, Paul; Lester, Leanne; Padley, Andrea; Sprigg, Lynn; Speers, David; Merritt, A; Coffin, Juli; Cross, Donna; Gething, Peter; Bowen, Asha

VERSION 1 – REVIEW

REVIEWER	Papenburg, Jesse McGill University, Pediatrics
REVIEW RETURNED	03-Aug-2021

GENERAL COMMENTS	This is a mixed-methods study that describes the acceptability of a minimally-invasive (nasal/oropharyngeal swab) COVID-19 screening protocol in 40 schools in Western Australia. 13,988 swabs were collected from students and staff between June and Sept 2020. The major findings were that there were zero infections identified and that participants reported high acceptability (71% of students reported no or minimal discomfort and most were willing to be re-swabbed [4% refusal rate]). The study is of modest novelty, and does not address the possible problem of reduced sensitivity of this alternate collection method, but does contribute to the literature by reporting on the acceptability of an approach to large-scale asymptomatic swabbing for SARS-CoV-2 in the school setting. MAJOR COMMENTS - This is a very labour and resource intensive intervention that had zero yield. This should be discussed. Although the protocol had high acceptability, is it worth doing in a low-transmission setting? What was the incidence of SARS-CoV-2 in WA during the study period? What were the costs of the screening program? How much class time did children miss because of it? How much work time did staff use for it? - Finding asymptomatic cases is most useful when it prevents froward transmission by preventing further contacts. What was the turnaround time for test results (mean/median)? MINOR COMMENTS: - Title: I don't think that the results demonstrate "efficiency" - Abstract: "no false positives". How can the authors state that? No other method was used to confirm the proposed protocol's positives.

	- Limitations: “possibility for bias will be addressed at the data analysis stage”. No such analysis was presented. - p. 6, line 47: the Xpert Xpress is not produced by bioMérieux. - Additional information on how potential participants were approached and on the informed consent process should be presented. - What was the Ct value of the in-house PCR positive / Cepheid Xpret negative sample?

REVIEWER	Braz-Silva, Paulo Henrique Universidade de Sao Paulo Faculdade de Odontologia, Division of General Pathology, Department of Stomatology
REVIEW RETURNED	05-Sep-2021

GENERAL COMMENTS	Dear authors, Thank you for the possibility to review this interesting and well conducted study. I have some suggestions in order to improve your manuscript. - Title: in my point of view, you have to state in your title the kind of swab collected (OP/Na). When we state only "swab" in COVID-19 context, its autommatic the association with nasopharyngeal swabs. (page 2/24) - I do not agree that sample size is a limitation of your study. (page 4/24) - Include the median age of the participants on table 1. (page 9/24) - It was not possible to see the figure 2. (page 10/24) - The discussion section is quite superficial. I suggest you to include 2 points: 1. Stress the importance of COVID-19 molecular surveillance for school safety, specially in countries which the pandemic is out of control. 2. Discuss the possibility of self colletion in these programs (saliva and OP/Na swabs). For this, I recommend you to include and discuss this reference: Braz-Silva PH, Mamana AC, Romano CM, Felix AC, de Paula AV, Fereira NE, Buss LF, Tozetto-Mendoza TR, Caixeta RAV, Leal FE, Grespan RMZ, Bizário JCS, Ferraz ABC, Sapkota D, Giannecchini S, To KK, Doglio A, Mendes-Correa MC. Performance of at-home self-collected saliva and nasal-oropharyngeal swabs in the surveillance of COVID-19. J Oral Microbiol. 2020 Dec 9;13(1):1858002. doi: 10.1080/20002297.2020.1858002 (page 11/24)

VERSION 1 – AUTHOR RESPONSE

Reviewer 1	
Comment	Response
This is a very labour and resource intensive intervention that had zero yield. This should be discussed. Although the protocol had high acceptability, is it worth doing in a low-transmission setting? What was the incidence of SARS-CoV-2 in WA during the study period? What were the costs of the screening program? How much class time did children miss because of it? How much work time did staff use for it?	These are reasonable questions to ask in a general sense, although we note they do not bear directly on the results presented in the paper. This project was initiated during the early stages of the COVID-19 pandemic, at a time when community transmission was growing in Australia and the future trajectory of the pandemic in WA was unknown and unknowable. In addition, the rate and role of asymptomatic infections in children was a major source of uncertainty with potentially significant consequences for public health and education policy. Mercifully, the initial wave in WA was contained and transmission dwindled across the subsequent months as this project rolled out. This context is now more explicitly explained in the final paragraph of the manuscript discussion however, none of that context has direct relevance to this submission - we do not present results or inference based on our measurements of infection prevalence. Rather, the focus is on the specific issue of swabbing methodology, performance, and acceptability. At a time when questions about transmission between children and in school settings are rising in prominence, we maintain that these results contribute information of widespread relevance and utility to those around the world planning and implementing child-focused SARS-CoV-2 epidemiological studies. When we embarked on this study, we had to choose the best way to swab children as quickly as possible and with minimal fuss in a school based setting. We chose the method discussed and demonstrated it to be well received. During the period of swabbing there were no community cases of COVID-19 in Western Australia, and this remained the case until 31 January 2021, with only

	occasional cases detected in hotel quarantine throughout this almost 10 month period.
Finding asymptomatic cases is most useful when it prevents froward transmission by preventing further contacts. What was the turnaround time for test results (mean/median)?	We aimed for test results to be available within 72 hours of swabbing no matter where they were collected in the large state of WA, recognising that for regional schools the turnaround time had a significant pre-analytical component due to sample transport. Despite the State's prioritisation of PCR for overseas arrivals at the time, this goal was achieved and the mean turnaround time for DETECT samples was 60 hours. When the study was designed, we also liaised carefully with the Western Australian public health units to plan an optimal approach for the transmission aspects of the study (see published protocol), but this did not eventuate as no COVID-19 cases were recorded.
Title: I don't think that the results demonstrate "efficiency"	We take on board this comment and have amended the title. Title now reads: Acceptability of OP/Na swabbing for SARS-CoV-2: A prospective observational cohort surveillance study in Western Australian schools
Abstract: "no false positives". How can the authors state that? No other method was used to confirm the proposed protocol's positives.	We describe the use of a second independent PCR platform for confirmatory testing (Cepheid). Across the two PCR platforms (in-house and Cepheid Xpert Xpress), there were no confirmed positive cases and as such no false positives reported. All negative controls were also negative.
Limitations: "possibility for bias will be addressed at the data analysis stage". No such analysis was presented.	This statement describes the intention in the protocol to deal with data bias had there been detection of positive cases and subsequent epidemiological analysis. As there were no positive cases detected this was not required. The text has been removed from the manuscript.
p. 6, line 47: the Xpert Xpress is not produced by bioMérieux.	Thank you for pointing out this oversight. Amended - text now reads:

	Any swab returning an in-house PCR positive result (CT value < 45) was subject to confirmatory testing with the Xpert Xpress SARS-CoV-2 assay (Cepheid, California, USA).
Additional information on how potential participants were approached and on the informed consent process should be presented.	This information is provided in the published protocol, referenced in this manuscript (reference 25, page 5). Some additional information has been added to the methods section of the current manuscript – text now reads: Prior to study commencement, written and video study and consent information was distributed by the schools to staff and parents, including study information and consent forms developed in consultation with a consumer advisory group and the Telethon Kids Institute Kulunga Aboriginal Research Development Unit. Staff and parents provided active informed consent through an online portal supported by the REDCap platform.
What was the Ct value of the in-house PCR positive / Cepheid Xpert negative sample?	The in-house PCR CT value was 37.69 (compared to assay positive control CT values 30-33). This is a weak PCR signal consistent with either false reactivity or genuine weak activity, depending on the prevalence. As there was no community transmission at the time and given the negative result on the confirmative Xpert platform this was very much in favour of false reactivity.
<u>Reviewer 2</u>	
Comment	Response
Title: in my point of view, you have to state in your title the kind of swab collected (OP/Na). When we state only "swab" in COVID-19 context, its automatic the association with nasopharyngeal swabs. (page 2/24)	We take on board this comment and have amended the title. Title now reads: Acceptability of OP/Na swabbing for SARS-CoV-2: A prospective observational cohort surveillance study in Western Australian schools
I do not agree that sample size is a limitation of your study. (page 4/24)	Thank you, the word ‘limit’ has been removed. Text now reads:

	The sample size of this study is dictated by pragmatic, budgetary and logistical considerations.
Include the median age of the participants on table 1. (page 9/24)	The median age of participants was 12 years for students and 48 years for teachers. This is now included in Table 1.
It was not possible to see the figure 2. (page 10/24)	Apologies for the inconvenience, a new version of the TIF file has been uploaded.
The discussion section is quite superficial. I suggest you to include 2 points: 1. Stress the importance of COVID-19 molecular surveillance for school safety, especially in countries which the pandemic is out of control. 2. Discuss the possibility of self colletion in these programs (saliva and OP/Na swabs). For this, I recommend you to include and discuss this reference: Braz-Silva PH, Mamana AC, Romano CM, Felix AC, de Paula AV, Fereira NE, Buss LF, Tozetto-Mendoza TR, Caixeta RAV, Leal FE, Grespan RMZ, Bizário JCS, Ferraz ABC, Sapkota D, Giannecchini S, To KK, Doglio A, Mendes-Correa MC. Performance of at-home self-collected saliva and nasal-oropharyngeal swabs in the surveillance of COVID-19. J Oral Microbiol. 2020 Dec 9;13(1):1858002. doi: 10.1080/20002297.2020.1858002 (page 11/24)	Thank you for your suggestions. The discussion has been updated to reflect these two points: 1. For school-aged children, closing schools to combat the spread of COVID-19 must be balanced against the very real challenges in mental health and inequality likely associated with missing out on the educational and social benefits of school attendance (32,33). Consequently, countries around the world have mobilised to implement mass testing in an effort to support the reopening of schools and other establishments. COVID-19 molecular surveillance will be important moving forwards to ensure the safety of schools and individuals, especially in high prevalence countries in which cases continue to climb. 2. In a large, representative cohort of school students and staff, our findings indicate that the vast majority of participants experienced minimal or no discomfort during an OP/Na swab. Almost all of those who were asked to participate a second time agreed, illustrating the high tolerance for repeat procedures which is desirable for optimised respiratory screening programs. This also suggests that individuals may be open to completing self-collected sampling, which has been shown to deliver adequate sensitivity for SARS-CoV-2 detection (37).
<u>Editor</u>	
Comment	Response
Please note that declarative titles are not part of the journal format. As such, please revise the title of your manuscript to include the research question, study design and setting. This is the preferred format of the journal. See published articles for examples.	Title now reads: Acceptability of OP/Na swabbing for SARS-CoV-2: A prospective observational cohort

	surveillance study in Western Australian schools
Please ensure that your abstract is formatted according to our Instructions for Authors: http://bmjopen.bmj.com/pages/authors/#research	Abstract has been updated to the required format. Text now reads: Objectives: When the COVID-19 pandemic was declared, Governments responded with lockdown and isolation measures to combat viral spread, including the closure of many schools. More than a year later, widespread screening for SARS-CoV-2 is critical to allow schools and other institutions to remain open. Here we describe the acceptability of a minimally-invasive COVID-19 screening protocol trialled by the Western Australian (WA) Government to mitigate the risks of and boost public confidence in schools remaining open. To minimise discomfort, and optimise recruitment and tolerability in unaccompanied children, a combined throat and nasal (OP/Na) swab was chosen over the nasopharyngeal swab commonly used, despite slightly reduced test performance. Design, setting and participants: Trialling of OP/Na swabbing took place as part of a prospective observational cohort surveillance study in 79 schools across Western Australia. Swabs were collected from 5,903 asymptomatic students and 1,036 asymptomatic staff in 40 schools monthly between June and September 2020. Outcome measures: PCR testing was performed with a two-step diagnostic and independent confirmatory PCR for any diagnostic PCR positives. Concurrent surveys, collected online through the REDCap platform, evaluated participant experiences of in-school swabbing. Results: 13,988 swabs were collected from students and staff. There were zero positive test results for SARS-CoV-2, including no false positives. Participants reported high acceptability: 71% of students reported no or minimal discomfort and most were willing to be re-swabbed (4% refusal rate). Conclusions: OP/Na swabbing is acceptable and repeatable in schoolchildren as young as 4 years old and may combat noncompliance rates by significantly increasing the

	acceptability of testing. This kind of minimally-invasive testing will be key to the success of ongoing, voluntary mass screening as society adjusts to a new 'normal' in the face of COVID-19. Trial registration: Australian New Zealand Clinical Trials Registry - ACTRN12620000922976
Please ensure that you have fully discussed the methodological limitations of the study in the discussion section of the main text	The following text has been added to the discussion section of the manuscript: This study was part of Western Australia's jurisdictional response to the COVID-19 pandemic in April 2020. At the time of design, the state had been in a complete lockdown for five weeks, and schools were closed. The study was designed and implemented to reassure families and the public that schools could re-open, and to inform the level of risk of transmission in a school setting. However, during this period of time, transmission of SARS-CoV-2 was so well controlled with public health measures that there were no detected community cases of COVID-19 for almost 10 months and as such there were also no confirmed cases in the study. Whilst this could be considered a methodological limitation, we have demonstrated the acceptability and ease of implementing a molecular based swabbing program in a school context with minimal disruption to students or educational outcomes.