RESEARCH ARTICLE



REVISED Point of care SARS-CoV-2 nucleic acid testing in schools

improves school attendance [version 2; peer review: 2

approved]

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Abstract

Background: National lockdowns have led to significant interruption to children's education globally. In the Autumn term in 2020, school absence in England and Wales was almost five times higher than the same period in 2019. Transmission of SARS-CoV-2 in schools and ongoing interruption to education remains a concern. However, evaluation of rapid point of care (POC) polymerase chain reaction (PCR) testing in British schools has not been undertaken. **Methods:** This is a survey of secondary schools in England that implemented PCR-based rapid POC testing. The study aims to measure the prevalence of SARS-CoV-2 infection in schools, to assess the impact of this testing on school attendance and closures, and to describe schools experiences with testing. All schools utilised the SAMBA II SARS-CoV-2 testing platform.

Results: 12 fee-paying secondary schools in England were included. Between September 1st 2020 and December 16th 2020, 697 on site rapid POC PCR tests were performed and 6.7% of these were positive for SARS-CoV-2 infection. There were five outbreaks in three schools during this time which were contained. Seven groups of close contacts within the school known as bubbles had to quarantine but there were no school closures. 84% of those tested were absent from school for less than one day whilst awaiting their test result. This potentially saved between 1047 and 1570 days off school in those testing negative compared to the NHS PCR laboratory test. Schools reported a positive impact of having a rapid testing platform as it allowed them to function as fully as possible during this pandemic. **Conclusions:** Rapid POC PCR testing platforms should be widely

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Any reports and responses or comments on the article can be found at the end of the article.

available and utilised in school settings. Reliable positive tests will prevent outbreaks and uncontrolled spread of infection within school settings. Reliable negative test results will reassure students, parents and staff and prevent disruption to education.

Keywords

SARS-CoV-2, school, testing, rapid, point of care

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Author roles: Collier DA: Conceptualization, Data Curation, Formal Analysis, Funding Acquisition, Methodology, Project Administration, Writing – Original Draft Preparation, Writing – Review & Editing; **Bousfield R**: Conceptualization, Writing – Original Draft Preparation, Writing – Review & Editing; **Gkrania-Klotsas E**: Conceptualization, Methodology, Writing – Original Draft Preparation, Writing – Review & Editing; **Gupta RK**: Conceptualization, Funding Acquisition, Methodology, Supervision, Writing – Original Draft Preparation, Writing – Review & Editing

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REVISED Amendments from Version 1

More details about the testing performance of the diagnostic platform have been included, as well as details of the samples tested. The discussion has been expanded to include the relevance of this study in the context of the changing landscape of the pandemic and its applicability in future pandemics. Minor grammatical changes have been made for clarity. One reference has been corrected and another updated to a more recent study.

Any further responses from the reviewers can be found at the end of the article

Summary

Testing could reduce SARS-CoV-2 transmission in schools and mitigate against school closures and COVID-19 related absences. We evaluated the impact of rapid point of care PCR testing for SARS-COV-2 in schools and found it identified cases promptly and reduced school absence in non-cases.

Introduction

The COVID-19 pandemic has had an indelible impact on the education of children in the United Kingdom¹. National lockdowns have led to significant interruption to children's education². Over the Autumn term in the 2020–2021 academic year, the average weekly absence from state-funded primary and secondary schools in England was 13% and this peaked at 28% in the last week of the Autumn term in December 2020 (school attendance during SARS-CoV-2 outbreak). This compared with an overall absence rate of 4.9% in Autumn 2019 before the COVID-19 pandemic³. Attendance at state-funded secondary schools in 151 local authorities in England fell from 88% in the week of the 10th of September 2020 to 68% by the week of the 11th of December 2020 (English secondary school attendance). Further interruptions must be avoided.

The availability of rapid point of care (POC) diagnostic testing has been shown to facilitate timely diagnoses in hospitals^{4–6}. However, less impressive results have been reported in community settings using antigen tests with lower sensitivity^{7,8}. Rapid, sensitive and specific SARS-CoV-2 POC testing could help to avoid school absence and school closures.

Methods

We conducted a survey of SARS-CoV-2 infection in secondary schools in England that had implemented PCR-based rapid POC testing for use in diagnosis and isolation of pupils and staff with SARS-CoV-2 infection on their school premises. All participating schools were fee-paying schools and boarding or mixed boarding/day schools. All schools utilised the SAMBA II SARS-CoV-2 testing platform. The tests were performed on combined nose and throat swab samples by a school nurse who had received training from the manufacturer. The limit of detection (LOD) of the SAMBA II SARS-CoV-2 test is 250 copies/ml (https://doi.org/10.1128/JCM.01262-20).

Schools were identified by convenience sampling either through the Independent Schools' Bursars Association, who cascaded the invite to join the study to the headteachers of their member schools or through our working knowledge of schools that had purchased their own testing platform. The headteacher of the schools were sent an electronic letter inviting their school to participate. The letter included the participant information and consent forms. Informed consent was obtained from the headteacher in an electronic format. Following this, the school was enrolled in the study. A survey was sent out to the school electronically which was completed by the school nurse and returned weekly. Fully anonymised risk factor data were gathered along with the number and results of SARS-CoV-2 tests carried out in each school (see Extended data 1)9. Data collected includes test performed from the 1st of September 2020 and will be collected up till the end of the academic year in August 2021. This initial report is based on data collected in the first term of the academic year up until the 16th of December 2020. The alpha variant was emerging as the dominant variant during this period and eventually replaced the preceding D614G wildtype variant (PHE Investigation of novel SARS-CoV-2 variant 202012/01: technical briefing 1¹⁰).

Data on new daily cases of COVID-19 stratified by age from South East, South West and East of England were downloaded from the Public Health England website. Data on state-funded school attendance during the COVID-19 was obtained from routinely published Department for Education data on attendance in education and early years settings during the COVID-19 outbreak (school attendance in England).

The main outcome is the proportional prevalence of SARS-CoV-2 infection at specific time points in the 2020/2021 academic year amongst those tested. Secondary outcomes include the impact of rapid POC SARS-CoV-2 testing on school attendance, school closure and closure of groups of close contacts within the school known as bubbles, which may be a year group, class, house or dorm. Qualitative accounts of participating school's experiences were collected as an open-ended survey question. These are presented as vignettes, in order to describe more fully the impact of SARS-CoV-2 rapid POC PCR testing in schools. Given that the choice of who to test followed the discretion of each school and may have differed at each school, details of implementing these tests and why students or staff were tested were collected.

Descriptive analyses of demographic and clinical data are presented as median and interquartile range (IQR) when continuous and as frequency and proportion (%) when categorical. The differences in continuous and categorical data were tested using the Mann-Whitney test and Chi-square test, respectively. Logistic regression was used to explore the association between a positive rapid POC result and *a priori* determined risk factors for SARS-CoV-2 infection, including age, sex, ethnicity and contact with a SARS-CoV-2 positive person. The final regression model included adjustment for age and sex and any other variable that had a p value of <0.05 in the univariable logistic regression analyses. Odd ratios are reported with 95% confidence intervals. Statistical analysis was done using STATA v.13.

We initially planned to recruit 30 schools across the United Kingdom with the anticipation that the number of schools acquiring a testing platform will increase over the academic year. However, when schools reopened in March 2021, twice weekly lateral flow testing with an antigen test became the government recommendation. Therefore, all schools enrolled up to the end of the autumn term were included in this study.

Ethics approval was granted by University of Cambridge Human Biology Research Ethics Committee- HRREC.202.0.39.

Results

Over the course of the Autumn term, 13 schools were recruited to the study and 12 of these returned data. Six schools were in South East, three in East and three in South West England. Schools were either exclusively boarding or mixed day and boarding. 697 SARS-CoV-2 rapid tests were performed between the 1st of September 2020 and the 16th of December 2020 (end of the Autumn term). The median age of those tested was 16 years (IQR 14-24), 44% (309/696) were male (Table 1). 30% (208/692) of those tested were staff, 60% (416/692) were students and 10% (68/692) were household members of staff. 64% of tests were done in symptomatic infection, the majority of whom had symptoms of either fever or cough and occasionally anosmia. Other common reasons for testing included contact testing (11.9%), asymptomatic screening (14.8%) and fitness to fly (6.2%). Less common reasons (2.7%) included visiting vulnerable relatives, testing prior to hospital admission and testing for reassurance. 97% (668/692) of tests were valid, 6.7% (45/668) of which were positive for SARS-CoV-2.

In September 2020, there was a relatively low prevalence of SARS-CoV-2 cases in the regions from which these schools were sampled and this increased over the course of the Autumn-Winter 2020 (Figure 1). In comparison, the overall number of cases of SARS-COV-2 diagnosed in the sampled schools remained relatively low (Figure 1) and did not increase as the second wave of the pandemic in the UK progressed. This was thought to be due to limited mixing between boarders and the local population.

Of note, a positive test for SARS-CoV-2 infection was associated with being symptomatic or being a contact of a COVID-19 case (Table 2). Seven asymptomatic cases were identified who were contacts of known SARS-CoV-2 positive cases. In the univariable logistic regression analyses, factors associated with a SARS-CoV-2 positive test result included having symptoms of anosmia [OR 7.3 (95% CI 2.9-18.5)], attending a school in the South East region [OR 4.2 (95% CI 1.8-9.7)] or South West region [OR 3.2 (95% CI 1.2-8.3)]. However, in the multivariable model adjusted for sex, age and all variables with a p value <0.05 in the univariable analyses, **Table 1. Clinical and demographic details of the study population.** *n/N is presented when data are missing, IQR interquartile range.

	Percentage, N=697 (*n/N)		
Median age in years (IQR)	16 (14-24) (608/697)		
Male	44.4 (309/696)		
Designation Student Staff Household member	60.1 (416/692) 30.1 (208/692) 9.8 (68/692)		
SARS-CoV-2 result Positive Negative Invalid	6.5 (45/692) 90.0 (623/692) 3.5 (24/692)		
Reason for test Symptoms Contact of COVID-19 positive person Screening Travel abroad Other	64.4 (427/663) 11.9 (79/663) 14.8 (98/663) 6.2 (41/663) 2.7 (18/663)		
Symptoms Cough Fever Anosmia Other	47.6 (201/422) 40.8 (172/422) 8.8 (37/422) 2.8 (12/422)		

only anosmia maintained a significant association with a positive SARS-CoV-2 test result [OR 5.5 (95% CI 2.1-14.7, p 0.001)].

Impact on school attendance

All infections occurred in eight out of the 12 schools. Two schools each had a single case and were able to limit transmission by identification and isolation of the infected individual. There were five outbreaks in three schools, defined as more than two cases diagnosed within two consecutive days. These outbreaks involved 16, five and four individuals in the affected schools. There were seven bubble closures and no school closures. The ability to exclude SARS-CoV-2 infection in symptomatic individuals was important in reducing school absence. The majority of individuals tested (84%) were absent from school for less than one day prior to receiving a rapid test result (Figure 2). This compared favourably with the NHS PCR test typically done in a drive-through testing centre or a test delivered my post. It usually takes between one to three days to return a test result (NHS coronavirus testing). Potentially, this cumulatively saves between 1,047 and 1,570 days off school (84% of all those testing negative). Participants reported that the use of an onsite rapid PCR tests helped the schools to

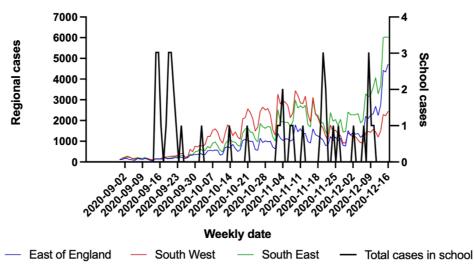


Figure 1. Weekly total regional COVID-19 cases numbers from East (blue), South West (red), South East (green) England on the left axis. Total weekly number of cases in schools sampled (black) on the right axis. Data on case numbers from East, South West and South East England regions were obtained from Public Health England website: https://coronavirus.data.gov.uk/details/download.

Table 2. Clinical and demographic factors associated with SARS-CoV-2 infection status. OR odds ratio, CI confidence interval. *n/N is presented when data are missing; - indicates where categories without any events were excluded from the analyses; ^a adjusted for age and sex, region and symptoms.

	Number	Risk of SARS-CoV-2 positivity	Unadjusted OR (95% CI)	P value	Adjusted OR ^a (95% CI)	P value
Age in years <16 ≥16	278 305	9.4 (26/278) 6.2 (19/305)	1 0.6 (0.3-1.2)	0.16		
Sex Female Male	377 290	6.4 (24/377) 7.2 (21/290)	1 1.1 (0.6-2.1)	0.66		
Designation Student Staff Household member	402 198 65	8.0 (32/402) 5.1 (10/198) 3.1 (2/65)	1 0.6 (0.3-1.3) 0.4 (0.1-1.6)	0.19 0.18		
Region East of England South East South West	264 265 139	2.7 (7/264) 10.2 (27/265) 7.9 (11/139)	1 4.2 (1.8-9.7) 3.2 (1.2-8.3)	0.001 0.02	1 2.6 (1.0-6.9) 3.1 (1.0-9.3)	0.06 0.05
Reason for test Symptoms Contact of COVID-19 case Screening Travel abroad Other	410 78 94 39 16	8.8 (36/410) 9.0 (7/78) 0 (0/94) 0 (0/39) 0 (0/16)	1 1.0 (0.4-2.4) - -	0.96		
Symptoms Cough Fever Anosmia Other	193 166 36 0	5.7 (11/193) 9.0 (15/166) 30.1 (11/36) 0 (0/12)	1 1.6 (0.7-3.7) 7.3 (2.9-18.5) -	0.23 <0.001	1 1.6 (0.7-3.7) 5.5 (2.1-14.7)	0.25 0.001

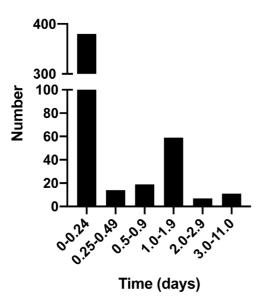


Figure 2. Days of absence from school whilst awaiting rapid point of care SARS-CoV-2 test result.

function as fully as possible during the pandemic (Extended data $2)^{11}$.

Discussion

The proportional prevalence of SARS-CoV-2 in our study population is high at 6% as the majority of those tested had symptoms or were COVID-19 contacts. Despite this, there were no school closures and absence from school was minimal. A nationwide surveillance study of COVID-19 infection in students and staff in English schools (COVID-19 Schools Infection Survey) reported a prevalence of SARS-CoV-2 infection in secondary school students and staff of 1.48% and 1.47%, respectively, in the first half of the Autumn term from the 3rd to the 19th of November 202012. The nationwide surveillance study included asymptomatic staff and students, which likely explains the difference in positivity rates between this survey population and the nationwide surveillance study. However, the incidence rates have been steadily increasing with the resultant increase in school absence and closure over the course of the Autumn term. 9-11% of children did not attend school for COVID-19 related reasons and up to 2% of state-funded schools were closed in the last week of the Autumn term (school attendance during SARS-CoV-2 outbreak). We estimate that having a rapid POC PCR-based test in these school saved between 1,047 and 1,570 days off school compared to the National Health Service / Public Health England PCR test and made a significant difference in the running of these schools.

New guidelines from the UK government to introduce mass testing in schools is welcome, if not overdue¹³. However, concerns have been raised about the ability of these lateral flow tests to accurately diagnose SARS-CoV-2 infection¹⁴. Although the specificity of these test are high, sensitivity may be as low

as 48% in asymptomatic⁸ and 58% in symptomatic individuals⁷ when self-administered. There is a trade-off between more expensive, highly accurate tests such as PCR tests and cheaper, less accurate, tests such as those based on lateral flow technology.

A limitation of the study is that the population may not be representative of most schools in England in terms of being able to afford these tests, having staff capacity to implement a testing program, and the characteristics of the students attending these schools. Although a direct comparison has not been made between a POC testing platform sited on the school premises and one off-site, it is likely that the logistics required to facilitate an off-site test will add further delays to turn-around times. The success of this strategy may not be solely due to the testing platform. These populations are largely closed with limited mixing with the wider population as indicated by the low number of positive cases in these schools compared with the background prevalence in the geographical regions where these schools were based.

Rapid diagnostic tests have a role to play in emerging infectious diseases as has been demonstrated in this study in schools, it can be rolled-out to assist in managing contacts, allowing prompt isolation of new cases and preventing absenteeism. We recommend that accurate, rapid POC PCR testing platforms should be widely available and utilised in school settings. We acknowledge that a barrier to implementing rapid POC PCR testing widely across all schools is cost. However, the cost to schools could be limited by government investment in these tests to support schools. We call for new research to develop cheaper but still accurate POC PCR tests. Furthermore, implementation could be managed by reserving more expensive POC PCR tests in higher risk settings like colleges and secondary schools whilst allowing for the use of cheaper but less accurate tests in younger ages where the risk of spreading infection is lower. Reliable positive tests will prevent outbreaks and uncontrolled spread of infection within school settings. Reliable negative test results will reassure students, parents and staff and prevent disruption of schooling.

Data availability

Underlying data

UCL Research Data Repository: Data underpinning Point of care SARS-CoV-2 nucleic acid testing in schools improves school attendance. https://doi.org/10.5522/04/16764511¹⁵.

Extended data

UCL Research Data Repository: Extended data 1 for Point of care SARS-CoV-2 nucleic acid testing in schools improves school attendance. https://doi.org/10.5522/04/16764535⁹.

UCL Research Data Repository: Extended data 2 for Point of care SARS-CoV-2 nucleic acid testing in schools improves school attendance. https://doi.org/10.5522/04/16766581¹¹.

Data are available under the terms of the Creative Commons Zero "No rights reserved" data waiver (CC0 1.0 Public domain dedication).

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Open Peer Review

Current Peer Review Status: 💙

Version 2

Reviewer Report 03 October 2022

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Sarah Logan 匝

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I have reviewed the revised manuscript and tried to comment that I am happy with the edits.

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Clinician in ID and parent of 3 children, the lived experience of school absences/ closures on the whole family and medical workforce cannot be underestimated!

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 30 September 2022

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I approve this submission for indexing.

Competing Interests: I am an editor for the Diagnostics section of the Infectious Diseases Society of America's COVID-19 Real-time Learning Network

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Version 1

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Reviewer Report 19 April 2022

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Summary:

Collier et al performed a retrospective survey-based analysis of school-based SARS-CoV-2 testing program using a point of care PCR assay, the SAMBA II. The authors analyzed data collected from September through December 2020 when SARS-CoV-2 prevalence was 6.7% in their schools. The majority of people were symptomatic and 84% of those tested with symptoms missed less than one day of school prior to being ruled out by the rapid PCR test. Compared to the testing program for the larger community, the authors estimate that the point of care PCR testing program saved between 1,047 and 1,570 days off from school.

Major comments:

- 1. The SARS-CoV-2 Omicron variant is much more transmissible than the viral lineages that were in circulation at the time of this study in the winter of 2020. Despite a much more established testing infrastructure, the Omicron variant spread widely, suggesting that diagnostic test performance regardless of assay type significantly declined. There are many possible reasons for this but it suggests that the efficacy of any testing program based on data from prior waves is at risk for being over-estimated if that program was implemented in the current environment.
- 2. Generalizable conclusions are a bit challenging to draw from this study. Additional information that would be helpful for the community include:
 - 1. Key aspects of the testing programs, such as criteria for testing, frequency of testing and body sampling site by school (if available). Each school's definition of 'bubble' can also help readers understand how many people would be in quarantine with each positive case.

- 2. Test characteristics of the SAMBA II including gene targets, limit of detection, turnaround time and literature supporting test performance.
- 3. Surveillance data documenting the predominating variants in circulation at the time of the study (see #1 above).
- 3. Similarly, would consider broadening the discussion to more critically examine the generalizability of results. Might an alternative explanation for the success of the testing program be due to the lack of mixing in the community, and not the characteristics of their point of care PCR testing strategy? Given that up to 90% of new infections occur from an asymptomatic index case, the fact that most (perhaps all?) cases detected in this program were symptomatic suggests a highly insular environment, which again may not be the case in most other settings.
- 4. Regarding the following statement: "However, concerns have been raised about the ability of these lateral flow tests to accurately diagnose SARS-CoV-2 infection" Would consider citing the more recent study by Deeks in BMJ (Deeks *et al.* (2021¹)).

Minor comments:

- 1. References 6 and 9 appear to be duplicated.
- 2. A turnaround time of 1 to 3 days is assumed for PCR testing through Public Health England. While this makes sense for 2020, is that still the case in 2022?
- 3. Schools were selected through a convenience sample. Is there any data to support or refute the fact that these schools are representative of schools throughout the UK and beyond?
- 4. With regards to the following statement: "Data collected includes test performed from the 1st of September 2020 and will be collected up till the end of the academic year in August 2021. This initial report is based on data collected in the first term of the academic year up until the 16th of December 2020.", it has been nearly 8 months since the end of August 2021, therefore a reader would reasonably expect that that data should be included in this report. Is there a reason it has not yet been included? If it cannot be added, would suggest modifying this statement to just state the study ended in December 2020.
- 5. In the results, it states that 697 tests were performed, however the denominators for gender, staff vs student, and household members are 696, 692, and 692, respectively. What is the reason for the discrepancy?
- 6. This statement could use further clarity: "No asymptomatic cases were identified amongst individuals tested for reasons such as asymptomatic screening, fitness to fly or other reasons."
 - 1. The way it is currently written implies there are positive tests from asymptomatic cases tested for other indications. However, my understanding based on the manuscript is that this program did not pick up any asymptomatic cases.

References

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Is the work clearly and accurately presented and does it cite the current literature? Partly

Is the study design appropriate and is the work technically sound? Yes

Are sufficient details of methods and analysis provided to allow replication by others? $\ensuremath{\mathsf{Yes}}$

If applicable, is the statistical analysis and its interpretation appropriate? $\ensuremath{\mathsf{Yes}}$

Are all the source data underlying the results available to ensure full reproducibility? $\ensuremath{\mathsf{Yes}}$

Are the conclusions drawn adequately supported by the results?

Partly

Competing Interests: I am an editor for the Diagnostics section of the Infectious Diseases Society of America's COVID-19 Real-time Learning Network

Reviewer Expertise: Clinical microbiology, infectious diseases, epidemiology, machine learning, clinical decision support

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 05 Aug 2022

Dami Collier, university college london, UK

Reviewer: Collier et al performed a retrospective survey-based analysis of school-based SARS-CoV-2 testing program using a point of care PCR assay, the SAMBA II. The authors analyzed data collected from September through December 2020 when SARS-CoV-2 prevalence was 6.7% in their schools. The majority of people were symptomatic and 84% of those tested with symptoms missed less than one day of school prior to being ruled out by the rapid PCR test. Compared to the testing program for the larger community, the authors estimate that the point of care PCR testing program saved between 1,047 and 1,570 days off from school.

Major comments:

The SARS-CoV-2 Omicron variant is much more transmissible than the viral lineages that were in circulation at the time of this study in the winter of 2020. Despite a much more established testing infrastructure, the Omicron variant spread widely, suggesting that diagnostic test

performance regardless of assay type significantly declined. There are many possible reasons for this but it suggests that the efficacy of any testing program based on data from prior waves is at risk for being over-estimated if that program was implemented in the current environment.

Author Response: As rightly pointed out by the reviewer there are many possible reasons why the Omicron variant spread widely. However, we do not agree that a reduction in diagnostic accuracy has been a major contributor to this. The S-gene target failure (SGTF) as a result of a deletion at nt207-212 (Δ 69-70) in the Spike gene was recognised relatively early in our setting. Most assays use targets other than the S-gene and although a weak or absent signal would be seen in the S-gene, a positive signal will be seen in other regions such as ORF1 and N-gene in targeted RT-PCRs.

Reviewer: Generalizable conclusions are a bit challenging to draw from this study. Additional information that would be helpful for the community include:

Key aspects of the testing programs, such as criteria for testing, frequency of testing and body sampling site by school (if available). Each school's definition of 'bubble' can also help readers understand how many people would be in quarantine with each positive case.

Author Response: This has now been included in the methods and references.

"All schools utilised the SAMBA II SARS-CoV-2 testing platform, which amplifies two regions of the genome ORF1ab and nucleocapsid protein. The tests were performed on combined nose and throat swab samples by a school nurse who had received training from the manufacturer. The two regions of the genome (open reading frame 1ab [ORF1ab] and nucleocapsid protein [N]) limit of detection (LOD) of the SAMBA II SARS-CoV-2 test is 250 copies/ml (https://doi.org/10.1128/JCM.01262-20)."

Reviewer: Test characteristics of the SAMBA II including gene targets, limit of detection, turnaround time and literature supporting test performance.

Author Response: This has now been included on the methods and references. See above.

Reviewer: Surveillance data documenting the predominating variants in circulation at the time of the study (see #1 above).

Author Response: This has now been included in the text.

"The alpha variant was emerging as the dominant variant during this period and eventually replaced the preceding D614G wildtype variant (PHE Investigation of novel SARS-CoV-2 variant 202012/01: technical briefing 1 https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/959438

Reviewer: Similarly, would consider broadening the discussion to more critically examine the generalizability of results. Might an alternative explanation for the success of the testing program be due to the lack of mixing in the community, and not the characteristics of their point of care PCR testing strategy? Given that up to 90% of new infections occur from an asymptomatic index

case, the fact that most (perhaps all?) cases detected in this program were symptomatic suggests a highly insular environment, which again may not be the case in most other settings.

Author Response: We agree and have broadened the discussion to include this.

"A limitation of the study is that the sample may not be representative of most schools in England in terms of being able to afford these tests, having staff capacity to implement a testing program, and the characteristics of the students attending these schools. Although a direct comparison has not been made between a POC testing platform sited on the school premises and one off-site, it is likely that the logistics required to facilitate an off-site test will add further delays to turn-around times. The success of this strategy may not be solely due to the testing strategy. These populations are largely closed with limited mixing with the wider population as indicated by the low number of positives in these schools compared with the background prevalence in the geographical regions where these schools were based."

Reviewer: Regarding the following statement: "However, concerns have been raised about the ability of these lateral flow tests to accurately diagnose SARS-CoV-2 infection" Would consider citing the more recent study by Deeks in BMJ (Deeks et al. (20211)).

Author Response: This reference has been cited as suggested.

"Deeks J J, Singanayagam A, Houston H, Sitch A J, Hakki S, Dunning J *et al.* SARS-CoV-2 antigen lateral flow tests for detecting infectious people: linked data analysis BMJ 2022; 376 :e066871 doi:10.1136/bmj-2021-066871"

Reviewer: *References 6 and 9 appear to be duplicated.*

Author Response: Our apologies. This has been corrected.

Reference 6 is:

Collier DA, Assennato SM, Warne B, Sithole N, Sharrocks K, Ritchie A, *et al.* Point of Care Nucleic Acid Testing for SARS-CoV-2 in Hospitalized Patients: A Clinical Validation Trial and Implementation Study. Cell Rep Med. 2020;1(5):100062.

Reference 9 is:

Mlcochova P, Collier D, Ritchie A, Assennato SM, Hosmillo M, Goel N, *et al.* Combined Pointof-Care Nucleic Acid and Antibody Testing for SARS-CoV-2 following Emergence of D614G Spike Variant. Cell Rep Med. 2020;1(6):100099.

Reviewer: A turnaround time of 1 to 3 days is assumed for PCR testing through Public Health England. While this makes sense for 2020, is that still the case in 2022?

Author Response: The turnaround time for PCR testing has varied depending on the stage of the pandemic with longer turnaround times during periods of higher incidence which the

resulting pressures of laboratories. The turnaround time quoted (supported by the reference) was the turnaround time at the time the study was conducted.

Reviewer: Schools were selected through a convenience sample. Is there any data to support or refute the fact that these schools are representative of schools throughout the UK and beyond?

Author Response: We stated in both the methods and references, these schools are feepaying schools and so not representative of schools throughout the UK.

"A limitation of the study is that the sample may not be representative of most schools in England in terms of being able to afford these tests, having staff capacity to implement a testing program, and the characteristics of the students attending these schools."

Reviewer: With regards to the following statement: "Data collected includes test performed from the 1st of September 2020 and will be collected up till the end of the academic year in August 2021. This initial report is based on data collected in the first term of the academic year up until the 16th of December 2020.", it has been nearly 8 months since the end of August 2021, therefore a reader would reasonably expect that that data should be included in this report. Is there a reason it has not yet been included? If it cannot be added, would suggest modifying this statement to just state the study ended in December 2020.

Author response: We stated in the methods the study was stopped after the initial phase. "We initially planned to recruit 30 schools across the United Kingdom with the anticipation that the number of schools acquiring a testing platform will increase over the academic year. However, when schools reopened in March 2021, twice weekly lateral flow testing with an antigen test became the government recommendation. Therefore, all schools enrolled up to the end of the autumn term were included in this study."

Reviewer: In the results, it states that 697 tests were performed, however the denominators for gender, staff vs student, and household members are 696, 692, and 692, respectively. What is the reason for the discrepancy?

Author response: 697 tests were done, however when data are missing, we present the denominator as non-missing data. Please refer to table 1. *n/N is presented when data are missing.

Reviewer: This statement could use further clarity: "No asymptomatic cases were identified amongst individuals tested for reasons such as asymptomatic screening, fitness to fly or other reasons."

The way it is currently written implies there are positive tests from asymptomatic cases tested for other indications. However, my understanding based on the manuscript is that this program did not pick up any asymptomatic cases.

Author response: This sentence has been clarified and now reads.

"Seven asymptomatic cases were identified who were contacts of known SARS-CoV-2 positive

cases"

Competing Interests: No competing interests were disclosed.

Reviewer Report 23 February 2022

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Sarah Logan 匝

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For understandable reasons there is quite a delay in getting this to publication and the landscape has changed. Nonetheless the number of school days saved by deployment of a rapid POC PCR based test is sizeable and the impact of a sensitive diagnostic test can have on enabling school attendance is a key point to learn for future.

More can be made in the discussion about the generalizability of this sort of approach in pandemics. Rapid roll out of diagnostics and evaluation of their impact over and above their PPV and NPV was a missing part of the approach to this pandemic. Therefore I do think that there is value in publication at this stage if the emphasis of the manuscript can be more on what can we learn and do better for next time.

Is the work clearly and accurately presented and does it cite the current literature? Partly

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others? $\ensuremath{\mathsf{Yes}}$

If applicable, is the statistical analysis and its interpretation appropriate?

I cannot comment. A qualified statistician is required.

Are all the source data underlying the results available to ensure full reproducibility? $\ensuremath{\mathsf{Yes}}$

Are the conclusions drawn adequately supported by the results?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Clinician in ID and parent of 3 children, the lived experience of school absences/ closures on the whole family and medical workforce cannot be underestimated!

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 05 Aug 2022

Dami Collier, university college london, UK

Reviewer: For understandable reasons there is quite a delay in getting this to publication and the landscape has changed. Nonetheless the number of school days saved by deployment of a rapid POC PCR based test is sizeable and the impact of a sensitive diagnostic test can have on enabling school attendance is a key point to learn for future.

Author Response: Many thanks to the reviewer for this comment. This is the main thrust of this article.

Reviewer: More can be made in the discussion about the generalizability of this sort of approach in pandemics.

Author Response: This has now been addressed in the discussion.

Reviewer: "Rapid diagnostic tests have a role to play in emerging infectious diseases and as has been demonstrated in this study in schools, it can be rolled-out to assist in managing contacts, allowing prompt isolation of new cases and preventing absenteeism."

Rapid roll out of diagnostics and evaluation of their impact over and above their PPV and NPV was a missing part of the approach to this pandemic. Therefore I do think that there is value in publication at this stage if the emphasis of the manuscript can be more on what can we learn and do better for next time.

Author Response: We wholeheartedly agree with this comment and indeed the landscape has changed since this study was conducted. We do believe that what this study shows is a workable option for managing COVID transmission in a closed setting. Its wider adoption may be limited by cost but early in an emerging epidemic when there isn't widespread community transmission, highly accurate, rapid tests such as these certainly have a role. In light of the changed landscape of the pandemic we have removed the recommendation that rapid POC PCR testing platforms should be widely available and utilised in school settings from the discussion.

"There is a trade-off between more expensive, highly accurate tests such as PCR tests and cheaper, less accurate, tests such as those based on lateral flow technology." And highlight, where they could potentially have worked, had these technologies been adopted in the Autumn of 2020.

"We call for new research to develop cheaper but still accurate POC PCR tests. Furthermore, implementation could be managed with more expensive POC PCR tests in higher risk settings and like colleges and secondary schools whilst allowing for the use of cheaper but less accurate tests in younger ages where the risk of spreading infection is lower."

Competing Interests: No competing interests were disclosed.