Evaluation of real-life use of Point-Of-Care Rapid Antigen TEsting for SARS-CoV-2 in schools (EPOCRATES)

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Abbreviations: ABM (agent-based model), Ct (cycle threshold), COVID-19 (Coronavirus disease 2019), D (day), ESCL (École Secondaire Calixa-Lavallée), LOD (limit of detection), PCR (polymerase chain reaction), PSNM (Pensionnat du Saint-Nom-de-Marie), RADT (rapid antigen detection test), SARS-CoV-2 (Severe acute respiratory syndrome coronavirus 2), TAT (turnaround time)

Table of Contents Summary: Rapid antigen tests were compared to standard PCR to diagnose SARS-CoV-2 infections in high-school students. They performed better in symptomatic individuals.

What's Known on This Subject

Rapid antigen detection tests (RADT) are often used to diagnose respiratory pathogens at the point-of-care. Their performance characteristics vary, but they usually have high specificity and moderate sensitivity compared with PCR.

What This Study Adds

RADT sensitivity ranged from 28.6% in asymptomatic individuals to 83.3% in symptomatic individuals. Return to school after 7 days of quarantine was safe in exposed students. Secondary cases were identified in 28% of classes with an index case.

Authors contribution statement:

Caroline Quach conceptualized and designed the study, acquired funding, carried out the data analysis and drafted the initial manuscript.

Marc Desforges, Annie-Claude Labbé, Cat Tuong Nguyen, Kate Zinszer, Jean Longtin, Ioannis Ragoussis and David L. Buckeridge conceptualized and designed the study.

Kelsey Adams, Marie-Ève Benoit collected data and managed and coordinated the research project on site.

Yves Petit, Dominic Besner, Zineb Laghdir, Geneviève Leduc managed and coordinated the research project on site.

Ana C. Blanchard carried out the data analysis and drafted the initial manuscript.

Olivier Séguin carried out the data analysis.

All authors critically reviewed, revised the manuscript and approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Abstract (246 words)

Background: We evaluated the use of rapid antigen detection tests (RADT) for the diagnosis of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in school settings to determine RADT's performance compared to PCR.

Methods: In this real-world, prospective observational cohort study, high-school students and staff were recruited from two high-schools in Montreal (Canada) and followed from January 25th to June 10th, 2021. Twenty-five percent of asymptomatic participants were tested weekly by RADT (nasal) and PCR (gargle). Class contacts of cases were tested. Symptomatic participants were tested by RADT (nasal) and PCR (nasal and gargle). The number of cases and outbreaks were compared to other high schools in the same area.

Results: Overall, 2,099 students and 286 school staff members consented to participate. The overall RADT's specificity varied from 99.8 to 100%, with a lower sensitivity, varying from 28.6% in asymptomatic to 83.3% in symptomatic participants. Secondary cases were identified in 10 of 35 classes. Returning students to school after a 7-day quarantine, with a negative PCR on D6-7 after exposure, did not lead to subsequent outbreaks. Of cases for whom the source was known, 37 of 57 (72.5%) were secondary to household transmission, 13 (25%) to intra-school transmission and one to community contacts between students in the same school.

Conclusion: RADT did not perform well as a screening tool in asymptomatic individuals. Reinforcing policies for symptom screening when entering schools and testing symptomatic individuals with RADT on the spot may avoid subsequent significant exposures in class.

Background

Timely diagnosis of infection enables outbreak control through rapid isolation of index cases and subsequent contact tracing [1, 2]. Diagnosis of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection is predominantly based on polymerase chain reaction (PCR) testing, which has a turnaround time (TAT) of 24-48 hours. Rapid antigen detection tests (RADT) were used for years to diagnose other respiratory pathogens, such as influenza and respiratory syncytial virus. RADT are inexpensive and can be used at the point-of-care. They usually have high specificity and moderate sensitivity compared with PCR[3-6]. Given their rapid TAT, RADT allow for efficient triage, management and cohorting of exposed individuals[7]. The potential use of RADT is especially relevant in school settings, where COVID-19 outbreaks can interrupt in-person teaching, contribute to social isolation and negatively impact learning [8-11].

RADT perform best in the early stages of infection, when viral load is generally high[12-15] and may help in situations where a person was exposed to a confirmed case of COVID-19. Reported RADT sensitivity ranges from 28.9% to 98.3%, with improved RADT sensitivity in samples with high viral loads and in symptomatic individuals, with a specificity of 99.5%[16, 17]. PCRs' usual limits of detection (LOD) is 600-1000 viral RNA copies/ml, whereas RADTs usually have LOD 2-3 logs higher (10^5 to 10^6)[18]. Many studies have indicated the importance of high viral load dynamics with infectiousness and transmissibility[19, 20]. There is a strong correlation between cycle threshold (Ct) values and the ability to recover infectious virus and thus transmissibility: for each unit increase in Ct value, the odds of recovering infectious virus decreased by 0.67 being under 10% when Ct-values were > 35. Ct values of 17 to 32 corresponded to 10^5 and 10^1 SARS-CoV-2 RNA copies/µL, respectively[21].

Children being the last group to be fully immunised, we aimed: 1) to determine the performance characteristics of RADT for SARS-CoV-2 compared to PCR in different groups of high-school students and staff and 2) to determine if serial testing of close COVID-19 contacts would allow for a safe and faster return to school.

Methods

Participating population

The study was conducted in two high schools (Montreal, Canada), of ~3000 students. Pensionnat du Saint-Nom-de-Marie (PSNM) is a private school in an affluent neighbourhood, with 80% of students from native-born families. École secondaire Calixa-Lavallée (ESCL) is a public school where students are predominantly from multiethnic, first-generation immigrant communities. Both schools followed the Ministry of Education recommendations during the COVID-19 pandemic, by forming "classroom bubbles" and providing in-person teaching, except for classes in secondary 3 to 5 (grades 9-11) that stayed home every other day. Masks were mandatory at all times, as of October 8th, 2020. Students, were ~30 per class and were seated one metre (three feet) from each other. They remained in the same classroom and teachers moved from one class to the next. School staff, including teachers and administrative personnel, were invited to participate. A first dose of COVID-19 vaccine was offered to staff members as of April 9th, 2021, and to students $\geq$ 12 years as of May 25th, 2021.

Study design and interventions

This was a real-world, prospective observational cohort study comparing RADT to PCR. Subjects were high-school students and staff from two schools followed from January 25th to June 10th, 2021.

The RADT used was a lateral flow immunoassay [PanBio™ COVID-19 Ag test (Abbott Laboratories, Illinois, USA)], authorised by Health Canada[22]. Nasal swabs were self-collected under the supervision of a research assistant who performed RADT on site. For symptomatic participants, the remaining buffer fluid after RADT was done was sent for PCR. In addition, spring water gargle specimens were collected for PCR testing[23]. Laboratory-developed PCR was performed in the CHU Sainte-Justine virology laboratory (Montreal, Canada), with a LOD of 400 copies/mL (based on Corman et al.[24]). Extraction and purification of genetic material (nasal and gargle specimens) was done with Roche's MagNA Pure 96 system. The laboratory testing protocol and the water gargle validation have been described elsewhere[25-28].

Decisions about management of cases and contacts were made by two members of the research team (AB, CQ), in collaboration with local public health (CT, OS), based on RADT and PCR results and history of exposures. The school principals (YP, DB) were actively involved in the study design and organisation throughout the study period.

1) Testing protocol in the absence of a known exposure:

    a. Asymptomatic students and staff: Nasal swabs and gargle specimens on a random sample of 25% of participants were collected weekly for RADT (nasal) and PCR (gargle), stratified by class.

b. Symptomatic students and staff: Gargle specimens for PCR and a nasal swab for RADT and PCR were performed on site. Results from RADT and PCR were officially reported to public health; an individual was considered infected if the PCR result was positive. If symptoms occurred while in school, the research team proceeded with sample procurement. If symptoms developed while at home, the participant could either get tested through the usual process of care or through a walkthrough process at school (by appointment, in a specific room away from public areas).

2) Management of exposed contacts of a positive individual in a class

Students and staff who were considered contacts of a confirmed COVID-19 positive individual were isolated at home. Students were allocated to either a 7- or 14-day quarantine, staffs were allocated to a 7-day quarantine, with tests (nasal RADT and gargle PCR) three days after last contact with the known positive case, and up to two days before the end of quarantine. RADT was performed in school on day (D)14, D21 and D28, if the initial PCR was negative. If symptoms developed, both the RADT and PCR were performed, as previously described. Students who did not consent to the study were quarantined for 14 days, even if their group was allocated to a 7-day quarantine. Students and staff concerned with significant off-campus exposure were provided to be tested through the project.

Outcomes

The primary outcome was to assess the performance characteristics of RADT in: a) asymptomatic participants randomly screened (compared to gargle PCR); b) asymptomatic close contacts of a

confirmed positive case (compared to PCR on nasal swab and gargle); c) symptomatic participants (compared to PCR on nasal swab and gargle).

Secondary outcomes included: a) number of positive students by RADT in groups exposed to a confirmed positive index case, allocated to early (on D8) versus standard (on D15) return to school (7 vs. 14 days of quarantine) and b) number of case clusters in schools. These clusters were compared to clusters in other high schools in Montreal during the same time frame, using public health data.

Statistical analysis

Descriptive statistics were used for characteristics of the cohort and test performance (sensitivity and specificity) of the RADT.

To determine the precision with which we would be able to estimate our primary outcome, we implemented an agent-based model (ABM) to estimate it through simulations, adapting a previously described school-based ABM[29] (Supplementary Appendix A). Based on this simulation, we expected that the number of infections and tests would be sufficient in one school but added an additional school to support generalizability of the findings, as well as to allow exploration of secondary objectives.

Ethical considerations

This project was approved by the CHU Ste-Justine Research Ethics Board (#MP-21-2021-3271). Written invitation letters to participate in the study were sent by schools' direction to parents and

staff explaining the study objectives, methods and expected impacts. Online informed parental consent, as well as assent, was required for all students. Parents who preferred to keep their children home for 14 days in case of a class contact could do so. Tests results were communicated to parents and students (aged $\geq$ 14 years) by the school (via email), as they became available.

This study was funded by the Québec Ministry of Health and Social Services.

Results

During the study period, 2,099 students and 286 school staff members consented to participate. Overall, the participation rate for students was 78.5% and 63.5% (Figure 1) and 94.4% and 89.5% for staff members.

RADT results and PCR validation (from gargle specimens only)

1) Asymptomatic students and staff

Of 5,583 RADT done on asymptomatic students (Table 1), seven had an invalid PCR result on the gargle sample, seven were equivocal and three were weak positive, of which one was negative when repeated the next day (and was excluded). Two students with equivocal or weak positive PCR results had a positive PCR result in the previous 90 days. The infection prevalence in asymptomatic participants was 0.30% (95% CI 0.18- 0.49). Therefore, the sensitivity of RADT in that population was 41.2% (95% CI 21.6-64.0), with a specificity of 100.0%.

Of 784 asymptomatic RADT screening tests done on asymptomatic randomly screened staff members, two gave invalid PCR results and six were lost. Only one RADT was positive, but the

PCR was negative on both the gargle and nasal specimens, giving a specificity of 99.8% (95% CI 99.3-100.0) (Table 1).

2) Asymptomatic exposed contacts in a classroom

A total of 1491 RADT tests and PCR were done on asymptomatic students exposed to a positive classmate index case at D3 and 2 days before returning to class. After excluding one equivocal PCR result, SARS-CoV-2 prevalence in this exposed group was 0.7% (95% CI 0.5-1.6). The sensitivity of RADT was 28.6% (95% CI 8.4-58.1) with a specificity of 99.6% (95% CI 99.1-99.9) (Table 1). Of 627 RADTs done for asymptomatic exposed contacts on D14, D21 and D28, only one was positive (also positive by PCR when tested on D12 – see outbreak section). A total of 61 RADT and PCRs were done for staff members on D3 and D7 after a contact with a positive index case in school (Table 1). All tests were negative.

3) Symptomatic students and staff

Overall, 235 students developed symptoms and were tested on site for SARS-CoV-2. As shown in Table 1, 10 had a positive RADT and 12 had a positive PCR [prevalence=5.1% (95% CI 2.7-8.7)]. The sensitivity of RADT in that population was 83.3% (95% CI 51.6-97.9) with a specificity of 100.0% (95% CI 98.4-100.0). Sixty-four staff members were tested on site for symptoms compatible with COVID-19. Only one had a positive RADT and PCR. In addition, one positive case was identified by PCR after a negative RADT (sensitivity of 50% (95% CI 1,3- =98,7) and specificity of 100%.

Outbreaks and comparison with other schools in the region

Of all participants, 76 PCR (gargle or nasal) positive cases were identified, including three cases in staff members. Of the 35 classes included in the study, 20 returned on D8 after contact, if the gargle PCR was negative on D6 or D7.

Secondary cases were identified in 10 classes. The number of secondary cases in each class were one (n=8 classes), three (n=1 class) and four (n=1 class). Overall, four secondary cases had a positive RADT, including three asymptomatic students and one symptomatic student who tested positive by RADT and PCR on D12, with symptoms starting on D9 after last contact with the positive classmate – a community exposure was also suspected. No tertiary case occurred. Outbreaks were limited to the classroom bubble and to school friends seen outside of school. When the source was known, 37/57 cases (72.5%) were secondary to household transmission, 13 (25%) to intra-school transmission and one to community contacts between students in the same school.

During the same period, outbreaks declared in other Montreal schools had a lower proportion of asymptomatic cases (31.8%) compared to ESCL (55.6%) and PSNM (85.7%) (Supplementary Appendix B).

Discussion

RADTs were purchased in many countries as an additional tool to prevent outbreaks. However, their use is limited by the paucity of evidence regarding their performance in school-aged children and their impact on allowing in-person schooling. In this study, we prospectively compared the performance of a COVID-19 RADT to PCR for the purpose of limiting transmission of SARS-

CoV-2 infection in a real-world setting in two high schools. In a context of low SARS-CoV-2 prevalence in school and higher prevalence in the community (5-7% test positivity in Montreal[30]), we observed only seven false positive RADT during the 5-month study (all in asymptomatic individuals) and the specificity of the RADT remained excellent in all circumstances (99.8 and 100%). However, the sensitivity was much lower, varying between 28.6% in asymptomatic to 83.3% in symptomatic students.

A recent large observational study described the use of RADT in asymptomatic individuals as beneficial, reporting a sensitivity of 64.4% (95% CI 58.3-70.2)[31]. However, as not all asymptomatic individuals included had a confirmatory PCR, this could be overestimated. In our study, only a few positive cases were detected by RADT (7/6358, 0.11% - students and staff combined) in asymptomatic individuals who were randomly tested. Ten additional cases were detected by PCR from gargle specimens. During the study, two full-time research assistants were in each school, in addition to local school staff who were supporting the study rollout. This level of required resources makes it difficult to justify the use of RADT for random screening of asymptomatic individuals given its low sensitivity in that setting.

On the other hand, RADT detected SARS-CoV-2 positive symptomatic cases in 15 minutes, allowing for prompt isolation, contact tracing, and testing – in collaboration with local public health. In this study, the overall sensitivity of RADT in symptomatic individuals (students and staff, combined) was 78.6% (95% CI 49.2-95.3). This finding is in agreement with other published studies[14, 15, 32-34]. Sood et al. recently described that the positive concordance of RADT was higher among symptomatic children (64.4%) compared to asymptomatic children (51.1%) presenting at

a walk-in testing site[33]. Similarly, L'Huillier et al. described a sensitivity of 73.0% in symptomatic vs. 43.3% in asymptomatic children[34]. The authors described the peak of RADT sensitivity as high as 100% on D2 post symptoms onset, with a subsequent decrease to 56% by D5. In our study, 225 of 235 symptomatic children had recorded their date of symptoms onset, with a median time of one day (range: 0-33 days). Overall, 46.7% (n=105/225) were tested with RADT and PCR on the day of symptoms onset. Our reported RADT sensitivity may have been higher had students been tested on subsequent days. However, the usefulness of RADT is precisely to control outbreaks and therefore delaying testing to enhance sensitivity would be counterproductive. This trade-off may not apply to the delta variant, for which the kinetic of infection may differ[35, 36].

RADT identified 28.6% of positive asymptomatic exposed school contacts, which was similar to that recently described by Torres et al. for non-household significant contacts (sensitivity: 35.7%)[37]. Although this percentage is relatively low, the rapid diagnosis of SARS-CoV-2 infection in exposed individuals allowed local public health to quickly manage these students' household contacts who, at the time, had to isolate until the result of the D3 testing. With changes in quarantine recommendations for vaccinated family members, the benefit of RADT in this specific population may be smaller. Of note, most positive cases in students, for which the source was known were due to intrafamilial and household SARS-CoV-2 transmission. In many of these instances, students were sent to school despite having a known positive contact. Active screening of symptoms and history of significant contact with known positive cases should be reinforced to prevent school outbreaks. Thirteen of 51 cases were acquired from school, with 15 cases belonging to the same class bubble (in five classes overall). Therefore, the asymptomatic nature of this

infection makes screening for school contacts essential. Our results demonstrate that using a more sensitive method, such as PCR, may be more reliable for that purpose.

This study had several limitations. First, we did not collect socio-demographic and behavioral data, including risk perception, adherence to public health measures, nor did we systematically document individual contacts with positive cases occurring outside of school. However, for the most part, we were able to identify when significant household transmission occurred and relied on the transparency of participants and local public health. We cannot infer whether PCR positive individuals were contagious. The study was performed before the advent of the delta variant in our region. Because RADT detects the N protein, we expect that its sensitivity and specificity would not be affected negatively, as viral loads of delta variant infections are reported to be higher[35]. Finally, the sensitivity of RADT in symptomatic individuals was based on a relatively small number (12 students and 2 staff members) of people with PCR-confirmed SARS-CoV-2 infections.

This is the largest study to date assessing the use of RADT in school settings. The strengths of this study included its prospective design, as well as the real-world use of RADT in comparison to PCR. We assigned participants to earlier versus standard return to school with serial RADT testing, showing that there were no secondary outbreaks when allowing students to return to school after a shorter quarantine. Although the current study was not powered to rule this out, this aligns with other recently published data[38] and may allow policymakers to consider reducing the duration of quarantine for exposed contacts, provided a PCR is negative on D6 or D7 following contact.

In conclusion, our findings contribute to the growing evidence that the use of RADT leads to rapid diagnosis of SARS-CoV-2 infection in symptomatic individuals in schools[39]. However, RADT does not perform well as a screening tool in asymptomatic individuals. In our study, teenagers were able to adequately proceed to self-collection of swabs, while supervised by a research assistant. It may be helpful to reinforce policies for symptom screening when entering schools, where symptomatic individuals, including students or staff could be tested with RADT on the spot. This would avoid subsequent significant exposures in class but would also allow students to attend school if symptoms were due to other viruses. A negative RADT could still mean that symptoms are due to SARS-CoV-2, but with a viral load too low to be detected and therefore less likely to transmit at that point. In such instance, a subsequent sample tested by PCR would be useful.

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Table 1. Performance of RADT in the different participant groups

RESULTS					CLINICAL PERFORMANCE OF RADT		
RADT (nasal)	PCR (gargle)				Sensitivity		Specificity
	POS	NEG	EQ/Weak POS	INV	Excluding EQ/Weak POS	Including EQ / Weak POS	
*Asymptomatic students**							
POS	7	1	0	0	41.2% (95% CI 21.6-64.0) (n=17)	26.9% (95% CI= 13.7-46.1) (n=26)	100%† (95% CI 99.9-100)
NEG	10	5549	9	7			
INV	0	0	0	0			
Asymptomatic students considered exposed contacts of positive index cases‡							
POS	4	6	0	0	28.6% (95% CI 8.4-58.1) (n=14)	26.7% (95% CI 7.8-55.1) (n=15)	99.6% (95% CI 99.1-99.9)
NEG	10	1470	1	0			
INV	0	0	0	0			
Symptomatic students§							
POS	10	0	0	0	83.3% (95% CI 51.6-97.9)	N/A	100.0% (95% CI 98.4-100.0)
NEG	2	224	0	0			
INV	0	0	0	0			
Asymptomatic staff members							
POS	0	1	0	0	N/A	N/A	99.8% (95% CI 99.3-100.0)
NEG	0	775	0	0			
INV	0	0	0	0			
Asymptomatic staff members considered exposed contacts of positive index cases							
POS	0	0	0	0	N/A	N/A	100.0% (95% CI 94.1-100.0)
NEG	0	61	0	0			
INV	0	0	0	0			
Symptomatic staff members							
POS	1	0	0	0	50.0% (95% CI 1.3-98.7)	N/A	100.0% (95% CI 94.3-100.0)
NEG	1	62	0	0			
INV	0	0	0	0			

RADT: rapid antigen detection test, PCR: polymerase chain reaction, POS: positive, NEG: negative, INV: invalid, EQ: equivocal, CI: confidence interval; N/A: non-applicable

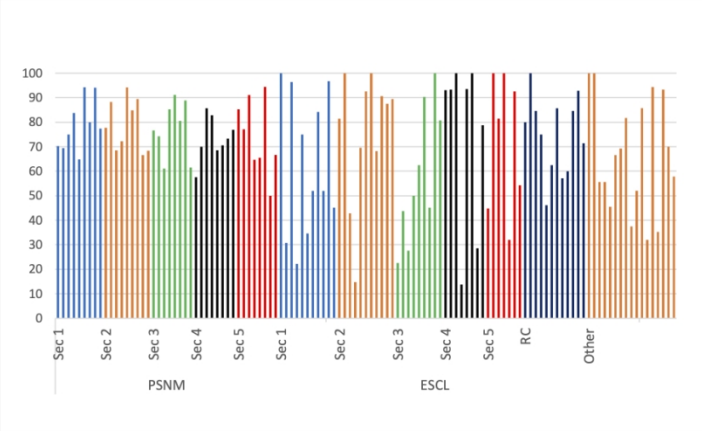
* Prevalence of SARS CoV-2 infection, based on PCR results (including equivocal and weakly positive results): 0.30% (95% CI 0.18-0.49)

†The specificity of RADT in asymptomatic students was 99.98% when adjusted to two decimal places

‡ Prevalence of SARS CoV-2 infection, based on PCR results (including equivocal and weakly positive results): 0.7% (95% CI 0.5-1.6)

§ Prevalence of SARS CoV-2 infection, based on PCR results (including equivocal and weakly positive results): 5.1% (95% CI 2.65-8.71)

Figure 1: Proportion of participating students per class and level



Sec: Secondary; RC: Reception class; PSNM: Pensionnat du Saint-Nom-de-Marie; ESCL : École Secondaire Calixa-Lavallée.

Sec: Secondary; RC: Reception class; PSNM: Pensionnat du Saint-Nom-de-Marie; ESCL : École Secondaire Calixa-Lavallée.

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Supplementary Appendix A : Sample size calculation

As the school populations were fixed in size, we determined the precision with which we would be able to estimate our primary outcome. Given the non-linear nature of the epidemic process and the complexity of the quarantine and testing policies proposed, it was not possible to estimate precision through a direct calculation. We therefore implemented an agent-based model (ABM) to estimate through simulations the number of tests that would be performed, the likely results of the tests, and other outcomes of interest in planning the study (e.g. number of days in school, number of secondary infections). We implemented a variation of a previously described school-based ABM to adapt the characteristics of the school[29]. For simplicity, we did not model household transmission explicitly, although we did allow for infection outside of the school. We also extended the model to include testing and quarantine, and we simulated random testing of students, routine testing of teachers, testing of symptomatic students and teachers and the first quarantine policy where a full 14-day quarantine was imposed for a class in which any student or teacher received a positive test (RADT or PCR). Based on the mean across 100 simulation runs for 182 days each, with an estimated sensitivity (compared to PCR) of the RADT of 0.41 (IQR: 0.39 – 0.42) as compared to the true (i.e., modelled) sensitivity of 0.40 and an estimated specificity of POC test of 0.99 (IQR: 0.99 – 0.99) as compared to the true specificity of 0.98, we expected that the number of infections and tests would be sufficient in one single school to estimate the accuracy of RADT with acceptable precision. An additional school was added to support generalizability of the findings, as well as to allow exploration of the secondary objectives.

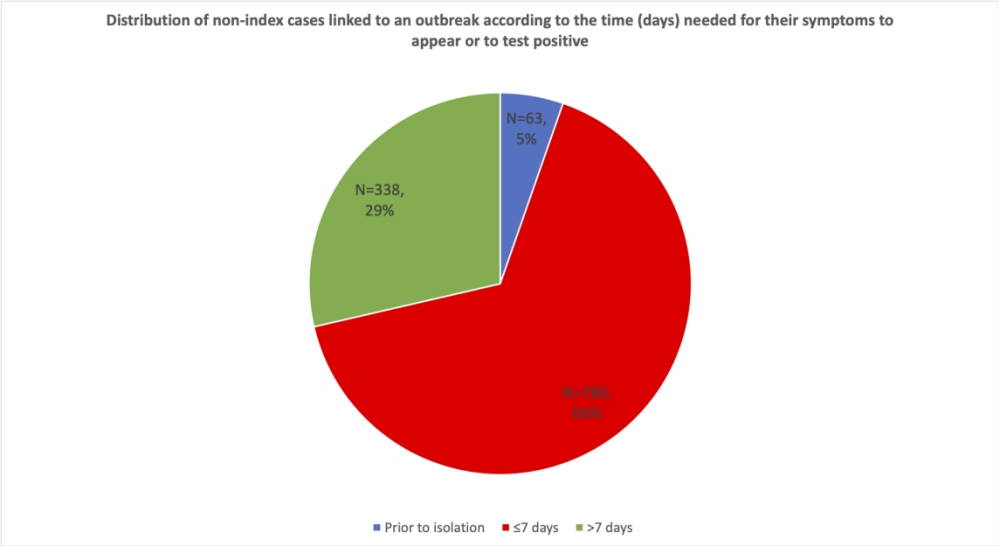
Supplementary Appendix B: Comparison of outbreaks to other high schools in Montreal using public health data during the same period

Data from Montréal Public Health showed that in other Montréal high schools (n=177), a range of 1 to 16 exposures and outbreaks per school (median: 1; IQR: 2) were observed during the study period, for a total of 358 outbreaks, one affecting two different schools. Schools declared that 1 to 52 cases (median: 4; IQR 5) were linked to an outbreak, for a total of 1181 cases. A range of 1 to 25 classes (median: 2, IQR: 3) were involved in outbreaks (n=161), for a total of 447 classes. Outbreaks at ESCL and PSNM comprised, on average, 3 and 2 cases, respectively. ESCL and PSNM had three outbreaks, with nine and seven students involved, from four and two groups, respectively, during the same period.

Despite active surveillance of SARS-CoV-2 infection through this study, there was no difference in outbreaks observed between participating schools and the rest of the Montréal high schools. However, outbreaks declared in other schools had a lower proportion of asymptomatic cases (31.8%) compared to ESCL (55.6%) and PSNM (85.7%). Participating schools had a lower proportion of cases linked to an outbreak present in school while contagious (28.6% and 6.7%), compared to the average in other schools of Montréal (n=241; 36.5%). Interestingly, data showed that 66.0% of cases linked to an outbreak in other high schools tested positive or started their symptoms within seven days of their first exposure (Supplementary Figure). Furthermore, 51.0% of the 741 cases linked to an outbreak who went to school while contagious were only processed by the Public Health team, due to capacity, after the recommended first testing date.

Using the number of classes where an outbreak occurred, assuming on average that one student is in class while contagious, we estimated that 50,010 high school students were isolated during the

study period in other high schools which, with 14 days of isolation, leads to an estimated 700,140 days or ~1,918 years of cumulative isolation. A safe, accelerated return to school could have possibly saved an estimated 350,070 days or ~959 years of cumulative isolation (Supplementary Table).



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Supplementary Table. Predicted days of isolation

January 25 to June 10 2021	*Average students per group*	*Groups*	*Total students put in isolation (instances)*	*Days of isolation (14 days)*	*Days of isolation (7 days)*
High school	30	1667	50010	700140	350070