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Analysis of a direct access testing system for the detection of SARS-CoV-2 in the paediatric population attending school

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Key words: SARS-CoV-2, children, testing system, nasopharyngeal swab
Parole chiave: SARS-CoV-2, children, testing system, nasopharyngeal swab

Abstract

Background. *During the COVID-19 pandemic, the paediatric population plays a minor role in the spread of the SARS-CoV-2 virus. However, in order to keep schools open and reduce SARS-CoV spreading, it is necessary to identify and isolate early SARS-CoV-2 positive paediatric patients even if they are asymptomatic. The aim of this study was to describe a setting for SARS-CoV 2 testing based on the spontaneous presentation of paediatric patients attending school without a medical prescription and explore its appropriateness.*
Study design. *Cross-sectional study.*
Methods. *The study performed between September 2020 and March 2021 among a sample of 13,283 paediatric patients who underwent a swab in four different hospital settings (school hot spot, emergency department, day hospital setting and hospital wards). For each patients we collected: date of swab execution, type of swab, execution setting of the swab, result of the swab, information about community spread of the virus in the 14 days prior to the swab execution, sex and age.*
Results. *In our sample, females accounted for 45.8%. The median age was 6.8 years (IQR 3.0-11.2) and the most frequent age category was between 6 and 11 years (27.9%).*
At multivariable models with a swab tested positive as outcome. The swabs executed in all the hospital settings had a lower likelihood of resulting positive compared with the school hot spot setting. Compared with adolescents aged between 14 and 19 years old, new-borns below 3 months (adjOR 1.83, 95% C.I. 1.14-3) and patients aged between 11 and 14 years old (adjOR 1.32, 95% C.I. 1.07-1.63) reported a higher probability of a swab tested positive. Instead, children aged between 3 months and 3 years (adjOR 0.77, 95% C.I. 0.61-0.96) and children aged between 3 years and 6 years (adjOR 0.66, 95% C.I. 0.53-0.83) were less likely to result positive. The higher was the mean of pooled Rt in the 14 days preceding the swab, the higher was the likelihood of resulting positive (adjOR 1.75, 95% C.I. 1.53-1.99).
Conclusion. *In conclusion, we found a high incidence of paediatric patients positive to the test for the detection of SARS-CoV-2 at the school hot spot compared with other settings during the period of observation. The free access modality to the nasopharyngeal swab was effective in identifying patients with COVID-19. Public health authorities should implement these testing modality in order to help reduce the spread of SARS-CoV-2 in school settings.*

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Introduction

COVID-19 epidemic spread out rapidly since its initial outbreak in China, forcing the World Health Organization (WHO) to declare the state of global pandemic on 11th March 2020 (1, 2). Within three years, over 700 million cases were reported, including over 6 million deaths (3).

Overall, during the pandemic, the pediatric population represented the lowest proportion of COVID-19 cases. Considering the early period of the pandemic, notification rates were lowest for this population, probably due to higher rates of asymptomatic and mild symptoms in children and lower testing rates rather than a reduced susceptibility (4). Indeed, it is well known that children tend to have a mild infection and 15-35% can be asymptomatic (5) reaching out to a lower number of hospitalizations or fatal outcomes than adults (6). Specifically in Italy, on August 2021 (i.e. the year when the present study was conducted), the 15.8% of total COVID-19 cases diagnosed involved children aged 0-19 years old (7). In particular, all case patients aged <18 years since the loosening of the first lockdown (4th May 2020), the majority of diagnosed cases occurred in adolescents aged 13-17 years (41.3%), followed by children aged 7-12 years (28.0%), 2-6 years (21.0%) and 0-1 year (7%). The hospitalisation rate was 4.8%, with the highest percentage of hospital admissions in infants aged ≤1 year (16.2%) (8). More recent data (2022), showed that, with the increasing vaccination coverage among adults, the pediatric population has become a relatively larger proportion of notified cases (4).

Many studies suggest that the paediatric population is a minor contributor to the diffusion of the virus, but it remains open to debate what proportion of this population may contribute to the spread (9). There are doubts about how much children actually contribute to virus transmission within the general population and whether they may be, due to some intrinsic characteristic of their young age, less infectious than adults. In favour of the latter assertion, there is the evidence that transmission in the family environment involves very rarely children as the source of the virus. However, it is possible that these data are affected by an underestimation due to the higher rate of asymptomaticity in children and, notoriously, milder symptoms, which makes the manifestation of the infection difficult to recognise (10). Indeed, from the above-mentioned surveillance data (8), it is difficult to tell whether children under 12 years of age are less likely to be infected or whether it is simply more complicated to identify positive cases due to a mostly asymptomatic presentation. In addition, the possible underestimation in the identification of paediatric SARS-CoV2 positive patients may also have been influenced by inadequate testing capacity or a lack of effort to recruit this population group, justified by a lower frequency of adverse consequences compared with adults and the elderly (11).

In particular, the lack of efficiency in tracking systems and the possible limited availability of diagnostic tests are likely to reduce the contact notification rate in the school context, in which, following the identification of SARS-CoV-2 positive individuals, an effective contact tracing strategy should be applied together with the administration of appropriate diagnostic tests to identify possible transmission to stem the growth of the new outbreak (11). Indeed, the European Centre for Disease Prevention and Control (ECDC) recommends that in the general population, but also and especially in educational establishments, a major effort should be made to offer diagnostic tests to the majority of asymptomatic cases to ensure timely isolation and adequate contact tracing, followed by eventual quarantine (12).

Last, to explore the characteristics of the SARS-CoV-2 infection among the paediatric population and the issue of asymptomaticity, studies about the seroprevalence (13) reported respectively that only 47% and 60% of the paediatric population tested positive for the presence of SARS-CoV2 antibodies complained of symptoms in accordance with the development of infection. These data suggest that around 50% of children who become infected with SARS-CoV2 are asymptomatic, thus contributing to the spread of the virus even though they are not clinically identifiable, making it very difficult to implement all the necessary measures to break the chain of contact.

Thus, in the school context, in line with the above-described data, the preventive measures implemented by most of countries in case of a suspected case agree that the student should self-isolate until a healthcare provider prescribes a test or decides that the student is not a suspected case (14). Focusing on Italy, the various scenarios in which paediatric patients need to undergo one of the diagnostic procedures to detect SARS-CoV2 positivity always require the intermediation of a general practitioner (GP) or a paediatrician (15). As far as we know, no one tried to investigate a different kind of setting as a valid alternative of testing in the paediatric population. The aim of this study was to describe a setting for SARS-CoV 2 testing based on the spontaneous presentation of paediatric patients without a medical prescription and explore its appropriateness by comparison with other settings.

Methods

Context and setting

The University Hospital *Azienda Ospedaliero-Universitaria (AOU) "Città della Salute e della Scienza"* in Turin (Piedmont region, Italy) constitutes one of the largest health care centres in Europe. Indeed, it is a complex of four interconnected hospitals (Molinette, Regina Margherita, S. Anna, and CTO) (16). In particular, the "Ospedale Infantile Regina Margherita" (OIRM) is a paediatric Hospital that seeks to prevent, diagnose and treat children's diseases. The hospital has surgical and medical specialties for the treatment of infants, children and adolescents in the Piedmont region and is able to treat rare, chronic and complex diseases. It provides treatment for onco-haematological diseases, stem cell transplants, heart surgery, brain surgery, burn treatment and infant surgery (17).

On 14th September 2020, a nasopharyngeal molecular swab (5, 18) execution centre for SARS-CoV-2 detection was opened at OIRM. This centre, called school hot spot (HS), was designed with the aim of quickly providing SARS-CoV-2 tests to school-age children. Patients accessed to the service sent by their GP or spontaneously if they referred to having symptoms of COVID-19 (19) or reported close contact with a positive patient according to ECDC guidelines (20). The HS was open from Monday to Saturday from 10.30 am to 3.00 pm and on Sunday 10.30 am to 01.00 pm.

Children entered the HS accompanied by a parent or a legal guardian and a paediatric nurse performed nasopharyngeal swabs. Access to the HS was free for all and no medical prescriptions were required.

In addition, at the OIRM, in the emergency room, SARS-CoV-2 nasopharyngeal swabs are performed on all paediatric patients who reported COVID-19 symptoms (19) or contact with COVID-19 positive patients in the previous 14 days in agreement with ECDC general guidance for management of persons who have had contact with COVID-19 cases (20, 21). Furthermore, patients admitted to the hospital wards, even in day hospital (DH), are subjected to a swab for the detection of SARS-CoV-2 before hospital admission.

To understand and comment the different

Table 1 - Description of learning activities in the period under examination.

Date	Type of learning activities
14/09/2020	Start of the school year (face-to-face teaching activity)
27/10/2020	Start of distance learning activities in the 14-19 age group (75% of total school time)
02/11/2020	Start of total distance learning activities in the 14-19 age group (100% of total school time)
29/11/2020	Start of total distance learning activities in the 12-19 age group (100% of total school time)
23/12/2020	Start of Holidays (closed school)
07/01/2021	Opening of schools in the 6-14 age group. Beginning of total distance learning activities in the 14-19 age group
16/01/2021	Start of partial distance learning activities in the 14-19 age group (50% of total school time)
08/03/2021	Start of total distance learning activities in the 12-19 age group (100% of total school time)
15/03/2021	Start of total distance learning activities in all age groups (100% of total school time)

risk of exposure to SARS-CoV-2, the percentage of distance learning activities in the various age groups appears to be an important information. Thus, to give context, Table 1 describes the percentages of distance learning activities in schools divided by date and age group.

Data collection

The present paper describes a cross-sectional study performed between 14th September 2020 and 18th March 2021 among a sample of 13,283 paediatric patients (aged 0-19 years) who underwent a swab at OIRM in four different hospital settings (HS, Emergency department, DH setting and hospital wards). The data collection ended on 18th March because the number of daily swabs had been significantly reduced due to the improvement of the epidemiological situation of SARS-CoV-2 infections. Hospital wards include COVID-19 ward where positive COVID-19 paediatric patients were hospitalized. Each record represented a unique patient as we considered only the first swab performed at the OIRM for each patient.

Two types of test on nasopharyngeal swabs were analysed: nucleic acid amplification test (NAAT), also called molecular test, and detection of virus-specific antigens by rapid antigen detection tests (RADTs), also called rapid test (22).

The data were collected from an internal database of the OIRM and included: date of swab execution, type of swab (NAAT or RADTs), execution setting of the swab (HS, emergency department, DH setting and hospital wards, result of the swab (positive, negative or indeterminate), sex and age of the paediatric patients.

Last, since the effective reproductive number (Rt), defined as averages of the number of people infected by a typical case at any given moment, play a central role in tracking infectious disease outbreaks, we recorded, for each swab performed, the mean value of the Rt in the Piedmont region calculated in the 14 days prior to the date of execution of the swab (23). The Rt values were collected from the weekly reports of the Italian ministry of health (24-26).

Statistical analysis

Descriptive analyses were performed for all variables. Age was categorized in 6 age groups according to the degree of school. In Italy, children less than three months old do not attend any type of school, children from 3 months to 3 years old attend the day nursery school, children from 3 to 6 years old attend kindergarten school, children between 6 years and 11 years of age attend primary school, children from 11 to 14 years old attend junior secondary school and children from 14 to 19 years old attend secondary school.

The Shapiro–Wilk test showed that the mean Rt did not have a normal distribution. Chi-squared tests and adjusted residuals (Mann Whitney U test where appropriate) were computed to assess differences between those who tested positive and those who tested negative.

To further describe the activity of the HS, descriptive statistics of the variables were stratified by setting and chi-squared tests and adjusted residuals (Kruskall Wallis test where appropriate) were calculated. In addition, we plotted a graph with the total number of swabs per week, the number of swabs that tested positive per week (only the HS spot subsample was considered), and the mean of pooled Rt in the 14 days preceding the swab.

Moreover, we calculated the weekly incidence of SARS-CoV-2 cases by using the positive cases found in our dataset and the overall population of Piedmont region (at 31 December 2020: 4,274,945 inhabitants). Weekly incidence was expressed as new positive cases per 100,000 inhabitants and the pattern was described through a graph where information about school closure dates was added (based on dates presented in Table 1).

To explore the appropriateness of the first access to the HS, our outcome was a nasopharyngeal swab tested positive (indeterminate results were considered as missing values). Thus, multivariable logistic regression models were carried out to understand if children accessing the HS were more likely to be positive compared with children accessing the other settings. In addition to the setting, the models were adjusted for age category, gender, mean of pooled Rt in the 14 days preceding the swab, and type of swab (results expressed as Odds Ratios (OR), 95% CI).

SPSS statistics (v27) was used and a two-tailed p-value < 0.05 was considered significant. Missing values were excluded.

Results

A total of 13,283 paediatric patients were included in our analysis. The median age was 6.8 years (IQR 3.0-11.2). The characteristics of the sample are described in Table 2. The mean of pooled Rt in the 14 days preceding the swab had a median of 1.18 (IQR=0.90-1.37), with a minimum of 0.68 in December 2020 and a maximum of 2.16 in October 2020.

According to the chi-square tests, the swabs tested positive more frequently among children above 6 years of age. The HS was the setting that presented the higher percentage of positive swabs and the NAAT was the type of swab that reported a higher frequency of positive results. Further details are reported in Table 2. In addition, the mean of pooled Rt in the 14 days preceding the swab had a different distribution across the swabs' results (Mann Whitney U test: <0.001), with a median of 1.31 (IQR=0.98-1.83) for children with a positive swab and a median of 1.18 (IQR=0.90-1.37) for those with a negative swab.

Focusing on the HS, the most frequent age category was between 6 and 11 years old. Compared with the other settings, the children and adolescents who accessed the HS were more frequently male and aged between 3 years and 14 years. Details are shown in Table 3. In addition, the mean of pooled Rt in the 14 days preceding the swab had a different distribution across the settings (Kruskall Wallis test p<0.001). Indeed, pairwise comparisons showed a different distribution of the Rt in the 14 days preceding the swab for the swab executed in the school hotspot setting (median 1.22, IQR 0.96-1.39) compared with the other settings (emergency department: median 1.05, IQR 0.89-1.31; DH: median 1.05, IQR 0.89-1.31; hospital wards: median 1.05, IQR 0.89-1.31).

Table 2 - Characteristics of the sample: overall and stratified by swabs' results

Characteristic	Overall (n=13,283) N (%)	Swabs' results		p-value
		Tested negative (n=11,771) N (%)	Tested positive (n=1,422) N (%)	
Gender				
Female	6,069 (45.8)	5,365 (89.0)	663 (11.0)	0.462
Male	7,191 (54.1)	6,385 (89.4)	757 (10.6)	
Age category				
0 to 2 months	278 (2.1)	248 (91.2)	24 (8.8)	**<0.001**
3 months to 2 years	3,031 (22.8)	2,782 (92.3)[a]	231 (7.7)[b]	
3 to 5 years	2,754 (20.7)	2519 (92.3)[a]	211 (7.7)[b]	
6 to 10 years	3,710 (27.9)	3,228 (87.3)[b]	470 (12.7)[a]	
11 to 13 years	2,206 (16.6)	1,868 (85.3)[b]	323 (14.7)[a]	
14 to 19 years	1,304 (9.8)	1,126 (87.4)[b]	163 (12.6)[a]	
Setting				
School hot spot (HS)	8,888 (66.9)	7,611 (85.9)[b]	1,245 (14.1)[a]	**<0.001**
Emergency department	2,771 (20.9)	2,609 (95.3)[a]	130 (4.7)[b]	
Day Hospital	1,248 (9.4)	1,204 (97.9)[a]	26 (2.1)[b]	
Hospital wards	376 (2.8)	347 (94.3)[a]	21 (5.7)[b]	
Type of swab				
Nucleic acid amplification test	12,787 (96.3)	11,291 (88.9)	1,412 (11.1)	**<0.001**
Rapid antigen detection test	496 (3.7)	480 (98.0)	10 (2.0)	

n = sample size
Figures are expressed as number (N) and percentages (%). Overall: column percentages. Swabs' results: row percentages.
p-value obtained via Chi-squared test.
[a] adjusted residual >1.96
[b] adjusted residual <-1.96

Figure 1 shows the total number of swabs per week (only school hotspot setting), number of swabs that tested positive per week (only school hotspot setting), and the mean of pooled Rt in the 14 days preceding the swab. The highest number of swabs were executed the week between the 2nd and the 8th November 2020 (n=663), followed by the week between 8th and 14th March 2021 (n=661) and the week between the 9th and the 15th November 2020 (n=647). Considering the percentage of executed swabs that resulted positive, the highest value occurred during the week between the 9th and the 15th November 2020 (25%) and the days from the 15th March 2021 and 18th March 2021 (25%), then the week between the 2nd and the 8th November 2020 (24%). In addition, Figure 2 shows the weekly incidence of SARS-CoV-2 positive cases per 100,000 inhabitants in our sample along with the dates of school opening/closure in Piedmont.

Last, Table 4 shows the multivariable models with a swab tested positive as outcome. The swabs executed in all the settings had a lower likelihood of resulting positive compared with the HS setting

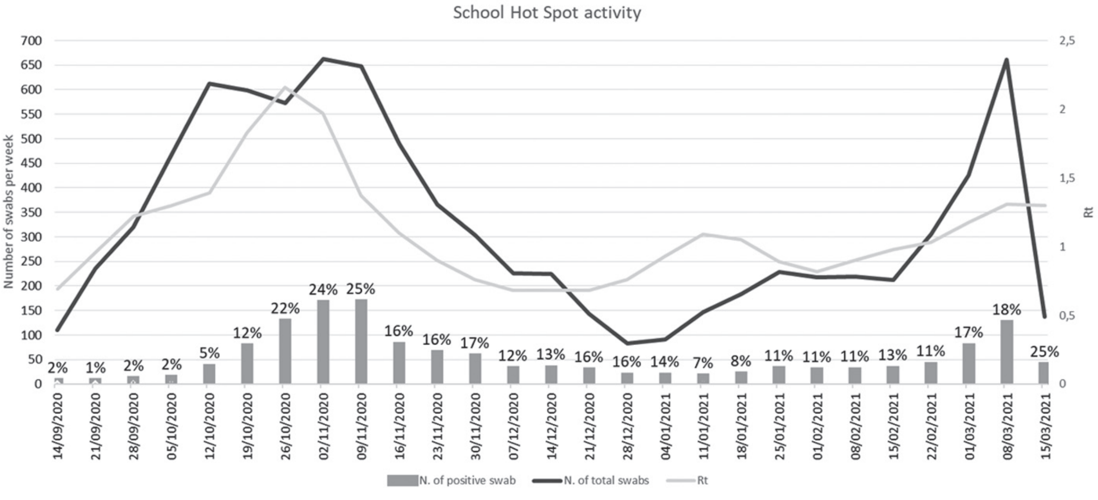

Figure 1 - School hot spot (HS): total number of swabs per week and number of swabs that tested positive per week from 14th September 2020 to 18th March 2021.

Figure legend: The Figure shows the trend of total number of swabs per week, number of swabs that tested positive per week from 14th September 2020 to 18th March 2021 (only school hotspot setting) and the mean of pooled Rt in the 14 days preceding the swab. Only the date of the first day of the week is shown. Above the number of swabs that tested positive, the percentage of positive swabs (out of the total number of swabs) is shown for each week. The week starting from 15th March 2021 consists of only 4 days as the data collection ended on 18th March 2021.

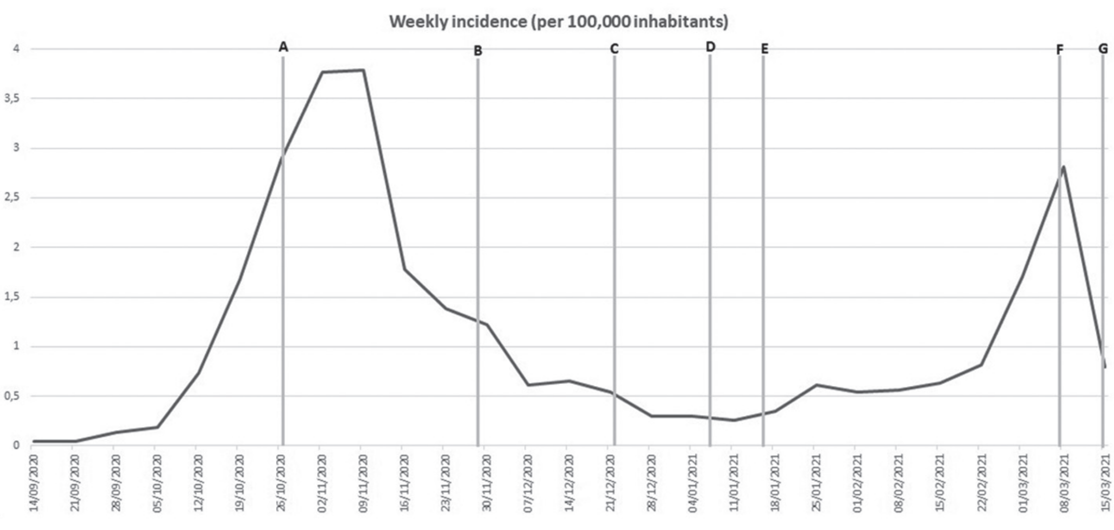

Figure 2 - Weekly incidence of SARS-CoV-2 cases per 100,000 inhabitants and dates of school closures from 14th September 2020 to 18th March 2021.

Figure legend: The Figure shows the weekly incidence of SARS-CoV-2 positive cases per 100,000 inhabitants along with the dates of school opening/closure in Piedmont. School (face-to-face) started on 14th September 2020. Dates are highlighted in capital letters, which represent: (A) Start of partial distance learning activities in the 14-19 age group (75% of total school time) (which became 100% on 2/11/2020); (B) Start of total distance learning activities in the 12-19 age group; (C) Start of Holidays (closed school); (D) Opening of schools in the 6-14 age group. Beginning of total distance learning activities in the 14-19 age group; (E) Start of partial distance learning activities in the 14-19 age group (50% of total school time); (F) Start of total distance learning activities in the 12-19 age group; (G) Start of total distance learning activities in all age groups.

Table 3 - Characteristics of the sample stratified by setting (overall sample and subsample with participants who tested positive)

Characteristic	School hot spot (HS)	Emergency department	Day Hospital	Hospital wards	p-value
	N (%)	N (%)	N (%)	N (%)	
Overall sample (n=13,283)					
Gender					
Female	4,126 (46.4)a	1,294 (47.0)	480 (38.5)b	169 (45.1)	<0.001
Male	4,757 (53.6)b	1,460 (53.0)	768 (61.5)a	206 (54.9)	
Age category					
0 to 2 months	13 (0.1)b	197 (7.1)a	29 (2.3)	39 (10.4)a	<0.001
3 months to 2 years	1,638 (18.4)b	1,087 (39.2)a	235 (18.8)b	71 (18.9)	
3 to 5 years	1,981 (22.3)a	448 (16.2)b	263 (21.1)	62 (16.5)b	
6 to 10 years	2,805 (31.6)a	513 (18.5)b	323 (25.9)	69 (18.4)b	
11 to 13 years	1,555 (17.5)a	384 (13.9)b	213 (17.1)	54 (14.4)	
14 to 19 years	896 (10.1)	142 (5.1)b	185 (14.8)a	81 (21.5)a	
Type of swab					
Nucleic acid amplification test	8,888 (100.0)a	2,297 (82.9)b	1,248 (100.0)a	3,54 (94.1)b	<0.001
Rapid antigen detection test	0 (0.0)b	474 (17.1)a	0 (0.0)b	22 (5.9)a	
Subsample: tested positive (n=1,422)					
Gender					
Female	591 (47.5)	58 (45.0)	8 (30.8)	6 (28.6)	0.116
Male	653 (52.5)	71 (55.0)	18 (69.2)	15 (71.4)	
Age category					
0 to 2 months	2 (0,2)b	17 (13,1)a	2 (7,7)a	3 (14,3)a	<0.001
3 months to 2 years	159 (12,8)b	60 (46,2)a	7 (26,9)	5 (23,8)	
3 to 5 years	188 (15,1)	14 (10,8)	3 (11,5)	6 (28,6)	
6 to 10 years	442 (35,5)a	18 (13,8)b	7 (26,9)	3 (14,3)	
11 to 13 years	301 (24,2)a	17 (13,1)b	4 (15,4)	1 (4,8)b	
14 to 19 years	153 (12,3)a	4 (3,1)b	3 (11,5)	3 (14,3)	
Type of swab					<0.001
Nucleic acid amplification test	1,245 (100.0)a	121 (93.1)b	26 (100.0)	20 (95.2)b	
Rapid antigen detection test	0 (0.0)b	9 (6.9)a	0 (0.0)	1 (4.8)a	

n = sample size
Figures are expressed as number (N) and column percentages (%).
p-value obtained via Chi-squared test.
[a] adjusted residual >1.96
[b] adjusted residual <-1.96

(p<0.001 for all settings). Compared with adolescents aged between 14 and 19 years old, new-borns below 3 months (p=0.012) and patients aged between 11 and 14 years old (p=0.009) reported a higher probability of a swab tested positive. Instead, children aged between 3 months and 3 years (p=0.020) and children aged between 3 years and 6 years (p<0.001) were less likely to result positive. The higher was the mean of pooled Rt in the 14 days preceding the swab, the higher was the likelihood of resulting

Table 4 - Multivariable logistic regression model: swab tested positive as outcome.

	Swab tested positive		
	adjOR	95% CI	p-value
Gender			
Female	Ref.		
Male	0.97	0.86-1.08	0.535
Age category			
14 to 19 years	Ref.		
0 to 2 months	1.85	1.14-3	0.012
3 months to 2 years	0.77	0.61-0.96	0.020
3 to 5 years	0.66	0.53-0.83	<0.001
6 to 10 years	1.1	0.9-1.34	0.343
11 to 13 years	1.32	1.07-1.63	0.009
Setting			
School hot spot (HS)	Ref.		
Emergency department	0.37	0.3-0.45	<0.001
Day Hospital	0.14	0.1-0.21	<0.001
Hospital wards	0.39	0.25-0.62	<0.001
Mean of pooled Rt in the 14 days preceding the swab	1.75	1.53-1.99	<0.001
Type of swab			
Nucleic acid amplification test	Ref.		
Rapid antigen detection test	0.33	0.17-0.63	0.001

Abbreviations: adjOR adjusted Odds Ratio, CI Confidence Interval, Rt effective reproductive number.

positive (p<0.001). Compared with children who received the NAAT, those who received the RADT were less likely to test positive (p=0.001).

Discussion

The aim of this study was to explore an organisational mode (the "school hot spot") for SARS-CoV-2 testing based on the spontaneous presentation of paediatric patients by analysing the results of tests for SARS-CoV-2 carried out in the HS and comparing these results with SARS-CoV-2 tests performed in other paediatric hospital settings.

The main results of the present study concern the multivariable model that showed a greater likelihood of testing positive in patients who swabbed at the HS compared with other settings. Indeed, the HS was aimed at patients with COVID-19 symptoms or with a history of close contact with a positive COVID-19 case, while the other settings had a different target population. In the emergency department, all patients were tested and the only patients who were not tested were those who had a short outpatient visit and had no history of close contact with COVID-19 patients. In DH service, only patients who had a negative history for COVID-19 symptoms or contact with COVID-19 patients were tested. Indeed, in DH, if the medical service was deferrable, patients with a history of COVID-19 were postponed. For this reason, in emergency department and DH, the incidence of positive swabs was lower. Last, swabs performed in the hospital wards reported a greater probability of being positive than the DH service because they also include swabs performed in the COVID-19 ward of the paediatric hospital. Thus, we can hypothesize that the HS organizational model has been used in an appropriate manner because the probability that a COVID-19 positive patient was swabbed at the HS was higher compared with other examined settings, suggesting that patients and their families are able to understand when the swab is needed without asking a doctor or they are properly addressed by their GP or paediatrician.

Moreover, the multivariable models revealed other remarkable associations. First, in agreement with the literature (27), our study found that new-borns are more likely to become infected than other paediatric patients. Then, we found that adolescents in the 11 to 13 age group had higher probability to test positive than patients in the 14 to 19 age group. A possible explanation for this could be that this age group attended face-to-face school more frequently and, consequently, was more exposed to the infection and was tested more (28-30). Surprisingly, children aged between 3 months and 2 years and children aged between 3 years and 5 years had lower probability to test positive than adolescents (14-19 years age group). Although this age group went to school for more time in presence than adolescents, COVID-19 cases are less easily identifiable because young children tend to have milder symptoms as reported in literature (14).

Understandably, children who received RADT were less likely to test positive. Indeed, this test was performed to patients only in the emergency department in case of a large influx of patients or when there was no time to wait for the result of the NAAT swab for the patient's emergency conditions. The NAAT swab is considered the reference standard diagnostic tool (31). In particular, a meta-analysis calculated a pooled sensitivity and specificity for molecular-based tests of 92.8% (95% CI, 88.9–95.4%) and 97.6% (95% CI, 96.6–98.3%), respectively, and for antigen-based tests of 70.6% (95% CI, 67.2–73.8%) and 98.9% (95% CI, 98.5–99.2%), respectively (31).

Finally, a higher mean of pooled Rt in the 14 days preceding the swab was associated with higher probability of being positive to the swab. As it is easy to understand, when the viral circulation is greater the probability of being symptomatic or having had contacts may also increase and, consequently, the swabs performed and the proportion of positives may increase too.

Last, it is worth noting that the paediatric patients most frequently tested at the OIRM were those between 6 and 11 years old. In the literature there is not an age range tested mostly in the paediatric population. The age group from 6 to 11 years attended school more in presence than older children (32) and, therefore, may have more chances of contagion and consequently may be more likely to be tested in our sample of children (33). In addition, we found that sex was not associated with a higher probability of being tested in paediatric population, as reported in the literature (33). In our sample, the swabs tested positive more frequently among children in the age group between 11 and 13 years. This might be partially explained by the fact that, in Italy, these group of children attended face to face school more than older children (32) and are more likely to be swabbed than younger children (34, 28). Also, compared with other settings, the HS was probably frequented more by children attending face-to-face learning compared with older ones. This could be due to the fact that face-to-face learning requires more frequent testing because the probability of having contact with positive people is higher. In literature, it is known that face-to-face learning increases the risk of contagion in children (28).

The present paper had some strengths and limitations that should be acknowledged. To the best of our knowledge, this was the first study that described a direct access testing modality for paediatric patients attending school. Furthermore, we analysed a large sample of paediatric patients spread over two waves of pandemics and in our sample of patients, some age groups attended face-to-face school more than others. However, the limitations were mainly related to the impossibility of correlating the patients' history and symptoms with the result of the tests obtained. Moreover, we do not know how many patients contacted a doctor before presenting to the school hotspot and consequently we do not know the percentage of patients who presented spontaneously and therefore what characteristics they had.

Nevertheless, the proposal of a new strategy of testing is urgent, especially among children and adolescents, and robust evidence on the most effective strategy still need to be demonstrated. As there is limited evidence of the effectiveness of school closures in containing the pandemic and, given the important health implications of school closures on young people's lives, it is important to implement preventive measures in order to reduce COVID-19 transmission and keep schools open (14). Indeed, it is essential to test symptomatic cases and contact tracing should be initiated promptly following identification of a confirmed case in order to isolate COVID-19 positive patients (35). This is even more important with the spread of several Variants of Concern (VOC). For instance, the Delta variant was declared a VOC in May 2021 (36) and was characterized by a higher transmission rate than other variants declared VOC in 2020, such as the Alpha variant (37). In particular, in populations where adults were vaccinated for COVID-19 but children were not vaccinated or are under-vaccinated, there was an estimate of increasing proportions of SARS-CoV-2 cases reported among children, due to the spread of Delta variant (38). In addition, at the end of 2021 the Omicron variant has begun to be detected (then becoming dominant) (39) and has been accompanied by significant changes in the presenting symptoms in children: it has been suggested that the suspicion for COVID-19 as cause for pediatric hospitalization should stay high, even in patients without typical respiratory symptoms (40). Last, with the overall increasing number of infections, also cases of hospitalization among children and adolescents can increase (38). Thus, increasing testing capacity appears necessary and the possibility of undergoing a swab for SARS-CoV-2 in direct access mode, as in our HS, could be implemented to carry out as many tests as possible (41).

In conclusion, we can hypothesize that the free presentation mode can be effective in identifying a high number of positive patients but also to be able to exclude the diagnosis of COVID-19 in many paediatric patients in order to allow a quick return to school (42). Particularly, this testing system should be addressed at older children because they are more likely to be infected in school settings (42, 43). In view of the need of keeping face-to-face learning activities and avoiding substantial loss of school days, future research should focus on evaluate the most quick and effective modality of testing in this population to help reduce the spread of SARS-CoV-2 in school settings and prevent issues due to school loss.

Riassunto

Analisi di un servizio di testing ad accesso diretto per la diagnosi di infezione da SARS-CoV-2 nella popolazione pediatrica in età scolare

Premesse. Durante la pandemia di COVID-19, popolazione pediatrica ha contribuito in minor misura alla diffusione del virus SARS-CoV-2. Nonostante ciò, al fine di garantire l'apertura delle scuole e limitare la diffusione del virus, è fondamentale identificare e isolare tempestivamente i pazienti pediatrici positivi anche se asintomatici. L'obiettivo dello studio è quello di descrivere una modalità di testing per SARS-CoV2 basata sull'accesso spontanteo dei pazienti pediatrici in età scolare senza necessità di prescrizione medica e valutare l'appropriatezza del ricorso al servizio.

Disegno dello studio. Cross-sectional study.

Metodi. Lo studio è stato condotto tra settembre 2020 e marzo 2021 ed ha coinvolto un campione di 13,283 pazienti pediatrici che si sono sottoposti a tampone nasofaringeo in 4 differenti setting ospedalieri (hot spot scolastico, pronto soccorso, day hospital e reparto ospedaliero). Per ciascun paziente sono stati registrati: sesso, età, data di esecuzione del tampone, tipo di tampone, setting di esecuzione, risultato del test, dati relativi alla diffusione del virus in comunità nei 14 giorni antecedenti all'esecuzione del tampone.

Risultati. Il campione in esame è costituito per il 45.8% da soggetti di sesso femminile. L'età mediana è pari a 6.8 anni (RIQ 3.0-11.2) e la fascia d'età maggiormente rappresentata è quella che va dai 6 e agli 11 anni (27.9%). I tamponi eseguiti in tutti I contesti ospedalieri hanno una probabilità inferiore di risultare positivi rispetto a quelli effettuati nel setting dell'hot spot. I bambini com meno di 3 mesi (adjOR 1.83, 95% C.I. 1.14-3) e I pazienti con età compresa tra 11 e 14 anni hanno (adjOR 1.32, 95% C.I. 1.07-1.63) hanno una maggiore probabilità di risultre positivi al test rispetto alla fascia 14-19 anni. Inoltre, I bambini di età compresa tra 3 mesi e 3 anni (adjOR 0.77, 95% C.I. 0.61-0.96) e I pazienti compresi nella fascia 3-6 anni (adjOR 0.66, 95% C.I. 0.53-0.83) hanno meno probabilità di risultare positivi al tampone. Maggiore era la media del valore Rt nei 14 giorni precedenti il tampone, maggiore era la probabilità di risultato positivo (adjOR 1,75, IC 95% 1,53-1,99).

Conclusioni. In conclusione, abbiamo riscontrato un'elevata incidenza di pazienti pediatrici positivi al test per la rilevazione di SARS-CoV-2 presso l'hot spot scolastico rispetto ad altre strutture durante il periodo di osservazione. La modalità di accesso libero, senza necessità di prescrizione medica, al tampone nasofaringeo è stata efficace nell'identificazione dei pazienti con COVID-19. Le autorità sanitarie pubbliche dovrebbero implementare queste modalità di test per aiutare a ridurre la diffusione di SARS-CoV-2 negli ambienti scolastici.

References

1. Zhu N, Zhang D, Wang W, et al. A Novel Coronavirus from Patients with Pneumonia in China, 2019. N Engl J Med. 2020 Feb 20; **382**(8): 727-33. doi: 10.1056/NEJMoa2001017. Epub 2020 Jan 24.
2. Costantino C, Cannizzaro E, Alba D, Conforto A, Cimino L, Mazzuco W. Sars-Cov-2 pandemic in the mediterranean area: epidemiology and perspectives. EuroMediterranean Biomed J. 2020; **15**(25): 102-6. doi: 10.3269/1970-5492 .2020.15.25
3. WHO Coronavirus (COVID-19) Dashboard. Latest update: 31 January 2023. Available from: https://covid19.who.int/
4. European Centre for Disease Prevention and Control (ECDC). SARS-CoV-2 in children (latest update 14 June 2022). Available from: https://www.ecdc.europa.eu/en/infectious-disease-topics/z-disease-list/covid-19/latest-evidence/sars-cov-2-children
5. Chen ZM, Fu JF, Shu Q, et al. Diagnosis and treatment recommendations for pediatric respiratory infection caused by the 2019 novel coronavirus.World J Pediatr. 2020 Jun; **16**(3): 240-46. doi: 10.1007/s12519-020-00345-5. Epub 2020 Feb 5.
6. European Center for Disease Prevention and Control (ECDC). COVID-19 in children and the role of school settings in COVID-19 transmission. Stockholm: ECDC; 2020.
7. Epicentro. Istituto Superiore di Sanità (ISS). Sorveglianza integrata COVID-19: i principali dati nazionali. 2021.
8. Bellino S, Rota MC, Riccardo F, et al. Pediatric COVID-19 Cases Prelockdown and Postlockdown in Italy. Pediatrics. 2021 Feb; **147**(2): e2020035238. doi: 10.1542/peds.2020-035238. Epub 2020 Nov 5.
9. Swiss National COVID-19 Science Task Force. The role of children (≤12 years of age) and adolescents (13-17 years of age) in the SARS-CoV-2 pandemic: A rapid review Questions. 2021.
10. Gaythorpe KAM, Bhatia S, Mangal T, et al. Children's role in the COVID-19 pandemic: a systematic review of early surveillance data on susceptibility, severity, and transmissibility. Publisher Correction: Sci Rep. 2021 Sep 16; **11**(1): 18814. doi: 10.1038/s41598-021-97183-w. Erratum for: Sci Rep. 2021 Jul 6; 11(1): 13903.
11. European Centre for Disease Prevention and Control (ECDC). COVID-19 associated with SARS-CoV-2 Multi-country (World). Stockholm: ECDC; 2020.
12. European Centre for Disease Prevention and Control (ECDC). COVID-19 testing strategies and objectives Key messages. Stockholm: ECDC; 2020.
13. Duysburgh ELS, Callies M, Kabouke I, et al. Prevalence and incidence of antibodies against sars-cov-2 in children and school staff mea-

sured between December 2020 and June 2021: an observational sero-prevalence prospective cohort study. Brussels: Sciensano; March 2021: -28.

14. Lo Moro G, Sinigaglia T, Bert F, Savatteri A, Gualano MR, Siliquini R. Reopening Schools during the COVID-19 Pandemic: Overview and Rapid Systematic Review of Guidelines and Recommendations on Preventive Measures and the Management of Cases. Int J Environ Res Public Health. 2020 Nov 27; **17**(23): 8839. doi: 10.3390/ijerph17238839.
15. Working Group ISS, Ministero della Salute, Ministero dell'Istruzione, INAIL, Fondazione Bruno Kessler, [Regione Emilia-Romagna, Regione Veneto. Operational guidance for the management of SARS-CoV-2 cases and outbreak in schools and kindergartens. Version of August 28, 2020]. Indicazioni operative per la gestione di casi e focolai di SARS-CoV-2 nelle scuole e nei servizi educativi dell'infanzia. Istituto Superiore di Sanità; 2020: 1-28 (Rapporto ISS COVID-19 n. 58/2020 Rev).
16. Bert F, Thomas R, Lo Moro G, et al. A new strategy to promote flu vaccination among health care workers: Molinette Hospital's experience. J Eval Clin Pract. 2020 Aug; **26**(4): 1205-11. doi: 10.1111/jep.13295. Epub 2019 Nov 7.
17. Città della Salute e della Scienza di Torino. A.O.U. Citta della Salute e della Scienza di Torino - Presentazione Regina Margherita. 2021.
18. World Health Organization (WHO). WHO Guidance Note. Laboratory testing for coronavirus disease (COVID-19) in suspected human cases‎ interim guidance. World Health Organization; 11 Spetember 2020.
19. Cui X, Zhao Z, Zhang T, et al. A systematic review and meta-analysis of children with coronavirus disease 2019 (COVID-19). J Med Virol. 2021 Feb; **93**(2): 1057-69. doi:10.1002/jmv.26398. Epub 2020 Sep 28.
20. European Centre for Disease Prevention and Control (ECDC). Contact tracing : P ublic health management of persons, including healthcare workers , having had contact with COVID-19 cases in the European Union Target audience Definition of contact persons Healthcare workers Contact management steps after a case is. ECDC Bull. 2020: 7-10.
21. European Centre for Disease Prevention and Control (ECDC). Contact tracing for COVID-19 : current evidence options for scale-up and an assessment of resources needed. ECDC Tech Rep. 2020: 1-9.
22. Adeyinka A, Bailey K, Pierre L, Kondamudi N. COVID 19 infection: Pediatric perspectives. J Am Coll Emerg Physicians Open. 2021 Jan 29; **2**(1): e12375. doi: 10.1002/emp2.12375.
23. Cori A, Ferguson NM, Fraser C, Cauchemez S. A new framework and software to estimate time-varying reproduction numbers during epidemics. Am J Epidemiol. 2013 Nov 1; **178**(9): 1505-12. doi: 10.1093/aje/kwt133. Epub 2013 Sep 15.
24. Alimohamadi Y, Taghdir M, Sepandi M. Estimate of the Basic Reproduction Number for COVID-19: A Systematic Review and Meta-analysis. J Prev Med Public Health. 2020 May; **53**(3): 151-7. doi: 10.3961/jpmph.20.076. Epub 2020 Mar 20.
25. Breban R, Vardavas R, Blower S. Theory versus data: how to calculate R0?. PLoS One. 2007 Mar 14; **2**(3): e282. doi: 10.1371/journal.pone.0000282.
26. Ministero della Salute. Nuovo coronavirus. 2021.
27. Kuttiatt VS, Abraham PR, Menon RP, Vaidya PC, Rahi M. Coronavirus disease 2019 in children: Clinical & epidemiological implications. Indian J Med Res. 2020 Jul & Aug; **152**(1 & 2): 21-40 10.4103/ijmr.IJMR_977_20.
28. Willeit P, Krause R, Lamprecht B, et al. Prevalence of RT-qPCR-detected SARS-CoV-2 infection at schools: First results from the Austrian School-SARS-CoV-2 prospective cohort study. Lancet Reg Health Eur. 2021 Jun; **5**: 100086. doi: 10.1016/j.lanepe.2021.100086. Epub 2021 Mar 23.
29. Riley S, Walters CE, Wang H, et al. REACT-1 round 7 updated report: regional heterogeneity in changes in prevalence of SARS-CoV-2 infection during the second national COVID-19 lockdown in England. medRxiv 2020 Dec 16. preprint doi: https://doi.org/10.1101/2020.12.15.20248244.
30. Riley S, Wang H, Eales O, et al. REACT-1 round 9 final report: Continued but slowing decline of prevalence of SARS-CoV-2 during national lockdown in England in February 2021. medRxiv 2021 Mar 6. preprint doi: https://doi.org/10.1101/2021.03.03.21252856.
31. Fragkou PC, Moschopoulos CD, Dimopoulou D, et al. Performance of point-of care molecular and antigen-based tests for SARS-CoV-2: a living systematic review and meta-analysis [published online ahead of print, 2022 Nov 3]. Clin Micro-

biol Infect. 2022;S1198-743X(22)00542-0. doi:10.1016/j.cmi.2022.10.028
32. Decreto del Presidente della Giunta Regionale 23 dicembre 2021, n. 100. Disposizioni attuative per la prevenzione e gestione dell'emergenza epidemiologica da COVID-19. Ordinanza ai sensi dell'art. 32, comma 3, della legge 23 dicembre 1978, n. 833, in materia di igiene e sanità pubblica. Misure urgenti per contrastare l'incremento della diffusione del contagio. Regione Piemonte BU51S4 23/12/2021.
33. European Centre for Disease Control (ECDC). COVID-19 in children and the role of school settings in COVID-19 transmission. Stockholm: ECDC; 2020.
34. Viner RM, Mytton OT, Bonell C, et al. Susceptibility to SARS-CoV-2 Infection Among Children and Adolescents Compared With Adults: A Systematic Review and Meta-analysis. JAMA Pediatr. 2021 Feb 1; **175**(2): 143-56. doi: 10.1001/jamapediatrics.2020.4573. Erratum in: JAMA Pediatr. 2021 Feb 1; **175**(2): 212.
35. European Centre for Disease Prevention and Control (ECDC). Objectives for COVID-19 testing in school settings - first update. Stockholm: ECDC; 21 August 2020: 19-22.
36. World Health Organization (WHO). Tracking SARS-CoV-2 Variants. World Health Organization; 4 Dec 2021: 1-13. Available on: https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/ [Last accessed: 2022 Aug 8].
37. Xia F, Yang X, Cheke RA, Xiao Y. Quantifying competitive advantages of mutant strains in a population involving importation and mass vaccination rollout. Infect Dis Model. 2021; **6**: 988-96. doi:10.1016/j.idm.2021.08.001. Epub 2021 Aug 8.
38. European Centre for Disease Prevention and Control (ECDC). Assessing SARS-CoV-2 circulation, variants of concern, non-pharmaceutical interventions and vaccine rollout in the EU/EEA, 15th update. Stokholm: ECDC; 10 June 2021.
39. European Centre for Disease Prevention and Control (ECDC). SARS-CoV-2 variants of concern as of 26 January 2023. Available on: https://www.ecdc.europa.eu/en/covid-19/variants-concern.
40. Kenney PO, Chang AJ, Krabill L, Hicar MD. Decreased Clinical Severity of Pediatric Acute COVID-19 and MIS-C and Increase of Incidental Cases during the Omicron Wave in Comparison to the Delta Wave. Viruses. 2023 Jan 7; **15**(1): 180. doi:10.3390/v15010180
41. Al-Hosani F, Al-Mazrouei S, Al-Memari S, Al-Yafei Z, Paulo MS, Koornneef E. A Review of COVID-19 Mass Testing in the United Arab Emirates. Front Public Health. 2021 May 12; **9**: 661134. doi: 10.3389/fpubh.2021.661134.
42. Irfan O, Li J, Tang K, Wang Z, Bhutta ZA. Risk of infection and transmission of SARS-CoV-2 among children and adolescents in households, communities and educational settings: A systematic review and meta-analysis. J Glob Health. 2021 Jul 17; **11**: 05013. doi: 10.7189/jogh.11.05013.
43. Yoon Y, Kim KR, Park H, Kim S, Kim YJ. Stepwise School Opening and an Impact on the Epidemiology of COVID-19 in the Children. J Korean Med Sci. 2020 Nov 30; **35**(46): e414. doi: 10.3346/jkms.2020.35.e414.

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