



SARS-CoV-2 transmission patterns in educational settings during the Alpha wave in Reggio-Emilia, Italy

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ABSTRACT

Different monitoring and control policies have been implemented in schools to minimize the spread of SARS-CoV-2. Transmission in schools has been hard to quantify due to the large proportion of asymptomatic carriers in young individuals. We applied a Bayesian approach to reconstruct the transmission chains between 284 SARS-CoV-2 infections ascertained during 87 school outbreak investigations conducted between March and April 2021 in Italy. Under the policy of reactive quarantines, we found that 42.5% (95%CrI: 29.5–54.3%) of infections among school attendees were caused by school contacts. The mean number of secondary cases infected at school by a positive individual during in-person education was estimated to be 0.33 (95%CrI: 0.23–0.43), with marked heterogeneity across individuals. Specifically, we estimated that only 26.0% (95%CrI: 17.6–34.1%) of students and school personnel who tested positive during in-person education caused at least one secondary infection at school. Positive individuals who attended school for at least 6 days before being isolated or quarantined infected on average 0.49 (95%CrI: 0.14–0.83) secondary cases. Our findings provide quantitative insights on the contribution of school transmission to the spread of SARS-CoV-2 in young individuals. Identifying positive cases within 5 days after exposure to their infector could reduce onward transmission at school by at least 30%.

1. Introduction

In the first two years of the COVID-19 pandemic, distance learning and reactive class closures have been extensively implemented in a variety of high-income countries to counter the spread of SARS-CoV-2 (Manica et al., 2021). Large outbreaks among school-age children have been reported in different countries (Manica et al., 2022a;

Stein-Zamir et al., 2020; Vardavas et al., 2022), and ad-hoc monitoring of the transmission during in-person education revealed a non-negligible proportion of secondary cases linked to school contacts (Vardavas et al., 2022; Tonon et al., 2021; Larosa et al., 2020; Meuris et al., 2021; Gamboa Moreno et al., 2021; Kremer et al., 2022; van Iersel et al., 2023; Pray et al., 2020; Peetluk et al., 2021; Macartney et al., 2020). Data from US and Sweden highlighted an increased risk of infection and

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COVID-19-related outcomes among people living with a child or a teacher attending school in person (Lessler et al., 2021; Vlachos et al., 2021), suggesting that SARS-CoV-2 transmission in educational settings should not be underestimated.

A variety of policies have been implemented across countries to monitor the viral spread in schools. These ranged from antigen or PCR testing of symptomatic individuals and close contacts of confirmed cases to regular screening using lateral flow device tests or salivary PCR tests applied to all students and school personnel, irrespectively of the observed cases (Kremer et al., 2022; Leng et al., 2022; Colosi et al., 2023). However, testing only symptomatic individuals was found to underestimate true positivity rates at schools (Kremer et al., 2022), and several studies have shown that symptom-based surveillance would likely miss a large share of infections in children (Liu et al., 2022; Poletti et al., 2021; Gettings et al., 2022).

A quantitative assessment of SARS-CoV-2 transmission in schools remains challenging, due to the relatively low likelihood of developing COVID-19 symptoms in young individuals (Meuris et al., 2021; Poletti et al., 2021; Levin et al., 2020), temporal changes in the policies implemented to counter the viral spread in schools (Manica et al., 2022a; Kremer et al., 2022), and the difficulties of monitoring systems and testing procedures in tracking the real number of infections in educational settings (Manica et al., 2022a; Tonon et al., 2021; Larosa et al., 2020; Meuris et al., 2021; Gamboa Moreno et al., 2021; Auger et al., 2022; Bilinski et al., 2022).

Previous studies have analyzed the contribution of open schools to the spread of SARS-CoV-2 by fitting mechanistic transmission models to aggregated data (e.g., observed prevalence of cases in students) (Leng et al., 2022; Colosi et al., 2023; Liu et al., 2022; Colosi et al., 2022), or by leveraging epidemiological links between confirmed SARS-CoV-2 infections in schools as identified from close contacts reported by each case (Manica et al., 2022a; Gettings et al., 2022). The likelihood of in-school transmission has also been investigated by analyzing phylogenetic relations inferred from whole-genome sequencing of positive samples, which could be used to determine transmission clusters (Kremer et al., 2022; Gettings et al., 2022), to estimate the secondary attack rate in schools (Kremer et al., 2022; Gettings et al., 2022), and to derive epidemiological links associated with maximum likelihood phylogenetic trees (Kremer et al., 2022).

Difficulties in identifying individual transmission events rise from positive individuals reporting more than one potential infector (Manica et al., 2022a; Kremer et al., 2022; Gettings et al., 2022), underreporting of cases in the considered population (Manica et al., 2022a; Kremer et al., 2022; Liu et al., 2022; Poletti et al., 2021; Gettings et al., 2022), and the lack of reliable data on the time of exposure(s) for positive individuals (Manica et al., 2022a).

A promising approach to quantify SARS-CoV-2 transmission across different settings is to probabilistically estimate transmission events in a Bayesian framework, by accounting for individuals' exposures to potential infectors as identified by public health officials, for the presence of non-infectious contacts, and for the generation interval between confirmed cases using data augmentation (Meuris et al., 2021; Kremer et al., 2022; Manica et al., 2023, 2022b).

In this study, we applied a Bayesian approach to reconstruct the transmission chains (who infected whom) between 284 SARS-CoV-2 positive individuals ascertained during 87 epidemiological investigations of clusters involving school children and personnel. The data was collected between March and April 2021 in the province of Reggio Emilia, Italy, when the Alpha variant was predominant in the population. We estimated the proportion of infections among students and school personnel that is attributable to contacts in schools and the average number of secondary cases infected by a positive individual during in-person education, therefore providing quantitative insights on SARS-CoV-2 transmission patterns in school facilities. The analysis encompasses several educational levels: daycare centers (<3 years of age), kindergartens (3–5 years), elementary schools (6–10 years), middle

schools (11–13 years), and high schools (14–19 years).

The strengths of this study rely on the solid approach used to infer likely transmission events occurred in school, the larger number of confirmed infections in children analyzed compared to other studies, the assessment of transmission risks before substantial vaccination had taken place in the school-aged population, and the minimization of the risks of bias in the identification of infections in the analyzed sample. Specifically, in the considered population, surveillance and control policies at school did not change during the study period and case contacts were identified and tested irrespectively of their clinical signs and of the number of ascertained secondary cases in schools. Implications of partial sampling of SARS-CoV-2 infections in school was also considered.

2. Methods

2.1. Study population

This study focuses on SARS-CoV-2 confirmed infections in both private and public schools and their identified contacts. The data was collected between March 1 and April 30, 2021 in the Italian province of Reggio Emilia (Northern Italy, Emilia-Romagna region, around 524,000 inhabitants, of which about 98,000 (19%) aged 0–19 years (Istituto Nazionale di Statistica, 2022)). According to genomic surveys data, during the study period, the Alpha variant accounted for more than 90% of SARS-CoV-2 infections in the considered population (Manica et al., 2023). Distance learning was imposed by national laws on all educational levels except daycare centers (i.e., where toddlers <3 years of age are cared for during the day while parents are at work) and kindergartens between March 2 and March 14, 2021, and extended to all levels between March 15 and April 6, 2021 (Ministero della Salute, 2021; Regione Emilia-Romagna, 2021a, 2021b) (see Fig. 1). Throughout the study period, compulsory masking was imposed during in-person education in all educational levels, except daycare centers and kindergartens. Additional measures were implemented in elementary, middle, and high schools to promote physical social distancing, including the use of single desks at least one meter apart from each other along with lunch breaks held on the single desks. For all school levels, temporal and spatial pathways were created for the different classes (i.e., groups of students attending the same set of lessons throughout the year) to minimize crowding at the different school entrances and exits (Larosa et al., 2020).

When in-person education was allowed, a reactive class quarantine protocol based on active surveillance of students was in place (Regione Emilia-Romagna, 2021a, 2021b). Specifically, laboratory-based antigen or Polymerase Chain Reaction (PCR) testing was mandatory for all individuals showing COVID-like symptoms. As soon as one student tested positive for SARS-CoV-2 (either antigen or PCR), a 14-day quarantine and PCR testing was imposed on all close contacts at school, defined as individuals (students or school personnel) who attended the same class or any activity conducted in the school with a SARS-CoV-2 confirmed infection up to 48 h before symptom onset or positive swab if asymptomatic (Djuric et al., 2022; Regione Emilia-Romagna 2021b). School personnel was not required to quarantine when showing a negative PCR test result. As soon as a teacher tested positive for SARS-CoV-2, distance learning was imposed on all their students until presenting a negative PCR test result.

Outside schools, isolation of infections ascertained in the general population, contact tracing, and testing of case contacts were in place throughout the study period (Manica et al., 2023). Positive individuals were isolated for a maximum of 21 days; isolation could be terminated earlier with a negative PCR result obtained no earlier than 14 days since the start of isolation. Close contacts of positive individuals were tested and quarantined for 10 days if they had a negative PCR test result at that date, or for 14 days without testing.

In Italy, COVID-19 vaccination started on December 27, 2020, and

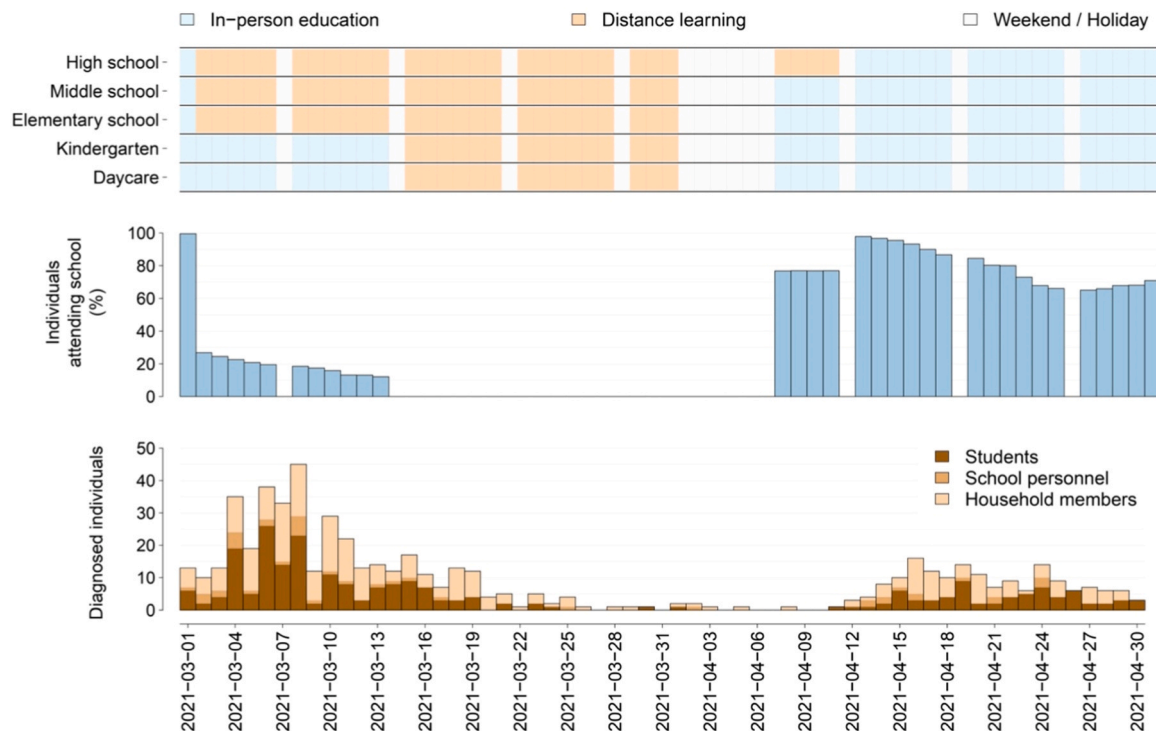


Fig. 1. Periods of in-person education (light blue) and distance learning (orange) for the different school levels in Reggio Emilia during the study period are shown in the top panel. Weekends and Easter holidays are represented in white. The middle panel shows the estimated overall percentage of individuals in the data (including negative individuals exposed to ascertained infections) attending school in person over time. Changes in the attending rate during in-person education are mainly driven by reactive quarantines at school. The bottom panel shows the cumulative number of individuals diagnosed with SARS-CoV-2 during outbreak investigations over time, stratified by students, school personnel, and their household members.

was not extended to children aged 12–15 years until June 2021 (AIFA, 2021a), and to children aged 5–11 years until December 2021 (AIFA, 2021b). Therefore, as of April 30, 2021 (the last date of our study period), less than 1% of individuals younger than 20 years of age were vaccinated in the Emilia-Romagna region (see eTable 1 in the Supplement). In the region, vaccination of school personnel started on February 22, 2021 (Ministero dell’Istruzione, 2021).

2.2. Data

Data on SARS-CoV-2 epidemiological investigations involving schools were routinely collected in 2021 as part of surveillance activities conducted in the province of Reggio Emilia. We analyzed data from 87 school outbreak investigations that occurred between March and April 2021, and that were associated with at least two SARS-CoV-2 infections confirmed via antigen or PCR testing in the same class or among individuals attending a specific activity conducted in the school.

Analyzed data included epidemiological records collected from 284 SARS-CoV-2 confirmed positive individuals among students and school personnel and their close contacts at school, covering five different school levels: daycare centers (<3 years of age), kindergartens (3–5 years), elementary schools (6–10 years), middle schools (11–13 years), and high schools (14–19 years). Information on the age, date of diagnosis, dates of negative tests, attended school level (if any), vaccination status, and dates of vaccine administration (if any) was collected for confirmed positive individuals. The date of symptom onset was collected for symptomatic cases. Multiple test results were available for the same individual because all case contacts identified in schools were tested both at the start and at the end of reactive quarantines in school. Tests were repeated for negative contacts with symptom onset within the quarantine period and for individuals reporting a contact with a positive case outside the school setting. Consecutive diagnosis dates between all confirmed infections within the same outbreak investigation were no

further than 12 days apart.

For approximately 40% of positive students and school personnel, their household was identified as the potential setting of infection. For these individuals, test results and vaccination status at the time of the outbreak investigation for their household members were also recorded. Individuals involved in the outbreak investigation were classified either as students, school personnel, or as individuals not attending school (e.g., household members of a student/school personnel). Individual records were available for all positive individuals involved in the outbreak investigation (284 individuals). The total number of school case contacts who were tested during an outbreak investigation was also provided. Students and school personnel who attended lessons with one confirmed infection or who had contact with a confirmed infection attending a specific activity conducted in the school were all considered school contacts. No individual information was available for the school contacts who tested negative for SARS-CoV-2 infection during the outbreak investigation (1267 individuals). Local health authorities collected data in a centralized database as part of the COVID-19 response activities, which were provided in anonymized form. Only one outbreak (7 positive cases) was discarded from the original data due to incomplete information on positive close contacts recorded at school.

2.3. Modeling SARS-CoV-2 transmission chains

Transmission chains between positive individuals were reconstructed via a Bayesian inference model, adapted from a similar approach previously applied to household contact tracing data (Manica et al., 2023, 2022b). The model exploits the temporal information on SARS-CoV-2 infections recorded in the dataset to probabilistically identify, for every case, the likely source of infection (from outside the school or from a specific school contact). To do this, we mechanistically modeled the force of infection exerted within the school on each individual over time, taking into account school closures implemented

because of tiered restrictions and reactive quarantines that occurred at school during each outbreak (see Figs. 1 and 2). The incidence of cases recorded in the general population was used to define the force of infection exerted on each individual outside the school. Available information on the vaccination history of individuals was considered to define their likelihood of getting infected after exposure and their contribution to onward transmission at school (see the Supplement for further details). The relative susceptibility of vaccinated individuals was assumed to be 50.8% 14 days after their first dose, and 18.1% 14 days after the second dose (Manica et al., 2023); we assumed that the infectiousness of breakthrough infections was reduced by 50% (Harris et al., 2021). Due to the lack of data and the negligible vaccination coverage among young individuals during the study period, negative school contacts were assumed to be unvaccinated. For each positive and symptomatic individual, the date of infection was imputed using the incubation period estimated for the Alpha variant in Italy (Manica et al., 2023). Following the same approach adopted in (Manica et al., 2023), the delays between the imputed infection date and the diagnosis of symptomatic cases were used to estimate a diagnostic delay distribution, which was employed for the imputation of the dates of infection of asymptomatic individuals. To account for uncertainty in infection dates, we re-sampled the set of imputed infection times for each ascertained infection 100 times. The generation time was assumed to follow a gamma distribution. Full information on the model is reported in the Supplement. In the baseline analysis, the likely source of infection was reconstructed only for students and school personnel, considering as a potential infector either a specific school attendee identified during the outbreak investigation or a generic contact occurring outside the school.

Model parameters were estimated via Markov Chain Monte Carlo (MCMC). For each set of imputed infection times, a separate MCMC was run with 50,000 iterations. Samples from the resulting posteriors were pooled together to obtain the final parameter distribution, and to estimate the likely source of infection of ascertained cases and the number

of secondary cases infected by positive individuals among school contacts. To assess heterogeneity in transmission, we fitted a negative binomial distribution to the estimated number of secondary cases infected by each positive individual. Results are presented in terms of average values and 95% credible intervals (CrI), computed over 50,000 reconstructed transmission chains (500 for each of the 100 sets of imputed infection times). The reconstruction of likely transmission chains was performed using a code developed ad-hoc by our team in the programming language C, available at <https://doi.org/10.5281/zenodo.8139018>.

2.4. Sensitivity analyses

We conducted two sensitivity analyses to include the available information on positive and negative household members of students and school personnel. In sensitivity analysis (a), we considered only school attendees with complete information on their household members (440 data records, see eTable 2), explicitly accounting for transmission events occurred between cohabiting individuals. In this case, information on the negative school exposures was not included due to the lack of sufficient data for these individuals. In sensitivity analysis (b), we considered all school attendees (either positive or negative) and their household members when reported, therefore including all records available in our data (1876 data records). The baseline analysis and the sensitivity analyses (a) and (b) were repeated to account for possible under-ascertainment of infections at schools (sensitivity analyses (c), (d), and (e)), considering the possibility of missing the detection of up to a maximum of five generations in the transmission chains (see eFigure 3 in the Supplement). Sensitivity analysis (f) was conducted by assuming that the school personnel was not quarantined after the diagnosis of a positive student. Sensitivity analysis (g) was performed by assuming that the school generation time follows the distribution of the generation time estimated from household data in (Manica et al., 2023), instead of

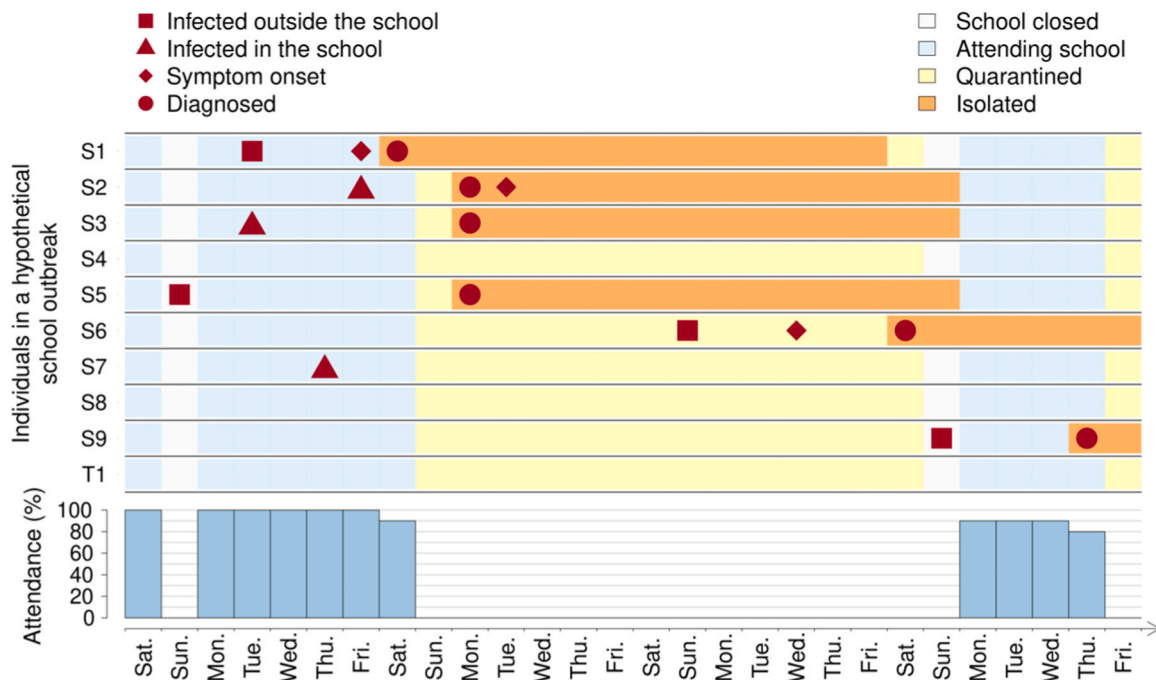


Fig. 2. Schematic representation of a hypothetical outbreak in school. Each row corresponds to a specific individual (either student S1-S9 or school personnel T1). The time of infection, symptom onset (if any), and diagnosis (if any) are indicated for each individual in red (triangles and squares indicate transmission occurring within and outside the school, respectively). For each individual, the attendance (blue), isolation (orange), and quarantine (yellow) periods are shown. Specifically, we assumed that each positive individual is isolated for 14 days starting from their date of diagnosis, and that 14 days of quarantine are imposed on school attendees involved in the same outbreak investigation the day after the first diagnosed infection in the school. Days of school closures are shown in white. The resulting daily percentage of individuals attending school among the involved school attendees, as computed for this illustrative case, is represented by the blue bars displayed in the bottom panel.

estimating the school generation time from inferred transmission links. Finally, additional sensitivity analyses were conducted to explore the impact of assuming no reduced transmissibility of breakthrough infections (h), a 50% lower protection against the infection provided by vaccination compared to our baseline assumption (i), and a different scaling factor for school transmission in daycare centers and kindergartens to reflect differences in social distancing measures implemented in young children and toddlers compared to higher educational levels (j). Full details are provided in the Supplement.

3. Results

3.1. Descriptive statistics

The dataset provided information collected during 87 school outbreak investigations, counting a cumulative number of 562 individuals who tested positive for SARS-CoV-2, 1267 individuals exposed at school and never testing positive, and 47 records of household members of school attendees who remained negative throughout the study period. Out of the 562 ascertained infections, 284 (50.5%) positive individuals were identified as students or school personnel. The information on the household members was available for 115 individuals regularly attending school (115/284, 40.5%). The mean number of individuals exposed to potential SARS-CoV-2 infection at school per outbreak was 17.8 (IQR: 15–20). The mean number of positive cases detected in each outbreak investigation, including household members when reported, was 6.5 (IQR: 4–8). The mean number of positive cases identified among school attendees per outbreak was 3.4 (IQR: 2–4). The average attack rate at school (i.e., the proportion of students/school personnel who resulted positive to SARS-CoV-2 from testing conducted during a school outbreak investigation) was 19.5% (IQR: 13.3–25.8%). Details on the analyzed data are reported in Table 1. Periods of in-person

Table 1
Description of the school attendees involved in the outbreak investigations.

Individuals Tested Positive For SARS-CoV-2 At School	
Total	284
Students	241 (84.9%)
School personnel	43 (15.1%)
Symptomatic:	
Students	145 (60.2%)
School personnel	38 (88.4%)
Gender:	
Male	143 (50.4%)
Female	141 (49.6%)
Age:	
0–2 years old	12 (4.2%)
3–5 years old	55 (19.4%)
6–10 years old	57 (20.1%)
11–13 years old	56 (19.7%)
14–19 years old	63 (22.2%)
20–39 years old	16 (5.6%)
40–60 years old	25 (8.8%)
School level:	
Daycare center	20 (7.0%)
Kindergarten	71 (25.0%)
Elementary school	68 (23.9%)
Middle school	61 (21.5%)
High school	64 (22.5%)
Vaccination status as of April 30, 2021:	
Received 1 dose only	25 (8.8%)
Received 2 doses	7 (2.5%)
Received 3 doses	0
NEGATIVE EXPOSURES IDENTIFIED AT SCHOOL	
Total	1267
Daycare center	85 (6.7%)
Kindergarten	259 (20.4%)
Elementary school	348 (27.5%)
Middle school	299 (23.6%)
High school	276 (21.8%)

education across different school levels during our study period are summarized in Fig. 1, along with our estimates of the percentage of students attending school over time as resulting from school closures and reactive quarantines at school, and with the number of diagnosed cases over time stratified by students, school personnel, and household members.

3.2. School generation time and likely source of infection of school attendees

From the Bayesian reconstruction of likely transmission chains, we estimated a mean generation time of 4.6 days (95%CrI: 1.9–8.4 days; eFigure 4 in the Supplement). Considering only individuals who were attending school in person and that were infected during school days, we estimated that school related contacts were their likely source of infection in 42.5% (95%CrI: 29.5–54.3%) of cases (see Fig. 3A). Consistent results were obtained across different sensitivity analyses (see Fig. 3A and eFigure 4 in the Supplement). According to our baseline analysis, no significant differences were found in the contribution of school contacts to the infection of students and school personnel, nor across different school levels (see Fig. 3B). However, an average lower contribution of school contacts to the infection was estimated for school personnel compared to students, possibly due to reduced proximity and duration of their social interactions. Estimates obtained in sensitivity analyses (c), (d), and (e) suggested that the probability of identifying an infected individual in school was 0.98 (95%CrI: 0.92–1), 0.72 (95%CrI: 0.42–0.98), and 0.98 (95%CrI: 0.94–1), respectively.

3.3. Onward transmission in school and timeliness of reactive quarantines

Our findings highlighted that a relatively low fraction of SARS-CoV-2 infections among school attendees caused onward transmission at school. According to our estimates, only 26.0% (95%CrI: 17.6–34.1%) of students and school personnel who tested positive during in-person education and who spent at least one day at school between infection and diagnosis, infected one or more school contact (see Fig. 4A). The number of secondary cases infected by positive individuals at school was estimated to follow a negative binomial distribution with shape parameter 0.80 (95%CrI: 0.19–2.52), resulting in a strong heterogeneity in transmission with 20% of positive students infecting 82.5% (95%CrI: 66.0–100%) of ascertained cases (Fig. 4A). The average number of secondary cases infected by a positive individual at school during in-person education was estimated to be 0.33 (95%CrI: 0.23–0.43, see Fig. 4B). Consistent results were obtained across different sensitivity analyses (see Fig. 4C). No significant differences were found across school levels (Fig. 4B).

Our estimates suggest that, when in-person education was allowed, 90.8% (95%CrI: 88.8–92.8%) of positive individuals among students and school personnel attended school for at least 1 day after infection and before being isolated or quarantined (Fig. 4D); 50.7% (95%CrI: 46.0–55.0%) attended school for more than 3 days after their infection, and 24.8% (95%CrI: 20.9–29.2%) attended for 6 days or more. By separately computing the number of secondary infections for individuals who attended school for 1–2 days, 3–5 days, or 6 days or more after their infection, we found that the heterogeneity in the transmission at schools is markedly driven by the delays in the identification of positive individuals (see Fig. 4E). We estimated that only 7.8% (95%CrI: 2.3–18.6%) of individuals attending school for only 1 or 2 days caused onward transmission in the school, with an average number of secondary infections of 0.29 (95%CrI: 0.13–0.54) (see Fig. 4F). We found that 45.9% (95%CrI: 20.9–65.1%) of positive individuals attending school for at least 6 days before being diagnosed caused at least one infection among school attendees, with an estimated average number of secondary infections of 0.49 (95%CrI: 0.14–0.83). Under reactive quarantines, the number of secondary cases infected by SARS-CoV-2 infections confirmed within 5 days after exposure to their infector was 30–40%

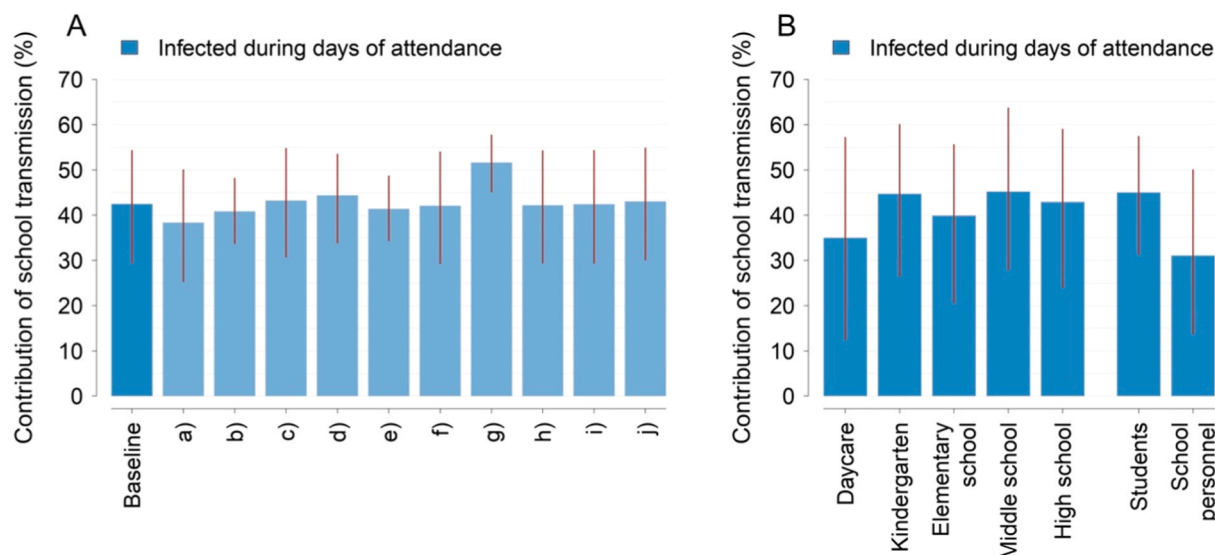


Fig. 3. Panel A shows the estimated percentage of positive students/school personnel who got infected as a result of contact with positive individuals attending school (bars represent mean model estimates; whiskers represent 95%CrI) as obtained for the baseline model and for the different sensitivity analyses (a: considering only data on confirmed infections among students and school personnel with information on their household members; b: considering all school contacts and household members when reported; c, d, and e: repetition of the baseline analysis and sensitivities (a) and (b), but accounting for possible under-ascertainment of infections at school; f: school personnel not quarantined; g: generation time taken from the literature instead of estimated from the transmission chain reconstruction; h: breakthrough infections assumed as infectious as unvaccinated infected individuals; i: vaccine effectiveness against the infection is 50% reduced compared to values assumed in the baseline scenario; j: a different scaling factor is assumed for the transmission in daycare centers and kindergartens compared to higher grades). Panel B shows the same quantity estimated under the baseline assumptions, stratified by school levels and by the status of the infectee (student or school personnel).

lower compared to other school attendees.

4. Discussion and conclusions

We analyzed data collected through epidemiological investigations of 87 potential school outbreaks of SARS-CoV-2 occurred in Italy between March 1 and April 30, 2021, when the Alpha variant was dominant. By reconstructing likely transmission chains, we investigated the spread of SARS-CoV-2 in educational settings. We found that almost half of the individuals who got infected on a day when they attended school were likely infected as a consequence of school related contacts. This estimate may represent the contribution of in-person education to the SARS-CoV-2 transmission among students and school personnel during the Alpha wave in Italy. Under reactive quarantines, and consistent with previous estimates obtained under different policies and epidemiological conditions (Tonon et al., 2021; Gamboa Moreno et al., 2021; Gettings et al., 2022; Alonso et al., 2022), we found that about 26% of students and school personnel infected during in-person education caused onward transmission. The average number of secondary cases caused by positive individuals at school during in-person education was estimated to be 0.33, in the same range (0.27–0.4) as estimated by other studies (Mossong et al., 2021; Bilinski et al., 2021), but slightly lower than previous estimates (mean: 0.5) from a school outbreak with over 80 positive students occurred in Lombardy in early 2021 (Manica et al., 2022a). Our results confirmed previous findings on the strong heterogeneity characterizing onward transmission of SARS-CoV-2 (Manica et al., 2022a; Macartney et al., 2020; Tupper and Colijn, 2021; Laxminarayan et al., 2020; Miller et al., 2020; Chen et al., 2021), highlighting that part of the heterogeneity observed at school may derive from the heterogeneity in diagnostic delays after infection.

Model results should be interpreted in light of the following conditions and limitations. Our estimates refer to school transmission that occurred during the Alpha wave, when the vaccination coverage in young individuals was negligible, compulsory masking was in place for elementary schools and higher grades, and reactive class quarantines and isolation of diagnosed infections were implemented. As such,

caution is advised when generalizing our results to consider the potential spread of SARS-CoV-2 under different epidemiological conditions. Our estimates suggest that, during the Alpha wave in Italy, identifying positive cases within 5 days after exposure to their infector could have reduced onward transmission in school by 30–40%. During the analyzed period, immediate testing of all household contacts of cases was in place, and backward tracing of contacts was applied to household members testing positive for SARS-CoV-2. This allowed the identification of many asymptomatic cases among young individuals at their early stage of infection (Djuric et al., 2022). Such a policy likely contributed to the reduction of SARS-CoV-2 transmission in schools, by increasing the ability of the public health system to identify potential school clusters. When accounting for potential under-ascertainment of infections among school contacts (sensitivity analyses (c), (d), and (e)) a slightly higher number of secondary cases per primary case was estimated (see Figs. 3A and 4C). These results are in line with previous studies showing that repeated mass testing in educational settings alongside isolation of close contacts has the potential to markedly reduce transmission risks in open schools (Leng et al., 2022; Colosi et al., 2023; Liu et al., 2022). While lifting compulsory masking in schools would be associated with an increased risk of infection for students and staff (Cowger et al., 2022; Science et al., 2022), vaccination of young individuals could significantly reduce the transmission of SARS-CoV-2 in educational settings (Colosi et al., 2022). Analyzed data consist of records collected in schools where ≥ 2 positive cases were detected. This means that we might have overestimated the chance of transmission in schools as our estimates are not informed by outbreak investigations revealing only one infection among tested students and school personnel (~60% of school outbreak investigations conducted during the study period (Djuric et al., 2022)). Despite the use of reliable data and solid statistical methods to infer likely transmission events, it is challenging to determine whether a person became infected in school or due to contacts occurring in the community as a direct result of schools being open (e.g., schoolmates using the same public transport). More in general, our results do not provide any indication of the overall contribution of in-person education to the spread of COVID-19 in the general

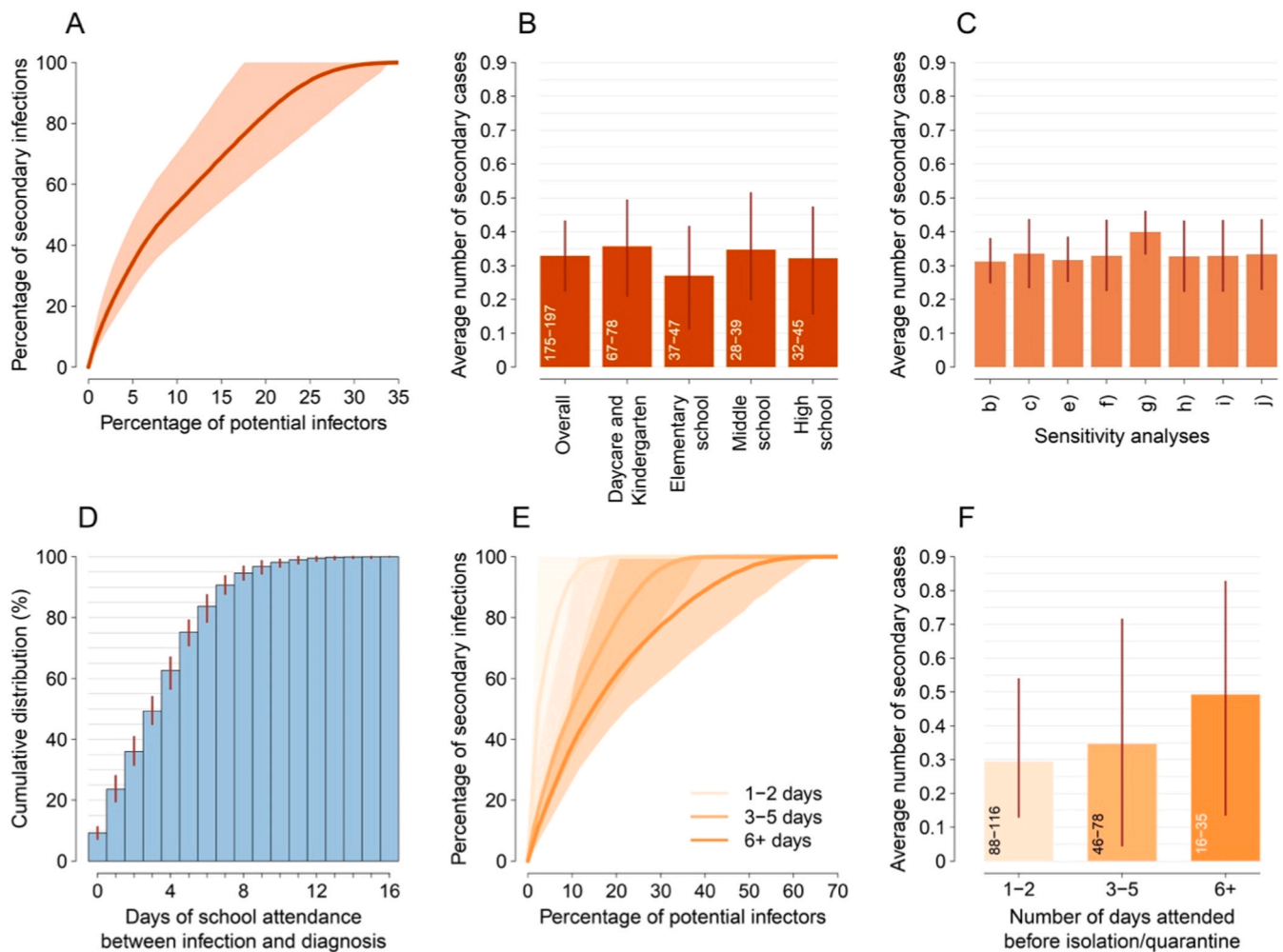


Fig. 4. Panel A shows the cumulative percentage of secondary infections due to school contacts caused by individuals who were either infected or diagnosed during in-person education and attended for at least one day after infection. Potential infectors are ordered from those who infected the largest number of secondary cases at school to those who did not infect any secondary case at school. Panel A shows that 26.0% of all potential infectors infected 100% of the secondary cases. The solid line represents the mean model estimate; the shaded area represents 95%CrI. Panel B represents the number of secondary cases caused at school by one infectious individual during in-person education, overall and stratified by school level. Bars represent mean model estimates; whiskers represent 95%CrI; displayed numbers represent the range of the number of potential infectors used for computing the number of secondary cases, which may change across reconstructed transmission chains. Panel C represents the number of secondary cases caused at school by one infectious individual during in-person education as obtained in the sensitivity analyses including complete information on the school-attending individuals (b: considering all school contacts and household members when reported; c and e: repetition of the baseline analysis and sensitivity (b), but accounting for possible under-ascertainment of infections at school; f: school personnel not quarantined; g: generation time taken from the literature instead of estimated from the transmission chain reconstruction; h: breakthrough infections assumed as infectious as unvaccinated infected individuals; i: vaccine effectiveness against the infection is 50% reduced compared to values assumed in the baseline scenario; j: a different scaling factor is assumed for the transmission in daycare centers and kindergartens compared to higher grades). Panel D shows the cumulative distribution of the number of days attending after infection and before isolation or quarantine among individuals that got infected or diagnosed during in-person education. Panel E shows the cumulative percentage of secondary infections due to school contacts caused by positive individuals who attended school for 1–2 days, 3–5 days, or 6 days or more after their infection and before isolation or quarantine. The figure shows that only 7.8% of positive individuals who attended school for 1–2 days infected a secondary case after their infection and before isolation or quarantine; similarly, only 27.6% of positive individuals who attended school for 3–5 days after their infection and before isolation or quarantine, and 45.9% of positive individuals who attended school for 6 days or more after their infection and before isolation or quarantine infected at least one secondary case. Panel F represents the number of secondary cases caused at school by one infectious individual during in-person education, stratified by the number of days they attended school before isolation or quarantine.

community. Finally, due to the lack of data, pre-existing immunity of individuals acquired from natural infection, and possible delays in class closures after notification of a case were not considered in our model.

Despite these limitations, the conducted analysis provides quantitative estimates of the potential spread of SARS-CoV-2 in educational environments during the Alpha wave in Italy. Solid estimates of the potential transmission of SARS-CoV-2 in schools are key to designing adequate surveillance and control protocols to reduce the risk of infection of students and school personnel, the loss of school days due to infection, and the potential spillover of cases in the general community.

Our findings suggest that in the absence of reactive class quarantines, transmission in schools would have resulted in approximately 0.5 secondary cases infected on average by each positive individual, while timely diagnoses of SARS-CoV-2 infections at school had the potential of reducing the number of secondary cases caused by school transmission by at least 30%. Furthermore, the school generation time was found to be shorter than the one identified from household data (Manica et al., 2023) (means: 4.6 vs 7.1 days), possibly due to the different age groups involved and consistent with the reduced opportunities of transmission determined by reactive quarantines in schools.

Consent for publication

Not applicable.

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Ethical statement

The collection of data used for this manuscript (surveillance and contact tracing data) is compulsory in Italy according to national laws on infectious diseases. The COVID-19 Italian National Working group on Bioethics has stated that consensus for the collection of this data in the context of the COVID-19 emergency is not mandatory (Rapporto ISS COVID-19 n. 34/2020), based on Guideline 12 of the WHO on ethical issues in public health surveillance. The legal ordinance n. 640 of February 28 2020, explicitly declares Istituto Superiore di Sanità as entitled to collect data for COVID-19 surveillance and contact tracing and that such data can be used and shared, upon anonymization, to advance scientific knowledge on this new disease.

CRedit authorship contribution statement

PPo, PPe, MA, PGR and SM conceived and supervised the study. CMG and PPo wrote the first draft of the manuscript. CMG wrote the code and performed the analyses. PM, MV, FV, OD, EB, EL, SC, MTC, PGR collected the epidemiological data. CMG, MM, GG, VM, AZ, VdA, FT, PPe, MA, PGR, SM and PPo interpreted results. All authors read, reviewed, and approved the final version and the submission of the manuscript. The corresponding author had final responsibility for the decision to submit for publication.

Declaration of Competing Interest

MA has received research funding from Seqirus. The funding is not related to COVID-19. All other authors declare no competing interest.

Data Availability

Data will be made available on request.

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Not applicable.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at [doi:10.1016/j.epidem.2023.100712](https://doi.org/10.1016/j.epidem.2023.100712).

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