

Project SEROCoVPOP-Schools

Final scientific report

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Assessing SARS-CoV-2 transmission dynamics within primary schools and day-care centers in the canton of Geneva: an epidemiological, virological and serological study

FINAL SCIENTIFIC REPORT: 29.11.2022 (updated on 13.12.2022)

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Abstract

The SEROCov-Schools study aimed to describe the transmission dynamics of SARS-CoV-2 infections in elementary schools and day-care centers and to assess the risk of introduction of the virus into children's households. To this end, we set up a prospective surveillance study involving two schools and three day-care centers in the canton of Geneva, i.e. 24 classes of children aged 1-2 to 6-7 years accompanied by their educational teams and their family members, for a total of more than 400 participants. By combining epidemiological, virological and serological data, we have shown the rapid spread of SARS-CoV-2 infections in institutions (child-to-child and child-to-adult transmission), and the introduction of the virus into households (including vaccinated parents), more markedly with each new variant. Young children are therefore an important source of extra-familial infections and play a crucial role in community transmission. They are a potential reservoir of the disease now that the majority of the adult and adolescent population is vaccinated.

Project background (based on scientific evidence available at the end of 2020)

The clinical presentation of SARS-CoV-2 infection differs between children and adults, with sub-clinical and mild illness being much more common in children (less than 10 years of age) (1-3). Only a minority of children require hospitalisation and the case fatality rate is very low ($\leq 1\%$) (4,5), although a small fraction of children can experience a severe post-infectious multisystem inflammatory syndrome (6).

This has created a perception that children are less susceptible to infection and do not play a substantial role in transmission (7).

Susceptibility to infection:

Despite their value, available clinical and seroprevalence data, as well as confirmed case statistics, do not provide a complete picture of the risk of infection among children. Indeed, during the first wave of the pandemic, **testing was limited**. Children were, and still are, less frequently tested for the virus due to both testing recommendations and the high frequency of mild or asymptomatic infections or atypical symptoms presentation (8,9). This increases the likelihood that index cases in children are missed, and severely limits the ability to determine their role in outbreaks.

Seroprevalence studies conducted in several countries including Switzerland (with a population-based study in the canton of Geneva) reported a lower proportion of children with antibodies against SARS-COV-2 compared to adults (10,11). As these studies were conducted during the lockdown with school closures or shortly after, when viral circulation was low in most countries, these findings could suggest that children are **less susceptible** to infection than adults, but may alternatively reflect shielding and changes in behaviour.

On the other hand, a study conducted between June and July 2020 in the canton of Zurich showed a **similar seroprevalence** between children and adults (12). The gap between children and adults could therefore have narrowed after the lifting of school closures.

Role in transmission:

Children play an important role in the **transmission of many respiratory viral diseases**, including beta-corona viruses. It is known that children are much more affected by common respiratory viruses due to limited prior exposure, immature immune systems, and more frequent physical contacts with others adults and children. Transmission of respiratory viruses like influenza has been well documented within schools (13) and between children and adults within household settings (14,15).

Multiple recent studies report biological data which show that 1) children can reach comparable viral loads as adults at the time of diagnosis and that 2) infectious virus can be isolated from the upper respiratory tract of children with SARS-CoV-2 (16-18). Thus, children may have a **similar shedding pattern** compared to adults, and it would be naïve not to consider them as transmitters. Factors influencing transmission, such as the absence of symptoms and a potential weaker aerosol production due to a smaller lung volume, are hardly studied (17-18).

A study conducted during the summer of 2020 in Germany showed that during periods of low incidence, there was no apparent transmission of the virus among children in day-care centers (19). From September 2020 on, as community transmission grew, **clusters** arose in educational settings catering for children of all ages. Even if the mode of transmission is not clear (adult-to-child, child-to-child and/or child-to-adult transmission), children have a large number of contacts in close contact settings such as childcare centres and schools. Therefore,

children may become a **significant source of extra-household infections** and have the potential to play a role in **community transmission**.

Public health challenges:

Day-care centers and schools play a critical role enabling pupils to receive both academic instruction and provide critical mental health and social support, especially for the most vulnerable ones. It is therefore a priority to keep them open. The **current lack of data on the role of primary schools and day-care centers in the transmission of the virus severely affects science-based public health strategies** to keep schools open while preventing the development of SARS-CoV-2 clusters in schools.

Unanswered questions on transmission and virus shedding also pose a **challenge for testing strategies**, such as now widely available SARS-CoV-2 antigen-based rapid diagnostic tests (RDTs), but also on **vaccination strategies**. The use of antigen-based RDTs is based on the detection of viral antigen, allowing identification of patients with higher viral loads that are most likely in their infectious period. Several validations are becoming available, and the World Health Organisation (WHO) has recently provided a recommendation for the use of such tests (20). If a vaccine is not available for the youngest ones, which is likely over the next months as testing is only now getting started with adolescents (and not even with children), children will likely serve as a reservoir of the virus, making it harder to end the pandemic.

In this study, we propose to **focus on children between 2 and 6 years of age**. Several studies have shown that the susceptibility of older children (and their seroprevalence) is comparable to that of adults (21-23), but younger children have been much less studied. Moreover, for young children social interactions are very important, online learning is difficult to envisage, physical distance cannot be implemented and masks are not systematically used or recommended.

Hypothesis and objectives

Hypothesis:

Although young children may be less susceptible to SARS-CoV-2 infection than older children and adults, their close and prolonged physical contacts with each other and with adults may render them important sources of transmission. Day-care centers and primary schools allow for efficient viral transmission between children, who could then be a vector for introduction into households and into the broader community. The extent to which this happens remains unclear.

Primary Objective:

To describe the transmission dynamics of SARS-CoV-2 infection within primary schools and day-care centers in a convenience sample of schools in the municipality of Geneva, and the risk of introduction of SARS-CoV-2 into the children's households.

Secondary Objectives:

1. To estimate the frequency of young children presenting anti SARS-CoV-2 antibodies at baseline (Work Package 1 [WP1]).

2. To estimate the SARS-CoV-2 infection attack rate among young children and their educators during the school year 2020-2021, during the school year 2021-2022 and over the study period (WP2).
3. To evaluate the classroom outbreak size within classes with a child or an educator who tested positive for SARS-CoV-2 (WP3).
4. To estimate the SARS-CoV-2 attack rate within the households of children who tested positive for SARS-CoV-2 (WP4).
5. To describe the clinical characteristics of children who tested positive for SARS-CoV-2 (WP2).
6. To estimate the infectiousness profile of the participants who tested positive for SARS-CoV-2 antigens (WP5).
7. To investigate chains of transmission within classes or households (WP3, WP4 and WP5).
8. To estimate the number of distinct introductions of SARS-CoV-2 in each class over the study period (WP5).
9. To monitor the circulation of other respiratory viruses among children during 1) the winter 2020/2021 when only non-pharmaceutical measures are in place and during 2) the winter 2021/2022, when a vaccine is widely delivered to the adult/adolescent population but most likely not to children (remaining a potential reservoir for SARS-CoV-2) (WP5). Note: we were not able to monitor the circulation of other respiratory viruses as planned, due to the much larger than expected number of outbreak investigations.

Regulatory authorization

This study was approved by the “Commission cantonale d'éthique de la recherche (CCER)” on January 12, 2020 (Project-ID 2020-02957).

Research and operating team

This interdisciplinary research project is the result of a close collaboration between the Unit of Population Epidemiology (UEP) of the University Hospitals of Geneva, the Emerging Viruses Laboratory of the University of Geneva (CRIVE), the Laboratory for the Characterization of Biological Networks of the Ecole Polytechnique Fédérale de Lausanne, the young participants, their parents and the staff of the institutions.

Project investigators were: Prof Stringhini (project leader), Prof Eckerle, Prof Guessous, Prof Posfay-Barbe, Dr Azman and Dr L'Huillier.

The field team was composed of 4 research nurses, 1 administrative assistant, 1 study coordinator, 1 medical doctor and 1 project manager.

Study design

SEROCovPOP-Schools is a prospective observational surveillance study, organized in five interconnected Work Packages (WP).

The study includes recruitment of children in schools and day-care centers, along with their educators (WP1), a surveillance (monitoring) phase (WP2) as well as outbreak investigation(s) in schools/day-care centers (WP3), including a follow-up phase (WP3 & WP4). It also combines epidemiologic data collection with serologic and molecular diagnostic tools and results (WP5).

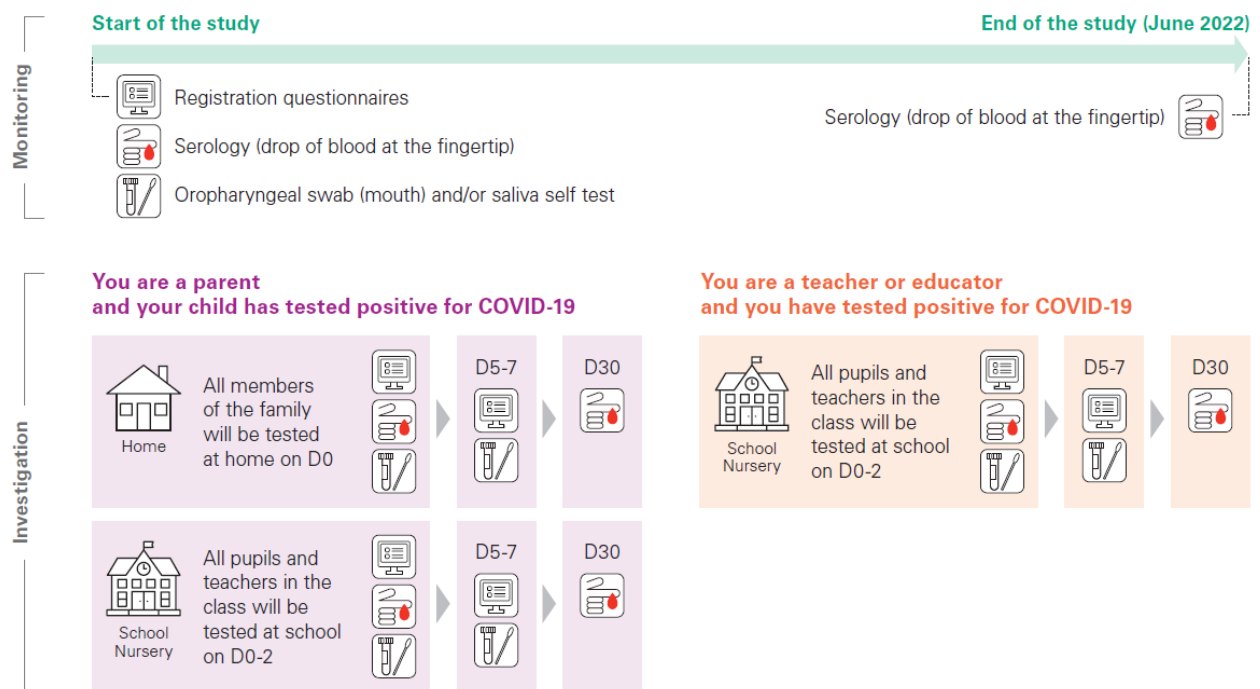


Figure 1. Overview of the SEROCovPOP-Schools study
D: Day

Participants

We included a convenience sample of children between 1-2 and 6-7 years of age (ages varied depending on the time of the school year, children who were about to celebrate their 2nd birthday were also considered eligible) from about 24 groups and classes of day-care centers and primary schools (nursery, 1P, 2P and 3P classes, i.e. the first three years of primary school) in the Geneva canton, along with their educators. Household members were invited to participate only if their child tested positive for SARS-CoV-2.

Work package 1: Recruitment

The SEROCov-POP-Schools project was divided into two phases. Phase 1 took place during the 2020/2021 school year and phase 2 during the 2021/2022 school year.

Preparation of Phase 1 began early 2021 with the recruitment of schools, day-care centers and participants. Phase 1 started on March 12th, 2021 and lasted until the end of the 2020/2021 school year.

Phase 2 of the study started in September 2021. A new recruitment phase took place in the same schools and day-care centers, as well as in another newly selected primary school.

Number of participating institutions and study participants

	Number of schools	Number of day-care centers	Number of Children	Number of Teachers / Educators	Number of Family members
PHASE 1 March 12 th , 2021 – July 23 rd , 2021	1	3	207	71	26
PHASE 2 September 1 st , 2021 – June 30 th , 2022	2	3	283	103	85

Tests and Questionnaires at Baseline

All included children and educators had a serology (capillary blood test) and a rapid antigen (phase 1) or RT-PCR (phase 2) test on an oropharyngeal swab at the beginning of the study. In phase 2, we also conducted a pilot evaluation of saliva sampling devices in the newly selected school, which demonstrated good acceptability and feasibility. Unfortunately, approximately one in three samples could not be analysed because of a limited quantity of saliva, which was not considered satisfactory enough to adopt this testing procedure.

Parents of the included children completed a short questionnaire at baseline, with questions about their participating child (age, sex, health status, previous exposure to SARS-CoV-2 or diagnosis of COVID-19), the household composition and parental socio-demographic characteristics.

All the included adults, i.e. educators and teachers, also completed a short questionnaire at baseline, with questions about their health, household composition, socioeconomic position, previous exposure to SARS-CoV-2 or diagnosis of COVID-19.

Last, a questionnaire on school/ day-care center prevention measures was also filled out by a key person within the institution.

All these questionnaires were completed online on the Specchio-COVID19 platform <https://www.specchio-covid19.ch/> (or on paper in a few specific cases).

Work package 2: Surveillance

Surveillance during phase 1 ran from recruitment until the end of the 2020/2021 school year, i.e. from March to July 2021.

Surveillance during phase 2 started in September 2021 and ran until February 2022. We had to stop this monitoring earlier than planned due to the change in cantonal recommendations regarding testing, declaration and isolation of positive cases in schools and nurseries (<https://www.ge.ch/document/covid-19-desescalade-mesures-protection-dans-ecoles-genevoises>). These measures included the end of classroom monitoring, and end of communication to school heads, teachers and parents when COVID-19 cases were detected. Because of these new cantonal policies, screening and self-tests were not recommended anymore, cases were not notified anymore and quarantine periods only depended on symptoms; this directly impacted the feasibility of the study which depended on participants or school declaration of symptomatic children.

Surveillance was performed using the Specchio-COVID19 platform, but also via direct contact with schools/day-care centers or parents.

Surveillance during phase 1 involved a weekly questionnaire for educators and parents of included children. They reported if the study participant or any member of his/her household had developed symptoms in the last week or had tested positive for SARS-CoV-2.

From September 2021 onwards, weekly questionnaire were replaced by regular contacts and weekly questionnaire with a key point of contact within each day-care center/school, who would report positive COVID-19 cases or children's sickness related absence within their institution.

School prevention measures questionnaires were repeated at the beginning of the 2021/2022 school year.

Regarding case declaration, any teacher who presented COVID-like symptoms was invited to perform a RT-PCR test and alert the research team as soon as possible in case the test was positive. The teacher would become an index case and trigger the initiation of WP3.

The same took place in case a child developed symptoms or if one of his/her household members had a positive test for SARS-CoV-2. In this case, the child was tested at the Geneva hospital (HUG) or at home by our mobile team. If he/she was positive, he/she became an index case and triggered the launch of both WP3 and WP4.

During the second winter of the pandemic (2021/2022), depending on the epidemiological situation, we considered conducting a monthly surveillance for other respiratory viruses in a subsample of our participants using a saliva sampling device, as the pilot evaluation demonstrated good acceptability and feasibility. However, we investigated so many outbreaks related to the Delta and Omicron variants that this regular surveillance could not be implemented.

At the end of phase 1, all participants leaving the study had a final serology performed at school by the research team.

A final serology took place at the end of phase 2 (end of 2021/2022 school year), in only one school because of low interest from parents in other schools. Indeed, after the Omicron wave a very large number of participants had been infected and saw no interest in serology testing.

Work package 3: School/day-care center outbreak follow-up

Once a positive case was declared, i.e. a child or an educator with a positive SARS-CoV-2 RT-PCR or rapid antigenic test, the school/day-care center outbreak follow-up phase was initiated.

Day 0 (D0) was defined as the day of the sampling of the case index's positive test.

Three school/day-care center visits following positive case declaration

Between D0 and D2, a mobile team visited the classroom/group to take an oropharyngeal swab and a drop of capillary blood from each participant. During phase 1, a rapid antigen test was performed on site with the oropharyngeal swab. From September 2021 onwards, a RT-PCR was performed at the HUG. On the day of the visit, parents and educators were asked to fill out an online questionnaire about the symptoms they may have, the onset time of each symptom and whether any of their household members were symptomatic.

Between D5 and D7, a second visit took place. During phase 1, a mobile team visited the class to take an oropharyngeal swab from each child and teacher and perform an antigen rapid test on site. From September 2021 onwards, a RT-PCR was performed. On the day of this second visit, parents and educators were also asked to fill out an online questionnaire about the symptoms they may have.

In December 2021 and January 2022, there were so many outbreaks that we did not always manage to organize two visits a few days apart, we therefore chose to have one visit during the first week after the case declaration.

At D30, all children and educators were offered a serology.

During phase 1, they also had to fill out an online questionnaire about the symptoms they may have had between visits 2 and 3. This was not the case anymore during phase 2.

Work package 4: Household outbreak follow-up

If a child was positive for SARS-CoV-2 in the surveillance (WP2) or class follow-up (WP3), visits took place at his/her house, or in the school/day-care center premises if many families were involved in the investigation.

Three household visits following positive case declaration

A mobile team visited the household of the positive child between D0 and D2. All household contacts were invited to participate in the outbreak investigation and follow-up. The mobile team took an oropharyngeal swab and a drop of capillary blood from each participating household member. During phase 1, a rapid antigen test was performed on site while from September 2021 onwards, a RT-PCR was performed. On the day of the visit, household contacts were asked to fill out an online questionnaire about the symptoms they may have, the specific timing of each symptom, if they were tested for SARS-CoV-2, the date and result of the test.

A second home visit took place between D5 and D7. During phase 1, an oropharyngeal swab and an antigen rapid test on site were performed on each household member. From September 2021 onwards, a RT-PCR was performed. On the day of the visit, household members were asked to fill out another similar online questionnaire as the one from the first visit.

A last household visit took place at D30, where all the household members (but the child who was tested at school) had a serology. During phase 1, they also had to fill out one last online questionnaire about the symptoms they may have or have had between visit 2 and visit 3. During phase 2, when most adults were vaccinated, serologies were not systematically offered to vaccinated participants, as the test performed by EPFL did not allow to differentiate between anti-SARS-CoV-2 antibodies following vaccination and/or infection (anti-S antibodies), or infection only (anti-N antibodies).

Work package 5: Laboratory analysis

Serological tests

Capillary blood samples were analyzed and anti-SARS-CoV-2 Spike IgG were assessed by the Laboratory of Biological Network Characterization, EPFL (PI: Prof. Sebastian Maerkl).

Virological investigations

Positive virological samples were sequenced in order to identify the strain, assess if different positive cases were linked and, with epidemiological information, reconstruct the chain of transmission between cases. When a participant had a positive RT-PCR test performed externally, we contacted the laboratory in order to retrieve the positive sample, provided the participant agreed. During the Omicron wave, most laboratories would throw away the samples very quickly (due to lack of space related to the huge number of samples), which prevented us from sequencing them all.

Results

Summary of key results:

Between March 12th, 2021 and February 18th, 2022, we investigated 11 outbreaks, related to Alpha, Delta and Omicron variants. Of note, there were so many case declarations in December 2021 and January 2022 that it was impossible to investigate all the cases that were reported. Overall, 62-87% of children had a negative serology at baseline vs 13-27% at the last visit.

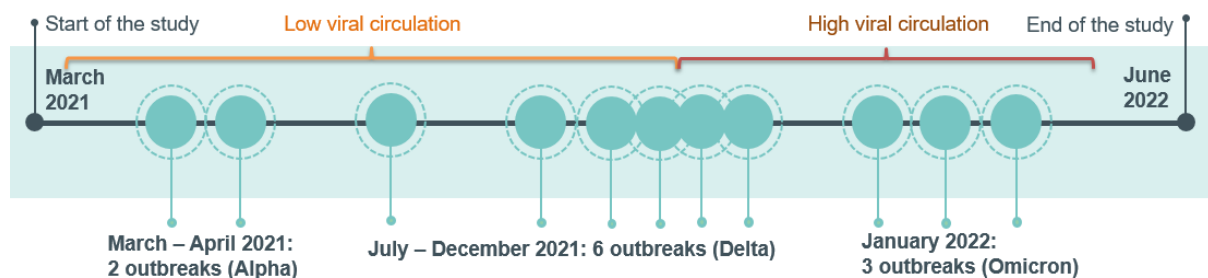


Figure 2. Timeline of the SEROCovPOP-Schools study and outbreak investigations

Conclusions:

This prospective day-care center/school-based study and epidemiological investigations into the different outbreaks already provide the followings:

- Evidence of child-to-child infection transmission with alpha, delta and omicron variants
- Evidence of child-to-adult infection transmission with alpha, delta and omicron variants
- Evidence of household infection introduction through children with alpha, delta and omicron variant
- Increased household infection introduction (including vaccinated parents) through children with Delta and even more with Omicron
- Evidence of rapid infection spread (child-to-child and child-to-adult transmission)
- Evidence of multiple introductions in school classes when incidence is high in the community

All above leading to:

- Higher transmission of infections in school settings with the Omicron variant than was reported with previous variants.
- Children appear to be an important source of extra-household infections and have a key role in community transmission.
- Increased potential for children to act as disease reservoirs as most of the adult and adolescent population get vaccinated

Limitations:

- Not all children and adults were tested in different outbreaks which could lead to an underestimation of the proportion of infected participants and infected family members

- Possible missed infections among adults vaccinated between D0-2 and D30 of outbreaks (distinction between infection-related and vaccine-related antibodies not possible)
- Lack of tests for household members of cases only detected by seroconversion at D30 with no positive tests, leading to a potential underestimation of secondary attack rates.

Publications:

We published two articles on two outbreaks related to the Alpha and Omicron variants:

<https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0272663>

[https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(22\)00267-5/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(22)00267-5/fulltext)

Recommendations

The following strategies would help reducing the overall SARS-CoV-2 virus circulation within the community.

- 1) Rapid testing of the case contacts within the school setting (ie: school classes) as soon as a positive case is identified within a classroom (adult or child). This allows the early identification of an outbreak, isolation of all positive cases and may interrupt chains of transmissions.
- 2) Short quarantine of the classroom if a large outbreak is identified (number to be determined), with testing at day 5 for coming back to school.
- 3) Isolating infected persons contributes to reducing transmission, however, a 5-day isolation period is too short and leads to a snowball effect with new infections occurring over a longer period of time after the outbreak onset

Of note, these other recommendations are based on a literature review and on observation, rather than being directly derived by our data:

- Weekly or regular pooled saliva PCR tests for children and school/day-care center staff
- Regular fresh air flow : opening windows and doors to allow better airflow
- Monitoring of CO2 levels in class/canteen with carbon-dioxide monitors
- Air filtration: portable air purifiers to decrease airborne virus quantity
- Limitation of classes/groups mixing as soon as a positive case is found in school/day-care center
- When possible, encourage masks wearing (even for children) for a short period of time if a positive case is found in a group
- Effective communication and awareness campaign targeted to parents
- Vaccination of school staff shall be encouraged

Scientific dissemination and impact

This study has had a scientific and societal impact locally, as well as nationally and internationally. Our team played a key role in **supporting and informing schools and families** during a stressful time of changing policies and measures that were sometimes difficult to follow and understand. The study provided an opportunity to conduct **science outreach** to the **children, teaching** them about testing, infection with the virus, antibody development through specially created illustrations, and answering their many questions during the visits. We also conveyed the idea that **science and research** could be fun (clowns accompanied us on the inclusion visits) and conducted by women, as our field team was all female. We made a point of keeping participants informed of our progress through regular **newsletters**, posts on the news section of the Specchio-COVID19 digital platform (<https://www.specchio-covid19.ch/actualites>) and an interactive **webinar** on "Children, teenagers and COVID-19" (February 2022). These activities are summarized in Figure 3.

Our findings were also shared with the *scientific community* through a **key note presentation at a congress** (Swiss National Science Foundation National Research Program 78, May 2022), and **scientific articles** (doi 10.1101/2021.10.26.21265509 / 10.1371/journal.pone.0272663, 10.1016/S1473-3099(22)00267-5), one of which was published in the Lancet Infectious Diseases. These publications were widely distributed on **social networks** (900 and 2100 tweets and shares, respectively). One other article is currently in preparation.

Our results were **regularly communicated** to the *Cantonal medical service* (Service du Médecin Cantonal, April 2021, September 2021, and December 2021) and to the *Federal Office of Public Health* (February 2022) in order to inform debates and decision-making in public health. We hope that this essential information will be used to adapt measures to protect children in their daily activities while allowing them to have the most "normal" life possible in this pandemic context.

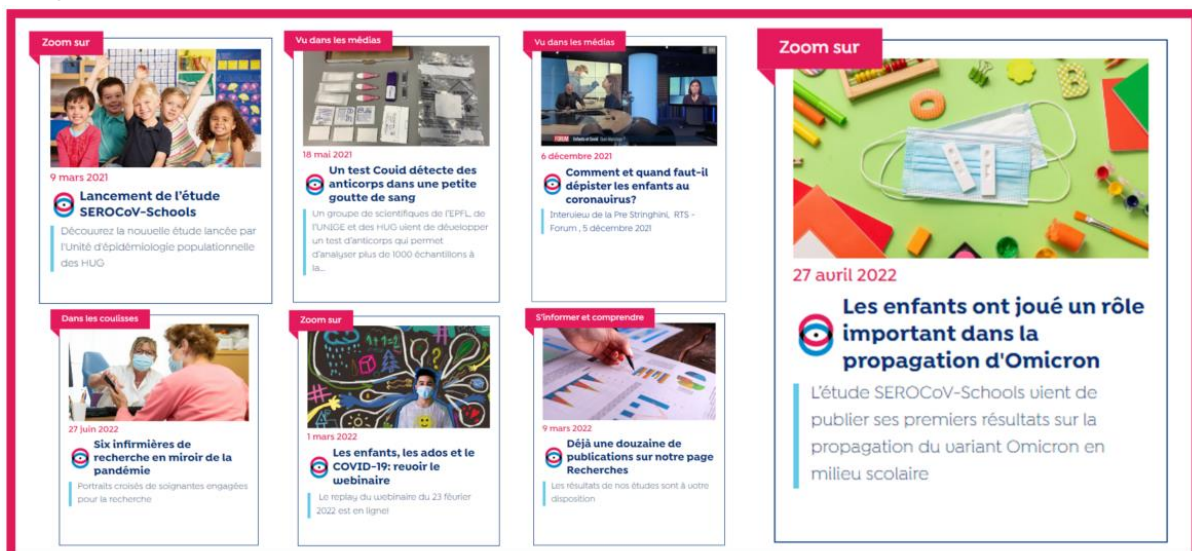


Figure 3. Selected articles intended for the scientific and non-scientific community and available on the Specchio-COVID19 platform.

Lastly, the groundbreaking work carried out by our team since the beginning of the study has been recognized: the SEROCov-Schools project has been awarded the “Prix Médecine et Société” by the University of Geneva in November 2022 (<https://www.specchio-covid19.ch/actualites/l-etude-serocov-schools-est-laureate-du-prix-medecine-et-societe>).

Conclusions

The fact that children are less frequently tested than the general adult population, the observation that they are less likely to suffer from severe forms, and the fact that virus circulation is tolerated to a certain extent in schools and classrooms have all influenced the perception of children’s potential role in SARS-CoV-2 transmission.

We conducted a longitudinal surveillance study, with several prospective outbreak investigations, to describe the transmission dynamics of SARS-CoV-2 infections within primary schools and day-care centers in Geneva, and the risk of introduction of SARS-CoV-2 into the children’s households. Combining epidemiological, serological and virological techniques, we observed clear dynamics of transmission including child-to-child but also child-to-adult and transmission to household members, even more so with the delta and omicron variants. Therefore, similarly to many other respiratory viral diseases, children play an important role in SARS-CoV-2 transmission. Infections can spread quickly within schools and day-care centers without being identified or noticed. Those “under the radar” infections may unknowingly be the start of many outbreaks within the community.

With younger children having a large number of close contacts, and the appearance of more contagious variants, controlling children’s infections through targeted measures and/or children’s vaccination will be key in decreasing SARS-CoV-2 community transmission and circulation. Systematic outbreak testing, for example inviting children to take a saliva test from the first positive case in the classroom or day-care center could be one of the first and easy measure to put in place to help decrease the spread of SARS-CoV-2 within those groups.

This becomes even more important as adults and children (> 5 years old) get vaccinated leading this last population segment to become a virus reservoir. Vaccination should be made available for the youngest children as quickly as possible.

The SEROCovPOP-Schools project has thus made an important contribution to better understanding the interplay between young children and the pandemic, which is one of the major societal issues of the last two years. It is distinguished by its local community anchorage and impact combined with internationally recognized scientific excellence.

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