

PREVALENCE AND INCIDENCE OF ANTIBODIES AGAINST SARS-COV-2 IN CHILDREN AND SCHOOL STAFF MEASURED BETWEEN DECEMBER 2020 AND JUNE 2021: AN OBSERVATIONAL SERO-PREVALENCE PROSPECTIVE COHORT STUDY

Findings of the first testing period

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WHO WE ARE

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For this, Sciensano builds on the more than 100 years of scientific expertise of the former Veterinary and Agrochemical Research Centre (CODA-CERVA) and the ex-Scientific Institute of Public Health (WIV-ISP).

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The KU Leuven logo consists of the text "KU LEUVEN" in white, uppercase, sans-serif font, centered within a dark blue rectangular box.

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Thank you very much!

MAIN FINDINGS

This study provides a representative estimate of the prevalence of anti-SARS-CoV-2 antibodies among pupils and school staff in Belgian primary and secondary schools at the end of the second wave.

Between 3 December 2020 and 28 January 2021, 12,4% (95% CI: 9.7 – 15.8) of pupils and 14,8% (95% CI: 12.2 - 18.0) of school staff in Belgian primary and the first two years of secondary schools had anti-SARS-CoV-2 antibodies. The prevalence among pupils and school staff is similar to the prevalence found in the general population.

Findings of the first testing period of this study (two additional testing period are planned) show that the prevalence of anti-SARS-CoV-2 antibodies is slightly lower among pupils than among school staff. However, this difference and the differences between pupils and staff of primary and secondary school are small and not statistically significant.

Regional differences in the prevalence of anti-SARS-CoV-2 antibodies were observed:

- Brussels: pupils: 24.0% (95% CI: 11.9 - 48.4) – school staff: 10.5% (95% CI 4.4 - 25.1)
- Flanders: pupils: 8.7% (95% CI: 6.4 – 11.6) – school staff: 13.2% (95% CI 9.7 – 17.8)
- Wallonia: pupils: 15.4% (95% CI: 10.8 – 22.0) – school staff: 17.7% (95% CI 13.6 – 23.2)

This is in line with the findings among Belgian blood donors and primary healthcare workers where similar regional differences are observed. However, data for the Brussels region are sparse and had a high degree of uncertainty (i.e. wide confidence limits), which prevents further interpretation or conclusions for this region.

Given the transmissible character of the disease, dependence of events is not unexpected. However, there was no evidence of important clustering of cases in schools during the first testing period, and thus no strong evidence of widespread transmission of SARS-CoV-2 in the school environment under current infection prevention and control measures.

Main conclusion and finding

This study provides a representative estimate of the prevalence of anti-SARS-CoV-2 antibodies among pupils and school staff in Belgian primary and secondary schools at the end of the second wave. The study found that schools providing face-to-face teaching did not result in disproportionate numbers of infected individuals. There are no important statistical or clinical differences in the sero-prevalence in primary and secondary school pupils and school staff on the one side and the broader community on the other side.

Based on our study findings, schools do not appear places where the coronavirus is more widespread or more likely to spread than elsewhere in the community.

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ABBREVIATIONS

BSL2	Biosafety Level 2
CI	Confidence Interval or Credible Interval
COVID-19	Coronavirus Disease of 2019
ELISA	Enzyme-linked Immunosorbent Assay
GEE	Generalized Estimating Equations
HCW	Healthcare Worker
IgG	Immunoglobulin G
IPC	Infection Prevention and Control
IQR	Interquartile Range
OD	Optical Density
PCR	Polymerase Chain Reaction
RBD	Receptor Binding Domain
RD	Risk Difference
RR	Relative Risk
SAR	Secondary Attack Rate
SARS-CoV-2	Severe Acute Respiratory Syndrome – Coronavirus 2
SD	Standard Deviation
WHO	World Health Organization

1. INTRODUCTION

Since the beginning of 2020 the world is under the spell of the new coronavirus, Severe Acute Respiratory Syndrome – Coronavirus 2 (SARS-CoV-2), which causes excess morbidity and mortality in adult populations and has led to an increased burden of the healthcare system globally. Until the 4th of March 2021, 115,927,475 confirmed coronavirus disease of 2019 (COVID-19) cases have been reported worldwide, among which 2,574,190 deaths (1). For Belgium this number was 777,608 confirmed cases and 22,169 confirmed COVID-19 deaths (2).

Based on several studies it seems that children are less affected by SARS-CoV-2 infections and potentially play a different role in dissemination of the SARS-CoV-2 virus compared to older adolescents and adults (3–7). It is unclear to which extent this is due to differences in exposure or routes of transmission or to an inherent decreased susceptibility to become infected or become symptomatic. However, a study conducted by us, found that children have a higher risk of getting infected in communities with high versus low viral circulation and transmission rates (8).

Between February 2020 and the 4th of March 2021, 1,782 confirmed COVID-19 cases were reported per 100,000 Belgian children less than 10 years of age and 6,221 confirmed COVID-19 cases per 100,000 youngsters between 10 and 19 years of age (2). During the same period 6,914 confirmed COVID-19 cases per 100,000 were recorded in the total Belgian population (2). These numbers should be interpreted cautiously because they depend on a continuously changing and age-dependent COVID-19 test strategy (9). The low number of confirmed cases in children younger than 10 years of age might also be partially explained by the reduced polymerase chain reaction (PCR) testing rates for the diagnosis of acute infection in the paediatric population. On the other hand, the burden of disease, and more specifically the mortality is also limited in the paediatric population. Between the beginning of the outbreak and the 4th of March 2021, Sciensano, the Belgian institute of public health, reported 8 COVID-19 related deaths in the age group 0 to 24 years of age (2).

At the end of 2020 – beginning 2021, studies on the prevalence of anti-SARS-CoV-2 antibodies in the Belgian population found a prevalence of 15.6% in the general population (healthy blood donors between 18 and 20 Jan 2021), 24.1% among hospital healthcare workers (representative sample of Belgian hospital healthcare workers between 27 - 31 Jan 2021) and 15.1% among primary healthcare workers (convenience sample of primary healthcare workers between 24 Dec 2020 and 8 Jan 2021) (2). To our knowledge there is no representative data on the sero-prevalence among Belgian children and school staff.

To gain insight in the transmission of the SARS-CoV-2 virus among school-aged children, especially in younger or asymptomatic subjects, it is necessary to combine data on active and past infections with SARS-CoV-2 virus in children and (pre-)adolescents. Two studies found that most children were apparently infected within the household (3,10). A surveillance study in Belgian schools indicated that teachers were more likely to be infected by their colleagues than by their students (11). A sero-prevalence study conducted in schools in Switzerland did not observe a high degree of clustering of seropositive cases within classes (12). A similar observation was made in a study among German teachers and pupils. The latter study also concluded that in a low prevalence setting these population groups were not the driving force of the disease transmission (13).

No data on the sero-prevalence in school staff and pupils from the same schools are available in Belgium, and data in the literature is equally limited. Nevertheless, such data are important to guide strategies to deal with the current epidemic (e.g. general school closure (whole region/country) or school or grade closure based on detected outbreaks).

The aim of this study is to assess the prevalence of anti-SARS-CoV-2 antibodies among children (age groups 7-9 and 13-14) and school staff in Belgian primary and secondary schools and to assess the incidence of seroconversion in this population during a follow-up period of 7 months. Additionally, by

collecting information of household members of the children and the school staff, we will gain more insight on COVID-19 disease within households in Belgium. The study also aims to generate knowledge on the clinical presentation of the disease among school-aged children and school staff and to evaluate the effect of some specific aspects of child behaviour and activities (e.g. participation in after school activities) on the infection rate among children. The study covers all regions in Belgium (Brussels-Capital, Flemish and Walloon Region).

In this report, we present a description of the study population and the prevalence of anti-SARS-CoV-2 antibodies during the first of three testing periods. This first testing period took place between December 3, 2020 and January 28, 2021. These findings and those from the second and third testing period will provide insight in the dynamics of the epidemic in schools and is useful for policy makers to decide on specific COVID-19 related measures for schools and school-aged children. This data might also guide the expert groups who provide advice on mitigation and vaccination strategies.

2. OBJECTIVES

The main objective of the complete study is to determine the prevalence and sero-conversion of antibodies against SARS-CoV-2 in a representative sample of school-aged children and school staff (primary and first grades of secondary school) in Belgium, at three different time points.

Secondary objectives are:

- Determine the cumulative incidence of SARS-CoV-2 between baseline (end first trimester) to the end of the school year in this sample
- Determine the proportion of asymptomatic infections with SARS-CoV-2 in this sample
- Gain insight in the role of SARS-CoV-2 infection in household members of children and school staff in this sample
- Investigate potential risk factors for infection among school-age children
- Investigate potential risk factors for infection among school staff

The objective of this report is to present a description of the study population and the prevalence of anti-SARS-CoV-2 antibodies during the first (December 3, 2020 to January 28, 2021) of three testing periods.

3. METHODS

This study is as a prospective observational cohort study that covers the second half of a single school year (December 2020 to June 2021).

The methodology was based on and in line with the ‘*Population-based age-stratified sero-epidemiological investigation protocol for COVID-19 virus infection*’ by WHO (14). The detailed study protocol is available on the Sciensano website:

https://www.sciensano.be/sites/default/files/federal_protocol_covid_seroprevalence_amendement_20201117_final_1.pdf

The study has been registered at ClinicalTrials.gov: <https://clinicaltrials.gov/ct2/show/NCT04613817>

3.1. STUDY SETTING AND POPULATION

The study population includes children and staff of primary and secondary schools in each of the Belgian provinces and in the capital region of Brussels. .

The children included belong to two predefined age groups: (1) children from the 2nd and 3rd grades (ages 7-9) in primary school, and (2) children from the 2nd year (ages 13-14) of secondary school. Teaching and supporting/non-teaching staff (e.g. administrative staff) with potential direct contact with pupils (i.e. presence at school at the same time as the pupils), were also included in this study.

Children and staff were recruited in the same schools using a two-stage randomized cluster design with proportional allocation by province and sociodemographic background. The aim was to recruit 20 pupils and 10 staff members in each school. The number of schools per province was determined from the paediatric population size on Jan 1st 2020 according to Statistics Belgium (15). Schools were selected at random from a list of all schools providing general education with a designated socio-economic profile in a random sample of districts selected with a probability proportional to their population size in each province. A unique “social quantile” was assigned to each district (i.e. quartiles when there were 4 districts, tertiles when there were 3 districts etc...) and schools with a corresponding social quantile were eligible for participation. The social background of schools was derived from data published by the respective authorities (i.e. the Flemish Government and the Fédération Wallonie-Bruxelles) (16–18).

A staff member from each participating school was designated as the local study-coordinator. He/she acts as contact person between the school and the Sciensano study team. His/her role is to facilitate the study at school level by e.g. scheduling the sampling appointments with the study nurse, support the nurse during the sample taking at school, contact the Sciensano study team in case of problems or questions, support the distribution of test results, completing the dedicated school questionnaires, etc.

3.2. STUDY DESIGN

Three consecutive testing periods have been planned, being: 1st period December 2020 – January 2021 (baseline), 2nd period March 2021 (M3), and 3rd period May – June 2021 (M6). At each period, biological data and basic information on socio-demographic characteristics (only during first time period), risk-behaviour and health characteristics including the presence of COVID-19 symptoms and previous conducted COVID-19 tests were/will be collected. Data collection was planned within a timeframe of maximum 4 weeks. Recruitment of schoolchildren and staff took place at the start of the first testing period.

Data on socio-demographic characteristics, risk-behaviour and health was/will be collected through a secured online questionnaire using the 'LimeSurvey' platform (LimeSurvey Version 3.22.24+200630). Parents/legal caregivers and staff members were/will be asked to complete a questionnaire providing basic information on socio-demographic characteristics at baseline, and risk-behaviour and health characteristics including the presence of COVID-19 symptoms at each of the testing points.

Anti-SARS-CoV-2 antibodies were/will be detected in saliva samples collected from each participating child and staff member using a saliva collection system (Oracol). Saliva samples were/will be either self-collected by the participants under supervision of a trained nurse or collected by a trained nurse. Samples were/will be transported to the Sciensano laboratory for analysis. Serological test results were/will be communicated to the children's parent/legal caregiver and staff after de-pseudonymisation by a designated member of the study team.

3.3. SAMPLE SIZE AND PROCEDURE

A required sample of 400 primary and 400 secondary schoolchildren and 400 staff members was determined based on a reported sero-prevalence of 6% in schoolchildren and 10% in staff in the Belgian population at the start of the school year (19). This sample size allowed us to estimate the seroprevalence with a margin of error of 2.3% for the children and 3% for the staff. Because up to 20 children and 10 staff were recruited in the same classes/schools we doubled the sample size to accommodate a design effect of 2 due to clustering of cases. Further we increased the target sample size to 820 children and 410 staff from each type of school to allow an equal distribution over the 41 clusters needed to ensure a proportionate distribution over the provinces.

3.4. DATA COLLECTION

Data on socio-demographic characteristics, risk-behaviour and health (questionnaire) and biological (saliva samples) data were/will be collected simultaneously.

3.4.1. Questionnaires

Information on demographic, socio-economic, risk- and protective behaviour characteristics (e.g. possible contact with COVID-19 cases since onset of the pandemic) and on COVID-19 symptomatology was collected with a baseline questionnaire (1st testing period) (see questionnaire <https://www.sciensano.be/nl/biblio/prevalence-and-incidence-antibodies-against-sars-cov-2-children-measured-one-year-belgium-a-sero-0>). The online questionnaire was to be completed by a parent/legal caregiver of the child or the staff member using a computer, tablet or smartphone. Additional information on preventive measures, school closures and SARS-CoV-2 outbreaks in the school was collected from the local study-coordinator with an online questionnaire.

3.4.2. Collection of biological samples

Saliva samples of the participants were collected using a saliva collection device (Oracol, Malvern Medical Developments, UK) as per the manufacturer instructions and previously validated protocol for the paediatric population. This entailed rubbing the oral swab with mild pressure against the buccal mucosa of the upper teeth during two minutes.

This saliva collection device was previously validated for the sampling of oral fluid and subsequent detection of anti-SARS-CoV-2 antibodies among children and adolescents in a pilot study in primary and secondary schools in two regions in the province of Limburg, Belgium (8, non-published data Sciensano laboratory). The same method was previously validated in Belgian adults by Sciensano and

thus allowed the use of the same method of sample collection and study procedures for the participating staff members (20).

Samples were kept refrigerated (2-8°C) before transport to the Sciensano laboratories in a cool box.

3.5. LABORATORY TESTING

Detection of anti-SARS-CoV-2 antibodies in saliva was done in the biosafety level 2 (BSL2) laboratories of Sciensano (Public Health Belgium). Samples were stored non-diluted at -80°C during +/- 1 month prior to analysis. Samples needed to contain a minimal volume of 110 microliter after centrifugation. Detection of anti-SARS-CoV-2 antibodies in saliva was done using an *in house* quantitative anti-RBD IgG (Receptor Binding Domain) ELISA. This assay has been validated for the use of oral fluid samples from children (84,62% sensitivity; 100% specificity; compared to serum; data on file) and adults. Using a predefined positivity cut off of optical density (OD) ratio ≥ 1.45 , a binary result was provided by the laboratory, classifying each sample as positive versus negative for the presence of antibodies against SARS-CoV-2. No second confirmatory assay was used.

The laboratory technician was blinded to the participants identifiers and survey data, including prior PCR positivity. Based on the child identifier (unique registration code), child data on the serological test results were linked with the questionnaire data.

3.6. DATA ANALYSIS

A flow chart presents the number of participants approached, eligible and included. Sero-prevalence estimates are based on complete data only (i.e. excluding collected samples that could not be analysed due to the lack of sufficient saliva). Descriptive statistics are reported with a 95% confidence interval (95%CI) for proportions and with their standard deviation (SD), interquartile range (IQR), or range as appropriate for continuous variables.

The sero-prevalence estimates and their 95%CI by age group and the staff are calculated as the percentage of specific IgG positive individuals. Standard errors and 95% confidence intervals of the sero-prevalence, and relative risk (RR) or risk difference (RD) for sero-positivity were estimated with generalized estimating equations (GEE) with a binomial distribution and exchangeable correlation structure (compound symmetry) to account for clustering of children and staff in schools and classes. A log link was used for the prevalence and RR but results were back transformed for reporting. The RD was estimated with an identity link. Estimates were not corrected for the lab-test performance or imperfect reference standard, but the sensitivity and specificity of the assay are reported above.

The sero-prevalence in teachers and pupils and in pupils from primary or secondary schools was compared by the RR and RD and associated 95% confidence intervals estimate with GEE.

A p-value of 5% or less was considered statistically significant. All data were analysed with R version 4.0 (R Foundation for Statistical Computing, Vienna, Austria, 2020).

3.7. ETHICS

The study was approved by the Commissie voor Medische Ethiek (Ethics Committee UZ Ghent) on 3 November 2020: B.U.N.: B6702020000744 - BC-08564. Approval of amendment (inclusion of school staff) on 20 November 2020.

4. RESULTS

4.1. GENERAL CHARACTERISTICS STUDY POPULATION

4.1.1. Sample composition and time

The first testing period ran from 3 December 2020 to 28 January 2021. Figure 1 shows the cumulative number of laboratory confirmed SARS-CoV-2 infection cases per 100,000 population over time for the three Belgian regions and for the whole country (2). The period in which laboratory specimens for SARS-CoV-2 antibody detection were sampled among the study participants is marked in grey and fell after the second wave which disproportionately affected Wallonia and Brussels. The baseline testing period was extended to a period of eight weeks, instead of the planned four weeks, due to the time needed to recruit all schools, winter holidays and the exam period at the end of the first trimester.

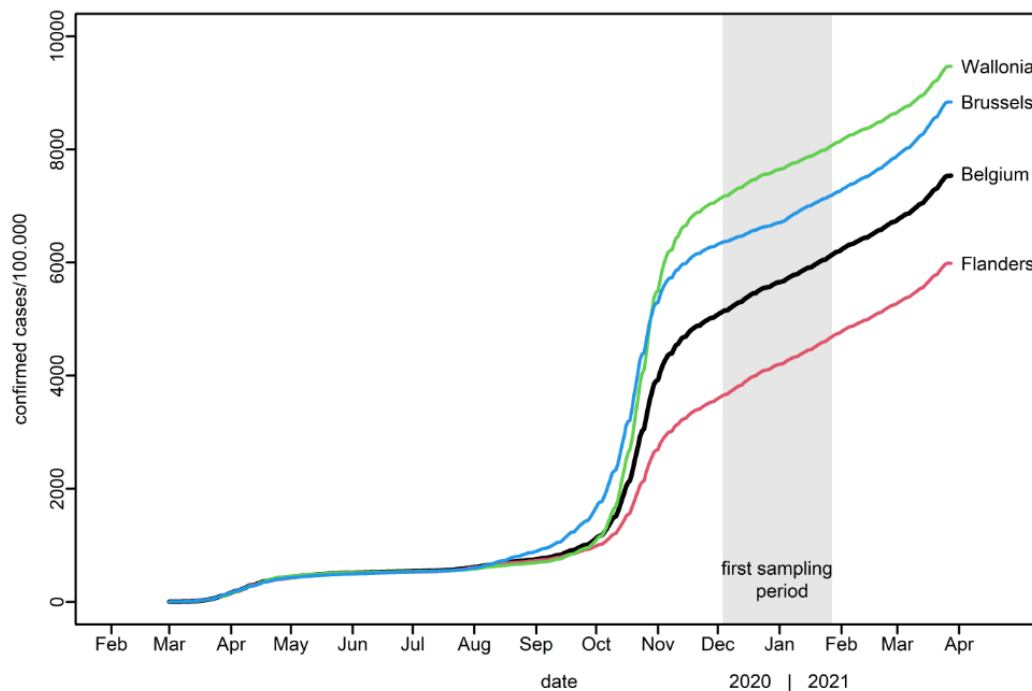
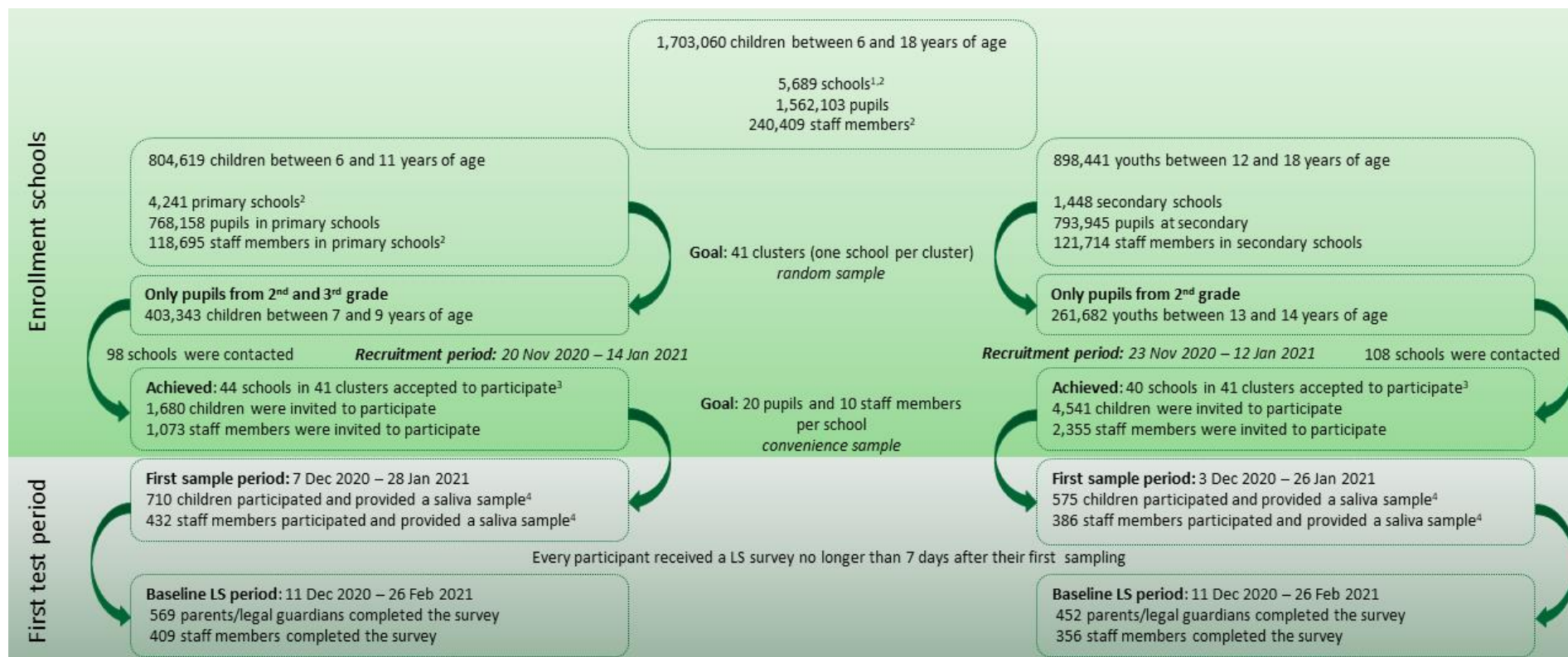


Figure 1: Study sampling period (grey colour) in relation to cumulative number of laboratory confirmed SARS-CoV-2 cases per 100,000 population, March 2020- April 2021, Belgium and by region (2)

Figure 2 gives an overview of the recruitment and the number of participants included in the study. In total 1,285 pupils participated; 710 pupils from the 2nd and 3rd grade of primary school (44 schools) and 575 pupils from the 2nd grade of secondary school (40 schools). The number of pupils was less than anticipated but the impact on the statistical power was limited and the geographic and social diversity was maintained. In total 818 staff members from schools participated; 432 from primary and 286 from secondary schools, which is in line with the targeted sample of 410 participants at each school level.



¹ Schools in Belgium starting from primary school (6-7 years of age) to secondary school (17-18 years of age), not including alternative education.

² Some pre-schools are included or pre-school staff is included.

³ In three clusters two schools were included (primary) – One cluster was not fulfilled (secondary).

⁴ A few schools had at the day of the first sample appointment more or less than the predefined sample size of 20 pupils and 10 staff.

Figure 2: Description sample recruitment and participation at first testing period (15,21–23)

4.1.2. Distribution of selected schools and school characteristics

Figure 3 shows the geographical distribution of the participating schools. The distribution is proportional to the population size of the respective provinces for which reason the province of Luxemburg only includes one cluster. Data from the province of Luxemburg will be aggregated with those from Namur when statistics at the provincial level will be provided in future reports.

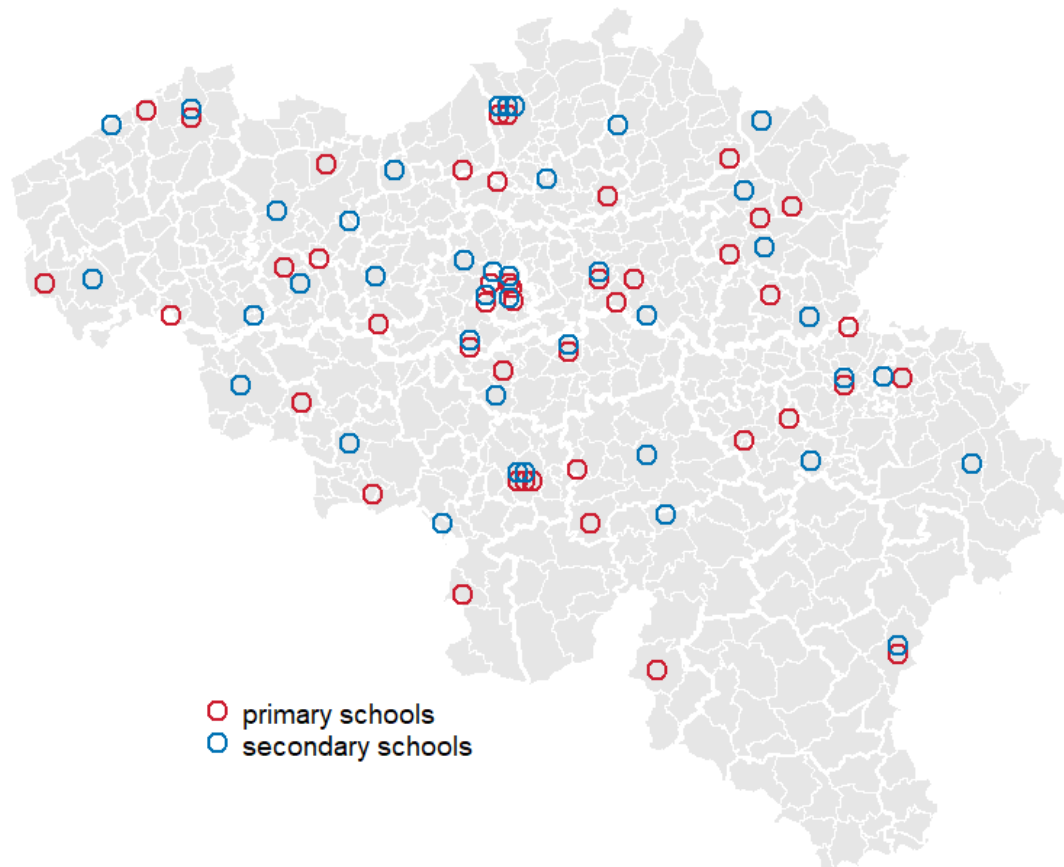


Figure 3: Distribution of primary and secondary schools included in the study

All 84 participating schools (44 primary and 40 secondary schools) completed a questionnaire with information on preventive measures, school closures and SARS-CoV-2 outbreaks in the school. Two schools have been closed (respectively one and eight days) since September 2020, and another 44 schools suspended one ($n = 17$) or more ($n=29$) classes (one school did not answer how many classes) for one ($n = 4$) to a maximum of 21 days (four schools did not answer how many days). Study participants from nine schools attended one of the suspended classes.

A large majority of schools reported confirmed COVID-19 cases among pupils ($n = 71$ schools; 1 – 93 pupils, 15 did not report the number of pupils) teaching staff ($n = 68$ schools; 1 – 25 staff, nine did not report the number of staff), or non-teaching staff ($n = 38$ schools, 1 – 6 staff, 6 did not report the number of non-teaching staff).

Table 1 gives an overview of the implementation of infection prevention and control (IPC) measures in the participating schools. Schools were asked to indicate how the measures were applied on a scale ranging from 1 (measure is not applied at all) to 5 (measure is fully applied) during the month

preceding the collection of saliva samples for our study. Table 1 gives the number and % of schools that indicated '4' or '5' on the scale, meaning they (fully) applied this measure.

Only 12 (14%) class rooms have a CO2 detector and 14 (17%) an active ventilation system, but all except 3 (96%) encourage teachers to ventilate the class passively between classes. Only 5 (6%) schools organize classes outside to a maximum extent. Breaks are organized such that contact between age groups is avoided in 30% of primary and 45% of secondary schools.

The frequency of cleaning was increased to a similar extent in class (n = 53, 63%) and staff rooms (n = 54, 64%). Toilets were cleaned more frequently in 75% of schools (n = 63), and surfaces are regularly disinfected in 67 (80%) of schools. Hand sanitizers are available for staff and pupils in 78 (93%) schools.

The number of staff members per room is limited in 66 (79%) schools, and 75 (89%) implemented strict regulations for staff regarding distance, ventilation and mask wear. In 71 (85%) schools lunches are organized in the pupils' class room or pupils have fixed places in the dining area. Fixed places in a classroom or fixed classrooms are more common in secondary (both 70%) than in primary (resp. 59% and 52%) schools.

In primary schools, staff maintain a safe distance between themselves (89%) or between staff and pupils (57%), and 84% wear masks when distancing is not possible. In 93% of secondary schools staff wear a mask indoor, even when distancing is possible, and 90% wear masks outdoor when a safe distance cannot be maintained.

Table 1: Number and percentage of schools indicating applying the infection prevention measures*

Preventive measure	Primary schools N=44 n (%)	Secondary schools N=40 n (%)	All schools N=84 n (%)
Class rooms have a CO2 meter	9 (21)	3 (8)	12 (14)
Schools have and use a ventilation system	9 (21)	5 (13)	14 (17)
Teachers are encourage to ventilate class rooms regularly	42 (96)	39 (98)	81 (96)
Classes take place as much as possible outside	3 (7)	2 (5)	5 (6)
Breaks are spread to decrease contact between different age groups	13 (30)	18 (45)	31 (37)
Class rooms are cleaned regularly and more frequent than previous school years	26 (59)	27 (68)	53 (63)
Staff rooms are cleaned regularly and more frequent than previous school years	29 (66)	25 (63)	54 (64)
Toilets are cleaned regularly and more frequent than previous school years	32 (73)	31 (78)	63 (75)
Surfaces that are touched regularly are daily disinfected	34 (77)	33 (83)	67 (80)
Number of staff per room is limited	33 (75)	33 (83)	66 (79)
Alcohol gel (or additional possibilities to clean hands) is available for pupils and staff	40 (91)	38 (95)	78 (93)
Pupils have one fixed place in a fixed class room	26 (59)	28 (70)	54 (64)
Teachers change between call rooms, not the pupils	23 (52)	28 (70)	51 (61)
Specific attention to follow preventive measures in staff room: 1. Wear a mask, 2 keep distance when eating or drinking, 3. Ventilate the room as much as possible.	39 (89)	36 (90)	75 (89)
Lunches are taken in the class room. If this is not possible pupils have a fixed place in the dining area	37 (84)	34 (85)	71 (85)
<i>Only for primary schools</i>			
Distance is maintained in contacts between adults	39 (89)		
Distance is maintained in contacts between staff and pupils	25 (57)		
Staff wears a mask if keeping distance cannot be guaranteed	37 (84)		
<i>Only for secondary</i>			
Staff and pupils always wear a mask inside		37 (93)	
Staff and pupils wear a mask outside unless they can keep sufficient distance		36 (90)	

* Number and % of schools that indicated on the scale ranging from 1 (meaning measure is not applied at all) to 5 (meaning measure is fully applied) a '4' or '5', meaning they indicated they applied this measure.

4.1.3. Pupils and school staff characteristics

Sociodemographic, health and behaviour related information of participating pupils and staff are given in Table 2 and 3. Questionnaire data are missing for 231 (18%) of the pupils and 43 (5%) of the school staff.

As given in Table 2, half of the participating pupils were female and half male. Among the school staff more than 70% of the participants were female which is a reflection of the gender distribution in this workforce. Both in primary and secondary schools, around 80% were teaching staff and 20% were supporting staff, administration and other. Our sample has a more or less equal number of participants among pupils and staff from each of the socioeconomic status tertiles.

Two thirds of primary school children and $\frac{3}{4}$ of secondary school children were from Belgian origin, defined as: being born in Belgium and none of their parents or grandparents born outside Belgium. The larger proportion of non-Belgian origin in primary schools is mainly due to differences in children from European, non-Belgian origin. "Origin" of staff was determined by their country of birth. The large majority (97.7% n = 749 out of 767 who answered this question) was born in Belgium, another 15 in a European country, and 3 in a country outside Europe.

Table 2: Sociodemographic characteristics of pupils and school staff

	Pupils		Staff	
	Primary 710	Secondary 575	Primary 432	Secondary 386
Total number				
Sex: M/F, (% male)	379/331 (53.4%)	298/277 (51.8%)	77/355 (17.8%)	135/251 (35.0%)
Age, years (mean, range)*	9 (6 – 12)	14 (13 – 16)	43 (21 – 65)	41 (22 – 66)
Region/province (% of total)	N (%)	N (%)	N (%)	N (%)
Brussels	96 (13.5%)	46 (8.0%)	53 (12.3%)	45 (11.7%)
Flanders, total	362 (51.0%)	341 (59.3%)	215 (49.8%)	214 (55.4%)
Antwerpen	67 (9.4%)	86 (15.0%)	49 (11.3%)	50 (13.0%)
Limburg	74 (10.4%)	63 (11.0%)	40 (9.3%)	40 (10.4%)
Vlaams Brabant	72 (10.1%)	72 (12.5%)	40 (9.3%)	40 (10.4%)
Oost-Vlaanderen	85 (12.0%)	64 (11.1%)	50 (11.6%)	44 (11.4%)
West-Vlaanderen	64 (9.0%)	56 (9.7%)	36 (8.3%)	40 (10.4%)
Wallonia, total	252 (35.5%)	188 (32.7%)	164 (38.0%)	127 (32.9%)
Brabant-Wallon	30 (4.2%)	31 (5.4%)	20 (4.6%)	13 (3.4%)
Hainaut	88 (12.4%)	49 (8.5%)	52 (12.0%)	53 (13.7%)
Liège	76 (10.7%)	66 (11.5%)	54 (12.5%)	42 (10.9%)
Namur	43 (6.1%)	23 (4.0%)	28 (6.5%)	13 (3.4%)
Luxembourg	15 (2.1%)	19 (3.3%)	10 (2.3%)	6 (1.6%)
School SES	N (%)	N (%)	N (%)	N (%)
Lower tertile	252 (35.5%)	167 (29.0%)	153 (35.4%)	125 (32.4%)
Middle tertile	262 (36.9%)	181 (31.5%)	165 (38.2%)	134 (34.7%)
Highest tertile	196 (27.6%)	227 (39.5%)	114 (26.4%)	127 (32.9%)
Rates below are based on the number of participants who complete the questionnaire				
Questionnaire completed	587 (82.7%)	467 (81.2%)	414 (95.8%)	361 (93.5%)
Origin (pupils only)*	N (%)	N (%)		
Belgian	400 (68.4%)	356 (77.1%)		
European/west	84 (14.4%)	35 (7.6%)		
Non-European	101 (17.3%)	71 (15.4%)		
School staff function*			N (%)	N (%)
Teaching staff			327 (80.3%)	287 (81.1%)
Non-teaching staff			80 (19.7%)	67 (18.9%)

F, female; N, number; M, male; SES, socioeconomic status

* Missing items:

- Age unknown for 1 pupil and 37 staff members;
- Origin: 2 in primary, 5 in secondary;
- School staff function: 7 in primary, 7 in secondary

Findings in Table 3 on behaviour and lifestyle show that both pupils and staff have travelled abroad since the start of the pandemic with a range from 22% in primary school staff to 33% in secondary school pupils. In 2020, more than half of the pupils participated in a summer camp and 56 – 76% in extra-curricular activities during the school year since September. Public transport is rarely (6-7%) used by pupils and staff of primary schools but this number increased to almost 50% of respondents in secondary school pupils.

Around 13% of the staff reported to have one or more chronic health conditions, whereas this was about 8% in secondary school pupils and less than 3% in primary school pupils. More than half of the participants reported one or more symptoms that could be related to a SARS-CoV-2 infection since the beginning of the epidemic (February 2020). This includes non-specific symptoms as cough, running nose, headache and diarrhoea. About 10% of the school staff and 2% of the pupils reported a previous PCR confirmed diagnosis of COVID-19. None of the participants was admitted to the hospital because of COVID-19 since the pandemic start.

Contacts with a person diagnosed with COVID-19 were more frequent among school staff (about 35%) than among pupils (21%).

Table 3: Health and lifestyle related characteristics of pupils and school staff*

	Pupils		Staff	
	Primary 587 (82.7%)	Secondary 467 (81.2%)	Primary 414 (95.8%)	Secondary 361 (93.5%)
Total number (% participants who completed questionnaire)				
Lifestyle	N (%)	N (%)	N (%)	N (%)
Public transport (1 times a week or more)	39 (6.7%)	221 (47.9%)	26 (6.3%)	52 (14.6%)
<i>Extra-curricular activities</i>				
Summertime school year	350 (60.3%)	245 (53.1%)		
	439 (75.7%)	260 (56.4%)		
Travel abroad	162 (27.9%)	154 (33.4%)	91 (22.2%)	107 (30.1%)
Health	N (%)	N (%)	N (%)	N (%)
Any chronic condition	15 (2.6%)	35 (7.6%)	53 (13.0%)	45 (12.8%)
Any COVID-19 symptom since March 2020	339 (69.9%)	226 (49.1%)	286 (69.9%)	249 (70.1%)
Previous COVID-19 infection (PCR confirmed diagnosis reported by subject)	15 (2.6%)	10 (2.2%)	37 (9.0%)	36 (10.1%)
Contact with a confirmed case	110 (19.0%)	108 (23.4%)	129 (31.5%)	137 (38.6%)

N, number

* Rates in this table are based on the number of participants who completed the questionnaire. Some items are additionally missing but the number of missing items is usually these are less than 10 items per category.

* Regarding information how the questions were asked and items assessed see questionnaire <https://www.sciensano.be/nl/biblio/prevalence-and-incidence-antibodies-against-sars-cov-2-children-measured-one-year-belgium-a-sero-0>.

4.2. PREVALENCE OF ANTI-SARS-COV-2 ANTIBODIES

Among 355 (28%) pupils and 189 (23%) school staff the collected volume of saliva was not sufficient for antibody testing (100 µL required). Prevalence estimates of anti-SARS-CoV-2 antibodies are based on data from participants for whom sufficient saliva was available for the assay. The total number of available data is reported in Table 4 and is thus different from the total study population as listed in Table 2.

Using the data of 930 included participants, our study found that in Belgium, in December 2020 – January 2021, 11.0% of the primary and 13.6% of the secondary school children had anti-SARS-CoV-2 antibodies. For school staff this percentage was respectively 16.1% for staff from primary schools and 13.6% for staff from secondary school (Table 4).

Regional differences in sero-prevalence are presented in Table 4. The data for the Brussels region are sparse due to a relatively large proportion of samples with an insufficient volume of saliva. Consequently the estimates for the region of Brussels are imprecise (wide confidence intervals), which prevents further inference or conclusions specific for this region.

Table 4: Number and adjusted prevalence of anti-SARS-CoV-2 antibodies (IgG) among primary (age 7-9) and secondary (age 13-14) school children and school staff, Belgium and three regions, 3 December 2020 until 28 January 2021

	Pupils		Staff	
	N positive /N total	Prevalence % (95% CI)	N positive /N total	Prevalence % (95% CI)
BELGIUM				
Primary school	53/479	11.0 (7.6 - 15.9)	49/305	16.1 (12.2 - 21.3)
Secondary school	58/451	13.6 (9.9 - 18.5)	44/324	13.6 (10.3 - 17.9)
TOTAL	111/930	12.4 (9.7 – 15.8)	93/629	14.8 (12.2 - 18.0)
REGIONS				
BRUSSELS				
Primary school	6/43	17.5 (7.2 - 42.6)	1/23	4.5 (1.0 - 20.6)
Secondary school	10/36	30.0 (11.4 - 79.2)	6/37	15.9 (7.2 - 34.9)
TOTAL	16/79	24.0 (11.9 - 48.4)	7/60	10.5 (4.4 - 25.1)
FLANDERS				
Primary school	21/265	7.9 (5.2 - 12.1)	22/163	13.3 (8.5 - 20.8)
Secondary school	26/281	9.5 (6.3 - 14.2)	24/184	13.0 (8.6 - 19.7)
TOTAL	47/546	8.7 (6.4 - 11.6)	46/347	13.2 (9.7 - 17.8)
WALLONIA				
Primary school	26/171	13.6 (7.5 - 24.8)	26/119	21.8 (15.5 - 30.4)
Secondary school	22/134	16.1 (11.8 - 22.0)	14/103	12.7 (8.9 - 18.1)
TOTAL	48/305	15.4 (10.8 - 22.0)	40/222	17.7 (13.6 - 23.2)

CI, confidence interval (adjusted for clustering of subjects); N, number.

The prevalence of antibodies was slightly lower in children than in school staff. However, none of the differences between primary and secondary school pupils, between primary and secondary school staff or between pupils and staff within school levels were statistically significant.

Analysis of the data also showed that positive anti-SARS-CoV-2 antibody test among pupils and/or staff were found in 69 (82%) of schools and were thus not clustered within a few schools.

Multiple log binomial regression of staff versus pupils and secondary versus primary schools adjusted for clustering reveals no significant differences. The RR (95%CI) is 1.23 (0.93 – 1.65, $p = 0.1$) in staff versus pupils and 1.02 (0.73 – 1.42; $p = 0.9$) in secondary versus primary schools.

Stratified simple log binomial regression shows a RR in secondary versus primary schools is 1.27 (0.78 – 2.06; $p = 0.3$) in pupils, and 0.84 (0.57 – 1.25; $p = 0.4$) in staff. The RR in staff versus pupils is 1.48 (0.99 – 2.22; $p = 0.06$) in primary schools, and 1.05 (0.70 – 1.58; $p = 0.8$) in secondary schools.

Corresponding risk differences estimated with binomial regression with an identity link show a RD (95%CI) of 2.9% (-0.9 – 6.7%; $p = 0.1$) in staff versus pupils and 0.7% (-3.8 – 5.2%; $p = 0.8$) in secondary versus primary schools in the multiple analysis. In the stratified analysis the RD is 2.9% (-3.1 – 8.9%; $p = 0.3$) in secondary versus primary pupils, -2.5 (-8.4 – 3.3; $p = 0.4$) in secondary versus primary staff, 5.3% (0 – 10.6%; $p = 0.5$) in primary staff versus pupils, and 0.6% (-4.8% - 6.1%) in secondary staff versus pupils.

5. CONCLUSIONS

We provide representative anti-SARS-CoV-2 antibodies prevalence estimates for Belgian school children and school staff.

The most important findings of this study can be summarized as follows:

- Our overall prevalence estimates of detectable anti-SARS-CoV-2 antibodies of **12.4% in pupils and 14.8% in school staff**, are comparable to estimates from mid-December 2020 in the UK (11.2% in pupils and 15.1% in school staff), but higher than the 7.8% in Swiss school children in November 2020 (24,12). Both countries, UK and Switzerland, provided face-to-face teaching. Representative and national school-based sero-prevalence studies are however scarce, only Austria, Chile, Germany and Switzerland have published national estimates for children in the school environment (25). Household studies often include school aged children as well, but estimates are generally higher than those from studies in school settings (25).
- Our study reflects **regional differences also seen in the daily and weekly reported COVID-19 cases in the Belgian population**, with a higher virus circulation in Wallonia and Brussels compared to the Flemish region (2). Our data provide a nationwide estimate and estimates for the Flemish and Walloon regions with a reasonable precision, but samples for Brussels should be interpreted cautiously due to the high degree of uncertainty (wide confidence intervals).
- We found **no statistical significant differences in the sero-prevalence estimates between children from primary schools and the second year of secondary school**. There is some evidence in the literature that the susceptibility for SARS-CoV-2 infection increases with age. A meta-analysis by Viner *et al* including studies published until September 2020 calculated a lower odds for infection in children of 0.52 and 0.72 in adolescents compared to adults (26). A systematic review and meta-analysis by Madewell estimated a secondary attack rate (SAR), the probability to become infected as a secondary case in the presence of a primary COVID-19 case, of 17% in children versus 28% in adults (27). Both in the Belgian school setting and the community, IPC (infection prevention and control) measures have been different depending on age. The largest differences related to extra-curricular activities, mask wearing, contact tracing, quarantine and testing procedures, but both age groups received face-to-face teaching. Analysis of our study data until the end of the study in June 2021, may reveal if our prevalence estimates are the result of effective IPC measures, but this is currently not possible. A pilot study in Limburg which also compared primary and secondary schools found no difference between both, in a region with a high number of confirmed cases in the community, while none of the youngest children were infected in the region with a low virus transmission (8).
- We found **no statistically significant differences in the prevalence of antibodies between school staff and pupils** and **no statistically significant differences between school staff from primary and secondary schools at the national level**. The similar sero-prevalence between the groups does show underreporting of cases among pupils when they are reported only as confirmed cases by positive PCR. Testing for acute infection is mainly symptom dependent but symptoms of disease are difficult to interpret, especially in children and adolescents. Both, 2/3 of the primary school pupils and of the school staff reported symptoms included in the list of COVID-19 associated symptoms since the start of the pandemic. Further analysis will provide insight in the asymptomatic case rate in both groups since we will have longitudinal data on the sero-prevalence and reported symptoms that cover relatively narrow time frames. For the present analysis, the relatively (vs. PCR) large rate of detected anti-SARS-CoV-2 antibodies among pupils should not be interpreted as widespread SARS-CoV-2 transmission in the school environment, nor do they imply that children are important or disproportionately frequent infectors.
- Given the transmissible character of the disease, dependence of events is not unexpected. However, there was **no evidence of important clustering of cases in schools** during the first

testing period, and thus no strong evidence of widespread transmission of SARS-CoV-2 in the school environment under current infection prevention and control measures.

- At national and regional level, we found **similar prevalence of antibodies in children and teaching staff compared to blood donors and healthcare workers**, collected during the same sampling period (Table 5). The earlier discussed study from the UK also found sero-prevalence estimates in the school community, children and teachers, similar to the local community seroprevalence (24). This indicates that schools providing face-to-face teaching did not result in disproportionate numbers of infected individuals.

Table 5: Prevalence of anti-SARS-CoV-2 antibodies (IgG and/or IgM) among different population groups in Belgium, Dec 2020 – Jan 2021

Population description	Time period	Prevalence of anti-SARS-CoV-2 antibodies (%; 95% CI)			
		Belgium	Brussels	Flanders	Wallonia
Pupils	3 Dec 2020 – 28 Jan 2021	12.4 (9.7-15.8)	24.0 (11.9-48.4)	8.7 (6.4-11.6)	15.4 (10.8-22.0)
School staff	3 Dec 2020 – 28 Jan 2021	14.8 (12.2-18.0)	10.5 (4.4 -25.1)	13.2 (9.7-17.8)	17.7 (13.6-23.2)
Blood donors	21 Dec 2020	16.3 (13.9-18.6)	23.2 (16.6-29.6)	9.0 (6.2-11.8)	27.3 (22.4-32.2)
Blood donors	6 Jan 2021	17.9 (15.4-20.6)	23.5 (17.0-30.1)	13.7 (10.4-16.9)	23.8 (19.2-28.7)
Hospital HCW	21-24 Dec 2020	19.7 (11.7-31.2)	NA	NA	NA
Primary HCW	24 Dec 2020 – 8 Jan 2021	15.1 (13.5-16.6)	18.5 (13.5-23.4)	11.3 (9.8-12.8)	20.4 (16.9-23.8)

CI, credible interval (for blood donors) or confidence interval (for HCW, pupils and school staff); HCW, healthcare workers

Our study and present reporting has limitations:

- Primary, due to insufficient saliva in the samples, 25% of the specimens could not be analysed for the presence or absence of antibodies. Combined with a participation rate slightly below expectation this resulted in a smaller study population than anticipated. However, our data still allow to provide nationwide sero-prevalence estimates and estimates for the regions of Flanders and Wallonia with a reasonable precision, but data for the Brussels Capital Region should be interpreted cautiously due to the high degree of uncertainty (wide confidence intervals).
- Secondly, we have not yet assessed the agreement between reported confirmed PCR cases, symptoms and sero-positivity or negativity and its impact on the estimates. This is planned in future reports.
- Third, the current reported testing period covered a longer time period than planned expanding to 8 weeks.
- Fourth, data on individual risks for infection was also limited for an assessment of common risk behaviours (extra-curricular activities, public transport, high risk contact) through the online questionnaire.
- Fifth, the absence of baseline data at start of the school year or from May-June 2020 and data on toddlers limits the conclusions we can formulate based on the data we collected in our study.

Sero-prevalence studies on themselves also come with limitations. They cannot provide us insight in the detailed transmission dynamics, including the direction of the transmission. A pre-print study by Theuring et al investigated the secondary attack rate in connected households to a randomly selected number of schools and found this to be 1.1% (28).

Main conclusion and finding

This study provides a representative estimate of the prevalence of anti-SARS-CoV-2 antibodies among pupils and school staff in Belgian primary and secondary schools at the end of the second wave. The study found that **schools providing face-to-face teaching did not result in disproportionate numbers of infected individuals**. There are no important statistical or clinical differences in the sero-prevalence in primary and secondary school pupils and school staff on the one side and the broader community on the other side.

A second testing round has already completed and will provide improved estimates for regions with missing data and include a larger sample size with interpretable serology test results. Additionally, this will enable us to follow up the epidemic evolution within the school communities in Belgium. Further assessment of risk factors for infection within this population will also still follow, providing additional insight in characteristics of those tested positive and negative. This study will also provide sampling at a moment that in the adult population a wide roll-out of vaccines is taking place.

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