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# BMJ Open

## Research protocol for Sentinel Schools study: Monitoring and evaluation of SARS-CoV-2 epidemic in Catalan educational settings.

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Manuscripts

## 1 **Research protocol for Sentinel Schools study: Monitoring and evaluation of SARS-CoV-** 2 **2 epidemic in Catalan educational settings.**

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15 59 **Key words:** COVID-19, severe acute respiratory syndrome coronavirus 2, School Settings,  
16 60 Sentinel Surveillance

## 17 61 **ABSTRACT**

### 18 62 **Introduction**

19  
20 63 Since the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) became of concern in  
21 64 January 2020 many preventive measures have been adopted in educational settings to ensure  
22 65 the control of coronavirus disease 2019 (COVID-19) pandemic among children and staff in  
23 66 schools. This study aims to set up a school sentinel surveillance network with the purpose of  
24 67 monitoring SARS-CoV-2 infection, seroprevalence as well as to analyse the impact of preventive  
25 68 interventions of SARS-CoV-2 in school settings. Additionally, we will assess diverse screening  
26 69 strategies in a cohort of students and school staff to monitor the screening acceptance and its  
27 70 potential impact. Altogether, we hope this study will enable the design of more effective  
28 71 strategies for the prevention of COVID-19 spread.

### 29 72 **Methods and analysis**

30  
31 73 The sentinel schools' study is a cross-sectional, school-based project including twenty-six  
32 74 participating sentinel schools in Catalonia (Spain). Children, adolescents and staff at the schools  
33 75 will be invited to participate. This project will be carried out from January, 2021 until June, 2022  
34 76 as follows: i) Twice yearly serological testing and molecular SARS-CoV-2 detection and  
35 77 questionnaires covering SARS-CoV-2 symptoms, tests, health, knowledge, attitudes and  
36 78 behaviours; ii) An environmental evaluation carried out in different classrooms; iii) SARS-CoV-2  
37 79 transmission dynamics and the impact of different variants among confirmed cases and  
38 80 classmates; iv) A participatory process by which the participants are invited to act as co-  
39 81 investigators to evaluate prevention strategies and provide recommendations to improve  
40 82 COVID-19 prevention in schools. Descriptive analysis will be performed for the main variables  
41 83 collected. The incidence and seroprevalence will be calculated and the association with socio-  
42 84 demographic factors and school characteristics will be determined using multivariate logistic  
43 85 regression.

### 44 86 **Ethics and dissemination**

45 87 Ethical approval was obtained from the IDIAPJGol and the Hospital Universitari Vall d'Hebron  
46 88 ethics committees. A report will be generated quarterly. Findings will be disseminated at  
47 89 national and international conferences and published in peer-reviewed journals.

### 48 90 **STRENGTHS AND LIMITATIONS OF THIS STUDY**

#### 49 91 **Strengths**

- 50  
51 92 - A multicentre study combining cross-sectional and longitudinal studies, collecting data from  
52 93 sentinel schools throughout Catalonia.

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- 94 - Planned to consolidate the sentinel school surveillance network to monitor and evaluate the  
95 epidemiology of SARS-CoV-2 in school settings and assess the effectiveness of future  
96 preventive and control measures, new diagnostic tests or vaccination.  
97 - Transdisciplinary and participatory research, carried out in collaboration with the education  
98 community to ensure that the prevention and control strategy for SARS-CoV-2 fits with the  
99 needs and expectations of schools.

#### 100 Limitations

- 101 - The participating school-population might not be representative of the entire Catalan school  
102 population distributed across all the territory.  
103 - Participation in periodic screenings could be low due to fear of testing the younger children  
104 or because of pandemic fatigue due to the large number of tests being performed.

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## 112 INTRODUCTION

113 Coronavirus disease 2019 (COVID-19), first reported from Wuhan city, China in December 2019<sup>1</sup>,  
114 was declared a Public Health Emergency of International Concern by the World Health  
115 Organization (WHO) on 30 January 2020 and defined as a pandemic on 11 March 2020. Although  
116 children were recognized as contributing to only a small proportion of laboratory-confirmed  
117 COVID-19 cases and rarely developing severe or fatal disease<sup>2, 3</sup>, their role in asymptomatic  
118 infection and transmission, which is well-described for other respiratory viral infections such as  
119 influenza, was uncertain at the point of these restrictions and is still under discussion.

120 On the declaration of the global COVID pandemic most countries closed their schools as part of  
121 their national lockdown measures<sup>4, 5</sup>, with more than 1 billion children and young people  
122 affected so far<sup>6</sup>. The closure of schools reduced the number of contacts within the population  
123 and, therefore, the subsequent transmission<sup>5</sup>. However, this measure can also cause  
124 considerable damage to children and their families with significant social and economic impacts,  
125 mainly on physical and mental health. On the other hand, most evidence from countries that  
126 have reopened schools or never closed them, suggests that schools have not been associated  
127 with significant increases in community transmission<sup>7-10</sup>. Thus, the transmission of SARS-CoV-2  
128 from paediatric patients both at home and in schools has been an intensely topic since the  
129 beginning of the COVID-19 pandemic, also regarding the emergency of new variant scenarios<sup>11-</sup>  
130 <sup>14</sup>.

131 Since Catalan schools reopened in September 2020 after 6-months of closure, there have been  
132 83,911 accumulated positive COVID-19 cases, of which 74,246 were students (5.16%) and 8,996  
133 school staff (5.49%)<sup>15</sup>. Likewise, a recent study that analysed the incidence dynamics of SARS-  
134 CoV-2 infection in children in the first term of the school reopening shows that the infection rate  
135 among children remained lower compared with the general population for pre-school (3-6  
136 years) and primary pupils (6-12 years) but was equal to it or higher in secondary students (12-  
137 18 years)<sup>16</sup>. Moreover, several studies have shown that in this pandemic very few cases infect  
138 many contacts (super-spreaders) while most cases either infect nobody or very few people and  
139 this includes paediatric index cases<sup>17-21</sup>. Defining host-related, viral and environmental patterns  
140 that determine these super-spreading situations is relevant to the tailoring of measures to  
141 minimize the transmission of SARS-CoV-2 in schools<sup>22</sup>.

142 Preventive interventions play an important role in working together to gain control of the  
143 COVID-19 pandemic, also in schools. In this sense, the social and behavioural sciences can  
144 provide valuable insights into managing the pandemic and its impacts<sup>23</sup>. Non-pharmacological  
145 preventive interventions in schools such as physical distancing, hygiene, use of masks, restricting  
146 interactions to clusters of students in bubble-groups, massive microbiological testing and other  
147 safety measures are essential to prevent transmission. These measures should be adapted to  
148 the setting and age group and prevent transmission while providing children with an optimal  
149 learning and social environment<sup>4</sup>. Furthermore, as it is known that SARS-CoV-2 transmission is  
150 via aerosols and virus-laden aerosols may easily accumulate in indoor environments, a proper  
151 ventilation of indoor spaces can be a great preventive measure. Additionally, the first set of  
152 COVID-19 vaccines provided a pharmacological intervention in the last quarter of 2020 when  
153 they received the authorization for emergency use by the European Medicines Agency (EMA)  
154 and the Food and Drug Agency in the United States<sup>24</sup>. So far, teaching and non-teaching staff  
155 and population over 16 years are being vaccinated as defined in the Spanish vaccination strategy  
156 raising hopes for a better control of the epidemic inside school settings. In this context, there is  
157 a need to understand the epidemiology of SARS-CoV-2 in children once the adult population has  
158 been vaccinated. The pandemic is moving very fast, and behaviours and attitudes may change  
159 in response to the COVID-19 pandemic. Understanding the drivers of vaccine acceptance will be  
160 crucial to the success of COVID-19 mass vaccination campaigns.

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3 161 Therefore, the use of periodical cross-sectional surveys on the knowledge, attitude and practice  
4 162 (KAP) associated with COVID-19 will allow rapid and adaptive monitoring of demographics,  
5 163 preventive behaviours, knowledge, and perceptions over time, among others, and can be useful  
6 164 in order to identify misinformation as they emerge.

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8 165 This article reports the design and protocol of a school-based study in several sentinel schools  
9 166 in Catalonia. The study is part of the COVID-19 monitoring and evaluation plan from the Ministry  
10 167 of Health of the Government of Catalonia, and it is conceived as a participatory and  
11 168 transdisciplinary research process where the students and school staff will be invited to  
12 169 participate. The monitoring and evaluation provide practical information for making timely  
13 170 decisions, addressing community needs, and identifying more effective strategies for the  
14 171 prevention of COVID-19 spread and future infectious threats. In addition, the protocol could be  
15 172 highly useful for adaption into other educational settings for the monitoring of the COVID-19  
16 173 pandemic.

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## 20 175 **GENERAL OBJECTIVES**

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23 176 1. To describe over time the knowledge, attitudes and behaviours (KAB) of students and school  
24 177 staff (teaching and non-teaching staff) towards SARS-CoV-2 infection and its prevention, as  
25 178 well as its impact in school settings.  
26 179 2. To assess over time the prevalence of SARS-CoV-2 infection and seroprevalence of  
27 180 antibodies against SARS-CoV-2 and to identify associated sociodemographic, biological,  
28 181 behavioural and environmental factors among both children and staff.  
29 182 3. To identify and describe multi-level determinants, barriers and needs of SARS-CoV-2  
30 183 prevention related measures in school settings over time.  
31 184 4. To assess the secondary attack rate of SARS-CoV-2 children index cases and its multilevel  
32 185 determinants and factors, both in school and family settings.  
33 186 5. To analyse the impact of preventive and control measures on the occurrence of SARS-CoV-  
34 187 2 in school settings.  
35 188 6. To pilot alternative testing and screening technologies and strategies, to assess their  
36 189 acceptability, feasibility and performance and the occurrence of SARS-CoV-2 infection  
37 190 among students over 12 years old and school staff.  
38 191 7. To analyse the impact of different SARS-CoV-2 variants' transmission in school settings.  
39 192 8. To facilitate a participatory process where the education community will act as co-  
40 193 researchers elaborating recommendations to improve the prevention and control measures  
41 194 in the school environment.  
42 195 9. To evaluate the impact on students' learning, attitudes and motivations of their  
43 196 participation in the research process and the teacher's perspectives on this impact.  
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## 45 198 **METHODS AND ANALYSIS**

### 46 199 **Study design and Setting**

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49 200 The population of Catalonia was 7,619,494 in 2019. The Catalan school system includes  
50 201 1,582,466 students, 117,398 teaching staff and 5,492 school centres<sup>25</sup>.

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53 202 This project is based on sentinel schools defined as a network of schools representing the  
54 203 diversity of schools and the scholar population in Catalonia, and chosen using the following  
55 204 criteria:

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58 205 • Volunteering/commitment of both the school management team and the teaching staff  
59 206 as well as the children's parents to participate in the project



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3 207 • Representation of schools located in the different Basic Health Areas (BHA) and  
4 208 territorial areas will be ensured taking into account tertiles of SARS-CoV-2 accumulated  
5 209 incidence and tertiles of socio-economic deprivation index<sup>26</sup>  
6 210 • Representation of schools with different characteristics:  
7 211 ○ Sociodemographic indicators. At least two-to-five high complexity schools  
8 212 characterized by low socioeconomic level and specific educational needs  
9 213 ○ Some schools located in rural areas<sup>27</sup>  
10 214 ○ Schools with all levels of education, small school size and school centres with  
11 215 professional training courses  
12 216 ○ Public, charter and private schools

15 217 The sentinel surveillance is carried out by means of serial cross-sectional and longitudinal school-  
16 218 based studies, direct observation, index case study and participatory research approach in  
17 219 children, adolescent and school staff from the selected sentinel schools. In a subset of schools  
18 220 (n=5), a cohort of students from first grade of secondary school to high school (12->18 years)  
19 221 and school staff has been established in order to monitor the COVID-19 incidence and the  
20 222 feasibility and acceptability of different periodical screening practices for COVID-19  
21 223 confirmation. All the study interventions will be carried out in two academic years starting from  
22 224 January 2021 to June 2022.

#### 25 225 **Study population (Inclusion criteria)**

- 26 226 • Students attending sentinel schools will be eligible for the study, from preschool (3-  
27 227 years-old) to high school (approximately 18-years-old)  
28 228 • School staff of the sentinel schools, including teachers, administrators, canteen and  
29 229 cleaning staff, and other adults working in the educational settings such as  
30 230 extracurricular education instructors

#### 33 231 **Informed consent**

34 232 Informed consent will be obtained from school staff, parents of children under 16 and pupils of  
35 233 16 years-old or older. Participants will be free to decline/withdraw consent at any time without  
36 234 providing a reason and without being subject to any resulting detriment.

#### 38 235 **Study procedures**

40 236 Summary information of questionnaires, biological samples and other information to be  
41 237 collected is provided in Table 1.

#### 43 238 Knowledge, attitudes and behaviours regarding COVID-19 (KAB) questionnaires and impact of 44 239 preventive and control measures

46 240 Each headteacher will send the study information pack (a study leaflet and the information  
47 241 sheet) and the link to the online informed consent and the baseline questionnaires by e-mail to  
48 242 the parents/guardians, school staff and older students (when necessary, on paper). We will send  
49 243 follow-up questionnaires twice a year. Three different questionnaire models will be designed:  
50 244 for teachers and other school staff (Questionnaire A); for students under 16, which will be  
51 245 answered by parents/guardian (Questionnaire B), and for students over 16 (Questionnaire C).  
52 246 The variables included in the KAB survey will be mainly based on the WHO recommendations,  
53 247 as described in WHO/Europe (2020)<sup>28</sup>.

#### 56 248 Prevalence of SARS-CoV-2 active infection and seroprevalence of antibodies against SARS-CoV- 57 249 2

58 250 *Cross-sectional study:* A field team (FT) made up of three nurses and a field coordinator will visit  
59 251 each school equipped with personal protective equipment to collect the samples for testing.

252 They will schedule the number of intervention days with each participating school depending on  
 253 school size. The following samples in the baseline and the following cross sectionals (twice  
 254 yearly) will be collected from all participants: i) Nasal swabs to perform a transcription-mediated  
 255 amplification assay (TMA) for detection of SARS-CoV-2; ii) Finger prick blood sample to assess  
 256 with a quick anti SARS-CoV-2 IgM/IgG antibody test.

257 *Longitudinal study:* Follow-up interventions will be scheduled twice yearly during the school year  
 258 as an alternative testing strategy. In each intervention, the FT will collect saliva and nasal  
 259 specimens for the detection of SARS-CoV-2 by molecular or antigenic tests, respectively. The  
 260 cohort participants will fill in an additional online epidemiological survey with information  
 261 related to SARS-CoV-2 infection, their symptomatology, exposure and vaccine status.

#### 262 Secondary attack rate and SARS-CoV-2 variants

263 This part of the study will be carried by the Paediatric Infectious Diseases and  
 264 Immunodeficiencies Unit at Hospital Universitari Vall d'Hebron (HUVH). Data on COVID-19 index  
 265 cases will be collected with appropriate social and geographical distribution. These cases will be  
 266 detected by the routine data provided by the Catalan Public Health Department or detected  
 267 during the study interventions and analysed in depth from then on. Data on demographic, social  
 268 and clinical features, vaccination status, comorbidities and clinical outcome will be collected.  
 269 School and household contacts will also be studied in depth to detect secondary cases. Samples  
 270 from the index case and all COVID-19 confirmed contacts will be sequenced using whole genome  
 271 sequencing (WGS) following the ARTIC Network protocol<sup>29</sup> for the characterization of SARS-CoV-  
 272 2 (lineage and mutations), molecular tracing of sequences, and measurement of the viral load  
 273 in these respiratory samples to assess its role in the transmission dynamics.

#### 274 Environmental determinants and barriers

275 The environmental evaluation will be carried out by the ISGlobal team to obtain information on  
 276 the structural characteristics of each participating sentinel school, ventilation practices and  
 277 other environmental prevention measures using the KKmoon carbon dioxide detector device.  
 278 This intervention will include: i) A structural evaluation by a field technician in at least one  
 279 classroom for each grade; ii) Online twice yearly surveys addressed to teachers and  
 280 headteachers regarding ventilation and other prevention practices; iii) Twice yearly 15-day  
 281 assessment of CO<sub>2</sub>, temperature and humidity – seven days assessed by the field technician and  
 282 the remainder as an experimenting tool for students – in 5 to 8 previously chosen classrooms.

#### 283 Participatory research

284 The project is conceived as a collaborative and transdisciplinary research project where the  
 285 education community and families participate in different phases of the research process. They  
 286 will act as co-researchers evaluating the prevention and control measure implementation of  
 287 SARS-CoV-2 infection in the school environment with a systemic perspective, as well as  
 288 elaborating their recommendations to improve the prevention and control strategy. This  
 289 approach will be implemented in collaboration with the EC funded project CONNECT, which aims  
 290 to improve science learning and increase students' motivation towards science careers by  
 291 engaging schools, scientists and families to solve local challenges.

292 Participation will entail discussion groups: i) Online focus groups with teachers. Preliminary  
 293 results of the bio-behavioural surveys will be shared and, based on these, they will be invited to  
 294 analyse problems, opportunities and needs, and to develop proposals for improvement of  
 295 prevention measures following a protocol; ii) Teachers conducting focus groups with their class-  
 296 group students and then families, reproducing a similar protocol; iii) The edited list of  
 297 recommendations will be presented by students to scientists and policy makers in an online  
 298 conference; iv) Elaboration of the final list of recommendations; v) Capital science survey: a pre-

299 and post-intervention survey addressed to pupils regarding the science learning and students'  
300 attitudes and motivation, and a pre- and post-intervention survey addressed to teachers  
301 regarding the education process.

302

303 Sample management, microbiological analysis and test result communication

304 As described above, diverse biological samples will be collected during the study.

305 The finger prick blood collected at the baseline and the follow-up will be processed at the time  
306 of collection to perform a quick SARS-CoV-2 serological test (COVID-19 IgG/IgM Rapid Test Kit,  
307 Lambra, Spain) with sensitivities of 97,2% (IgG) and 87,9% (IgM), and specificities of 100% for  
308 both immunoglobulins as the manufacturers describe. This approach will be used to assess the  
309 exposure to SARS-CoV-2 infection or vaccination by the presence of antibodies. In addition, the  
310 nasal swab sample collected in the longitudinal study will be processed at the time of collection  
311 for detection of SARS-CoV-2 antigen using the Panbio COVID-19 Ag Rapid Test (Abbot, USA) with  
312 a sensitivity of 93.3% (95% CI: 83.8-98.2%) and specificity of 99.4% (95% CI: 97.0-100%) as the  
313 manufacturers describe. The nursing team will upload the rapid test results on an online  
314 research database using electronic tablets. These results will be introduced afterwards to the  
315 electronic health record of all participants, who will be able to consult them in the online patient  
316 health portal (La Meva Salut app). In case of Ag positive with IgG negative, the COVID-school  
317 manager, a new sanitary staff role acting as a liaison between the primary care team and the  
318 school centres, will activate the public health protocol established by the Catalan Ministry of  
319 Health<sup>30</sup>.

320 Nasal swabs and saliva samples will be maintained at 4°C during sampling procedures and  
321 transport to laboratory facilities. A molecular assay based on the transcription mediated  
322 amplification assay (Procleix SARS-CoV-2, Grifols) will be conducted in HUVH for detection of  
323 SARS-CoV-2 in nasal swabs, and RT-PCR assay (Allplex SARS-CoV-2/FluA/FluB/RSV, Werfen) will  
324 be conducted at the Hospital Universitari Germans Trias i Pujol (HUGTiP) laboratories to  
325 determine SARS-CoV-2 infection in saliva specimens. If the TMA assay (HUVH) or RT-PCR assay  
326 (HUGTiP) is positive, an active infection will be confirmed. Once the nasal samples have been  
327 tested, all positive specimens will be stored in sample collection C.0001145 on the *Instituto de*  
328 *Salud Carlos III* register. On the other hand, saliva samples with positive SARS-CoV-2 results will  
329 be frozen and stored at the IGTP-HUGTiP Biobank and conserved for two years. TMA/PCR results  
330 will be uploaded by the microbiology laboratories to the electronic health record, and the  
331 participants and their general practitioners or paediatricians will be able to check them.

332 Regarding the transmissibility study, nasopharyngeal or nasal swab samples from index cases  
333 and positive secondary cases will be sent to the HUVH laboratory for genetic SARS-CoV-2  
334 characterisation, to measure the viral load and to detect other respiratory viruses. The genetic  
335 characterisation of SARS-CoV-2 will be performed through WGS according to the ARTIC Network  
336 protocol<sup>29</sup> by using MiSeq and NextSeq 2000 platforms (Illumina, CA, USA). Other respiratory  
337 viruses will be detected by a real-time multiplex RT-PCR assay (Allplex Respiratory Panel Assay,  
338 Seegene); total nucleic acids will be extracted using NucliSENS EasyMAG (bioMérieux, Marcy  
339 l'Etoile, France) or Microlab STARlet System (Hamilton, CA, USA) according to the  
340 manufacturer's instructions. Additionally, to measure the SARS-CoV-2 viral load, an in-house  
341 quantitative RT-PCR assay using the primer/probe set targeting the nucleocapsid protein (N1)  
342 and the human RNase P (housekeeping gene) from the CDC 2019-nCoV Real-Time RT-PCR  
343 Diagnostic Panel will be carried out. The Ct values of the viral target will be normalized to a  
344 housekeeping gene based on the  $\Delta$ Ct method (Ct<sub>sample</sub> - Ct<sub>housekeeping gene</sub>) in order to  
345 minimize the variations due to the non-standardized collection of a heterogenous specimens.

### 346 **Data management, data protection and patient confidentiality**

347 Informed consents and the different surveys will be designed and published by means of the  
 348 EUSurvey management system, an official online survey management tool of the European  
 349 Commission. For those participants for whom online access is not possible, printed surveys will  
 350 be distributed by the field team and afterwards digitalized. The periodical surveys from the  
 351 cohort study will be published by means of the OpenTIC software.

352 After giving their consent to participate (or allow their child to participate), each participant will  
 353 be allocated a unique participant ID number on enrolment to the study. This unique identifier  
 354 will serve as a link to all the data needed for the study (questioners, biological samples). The file  
 355 that relates the identifier or pseudonym to the personally identifiable data will be encrypted  
 356 and the access to this file will be restricted to a very small number of authorized persons (EM,  
 357 YD, JA, LA). The process will comply with the General Data Protection Regulation (GDPR)  
 358 requirements.

#### 359 **Study definitions:**

360 Given that all the participants attending the school should be asymptomatic, a confirmed COVID-  
 361 19 case will be defined as any individual testing SARS-CoV-2 positive by molecular assays (PCR  
 362 or TMA-based) or COVID-19 Ag Rapid Test (RAT) in a respiratory or saliva specimen<sup>31</sup>.

363 A paediatric index case will be established when the child is the first confirmed COVID-19 case  
 364 in the classroom noticed by health authorities or the research team<sup>21</sup>. A secondary case will be  
 365 defined as a classmate or household contact subsequently testing positive for SARS-CoV-2 by  
 366 molecular assay or RAT. Close contacts will be defined as all people who have shared space with  
 367 a positive COVID-19 less than 2 metres away, for more than 15 minutes, without protection and  
 368 from the 48 hours prior to the onset of symptoms. If the positive person has not had symptoms,  
 369 onset will be defined as the date of performing the diagnostic test.

#### 370 **Variables collected**

- 371 i) Individual data
- 372 • Sociodemographic and socioeconomic indicators: age, gender, ethnic origin,  
 373 household and career, economic status, job situation of their parents in the case of  
 374 pupils
  - 375 • Clinical data and infection by SARS-CoV-2: symptoms, hospitalization, exposure,  
 376 contact with positive cases
  - 377 • Attitude, behaviour and knowledge regarding COVID-19 and preventive measures
  - 378 • Pandemic impact indicators such as changes on mental and physic health and the  
 379 purchasing power of parents and school staff
  - 380 • Vaccination data: manufacturer, number of doses, date of doses, refusal to  
 381 vaccinate (date and reason)
  - 382 • Attitude and usability of focus groups regarding scientific contribution
- 383 ii) Collective data
- 384 Number of classrooms, number of tables/classroom, number of pupils/m<sup>2</sup>, school  
 385 surface, schoolyard surface, concentration of CO<sub>2</sub>, temperature and humidity in the  
 386 classrooms.
- 387 iii) Ecological data
- 388 These data will be collected and provided by the Primary Care Services Information  
 389 System (SISAP) and the Data analytics program for health research and innovation  
 390 (PADRIS) and will include data from different data sources in order to obtain the  
 391 information mentioned below:

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- 392 • Number of new COVID-19 confirmed cases or tested positive for SARS-CoV-2 by  
393 TMA/PCR or RAT /total of residents.
- 394 • Number of new COVID-19 confirmed cases or tested positive for SARS-CoV-2 by  
395 TMA/PCR or RAT/total of tested people.
- 396 • Number of new COVID-19 confirmed cases or tested positive for SARS-CoV-2 by  
397 TMA/PCR or RAT/total of suspected cases.
- 398 • Number of confined classrooms/total number of classrooms.

### 399 **Data analysis plan and sample size**

400 We estimate a 70% participation among the total of 11,000 individuals who are on the census  
401 at the 26 sentinel schools. A descriptive analysis will be performed for all the main  
402 aforementioned variables collected: participant's sociodemographic characteristics, SARS-CoV-  
403 2 infection characterization, its associated factors, behaviour information and other outcomes  
404 of interest. For quantitative variables, we will use measures of central tendency and dispersion  
405 (mean, standard deviation, median, interquartile range, 95% confidence interval). For  
406 qualitative variables, we will calculate absolute frequencies and percentages. To estimate the  
407 statistical significance of time trends in SARS-CoV-2 laboratory confirmed cases we will use  
408 multivariate logistic regression analysis with robust standard errors clustered at the individual-  
409 level and school-level, adjusting for sociodemographic, environmental and school structural  
410 variables.

411 In order to address the fourth objective related to the transmissibility study, a descriptive  
412 analysis will be performed for all cases and contacts identified in school clusters. Analyses will  
413 include chi-square and independent sample t-test procedures to assess differences between  
414 super-spreaders and non-spreaders for index cases and secondary cases using socio-  
415 demographics, number of classmates and household contacts, clinical and environmental  
416 variables. Finally, we will use univariate and multivariate logistic regression models to assess the  
417 association between transmission risk factors and SARS-CoV-2 infection among index cases and  
418 close contacts. All models will be adjusted for gender, age, vaccination status, number of  
419 classmates, and household contacts and whether or not the index cases are symptomatic.

420 Global data on the COVID-19 epidemic in Catalonia and the school basic health area (BHA) will  
421 be collected to contextualize the current epidemic situation. Data will be provided globally and  
422 stratified by age groups and collectives. This data will be provided by the Catalan Agency for  
423 Quality and Health Assessment (AQuAS) and SISAP. Analysis of the interrupted time series of  
424 SARS-CoV-2 seroprevalence and COVID-19 confirmed cases will be performed to assess the  
425 public health implemented measures including vaccination programmes. The confirmed cases  
426 will be modelled as ARIMA processes to estimate the expected numbers to be compared to  
427 those observed and estimate the impact of the different analysed measures, to do this we will  
428 calculate absolute and relative changes between expected-observed confirmed cases in each  
429 time point of the implemented measures. Analysis will be conducted in R (R Core Team, 2014).

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### 431 **ETHICS AND DISSEMINATION**

432 The ethical aspects of the present study include:

- 433 • Recruitment of participants with informed consent
- 434 • Collection and storage of biological samples
- 435 • Questionnaires with non-anonymized data
- 436 • Collection and storage of personal data

437 The confidentiality of data and other ethical considerations will be managed in accordance with  
438 the recommendations of the Spanish Law 14/2007 of 3 July, on Biomedical Research and the

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3 439 Spanish Royal Decree RD 1716/2011 of 18 November, which lays down the basic requirements  
4 440 for the authorisation and operation of biobanks for purposes of Biomedical Research and the  
5 441 treatment of biological samples of human origin. Informed consent is required for this project  
6 442 as is established in article 59 of the law.

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8 443 The necessary measures will be taken to ensure the protection of personal data and their  
9 444 confidentiality, in accordance with EU Regulation 2016/679 of the European Parliament and of  
10 445 the Council of 27 April 2016 on the protection of natural persons with regard to the processing  
11 446 of personal data and on the free movement of such data (RGPD), and in the Spanish Organic Law  
12 447 3/2018 of 5 December, for the protection of personal data and Guarantee of digital rights (LOPD-  
13 448 GDD).

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15 449 The data protection office of the Ministry of Health of the Government of Catalonia has reached  
16 450 an agreement signed by all the organizations in the research team to align with all the ethical  
17 451 considerations mentioned above and recommended by the same office.

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19 452 The data and results provided by this project will be valuable in the current context of the public  
20 453 health emergency of international concern declared by the WHO for the COVID-19 pandemic  
21 454 and taking into account the urgent need for information coming from COVID-19 studies.

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23 455 The CEEISCAT research team will generate a quarterly report with qualitative and quantitative  
24 456 data to give feedback to the stakeholders. Findings from this study will be disseminated at  
25 457 national and international conferences, reported on the public webpage of the project and  
26 458 published in peer-reviewed journals.

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#### 30 460 **Study registration**

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32 461 Ethical approval was obtained from the Foundation University Institute for Research in Primary  
33 462 Health Care Jordi Gol i Gurina (IDIAPJGol) ethics committee with code 20/192-PCV on 17  
34 463 December 2020 and the Hospital Universitari Vall d'Hebron ethics committee with code  
35 464 PR(AMI)668/2020.

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#### 38 39 466 **AUTHORS' CONTRIBUTIONS**

40  
41 467 All authors have read, reviewed and agreed to the finalized submitted version of the manuscript.  
42 468 Conceptualisation: JC. Design study: JC, CF, AS, AB, JR, JS, PS, AS and MG. Operational procedures: JC, JR,  
43 469 AB, CF, AC, JS, MG, AA, TP, IB, JF, RM, PS, AS, and JB. Resources: RF, JM, JMA, CC and JB. Writing and draft  
44 470 preparation: AB, CF, AC. Writing, review and edition; all authors.

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48  
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51 475 during its execution, analyses, interpretation of the data or decision to submit result.

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#### 54 55 477 **COMPETING INTEREST STATEMENT**

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57 478 All of the authors declare that they have no conflicts of interest.

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3 480 **PATIENT AND PUBLIC INVOLVEMENT**

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5 481 No patient involved  
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8 483 **REFERENCES**

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577 **Table 1. Summary information of study procedures.**

Type of intervention	Determination	Type of Test	Coordination	Frequency
<b>Bio-behavioural questionnaires</b>			CEEISCAT	
- Questionnaire A (teaching and non-teaching staff) - Questionnaire B (parents or foster parents of students under 16 years old) - Questionnaire C (16-years-old or older students)				Once during 2020-2021 school year and twice during 2021-2022 school year
<b>Biological sampling</b>			CEEISCAT	
<u>Baseline</u> - Blood from finger prick - Nasal swab sample	Ab anti-SARS-CoV-2 Viral RNA (SARS-CoV-2)	LFA TMA		Once during 2020-2021 school year and twice during 2021-2022 school year
<u>Longitudinal study</u> (> 1 <sup>st</sup> grade of middle school and school staff) - Saliva sample - Nasal swab sample	Viral RNA (SARS-CoV-2) SARS-CoV-2 Ag rapid test	RT-PCR LFA		Bi-monthly
<b>Environmental and structural evaluation in each sentinel school</b>			ISGlobal	
- Environmental questionnaires (Directors and teachers) - Structural and environmental evaluation by a field technician - CO <sub>2</sub> , humidity and temperature measurements	Prevention measures (e.g. ventilation practices)			Once during 2020-2021 school year and twice during 2021-2022 school year
<b>Transmissibility study</b>			HUVH	
- COVID-19 index cases - Household and classmate contacts evaluation - Secondary attack rate	Viral coinfections Viral RNA (SARS-CoV-2) SARS-CoV-2 characterisations Viral load measurement	RT-PCR TMA/PCR Whole genome sequencing Quantitative PCR assay		
<b>Participatory research</b>			Living lab (IRSIcaixa)	
- Scientific capital surveys - Focus groups - List of recommendations - Annual school conference				Once during 2020-2021 school year and twice during 2021-2022 school year

578 Ab: antibodies; Ag: antigens; LFA: Lateral flow assay; TMA: Transcription mediated amplification assay

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## STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page No
<b>Title and abstract</b>	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found	1-2
<b>Introduction</b>			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	5
<b>Methods</b>			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	6-7
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	9-10
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6-8
Bias	9	Describe any efforts to address potential sources of bias	NA
Study size	10	Explain how the study size was arrived at	5-6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	9
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	10
		(b) Describe any methods used to examine subgroups and interactions	10
		(c) Explain how missing data were addressed	NA
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	10
		(e) Describe any sensitivity analyses	NA

Continued on next page

<b>Results</b>			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	NA
		(b) Give reasons for non-participation at each stage	NA
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	NA
		(b) Indicate number of participants with missing data for each variable of interest	NA
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	NA
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	NA
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	NA
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	NA
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	NA
		(b) Report category boundaries when continuous variables were categorized	NA
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
<b>Discussion</b>			
Key results	18	Summarise key results with reference to study objectives	NA
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	NA
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	NA
Generalisability	21	Discuss the generalisability (external validity) of the study results	NA
<b>Other information</b>			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	14

\*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at [www.strobe-statement.org](http://www.strobe-statement.org).

# BMJ Open

## Study protocol for monitoring SARS-CoV-2 infection and its determinants in Catalonia (Spain): an observational and participatory research approach in a Sentinel Network of Schools.

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<b>Primary Subject Heading</b>:	Public health

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Secondary Subject Heading:	Epidemiology, Paediatrics
Keywords:	COVID-19, Community child health < PAEDIATRICS, PUBLIC HEALTH, Epidemiology < INFECTIOUS DISEASES



## 1 Study protocol for monitoring SARS-CoV-2 infection and its determinants in Catalonia 2 (Spain): an observational and participatory research approach in a Sentinel Network 3 of Schools.

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18 60 **Key words:** COVID-19, severe acute respiratory syndrome coronavirus 2, School Settings,  
19 61 Sentinel Surveillance

## 20 62 **ABSTRACT**

### 21 63 **Introduction**

22  
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24 64 Since the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) became of concern in  
25 65 January 2020 many preventive measures have been adopted in educational settings to ensure  
26 66 the control of coronavirus disease 2019 (COVID-19) pandemic among children and staff in  
27 67 schools. This study aims to set up a school sentinel surveillance network with the purpose of  
28 68 monitoring SARS-CoV-2 infection, seroprevalence as well as to analyse the impact of preventive  
29 69 interventions of SARS-CoV-2 in school settings. Additionally, we will assess diverse screening  
30 70 strategies in a cohort of students and school staff to monitor the screening acceptance and its  
31 71 potential impact. Altogether, we hope this study will enable the design of more effective  
32 72 strategies for the prevention of COVID-19 spread.

### 33 73 **Methods and analysis**

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36 74 The sentinel schools' study is a cross-sectional, school-based project including twenty-six  
37 75 participating sentinel schools in Catalonia (Spain). Children, adolescents and staff at the schools  
38 76 will be invited to participate. This project will be carried out from January, 2021 until June, 2022  
39 77 as follows: i) Twice yearly serological testing and molecular SARS-CoV-2 detection and  
40 78 questionnaires covering SARS-CoV-2 symptoms, tests, health, knowledge, attitudes and  
41 79 behaviours; ii) An environmental evaluation carried out in different classrooms; iii) SARS-CoV-2  
42 80 transmission dynamics and the impact of different variants among confirmed cases and  
43 81 classmates; iv) A participatory process by which the participants are invited to act as co-  
44 82 investigators to evaluate prevention strategies and provide recommendations to improve  
45 83 COVID-19 prevention in schools. Descriptive analysis will be performed for the main variables  
46 84 collected. The incidence and seroprevalence will be calculated and the association with socio-  
47 85 demographic factors and school characteristics will be determined using multivariate logistic  
48 86 regression.

### 49 87 **Ethics and dissemination**

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52 88 Ethical approval was obtained from the IDIAPJGol and the Hospital Universitari Vall d'Hebron  
53 89 ethics committees. A report will be generated quarterly. Findings will be disseminated at  
54 90 national and international conferences and published in peer-reviewed journals.

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### 58 92 **STRENGTHS AND LIMITATIONS OF THIS STUDY**



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93 Strengths

- 94 - A multicentre study combining cross-sectional and longitudinal studies, collecting data from
- 95 sentinel schools throughout Catalonia.
- 96 - Planned to consolidate the sentinel school surveillance network to monitor and evaluate the
- 97 epidemiology of SARS-CoV-2 in school settings and assess the effectiveness of future
- 98 preventive and control measures, new diagnostic tests or vaccination.
- 99 - Transdisciplinary and participatory research, carried out in collaboration with the education
- 100 community to ensure that the prevention and control strategy for SARS-CoV-2 fits with the
- 101 needs and expectations of schools.

102 Limitations

- 103 - The participating school-population might not be representative of the entire Catalan school
- 104 population distributed across all the territory.
- 105 - Participation in periodic screenings could be low due to fear of testing the younger children
- 106 or because of pandemic fatigue due to the large number of tests being performed.

107

## 108 INTRODUCTION

109 Coronavirus disease 2019 (COVID-19), first reported from Wuhan city, China in December 2019<sup>1</sup>,  
110 was declared a Public Health Emergency of International Concern by the World Health  
111 Organization (WHO) on 30 January 2020 and defined as a pandemic on 11 March 2020. Although  
112 children were recognized as contributing to only a small proportion of laboratory-confirmed  
113 COVID-19 cases and rarely developing severe or fatal disease<sup>2, 3</sup>, their role in asymptomatic  
114 infection and transmission, which is well-described for other respiratory viral infections such as  
115 influenza, was uncertain at the point of these restrictions and is still under discussion.

116 On the declaration of the global COVID-19 pandemic most countries closed their schools as part  
117 of their national lockdown measures<sup>4, 5</sup>, with more than 1 billion children and young people  
118 affected so far<sup>6</sup>. The closure of schools reduced the number of contacts within the population  
119 and, therefore, the subsequent transmission<sup>5</sup>. However, this measure can also cause  
120 considerable damage to children and their families with significant social and economic impacts,  
121 mainly on physical and mental health<sup>7-11</sup>. On the other hand, most evidence from countries that  
122 have reopened schools or never closed them, suggests that schools have not been associated  
123 with significant increases in community transmission<sup>12-15</sup>. Thus, the transmission of SARS-CoV-2  
124 from paediatric patients both at home and in schools has been an intensely topic since the  
125 beginning of the COVID-19 pandemic, also regarding the emergency of new variant scenarios<sup>16-</sup>  
126 <sup>19</sup>.

127 Since Catalan schools reopened in September 2020 after 6-months of closure, there have been  
128 83,911 accumulated positive COVID-19 cases, of which 74,246 were students (5.16%) and 8,996  
129 school staff (5.49%)<sup>20</sup>. Likewise, a recent study that analysed the incidence dynamics of SARS-  
130 CoV-2 infection in children in the first term of the school reopening shows that the infection rate  
131 among children remained lower compared with the general population for pre-school (3-6  
132 years) and primary pupils (6-12 years) but was equal to it or higher in secondary students (12-  
133 18 years)<sup>21</sup>. Moreover, several studies have shown that in this pandemic very few cases infect  
134 many contacts (super-spreaders) while most cases either infect nobody or very few people and  
135 this includes paediatric index cases<sup>22-26</sup>. Defining host-related, viral and environmental patterns  
136 that determine these super-spreading situations is relevant to the tailoring of measures to  
137 minimize the transmission of SARS-CoV-2 in schools<sup>27</sup>.

138 Preventive interventions play an important role in working together to gain control of the  
139 COVID-19 pandemic, also in schools. In this sense, the social and behavioural sciences can  
140 provide valuable insights into managing the pandemic and its impacts<sup>28</sup>. Non-pharmacological  
141 preventive interventions in schools such as physical distancing, hygiene, use of masks, restricting  
142 interactions to clusters of students in bubble-groups, massive microbiological testing and other  
143 safety measures are essential to prevent transmission<sup>29</sup>. These measures should be adapted to  
144 the setting and age group and prevent transmission while providing children with an optimal  
145 learning and social environment<sup>4</sup>. Furthermore, as it is known that SARS-CoV-2 transmission is  
146 via aerosols and virus-laden aerosols may easily accumulate in indoor environments, a proper  
147 ventilation of indoor spaces can be a great preventive measure<sup>29</sup>. Additionally, the first set of  
148 COVID-19 vaccines provided a pharmacological intervention in the last quarter of 2020 when  
149 they received the authorization for emergency use by the European Medicines Agency (EMA)  
150 and the Food and Drug Agency in the United States<sup>30</sup>. So far, teaching and non-teaching staff  
151 and population over 12 years are being vaccinated as defined in the Spanish vaccination strategy  
152 raising hopes for a better control of the epidemic inside school settings. In this context, there is  
153 a need to understand the epidemiology of SARS-CoV-2 in children once the adult population has  
154 been vaccinated. The pandemic is moving very fast, and behaviours and attitudes may change  
155 in response to the COVID-19 pandemic. Understanding the drivers of vaccine acceptance will be  
156 crucial to the success of COVID-19 mass vaccination campaigns.

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3 157 Therefore, the use of periodical cross-sectional surveys on the knowledge, attitude and practice  
4 158 (KAP) associated with COVID-19 will allow rapid and adaptive monitoring of demographics,  
5 159 preventive behaviours, knowledge, and perceptions over time, among others, and can be useful  
6 160 in order to identify misinformation as they emerge.  
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8 161 This article reports the design and protocol of a school-based study in several sentinel schools  
9 162 in Catalonia. The study is part of the COVID-19 monitoring and evaluation plan from the Ministry  
10 163 of Health of the Government of Catalonia, and it is conceived as a participatory and  
11 164 transdisciplinary research process where the students and school staff will be invited to  
12 165 participate. The monitoring and evaluation provide practical information for making timely  
13 166 decisions, addressing community needs, and identifying more effective strategies for the  
14 167 prevention of COVID-19 spread and future infectious threats. In addition, the protocol could be  
15 168 highly useful for adaption into other educational settings for the monitoring of the COVID-19  
16 169 pandemic.  
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## 20 171 **GENERAL OBJECTIVES**

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23 172 1. To describe over time the knowledge, attitudes and behaviours (KAB) of students and school  
24 173 staff (teaching and non-teaching staff) towards SARS-CoV-2 infection and its prevention, as  
25 174 well as its impact in school settings.  
26 175 2. To assess over time the prevalence of SARS-CoV-2 infection and seroprevalence of  
27 176 antibodies against SARS-CoV-2 and to identify associated sociodemographic, biological,  
28 177 behavioural and environmental factors among both children and staff.  
29 178 3. To identify and describe multi-level determinants, barriers and needs of SARS-CoV-2  
30 179 prevention related measures in school settings over time.  
31 180 4. To assess the secondary attack rate of SARS-CoV-2 children index cases and its multilevel  
32 181 determinants and factors, both in school and family settings.  
33 182 5. To analyse the impact of preventive and control measures on the occurrence of SARS-CoV-  
34 183 2 in school settings.  
35 184 6. To pilot alternative testing and screening technologies and strategies, to assess their  
36 185 acceptability, feasibility and performance and the occurrence of SARS-CoV-2 infection  
37 186 among students and school staff.  
38 187 7. To analyse the impact of different SARS-CoV-2 variants' transmission in school settings.  
39 188 8. To facilitate a participatory process where the education community will act as co-  
40 189 researchers elaborating recommendations to improve the prevention and control measures  
41 190 in the school environment.  
42 191 9. To evaluate the impact on students' learning, attitudes and motivations of their  
43 192 participation in the research process and the teacher's perspectives on this impact.  
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## 45 194 **METHODS AND ANALYSIS**

### 46 195 **Study design and Setting**

47  
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50 196 The population of Catalonia was 7,619,494 in 2019. The Catalan school system includes  
51 197 1,582,466 students, 117,398 teaching staff and 5,492 school centres<sup>31</sup>.

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54 198 This project is based on sentinel schools defined as a network of schools representing the  
55 199 diversity of schools and the scholar population in Catalonia, and chosen using the following  
56 200 criteria:

- 57  
58 201 • Volunteering/commitment of both the school management team and the teaching staff  
59 202 as well as the children's parents to participate in the project

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- 203 • Representation of schools located in the different Basic Health Areas (BHA) and territorial areas will be ensured taking into account tertiles of SARS-CoV-2 accumulated incidence and tertiles of socio-economic deprivation index<sup>32</sup>
- 206 • Representation of schools with different characteristics:
  - 207 ○ Sociodemographic indicators. At least two-to-five high complexity schools characterized by low socioeconomic level and specific educational needs
  - 208 ○ Some schools located in rural areas<sup>33</sup>
  - 209 ○ Schools with all levels of education, small school size and school centres with professional training courses
  - 210 ○ Public, charter and private schools
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213 The sentinel surveillance is carried out by means of serial cross-sectional and longitudinal school-based studies, direct observation, index case study and participatory research approach in children, adolescent and school staff from the selected sentinel schools. In a subset of schools (n=5), a cohort of students from first grade of secondary school to high school (12->18 years) and school staff has been established in order to monitor the COVID-19 incidence and the feasibility and acceptability of different periodical screening practices for COVID-19 confirmation. All the study interventions will be carried out in two academic years starting from January 2021 to June 2022 and the analysis will take place from June 2022 until the end of 2022.

#### 221 **Study population (Inclusion criteria)**

- 222 • Students attending sentinel schools will be eligible for the study, from preschool (3-years-old) to high school (approximately 18-years-old)
- 223
- 224 • School staff of the sentinel schools, including teachers, administrators, canteen and cleaning staff, and other adults working in the educational settings such as
- 225 extracurricular education instructors
- 226

#### 227 **Informed consent**

228 Informed consent will be obtained from school staff, parents of children under 16 and pupils of 16 years-old or older. Participants will be free to decline/withdraw consent at any time without providing a reason and without being subject to any resulting detriment.

#### 231 **Study procedures**

232 Summary information of questionnaires, biological samples and other information to be collected is provided in Table 1.

#### 234 Knowledge, attitudes and behaviours regarding COVID-19 (KAB) questionnaires and impact of preventive and control measures

236 Each headteacher will send the study information pack (a study leaflet and the information sheet) and the link to the online informed consent and the baseline questionnaires by e-mail to the parents/guardians, school staff and older students (when necessary, on paper). We will send follow-up questionnaires twice a year. Three different questionnaire models will be designed: for teachers and other school staff (Questionnaire A); for students under 16, which will be answered by parents/guardian (Questionnaire B), and for students over 16 (Questionnaire C). The variables included in the KAB survey will be mainly based on the WHO recommendations, as described in WHO/Europe (2020)<sup>34</sup>.

#### 244 Prevalence of SARS-CoV-2 active infection and seroprevalence of antibodies against SARS-CoV-2

246 *Cross-sectional study:* A field team (FT) made up of three nurses and a field coordinator will visit each school equipped with personal protective equipment to collect the samples for testing.

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3 248 They will schedule the number of intervention days with each participating school depending on  
4 249 school size. The following samples in the baseline and the following cross sectionals (twice  
5 250 yearly) will be collected from all participants: i) Nasal swabs to perform a transcription-mediated  
6 251 amplification assay (TMA) for detection of SARS-CoV-2; ii) Finger prick blood sample to assess  
7 252 with a quick anti SARS-CoV-2 IgM/IgG antibody test.

9 253 *Longitudinal study:* Follow-up interventions will be scheduled twice monthly during the school  
10 254 year as an alternative testing strategy. In each intervention, the FT will collect saliva and nasal  
11 255 specimens for the detection of SARS-CoV-2 by molecular or antigenic tests, respectively. The  
12 256 cohort participants will fill in an additional online epidemiological survey with information  
13 257 related to SARS-CoV-2 infection, their symptomatology, exposure and vaccine status.

#### 15 258 Secondary attack rate and SARS-CoV-2 variants

17 259 This part of the study will be carried by the Paediatric Infectious Diseases and  
18 260 Immunodeficiencies Unit at Hospital Universitari Vall d'Hebron (HUVH). Data on COVID-19 index  
19 261 cases will be collected with appropriate social and geographical distribution. These cases will be  
20 262 detected by the routine data provided by the Catalan Public Health Department or detected  
21 263 during the study interventions and analysed in depth from then on. Data on demographic, social  
22 264 and clinical features, vaccination status, comorbidities and clinical outcome will be collected.  
23 265 School and household contacts will also be studied in depth to detect secondary cases. Samples  
24 266 from the index case and all COVID-19 confirmed contacts will be sequenced using whole genome  
25 267 sequencing (WGS) following the ARTIC Network protocol<sup>35</sup> for the characterization of SARS-CoV-  
26 268 2 (lineage and mutations), molecular tracing of sequences, and measurement of the viral load  
27 269 in these respiratory samples to assess its role in the transmission dynamics.

#### 30 270 Environmental determinants and barriers

32 271 The environmental evaluation will be carried out by the ISGlobal team to obtain information on  
33 272 the structural characteristics of each participating sentinel school, ventilation practices and  
34 273 other environmental prevention measures using the KKmoon carbon dioxide detector device.  
35 274 This intervention will include: i) A structural evaluation by a field technician in at least one  
36 275 classroom for each grade; ii) Online twice yearly surveys addressed to teachers and  
37 276 headteachers regarding ventilation and other prevention practices; iii) Twice yearly 15-day  
38 277 assessment of CO<sub>2</sub>, temperature and humidity – seven days assessed by the field technician and  
39 278 the remainder as an experimenting tool for students – in 5 to 8 previously chosen classrooms.

#### 41 279 Participatory research

43 280 The project is conceived as a collaborative and transdisciplinary research project where the  
44 281 education community and families participate in different phases of the research process. They  
45 282 will act as co-researchers evaluating the prevention and control measure implementation of  
46 283 SARS-CoV-2 infection in the school environment with a systemic perspective, as well as  
47 284 elaborating their recommendations to improve the prevention and control strategy. This  
48 285 approach will be implemented in collaboration with the EC funded project CONNECT, which aims  
49 286 to improve science learning and increase students' motivation towards science careers by  
50 287 engaging schools, scientists and families to solve local challenges.

53 288 Participation will entail discussion groups: i) Online focus groups with teachers. Preliminary  
54 289 results of the bio-behavioural surveys will be shared and, based on these, they will be invited to  
55 290 analyse problems, opportunities and needs, and to develop proposals for improvement of  
56 291 prevention measures following a protocol; ii) Teachers conducting focus groups with their class-  
57 292 group students and then families, reproducing a similar protocol; iii) The edited list of  
58 293 recommendations will be presented by students to scientists and policy makers in an online  
59 294 conference; iv) Elaboration of the final list of recommendations; v) Capital science survey: a pre-

295 and post-intervention survey addressed to pupils regarding the science learning and students'  
296 attitudes and motivation, and a pre- and post-intervention survey addressed to teachers  
297 regarding the education process.

298

#### 299 Sample management, microbiological analysis and test result communication

300 As described above, diverse biological samples will be collected during the study.

301 The finger prick blood collected at the baseline and the follow-up will be processed at the time  
302 of collection to perform a quick SARS-CoV-2 serological test (COVID-19 IgG/IgM Rapid Test Kit,  
303 Lambra, Spain) with sensitivities of 97,2% (IgG) and 87,9% (IgM), and specificities of 100% for  
304 both immunoglobulins as the manufacturers describe. This approach will be used to assess the  
305 exposure to SARS-CoV-2 infection or vaccination by the presence of antibodies. In addition, the  
306 nasal swab sample collected in the longitudinal study will be processed at the time of collection  
307 for detection of SARS-CoV-2 antigen using the Panbio COVID-19 Ag Rapid Test (Abbot, USA) with  
308 a sensitivity of 93.3% (95% CI: 83.8-98.2%) and specificity of 99.4% (95% CI: 97.0-100%) as the  
309 manufacturers describe. The nursing team will upload the rapid test results on an online  
310 research database using electronic tablets. These results will be introduced afterwards to the  
311 electronic health record of all participants, who will be able to consult them in the online patient  
312 health portal (La Meva Salut app). In case of Ag positive with IgG negative, the COVID-school  
313 manager, a new sanitary staff role acting as a liaison between the primary care team and the  
314 school centres, will activate the public health protocol established by the Catalan Ministry of  
315 Health<sup>36</sup>.

316 Nasal swabs and saliva samples will be maintained at 4°C during sampling procedures and  
317 transport to laboratory facilities. A molecular assay based on the transcription mediated  
318 amplification assay (Procleix SARS-CoV-2, Grifols) will be conducted in HUVH for detection of  
319 SARS-CoV-2 in nasal swabs, and RT-PCR assay (Allplex SARS-CoV-2/FluA/FluB/RSV, Werfen) will  
320 be conducted at the Hospital Universitari Germans Trias i Pujol (HUGTiP) laboratories to  
321 determine SARS-CoV-2 infection in saliva specimens. If the TMA assay (HUVH) or RT-PCR assay  
322 (HUGTiP) is positive, an active infection will be confirmed. Once the nasal samples have been  
323 tested, all positive specimens will be stored in sample collection C.0001145 on the *Instituto de*  
324 *Salud Carlos III* register. On the other hand, saliva samples with positive SARS-CoV-2 results will  
325 be frozen and stored at the IGTP-HUGTiP Biobank and conserved for two years. TMA/PCR results  
326 will be uploaded by the microbiology laboratories to the electronic health record, and the  
327 participants and their general practitioners or paediatricians will be able to check them.

328 Regarding the transmissibility study, nasopharyngeal or nasal swab samples from index cases  
329 and positive secondary cases will be sent to the HUVH laboratory for genetic SARS-CoV-2  
330 characterisation, to measure the viral load and to detect other respiratory viruses. The genetic  
331 characterisation of SARS-CoV-2 will be performed through WGS according to the ARTIC Network  
332 protocol<sup>35</sup> by using MiSeq and NextSeq 2000 platforms (Illumina, CA, USA). Other respiratory  
333 viruses will be detected by a real-time multiplex RT-PCR assay (Allplex Respiratory Panel Assay,  
334 Seegene); total nucleic acids will be extracted using NucliSENS EasyMAG (bioMérieux, Marcy  
335 l'Etoile, France) or Microlab STARlet System (Hamilton, CA, USA) according to the  
336 manufacturer's instructions. Additionally, to measure the SARS-CoV-2 viral load, an in-house  
337 quantitative RT-PCR assay using the primer/probe set targeting the nucleocapsid protein (N1)  
338 and the human RNase P (housekeeping gene) from the CDC 2019-nCoV Real-Time RT-PCR  
339 Diagnostic Panel will be carried out. The Ct values of the viral target will be normalized to a  
340 housekeeping gene based on the  $\Delta$ Ct method (Ct<sub>sample</sub> - Ct<sub>housekeeping gene</sub>) in order to  
341 minimize the variations due to the non-standardized collection of a heterogenous specimens.

### 342 **Data management, data protection and patient confidentiality**

343 Informed consents and the different surveys will be designed and published by means of the  
 344 EUSurvey management system, an official online survey management tool of the European  
 345 Commission. For those participants for whom online access is not possible, printed surveys will  
 346 be distributed by the field team and afterwards digitalized. The periodical surveys from the  
 347 cohort study will be published by means of the OpenTIC software.

348 After giving their consent to participate (or allow their child to participate), each participant will  
 349 be allocated a unique participant ID number on enrolment to the study. This unique identifier  
 350 will serve as a link to all the data needed for the study (questioners, biological samples). The file  
 351 that relates the identifier or pseudonym to the personally identifiable data will be encrypted  
 352 and the access to this file will be restricted to a very small number of authorized persons (EM,  
 353 YD, JA, LA). The process will comply with the General Data Protection Regulation (GDPR)  
 354 requirements.

#### 355 **Study definitions:**

356 Given that all the participants attending the school should be asymptomatic, a confirmed COVID-  
 357 19 case will be defined as any individual testing SARS-CoV-2 positive by molecular assays (PCR  
 358 or TMA-based) or COVID-19 Ag Rapid Test (RAT) in a respiratory or saliva specimen<sup>37</sup>.

359 A paediatric index case will be established when the child is the first confirmed COVID-19 case  
 360 in the classroom noticed by health authorities or the research team<sup>26</sup>. A secondary case will be  
 361 defined as a classmate or household contact subsequently testing positive for SARS-CoV-2 by  
 362 molecular assay or RAT. Close contacts will be defined as all people who have shared space with  
 363 a positive COVID-19 less than 2 metres away, for more than 15 minutes, without protection and  
 364 from the 48 hours prior to the onset of symptoms. If the positive person has not had symptoms,  
 365 onset will be defined as the date of performing the diagnostic test.

#### 366 **Variables collected**

- 367 i) Individual data
- 368 • Sociodemographic and socioeconomic indicators: age, gender, ethnic origin,  
 369 household and career, economic status, job situation of their parents in the case of  
 370 pupils
  - 371 • Clinical data and infection by SARS-CoV-2: symptoms, COVID-19 chronic symptoms,  
 372 the duration of symptoms, reinfection of COVID-19, hospitalization, exposure,  
 373 contact with positive cases
  - 374 • Attitude, behaviour and knowledge regarding COVID-19 and preventive measures
  - 375 • Pandemic impact indicators such as changes on mental and physic health and the  
 376 purchasing power of parents and school staff
  - 377 • Vaccination data: manufacturer, number of doses, date of doses, side effects of  
 378 COVID-19 vaccine, refusal to vaccinate (date and reason)
  - 379 • Attitude and usability of focus groups regarding scientific contribution
- 380 ii) Collective data
- 381 Number of classrooms, number of tables/classroom, number of pupils/m<sup>2</sup>, school  
 382 surface, schoolyard surface, concentration of CO<sub>2</sub>, temperature and humidity in the  
 383 classrooms.
- 384 iii) Ecological data
- 385 These data will be collected and provided by the Primary Care Services Information  
 386 System (SISAP) and the Data analytics program for health research and innovation  
 387 (PADRIS) and will include data from different data sources in order to obtain the  
 388 information mentioned below:

- 1  
2  
3 389           • Number of new COVID-19 confirmed cases or tested positive for SARS-CoV-2 by  
4 390           TMA/PCR or RAT /total of residents.  
5 391           • Number of new COVID-19 confirmed cases or tested positive for SARS-CoV-2 by  
6 392           TMA/PCR or RAT/total of tested people.  
7  
8 393           • Number of new COVID-19 confirmed cases or tested positive for SARS-CoV-2 by  
9 394           TMA/PCR or RAT/total of suspected cases.  
10 395           • Number of confined classrooms/total number of classrooms.

#### 11 396 **Data analysis plan and sample size**

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13 397 We estimate a participation of 50-70% among the total of 11,000 individuals who are on the  
14 398 census at the 26 sentinel schools since not all potential participants are aware of the public  
15 399 health concern and due to other barriers. A descriptive analysis will be performed for all the  
16 400 main aforementioned variables collected: participant's sociodemographic characteristics, SARS-  
17 401 CoV-2 infection characterization, its associated factors, behaviour information and other  
18 402 outcomes of interest. For quantitative variables, we will use measures of central tendency and  
19 403 dispersion (mean, standard deviation, median, interquartile range, 95% confidence interval). For  
20 404 qualitative variables, we will calculate absolute frequencies and percentages. To estimate the  
21 405 statistical significance of time trends in SARS-CoV-2 laboratory confirmed cases we will use  
22 406 multivariate logistic regression analysis with robust standard errors clustered at the individual-  
23 407 level and school-level, adjusting for sociodemographic, environmental and school structural  
24 408 variables.

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26  
27 409 In order to address the fourth objective related to the transmissibility study, a descriptive  
28 410 analysis will be performed for all cases and contacts identified in school clusters. Analyses will  
29 411 include chi-square and independent sample t-test procedures to assess differences between  
30 412 super-spreaders and non-spreaders for index cases and secondary cases using socio-  
31 413 demographics, number of classmates and household contacts, clinical and environmental  
32 414 variables. Finally, we will use univariate and multivariate logistic regression models to assess the  
33 415 association between transmission risk factors and SARS-CoV-2 infection among index cases and  
34 416 close contacts. All models will be adjusted for gender, age, vaccination status, number of  
35 417 classmates, and household contacts and whether or not the index cases are symptomatic.

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37  
38 418 Global data on the COVID-19 epidemic in Catalonia and the school basic health area (BHA) will  
39 419 be collected to contextualize the current epidemic situation. Data will be provided globally and  
40 420 stratified by age groups and collectives. This data will be provided by the Catalan Agency for  
41 421 Quality and Health Assessment (AQuAS) and SISAP. Analysis of the interrupted time series of  
42 422 SARS-CoV-2 seroprevalence and COVID-19 confirmed cases will be performed to assess the  
43 423 public health implemented measures including vaccination programmes. The confirmed cases  
44 424 will be modelled as ARIMA processes to estimate the expected numbers to be compared to  
45 425 those observed and estimate the impact of the different analysed measures, to do this we will  
46 426 calculate absolute and relative changes between expected-observed confirmed cases in each  
47 427 time point of the implemented measures. Analysis will be conducted in R (R Core Team, 2014).

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#### 51 429 **PATIENT AND PUBLIC INVOLVEMENT (PPI)**

52 430 We will convene a virtual PPI panel, who will contribute to the dissemination of findings.

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#### 55 432 **ETHICS AND DISSEMINATION**

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57 433 The ethical aspects of the present study include:  
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- 434 • Recruitment of participants with informed consent
- 435 • Collection and storage of biological samples
- 436 • Questionnaires with non-anonymized data
- 437 • Collection and storage of personal data

438 The confidentiality of data and other ethical considerations will be managed in accordance with  
439 the recommendations of the Spanish Law 14/2007 of 3 July, on Biomedical Research and the  
440 Spanish Royal Decree RD 1716/2011 of 18 November, which lays down the basic requirements  
441 for the authorisation and operation of biobanks for purposes of Biomedical Research and the  
442 treatment of biological samples of human origin. Informed consent is required for this project  
443 as is established in article 59 of the law.

444 The necessary measures will be taken to ensure the protection of personal data and their  
445 confidentiality, in accordance with EU Regulation 2016/679 of the European Parliament and of  
446 the Council of 27 April 2016 on the protection of natural persons with regard to the processing  
447 of personal data and on the free movement of such data (RGPD), and in the Spanish Organic Law  
448 3/2018 of 5 December, for the protection of personal data and Guarantee of digital rights (LOPD-  
449 GDD).

450 The data protection office of the Ministry of Health of the Government of Catalonia has reached  
451 an agreement signed by all the organizations in the research team to align with all the ethical  
452 considerations mentioned above and recommended by the same office.

453 The data and results provided by this project will be valuable in the current context of the public  
454 health emergency of international concern declared by the WHO for the COVID-19 pandemic  
455 and taking into account the urgent need for information coming from COVID-19 studies.

456 The CEEISCAT research team will generate a quarterly report with qualitative and quantitative  
457 data to give feedback to the stakeholders. Findings from this study will be disseminated at  
458 national and international conferences, reported on the public webpage of the project and  
459 published in peer-reviewed journals.

460

#### 461 **Study registration**

462 Ethical approval was obtained from the Foundation University Institute for Research in Primary  
463 Health Care Jordi Gol i Gurina (IDIAPJGol) ethics committee with code 20/192-PCV on 17  
464 December 2020 and the Hospital Universitari Vall d'Hebron ethics committee with code  
465 PR(AMI)668/2020.

466

#### 467 **AUTHORS' CONTRIBUTIONS**

468 All authors have read, reviewed and agreed to the finalized submitted version of the manuscript.  
469 Conceptualisation: JC. Design study: JC, CF, AS, AB, JR, JS, PS, AS and MG. Operational procedures: JC, JR,  
470 AB, CF, AC, JS, MG, AA, TP, IB, JF, RM, PS, AS, MS and JB. Resources: RF, JM, JMA, CC and JB. Writing and  
471 draft preparation: AB, CF, AC, AS, MS and RM. Writing, review and edition; all authors.

472

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476 during its execution, analyses, interpretation of the data or decision to submit result.

477

478 **COMPETING INTEREST STATEMENT**

479 All of the authors declare that they have no conflicts of interest.

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For peer review only

592 **Table 1. Summary information of study procedures.**

Type of intervention	Determination	Type of Test	Coordination	Frequency
<b>Bio-behavioural questionnaires</b>			CEEISCAT	
- Questionnaire A (teaching and non-teaching staff) - Questionnaire B (parents or foster parents of students under 16 years old) - Questionnaire C (16-years-old or older students)				Once during 2020-2021 school year and twice during 2021-2022 school year
<b>Biological sampling</b>			CEEISCAT	
<b>Baseline</b> - Blood from finger prick - Nasal swab sample	Ab anti-SARS-CoV-2 Viral RNA (SARS-CoV-2)	LFA TMA		Once during 2020-2021 school year and twice during 2021-2022 school year
<b>Longitudinal study (&gt; 1<sup>st</sup> grade of middle school and school staff)</b> - Saliva sample - Nasal swab sample	Viral RNA (SARS-CoV-2) SARS-CoV-2 Ag rapid test	RT-PCR LFA		Bi-monthly
<b>Environmental and structural evaluation in each sentinel school</b>			ISGlobal	
- Environmental questionnaires (Directors and teachers) - Structural and environmental evaluation by a field technician - CO <sub>2</sub> , humidity and temperature measurements	Prevention measures (e.g. ventilation practices)			Once during 2020-2021 school year and twice during 2021-2022 school year
<b>Transmissibility study</b>			HUVH	
- COVID-19 index cases - Household and classmate contacts evaluation - Secondary attack rate	Viral coinfections Viral RNA (SARS-CoV-2) SARS-CoV-2 characterisations Viral load measurement	RT-PCR TMA/PCR Whole genome sequencing Quantitative PCR assay		
<b>Participatory research</b>			Living lab (IRSIcaixa)	
- Scientific capital surveys - Focus groups - List of recommendations - Annual school conference				Once during 2020-2021 school year and twice during 2021-2022 school year

593 Ab: antibodies; Ag: antigens; LFA: Lateral flow assay; TMA: Transcription mediated amplification assay

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## STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page No
<b>Title and abstract</b>	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1-2
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	
<b>Introduction</b>			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	5
<b>Methods</b>			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	6-7
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	9-10
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6-8
Bias	9	Describe any efforts to address potential sources of bias	NA
Study size	10	Explain how the study size was arrived at	5-6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	9
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	10
		(b) Describe any methods used to examine subgroups and interactions	10
		(c) Explain how missing data were addressed	NA
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	10
		(e) Describe any sensitivity analyses	NA

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<b>Results</b>			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	NA
		(b) Give reasons for non-participation at each stage	NA
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	NA
		(b) Indicate number of participants with missing data for each variable of interest	NA
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	NA
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	NA
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	NA
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	NA
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	NA
		(b) Report category boundaries when continuous variables were categorized	NA
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
<b>Discussion</b>			
Key results	18	Summarise key results with reference to study objectives	NA
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	NA
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	NA
Generalisability	21	Discuss the generalisability (external validity) of the study results	NA
<b>Other information</b>			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	14

\*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at [www.strobe-statement.org](http://www.strobe-statement.org).