



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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ABSTRACT

Introduction Since the SARS-CoV-2 became of concern in January 2020, many preventive measures have been adopted in educational settings to ensure the control of COVID-19 pandemic among children and staff in schools. This study aims to set up a school sentinel surveillance network with the purpose of monitoring SARS-CoV-2 infection, seroprevalence as well as to analyse the impact of preventive interventions of SARS-CoV-2 in school settings. Additionally, we will assess diverse screening strategies in a cohort of students and school staff to monitor the screening acceptance and its potential impact. Altogether, we hope this study will enable the design of more effective strategies for the prevention of COVID-19 spread.

Methods and analysis The sentinel schools' study is a cross-sectional, school-based project including 26 participating sentinel schools in Catalonia (Spain). Children, adolescents and staff at the schools will be invited to participate. This project will be carried out from January 2021 to June 2022 as follows: (1) twice yearly serological testing and molecular SARS-CoV-2 detection and questionnaires covering SARS-CoV-2 symptoms, tests, health, knowledge, attitudes and behaviours; (2) an environmental evaluation carried out in different classrooms; (3) SARS-CoV-2 transmission dynamics and the impact of different variants among confirmed cases and classmates; (4) a participatory process by which the participants are invited to act as coinvestigators to evaluate prevention strategies and provide recommendations to improve COVID-19 prevention in schools. Descriptive analysis will be performed for the main variables collected. The incidence and seroprevalence will be calculated and the association with sociodemographic factors and school characteristics will be determined using multivariate logistic regression.

Ethics and dissemination Ethical approval was obtained from the IDIAPJGol and the Hospital Universitari Vall d'Hebron ethics committees. A report will be generated quarterly.

Strengths and limitations of this study

- A multicentre study combining cross-sectional and longitudinal studies, collecting data from sentinel schools throughout Catalonia.
- Planned to consolidate the sentinel school surveillance network to monitor and evaluate the epidemiology of SARS-CoV-2 in school settings and assess the effectiveness of future preventive and control measures, new diagnostic tests or vaccination.
- Transdisciplinary and participatory research, carried out in collaboration with the education community to ensure that the prevention and control strategy for SARS-CoV-2 fits with the needs and expectations of schools.
- The participating school population might not be representative of the entire Catalan school population distributed across all the territory.
- Participation in periodic screenings could be low due to fear of testing the younger children or because of pandemic fatigue due to the large number of tests being performed.

Findings will be disseminated at national and international conferences and published in peer-reviewed journals.

INTRODUCTION

COVID-19, first reported from Wuhan city, China, in December 2019,¹ was declared a Public Health Emergency of International Concern by the WHO on 30 January 2020 and defined as a pandemic on 11 March 2020. Although children were recognised as contributing to only a small proportion of laboratory-confirmed COVID-19 cases and rarely developing severe or fatal

disease,^{2,3} their role in asymptomatic infection and transmission, which is well described for other respiratory viral infections such as influenza, was uncertain at the point of these restrictions and is still under discussion.

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

Since Catalan schools reopened in September 2020 after 6 months of closure, there have been 83 911 accumulated positive COVID-19 cases, of which 74 246 were students (5.16%) and 8996 school staff (5.49%).²⁰ Likewise, a recent study that analysed the incidence dynamics of SARS-CoV-2 infection in children in the first term of the school reopening shows that the infection rate among children remained lower compared with the general population for preschool (3–6 years) and primary pupils (6–12 years) but was equal to it or higher in secondary students (12–18 years).²¹ Moreover, several studies have shown that in this pandemic very few cases infect many contacts (super-spreaders), while most cases either infect nobody or very few people and this includes paediatric index cases.^{22–26} Defining host-related, viral and environmental patterns that determine these super-spreading situations is relevant to the tailoring of measures to minimise the transmission of SARS-CoV-2 in schools.²⁷

Preventive interventions play an important role in working together to gain control of the COVID-19 pandemic and also in schools. In this sense, the social and behavioural sciences can provide valuable insights into managing the pandemic and its impacts.²⁸ Non-pharmacological preventive interventions in schools such as physical distancing, hygiene, use of masks, restricting interactions to clusters of students in bubble groups, massive microbiological testing and other safety measures are essential to prevent transmission.²⁹ These measures should be adapted to the setting and age group and prevent transmission while providing children with an optimal learning and social environment.⁴ Furthermore, as it is known that SARS-CoV-2 transmission is via aerosols and virus-laden aerosols may easily accumulate in indoor environments, a proper ventilation of indoor spaces can be a great preventive measure.²⁹ Additionally, the first set of COVID-19 vaccines provided a pharmacological intervention in the last quarter of 2020 when they received

the authorisation for emergency use by the European Medicines Agency and the Food and Drug Agency in the USA.³⁰ So far, teaching and non-teaching staff and population over 12 years are being vaccinated as defined in the Spanish vaccination strategy raising hopes for a better control of the epidemic inside school settings. In this context, there is a need to understand the epidemiology of SARS-CoV-2 in children once the adult population has been vaccinated. The pandemic is moving very fast, and behaviours and attitudes may change in response to the COVID-19 pandemic. Understanding the drivers of vaccine acceptance will be crucial to the success of COVID-19 mass vaccination campaigns.

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

This article reports the design and protocol of a school-based study in several sentinel schools in Catalonia. The study is part of the COVID-19 monitoring and evaluation plan from the Ministry of Health of the Government of Catalonia, and it is conceived as a participatory and transdisciplinary research process where the students and school staff will be invited to participate. The monitoring and evaluation provide practical information for making timely decisions, addressing community needs and identifying more effective strategies for the prevention of COVID-19 spread and future infectious threats. In addition, the protocol could be highly useful for adaptation into other educational settings for the monitoring of the COVID-19 pandemic.

GENERAL OBJECTIVES

1. To describe over time the knowledge, attitudes and behaviours (KAB) of students and school staff (teaching and non-teaching staff) towards SARS-CoV-2 infection and its prevention as well as its impact in school settings.
2. To assess over time the prevalence of SARS-CoV-2 infection and seroprevalence of antibodies against SARS-CoV-2 and to identify associated sociodemographic, biological, behavioural and environmental factors among both children and staff.
3. To identify and describe multilevel determinants, barriers and needs of SARS-CoV-2 prevention related measures in school settings over time.
4. To assess the secondary attack rate of SARS-CoV-2 children index cases and its multilevel determinants and factors, both in school and family settings.
5. To analyse the impact of preventive and control measures on the occurrence of SARS-CoV-2 in school settings.
6. To pilot alternative testing and screening technologies and strategies to assess their acceptability, feasibility and performance and the occurrence of SARS-CoV-2 infection among students and school staff.

7. To analyse the impact of different SARS-CoV-2 variants' transmission in school settings.
8. To facilitate a participatory process where the education community will act as coresearchers elaborating recommendations to improve the prevention and control measures in the school environment.
9. To evaluate the impact on students' learning, attitudes and motivations of their participation in the research process and the teacher's perspectives on this impact.

METHODS AND ANALYSIS

Study design and setting

The population of Catalonia was 7 619 494 in 2019. The Catalan school system includes 1 582 466 students, 117 398 teaching staff and 5492 school centres.³¹

This project is based on sentinel schools defined as a network of schools representing the diversity of schools and the scholar population in Catalonia and chosen using the following criteria:

- ▶ Volunteering/commitment of both the school management team and the teaching staff as well as the children's parents to participate in the project.
- ▶ 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 socioeconomic deprivation index³²
- ▶ Representation of schools with different characteristics:
 - Sociodemographic indicators. At least two-to-five high complexity schools characterised by low socioeconomic level and specific educational needs.
 - Some schools located in rural areas.³³
 - Schools with all levels of education, small school size and school centres with professional training courses.
 - Public, charter and private schools.

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.

Study population (inclusion criteria)

- ▶ Students attending sentinel schools will be eligible for the study, from preschool (3 years old) to high school (approximately 18 years old).
- ▶ School staff of the sentinel schools, including teachers, administrators, canteen and cleaning staff, and other

adults working in the educational settings such as extracurricular education instructors.

Informed consent

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.

Study procedures

Summary information of questionnaires, biological samples and other information to be collected is provided in [table 1](#).

KAB questionnaires regarding COVID-19 and impact of preventive and control measures

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 email 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 years, which will be answered by parents/guardian (questionnaire B) and for students over 16 years (questionnaire C). The variables included in the KAB survey will be mainly based on the WHO recommendations, as described in WHO/Europe (2020).³⁴

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

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. They will schedule the number of intervention days with each participating school depending on school size. The following samples in the baseline and the following cross sectionals (twice yearly) will be collected from all participants: (1) nasal swabs to perform a transcription-mediated amplification assay (TMA) for detection of SARS-CoV-2 and (2) finger prick blood sample to assess with a quick anti SARS-CoV-2 IgM/IgG antibody test.

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

Secondary attack rate and SARS-CoV-2 variants

This part of the study will be carried by the Paediatric Infectious Diseases and Immunodeficiencies Unit at Hospital Universitari Vall d'Hebron (HUVH). Data on COVID-19 index cases will be collected with appropriate

Table 1 Summary information of study procedures

Type of intervention	Determination	Type of test	Coordination	Frequency
Biobehavioural questionnaires			CEEISCAT	
<ul style="list-style-type: none"> ▶ 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
Biological sampling			CEEISCAT	
Baseline				
<ul style="list-style-type: none"> ▶ Blood from finger prick ▶ Nasal swab sample 	Ab anti-SARS-CoV-2	LFA		Once during 2020–2021 school year and twice during 2021–2022 school year
Longitudinal study (> 1st grade of middle school and school staff)	Viral RNA (SARS-CoV-2)	TMA		
<ul style="list-style-type: none"> ▶ Saliva sample ▶ Nasal swab sample 	Viral RNA (SARS-CoV-2)	RT-PCR		Once during 2020–2021 school year and twice during 2021–2022 school year
	SARS-CoV-2 Ag rapid test	LFA		Bi-monthly
Environmental and structural evaluation in each sentinel school			ISGlobal	
<ul style="list-style-type: none"> ▶ Environmental questionnaires (directors and teachers) ▶ Structural and environmental evaluation by a field technician ▶ CO₂, humidity and temperature measurements 	Prevention measures (eg, ventilation practices)			Once during 2020–2021 school year and twice during 2021–2022 school year
Transmissibility study			HUVH	
<ul style="list-style-type: none"> ▶ COVID-19 index cases ▶ Household and classmate contacts evaluation ▶ Secondary attack rate 	Viral coinfections	RT-PCR		
	Viral RNA (SARS-CoV-2)	TMA/PCR		
	SARS-CoV-2 characterisations	Whole-genome sequencing		
	Viral load measurement	Quantitative PCR assay		
Participatory research			Living lab (IRSiCaixa)	
<ul style="list-style-type: none"> ▶ Scientific capital surveys ▶ Focus groups ▶ List of recommendations ▶ Annual school conference 				Once during 2020–2021 school year and twice during 2021–2022 school year

Ab, antibodies; Ag, antigens; CEEISCAT, Centre for Epidemiological Studies of HIV/SIDA and STI of Catalonia; HUVH, Hospital Universitari Vall d'Hebron; LFA, lateral flow assay; TMA, transcription-mediated amplification assay.

social and geographical distribution. These cases will be detected by the routine data provided by the Catalan Public Health Department or detected during the study interventions and analysed in depth from then on. Data on demographic, social and clinical features, vaccination status, comorbidities and clinical outcome will be collected. School and household contacts will also be studied in depth to detect secondary cases. Samples from the index case and all COVID-19 confirmed contacts will be sequenced using whole-genome sequencing (WGS) following the ARTIC Network protocol³⁵ for the characterisation of SARS-CoV-2 (lineage and mutations), molecular tracing of sequences and measurement of the viral load in these respiratory samples to assess its role in the transmission dynamics.

Environmental determinants and barriers

The environmental evaluation will be carried out by the ISGlobal team to obtain information on the structural characteristics of each participating sentinel school, ventilation practices and other environmental prevention measures using the KKmoon carbon dioxide detector device. This intervention will include: (1) a structural

evaluation by a field technician in at least one classroom for each grade; (2) online twice yearly surveys addressed to teachers and headteachers regarding ventilation and other prevention practices; (3) twice yearly 15-day assessment of CO₂, temperature and humidity—7 days assessed by the field technician and the remainder as an experimenting tool for students—in five to eight previously chosen classrooms.

Participatory research

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

Participation will entail discussion groups: (1) online focus groups with teachers. Preliminary results of the biobehavioural surveys will be shared, and based on these, they will be invited to analyse problems, opportunities and needs and to develop proposals for improvement of prevention measures following a protocol; (2) teachers conducting focus groups with their class group students and then families, reproducing a similar protocol; (3) the edited list of recommendations will be presented by students to scientists and policy makers in an online conference; (4) elaboration of the final list of recommendations; (5) capital science survey: a preintervention and postintervention survey addressed to pupils regarding the science learning and students' attitudes and motivation, and a preintervention and postintervention survey addressed to teachers regarding the education process.

Sample management, microbiological analysis and test result communication

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

The finger prick blood collected at the baseline and the follow-up will be processed at the time of collection to perform a quick SARS-CoV-2 serological test (COVID-19 IgG/IgM Rapid Test Kit, Lambra, Spain) with sensitivities of 97.2% (IgG) and 87.9% (IgM), and specificities of 100% for both immunoglobulins as the manufacturers describe. This approach will be used to assess the exposure to SARS-CoV-2 infection or vaccination by the presence of antibodies. In addition, the nasal swab sample collected in the longitudinal study will be processed at the time of collection for detection of SARS-CoV-2 antigen using the Panbio COVID-19 Ag Rapid Test (Abbot, USA) with a sensitivity of 93.3% (95% CI 83.8% to 98.2%) and specificity of 99.4% (95% CI 97.0% to 100%) as the manufacturers describe. The nursing team will upload the rapid test results on an online research database using electronic tablets. These results will be introduced afterwards to the electronic health record of all participants who will be able to consult them in the online patient health portal (La Meva Salut app). In case of Ag positive with IgG negative, the COVID-school manager, a new sanitary staff role acting as a liaison between the primary care team and the school centres, will activate the public health protocol established by the Catalan Ministry of Health.³⁶

Nasal swabs and saliva samples will be maintained at 4°C during sampling procedures and transport to laboratory facilities. A molecular assay based on the TMA (Procleix SARS-CoV-2, Grifols) will be conducted in HUVH for detection of SARS-CoV-2 in nasal swabs, and RT-PCR assay (Allplex SARS-CoV-2/FluA/FluB/RSV, Werfen) will be conducted at the Hospital Universitari Germans Trias i Pujol (HUGTiP) laboratories to determine SARS-CoV-2 infection in saliva specimens. If the TMA assay (HUVH) or RT-PCR assay (HUGTiP) is positive, an active infection will be confirmed. Once the nasal samples have been tested, all positive specimens will be stored in sample collection C.0001145 on the *Instituto de Salud*

Carlos III register. However, saliva samples with positive SARS-CoV-2 results will be frozen and stored at the IGTP-HUGTiP Biobank and conserved for 2 years. TMA/PCR results will be uploaded by the microbiology laboratories to the electronic health record, and the participants and their general practitioners or paediatricians will be able to check them.

Regarding the transmissibility study, nasopharyngeal or nasal swab samples from index cases and positive secondary cases will be sent to the HUVH laboratory for genetic SARS-CoV-2 characterisation, to measure the viral load and to detect other respiratory viruses. The genetic characterisation of SARS-CoV-2 will be performed through WGS according to the ARTIC Network protocol³⁵ by using MiSeq and NextSeq 2000 platforms (Illumina, California, USA). Other respiratory viruses will be detected by a real-time multiplex RT-PCR assay (Allplex Respiratory Panel Assay, Seegene); total nucleic acids will be extracted using NucliSENS EasyMAG (bioMérieux, Marcy l'Etoile, France) or Microlab STARlet System (Hamilton, California, USA) according to the manufacturer's instructions. Additionally, to measure the SARS-CoV-2 viral load, an in-house quantitative RT-PCR assay using the primer/probe set targeting the nucleocapsid protein (N1) and the human RNase P (housekeeping gene) from the CDC 2019-nCoV Real-Time RT-PCR Diagnostic Panel will be carried out. The Ct values of the viral target will be normalised to a housekeeping gene based on the Δ Ct method (Ct_{sample} - Ct_{housekeeping gene}) in order to minimise the variations due to the non-standardised collection of a heterogenous specimens.

Data management, data protection and patient confidentiality

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

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

Study definitions

Given that all the participants attending the school should be asymptomatic, a confirmed COVID-19 case will be defined as any individual testing SARS-CoV-2 positive

by molecular assays (PCR or TMA-based) or COVID-19 Ag Rapid Test (RAT) in a respiratory or saliva specimen.³⁷

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

Variables collected

Individual data

- ▶ Sociodemographic and socioeconomic indicators: age, gender, ethnic origin, household and career, economic status and job situation of their parents in the case of pupils.
- ▶ Clinical data and infection by SARS-CoV-2: symptoms, COVID-19 chronic symptoms, the duration of symptoms, reinfection of COVID-19, hospitalisation, exposure and contact with positive cases.
- ▶ Attitude, behaviour and knowledge regarding COVID-19 and preventive measures.
- ▶ Pandemic impact indicators such as changes on mental and physic health and the purchasing power of parents and school staff.
- ▶ Vaccination data: manufacturer, number of doses, date of doses, side effects of COVID-19 vaccine and refusal to vaccinate (date and reason).
- ▶ Attitude and usability of focus groups regarding scientific contribution.

Collective data

Number of classrooms, number of tables/classroom, number of pupils/m², school surface, schoolyard surface, concentration of CO₂, temperature and humidity in the classrooms.

Ecological data

These data will be collected and provided by the Primary Care Services Information System (SISAP) and the data analytics programme for health research and innovation (PADRIS) and will include data from different data sources in order to obtain the information mentioned further:

- ▶ Number of new COVID-19 confirmed cases or tested positive for SARS-CoV-2 by TMA/PCR or RAT /total of residents.
- ▶ Number of new COVID-19 confirmed cases or tested positive for SARS-CoV-2 by TMA/PCR or RAT/total of tested people.
- ▶ Number of new COVID-19 confirmed cases or tested positive for SARS-CoV-2 by TMA/PCR or RAT/total of suspected cases.

- ▶ Number of confined classrooms/total number of classrooms.

Data analysis plan and sample size

We estimate a participation of 50%–70% among the total of 11 000 individuals who are on the census at the 26 sentinel schools since not all potential participants are aware of the public health concern and due to other barriers. A descriptive analysis will be performed for all the main aforementioned variables collected: participant's sociodemographic characteristics, SARS-CoV-2 infection characterisation, its associated factors, behaviour information and other outcomes of interest. For quantitative variables, we will use measures of central tendency and dispersion (mean, SD, median, IQR and 95% CI). For qualitative variables, we will calculate absolute frequencies and percentages. To estimate the statistical significance of time trends in SARS-CoV-2 laboratory confirmed cases, we will use multivariate logistic regression analysis with robust SEs clustered at the individual level and school level, adjusting for sociodemographic, environmental and school structural variables.

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

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

Patient and public involvement (PPI)

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

ETHICS AND DISSEMINATION

The ethical aspects of the present study include:

- ▶ Recruitment of participants with informed consent.
- ▶ Collection and storage of biological samples.
- ▶ Questionnaires with non-anonymised data.
- ▶ Collection and storage of personal data.

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

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

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

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

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

This study involves human participants and was approved by Ethical approval from Foundation University Institute for Research in Primary Health Care Jordi Gol i Gurina (IDIAPJGol) ethics committee with code 20/192-PCV on 17 December 2020 and the Hospital Universitari Vall d'Hebron ethics committee with code PR(AMI)668/2020. Participants gave informed consent to participate in the study before taking part.

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