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# BMJ Open Protocol for a prospective quasi-experimental study on SARS-CoV-2 transmission during outdoor sports events in France: the COVID-ESO project

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## ABSTRACT

**Introduction** The spread of SARS-CoV-2 and its variants in the community remains a major concern despite the application of control measures including the banning of mass sporting events. The circulation of SARS-CoV-2 within the general population, and potentially within the population practicing outdoor sports activities, suggests contexts conducive to the transmission of the virus. We hypothesise that outdoor sports events (OSEs) do not present a higher risk of SARS-CoV-2 contamination. The objective of the COVID-ESO project is to measure if individuals participating in OSE present a similar risk of SARS-CoV-2 transmission compared with individuals not participating in OSE, in France.

**Methods and analysis** The COVID-ESO project is a prospective, quasi-experimental study to be conducted in volunteer individuals likely to participate in OSE. Six events are targeted across France to be included. Three sport trials will be eligible for the study: running, cycling and triathlon. Each individual participating in the OSE will choose one of his or her usual training partner to be eligible for the unexposed control group. Individuals will be matched (1:1) on age, sex and the district of residence. Individuals assigned to the exposed group will participate in the OSE, whereas individuals assigned to the unexposed group will not participate in the OSE. All individuals will be asked to perform saliva tests on the day of the event and 7 days after the event. A questionnaire including sociodemographic, clinical and exposure data to SARS-CoV-2 will be sent by email for both groups on the day before the event and 7 days after the event. Differences in SARS-CoV-2 infection rates between the exposed versus the unexposed group will be analysed by fitting a conditional logistic regression model, adjusted for potential confounders. As the sport events unfold, data will be analyzed by performing sequential meta-analyses.

**Ethics and dissemination** This protocol has been approved by the ethical committee. Ethical approval has been obtained for the Clinical research and committee of South West of France, 10 June 2021. COMITE DE PROTECTION DES PERSONNES DU SUD-OUEST ET OUTRE-MER 4 under the reference number 21.03.23.71737/CPP2021-04-045 a COVID/2021-A00845-36. Findings

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ The COVID-ESO study is a prospective, quasi-experimental study in a population participating in outdoor sports events.
- ⇒ To increase study adherence, saliva tests will be performed on participants.
- ⇒ Due to ethical issues, randomisation was not possible in this study.
- ⇒ The outdoor sports event could be the source of incident COVID-19 cases among the exposed group, and therefore, contribute to generating potential SARS-CoV-2 clusters.

generated from this study will be shared to national health and sport authorities.

## BACKGROUND

Coronaviruses are RNA viruses<sup>1</sup> that cause mild to moderate respiratory infections in humans with symptoms similar to a common cold.

Since 11 March 2020, the world has been facing the pandemic caused by the strain of SARS-CoV-2.<sup>2</sup> This virus but also its new variants<sup>3</sup> circulate actively in the community despite available vaccines and the application of control measures including social distancing measures, quarantines, lockdown as well as the banning of mass sporting events. In France, from 3 January 2020 to 26 October 2021, there have been more than 6 900 000 confirmed cases of COVID-19 with almost 115 000 deaths, reported. As of 17 October 2021, the COVID-19 vaccination coverage is estimated at 67.8%.<sup>4</sup>

SARS-CoV-2 is mainly transmitted through droplets emitted by orotracheal secretions when speaking, coughing, sneezing or exhaling even though there are few



situations where airborne transmission has been documented.<sup>5</sup> SARS-CoV-2 infects all age groups, primarily affecting people ages over 65, as well as those with comorbidities such as cardiovascular disease, diabetes, chronic respiratory disease, immunosuppression or obesity presenting a higher risk of developing severe forms.<sup>6</sup> In view of these data, populations of athletes, potentially eligible for registering to outdoor sports events (OSEs), therefore, appear to be little exposed to a worrisome prognosis of the disease.<sup>7</sup>

Several studies explored the risk of SARS-CoV-2 transmission in an outdoor context, and concluded to a lower risk of the virus to be transmitted in a such setting.<sup>8</sup> Indeed, SARS-CoV-2 transmission has been documented to be greater in confined settings whereas fewer infections occurred in an outdoor environment, in particular when social distancing and health protocols are respected.<sup>9</sup>

The active circulation of SARS-CoV-2 within the general population, and potentially within the population practicing outdoor sports activities, suggests contexts conducive to the transmission of the virus. Health prevention and control protocols make it possible to limit the spread of this virus. Nevertheless, despite the availability of vaccines, the occurrence of potentially highly contagious variants or vaccine hesitancy might require appropriate protocols to reinforce individual safety during outdoor events. Given how the virus spreads and the physical barriers put in place, we hypothesise that OSEs do not present a higher risk of SARS-CoV-2 contamination. However, little information is known on the risk of transmission of SARS-CoV-2 in OSEs.

The main objective of the COVID-ESO project is to measure if individuals participating in OSEs present a similar risk of SARS-CoV-2 transmission comparing to individuals not participating in OSEs, in France.

## METHODS

### Study design and setting

This prospective, interventional, quasi-experimental study<sup>10</sup> will be carried out in volunteer individuals likely to participate in OSEs. At the time of the protocol was drafted, six events were targeted across France to be included in the COVID-ESO project. Three sport trials will be eligible for the study: running, cycling and triathlon.

### Recruitment

Any adult patient aged over 18, having a French social security number, fluent in French and understanding of the French language, having a medical certificate allowing sport practice and who gives informed consent, is eligible for the study. Any patient who does not meet the aforementioned criteria and/or meet the following criteria will be excluded from the study:

- ▶ Participant with respiratory symptoms or other clinical features suggesting COVID-19.

- ▶ Individual diagnosed positive for COVID-19 less than 3 months before the event.
- ▶ Individual involved as a volunteer in the organisation of the event.
- ▶ Pregnant or breastfeeding women.
- ▶ Individuals with risk factors of developing a severe form of COVID-19.<sup>11</sup>

Each individual participating in the OSE will choose one of his or her usual training partner to be eligible for the unexposed control group. Individuals will be matched (1:1) on three variables known to be factors that influence exposure to sports practice and/or condition SARS-CoV-2 infection: age ( $\pm 5$  years), sex and the administrative district of residence.

Individuals assigned to the exposed group will participate in the OSE, whereas individuals assigned to the unexposed group will not participate in the OSE as shown in [figure 1](#). Athletes are aware of the future OSE where they would like to participate. Registration to the OSE is based on a voluntary basis but is a prerequisite for participating in the COVID-ESO study. Eligible criteria of both groups will be assessed through an information letter to be filled in at the time of registration for the event. All individuals participating in the study will be asked to perform saliva tests on the day of the event and 7 days after the event. The time interval of 7 days between the two saliva tests was chosen given the mean incubation period of SARS-CoV-2 estimated at 5–7 days<sup>12 13</sup> and also considering that the majority of SARS-CoV-2 infections occur before 7 days after exposure.<sup>14</sup> The day prior to the event, a questionnaire will be sent by email to all individuals in order to assess baseline characteristics and exposures related to COVID-19. A second questionnaire will be sent by email to assess exposures to COVID-19 between the event and day 7. During the time of the event, unexposed individuals will be asked to keep their daily routine. Measurement of the exposure during the time of event for the unexposed group will be assessed in the questionnaire administered at day 7. The exposed and the unexposed individuals must not have contact 10 days before the event up until 8 days after the event

### Patient and public involvement

No patient is involved in the study.

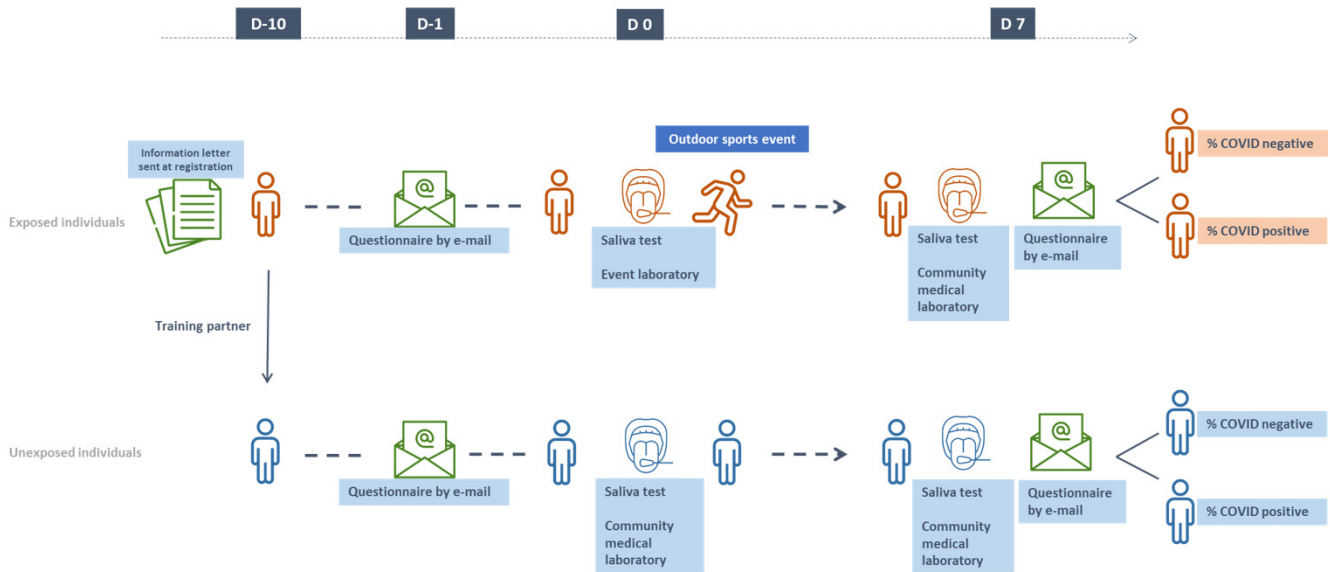
Aggregated results will be disseminated by email sent to all the participants of the study.

### Data collection

Data will be collected on an electronic case report form (CRF) designed especially for the purpose of the project and stored on the Logicoss software platform (<https://www.logicoss.com/>). A questionnaire including socio-demographic, clinical and exposure data to COVID-19 will be carried out for both groups on the day before the event and 7 days after the event.

### Biological sample collection and testing

A saliva test will be performed and tested for the presence of SARS-CoV-2 RNA by real-time reverse-transcription



**Figure 1** Description of the COVID-ESO study.

PCR (ThermoFisher TaqPath kit) for each individual who meets inclusion criteria. The unexposed group will perform saliva tests in community medical testing laboratories on day 0 and day 7 after the event. Participants to the event will be tested on the event location on day 0 before the start of the event and in a community medical testing laboratory on day 7 after the event. The results of the presence or absence of SARS-CoV-2 will be shared to the prescriber based on their license number to keep professional secrecy.

## Statistical methods

### Sample size

Under the alternative hypothesis H1 of an identical probability of infection of the exposed and unexposed groups fixed at 400/100 000 (0.4%), 2134 participants must be included in the study (1067 per group) so that the upper limit of the one-sided 95% CI (or equivalent to the upper limit of the two-sided 90% CI) excludes a difference in the probability of contamination to the detriment of the exposed group of 0.8% in 90% of cases (power=0.90).<sup>15</sup> The aim is to reject the null hypothesis of a probability of infection multiplied by 3.0 to the detriment of the exposed group. **Table 1** presents the sample size calculation.

### Statistical analyses

The probability of infection (positive tests between the first and the second sample) will be estimated in the exposed and unexposed groups with their 95% CIs, athletes (exposed or non-exposed) with a first positive test being previously excluded from the analysis. As the infection rate is low, the estimated probability of infection is almost numerically identical to the weekly infectious rate.

Age, sex and administrative district of residence of the individuals in each exposed/non-exposed pair will

be analysed in order to have a detailed analysis of the pairing structure. Individuals with a first positive test will be excluded from the analysis. The remaining exposed (respectively non-exposed) individual of the pair will then be re-matched to a pair of which the non-exposed individual (respectively exposed) will be the closest to it in terms of the three matched factors. Since the study design is strictly matched (1:1 matching), the main analysis of this study will be performed by fitting a conditional logistic regression model.<sup>16</sup> An adjusted conditional

**Table 1** Sample size calculation

Incidence* in both groups under H1	Incidence* in the exposed group under H0	Power	Size in each group	Total size
150	450	50%	901	1802
		60%	1200	2400
		70%	1566	3132
		80%	2059	4118
		90%	2852	5704
400	1200	50%	337	674
		60%	449	898
		70%	586	1172
		80%	771	1542
		90%†	1067	2134
750	2250	50%	567	1134
		60%	410	820
		70%	312	624
		80%	239	478
		90%	180	360

\*Weekly incidence per 100 000 individuals (considered as identical to the probability of a SARS-CoV-2 infection in the general population).  
 †Power calculation stated in the COVID-ESO study protocol.

logistic regression model will estimate the OR associated with exposure to outdoor sports practice and its CI. This analysis will then be completed by adjusting a model taking into account two other potential confounding factors: the size of the household (including the number of children) and the profession (ie, caregivers, teachers).<sup>17</sup> These potential confounders will be taken into account using indicator covariates introduced into the model predictor.

As the sport events unfold, data will be analysed using a group sequential Bayesian approach.<sup>18 19</sup> The cumulative information provided by each OSE will be taken into account to provide a more precise estimation of the parameter and the corresponding odds-ratio distributions. The upper limit of the 95% one-side credibility interval of the OR will be compared with the numerical value 3. Analyses will be carried out using R V.4.1.0.

### Data management and archiving

#### Case report form

All required information will be recorded on an electronic questionnaire in a clear and legible manner, and justification must be provided for all missing data. Data entry errors will be limited by predefining plausibility checks in the online questionnaire.

Transfer of the data from the Dokever society (<https://www.dokever.com/>) through the Logicoss platform to the coordinating centre in Lyon, France will be performed via the electronic questionnaire following approval by the French National Commission for Data Protection (Commission Nationale de l'Informatique et des Libertés).

#### Data management

Collected data will be computerised by the Dokever society. Databases will be anonymous and locked with a password known only by the scientific staff. These data will be kept for a minimum of 15 years after the end of the study.

#### Archiving

According to French law, the sponsor will keep the study documents (protocol and annexes, possible amendments, information forms, CRF, statistical analysis plan and output and the final study report) for a minimum of 15 years. After this period, the sponsor will be consulted before any data are destroyed. Study-related documents and reports may be subject to audit or inspection by the sponsor and/or other authorised bodies. This study is part of the 'reference methodology' (MR-001) in application of article 54, paragraph 5, of French law No. 78-17 of 6 January 1978. This change was approved on 5 January 2006 and modified on 21 July 2016. The Hospices Civils de Lyon, the promoter of the study, has signed a commitment to comply to this reference methodology.

#### Confidentiality

In accordance with the provisions concerning the confidentiality of data to which the persons responsible for the quality control of research involving the human

person have access (Article L.1121-3 of the Public Health Code), in accordance with the provisions relating to the confidentiality of information concerning in particular the tests, the persons who are suitable for them and the results obtained (article R. 5121-13 of the public health code), the persons having direct access to the data will take all the necessary precautions to ensure the confidentiality of information relating to the tests, to the persons who take part in them and in particular as regards their identity as well as the results obtained.

These people, like the investigators themselves, are subject to professional secrecy (under the conditions defined by articles 226-13 and 226-14 of the penal code).

### ETHICS AND DISSEMINATION

#### Ethical approval

Ethical approval has been obtained for the Clinical research and committee of South West of France, 10 June 2021. COMITE DE PROTECTION DES PERSONNES DU SUD-OUEST ET OUTRE-MER 4 under the reference number 21.03.23.71737/CPP2021-04-045 a COVID/2021-A00845-36

#### Informed consent

All participants of the study will be informed of the objectives and their rights to refuse to participate in the study or withdraw at any time using simple, understandable terms. This information will be provided by an information and consent form given to each participant. According to French law, voluntary, written informed consent will be obtained by the investigator before inclusion for the epidemiological data, and for the collection of biological data.

#### Regulatory compliance

The research will be conducted in accordance with applicable laws and regulations currently in place in France.

#### Withdrawal criteria

Subjects may request to withdraw from the study at any time and for any reason without having to justify. In the event of a premature withdrawal, the investigator must document the participant's reasons for withdrawal as completely as possible.

#### Stopping the research study

The sponsors reserve the right to interrupt the study at any time if the objectives are not being met. In the event of premature termination of the study for security reasons, the information will be transmitted by the sponsor to all concerned parties and to the ethical committee within 15 days.

#### Protocol amendments

In the eventuality of changes in the existing protocol that significantly affect the scope or the scientific quality of the investigation, an amendment containing a verbatim description of the changes and reference (date and

number) to the submission that contained the original protocol will be submitted to the ethical committee for their approval.

### Dissemination

Results and scientific reports that emerge from this study will be made publically available under the responsibility of the principal investigator in agreement with the associated investigators. Results will be reported following the guidelines from the STrengthening the Reporting of OBservational studies in Epidemiology consortium ([www.strobe-statement.org/](http://www.strobe-statement.org/)). Publication rules will follow international recommendations. The findings will also be shared with national health and sport authorities.

Authorship will follow the guidelines established by the International Committee of Medical Journal Editors (<http://www.icmje.org/>), which require substantive contributions to the design, conduct, and interpretation and reporting of an epidemiological study.

### DISCUSSION

The COVID-ESO project will provide original results that could:

#1 constitute additional evidence for a better understanding of SARS-CoV-2 transmission in a population participating in OSEs.

#2 pave the way for tailored recommendations or supplement current recommendations in terms of control measures by acquiring data on the SARS-CoV-2 transmission in this specific setting.

#3 identify subpopulations at increased risk of transmission of SARS-CoV-2 in OSEs.

#4 help to identify areas or contact opportunities that are more at risk of exposure to the SARS-CoV-2 during the event.

Nevertheless, the OSE could be the source of incident COVID-19 cases among the exposed group and therefore contribute to generating potential SARS-CoV-2 clusters.

In addition, symptomatic individuals will not be included in the study although it is well documented that symptomatic individuals are more contagious, therefore, more likely to disseminate SARS-CoV-2 than asymptomatic or paucisymptomatic individuals.<sup>20</sup>

The choice of performing saliva tests was made to reduce the number of individuals lost to follow-up and increase the likelihood of participating in the study, as saliva tests are less invasive than nasopharyngeal swabs, with acceptable sensitivity and specificity values.<sup>21</sup> A measurement bias might occur as not all laboratory tests will be performed in a centralised testing platform. Questionnaires will be sent electronically which might induce a recall bias and an information bias, as data will be declarative and based on trust. No blinding experiment was possible in this situation as the participants need to know whether they are attending to the OSE or not. To limit lost to follow-up, in particular after the event, a financial

reward will be offered to all participants of the study who had fully completed both tests and questionnaires.

Furthermore, considering that the events need to be organised ahead of time made the authors choose a quasi-experimental design where randomisation was not possible. Allocating eligible individuals at random might have generated significant disappointment among the athletes who have been preparing for a long time (training, diet) with the objective and hope of participating in the event. The human aspect cannot be neglected in that sense.

Additionally, the window of opportunity of conducting such studies is very narrow, as a right balance needs to be found between outbreak situations and 'normal' life. At the same time, the emergence of new variants and future vaccine roll-out may hinder the execution of the study. Evidence suggests that SARS-CoV-2 is susceptible to seasonal oscillations that could interfere with the study implementation.<sup>22</sup> Also, the organisation of the events depends on the weather and climate conditions, which could hamper the smooth implementation of the sports trials. For instance, a triathlon trial can hardly be run in the winter period.

Finally, this protocol has been initially drafted at the time where OSEs were strictly forbidden in France and when the SARS-CoV-2 incidence rate in the community was very high. Data might evolve over time also considering that more and more individuals are being vaccinated. Instead of being an experimental study prior to the resumption of OSEs but more as a population-based study using real world data aiming at comforting athletes regarding the risk of infection following OSEs.

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