ENE-COVID19
NATIONAL STUDY OF SARS-CoV2 SERO-EPIDEMIOLOGY IN SPAIN
EXECUTIVE SUMMARY

SUMMARY

To better understand the real dimension of COVID-19 epidemic, Spain has launched a population-based sero-epidemiological study (ENE-COVID) to monitor the infection dynamics across its territory in order to inform the future Public Health Policies related to COVID-19.

Given geographical differences in SARS-CoV-2 spread in the Spanish territory, ENE-COVID is been designed to offer estimations of past and present infection prevalence down to the province[1] level (NUTS 3), and will provide updated information on the epidemic evolution during two months.

This prospective study intends to include 60,000 people conforming two population-based cohorts equally representative of the whole country, the second one starting a week apart from the first cohort. Following WHO recommendations, ENE-COVID uses households as the basic sampling unit. Both cohorts are revisited two more times to collect epidemiological information and specimens after 3 weeks of enrollment.

At every visit, participants will answer a brief questionnaire with demographic information as well as COVID19 diagnosis, symptoms and risk factors, a IgG/IGM Rapid Test (lateral flow chromatographic immunoassay) will be applied using finger-prick capillary blood. Finally, a venous blood sample will be taken in those participants agreeing to provide it to determine SARS-CoV-2 antibodies using a more precise method (chemiluminescent microparticle immunoassay: CMIA).

To conduct this survey within the highest standards of efficiency and reliability, the study counts on:

a) The collaboration of the **Spanish National Statistics Institute (INE)**, to support sample selection and provision of relevant information on participants already available in their databases.

b) The collaboration of the 17 administrative **regions in Spain (Comunidades Autónomas-NUTS 2)**, that will adapt the logistics required for the study to their realities, and provide the healthcare personnel needed to carry out the study.

[1] 50 administrative provinces plus 2 autonomous regions

INTRODUCTION

The monitoring system for COVID-19 of the National Network for Epidemiological Surveillance has been constantly adapting the information provided by the different regions to the different stages of this pandemic. Nevertheless, the available information nowadays is not sufficient to characterise accurately the time-evolution and geographical distribution of the epidemic, being this characterisation a critical tool for implementing more informed Public Health Policies. Asymptomatic or mild-symptomatic cases, as well as other moderate to severe non-diagnosed patients could represent a high portion of affected people.

The limitations of the data gathering process currently in place prevent us:

a) To know the real dimension of the total number of infected people, either at national, regional and local level.

b) To monitor the disease spreading process, considering that within a confinement situation, is very important to elucidate to which extent new infections are due to community transmission or occurring inside households, as the contention measures may differ.

SPECIFIC OBJECTIVES

1. Estimate the prevalence of infection for SARS-Cov2, by determining antibodies against the virus, in Spain, by Autonomous Communities (CCAA-NUTS 2) and by Provinces (NUTS 3), as well as by age and sex.

2. To evaluate changes in this prevalence and to monitor the evolution of the epidemic, paying particular attention to new infections due to community transmission.

METHODOLOGY

- Sample Design

Participants were selected through a stratified two-stage sampling. To ensure representativeness at the provincial, regional and national level, the first stratification level corresponds to the 50 provinces together with the two autonomous cities of Ceuta and Melilla. The second level takes into account population density, classifying municipalities according to their size into 4 categories (from less than 5,000 to greater than 100,000 inhabitants). Within each stratum, the census sections are the sampling unit at the first stage, being households the unit for the second stage.

The number of participants required to estimate a seroprevalence of 5% or higher -including an inflation factor to account for the correlation between dwellers in the same household- was taken as the minimum sample required at the province level. This figure was amplified to allow for a non-response of 33%. At the Autonomous Community level, the minimum sample was also calculated in a similar way, but imposing greater precision. The final sample was then selected combining a uniform distribution per province (half of the total sample allocated there), with a

proportional distribution according to the above-mentioned categories of municipalities. With these criteria in mind, ENE-Covid will try to contact 36,000 Spanish households distributed in 1,500 census sections to invite their 90,000 dwellers to participate, in order to obtain a final sample of around 60,000 people.

- Serological determination

Being COVID-19 a new disease, all diagnostic tools, including antibody tests are still under development. There is no gold-standard for these techniques. Since our goal is to get an estimation of the percentage of people with antibodies against SARS-CoV-2, two complementary tests will be used.

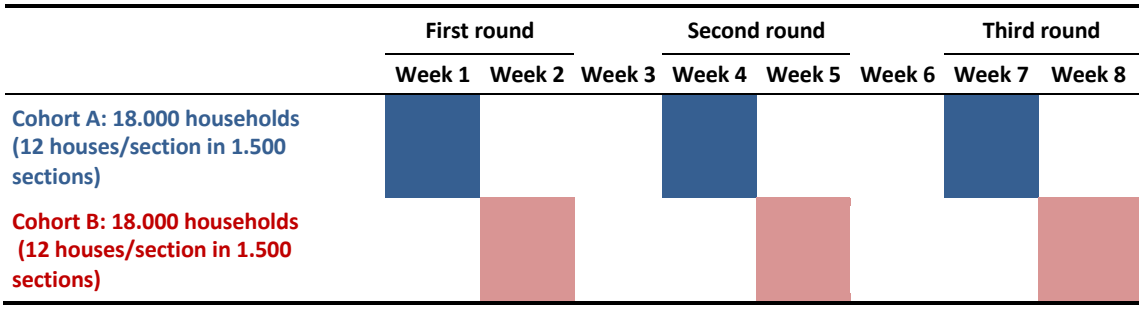
The study includes, as a first tool, a rapid immunochromatographic test (lateral flow chromatographic immunoassay), using finger-prick blood, providing IgG/IgM results in 10 minutes. Furthermore, blood samples will be taken from participants who consent to donate them (60% of the whole sample) at the same moment and will be transferred to selected laboratories to quantify IgG using an immunoassay with high sensitivity and specificity (CMIA). Results from this technique will serve to recalibrate those obtained with the rapid test, which seems to have lower sensitivity.

- Epidemiological information

The study includes a short epidemiological questionnaire to obtain the necessary information to know the existence of a previous diagnosis of COVID19, the presence or history of symptoms compatible with this disease and the main known risk factors. The epidemiological questionnaire explores possible sources of infection and characteristics of the subjects and, specifically, collects all the information necessary to characterize the participants as negative, asymptomatic, or people with possible present or past COVID19 involvement.

- Field work

In a first round, we expect to collect the information from the 36.000 households in a two week time. At least 3 monitoring rounds will be needed, with 1 week of separation between them. The first week, 12 randomly selected households from each census track (cohort A) will be recruited; the remaining 12 households from each census track will be invited to participate in the second week (cohort B).



- Information provided to participants

Participants will be informed about the results of the rapid test. An information sheet has been prepared explaining that a positive result only shows previous contact with the virus, but it cannot be understood as a COVID-19 diagnosis, nor give us information about infectiveness.

- Survey takers, training

A specific training programme for survey takers is already undergoing. It includes a virtual course to give health workers detailed information about the study goals and procedures, the way information is collected, the right way to perform the rapid tests and the right procedure for sample collection and transportation, taking into account biosecurity issues. All technical specifications are included in the study protocols.

- Ethical considerations

ENE-Covid was reviewed and approved by the Ethics Committee at the Carlos III Institute of Health. Different forms of informed consent are available for adult people, teenagers, parents of participant children and tutors of disabled participants.

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