SEROPREVALENCE SARS-COV-2 IN BLOOD DONORS

The study will be coordinated by the service Epidemiology of Infectious Diseases (contact: Robby De Pauw) of the scientific directorate of Epidemiology and public health, Sciensano. Laboratory analysis will be performed by the service Immune response of the scientific directorate of Infectious diseases in humans (contact: Isabelle Desombere).

The study collaborates with 'Rode Kruis Vlaanderen' (contact: An Muylaert) for the collection of residual samples of blood donors in Flanders, and 'Service du Sang de la Croix-Rouge de Belgique' (contact: Marie-Pierre Rodenbach).

BACKGROUND

In December 2019, public health authorities in Wuhan, China, reported a cluster of patients with an acute respiratory syndrome of unknown cause. A novel coronavirus, later called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was soon identified as the causative agent. The initial outbreak spread rapidly in Wuhan, China and later also globally with outbreaks and clusters observed in Asia, Europe, Australia, Africa and the Americas. This disease is now referred to as coronavirus disease 2019 (COVID-19).

Sciensano has a legally established research and surveillance mission in the framework of public health in Belgium and has set up various surveillance systems since the beginning of the COVID- 19 epidemic, amongst others, in laboratories, hospitals and a general practitioner network. However, data on the healthy population, previously infected by SARS-CoV-2 but not tested, is still lacking. In general, only little is known on the number of asymptomatic patients or patients with only mild symptoms as they are currently not being tested. The testing methodology currently used for diagnosis, namely PCR, only allows to identify current infections. Previous exposure can be identified by the detection of antibodies against the virus using serological testing strategies. The presence of antibodies may indicate a certain protection against new disease and therefore their prevalence in individuals and the population could play an important role in further control of and policy making for the COVID-19 epidemic. However, there are still uncertainties and further research is needed.

OBJECTIVES

The overall objective of the study is to monitor the prevalence of antibodies against SARS-CoV-2 in the healthy Belgian adult population during the COVID-19 outbreak. In order to identify subgroups with higher or lower exposures to the virus, age- gender- and region-specific seroprevalences will be determined.

METHODS

STUDY DESIGN

A repeated cross-sectional study will be carried out with collection of residual blood samples from Belgian blood donors (majority new individuals each time) in collaboration with Rode Kruis Vlaanderen. Sample collection will be repeated every two weeks in order to monitor the prevalence of antibodies during the COVID-19 epidemic. In addition, the age, gender and province of the donor will be collected together with the date of donation.

The study population, persons donating blood during the COVID-19 crisis in Flanders, is expected to be a subset of the healthy Belgian population aged 18 years or older. In addition to systematically applied inclusion and exclusion criteria for blood donation , persons with COVID-19 symptoms, such as fever, coughing, sore throat,… in the past 14 days, or persons with a family member or contact with a positive COVID-19 patient are not allowed to donate blood. Blood donors are excluded from the study if they did not give their consent for the use of residual blood of their donation for scientific research which is asked as an opt-in in the medical questionnaire. In addition, they are excluded if they indicate that their coded personal data can't be used for scientific research (opt-out).

Serological tests will be performed at the service of Immune response at Sciensano. Blood donors will not be informed on the outcome of the serological test as results will not be immediately available. Furthermore, the serological tests are still in an experimental phase and have not yet been validated for diagnostic purposes.

SAMPLING AND SAMPLE SIZE

Based on the expected regional, sex, and age distribution of the blood donors, a total of 900 samples are first drawn from all samples sent to Sciensano. This sample size allows for a precision of 3% (or 95% CI width of 6%), assuming a population-prevalence of 30%. Sampling was increased to 1200 from January 2021 onwards to preserve the precision of 3% for seroprevalence estimates of 50% (Arya et al., 2012).

DATA ANALYSIS

The main objective of this study is to evaluate and surveille trends in the presence of antibodies against SARS-CoV-2 among the Belgian population. To this end, the red cross (Rode Kruis Vlaanderen and Service du Sang de la Croix-Rouge de Belgique) provide samples every two weeks (up to January 2021) or every month (from January 2021 onwards) to be analyzed. To yield valid estimates for the population, samples are corrected for sampling bias via the known distribution of the population with respect to age, sex and region of the different samples. In addition, the estimates are corrected for test imperfectness. Hereafter, the analytical solution for these constraints is briefly explained.

Sampling bias

To generalize the results obtained by the current study from a sample to the Belgian population, a robust Bayesian method is applied, i.e. Multilevel regression with poststratification (MRP) (Buttice & Highton, 2013). This approach yields similar results as the well-known weighted approach that is implemented in the survey-package, but has the advantage of being more flexible in the generated output (e.g. test imperfectness can immediately be integrated in the estimation process).

Test-Imperfectness

To adress the issue of test-imperfectness, we integrated the test performance in terms of its sensitivity and specificity. Over time, two different test kits have been applied, including the Wantai ELISA Total Ab test up to march 2021, and the Wantai ELISA IgG test from march 2021 onwards. Estimates for test imperfectness for the Wantai ELISA Total Ab test were derived from cochrane review by Deeks et al. (Deeks et al., 2020). These estimates are summarized in **table 1**. Estimates of test imperfectness for the Wantai ELISA IgG test were extracted from the manufacturer's information sheet, and are summarized in **table 2**.

Table 1. Result for diagnostic accuracy "Wantai Total Ab"

Publication	TP	FP	FN	TN
Lassauniere et al. (2020)	28	0	2	82
Lou et al. (2020)	78	0	2	300
Zhao et al. (2020)	127	4	27	667

TP, true positive; FP, false positive; FN, false negative, TN, true negative

Table 2: Result for diagnostic accuracy "Wantai IgG"

Publication	TP	FP	FN	TN
Manufacturer	75	0	4	75

TP, true positive; FP, false positive; FN, false negative, TN, true negative

Statistics

All analysis are performed in R (R Core Team (2018), available from https://www.R-project.org/). and Bayesian analysis is performed with Stan using the R-integrated package R-Stan (https://mc-stan.org/users/interfaces/rstan). The Stan-modeling code can be found here (https://github.com/rdpauw/BelSero), and will be updated in case of any major changes.

MORE INFORMATION

More information on Bayesian post-stratification can be found here (https://mc-stan.org/docs/2_26/stan-users-guide/poststratification.html).

More information on correction for test imperfectness can be found in the manuscript by Flor et al. (Flor et al., 2020).

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