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PREVALENCE AND INCIDENCE OF ANTIBODIES AGAINST SARS-COV-2 AMONG PRIMARY HEALTHCARE PROVIDERS IN BELGIUM DURING ONE YEAR OF THE COVID-19 EPIDEMIC: PROSPECTIVE COHORT STUDY PROTOCOL

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PREVALENCE AND INCIDENCE OF ANTIBODIES AGAINST SARS-COV-2 AMONG PRIMARY HEALTHCARE PROVIDERS IN BELGIUM DURING ONE YEAR OF THE COVID-19 EPIDEMIC: PROSPECTIVE COHORT STUDY PROTOCOL

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ABSTRACT

Introduction

National severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) seroprevalence data provides essential information about population exposure to the virus and helps predict the future course of the epidemic. Early cohort studies have suggested declines in levels of antibodies in individuals, associated with, for example, illness severity, age and co-morbidities. This protocol focuses on the seroprevalence among primary health care providers (PHCPs) in Belgium. They manage the vast majority of COVID-19 patients in addition to other patients and therefore play an essential role in the efficient organisation of health care. Currently, evidence is lacking on 1. how many PHCPs get infected with SARS-CoV-2 in Belgium, 2. the rate at which this happens, 3. their clinical spectrum, 4. their risk factors, 5. the effectiveness of the measures to prevent infection and 6. the accuracy of the serology-based point-of-care test in a primary care setting.

Methods and analysis

This study will be set up as a prospective cohort study. General practitioners (GPs) and other PHCPs (working in a GP practice) will be recruited via professional networks and professional media outlets to register online to participate. Registered GPs and other PHCPs will be asked at each testing point (n=9) to perform a capillary blood sample antibody point-of-care test (OrientGene®) and complete an online questionnaire. The primary outcomes are the prevalence and incidence of antibodies against SARS-CoV-2 in PHCPs during a 12-month follow-up period. Secondary outcomes include the longevity of antibodies against SARS-CoV-2.

Ethics and dissemination:

Ethical approval has been granted by the Ethics Committee of the University Hospital Antwerp/University of Antwerp (Belgian registration number: 3002020000237). Alongside journal publications, dissemination activities include the publication of monthly reports to be shared with the participants and the general population through the publicly available website of the Belgian health authorities (Sciensano).

Registration:

Trial registration number: NCT04779424

Key words: cohort study; primary care; SARS-CoV-2; COVID-19; prevalence; incidence; antibodies; seroprevalence

Article summary

Strengths and limitations of this study

- This large cohort study will provide regular, timely and precise data at national level on prevalence and incidence of antibodies against SARS-CoV-2 among primary health care providers (PHCPs) managing the vast majority of COVID-19 and other patients and therefore essential to organise health care efficiently.
- This study will familiarise PHCPs with the use of serology-based point-of-care tests (POCTs) and validate the POCT in a primary care setting.
- Missing data points and the use of a convenience sample could limit the validity of the study results.

For peer review only

Introduction

As of 16th May 2021, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has infected over 162 million people worldwide (over 1 030 000 in Belgium) and caused over 3.3 million deaths from coronavirus disease (COVID-19) worldwide (over 24 000 in Belgium).¹ COVID-19 is a lethal respiratory tract infection (RTI), but infection with SARS-CoV-2 can also be mild and even asymptomatic.

SARS-CoV-2 seroprevalence estimates provide essential information about population exposure to infection and help predict the future course of the epidemic.^{2 3} When setting up this study seroprevalence studies in Iceland⁴ and Spain⁵ showed different levels of population antibody positivity, lasting up to 4 months in Iceland. In addition, early cohort studies have suggested waning of antibody levels in individuals, associated with for example illness severity, age and co-morbidities.⁶⁻⁸ Meanwhile, other seroprevalence studies showed antibody positivity lasting up to 9 months.^{9 10} For Belgium, Sciensano (the Belgian national scientific institute, www.sciensano.be) performs national seroprevalence studies of SARS-CoV-2 antibodies in several relevant populations including schools,¹¹ hospital personnel¹² and nursing homes¹³.

This protocol focuses on the seroprevalence among primary care health care providers (PHCPs). They manage the vast majority of COVID-19 and other patients and therefore play an essential role in the efficient organisation of healthcare.^{14 15} Among the PHCPs, general practitioners (GPs) in particular, act as gatekeepers to the next levels of care. Therefore, preserving the capacity of GPs, together with that of their co-workers, throughout the COVID-19 epidemic is essential.¹⁶ In Belgium, this is particularly concerning given the GP workforce consists of mainly older adults and is therefore at higher risk for COVID-19-related morbidity and mortality.¹⁷ In Italy GPs represented up to 38% of the physicians who died from COVID-19 early on in the epidemic.¹⁸

However, current evidence is lacking on 1. how many PHCPs are infected by SARS-CoV-2 or have COVID-19 in Belgium, 2. the rate at which this occurs, 3. their clinical spectrum, 4. their risk factors, 5. the effectiveness of the measures to prevent this from happening and 6. the accuracy of the immunological serology-based point-of-care test (POCT) used by PHCPs.

During the COVID-19 crisis POCTs have been developed to identify the presence of antibodies for SARS-CoV-2. Compared to laboratory tests, a valid easy-to-use POCT will speed up the availability of the test results for both the participants and the national health authorities. Furthermore, by using POCTs in this study, PHCPs will have the opportunity to become more familiar with this type of technology.

Sciensano has validated five POCTs using finger prick blood, identifying one test with appropriate sensitivity (92.9%) and specificity (96.3%) for use in seroprevalence studies.¹⁹ We use this Orientgene® POCT for the present study.

If (Belgian) primary care cannot be delivered safely, the COVID-19 epidemic will disrupt public health by failing to deliver non-COVID-19 related healthcare and to (continue to) keep off the pressure from the next levels of care during the current epidemic. Therefore, we need to monitor their health and the effectiveness of, and the need for, infection prevention and control measures during epidemics. In addition, the follow-up of a cohort of PHCPs will help us to understand the duration and nature of antibodies generated in response to SARS-CoV-2 infection as well as those generated in response to vaccination.²⁰ Whether and for how long antibody response protects those infected with SARS-CoV-2 from future infections or illness will determine the value of serological tests.²¹

Primary objectives

1. Assess the prevalence of antibodies against SARS-CoV-2 among PHCPs (PHCPs = GPs and other PHCPs in their practice) in Belgium at timepoint 1 and at different timepoints during a 12-month follow-up period.
2. Assess the monthly and annual incidence of antibodies against SARS-CoV-2 among PHCPs in Belgium during a 12-month follow-up period

Secondary objectives

1. Assess the longevity of the serological antibody response among seropositive PHCPs.
2. Assess the proportion of asymptomatic cases among (new) cases (that develop during follow-up).
3. Assess the determinants (risk and predictive factors) of SARS-CoV-2 infection in PHCPs.
4. Validate the serology-based POCT in a primary care setting (Phase 3 validation).
5. Familiarise PHCPs with the use of serology-based point-of-care tests.

Once vaccination of PCHPs starts, this study will take into account vaccination rates when reporting the seroprevalence and be able to assess waning of antibodies after vaccination.

Methods and analysis

The aim of this study is to broaden the knowledge on SARS-CoV-2 infection in Belgian primary care and to contribute to scientific research, health service and policy management supporting the fight against this epidemic.

STUDY POPULATION

Inclusion Criteria:

- Any GP working in Belgium (including those in professional training) currently working in primary care and any PHCP from the same GP practice who physically manages (examines, tests, treats) patients,
- Participants must be able to comply with the study protocol and provide informed consent to participate in the study.

Exclusion Criteria:

- Staff hired on a temporary (interim) basis will be excluded as follow-up over time will be compromised.
- Administrative staff or technical staff without any prolonged (longer than 15 minutes) face to face contact with patients are not eligible.
- PHCPs who were not professionally active during the inclusion period will not be eligible

STUDY DESIGN

This study will be set up as a prospective cohort study.

Recruitment

PHCPs will be recruited prior to the first and second testing points (registration will be possible between 15 November 2020 and 15 January 2021). PHCPs working in clinical practice in Belgium will be invited to register online for participation in this national epidemiological study and will be asked to invite the other PHCPs in their practice to do the same. We will emphasize that PHCPs that have already been diagnosed with COVID-19 are also eligible. Information about the study will be disseminated to GPs and PHCPs via professional organisations (Domus Medica and College de Médecine Générale), university networks across the country and through professional media channels. The convenience sample of participants will be checked to ensure that it is representative in terms of geographic and demographic qualities.²²

Data Collection

Upon inclusion in the study, participants will be assigned a unique study code by the researchers, who will manage the key between these codes and the identification data. They will receive testing material at their place of work through regular mail. At the first testing time-point (T1) they will receive an invitation by email (including a personalised link to an online questionnaire in French and Dutch) inviting them to:

1. Auto-collect a capillary blood sample and analyse it using the OrientGene® POCT.
2. Complete a baseline questionnaire through a secured online platform hosted by Sciensano (Limesurvey).

The baseline questionnaire at the first testing point will ask for their informed consent and will ask for information about;

- The result of the POCT,
- basic socio-demographic data, (age, gender, composition of household – e.g. presence of school-aged children in the house)
- professional data, (practice patient size)
- health status, (pre-existing health conditions, regular medication use, presence of symptoms since the start of the epidemic, previous positive test results for COVID-19)
- Professional exposure, (contact with confirmed cases, use of infection prevention and control measures and
- the availability of personal protective equipment (practice organisational aspects, delayed care for non-urgent conditions) (see supplementary materials).

A follow-up questionnaire will be sent for each of the subsequent testing timepoints. In addition to the POCT result, it will collect information on:

- the health status, including the presence of symptoms,
- vaccination status (date of vaccination, type of vaccine, number of doses, presence of side-effects)
- professional exposure, (contact with confirmed cases, use of infection prevention and control measures (see supplementary materials).

Phase 3 validation of the POCT

To validate the POCT, a sub-sample of participants will be asked to provide a serum sample. This sub-sample will be made up of all those participants that were seropositive for SARS-CoV-2 on the POCT at T1 and a random sample of participants that were seronegative at T1.

The participants will be sent material to collect the blood sample (Becton Dickinson Vacutainer® SSTTM ii Advance; ref 368879) along with postal materials (in accordance with the UN 3373 packaging norms) and instructions on how to send it to the laboratory of clinical biology of the University Hospital of Antwerp (UZA) (a reference laboratory chosen by Sciensano). Participants will be asked to send their blood sample the same day it is taken, and analysis will be undertaken within 24 hours of reception. Analysis will be done with a reference standard using the following testing algorithm: serum samples will be tested first on the ELECSYS Anti-SARS-CoV-2 S assay (Roche, Basel, Switzerland), if the cut-off index (COI) is between 0.6-3.0 the sample will be tested on the ATELLICA IM SARS-CoV-2 assay (Siemens, Munich, Germany), and if discordant results it will be tested on the LIAISON SARS-CoV-2 S1/S2 IgG assay (DiaSorin, Saluggia, Italy), using a two out of three 'reference standard'. The analytical and clinical performance of these three commercially available, fully automated SARS-CoV-2 antibody assays was investigated at University hospital of Antwerp (UZA) and the relevance of this testing algorithm explained and illustrated (personal communication Bart Peeters). Analytical performance of all three assays was acceptable and comparable with results found in other studies.²³⁻²⁶

Participants of this sub-sample will receive a 25€ voucher by way of compensation for the time and effort invested. The results of the serum sample will be communicated to participants via regular mail.

Follow-up

The study will last 12 months. Epidemiological data collected through the online questionnaires and self-sampling using the POCT will occur monthly for six months with one sample collection at nine and the final one at 12 months (Table 1). This corresponds to a total of nine testing timepoints. This number will however depend on the evolution of the epidemic. At each testing time-point, participants will be asked to perform the POCT within a timeframe of maximum 5 days. For the sub-sample providing a serum sample, participants will be asked to take the serum sample at the same time (just prior) to performing the POCT.

The result of the POCT will be entered as a variable in the online questionnaire. Data analysis will be performed and reported after each relevant testing period and at the end of the study. All pseudonymised data collected will safely be stored by Sciensano for 10 years after completion of the study.

Table 1. Timing of data collection

	T1	T2	T3	T4	T5	T6	T7	T8	T9	Total
	M0	M1	M2	M3	M4	M5	M6	M9	M12	9
POCT	X	X	X	X	X	X	X	X	X	9
Baseline Q	X									1
Follow-up Q		X	X	X	X	X	X	X	X	8
Serum		X								1

T: testing point, M: month, Q: questionnaire

SAMPLE SIZE

This study aims to include 5000 PHCPs with a 4 GPs to 1 other PHCP ratio considering the following sample size considerations regarding the different objectives of the proposed study.

To estimate a prevalence ranging from 5% to 10%, the current estimates for SARS-CoV-2 seroprevalence in the general population and hospital care providers, with a precision ranging from 2% to 1% and a 95% confidence level, a sample size ranging from 504 to 3554 PHCPs is required (Binomial 'exact' calculation), respectively. Since PHCPs will be clustered in their practices, we must correct the sample size. For an average of 2.5 PHCPs per practice (m) and an intraclass correlation of 0.2 (ρ) the design effect ($=1+(m-1)*\rho$) is 1.3. The corrected sample size ranges from 655 to 4620 PHCPs. Higher seroprevalence and non-response, both of which are to be expected, will reduce the precision of the estimates as will stratification by region or province. For example, with a sample size of 4620 PHCPs distributed equally over eleven strata, which corresponds to the number of provinces in Belgium ($n=10$) plus Brussels, the precision will range between 2.5% and 3.5% for a prevalence ranging from 5% to 10%, respectively.

1
2
3 Since multivariate prediction research for each determinant studied requires at least 10
4 subjects in the smallest category of the outcome variable to allow proper statistical
5 modelling,^{27 28} a model including 25 determinants would require 250 seropositive participants,
6 which corresponds to a 5% seroprevalence in 5000 or a 10% seroprevalence in 2500
7 PHCPs, not taking into account interaction terms in the model. The number of determinants
8 that can be assessed in multivariable analysis to predict new cases will depend on the
9 incidence. For example, to be able to assess 10 determinants would require 100 new cases
10 or 3% new cases in 3600 PHCPs or 4700 PHCPs considering a design effect of 1.3. A lower
11 incidence or lower sample size would further limit the number of determinants that can be
12 modelled. Using more recently described methods to calculate the sample size required for
13 developing a clinical prediction model would also require a sample size of substantially more
14 than 2000 participants (n=2283, with 228 events and 9.1 events per predictor) to meet the 4
15 criteria described by Riley RD et al. in case of a Mean Average Prediction Error (MAPE) of
16 0.025.²⁹

17
18 To estimate an incidence of 3% with a precision of 1% and a 95% confidence level, a sample
19 size of 1212 PHCPs is required or 1576 PHCPs considering a design effect of 1.3 (4160
20 PHCPs to estimate an incidence of 2% with a precision of 0.5% and considering clustering).
21 To be able to validate the POCT's accuracy in the primary care setting, i.e. estimate the
22 POCT's sensitivity (92.9%) with a lower limit of its 95%CI of 90% and its specificity (96.3%)
23 with a lower limit of its 95%CI of 95%, a sample of 301 PHCPs seropositive on the reference
24 standard (for sensitivity) and 810 PHCPs seronegative on the reference standard (for
25 specificity) is required, which corresponds to for example 6% seroprevalence in 5022
26 PHCPs. To reduce the burden on the participants and the costs of the study all those with a
27 positive POCT and only a (random) sample of 900 PHCPs with a negative POCT will be
28 assessed with the reference standard, and inverse probability weighting will be applied to
29 correct for missing reference standard data by design.³⁰⁻³²

30
31 A sample size of 5000 would also allow us to estimate the longevity of the antibody response
32 among the PHCPs seropositive on the POCT. For example, starting from 300 PHCPs
33 seropositive based on the POCT, a decrease of 10% in seroprevalence can be estimated
34 with a precision of 4% and a 95% confidence level. Smaller decreases in seroprevalence
35 and/or estimating with lower precision would require less than 5000 PHCPs to identify
36 sufficient PHCPs seropositive on the POCT. Clustering will most likely not be an issue here
37 since the waning of antibodies will most likely not be correlated among PHCPs working in the
38 same practice.
39

40 41 **DATA PROTECTION**

42 As described above, epidemiological and serological data will be linked via a unique identifier
43 code assigned to each participant. The same unique identifier code will be entered in each
44 questionnaire, enabling the link for data analysis. This code will stay the same throughout the
45 study. The key between the codes and the identification data of the participants will be kept
46 in a secure and protected way by the principal investigators and the researchers, and
47 destroyed upon completion of the study. The personal data processing activities for the
48 proposed research project will be submitted to the UAntwerpen Data Protection Office to
49 review its completeness and compliance with the General Data Protection Regulation
50 (GDPR) and to ask for formal approval. To control digital access only by authorized people
51 on all devices (desktops, laptops, external drives, ...) at all locations (work, home, and
52 travel), complex passwords are used, up-to-date anti-virus and firewall protection is run.
53 Using the ICT services of UAntwerp, ULiège and Sciensano assures that the data will be
54 backed up on a regular basis. The research team ensures that their personal computer
55 system is always up-to-date, and does not switch off the automatic installation of updates.
56

57 58 **DATA ANALYSIS**

59 Data analysis will be done jointly by the principal investigators, researchers and team
60 involved in this study with the University of Antwerp team taking the lead. Questionnaire

1
2
3 responses will be coded. Data will be cleaned and validated; incomplete questionnaires will
4 be manually checked to see if they can be included. Analysis will be mainly descriptive and
5 done on R version 3.6.3 or equivalent.

6 Among others, the following indicators will be calculated, considering clustering of PHCPs in
7 the same practice whenever appropriate:
8

- 9 1. Seroprevalence of SARS-CoV-2: number of participants in whom presence of specific
10 SARS-CoV-2 IgG is detected by the POCT / Total number of participants tested with the
11 POCT
- 12 2. Prevalence of reported COVID-19 cases: number of participants who self-report at
13 baseline that SARS-CoV-2 infection (symptomatic and asymptomatic) was detected / Total
14 number of participants responding to the baseline questionnaire
- 15 3. SARS-CoV-2 seroconversion rate: number of participants in whom presence of specific
16 SARS-CoV-2 IgM and/or IgG is detected by POCT at follow-up / Total number of
17 participants followed-up not sero-converted before (based on prior POCT results), monthly
18 during 12 months of follow-up.
- 19 4. Incidence of reported COVID-19: number of participants who self-report new SARS-CoV-2
20 infections (symptomatic and asymptomatic) at follow-up / Total number of participants not
21 yet infected before (based on prior self-reporting and POCT results) and responding to the
22 follow-up questionnaire, monthly during 12 months of follow-up.
- 23 5. SARS-CoV-2 antibodies longevity: number of participants in whom presence of specific
24 SARS-CoV-2 IgG is no longer detected by POCT at follow-up / Total number of
25 participants followed-up sero-converted before (based on prior POCT results), monthly
26 during 12 months of follow-up.
27
28

29
30 To assess determinants of SARS-CoV-2 seroprevalence and seroconversion in PHCPs,
31 among which the availability and use of different preventive measures against SARS-CoV-2
32 infection, univariable and multivariable regression analysis, considering the clustering of
33 participants at their practices, will be performed, e.g. generalised estimating equations.³³
34 Model calibration will be assessed using calibration plots and the Hosmer-Lemeshow
35 goodness-of-fit test.³⁴ Its discrimination will be estimated with the area under the receiving
36 operator characteristic (ROC) curve.
37

38 **Data Analysis Phase 3 validation POCT**

39
40 To validate the POCT in a primary care setting, we will estimate the following test
41 characteristics:
42

- 43 1. SARS-CoV-2 POCT sensitivity: number of participants testing positive on the SARS-CoV-
44 2 POCT / Total number of participants testing positive on the reference standard.
- 45 2. SARS-CoV-2 POCT specificity: number of participants testing negative on the SARS-CoV-
46 2 POCT / Total number of participants testing negative on the reference standard.
47
48

49 These estimates will be corrected for missing reference standard data by inverse probability
50 weighting to infer what the reference standard results might have been had the entire study
51 sample been verified.³⁰⁻³² To show which participants are missing a reference standard result
52 a flow chart will be provided (Figure 1).
53

54 **Vaccination**

55 The start of the vaccination of PHCPs during the study follow-up provided the opportunity to
56 monitor its progress (at regional level). Obviously, the PHCPs vaccination status was
57 considered when assessing the primary and secondary outcomes of this study.
58

59 **BIAS AND LIMITATIONS**

60

1
2
3 The study results will be based on a convenience sample. However the sample will cover a
4 large proportion of geographically well distributed PHCPs.
5

6 Selection bias is possibly because of the “late” start of the study: if all the most vulnerable
7 PHCPs have already been infected at the time of the start of this study, then the incidence
8 among the remaining PHCPs may be lower (because better immune system, more adherent
9 to personal protection guidelines etc...). Hence, as in the ongoing seroprevalence study, we
10 will explicitly ask for participation regardless of previous SARS-CoV-2 testing and test
11 results.
12

13 Insufficient sample size: due to the current heavy workload in Belgian primary care and time
14 constraints, it might be difficult to recruit PHCPs into this study. However, we will aim for a
15 security margin in the number of participants and have good experience in the ongoing
16 seroprevalence study.
17

18 Loss to follow-up or missing data will be possible, for example if a PHCP becomes sick in
19 between two data collection points without providing immediate samples and is isolated at
20 home, or if participant does not provide data at one point because of heavy workload etc. In
21 these cases, the PHCP will be invited to come back in the study and participate in the
22 following data collection time-point. However, in the current outbreak situation PHCPs are
23 supposedly highly interested in knowing their infection status and therefore in participating in
24 the study. Furthermore, their profession might make them more inclined to contribute to
25 medical research. Finally, the duration of follow-up being relatively short, drop out should be
26 minimized. All efforts will be made to maintain the motivation of participants to participate at
27 each time-point by: keeping them regularly updated of the results of the study, being
28 attentive to questions and concerns: keeping communication to a minimum (to avoid
29 overburdening them) and wherever possible communication with participants in their own
30 language.³⁵
31
32

33 Under- and overestimation of the presence of SARS-CoV-2 among this population due to
34 imperfect testing methods (imperfect sensitivity and specificity). However, this bias will be
35 minimized by using best available POCT.¹⁹
36
37

38 **PATIENT & PUBLIC INVOLVEMENT**

39 Patients or the public were not involved in the design, or conduct, or reporting, or
40 dissemination plans of our research. The research team however involved potential study
41 subjects, i.e. PHCPs.
42

43 **Ethics and dissemination**

44 Ethical approval has been granted by Ethics Committee of the University Hospital
45 Antwerp/University of Antwerp (Belgian registration number: 3002020000237). Anonymous
46 study results will be made accessible and available as soon as possible after each testing
47 point and at the end of the study to public health authorities involved in management of the
48 COVID-19 epidemic in Belgium. This will be done through a policy brief or press release.
49 Sciensano will coordinate the distribution of results. These results will also be published on a
50 dedicated, public webpage of the Sciensano COVID-19 dashboard.³⁶
51 The general population will also be informed of the results through press communications.
52 This will be done by the communication departments of the University of Antwerp and the
53 University of Liège, Sciensano and the other study partners.
54 Scientific peer-reviewed publications (possible short communication, regular paper) will be
55 prepared to add to the body of evidence and availability for the global scientific community
56 and public health decision makers.
57
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4 **Authors' contributions:**•The study concept and design was conceived by SC, NA,
5 BS and ED. SC, NA and BS will conduct registration and data collection. Analysis will
6 be performed by RB. NA prepared the first draft of the manuscript. All authors
7 provided edits and critiqued the manuscript for intellectual content.
8

9
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12

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Figures

Figure 1. Participant flow uploaded separately

For peer review only

Supplementary materials

Prevalence and incidence of antibodies against SARS-CoV-2 among primary healthcare providers in Belgium – consent & baseline questionnaire

uploaded separately

Prevalence and incidence of antibodies against SARS-CoV-2 among primary healthcare providers in Belgium – Follow-up questionnaire

uploaded separately

For peer review only

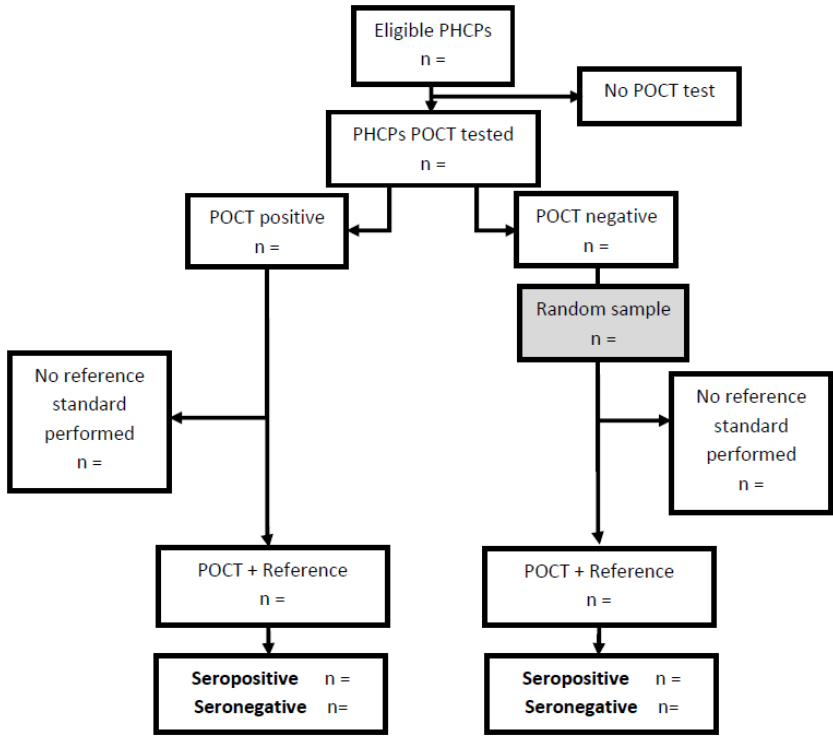


Figure 1: Participant flow
612x469mm (38 x 38 DPI)

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Prevalence and incidence of antibodies against SARS-CoV-2 among primary healthcare providers in Belgium – consent and baseline T2 questionnaire

Dear Participant,

Thank you for your registration for the CHARMING study. We have provided you with your personal study materials for the first three testing time points.

Here we first ask for your formal consent to the study. All questions in the consent section need to be answered before you can proceed. Next we ask for your results on the rapid test, and questions about your health, household, practice and views on the SARS-COV2 pandemic.

If you have questions about CHARMING, please email us at covid-dmg@uliege.be (<mailto:covid-dmg@uliege.be>).

Many thanks in advance for carefully completing this questionnaire. We hope this will go smoothly for you.

The CHARMING study team



There are 74 questions in this survey.

E - Consent

Before giving your consent it is important that you have reviewed the information document about this study available in French **here**

(<https://dox.uliege.be/index.php/s/n64T153cp07BOKG>) and in Dutch **here**

(<https://dox.uliege.be/index.php/s/OYp4cllx8oxERBt>).

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1 Your study code (C followed by 4 numbers; see our email of 25.01.2021 with your link to this questionnaire): *

Please write your answer here:

2
I have received an information sheet (version 2.2, 26-11-2020). All my questions concerning this study have been answered satisfactorily. I was given sufficient time to reflect before agreeing to participate in this study. *

Please choose **only one** of the following:

Yes

3
My participation is voluntary. I have the right to withdraw my consent at any time without giving a reason. *

Please choose **only one** of the following:

Yes

4
In order to meet the needs of this study, I consent to the collection and use of my data (including the result of the rapid test). *

Please choose **only one** of the following:

Yes

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5
I authorise the consultation of my data to the persons collaborating in this research (these persons are listed in the information form). *

Please choose **only one** of the following:

Yes

6
I agree that the data recorded in this study will be kept for 20 years and may be processed for future research on respiratory infections and coronaviruses. *

Please choose **only one** of the following:

Yes

7
I agree to provide a blood sample to validate the rapid test. *

Please choose **only one** of the following:

Yes

No

8
I agree to provide a blood sample to examine the T-cell response. ^[L]_[SEP] *

Please choose **only one** of the following:

Yes

No

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I agree that the blood samples taken in this study will be stored for 20 years and can be processed at a later date. *

Please choose **only one** of the following:

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After this study, I agree to be approached for further research. *

Please choose **only one** of the following:

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I wish to participate in this survey. *

Please choose **only one** of the following:

Yes

Results of the rapid test

12 *Date on which you carried out the rapid test (dd.mm.yyyy)? **

Please enter a date:

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Did the control line "C" change from blue to red?

If not, the test is invalid.

*

Please choose **only one** of the following:

Yes

No

14

Result of your quick test for IgG?

A red line visible next to G = positive (see figure).

*

Only answer this question if the following conditions are met:

Answer was 'Yes' at question '13 [Q00013]' (Did the control line "C" change from blue to red? If not, the test is invalid.)

Please choose **only one** of the following:

Positive

Negative

Unclear

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15 Result of your quick test for IgM?

A red line visible next to M = positive (see figure).

*

Only answer this question if the following conditions are met:

Answer was 'Yes' at question '13 [Q00013]' (Did the control line "C" change from blue to red? If not, the test is invalid.)

Please choose **only one** of the following:

- Positive
- Negative
- Unclear

16 Date on which you completed this questionnaire (dd.mm.yyyy)? *

Please enter a date:

17 How many sealed tests do you have left after this testing time point? *

❗ Choose one of the following answers

Please choose **only one** of the following:

- 0 sealed tests
- 1 sealed test
- 2 sealed tests
- 3 sealed tests
- 4 sealed tests
- 5 sealed tests

18

Do you smoke? *

❗ If you choose 'not for _____ years' please also specify your choice in the accompanying text field.

❗ Only numbers may be entered in 'not for _____ years' accompanying text field.

Please choose **only one** of the following:

- Yes
- I have stopped smoking
- I have never smoked

19 How many years ago did you stop smoking?

Only answer this question if the following conditions are met:

Answer was 'I have stopped smoking' at question '18 [Q00018]' (Do you smoke?)

Please write your answer here:

years

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How many alcoholic drinks do you consume per week? *

Please choose **only one** of the following:

- 0
- 1 - 5
- 6 - 10
- 11 - 15
- 16 - 20
- > 20

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21 Have you been vaccinated against pneumococcus? *

Please choose **only one** of the following:

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- Yes
 - No
 - I don't know

22 Have you been vaccinated against influenza for this winter season (2020-2021)?

*

Please choose **only one** of the following:

- Yes
- No
- I don't know yet

23 Have you been vaccinated against COVID-19? *

Please choose **only one** of the following:

- Yes
- No

24 Which vaccine did you receive? *

Only answer this question if the following conditions are met:

Answer was 'Yes' at question '23 [Q00023]' (Have you been vaccinated against COVID-19?)

Please choose **only one** of the following:

Pfizer/BioNTech

Moderna

Oxford/AstraZeneca

Other

25 How many doses have you received? *

Only answer this question if the following conditions are met:

Answer was 'Yes' at question '23 [Q00023]' (Have you been vaccinated against COVID-19?)

Please choose **only one** of the following:

1 dose

2 doses

26 When did you receive the first dose of the vaccine (dd.mm.yyyy)?

Only answer this question if the following conditions are met:

Answer was 'Yes' at question '23 [Q00023]' (Have you been vaccinated against COVID-19?)

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27

Do you have one or more chronic diseases? *

Please choose **only one** of the following: Yes No

28 What chronic disease(s) do you have? (multiple answers possible) *

Only answer this question if the following conditions are met:

Answer was 'Yes' at question '27 [Q00027]' (Do you have one or more chronic diseases?)

Please choose **all** that apply: Hypertension Diabetes Obesity Other

29 Please list other chronic diseases

Only answer this question if the following conditions are met:

Answer was at question '28 [Q00028]' (What chronic disease(s) do you have? (multiple answers possible))

Please write your answer here:

30 Do you take medicines for chronic diseases? *

Only answer this question if the following conditions are met:

Answer was 'Yes' at question '27 [Q00027]' (Do you have one or more chronic diseases?)

Please choose **only one** of the following:

- Yes
- No

31 If yes which ones? *

Only answer this question if the following conditions are met:

Answer was 'Yes' at question '30 [Q00030]' (Do you take medicines for chronic diseases?)

Please choose **all** that apply:

- ACE inhibitors
- Immunosuppressants
- Corticosteroids (also inhalation)
- NSAID
- Other

32 Other medicines for chronic disease

Only answer this question if the following conditions are met:

Answer was at question '31 [Q00031]' (If yes which ones?)

Please write your answer here:

33 Other medicines in the last six months

Only answer this question if the following conditions are met:

Answer was 'Yes' at question ' [Q00034]' (Have you taken medicines other than those for chronic diseases in the last six months?)

Please write your answer here:

34 Have you taken medicines other than those for chronic diseases in the last six months? *

Please choose **only one** of the following:

- Yes
- No

Your general practice

35 I work in general practice as... *

Please choose **only one** of the following:

- General practitioner
- General practitioner in training
- Other healthcare providers, e.g. nurse, dietician, ...

36 Which year of your training are you in?

Only answer this question if the following conditions are met:

Answer was 'General practitioner in training' at question '35 [Q00035]' (I work in general practice as...)

Please choose **only one** of the following:

- Year 1
- Year 2
- Year 3

37 Please select your profession *

Only answer this question if the following conditions are met:

Answer was 'Other healthcare providers, e.g. nurse, dietician, ...' at question '35 [Q00035]' (I work in general practice as...)

Please choose **only one** of the following:

- Nurse
- Psychologist
- Dietician
- Speech therapist
- Other

38 I have been doing this job for...

*

Please choose **only one** of the following:

- Less than 2 years
- 2 to 5 years
- 6 to 10 years
- More than 10 years

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39 I also work at... *

Please choose **all** that apply:

- As CRA (coordinating and advising doctor)
- In a hospital
- In an institution (e.g. psychiatry, care for the disabled, ...)
- I don't have any other activity
- Other:

40 Which other healthcare professionals work in your practice? (multiple answers possible) *

Please choose **all** that apply:

- General practitioner
- Dietician
- Psychologist
- Nurse
- Practice assistant
- None of the above
- Other:

41 What is the (estimated) number of patients assigned to your practice? *

Please write your answer here:

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42 What is the (estimated) proportion of patients younger than 15 years of age (%) ? *

● Your answer must be between 0 and 100

Please write your answer here:

%

43 What is the (estimated) proportion of patients over 65 years of age (%)? *

● Your answer must be between 0 and 100

Please write your answer here:

%

44 What is the estimated proportion of patients with increased benefits (%) ? *

● Your answer must be between 0 and 100

Please write your answer here:

%

45 What is the (estimated) proportion of patients with a migration background (%) ? *

Please write your answer here:

%

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46 What is the (estimated) proportion of patients who do not speak Dutch, French or German (%) ? *

Please write your answer here:

%

Your household

47 What is the composition of your household? *

ⓘ Each answer must be at least 0

Please write your answer(s) here:

How many family members does your household include, including yourself?

How many children attend a crèche (less than 2.5 years) ?

How many children attend pre-school (2,5 to 6 years)?

How many children attend primary school (typically 6 to 12 years)?

How many children attend secondary school (typically 12 - 18 years)?

How many household members are university/college students (typically aged over 18 years) AND sleeping in the family home more than 3 nights per week?

How many household members (typically over 18 years) in employment AND sleeping in the family home more than 3 nights per week?

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48 Is your partner employed in healthcare with patient contact? *

Please choose **only one** of the following:

- Yes
- No
- Not applicable

49 How many household members had complaints this year that are compatible with COVID-19, including yourself? *

Please write your answer here:

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50 If you had complaints, what were they? (multiple answers possible) *

Only answer this question if the following conditions are met:

Answer was greater than or equal to '1' at question '49 [Q00049]' (How many household members had complaints this year that are compatible with COVID-19, including yourself?)

Please choose **all** that apply:

I didn't have any complaints

Cough

Headache

Sore throat

Fever

Shortness of breath

Runny nose

Muscle pain

Loss of sense of smell

Loss of taste

General weakness/ fatigue

Nausea/ vomiting

Diarrhoea

Other:

51 How many members of your household, including yourself, have been tested for COVID-19 (excluding tests for research purposes)? *

Please write your answer here:

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52 How often have you been tested (except for the research purposes)? *

Please write your answer here:

times

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53 How many days have you spent in quarantine? *

Please choose **only one** of the following:

- 0 days
- up to 5 days
- up to 7 days
- up to 10 days
- up to 14 days
- up to 20 days
- more than 20 days

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54 Have you ever tested positive for COVID-19? *

Please choose **only one** of the following:

- Yes
- No

55 If you tested positive, when was the positive sample taken? *

Only answer this question if the following conditions are met:

Answer was 'Yes' at question '54 [Q00054]' (Have you ever tested positive for COVID-19?)

Please choose **only one** of the following:

- February
- March
- April
- May
- June
- July
- August
- September
- October
- November
- December
- January 2021

56 if you know the exact date of the positive sample enter it here:

Only answer this question if the following conditions are met:

Answer was 'Yes' at question '54 [Q00054]' (Have you ever tested positive for COVID-19?)

Please enter a date:

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57

For the positive test result which test(s) was/were used? (multiple answers possible) *

Only answer this question if the following conditions are met:

Answer was 'Yes' at question '54 [Q00054]' (Have you ever tested positive for COVID-19?)

Please choose **all** that apply:

- PCR (for virus detection)
- Rapid test (for virus detection)
- Blood sample (for antibody detection)
- Rapid test (for antibody detection)

Other:

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If you tested positive, who was the suspected source of the infection? *

Only answer this question if the following conditions are met:

Answer was 'Yes' at question '54 [Q00054]' (Have you ever tested positive for COVID-19?)

Please choose **all** that apply:

- Patient
- Co-worker
- Family member

Other:

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59 If you were treated for COVID-19, what treatment did you have? *

Only answer this question if the following conditions are met:

Answer was 'Yes' at question '54 [Q00054]' (Have you ever tested positive for COVID-19?)

Please choose **all** that apply:

Symptomatic treatment of pain, fever and other complaints

Hydroxychloroquine

Antibiotics

No treatment

Other:

60 If you were admitted for COVID-19, how many days did you spend in hospital?

(if you were not admitted to hospital put '0') *

Only answer this question if the following conditions are met:

Answer was 'Yes' at question '54 [Q00054]' (Have you ever tested positive for COVID-19?)

Please write your answer here:

days

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61

If you were admitted for COVID-19, how many days did you stay in intensive care? (if you were not admitted to intensive care put '0') *

Only answer this question if the following conditions are met:

Answer was 'Yes' at question '54 [Q00054]' (Have you ever tested positive for COVID-19?)

Please write your answer here:

days

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62 How many household members have tested positive for COVID-19, **not** including yourself? *

Please write your answer here:

63 How many household members have been admitted to hospital for (suspected) COVID-19, **not** including yourself? *

Please write your answer here:

64 How many household members have been treated for (suspected) COVID-19, **not** including yourself? *

Please write your answer here:

Risk factors for COVID-19

65 Have you continued to work since the outbreak? *

Please choose **only one** of the following:

- Yes
 No

66 Have you been in physical contact with patients with confirmed COVID-19 since the outbreak? *

Please choose **only one** of the following:

- Yes
 No

67 If so, how many? *

Only answer this question if the following conditions are met:

Answer was 'Yes' at question '66 [Q00066]' (Have you been in physical contact with patients with confirmed COVID-19 since the outbreak?)

Please choose **only one** of the following:

- 1 - 5 patients
 6 - 10 patients
 11 - 15 patients
 16 - 20 patients
 > 20 patients

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68 Have you lacked protective equipment since the outbreak? *

Please choose **only one** of the following:

Yes

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69 If so which equipment? (multiple answers possible) *

Only answer this question if the following conditions are met:

Answer was 'Yes' at question '68 [Q00068]' (Have you lacked protective equipment since the outbreak?)

Please choose **all** that apply:

Gloves

Surgical mouth mask

Other mouth mask (FFP2 or FFP3)

Safety goggles

Apron / body protection

Other:

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70 If available, which protective material do you use in patients with (suspected) COVID-19)? (multiple answers possible) *

Please choose **all** that apply:

Gloves

Surgical mouth mask

Other mouth mask (FFP2 or FFP3)

Safety goggles

Apron/body protection

Other:

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71
If available, what protective material do you use with your other patients? (multiple answers possible) *

Please choose **all** that apply:

- Gloves
- Surgical mouth mask
- Other mouth mask (FFP2 or FFP3)
- safety goggles
- Apron/body protection

Other:

72 Have you participated in the COVID patient triage? *

Please choose **only one** of the following:

- Yes
- No

73 If so, how many patients did you physically examine who subsequently turned out to be COVID-19 positive? *

Only answer this question if the following conditions are met:

Answer was 'Yes' at question '72 [Q00072]' (Have you participated in the COVID patient triage?)

Please choose **only one** of the following:

- 0 patients
- 1 - 5 patients
- 6 - 10 patients
- 11 - 15 patients
- 16 - 20 patients
- > 20 patients

74

Indicate to what extent you agree with the following statements

(1= totally disagree; 5= totally agree): *

Please choose the appropriate response for each item:

	1	2	3	4	5
The personal protection equipment that I use, protects me sufficiently against more contagious variants of SARS-CoV-2.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
A temporary ban on non-essential international travel is needed.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
I am sure I am already infected with COVID-19.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
I will certainly be infected with COVID-19 during this epidemic.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
I am afraid I am contaminating my relatives.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
The guidelines for primary care are clearly communicated.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
The guidelines for primary care are scientifically based.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
The Belgian healthcare system is strong enough to cope with this epidemic.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
The testing capacity in Belgium is sufficient.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Rapid diagnostic tests are relevant for general practice.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Rapid diagnostic tests for SARS-CoV-2 viral detection are manageable for general practice.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

	1	2	3	4	5
The measures imposed by the government are sufficient.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Everyone should wear a mask if they go outdoors.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
I have every confidence in the scientific COVID-19 expert committee.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Most of my patients follow the rules of 'social distancing'.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Most of my patients adhere to hygiene rules.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
La plupart de mes patients symptomatiques respectent les règles de quarantaine.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
This period is more stressful than during a busy flu period.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
I want to get the COVID-19 vaccination as soon as it is available.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Thank you very much for completing this questionnaire.

You will shortly receive an email that will explain what your test result means. We will send you an overview of your consent to participate in the study in the coming weeks.

The CHARMING study team



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Submit your survey.

Thank you for completing this survey.

Prevalence and incidence of antibodies against SARS-CoV-2 among primary healthcare providers in Belgium - Follow-up questionnaire February 2021

Dear Participant,

Thank you for your participation in CHARMING. This follow-up questionnaire refers to the period since the last testing period.

Many thanks in advance for carefully completing this questionnaire. We hope this will go smoothly for you.

The CHARMING study team

PS If you have questions about CHARMING, please email us at covid-dmg@uliege.be (mailto:covid-dmg@uliege.be).



There are 46 questions in this survey.

Part 1

1 Your personal study code (C followed by 4 numbers; see our email of 26.02.2021 with your link to this questionnaire): *

Please write your answer here:

Part 2

For peer review only - <http://bmjopen.bmj.com/site/about/guidelines.xhtml>

Instructions on how to perform the rapid test can be found in French **here**

(<https://dox.uliege.be/index.php/s/1duglah08HN8Ylr>) and in Dutch **here**

(<https://dox.uliege.be/index.php/s/hqqiswSGBxKw3yf>). Short instruction videos are available here:

- French test on yourself : <https://vimeo.com/492411023/7b2bedb700>

(<https://vimeo.com/492411023/7b2bedb700>)

- French test on someone else: <https://vimeo.com/492427669/b42bb624b6>

(<https://vimeo.com/492427669/b42bb624b6>)

- Dutch test on yourself: <https://vimeo.com/492430777/92626224d1>

(<https://vimeo.com/492430777/92626224d1>)

- Dutch test on someone else : <https://vimeo.com/492428827/d565f20bc2>

(<https://vimeo.com/492428827/d565f20bc2>)

2 *Date on which you carried out the rapid test (dd.mm.yyyy)? **

Please enter a date:

3
Did the control line "C" change from blue to red?
If not, the test is invalid.

*

Please choose **only one** of the following:

Yes

No

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4 Result of your quick test for IgG?

A red line visible next to G = positive (see figure).

*

Please choose **only one** of the following:

- Positive
 Negative
 Unclear

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5 Result of your quick test for IgM?

A red line visible next to M = positive (see figure).

*

Please choose **only one** of the following:

- Positive
 Negative
 Unclear

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6 Date on which you completed this questionnaire (dd.mm.yyyy)? *

Please enter a date:

7 How many sealed tests do you have left after this testing time point? *

Please choose **only one** of the following:

- 0 sealed tests
- 1 sealed test
- 2 sealed tests
- 3 sealed tests
- 4 sealed tests
- 5 sealed tests

Part 3

8 Since **your first** testing period (end December 2020 or end January 2021), how many days have you spent in quarantine? *

Please choose **only one** of the following:

- 0 days
- up to 5 days
- up to 7 days
- up to 10 days
- up to 14 days
- up to 20 days
- more than 20 days

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9 Since **your first** testing period (end December 2020 or end January 2021), how often have you been tested for COVID-19 (except for research purposes)? *

Please write your answer here:

times

10 I work in general practice as... *

Please choose **only one** of the following:

- General practitioner
- General practitioner in training
- Other healthcare providers, e.g. nurse, dietician, ...

11 Please select your profession *

Please choose **only one** of the following:

- Nurse
- Psychologist
- Dietician
- Speech therapist

Other

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12 Since the **last** testing period I have also worked... *

Please choose **all** that apply:

- As CRA (coordinating and advising doctor)
- In a hospital
- In an institution (e.g. psychiatry, care for the disabled, ...)
- I don't have any other activity
- Other:

Part 4

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13 Since the last testing phase of CHARMING how many family members had complaints that are compatible with COVID-19, including yourself? *

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14 If you had complaints, since the last testing period, what were they? (multiple answers possible) *

Please choose **all** that apply:

I didn't have any complaints

Cough

Headache

Sore throat

Fever

Shortness of breath

Runny nose

Muscle pain

Loss of sense of smell

Loss of taste

General weakness/ fatigue

Nausea/ vomiting

Diarrhoea

Other:

15 Since the last testing period how many family members, including yourself, have been tested for COVID-19 (excluding tests for research purposes)? *

Please write your answer here:

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16 Have you tested positive for COVID-19 since the last testing period? (multiple answers possible) *

Please choose **only one** of the following:

Yes

No

17 For the positive test result which test(s) was/were used? (multiple answers possible) *

Please choose **all** that apply:

PCR (for virus detection)

Rapid test (for virus detection)

Blood sample (for antibody detection)

Rapid test (for antibody detection)

Other:

18 If you tested positive when was the positive sample taken (dd.mm.yyyy)?

Please enter a date:

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19 If you were treated for COVID-19, what treatment did you have? *

Please choose **all** that apply:

Symptomatic treatment of pain, fever and other complaints

Hydroxychloroquine

Antibiotics

No treatment

Other:

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20 If you tested positive, who was the suspected source of the infection? *

Please choose **all** that apply:

Patient

Co-worker

Family member

Other:

21 If you were admitted for COVID-19, how many days did you spend in hospital?

(if you were not admitted to hospital put '0') *

Please write your answer here:

days

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If you were admitted for COVID-19, how many days did you stay in intensive care? (if you were not admitted to intensive care put '0') *

Please write your answer here:

days

23 Since the last testing period how many family members have tested positive for COVID-19, **not** including yourself? *

Please write your answer here:

24 Since the last testing period how many family members have been admitted to hospital for (suspected) COVID-19, **not** including yourself? *

Please write your answer here:

25 Since the last testing period how many family members have been treated for (suspected) COVID-19, **not** including yourself? *

Please write your answer here:

Part 5

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26 Have you continued to work in primary care since the last testing period? *

Please choose **only one** of the following:

- Yes
- No

27 Have you been in physical contact with patients with confirmed COVID-19 since the last testing period? *

Please choose **only one** of the following:

- Yes
- No

28 If so, how many? *

Please choose **only one** of the following:

- 1 - 5 patients
- 6 - 10 patients
- 11 - 15 patients
- 16 - 20 patients
- > 20 patients

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29 Have you lacked protective equipment since the **last** testing period? *

Please choose **only one** of the following:

Yes

No

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30 If so which equipment? (multiple answers possible) *

Please choose **all** that apply:

Gloves

Surgical mouth mask

Other mouth mask (FFP2 or FFP3)

Safety goggles

Apron / body protection

Other:

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31 If available, which protective material have you used since the last testing period in patients with (suspected) COVID-19)? (multiple answers possible) *

Please choose **all** that apply:

Gloves

Surgical mouth mask

Other mouth mask (FFP2 or FFP3)

Safety goggles

Apron/body protection

Other:

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If available, what protective material have you used with your other patients? (multiple answers possible) *

Please choose **all** that apply:

- Gloves
- Surgical mouth mask
- Other mouth mask (FFP2 or FFP3)
- safety goggles
- Apron/body protection

Other:

33 Have you participated in the COVID patient triage since the last testing period? *

Please choose **only one** of the following:

- Yes
- No

34 If so, how many patients did you physically examine who subsequently turned out to be COVID-19 positive? *

Please choose **only one** of the following:

- 0 patients
- 1 - 5 patients
- 6 - 10 patients
- 11 - 15 patients
- 16 - 20 patients
- > 20 patients

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35 Have you been vaccinated against COVID-19? *

Please choose **only one** of the following:

Yes

No

36 Which vaccine did you receive? *

Please choose **only one** of the following:

Pfizer/BioNTech

Moderna

Oxford/AstraZeneca

Other

37 How many doses have you received? *

Please choose **only one** of the following:

1 dose

2 doses

38 When did you receive the **first** dose of the vaccine (dd.mm.yyyy)? *

Please enter a date:

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39 Did you experience side-effects after receiving the **first** dose? *

Please choose **only one** of the following:

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- No side-effects
 - Negligible side-effects
 - Mild side-effects
 - Moderate side-effects
 - Severe side-effects

40 For how many days did you experience the following side-effects after the **first** dose (if you did not experience the side-effect put '0'): *

41 What other moderate or severe side-effects did you experience after receiving the **first** dose?

Please write your answer here:

42 When did you receive the **second** dose of the vaccine (dd.mm.yyyy)? *

Please enter a date:

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43 Did you experience side-effects after receiving the **second** dose? *

Please choose **only one** of the following:

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- No side-effects
 - Negligible side-effects
 - Mild side-effects
 - Moderate side-effects
 - Severe side-effects

44 For how many days after receiving the **second** dose of the vaccine did you experience the following side-effects (if you did not experience the side-effect put '0')? *

45 What other moderate or severe side-effects did you experience after receiving the **second** dose?

Please write your answer here:

46

Indicate to what extent you agree with the following statements

(1= totally disagree; 5= totally agree): *

Please choose the appropriate response for each item:

	1	2	3	4	5
The personal protection equipment that I use, protects me sufficiently against more contagious variants of SARS-CoV-2.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
A temporary ban on non-essential international travel is still needed.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
The Belgian healthcare system is strong enough to cope with this epidemic.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
The testing capacity in Belgium is sufficient.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Rapid diagnostic tests are relevant for general practice.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Rapid diagnostic tests for SARS-CoV-2 viral detection are manageable for general practice.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
The measures imposed by the government are sufficient.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Everyone should wear a mask when they work inside with other people.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
I have every confidence in the scientific COVID-19 expert committee.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Most of my patients follow the rules of 'social distancing'.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Most of my patients adhere to hygiene rules.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

	1	2	3	4	5
Most of my symptomatic patients respect the quarantine rules.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
This period is more stressful than during a busy flu period.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
For health care personnel the COVID-19 vaccination should be obligatory.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Thank you very much for completing this questionnaire.

You will shortly receive an email that will explain what your test result means.

If you experience side-effects after receiving the vaccination you can report them officially here:

In Dutch: <https://www.fagg.be/nl/bijwerking> (<https://www.fagg.be/nl/bijwerking>)

In French: https://www.afmps.be/fr/effet_indesirable (https://www.afmps.be/fr/effet_indesirable)

The CHARMING study team



21.03.2021 – 20:58

Submit your survey.

Thank you for completing this survey.

BMJ Open

PREVALENCE AND INCIDENCE OF ANTIBODIES AGAINST SARS-COV-2 AMONG PRIMARY HEALTHCARE PROVIDERS IN BELGIUM DURING ONE YEAR OF THE COVID-19 EPIDEMIC: PROSPECTIVE COHORT STUDY PROTOCOL

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PREVALENCE AND INCIDENCE OF ANTIBODIES AGAINST SARS-COV-2 AMONG PRIMARY HEALTHCARE PROVIDERS IN BELGIUM DURING ONE YEAR OF THE COVID-19 EPIDEMIC: PROSPECTIVE COHORT STUDY PROTOCOL

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ABSTRACT

Introduction

National severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) seroprevalence data provides essential information about population exposure to the virus and helps predict the future course of the epidemic. Early cohort studies have suggested declines in levels of antibodies in individuals, associated with, for example, illness severity, age and co-morbidities. This protocol focuses on the seroprevalence among primary health care providers (PHCPs) in Belgium. PHCPs manage the vast majority of (COVID-19) patients and therefore play an essential role in the efficient organisation of health care. Currently, evidence is lacking on 1. how many PHCPs get infected with SARS-CoV-2 in Belgium, 2. the rate at which this happens, 3. their clinical spectrum, 4. their risk factors, 5. the effectiveness of the measures to prevent infection and 6. the accuracy of the serology-based point-of-care test in a primary care setting.

Methods and analysis

This study will be set up as a prospective cohort study. General practitioners (GPs) and other PHCPs (working in a GP practice) will be recruited via professional networks and professional media outlets to register online to participate. Registered GPs and other PHCPs will be asked at each testing point (n=9) to perform a capillary blood sample antibody point-of-care test targeting IgM and IgG against the receptor binding domain of SARS-CoV-2 and complete an online questionnaire. The primary outcomes are the prevalence and incidence of antibodies against SARS-CoV-2 in PHCPs during a 12-month follow-up period. Secondary outcomes include the longevity of antibodies against SARS-CoV-2.

Ethics and dissemination:

Ethical approval has been granted by the Ethics Committee of the University Hospital Antwerp/University of Antwerp (Belgian registration number: 3002020000237). Alongside journal publications, dissemination activities include the publication of monthly reports to be shared with the participants and the general population through the publicly available website of the Belgian health authorities (Sciensano).

Registration:

Trial registration number: NCT04779424

Key words: cohort study; primary care; SARS-CoV-2; COVID-19; prevalence; incidence; antibodies; seroprevalence

Article summary

Strengths and limitations of this study

- This large cohort study can provide precise estimates of the prevalence and incidence of antibodies against SARS-CoV-2 among primary health care providers (PHCPs) at national level.
- This study uses a serology-based point-of-care test (POCT) validated in a laboratory setting and validates this POCT in a primary care setting.
- The POCT used targets IgM and IgG against the receptor binding domain of SARS-CoV-2 and can therefore also provide valuable information in a vaccinated population.
- Regular online data collection provides timely data that can be compared to that of the general population and other population groups, e.g. health care workers in hospitals and nursing homes.
- Missing data points, reduced POCT accuracy and the use of a convenience sample could limit the validity of the study results.

Introduction

As of 16th May 2021, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has infected over 162 million people worldwide (over 1 030 000 in Belgium) and caused over 3.3 million deaths from coronavirus disease (COVID-19) worldwide (over 24 000 in Belgium).¹ COVID-19 is a lethal respiratory tract infection (RTI), but infection with SARS-CoV-2 can also be mild and even asymptomatic.

SARS-CoV-2 seroprevalence estimates provide essential information about population exposure to infection and help predict the future course of the epidemic.^{2,3} When setting up this study seroprevalence studies in Iceland⁴ and Spain⁵ showed different levels of population antibody positivity, lasting up to at least 4 months in Iceland. In addition, early cohort studies have suggested waning of antibody levels in individuals, associated with for example illness severity, age and co-morbidities.⁶⁻⁸ Meanwhile, other seroprevalence studies showed antibody positivity lasting up to 9 months.^{9,10} For Belgium, Sciensano (the Belgian national scientific institute, www.sciensano.be) performs national seroprevalence studies of SARS-CoV-2 antibodies in several relevant populations including schools,¹¹ hospital personnel¹² and nursing homes¹³.

This protocol focuses on the seroprevalence among primary health care providers (PHCPs). They manage the vast majority of COVID-19 and other patients and therefore play an essential role in the efficient organisation of healthcare.^{14,15} Among the PHCPs, general practitioners (GPs) in particular, act as gatekeepers to the next levels of care. Therefore, preserving the capacity of GPs, together with that of their co-workers, throughout the COVID-19 epidemic is essential.¹⁶ In Belgium, this is particularly concerning given the GP workforce consists of mainly older adults and is therefore at higher risk for COVID-19-related morbidity and mortality.¹⁷ In Italy GPs represented up to 38% of the physicians who died from COVID-19 early on in the epidemic.¹⁸

However, current evidence is lacking on 1. how many PHCPs are infected by SARS-CoV-2 or have COVID-19 in Belgium, 2. the rate at which this occurs, 3. their clinical spectrum, 4. their risk factors, 5. the effectiveness of the measures to prevent this from happening and 6. the accuracy of the immunological serology-based point-of-care test (POCT) used by PHCPs.

During the COVID-19 crisis POCTs have been developed to identify the presence of antibodies for SARS-CoV-2. Compared to laboratory tests, a valid easy-to-use POCT will speed up the availability of the test results for both the participants and the national health authorities. Furthermore, by using POCTs in this study, PHCPs will have the opportunity to become more familiar with this type of technology.

Sciensano has validated five POCTs using finger prick blood, identifying one test with appropriate sensitivity (92.9%) and specificity (96.3%) for use in seroprevalence studies.¹⁹ We use this POCT for the present study. It targets IgM and IgG against the receptor binding domain (RBD) of SARS-CoV-2 and can therefore also provide valuable information in a vaccinated population.

If (Belgian) primary care cannot be delivered safely, the COVID-19 epidemic will disrupt public health by failing to deliver non-COVID-19 related healthcare and will be unable to (continue to) support the next levels of care during the current epidemic. Therefore, we need to monitor their health and the effectiveness of, and the need for, infection prevention and control measures during epidemics. In addition, the follow-up of a cohort of PHCPs will help us to understand the duration and nature of antibodies generated in response to SARS-CoV-2 infection as well as those generated in response to vaccination.²⁰ Whether and for how long

antibody response protects those infected with SARS-CoV-2 from future infections or illness will determine the value of serological tests.²¹

Primary objectives

1. Assess the prevalence of antibodies against SARS-CoV-2 among PHCPs (PHCPs = GPs and other PHCPs in their practice) in Belgium at timepoint 1 and at different timepoints during a 12-month follow-up period.
2. Assess the monthly and annual incidence of antibodies against SARS-CoV-2 among PHCPs in Belgium during a 12-month follow-up period

Secondary objectives

1. Assess the longevity of the serological antibody response among seropositive PHCPs.
2. Assess the proportion of asymptomatic cases among (new) cases (that develop during follow-up).
3. Assess the determinants (risk and predictive factors) of SARS-CoV-2 infection in PHCPs.
4. Validate the serology-based POCT in a primary care setting (Phase 3 validation).
5. Familiarise PHCPs with the use of serology-based point-of-care tests.

Once vaccination of PCHPs starts, this study will take into account vaccination rates when reporting the seroprevalence and be able to assess waning of antibodies after vaccination.

Methods and analysis

The aim of this study is to broaden the knowledge on SARS-CoV-2 infection in Belgian primary care and to contribute to scientific research, health service and policy management supporting the fight against this epidemic.

STUDY POPULATION

Inclusion Criteria:

- Any GP working in Belgium (including those in professional training) currently working in primary care and any PHCP from the same GP practice who physically manages (examines, tests, treats) patients,
- Participants must be able to comply with the study protocol and provide informed consent to participate in the study.

Exclusion Criteria:

- Staff hired on a temporary (interim) basis will be excluded as follow-up over time will be compromised.
- Administrative staff or technical staff without any prolonged (longer than 15 minutes) face to face contact with patients are not eligible.
- PHCPs who were not professionally active during the inclusion period will not be eligible

STUDY DESIGN

This study will be set up as a prospective cohort study.

Recruitment

PHCPs will be recruited prior to the first and second testing points (registration will be possible between 15 November 2020 and 15 January 2021). PHCPs working in clinical practice in Belgium will be invited to register online for participation in this national epidemiological study and will be asked to invite the other PHCPs in their practice to do the same. We will emphasize that PHCPs that have already been diagnosed with COVID-19 are also eligible. Information about the study will be disseminated to GPs and PHCPs via professional organisations (Domus Medica and College de Médecine Générale), university networks across the country and through professional media channels. The convenience

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2
3 sample of participants will be checked to ensure that it is representative in terms of
4 geographic and demographic qualities.²²
5

6 **Data Collection**

7 Upon inclusion in the study, participants will be assigned a unique study code by the
8 researchers, who will manage the key between these codes and the identification data. They
9 will receive testing material at their place of work through regular mail. At the first testing
10 time-point (T1) they will receive an invitation by email (including a personalised link to an
11 online questionnaire in French and Dutch) inviting them to:

- 12 1. Auto-collect a capillary blood sample and analyse it using the POCT (OrientGene®).
- 13 2. Complete a baseline questionnaire through a secured online platform hosted by
14 Sciensano (Limesurvey).
15

16
17 The baseline questionnaire at the first testing point will ask for their informed consent and will
18 ask for information about;

- 19 - The result of the POCT,
- 20 - basic socio-demographic data, (age, gender, composition of household – e.g. presence of
21 school-aged children in the house)
- 22 - professional data, (practice patient size)
- 23 - health status, (pre-existing health conditions, regular medication use, presence of
24 symptoms since the start of the epidemic, previous positive test results for COVID-19)
- 25 - Professional exposure, (contact with confirmed cases, use of infection prevention and
26 control measures and
- 27 - the availability of personal protective equipment (practice organisational aspects, delayed
28 care for non-urgent conditions) (see supplementary materials).
29

30
31 A follow-up questionnaire will be sent for each of the subsequent testing timepoints. In
32 addition to the POCT result, it will collect information on:

- 33 - the health status, including the presence of symptoms,
- 34 - vaccination status (date of vaccination, type of vaccine, number of doses, presence of
35 side-effects)
- 36 - professional exposure, (contact with confirmed cases, use of infection prevention and
37 control measures (see supplementary materials).
38

39 **Phase 3 validation of the POCT**

40 To validate the POCT, a sub-sample of participants will be asked to provide a serum sample.
41 This sub-sample will be made up of all those participants that were seropositive for SARS-
42 Cov-2 on the POCT at T1 and a random sample of participants that were seronegative at T1.
43

44
45 The participants will be sent material to collect the blood sample (Becton Dickinson
46 Vacutainer® SSTTM ii Advance; ref 368879) along with postal materials (in accordance with
47 the UN 3373 packaging norms) and instructions on how to send it to the laboratory of clinical
48 biology of the University Hospital of Antwerp (UZA) (a reference laboratory chosen by
49 Sciensano). Participants will be asked to send their blood sample the same day it is taken,
50 and analysis will be undertaken within 24 hours of reception. Analysis will be done with a
51 reference standard using the following testing algorithm: serum samples will be tested first on
52 the ELECSYS Anti-SARS-CoV-2 S assay (Roche, Basel, Switzerland), if the cut-off index
53 (COI) is between 0.6-3.0 the sample will be tested on the ATELLICA IM SARS-CoV-2 assay
54 (Siemens, Munich, Germany), and in case of discordant results it will be tested on the
55 LIAISON SARS-CoV-2 S1/S2 IgG assay (DiaSorin, Saluggia, Italy), using a two out of three
56 'reference standard'. The analytical and clinical performance of these three commercially
57 available, fully automated SARS-CoV-2 antibody assays was investigated at University
58 hospital of Antwerp (UZA) and the relevance of this testing algorithm explained and
59
60

illustrated (personal communication Bart Peeters). Analytical performance of all three assays was acceptable and comparable with results found in other studies.²³⁻²⁶

Participants of this sub-sample will receive a 25€ voucher by way of compensation for the time and effort invested. The results of the serum sample will be communicated to participants via regular postal services.

Follow-up

The study will last 12 months. Epidemiological data collected through the online questionnaires and self-sampling using the POCT will occur monthly for six months with one sample collection at nine and the final one at 12 months (Table 1). This corresponds to a total of nine testing timepoints. This number will however depend on the evolution of the epidemic. At each testing time-point, participants will be asked to perform the POCT within a timeframe of maximum 5 days. For the sub-sample providing a serum sample, participants will be asked to take the serum sample at the same time (just prior) to performing the POCT.

The result of the POCT will be entered as a variable in the online questionnaire. Data analysis will be performed and reported after each relevant testing period and at the end of the study. All pseudonymised data collected will be stored securely by Sciensano for 10 years after completion of the study.

Table 1. Timing of data collection

	T1	T2	T3	T4	T5	T6	T7	T8	T9	Total
	M0	M1	M2	M3	M4	M5	M6	M9	M12	9
POCT	X	X	X	X	X	X	X	X	X	9
Baseline Q	X									1
Follow-up Q		X	X	X	X	X	X	X	X	8
Serum		X								1

T: testing point, M: month, Q: questionnaire

SAMPLE SIZE

This study aims to include 5000 PHCPs with a 4 GPs to 1 other PHCP ratio considering the following sample size considerations regarding the different objectives of the proposed study.

To estimate a prevalence ranging from 5% to 10%, the current estimates for SARS-CoV-2 seroprevalence in the general population and hospital care providers, with a precision ranging from 2% to 1% and a 95% confidence level, a sample size ranging from 504 to 3554 PHCPs is required (Binomial 'exact' calculation), respectively. Since PHCPs will be clustered in their practices, we must correct the sample size. For an average of 2.5 PHCPs per practice (m) and an intraclass correlation of 0.2 (ρ) the design effect ($=1+(m-1)*\rho$) is 1.3. The corrected sample size ranges from 655 to 4620 PHCPs. Higher seroprevalence and non-response, both of which are to be expected, will reduce the precision of the estimates as will stratification by region or province. For example, with a sample size of 4620 PHCPs distributed equally over eleven strata, which corresponds to the number of provinces in

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3 Belgium (n=10) plus Brussels, the precision will range between 2.5% and 3.5% for a
4 prevalence ranging from 5% to 10%, respectively.
5

6 Since multivariate prediction research for each determinant studied requires at least 10
7 subjects in the smallest category of the outcome variable to allow proper statistical
8 modelling,^{27 28} a model including 25 determinants would require 250 seropositive participants,
9 which corresponds to a 5% seroprevalence in 5000 or a 10% seroprevalence in 2500
10 PHCPs, not taking into account interaction terms in the model. The number of determinants
11 that can be assessed in multivariable analysis to predict new cases will depend on the
12 incidence. For example, to be able to assess 10 determinants would require 100 new cases
13 or 3% new cases in 3600 PHCPs or 4700 PHCPs considering a design effect of 1.3. A lower
14 incidence or lower sample size would further limit the number of determinants that can be
15 modelled. Using more recently described methods to calculate the sample size required for
16 developing a clinical prediction model would also require a sample size of substantially more
17 than 2000 participants (n=2283, with 228 events and 9.1 events per predictor) to meet the 4
18 criteria described by Riley RD et al. in case of a Mean Average Prediction Error (MAPE) of
19 0.025.²⁹
20

21 To estimate an incidence of 3% with a precision of 1% and a 95% confidence level, a sample
22 size of 1212 PHCPs is required or 1576 PHCPs considering a design effect of 1.3 (4160
23 PHCPs to estimate an incidence of 2% with a precision of 0.5% and considering clustering).
24 To be able to validate the POCT's accuracy in the primary care setting, i.e. estimate the
25 POCT's sensitivity (92.9%) with a lower limit of its 95%CI of 90% and its specificity (96.3%)
26 with a lower limit of its 95%CI of 95%, a sample of 301 PHCPs seropositive on the reference
27 standard (for sensitivity) and 810 PHCPs seronegative on the reference standard (for
28 specificity) is required, which corresponds to for example 6% seroprevalence in 5022
29 PHCPs. To reduce the burden on the participants and the costs of the study all those with a
30 positive POCT and only a (random) sample of 900 PHCPs with a negative POCT will be
31 assessed with the reference standard, and inverse probability weighting will be applied to
32 correct for missing reference standard data by design.³⁰⁻³²
33

34 A sample size of 5000 would also allow us to estimate the longevity of the antibody response
35 among the PHCPs seropositive on the POCT. For example, starting from 300 PHCPs
36 seropositive based on the POCT, a decrease of 10% in seroprevalence can be estimated
37 with a precision of 4% and a 95% confidence level. Smaller decreases in seroprevalence
38 and/or estimating with lower precision would require less than 5000 PHCPs to identify
39 sufficient PHCPs seropositive on the POCT. Clustering will most likely not be an issue here
40 since the waning of antibodies will most likely not be correlated among PHCPs working in the
41 same practice.
42
43

44 **DATA PROTECTION**

45 As described above, epidemiological and serological data will be linked via a unique identifier
46 code assigned to each participant. The same unique identifier code will be entered in each
47 questionnaire, enabling the link for data analysis. This code will remain the same throughout
48 the study. The key between the codes and the identification data of the participants will be
49 kept in a secure and protected way by the principal investigators and the researchers, and
50 destroyed upon completion of the study. The personal data processing activities for the
51 proposed research project will be submitted to the UAntwerpen Data Protection Office to
52 review its completeness and compliance with the General Data Protection Regulation
53 (GDPR) and to ask for formal approval. To control digital access only by authorized people
54 on all devices (desktops, laptops, external drives, ...) at all locations (work, home, and
55 travel), complex passwords are used, up-to-date anti-virus and firewall protection is run.
56 Using the ICT services of UAntwerp, ULiège and Sciensano assures that the data will be
57 backed up on a regular basis. The research team ensures that their personal computer
58 system is always up-to-date, and does not switch off the automatic installation of updates.
59
60

DATA ANALYSIS

Data analysis will be done jointly by the principal investigators, researchers and team involved in this study with the University of Antwerp team taking the lead. Questionnaire responses will be coded. Data will be cleaned and validated; incomplete questionnaires will be manually checked to see if they can be included. Analysis will be mainly descriptive and done on R version 3.6.3 or equivalent.

Among others, the following indicators will be calculated, considering clustering of PHCPs in the same practice whenever appropriate:

1. Seroprevalence of SARS-CoV-2: number of participants in whom presence of specific SARS-CoV-2 IgG is detected by the POCT / Total number of participants tested with the POCT
2. Prevalence of reported COVID-19 cases: number of participants who self-report at baseline that SARS-CoV-2 infection (symptomatic and asymptomatic) was detected / Total number of participants responding to the baseline questionnaire
3. SARS-CoV-2 seroconversion rate: number of participants in whom presence of specific SARS-CoV-2 IgM and/or IgG is detected by POCT at follow-up / Total number of participants followed-up not sero-converted before (based on prior POCT results), monthly during 12 months of follow-up.
4. Incidence of reported COVID-19: number of participants who self-report new SARS-CoV-2 infections (symptomatic and asymptomatic) at follow-up / Total number of participants not yet infected before (based on prior self-reporting and POCT results) and responding to the follow-up questionnaire, monthly during 12 months of follow-up.
5. SARS-CoV-2 antibodies longevity: number of participants in whom presence of specific SARS-CoV-2 IgG is no longer detected by POCT at follow-up / Total number of participants followed-up sero-converted before (based on prior POCT results), monthly during 12 months of follow-up.

To assess determinants of SARS-CoV-2 seroprevalence and seroconversion in PHCPs, among which the availability and use of different preventive measures against SARS-CoV-2 infection, univariable and multivariable regression analysis, considering the clustering of participants at their practices, will be performed, e.g. generalised estimating equations.³³ Model calibration will be assessed using calibration plots and the Hosmer-Lemeshow goodness-of-fit test.³⁴ Its discrimination will be estimated with the area under the receiving operator characteristic (ROC) curve.

Data Analysis Phase 3 validation POCT

To validate the POCT in a primary care setting, we will estimate the following test characteristics:

1. SARS-CoV-2 POCT sensitivity: number of participants testing positive on the SARS-CoV-2 POCT / Total number of participants testing positive on the reference standard.
2. SARS-CoV-2 POCT specificity: number of participants testing negative on the SARS-CoV-2 POCT / Total number of participants testing negative on the reference standard.

These estimates will be corrected for missing reference standard data by inverse probability weighting to infer what the reference standard results might have been had the entire study sample been verified.³⁰⁻³² To show which participants are missing a reference standard result a flow chart will be provided (Figure 1).

Vaccination

1
2
3 The start of the vaccination of PHCPs during the study follow-up provided the opportunity to
4 monitor its progress (at regional level). Obviously, the PHCPs vaccination status was
5 considered when assessing the primary and secondary outcomes of this study.
6

7 **BIAS AND LIMITATIONS**

8 The study results will be based on a convenience sample. However the sample will cover a
9 large proportion of geographically well distributed PHCPs.
10

11 Selection bias is possibly because of the “late” start of the study: if all the most vulnerable
12 PHCPs have already been infected at the time of the start of this study, then the incidence
13 among the remaining PHCPs may be lower (because better immune system, more adherent
14 to personal protection guidelines etc...). Hence, as in the ongoing seroprevalence study, we
15 will explicitly ask for participation regardless of previous SARS-CoV-2 testing and test
16 results.
17

18
19 Insufficient sample size: due to the current heavy workload in Belgian primary care and time
20 constraints, it might be difficult to recruit PHCPs into this study. However, we will aim for a
21 security margin in the number of participants and have good experience in the ongoing
22 seroprevalence study.
23

24 Loss to follow-up or missing data will be possible, for example if a participant becomes sick
25 in between two data collection points without providing immediate samples and is isolated at
26 home, or if a participant does not provide data at one point because of heavy workload etc.
27 In these cases, the participant will be invited to come back in the study and participate in the
28 following data collection time-point. However, in the current outbreak situation PHCPs are
29 supposedly very interested in knowing their infection status and therefore in participating in
30 the study. Furthermore, their profession might make them more inclined to contribute to
31 medical research. Finally, the duration of follow-up being relatively short, drop out should be
32 minimized. All efforts will be made to maintain the motivation of participants to participate at
33 each time-point by: keeping them regularly updated of the results of the study, being
34 attentive to questions and concerns: keeping communication to a minimum (to avoid
35 overburdening them) and wherever possible communication with participants in their own
36 language.³⁵
37

38
39 Under- and overestimation of the presence of SARS-CoV-2 among this population due to
40 imperfect testing methods (imperfect sensitivity and specificity). However, this bias will be
41 minimized by using best available POCT.¹⁹
42

43 **PATIENT & PUBLIC INVOLVEMENT**

44 Patients or the public were not involved in the design, or conduct, or reporting, or
45 dissemination plans of our research. The research team however involved potential study
46 subjects, i.e. PHCPs.
47

48 **Ethics and dissemination**

49 Ethical approval has been granted by Ethics Committee of the University Hospital
50 Antwerp/University of Antwerp (Belgian registration number: 3002020000237). Anonymous
51 study results will be made accessible and available as soon as possible after each testing
52 point and at the end of the study to public health authorities involved in management of the
53 COVID-19 epidemic in Belgium. This will be done through a policy brief or press release.
54 Sciensano will coordinate the distribution of results. These results will also be published on a
55 dedicated, public webpage of the Sciensano COVID-19 dashboard.³⁶
56

57 The general population will also be informed of the results through press communications.
58 This will be done by the communication departments of the University of Antwerp and the
59 University of Liège, Sciensano and the other study partners.
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3 Scientific peer-reviewed publications (possible short communication, regular paper) will be
4 prepared to add to the body of evidence and availability for the global scientific community
5 and public health decision makers.
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4 **Authors' contributions:** The study concept and design was initiated by SC, NA, BS
5 and ED and finalized with contributions from JV, ADS, SH, AVdB, ID, PVD, HG. SC,
6 NA and BS will conduct registration and data collection. Analysis will be performed by
7 RB. NA prepared the first draft of the manuscript. All authors (NA, BS, RB, JV, ADS,
8 SH, AVdB, ID, PVD, HG, LB, ED and SC) provided edits and critiqued the manuscript
9 for intellectual content, approved the submitted version, will be involved in the
10 interpretation of data, and agree to be accountable for all aspects of the work.
11
12

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14 [OZ8478]'
15
16

17 **Competing interests statement:** None declared.
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Figures

Figure 1. Participant flow uploaded separately

For peer review only

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3 **Supplementary materials**

4 Prevalence and incidence of antibodies against SARS-CoV-2 among
5 primary healthcare providers in Belgium – consent & baseline
6 questionnaire
7
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9 uploaded separately
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11 Prevalence and incidence of antibodies against SARS-CoV-2 among
12 primary healthcare providers in Belgium – Follow-up questionnaire
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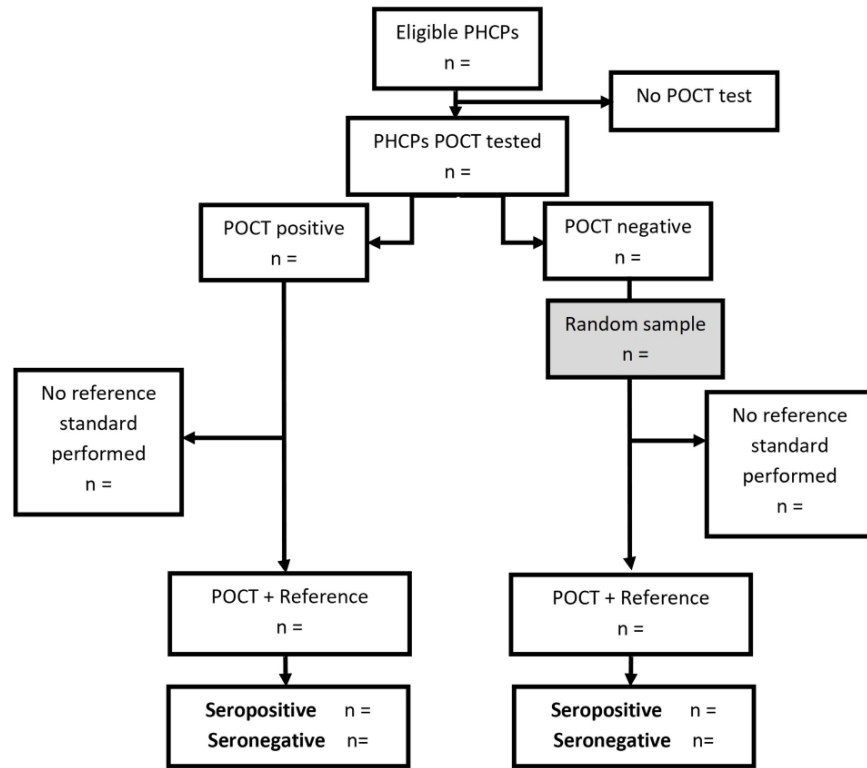


Figure 1: Participant flow

93x93mm (300 x 300 DPI)

Prevalence and incidence of antibodies against SARS-CoV-2 among primary healthcare providers in Belgium – consent and baseline T2 questionnaire

Dear Participant,

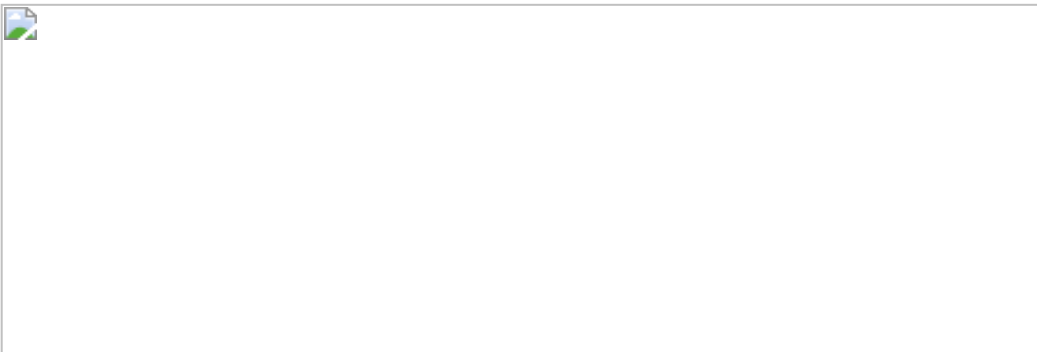
Thank you for your registration for the CHARMING study. We have provided you with your personal study materials for the first three testing time points.

Here we first ask for your formal consent to the study. All questions in the consent section need to be answered before you can proceed. Next we ask for your results on the rapid test, and questions about your health, household, practice and views on the SARS-COV2 pandemic.

If you have questions about CHARMING, please email us at covid-dmg@uliege.be (<mailto:covid-dmg@uliege.be>).

Many thanks in advance for carefully completing this questionnaire. We hope this will go smoothly for you.

The CHARMING study team



There are 74 questions in this survey.

E - Consent

Before giving your consent it is important that you have reviewed the information document about this study available in French **here**

(<https://dox.uliege.be/index.php/s/n64T153cp07BOKG>) and in Dutch **here**

(<https://dox.uliege.be/index.php/s/OYp4cllx8oxERBt>).

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1 Your study code (C followed by 4 numbers; see our email of 25.01.2021 with your link to this questionnaire): *

Please write your answer here:

2
I have received an information sheet (version 2.2, 26-11-2020). All my questions concerning this study have been answered satisfactorily. I was given sufficient time to reflect before agreeing to participate in this study. *

Please choose **only one** of the following:

Yes

3
My participation is voluntary. I have the right to withdraw my consent at any time without giving a reason. *

Please choose **only one** of the following:

Yes

4
In order to meet the needs of this study, I consent to the collection and use of my data (including the result of the rapid test). *

Please choose **only one** of the following:

Yes

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5
I authorise the consultation of my data to the persons collaborating in this research (these persons are listed in the information form). *

Please choose **only one** of the following:

Yes

6
I agree that the data recorded in this study will be kept for 20 years and may be processed for future research on respiratory infections and coronaviruses. *

Please choose **only one** of the following:

Yes

7
I agree to provide a blood sample to validate the rapid test. *

Please choose **only one** of the following:

Yes

No

8
I agree to provide a blood sample to examine the T-cell response. ^[L]_[SEP] *

Please choose **only one** of the following:

Yes

No

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9
I agree that the blood samples taken in this study will be stored for 20 years and can be processed at a later date. *

Please choose **only one** of the following:

10 Yes

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After this study, I agree to be approached for further research. *

Please choose **only one** of the following:

24 Yes

25 No

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11
I wish to participate in this survey. *

Please choose **only one** of the following:

46 Yes

47 Results of the rapid test

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12 *Date on which you carried out the rapid test (dd.mm.yyyy)? **

Please enter a date:

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13
Did the control line "C" change from blue to red?
If not, the test is invalid.

*

Please choose **only one** of the following:

Yes

No

14

Result of your quick test for IgG?

A red line visible next to G = positive (see figure).

*

Only answer this question if the following conditions are met:

Answer was 'Yes' at question '13 [Q00013]' (Did the control line "C" change from blue to red? If not, the test is invalid.)

Please choose **only one** of the following:

Positive

Negative

Unclear

15 Result of your quick test for IgM?

A red line visible next to M = positive (see figure).

*

Only answer this question if the following conditions are met:

Answer was 'Yes' at question '13 [Q00013]' (Did the control line "C" change from blue to red? If not, the test is invalid.)

Please choose **only one** of the following:

- Positive
- Negative
- Unclear

16 Date on which you completed this questionnaire (dd.mm.yyyy)? *

Please enter a date:

17 How many sealed tests do you have left after this testing time point? *

! Choose one of the following answers

Please choose **only one** of the following:

- 0 sealed tests
- 1 sealed test
- 2 sealed tests
- 3 sealed tests
- 4 sealed tests
- 5 sealed tests

18

Do you smoke? *

❗ If you choose 'not for _____ years' please also specify your choice in the accompanying text field.

❗ Only numbers may be entered in 'not for _____ years' accompanying text field.

Please choose **only one** of the following:

- Yes
- I have stopped smoking
- I have never smoked

19 How many years ago did you stop smoking?

Only answer this question if the following conditions are met:

Answer was 'I have stopped smoking' at question '18 [Q00018]' (Do you smoke?)

Please write your answer here:

years

20

How many alcoholic drinks do you consume per week? *

Please choose **only one** of the following:

- 0
- 1 - 5
- 6 - 10
- 11 - 15
- 16 - 20
- > 20

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21 Have you been vaccinated against pneumococcus? *

Please choose **only one** of the following:

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- Yes
 - No
 - I don't know

22 Have you been vaccinated against influenza for this winter season (2020-2021)?

*

Please choose **only one** of the following:

- Yes
- No
- I don't know yet

23 Have you been vaccinated against COVID-19? *

Please choose **only one** of the following:

- Yes
- No

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24 Which vaccine did you receive? *

Only answer this question if the following conditions are met:
Answer was 'Yes' at question '23 [Q00023]' (Have you been vaccinated against COVID-19?)

Please choose **only one** of the following:

- Pfizer/BioNTech
- Moderna
- Oxford/AstraZeneca
- Other

25 How many doses have you received? *

Only answer this question if the following conditions are met:
Answer was 'Yes' at question '23 [Q00023]' (Have you been vaccinated against COVID-19?)

Please choose **only one** of the following:

- 1 dose
- 2 doses

26 When did you receive the first dose of the vaccine (dd.mm.yyyy)?

Only answer this question if the following conditions are met:
Answer was 'Yes' at question '23 [Q00023]' (Have you been vaccinated against COVID-19?)

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27

Do you have one or more chronic diseases? *

Please choose **only one** of the following:

Yes

No

28 What chronic disease(s) do you have? (multiple answers possible) *

Only answer this question if the following conditions are met:

Answer was 'Yes' at question '27 [Q00027]' (Do you have one or more chronic diseases?)

Please choose **all** that apply:

Hypertension

Diabetes

Obesity

Other

29 Please list other chronic diseases

Only answer this question if the following conditions are met:

Answer was at question '28 [Q00028]' (What chronic disease(s) do you have? (multiple answers possible))

Please write your answer here:

30 Do you take medicines for chronic diseases? *

Only answer this question if the following conditions are met:

Answer was 'Yes' at question '27 [Q00027]' (Do you have one or more chronic diseases?)

Please choose **only one** of the following:

- Yes
- No

31 If yes which ones? *

Only answer this question if the following conditions are met:

Answer was 'Yes' at question '30 [Q00030]' (Do you take medicines for chronic diseases?)

Please choose **all** that apply:

- ACE inhibitors
- Immunosuppressants
- Corticosteroids (also inhalation)
- NSAID
- Other

32 Other medicines for chronic disease

Only answer this question if the following conditions are met:

Answer was at question '31 [Q00031]' (If yes which ones?)

Please write your answer here:

33 Other medicines in the last six months

Only answer this question if the following conditions are met:

Answer was 'Yes' at question ' [Q00034]' (Have you taken medicines other than those for chronic diseases in the last six months?)

Please write your answer here:

34 Have you taken medicines other than those for chronic diseases in the last six months? *

Please choose **only one** of the following:

- Yes
- No

Your general practice

35 I work in general practice as... *

Please choose **only one** of the following:

- General practitioner
- General practitioner in training
- Other healthcare providers, e.g. nurse, dietician, ...

36 Which year of your training are you in?

Only answer this question if the following conditions are met:

Answer was 'General practitioner in training' at question '35 [Q00035]' (I work in general practice as...)

Please choose **only one** of the following:

- Year 1
- Year 2
- Year 3

37 Please select your profession *

Only answer this question if the following conditions are met:

Answer was 'Other healthcare providers, e.g. nurse, dietician, ...' at question '35 [Q00035]' (I work in general practice as...)

Please choose **only one** of the following:

- Nurse
- Psychologist
- Dietician
- Speech therapist
- Other

38 I have been doing this job for...

*

Please choose **only one** of the following:

- Less than 2 years
- 2 to 5 years
- 6 to 10 years
- More than 10 years

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39 I also work at... *

Please choose **all** that apply:

- As CRA (coordinating and advising doctor)
- In a hospital
- In an institution (e.g. psychiatry, care for the disabled, ...)
- I don't have any other activity
- Other:

40 Which other healthcare professionals work in your practice? (multiple answers possible) *

Please choose **all** that apply:

- General practitioner
- Dietician
- Psychologist
- Nurse
- Practice assistant
- None of the above
- Other:

41 What is the (estimated) number of patients assigned to your practice? *

Please write your answer here:

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42 What is the (estimated) proportion of patients younger than 15 years of age (%) ? *

🚫 Your answer must be between 0 and 100

Please write your answer here:

%

43 What is the (estimated) proportion of patients over 65 years of age (%)? *

🚫 Your answer must be between 0 and 100

Please write your answer here:

%

44 What is the estimated proportion of patients with increased benefits (%) ? *

🚫 Your answer must be between 0 and 100

Please write your answer here:

%

45 What is the (estimated) proportion of patients with a migration background (%) ? *

Please write your answer here:

%

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46 What is the (estimated) proportion of patients who do not speak Dutch, French or German (%) ? *

Please write your answer here:

%

Your household

47 What is the composition of your household? *

ⓘ Each answer must be at least 0

Please write your answer(s) here:

How many family members does your household include, including yourself?

How many children attend a crèche (less than 2.5 years) ?

How many children attend pre-school (2,5 to 6 years)?

How many children attend primary school (typically 6 to 12 years)?

How many children attend secondary school (typically 12 - 18 years)?

How many household members are university/college students (typically aged over 18 years) AND sleeping in the family home more than 3 nights per week?

How many household members (typically over 18 years) in employment AND sleeping in the family home more than 3 nights per week?

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48 Is your partner employed in healthcare with patient contact? *

Please choose **only one** of the following:

- Yes
- No
- Not applicable

49 How many household members had complaints this year that are compatible with COVID-19, including yourself? *

Please write your answer here:

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50 If you had complaints, what were they? (multiple answers possible) *

Only answer this question if the following conditions are met:

Answer was greater than or equal to '1' at question '49 [Q00049]' (How many household members had complaints this year that are compatible with COVID-19, including yourself?)

Please choose **all** that apply:

I didn't have any complaints

Cough

Headache

Sore throat

Fever

Shortness of breath

Runny nose

Muscle pain

Loss of sense of smell

Loss of taste

General weakness/ fatigue

Nausea/ vomiting

Diarrhoea

Other:

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51 How many members of your household, including yourself, have been tested for COVID-19 (excluding tests for research purposes)? *

Please write your answer here:

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52 How often have you been tested (except for the research purposes)? *

Please write your answer here:

times

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53 How many days have you spent in quarantine? *

Please choose **only one** of the following:

- 0 days
- up to 5 days
- up to 7 days
- up to 10 days
- up to 14 days
- up to 20 days
- more than 20 days

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54 Have you ever tested positive for COVID-19? *

Please choose **only one** of the following:

- Yes
- No

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55 If you tested positive, when was the positive sample taken? *

Only answer this question if the following conditions are met:

Answer was 'Yes' at question '54 [Q00054]' (Have you ever tested positive for COVID-19?)

Please choose **only one** of the following:

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- February
 - March
 - April
 - May
 - June
 - July
 - August
 - September
 - October
 - November
 - December
 - January 2021

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56 if you know the exact date of the positive sample enter it here:

Only answer this question if the following conditions are met:

Answer was 'Yes' at question '54 [Q00054]' (Have you ever tested positive for COVID-19?)

Please enter a date:

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57

For the positive test result which test(s) was/were used? (multiple answers possible) *

Only answer this question if the following conditions are met:
Answer was 'Yes' at question '54 [Q00054]' (Have you ever tested positive for COVID-19?)

Please choose **all** that apply:

- PCR (for virus detection)
- Rapid test (for virus detection)
- Blood sample (for antibody detection)
- Rapid test (for antibody detection)
- Other:

58

If you tested positive, who was the suspected source of the infection? *

Only answer this question if the following conditions are met:
Answer was 'Yes' at question '54 [Q00054]' (Have you ever tested positive for COVID-19?)

Please choose **all** that apply:

- Patient
- Co-worker
- Family member
- Other:

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59 If you were treated for COVID-19, what treatment did you have? *

Only answer this question if the following conditions are met:

Answer was 'Yes' at question '54 [Q00054]' (Have you ever tested positive for COVID-19?)

Please choose **all** that apply:

Symptomatic treatment of pain, fever and other complaints

Hydroxychloroquine

Antibiotics

No treatment

Other:

60

If you were admitted for COVID-19, how many days did you spend in hospital?

(if you were not admitted to hospital put '0') *

Only answer this question if the following conditions are met:

Answer was 'Yes' at question '54 [Q00054]' (Have you ever tested positive for COVID-19?)

Please write your answer here:

days

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61
If you were admitted for COVID-19, how many days did you stay in intensive care? (if you were not admitted to intensive care put '0') *

Only answer this question if the following conditions are met:

Answer was 'Yes' at question '54 [Q00054]' (Have you ever tested positive for COVID-19?)

Please write your answer here:

days

62 How many household members have tested positive for COVID-19, **not** including yourself? *

Please write your answer here:

63 How many household members have been admitted to hospital for (suspected) COVID-19, **not** including yourself? *

Please write your answer here:

64 How many household members have been treated for (suspected) COVID-19, **not** including yourself? *

Please write your answer here:

Risk factors for COVID-19

65 Have you continued to work since the outbreak? *

Please choose **only one** of the following:

- Yes
- No

66 Have you been in physical contact with patients with confirmed COVID-19 since the outbreak? *

Please choose **only one** of the following:

- Yes
- No

67 If so, how many? *

Only answer this question if the following conditions are met:

Answer was 'Yes' at question '66 [Q00066]' (Have you been in physical contact with patients with confirmed COVID-19 since the outbreak?)

Please choose **only one** of the following:

- 1 - 5 patients
- 6 - 10 patients
- 11 - 15 patients
- 16 - 20 patients
- > 20 patients

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68 Have you lacked protective equipment since the outbreak? *

Please choose **only one** of the following:

- Yes
- No

69 If so which equipment? (multiple answers possible) *

Only answer this question if the following conditions are met:
Answer was 'Yes' at question '68 [Q00068]' (Have you lacked protective equipment since the outbreak?)

Please choose **all** that apply:

- Gloves
- Surgical mouth mask
- Other mouth mask (FFP2 or FFP3)
- Safety goggles
- Apron / body protection
- Other:

70 If available, which protective material do you use in patients with (suspected) COVID-19)? (multiple answers possible) *

Please choose **all** that apply:

- Gloves
- Surgical mouth mask
- Other mouth mask (FFP2 or FFP3)
- Safety goggles
- Apron/body protection
- Other:

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71
If available, what protective material do you use with your other patients? (multiple answers possible) *

Please choose **all** that apply:

- Gloves
- Surgical mouth mask
- Other mouth mask (FFP2 or FFP3)
- safety goggles
- Apron/body protection

Other:

72 Have you participated in the COVID patient triage? *

Please choose **only one** of the following:

- Yes
- No

73 If so, how many patients did you physically examine who subsequently turned out to be COVID-19 positive? *

Only answer this question if the following conditions are met:

Answer was 'Yes' at question '72 [Q00072]' (Have you participated in the COVID patient triage?)

Please choose **only one** of the following:

- 0 patients
- 1 - 5 patients
- 6 - 10 patients
- 11 - 15 patients
- 16 - 20 patients
- > 20 patients

74

Indicate to what extent you agree with the following statements

(1= totally disagree; 5= totally agree): *

Please choose the appropriate response for each item:

	1	2	3	4	5
The personal protection equipment that I use, protects me sufficiently against more contagious variants of SARS-CoV-2.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
A temporary ban on non-essential international travel is needed.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
I am sure I am already infected with COVID-19.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
I will certainly be infected with COVID-19 during this epidemic.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
I am afraid I am contaminating my relatives.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
The guidelines for primary care are clearly communicated.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
The guidelines for primary care are scientifically based.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
The Belgian healthcare system is strong enough to cope with this epidemic.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
The testing capacity in Belgium is sufficient.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Rapid diagnostic tests are relevant for general practice.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Rapid diagnostic tests for SARS-CoV-2 viral detection are manageable for general practice.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

	1	2	3	4	5
The measures imposed by the government are sufficient.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Everyone should wear a mask if they go outdoors.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
I have every confidence in the scientific COVID-19 expert committee.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Most of my patients follow the rules of 'social distancing'.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Most of my patients adhere to hygiene rules.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
La plupart de mes patients symptomatiques respectent les règles de quarantaine.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
This period is more stressful than during a busy flu period.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
I want to get the COVID-19 vaccination as soon as it is available.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Thank you very much for completing this questionnaire.

You will shortly receive an email that will explain what your test result means. We will send you an overview of your consent to participate in the study in the coming weeks.

The CHARMING study team



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Submit your survey.
Thank you for completing this survey.

Prevalence and incidence of antibodies against SARS-CoV-2 among primary healthcare providers in Belgium - Follow-up questionnaire February 2021

Dear Participant,

Thank you for your participation in CHARMING. This follow-up questionnaire refers to the period since the last testing period.

Many thanks in advance for carefully completing this questionnaire. We hope this will go smoothly for you.

The CHARMING study team

PS If you have questions about CHARMING, please email us at covid-dmg@uliege.be (<mailto:covid-dmg@uliege.be>).



There are 46 questions in this survey.

Part 1

1 Your personal study code (C followed by 4 numbers; see our email of 26.02.2021 with your link to this questionnaire): *

Please write your answer here:

Part 2

For peer review only - <http://bmjopen.bmj.com/site/about/guidelines.xhtml>

Instructions on how to perform the rapid test can be found in French **here**

(<https://dox.uliege.be/index.php/s/1duglah08HN8Ylr>) and in Dutch **here**

(<https://dox.uliege.be/index.php/s/hqqiswSGBxKw3yf>). Short instruction videos are available here:

- French test on yourself : <https://vimeo.com/492411023/7b2bedb700>

(<https://vimeo.com/492411023/7b2bedb700>)

- French test on someone else: <https://vimeo.com/492427669/b42bb624b6>

(<https://vimeo.com/492427669/b42bb624b6>)

- Dutch test on yourself: <https://vimeo.com/492430777/92626224d1>

(<https://vimeo.com/492430777/92626224d1>)

- Dutch test on someone else : <https://vimeo.com/492428827/d565f20bc2>

(<https://vimeo.com/492428827/d565f20bc2>)

2 *Date on which you carried out the rapid test (dd.mm.yyyy)? **

Please enter a date:

3
Did the control line "C" change from blue to red?
If not, the test is invalid.

*

Please choose **only one** of the following:

Yes

No

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4 Result of your quick test for IgG?

A red line visible next to G = positive (see figure).

*

Please choose **only one** of the following:

- Positive
 Negative
 Unclear

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5 Result of your quick test for IgM?

A red line visible next to M = positive (see figure).

*

Please choose **only one** of the following:

- Positive
 Negative
 Unclear

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6 Date on which you completed this questionnaire (dd.mm.yyyy)? *

Please enter a date:

7 How many sealed tests do you have left after this testing time point? *

Please choose **only one** of the following:

- 0 sealed tests
- 1 sealed test
- 2 sealed tests
- 3 sealed tests
- 4 sealed tests
- 5 sealed tests

Part 3

8 Since **your first** testing period (end December 2020 or end January 2021), how many days have you spent in quarantine? *

Please choose **only one** of the following:

- 0 days
- up to 5 days
- up to 7 days
- up to 10 days
- up to 14 days
- up to 20 days
- more than 20 days

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9 Since **your first** testing period (end December 2020 or end January 2021), how often have you been tested for COVID-19 (except for research purposes)? *

Please write your answer here:

times

10 I work in general practice as... *

Please choose **only one** of the following:

- General practitioner
- General practitioner in training
- Other healthcare providers, e.g. nurse, dietician, ...

11 Please select your profession *

Please choose **only one** of the following:

- Nurse
- Psychologist
- Dietician
- Speech therapist

Other

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12 Since the **last** testing period I have also worked... *

Please choose **all** that apply:

- As CRA (coordinating and advising doctor)
- In a hospital
- In an institution (e.g. psychiatry, care for the disabled, ...)
- I don't have any other activity
- Other:

Part 4

13 Since the last testing phase of CHARMING how many family members had complaints that are compatible with COVID-19, including yourself? *

Please write your answer here:

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14 If you had complaints, since the last testing period, what were they? (multiple answers possible) *

Please choose **all** that apply:

I didn't have any complaints

Cough

Headache

Sore throat

Fever

Shortness of breath

Runny nose

Muscle pain

Loss of sense of smell

Loss of taste

General weakness/ fatigue

Nausea/ vomiting

Diarrhoea

Other:

15 Since the last testing period how many family members, including yourself, have been tested for COVID-19 (excluding tests for research purposes)? *

Please write your answer here:

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16 Have you tested positive for COVID-19 since the last testing period? (multiple answers possible) *

Please choose **only one** of the following:

- Yes
- No

17 For the positive test result which test(s) was/were used? (multiple answers possible) *

Please choose **all** that apply:

- PCR (for virus detection)
- Rapid test (for virus detection)
- Blood sample (for antibody detection)
- Rapid test (for antibody detection)
- Other:

18 If you tested positive when was the positive sample taken (dd.mm.yyyy)?

Please enter a date:

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19 If you were treated for COVID-19, what treatment did you have? *

Please choose **all** that apply:

Symptomatic treatment of pain, fever and other complaints

Hydroxychloroquine

Antibiotics

No treatment

Other:

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20 If you tested positive, who was the suspected source of the infection? *

Please choose **all** that apply:

Patient

Co-worker

Family member

Other:

21 If you were admitted for COVID-19, how many days did you spend in hospital?

(if you were not admitted to hospital put '0') *

Please write your answer here:

days

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22
If you were admitted for COVID-19, how many days did you stay in intensive care? (if you were not admitted to intensive care put '0') *

Please write your answer here:

days

23 Since the last testing period how many family members have tested positive for COVID-19, **not** including yourself? *

Please write your answer here:

24 Since the last testing period how many family members have been admitted to hospital for (suspected) COVID-19, **not** including yourself? *

Please write your answer here:

25 Since the last testing period how many family members have been treated for (suspected) COVID-19, **not** including yourself? *

Please write your answer here:

Part 5

26 Have you continued to work in primary care since the last testing period? *

Please choose **only one** of the following:

- Yes
- No

27 Have you been in physical contact with patients with confirmed COVID-19 since the last testing period? *

Please choose **only one** of the following:

- Yes
- No

28 If so, how many? *

Please choose **only one** of the following:

- 1 - 5 patients
- 6 - 10 patients
- 11 - 15 patients
- 16 - 20 patients
- > 20 patients

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29 Have you lacked protective equipment since the **last** testing period? *

Please choose **only one** of the following:

Yes

No

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30 If so which equipment? (multiple answers possible) *

Please choose **all** that apply:

Gloves

Surgical mouth mask

Other mouth mask (FFP2 or FFP3)

Safety goggles

Apron / body protection

Other:

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31 If available, which protective material have you used since the last testing period in patients with (suspected) COVID-19)? (multiple answers possible) *

Please choose **all** that apply:

Gloves

Surgical mouth mask

Other mouth mask (FFP2 or FFP3)

Safety goggles

Apron/body protection

Other:

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32
If available, what protective material have you used with your other patients? (multiple answers possible) *

Please choose **all** that apply:

- Gloves
- Surgical mouth mask
- Other mouth mask (FFP2 or FFP3)
- safety goggles
- Apron/body protection

Other:

33 Have you participated in the COVID patient triage since the last testing period? *

Please choose **only one** of the following:

- Yes
- No

34 If so, how many patients did you physically examine who subsequently turned out to be COVID-19 positive? *

Please choose **only one** of the following:

- 0 patients
- 1 - 5 patients
- 6 - 10 patients
- 11 - 15 patients
- 16 - 20 patients
- > 20 patients

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35 Have you been vaccinated against COVID-19? *

Please choose **only one** of the following:

- Yes
- No

36 Which vaccine did you receive? *

Please choose **only one** of the following:

- Pfizer/BioNTech
- Moderna
- Oxford/AstraZeneca
- Other

37 How many doses have you received? *

Please choose **only one** of the following:

- 1 dose
- 2 doses

38 When did you receive the **first** dose of the vaccine (dd.mm.yyyy)? *

Please enter a date:

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39 Did you experience side-effects after receiving the **first** dose? *

Please choose **only one** of the following:

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- No side-effects
 - Negligible side-effects
 - Mild side-effects
 - Moderate side-effects
 - Severe side-effects

40 For how many days did you experience the following side-effects after the **first** dose (if you did not experience the side-effect put '0'): *

41 What other moderate or severe side-effects did you experience after receiving the **first** dose?

Please write your answer here:

42 When did you receive the **second** dose of the vaccine (dd.mm.yyyy)? *

Please enter a date:

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43 Did you experience side-effects after receiving the **second** dose? *

Please choose **only one** of the following:

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- No side-effects
 - Negligible side-effects
 - Mild side-effects
 - Moderate side-effects
 - Severe side-effects

44 For how many days after receiving the **second** dose of the vaccine did you experience the following side-effects (if you did not experience the side-effect put '0')? *

45 What other moderate or severe side-effects did you experience after receiving the **second** dose?

Please write your answer here:

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Indicate to what extent you agree with the following statements

(1= totally disagree; 5= totally agree): *

Please choose the appropriate response for each item:

	1	2	3	4	5
The personal protection equipment that I use, protects me sufficiently against more contagious variants of SARS-CoV-2.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
A temporary ban on non-essential international travel is still needed.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
The Belgian healthcare system is strong enough to cope with this epidemic.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
The testing capacity in Belgium is sufficient.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Rapid diagnostic tests are relevant for general practice.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Rapid diagnostic tests for SARS-CoV-2 viral detection are manageable for general practice.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
The measures imposed by the government are sufficient.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Everyone should wear a mask when they work inside with other people.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
I have every confidence in the scientific COVID-19 expert committee.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Most of my patients follow the rules of 'social distancing'.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Most of my patients adhere to hygiene rules.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

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	1	2	3	4	5
Most of my symptomatic patients respect the quarantine rules.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
This period is more stressful than during a busy flu period.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
For health care personnel the COVID-19 vaccination should be obligatory.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Thank you very much for completing this questionnaire.

You will shortly receive an email that will explain what your test result means.

If you experience side-effects after receiving the vaccination you can report them officially here:

In Dutch: <https://www.fagg.be/nl/bijwerking> (<https://www.fagg.be/nl/bijwerking>)

In French: https://www.afmps.be/fr/effet_indesirable (https://www.afmps.be/fr/effet_indesirable)

The CHARMING study team



21.03.2021 – 20:58

Submit your survey.

Thank you for completing this survey.