Prevalence and incidence of antibodies against SARS-CoV-2 among primary healthcare providers in Belgium during 1 year of the COVID-19 epidemic: prospective cohort study protocol

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ABSTRACT

Introduction National SARS-CoV-2 seroprevalence data provide essential information about population exposure to the virus and help 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 comorbidities. This protocol focuses on the seroprevalence among primary healthcare providers (PHCPs) in Belgium. PHCPs manage the vast majority of (COVID-19) patients and therefore play an essential role in the efficient organisation of healthcare. 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 (POCT) 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 POCT 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 of 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).

Trial registration number NCT04779424.

INTRODUCTION

As of 16 May 2021, SARS-CoV-2 has infected over 162 million people worldwide (over 1 030 000 in Belgium) and caused over 3.3 million deaths from COVID-19 worldwide (over 24 000 in Belgium).1 COVID-19 is a lethal respiratory tract infection, 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 comorbidities. \(^6\)–\(^8\) Meanwhile, other seroprevalence studies showed antibody positivity lasting up to 9 months. \(^3\)\(^10\) 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 personnel, \(^12\) and nursing homes. \(^13\)

This protocol focuses on the seroprevalence among primary healthcare 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 coworkers, 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 of 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 with 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 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**

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

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

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 was 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 and 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 min) 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 emphasise 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 geographical and demographic qualities.22

Data collection

On 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 timepoint (T1), they will receive an invitation by email (including a personalised link to an online questionnaire in French and Dutch) inviting them to:

1. Autocollect a capillary blood sample and analyse it using the POCT (OrientGene).
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 sociodemographic data (age, gender, composition of household, for example, 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).
   - The availability of personal protective equipment (practice organisational aspects, delayed care for non-urgent conditions) (see online supplemental 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 and presence of side effects).
- Professional exposure (contact with confirmed cases, use of infection prevention and control measures) (see online supplemental materials).

Phase III validation of the POCT

To validate the POCT, a subsample of participants will be asked to provide a serum sample. This subsample will be made up of all those participants who were seropositive for SARS-Cov-2 on the POCT at T1 and a random sample of participants who 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 (UA) (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 is between 0.6 and 3.0, the sample will be tested on the ATELLICA IM SARS-CoV-2 assay (Siemens, Munich, Germany), and in case of 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 standards’. The analytical and clinical performance of these three commercially available, fully automated SARS-CoV-2 antibody assays was investigated at UZA, and the relevance of this testing algorithm was explained and illustrated (B Peeters, personal communication, 2020). Analytical performance of all three assays was acceptable and comparable with results found in other studies.23–26

Participants of this subsample 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 6 months with one sample collection at 9 months and the final one at 12 months (table 1). This corresponds to a total of nine testing timepoints. This number, however, will depend on the evolution of the epidemic. At each testing timepoint, participants will be asked to perform the POCT within a time frame of maximum 5 days. For the subsample 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.

Sample size

This study aimed 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% at 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 (r), the design effect (1+[(m-1)×r]) 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 11 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.

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

To estimate an incidence of 5% with a precision of 1% at a 95% confidence level, a sample size of 1212 PHCPs is required or 1576 PHCPs considering a design effect of 1.3 (4160 PHCPs to estimate an incidence of 2% with a precision of 0.5% and considering clustering).

To be able to validate the POCT’s accuracy in the primary care setting, that is, to estimate the POCT’s sensitivity (92.9%) with a lower limit of its 95% CI of 90% and its specificity (96.3%) with a lower limit of its 95% CI of 95%, a sample of 301 PHCPs seropositive on the reference standard (for sensitivity) and 810 PHCPs seronegative on the reference standard (for specificity) is required, which corresponds to for example 6% seroprevalence in 5022 PHCPs. To reduce the burden on the participants and the costs of the study, all those with a positive POCT and only a (random) sample of 900 PHCPs with a negative POCT will be assessed with the reference standard, and inverse probability weighting will be applied to correct for missing reference standard data by design.30–32

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

### Data protection

As described previously, epidemiological and serological data will be linked via a unique identifier code assigned to each participant. The same unique identifier code will be entered in each questionnaire, enabling the link for data analysis. This code will remain the same throughout the study. The key between the codes and the identification data of the participants will be kept in a secure location (desktops, laptops, external drives, etc) at all locations (work, home and travel), complex passwords are used, and up-to-date access only by authorised people on all devices (desktops, laptops, external drives, etc) at all locations (work, home and travel), complex passwords are used, and up-to-date access only by authorised people on all devices (desktops, laptops, external drives, etc).
antivirus and firewall protection is run. Using the Information and Communication Technology (ICT) services of UAntwerp, ULiège and Sciensano assures that the data will be backed up on a regular basis. The research team ensures that their personal computer system is always up-to-date and does not switch off the automatic installation of updates.

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 V.3.6.3 or equivalent.

Among others, the following indicators will be calculated, considering clustering of PHCPs in the same practice whenever appropriate:
▶ 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.
▶ 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.
▶ 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 seroconverted before (based on prior POCT results), monthly during 12 months of follow-up.
▶ 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.
▶ SARS-CoV-2 antibody 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 seroconverted 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, which include the availability and use of different preventive measures against SARS-CoV-2 infection, univariable and multivariable regression analyses, considering the clustering of participants at their practices, will be performed, for example, generalised estimating equations. Model calibration will be assessed using calibration plots and the Hosmer-Lemeshow goodness-of-fit test. Discrimination will be estimated with the area under the receiver operating characteristic curve.

Data analysis phase III validation POCT
To validate the POCT in a primary care setting, we will estimate the following test characteristics:
▶ 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.
▶ 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. To show which participants are missing a reference standard result, a flowchart will be provided (figure 1).

Vaccination
The start of the vaccination of PHCPs during the study follow-up will provide the opportunity to monitor its progress (at regional level). Obviously, the PHCPs’ vaccination status will be considered when assessing the primary and secondary outcomes of this study.

Bias and limitations
The study results will be based on a convenience sample. However, the sample will cover a large proportion of geographically well-distributed PHCPs.

Selection bias is possibly because of the ‘late’ start of the study: if all the most vulnerable PHCPs have already been infected at the time of the start of this study, then the incidence among the remaining PHCPs may be lower (because better immune system, more adherent to personal protection guidelines, etc). Hence, as in an earlier seroprevalence study, we will explicitly ask for participation regardless of previous SARS-CoV-2 testing and test results.
Insufficient sample size: due to the current heavy workload in Belgian primary care and time constraints, it might be difficult to recruit PHCPs into this study. However, we will aim for a security margin in the number of participants and have good experience in the earlier seroprevalence study.35

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

Underestimation and overestimation of the presence of SARS-CoV-2 among this population due to imperfect testing methods (imperfect sensitivity and specificity). However, this bias will be minimised by using best available POCT.19

Patient and public involvement

Patients or the public were not involved in the design, conduct, reporting or dissemination plans of our research. The research team, however, involved potential study subjects, that is, PHCPs.

Ethics and dissemination

Ethical approval has been granted by ethics committee of the UZA/University of Antwerp (Belgian registration number: 3002020000237). Anonymous study results will be made accessible and available as soon as possible after each testing point and at the end of the study to public health authorities involved in management of the COVID-19 epidemic in Belgium. This will be done through a policy brief or press release. Sciensano will coordinate the distribution of results. These results will also be published on a dedicated, public webpage of the Sciensano COVID-19 dashboard.37

The general population will also be informed of the results through press communications. This will be done by the communication departments of the University of Antwerp and the University of Liège, Sciensano and the other study partners.

Scientific peer-reviewed publications (possible short communication, regular paper) will be prepared to add to the body of evidence and availability for the global scientific community and public health decision makers.

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Correction notice This article has been corrected since it was published. Joint first authorship and equal contribution details have been added.

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Contributors The study concept and design were initiated by SC, NA, BS and ED and finalised with contributions from JYV, ADS, SH, AVdB, ID, PVD and HG. SC, NA and BS conducted registration and data collection. Analysis was performed by RB. NA prepared the first draft of the manuscript. All authors provided edits and critiqued the manuscript for intellectual content, approved the submitted version, were involved in the interpretation of data and agreed to be accountable for all aspects of the work.

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REFERENCES


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://doc.uliege.be/index.php/s/n64T153cp07BOkG) and in Dutch here (https://doc.uliege.be/index.php/s/OYp4cllx8oxERBt).
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
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. *

Please choose only one of the following:

- Yes
- No
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:

- Yes
- No

10
After this study, I agree to be approached for further research. *
Please choose only one of the following:

- Yes
- No

11
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:

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
21 Have you been vaccinated against pneumococcus? *
Please choose only one of the following:

☐ 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?)

Please enter a date:
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
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:
______________________________
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:

%
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? *

1 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?
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:
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: __________________________
52 How often have you been tested (except for the research purposes)? *

Please write your answer here:

times

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

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:
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: __________
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
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
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:
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:

<table>
<thead>
<tr>
<th>Statement</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>The personal protection equipment that I use, protects me sufficiently against more contagious variants of SARS-CoV-2.</td>
<td></td>
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<tr>
<td>A temporary ban on non-essential international travel is needed.</td>
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<tr>
<td>I am sure I am already infected with COVID-19.</td>
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<tr>
<td>I will certainly be infected with COVID-19 during this epidemic.</td>
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<tr>
<td>I am afraid I am contaminating my relatives.</td>
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<tr>
<td>The guidelines for primary care are clearly communicated.</td>
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<tr>
<td>The guidelines for primary care are scientifically based.</td>
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<tr>
<td>The Belgian healthcare system is strong enough to cope with this epidemic.</td>
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<tr>
<td>The testing capacity in Belgium is sufficient.</td>
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<tr>
<td>Rapid diagnostic tests are relevant for general practice.</td>
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<tr>
<td>Rapid diagnostic tests for SARS-CoV-2 viral detection are manageable for general practice.</td>
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</tr>
<tr>
<td><strong>Question</strong></td>
<td>1</td>
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<tr>
<td>The measures imposed by the government are sufficient.</td>
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<tr>
<td>Everyone should wear a mask if they go outdoors.</td>
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<tr>
<td>I have every confidence in the scientific COVID-19 expert committee.</td>
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<tr>
<td>Most of my patients follow the rules of 'social distancing'.</td>
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<tr>
<td>Most of my patients adhere to hygiene rules.</td>
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<tr>
<td>La plupart de mes patients symptomatiques respectent les règles de quarantaine.</td>
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<tr>
<td>This period is more stressful than during a busy flu period.</td>
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<tr>
<td>I want to get the COVID-19 vaccination as soon as it is available.</td>
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</tbody>
</table>

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
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

Instructions on how to perform the rapid test can be found in French [here](https://dox.uliege.be/index.php/s/1duglah08HN8YIr) 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
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

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

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
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
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: __________________________
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:
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: [Blank]

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

Please enter a date:

[Blank]
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: [

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

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

- [ ] Yes
- [ ] No

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: ________________________________

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: ________________________________
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
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<table>
<thead>
<tr>
<th>Question</th>
<th>Answer Options</th>
</tr>
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<tbody>
<tr>
<td>35 Have you been vaccinated against COVID-19?</td>
<td>Yes, No</td>
</tr>
<tr>
<td>36 Which vaccine did you receive?</td>
<td>Pfizer/BioNTech, Moderna, Oxford/AstraZeneca, Other</td>
</tr>
<tr>
<td>37 How many doses have you received?</td>
<td>1 dose, 2 doses</td>
</tr>
<tr>
<td>38 When did you receive the first dose of the vaccine (dd.mm.yyyy)?</td>
<td>Enter a date</td>
</tr>
</tbody>
</table>

39 Did you experience side-effects after receiving the **first** dose? *
Please choose only one of the following:

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

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

- 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:

<table>
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<td>The testing capacity in Belgium is sufficient.</td>
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<tr>
<td>Rapid diagnostic tests are relevant for general practice.</td>
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<tr>
<td>Rapid diagnostic tests for SARS-CoV-2 viral detection are manageable for general practice.</td>
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<tr>
<td>The measures imposed by the government are sufficient.</td>
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<tr>
<td>Everyone should wear a mask when they work inside with other people.</td>
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<tr>
<td>I have every confidence in the scientific COVID-19 expert committee.</td>
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<tr>
<td>Most of my patients follow the rules of 'social distancing'.</td>
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<tr>
<td>Most of my patients adhere to hygiene rules.</td>
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</tbody>
</table>
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
In French: 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.