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

Version 2.3 – 6/11/2020

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1. Background

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has already infected over 45 million people worldwide (over 450,000 in Belgium) and caused over 1.2 million people to die from coronavirus disease (COVID-19) worldwide (over 12,000 in Belgium) by early November 2020. COVID-19 is a lethal respiratory tract infection (RTI), but infection with SARS-CoV-2 can also be mild and even asymptomatic.
National SARS-CoV-2 seroprevalence provide essential information about population exposure to infection and to understand the future course of the epidemic.[1 2] Seroprevalence studies in Iceland[3] and Spain[4] showed different levels of population antibody positivity, with antibody positivity over 4 months in Iceland. Meanwhile, cohort studies have suggested substantial waning of antibody levels in individuals, associated with for example illness severity, age and co-morbidities.[5-7] For Belgium, Sciensano (www.sciensano.be) coordinates national seroprevalence studies of SARS-CoV-2 antibodies in several relevant populations (Table 1).

This protocol focuses on the seroprevalence in primary care health care providers (PHCPs). They manage the vast majority of COVID-19 and other patients and therefore are essential to organise health care efficiently.[8 9] Among the primary health care providers (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-worker, throughout the COVID-19 epidemic is essential. In Belgium, this is particularly a reason for concern as the GP workforce consists of older adults and is therefore at higher risk for COVID-19 morbidity and mortality. GPs represented up to 38% of the physicians who died from COVID-19 in Italy early in the epidemic.[10]

Currently however evidence is lacking on 1. how many PHCPs get infected or diseased 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 this from happening and 6. the accuracy of the immunological serology based point-of-care test in a primary care setting.

Table 1. Populations of Sciensano coordinated SARS-CoV-2 seroprevalence studies

General population (via blood donors)
General population (via their national health interview survey)
School aged children
Nursing home residents and personnel
Hospital health care workers
Primary health care workers
Workforce

In Flanders, one of the three regions in Belgium, a seroprevalence study in PHCPs is ongoing, using dried blood spot (DBS) (self-)sampling of capillary blood and a Luminex bead-based assay developed by the group of Kevin Ariën at the Institute of Tropical Medicine (ITM; www.itg.be) (see Appendix 1).[11] Meanwhile, Sciensano validated five point-of-care tests (POCT), identifying one test with appropriate sensitivity and specificity for use in seroprevalence studies.[12]
A valid easy-to-use point-of-care test (POCT) will further minimize the potential risks of (cross)-contamination, will familiarise PHCPs with the use of this POCT and could substantially improve the timeliness of the availability of the test results both to the participants and to Sciensano compared to any laboratory test. To produce results that are valid for the entire Belgian territory however the expansion of the ongoing study from Flanders to Belgium is required.

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 assess the number of (asymptomatic) SARS-CoV-2 infections among PHCPs next to efficiently monitor their health and the effectiveness of/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.[13] It might also help us understand the response generated by vaccination. 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.[14]

2. Methods

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 supporting the fight against this epidemic.

2.1 OBJECTIVES

Primary objectives
- Assess the prevalence of antibodies against SARS-CoV-2 in primary health care providers (PHCPs; general practitioners (GPs) and 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 immunological serology-based POCT in a primary care setting (Phase 3 validation).
- Familiarise PHCPs with the use of immunological serology-based point of care tests.
- Assess the agreement between POCT and DBS results in a primary care setting.

2.2. STUDY POPULATION

Inclusion Criteria:

- Any Belgian general practitioner (GP) (including those in professional training) currently working in primary care and any other primary health care providers (PHCPs) from the same GP practice who physically manage (examine, test, treat) patients/clients (frontline PHCP), are able to comply with the study protocol and provided informed consent to participate in the study (see Appendix 2 and 3 for the information and consent form, respectively). Also PHCPs having been diagnosed with COVID-19 are included.

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 contact with patients/clients will also be excluded.

- PHCPs who were not active during the inclusion period will automatically be excluded.

2.3. STUDY DESIGN

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

PHCPs will be recruited close to the first testing point. All Belgian GPs in clinical practice 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. Registered PHCPs will be informed in more detail about the study. A model and demography informed sample[15] of registered GPs and other PHCPs will be asked to provide informed consent and will be assigned a unique study code by the researchers, who will manage the key between these codes and the identification data. Next they will be asked at each testing point to 1. perform a POCT (OrientGene®) and 2. complete a questionnaire through a secured online application hosted by Sciensano. The baseline questionnaire at the first testing point will include information about; basic socio-demographics, health status, including presence of symptoms since the start of the epidemic, implementation of infection prevention and control measures and the availability of personal protective equipment (practice organisational aspects, delayed care for non-urgent conditions) (see Appendix 4). At each of the following testing points information on the health status, including the presence of symptoms, and preventive measures since the previous testing point will be collected with a follow-up questionnaire through the same secured online application (see Appendix 5). The PHCPs will be provided with a link to enter their data, which will be immediately available for Sciensano and accessible for the research team. To validate the POCT, all PHCPs that were seropositive and a random sample of PHCPS that were seronegative on the POCT at the first testing point and provided consent for a serum sample, will be asked to provide a serum sample, which will be

transferred to the laboratory of clinical biology of the University Hospital of Antwerp (UZA) for analysis with a reference standard. As reference standard the following testing algorithm will be use, i.e. 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 study will last twelve months with epidemiological data collected through the online questionnaires and biological sample collection monthly for six months and one sample collection at nine and one at twelve months (Table 2). This corresponds to a total of nine testing time points. This number will however depend on the evolution of the epidemic. Each testing point, the POCTs will be performed ideally within a timeframe of maximum 5 days. At the testing point to validate the POCT, the serum sample should be taken at the same time, i.e. just prior to performing the POCT.

Table 2. Timing of data collection

	T1	M1	M2	M3	M4	M5	M6	M9	M12	Total
POCT	x	x	x	x	x	x	x	x	x	9
Baseline	x									1
Follow-up		x	x	x	x	x	x	x	x	8
Serum			x							1
Picture				x						

x: the timing of this data collection is more flexible

The result of the POCT will be entered as a variable in the online questionnaire.

All data analysis will be performed and reported after each relevant testing period and at the end of the study.

2.4 SAMPLE SIZE

This study aims to include 5,000 PHCPs with a 4 GPs to 1 other PHCP ratio taking into account 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 have to correct the sample size. For an average of 2.5 PHCPs per practice (m) and an intraclustercorrelation of 0.2 (rho) 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 and Brussels. 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.
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, [16 17] 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 taking into account a design effect of 1.3. A lower incidence or lower sample size would further limit the number of determinants that can be modelled.
To estimate an incidence of 3% with a precision of 1% and a 95% confidence level, a sample size of 1212 PHCPs is required or 1576 PHCPs taking into account a design effect of 1.3 (4160 PHCPs to estimate an incidence of 2% with a precision of 0.5% and taking into account clustering).
To be able to validate the POCT's accuracy in the primary care setting, i.e. 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 to 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.[18-20]
A sample size 5,000 would also allow us to estimate the longevity of the serological antibody response among the PHCPs seropositive on the POCT. For example starting from 300 PHCPs seropositive on the POCT a decrease of 10% in seroprevalence can be estimated with a precision of 4% and a 95% confidence level. Smaller decreases in seroprevalence and/or estimating with lower precision would requires 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.
This study will also allow to assess the agreement between DBS and POCT, and consequently help interpret ongoing and design future studies. Based on 500 paired samples either small differences in paired proportion of up to 2% can be detected as well as lower than 'perfect' agreement based on Cohen's kappa.

2.5. SAMPLING PROCEDURE

To select the PHCP to be included in the sample, we first invite all Belgian GPs via their scientific organisations, i.e. Domus medica in Flanders, Collège de Médecine Générale (CMG) in Wallonia, and both in Brussels to register for participation through their secured online applications. Once registered GPs are subsequently invited by an automatically send e-mail to distribute the invitation to the other PHCPs working in their practice. PHCPs who are willing to participate can register through the same secured online application. All registered PHCPs will receive information on the study and be provided with the opportunity to ask questions by e-mail. A model and demography informed sample[15] of registered GPs and other PHCPs, i.e. a sample representative for the GPs' practice type (solo, duo or group) and location and their age and gender, will be asked to consent to participation online as well. If the number of registered PHCPs does not allow for such a sample of 4000 GPs and 1000 other PHCPs, the information of the participating practices and PHCPS will be used to correct the outcome estimates.

2.6. DATA COLLECTION

2.6.1. Information collected

POCT result data and epidemiological data will be collected simultaneously at baseline (T1), and then monthly for six months, at nine month and finally at twelve months (depending on the evolution of the epidemic) (see Table 2).

In Flanders and Wallonia, one (postdoctoral) researcher will be designated to coordinate the study locally (ideally a staff member of an academic department of primary care experienced in

primary care research) and communicate with the principle investigators. The (postdoctoral) researchers will be responsible of setting up a small team or service to:

- Help in the participants selection and inform the participants (see above),

- Explain, provide and collect the informed consent for each of the participants,

- Distribute the study material, c.q. the POCT with instructions, to the participants via regular mail at each study testing time point,

- Enable subsequent collection of data on the test result and additional epidemiological data via the online questionnaires that is immediately available to the principle investigators and can be accessed by the researchers, by sending an e-mail to the participants providing them with the appropriate link,

- Ensure any other logistical support required for the study.

Biological samples/Serological data will be collected via

- At each timepoint, the participating PHCPs will provide a capillary blood sample of and by themselves and have it analysed by the OrientGene[1] POCT. The study material will be sent well in advance to allow the participating PHCPs to take their sample within a timeframe of maximum 5 days;

- Alll PHCPs that tested positive and a random sample of 900 PHCPs that tested negative on the POCT on the first timepoint and provided consent for a serum sample will be asked to provide a serum sample and have it transferred to and analysed by the reference standard at UZA, i.e. 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 then confirmation on the ATELLICA IM SARS-CoV-2 assay (Siemens, Munich, Germany), and if discordant results 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 commercial, fully-automated SARS-CoV-2 antibody assays was investigated at 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.[21-24]

Epidemiological data will be collected at each study timepoint via the online baseline and follow-up questionnaire presented in Appendix 3 and 4, respectively. These questionnaires are based on the ones used in the ongoing seroprevalence study in Flemish primary care (see Appendix 1). The questionnaires will be available in Dutch and French. They will be completed

[1] Sciensano validated the OrientGene, coated with receptor binding domain (RBD), by comparing this POCT's results with results obtained with the Wantai SARS-CoV-2 total Ig ELISA, also RBD-coated, found a sensitivity of 92.9% and a specificity of 96.7%, i.e. the best results of the five POCTs tested, and concluded that the OrientGene POCT is best suited for screening purposes using finger prick blood in a large-based population setting (personal communication); Rapport n° D/2020/14.440/72

online by the participants at each timepoint, and will include their unique identifier code. At each timepoint the participants will receive the link to the appropriate questionnaire via e-mail.

Information collected will include the POCT test result, basic socio-demographic characteristics (age, gender, practice patient size…), professional exposure (specific function, contact with confirmed case etc.), and health characteristics (co-morbidities, presence of symptoms, use of medications). This information will be needed to assess the association between the presence and clinical presentation of the disease and these potential risk factors.

For a selection of PHCPs we will also have the result of the reference standard to validate the POCT's accuracy in the primary care setting.

All pseudonymised data collected will safely stored by Sciensano for 10 years after completion of the study.

2.6.2. Laboratory specimen collection, transport and analysis

The PHCPs consenting to and selected for the validation of the POCT's in the primary care setting will be provided with a serum tube (Becton Dickinson Vacutainer® SST™ ii Advance; ref 368879) and any other materials needed to transport their serum sample to the UZA laboratory of clinical biology. They will be asked to organise the collection of their serum samples themselves at a pre-arranged time. The samples can for example be taken by another PHCP in their practice or by a PHCP they collaborate with. The samples will be stored at ambient temperature until they are picked-up for transport (option 1) or sent in accordance with the UN 3373 packaging norm via regular mail (option 2).

Option 1: The serum samples will picked-up by a courier service on the day the sample taking and collection is arranged, stored at ambient during transport and delivered the same day the UZA laboratory of clinical biology.

Option 2: The serum samples will be sent in accordance with the UN3373 packaging norm via regular mail on the same day the sample was taken to the UZA laboratory of clinical biology.

Upon arrival at the UZA laboratory of clinical biology the samples will be processed and analysis using the testing algorithm started within 24 hours, i.e. 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'.

2.7. DATA ANALYSIS

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 must stay the same during the entire duration of follow-up. The key between the codes and the identification data of the participants will be kept in a secure and protected way by the principle investigators and the researchers, and destroyed upon completion of the study. The personal data processing activities for the proposed research

project will be submitted to the UAntwerpen Data Protection Office to review its completeness and compliance with the General Data Protection Regulation (GDPR) and to ask for formal approval. To control digital access only by authorized people on all devices (desktops, laptops, external drives, …) at all locations (work, home and travel), complex passwords are used, up-to-date anti-virus and firewall protection is run. Using the ICT services of UAntwerp, ULiège and Sciensano assures that the data will be backed up at 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. Non-digital information, e.g. informed consent forms, are stored separate and secure.

Epidemiological data

Analysis will be done jointly by the principle 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 SAS 9.4 or equivalent.

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

- "Seroprevalence of SARS-CoV-2": number of PHCPs in whom presence of specific SARS-CoV-2 IgG is detected by the POCT / Total number of PHCP tested with the POCT

- "Prevalence of reported COVID-19 cases": number of PHCPs who self-report at baseline that SARS-CoV-2 infection (symptomatic and asymptomatic) was detected / Total number of PHCPs responding to the baseline questionnaire

- "SARS-CoV-2 seroconversion rate": number of PHCPs in whom presence of specific SARS-CoV-2 IgM and/or IgG is detected by POCT at follow-up / Total number of PHCP followed-up not sero-converted before (based on prior POCT results), monthly during 12 months of follow-up.

- "Incidence of reported COVID-19": number of PHCPs who self-report new SARS-CoV-2 infections (symptomatic and asymptomatic) at follow-up / Total number of PHCPs 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 antibodies longevity": number of PHCPs in whom presence of specific SARS-CoV-2 IgG is no longer detected by POCT at follow-up / Total number of PHCP 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, taking into account the clustering of PHCPs in their practice, will be performed, e.g. generalised estimating equations.[25] Model calibration will be assessed using calibration plots and the Hosmer-Lemeshow goodness-of-fit test.[26] It discrimination will be estimated with the area under the receiving operator characteristic (ROC) curve. For internal validation bootstrapping will be applied. The final model's parameter will be converted into a prediction rule and simplified risk score.[27]

To assess the agreement between the POCT and DBS results differences in paired proportions will be assessed using McNemar's test and Cohen's kappa will be calculated.

Data analysis will be done by the researcher team using statistical software already available to the analysis team (including STATA 14 / SAS / R), while having the necessary licenses.

Laboratory data

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

- "SARS-CoV-2 POCT sensitivity": number of PHCPs testing positive on the SARS-CoV-2 POCT / Total number of PHCP testing positive on the reference standard.

- "SARS-CoV-2 POCT specificity": number of PHCPs testing negative on the SARS-CoV-2 POCT / Total number of PHCP 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 all participants been verified.[18-20] To show which participants are missing a reference standard result a flow chart will be provided (Figure 1).

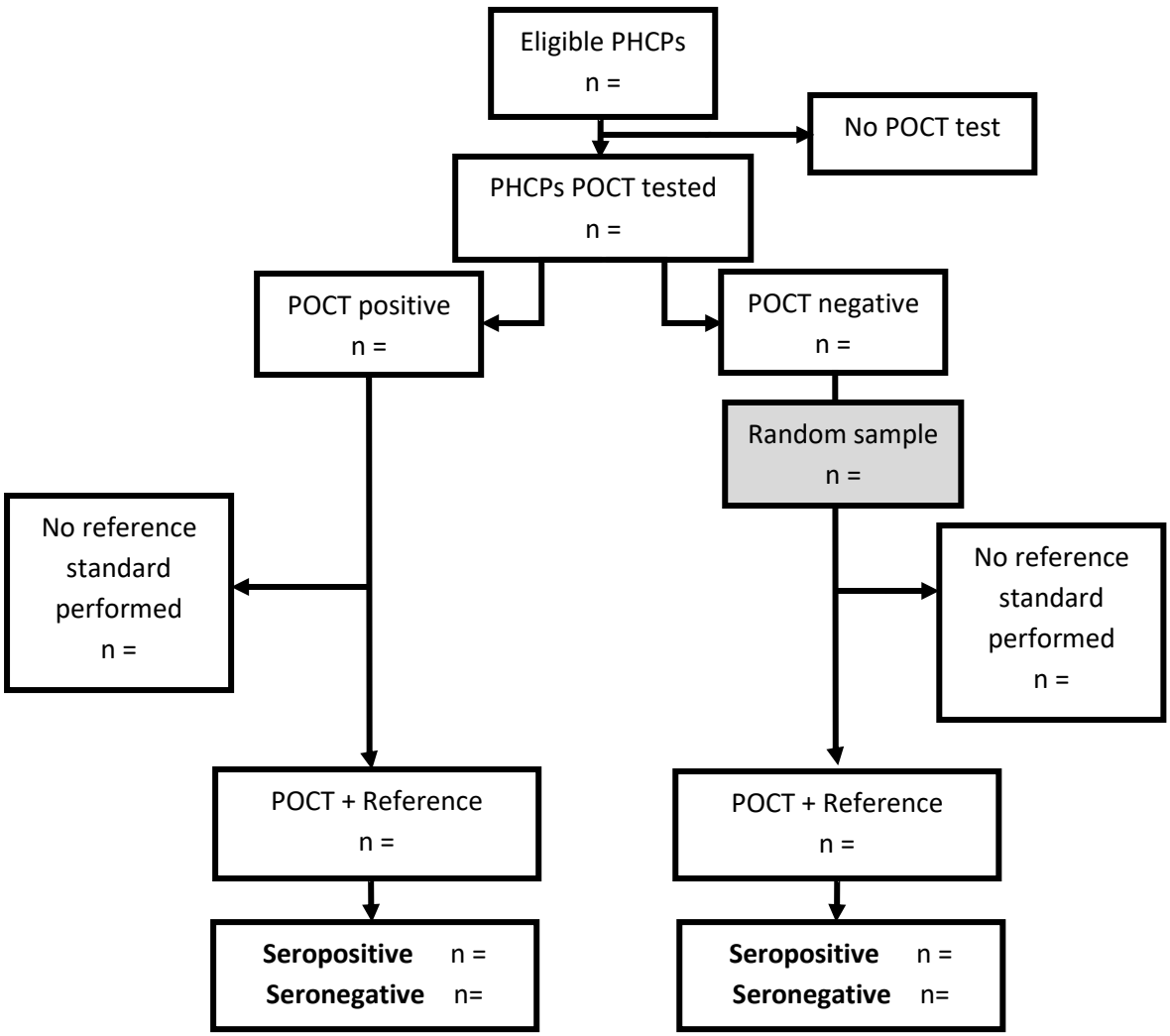

Figure 1. Participant flow

2.8. QUALITY ASSURANCE

As for the questionnaires, this protocol has been and will be reviewed by other researchers and experts in the field. The informed consent and the questionnaire will be available in two languages (French and Dutch). Results from the reference standard will be validated by the scientists in charge of the assays. Data analysis will be done by the researchers in collaboration with appropriate experts, including statisticians with expertise in the analysis of longitudinal data.

2.9. BIAS AND LIMITATIONS

- Potential selection bias 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 the ongoing seroprevalence study, we will explicitly ask for participation regardless 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 ongoing seroprevalence study.

- Loss of follow-up or missing data will be possible, for example if a PHCP becomes sick in between two data collection points without providing immediate samples and is isolated at home, or if participant does not provide data at one point because of heavy workload etc. In these cases, the PHCP 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 highly 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, loss of follow-up should be minimized.

- Under- and overestimation of the presence of SARS-CoV-2 among this population due to:
- imperfect testing methods (imperfect sensitivity and specificity)=> however, bias minimized by using best available POCT
  errors in the data collection => however, staff in charge of collecting the samples are experienced PHCPs and questionnaires will be as short and clear as possible to ensure completeness and accuracy of data and minimize reporting bias.

2.10. PROTECTION OF HUMAN SUBJECTS

2.10.1. Risks

The risks for participants are minimal, they include side effects of the sampling procedures. A capillary blood test requires puncturing of the skin of a fingertip with a very thin needle. A serum sample requires puncturing a vein through the skin. Although most PHCPs are aware of the risks, all participants will be clearly informed about these complications inherent to blood collection (pain/discomfort at the puncturing site, subcutaneous bleeding), that are minimized

by providing clear instructions to of the PHCPs in charge of collecting the samples. The POCT will be accompanied by an instruction video and a package insert with written instructions.

2.10.2. Benefits

In this challenging COVID-19 situation, PHCPs would be eager to benefit from monthly serological testing and follow-up they would otherwise not have. They would also benefit from the experience of being able to perform a POCT that is not yet routinely performed in Belgium during this COVID-19 epidemics. To date those who (continue to) test positive should however not consider themselves protected and adhere to the same infection prevention and control measures as those who tested negative.

2.10.3. Confidentiality

Samples results and questionnaires will be pseudonymized via an individual code attributed to each participant. None of the researchers who will analyse the data will be involved in data collection, nor in the care of COVID-19 patients.

2.10.4. Biological specimen

Any sample entering the Biobank Antwerpen, Antwerp, Belgium (ID: BE 71030031000) will be stored after for a duration of 10 years after which it will be destroyed. If participant wish that their biological specimens be destroyed upon completion of the study, this will need to be mentioned in the informed consent form.

2.10.5. Informed consent

Information on the study will be provided online by the researchers and informed consent will be obtained from all participants, in their working language. The information and consent forms can be found in appendix 1 and 2, respectively.

2.10.6. Ethical committee clearance

We will submit the proposed study for ethics approval to the ethics committee of the Antwerp University Hospital/University of Antwerp.

2.10.7. Insurance

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2.10.8. Data processing and protection (GDPR)

A full data management plan (DMP) will be submitted to the University of Antwerp's Data Protection Office (DPO) for review if and confirmation that the register for personal data processing activities for this study is complete and in compliance with the General Data Protection Regulation (GDPR).

2.11. DISTRIBUTION OF RESULTS

The study protocol will be registered at Clinicaltrials.gov.

Anonymous study results should 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 can be done through a policy brief or presentation. Sciensano will coordinate the distribution of results. These results will be also published on the relevant websites of these institutions.

The general public will also be informed regarding these anonymous results through press communications. This will be done by the communication departments of the study PI, of Sciensano and of the study partners.

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

2.12. PRACTICAL CONSIDERATIONS

2.12.1. Timeline

- Study start date: ASAP, ideally during the week of 16 November.

- Estimated study completion date: last study testing time point is 12 months after the first study testing point. The researchers aim to report on the processed and analysed data after each testing time point and within six months of the last study testing point. Seroprevalence data will however be available to Sciensano in near real-time.

2.12.2. Field work

- Ordering of the POCTs for the seroprevalence study will be done by Sciensano. All other study material will be purchased, prepared and dispatched by the researchers and their subcontractors.

- Werminval will prepare and dispatch the study materials we provide them with.
They will send out study materials for 3 testing time points in a bubble envelop (Article code 28145 (A5 Formaat, 21 x 26.5 cm); UAntwerpen) one week before the first, the fourth and the seventh testing time point, i.e.:

  - POCTs (OrientGene®) and buffer solution
  - Alcohol pads (A18704; ROMED
  - Finger pickers (Safetylancet dispsable ERGOLANCE Pink 21G)
  - Band-Aids (20067 Novospot-vivastrip D23mm)
  - Zip-bags (A19769; 120x180mm)

In case of option 2:

They will also sent out the study materials for the serum sample collection in a bubble envelop (Article code 28145 (A5 Formaat, 21 x 26.5 cm); UAntwerpen) one week in advance of the third testing time point, i.e.:

- *Serum tube (Becton Dickinson Vacutainer® SSTTM ii Advance; ref 368879)*
- *Absorbent material (Article Q90102 (Absorbent paper 86ml, 76x152mm; MLS)*
- *Laboratory mailbag (Artikcle O50124; 165 x 265 mm; MLS)_*
- *Protecting envelop (Artikel code 28145 (A5 Formaat, 21 x 26.5 cm; UAntwerpen)*
- *Bubble envelop (Mail Lite bubble envelop A/000 110 (B) x 160 (H) mm; UAntwerpen)*
- *Requisition form (UAntwerpen)*
- *UN 3373 sticker/image to print on label paper (Avery LR 7165, UAntwerpen)*

In case of option 1:

iHCT (or EUROSPRINTER) will organize collection of the serum samples on the day the sample taking and collection is arranged, storage at ambient during transport and delivery of the samples the same day the UZA laboratory of clinical biology.

- The UZA laboratory of clinical biology the samples will process upon arrival and start analyzing them using the testing algorithm within 24 hours, i.e. 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'.

- Epidemiological and laboratory data will be analysed by the researchers (see above).

- A budget of € 1,779,125 (including 17% overhead and 21% taxes) was estimated and approved by Sciensano on the 30th of September 2020.

2.13 SPECIAL CONSIDERATIONS AND CIRCUMSTANCES

Given the uncertainty about the future development of the COVID-19 epidemic, adaptation of the testing time points (more or less frequent sampling) and earlier termination or extension of the study might be considered and needed.

2.14. EXPECTED OUTCOME

The benefits to get out of the achievement of this study would be numerous:

- Data on the current burden of COVID-19 in asymptomatic PHCPs is currently missing worldwide and would help to understand better the dynamics of the disease. This would help inform scientist and policy makers thus optimizing infection prevention and control practices.

- Furthermore, PHCPs represent an important element in the infection transmission chain, as they are both highly exposed to infectious cases and to vulnerable population. This is why getting a better picture of the proportion of infected PHCPs could help to review the measures to protect them from infectious threats, thereby protecting the general population.

3. Appendices

APPENDIX 1: SEROPREVALENCE STUDY IN FLANDERS

In Flanders a seroprevalence study aiming to provide valid answers to similar research questions is ongoing. Given the late seroconversion found in COVID-19 patients,[28 29] their immunological serology-based tests rely on sensitive immunoassays, like the Luminex bead-based assay developed by the group of Kevin Ariën (ITM; www.itg.be).[11] To provide a sample for the serological tests, dried blood spot (DBS) (self-)sampling of capillary blood is used. This is a globally adopted, minimally invasive and transmission safe option.[30] Moreover, it is shown to be stable over time and producing valid results in Belgian nursing home residents and personnel (personal communication Piet Cools, UGent). Out of 440 paired samples (Whatmann DBS and serum sample) all serum samples were screened with the Abbott IgG chemiluminescent microparticle immunoassay. Next, the DBS from all 129 positive and a random sample of 144 negative sera were analysed with the EUROIMMUN ELISA, showing over 96% sensitivity and over 98.5 specificity.

The GPs and other PHCPs participating in this prospective cohort study (UAntwerpen COVID BOF 42828) and have consented to provide a DBS and additional testing will also be invited for the national seroprevalence study. Their DBS samples will continue to be returned to the laboratory of medical microbiology of the University of Antwerp via regular mail. The DBS received, which will be processed and analyzed at the laboratory of medical microbiology of the University of Antwerp and at the Institute of Tropical Medical (ITM) in Antwerp using a validated protocol.

In brief, from each DBS 2 discs (4mm) are punched in an Eppendorf tube (1.5 mL), 160 µL of the PBS-BN (dulbecco's phosphate buffered saline (DPBS, Gilco, ref: 14190-094) with 1% bovine serum albumin (BSA, Sigma, ref: A7030-100G) is added before incubating overnight at room temperature by shaking conditions. After elution 15 µL of eluate is sent at room temperature to ITM for analysis. The rest of the eluate is stored at 4°C. At ITM Joachim Mariën and Kevin Ariën developed a highly specific (99%) and sensitive (96%) Luminex SARS-CoV-2 antibody detection assay using nucleocapsid protein (NP), receptor-binding domain (RBD) and S protein subunits S1S2 antigens together.[11] This test is validated for serum, and seems to perform equally well with eluates from DBS (unpublished data). Validation of the Luminex assay using a sample of DBS with paired positive and negative sera provided by Piet Cools is ongoing at ITM.

Results will continue to be communicated to all participants providing DBS in an encrypted way (a valid personal e-mail address will be asked in the baseline questionnaire). However, as these tests are done for research and not diagnostic purposes, and depending on lab capacity, communication of the results will take longer compared to diagnostic testing.

The results will also be available to assess the agreement between the DBS and POCT in the proposed project.

APPENDIX 2: INFORMATION FORM

Dutch version: https://dox.uliege.be/index.php/s/YaJm2hfsyvwwer7

French version: https://dox.uliege.be/index.php/s/MqlWBMx0KinY8y8

APPENDIX 3: CONSENT FORM (DUTCH VERSION)

Voor u kan starten moet u eerst instemmen met deelname. Zonder uw toestemming, mogen we uw antwoorden niet verwerken. Het is belangrijk dat u weet waarom de studie wordt afgenomen, wat er met de resultaten gebeurt en wat uw rechten zijn. Deze informatie vindt u terug in het informatieformulier dat u eerder heeft ontvangen.

- ☐ Mijn studiecode: __ __ __ __
- ☐ Ik heb het informatieformulier (Versie 2.2, 19-11-2020) gelezen. Ik kon vragen stellen. Mijn vragen zijn goed beantwoord. Ik had genoeg tijd om te beslissen over deelname.
- ☐ Ik weet dat deelname vrijwillig is. Ook weet ik dat ik op ieder moment kan beslissen om toch niet mee te doen. Daarvoor hoef ik geen reden te geven.
- ☐ Ik geef toestemming voor het verzamelen en gebruiken van mijn gegevens, waaronder mijn resultaat op de sneltest, om de onderzoeksvragen in dit onderzoek te beantwoorden.
- ☐ Ik weet dat voor de controle van het onderzoek sommige mensen toegang tot al mijn gegevens kunnen krijgen. Die mensen staan vermeld in het informatieformulier. Ik geef toestemming voor die inzage door deze personen.

- ☐ Ik geef toestemming om mijn gegevens 20 jaar te bewaren en te gebruiken voor toekomstig onderzoek op het gebied van luchtweg- en coronavirusinfecties.
- ☐ Ik wil meedoen aan dit onderzoek.

- ☐ Ik geef ook toestemming om een extra veneus bloedstaal te leveren om de sneltest te valideren.

- ☐ Ik geef ook toestemming om een extra veneus bloedstaal te leveren om de T-cel respons te onderzoeken

- ☐ Ik geef ook toestemming om mijn bloedstaal na dit onderzoek te bewaren en om dit later nog voor ander en/of meer onderzoek te gebruiken, zoals in de informatiebrief staat.

- ☐ Ik geef ook toestemming om mij na dit onderzoek te benaderen voor vervolgonderzoek.

APPENDIX 4: BASELINE QUESTIONNAIRE (DUTCH VERSION)

Geachte huisarts
Geachte medewerker

Gelieve onderstaande vragenlijst in te vullen.

Algemeen

1. Uw studiecode: __ __ __ __
2. Datum waarop u de sneltest uitvoerde? (dd/mm/jjjj): ____/____/_____
3. Resultaat van uw sneltest?
   IgM
   - □ positief
   - □ negatief
   - □ onduidelijk

   IgG
   - □ positief
   - □ negatief
   - □ onduidelijk

   □ ongeldig
4. Datum waarop u deze vragenlijst invult? (dd/mm/jjjj): ____/____/_____
5. Rookt u?
   - □ ja
   - □ niet meer: _____ jaar gestopt
   - □ nee
6. Hoeveel consumpties alcohol drinkt u per week?
   - □ 0
   - □ 1- 5
   - □ 6 – 10
   - □ 11 – 15
   - □ 16 – 20
   - □ > 20
7. Heeft u een of meer chronische ziekten (co-morbiditeit, zo ja welke?):
   - □ ja, namelijk (meerdere antwoorden mogelijk)
     - □ hypertensie
     - □ diabetes
     - □ obesitas
     - □ andere, namelijk
     - 1. ……..
     - 2. ……
     - 3. ……..
   - □ nee
8. Was u eind 2019 gevaccineerd tegen influenza?
   - □ ja
   - □ nee
9. Zal u eind 2020 gevaccineerd zijn tegen influenza?
   - □ ja
   - □ nee
   - □ weet niet
10. Bent u gevaccineerd tegen pneumokokken?
    - □ ja
    - □ nee

11. Gebruikt u chronisch geneesmiddelen?
    - □ ja, namelijk (meerdere antwoorden mogelijk)
        - □ ACE inhibitoren
        - □ immunosuppressiva
        - □ corticosteroïden (ook inhalatie)
        - □ NSAID
        - □ andere, namelijk
        1. ……..
        2. ……
        3. ……..
    - □ nee
12. Heeft u andere geneesmiddelen gebruikt het voorbije half jaar (zo ja, welke)?
    - □ ja, namelijk
        1. ……..
        2. ……
        3. ……..
    - □ nee
13. Ik ben werkzaam in de huisartspraktijk als
    - □ Huisarts
    - □ Andere zorgverleners, bv. Verpleegkundige, diëtist, …
    - □ Andere medewerkers, bv. secretariaatsmedewerker
14. Ik doe dit werk al
    - □ Minder dan 2 jaar
    - □ 2 tot 5 jaar
    - □ 6 tot 10 jaar
    - □ Meer dan 10 jaar
15. Ik werk ook
    - □ Als CRA (coördinerende en raadgeven arts)
    - □ In een ziekenhuis
    - □ In een instelling (bv. psychiatrie, gehandicaptenzorg, …)
    - □ Ergens anders, namelijk

    1. ……..
    2. ……
    3. ……..

Vragen over uw huisartspraktijk

16. Werken er andere zorgverleners (niet huisartsen) in uw praktijk?
    - □ ja, namelijk
        - □ diëtist
        - □ psycholoog
        - □ verpleegkundige
        - □ praktijkassistent
        - □ andere, namelijk
        1. ……..
        2. ……
        3. ……..
    - □ nee

17. Wat is het (geschatte) aantal patiënten dat is toegewezen aan uw praktijk?
    □ < 500
    □ 500-750
    □ 750-1000
    □ 1000-1250
    □ 1250-1500
    □ 1500-2000
    □ 2000-3000
    □ 3000-4000
    □ > 4000
18. Wat is het (geschatte) aandeel patiënten jonger dan 15 jaar? ____ %
19. Wat is het (geschatte) aandeel patiënten ouder dan 65 jaar? ____ %
20. Wat is het geschatte aandeel patiënten met verhoogde tegemoetkoming? ____ %
21. Wat is het (geschatte) aandeel patiënten met migratieachtergrond? ____ %
22. Wat is het (geschatte) aandeel patiënten dat geen Nederlands, Frans of Duits spreekt? ____ %

<u>Vragen over uw gezin</u>

23. Is uw partner tewerkgesteld in de zorg met patiëntencontact?
    □ ja
    □ nee
24. Hoeveel gezinsleden telt uw huishouden, uzelf inbegrepen? ____
    - □ Hoeveel kinderen dat naar de crèche gaat? ____
    - □ Hoeveel kinderen jonger dan 6 jaar? ____
    - □ Hoeveel kinderen tussen 6 en 18 jaar? ____
    - □ Hoeveel studerende gezinsleden ouder dan 18 jaar? ____
    - □ Hoeveel werkende gezinsleden ouder dan 18 jaar? ____
25. Hoeveel gezinsleden hadden dit jaar klachten die bij COVID-19 passen, uzelf inbegrepen? ____
    - Als u klachten had, welk klachten waren dat dan?
        □ hoest
        □ hoofdpijn
        □ keelpijn
        □ koorts
        □ kortademigheid
        □ neusloop
        □ spierpijn
        □ verlies van geur
        □ verlies van smaak
        □ algemene zwakte/vermoeidheid
        □ misselijkheid/braken
        □ diarree
        □ andere, namelijk
        ……..

26. Hoeveel gezinsleden zijn getest voor COVID-19, uzelf inbegrepen (testen voor onderzoeksdoeleinden niet meegerekend)? ____
    - Hoe vaak bent u al getest? _____
    - Wanneer bent u voor de eerste keer? (dd/mm/jjjj): ____/____/_____
    - Op basis van welk staalmateriaal?
        - □ nasopharyngeale wisser
        - □ gecombineerde keel-neus wisser
        - □ bloedname
        - □ andere, namelijk
        - ……..
    - Met welke test(en)?
        - □ virusdetectie
        - □ antilichaamdetectie
        - □ andere, namelijk
        - ……..
    - Wanneer bent u voor de tweede keer getest? (dd/mm/jjjj): ____/____/_____
    - Op basis van welk staalmateriaal?
        - □ nasopharyngeale wisser
        - □ gecombineerde keel-neus wisser
        - □ bloedname
        - □ andere, namelijk
        - ……..
    - Met welke test(en)?
        - □ virusdetectie
        - □ antilichaamdetectie
        - □ andere, namelijk
        - ……..
    - Wanneer bent u voor de derde keer getest? (dd/mm/jjjj): ____/____/_____
    - Op basis van welk staalmateriaal?
        - □ nasopharyngeale wisser
        - □ gecombineerde keel-neus wisser
        - □ bloedname
        - □ andere, namelijk
        - ……..
    - Met welke test(en)?
        - □ virusdetectie
        - □ antilichaamdetectie
        - □ andere, namelijk
        - ……..

27. Hoeveel gezinsleden testten positief voor COVID-19, uzelf inbegrepen? ____
    - Als u positief testte, wanneer werd het positieve staal afgenomen? (dd/mm/jjjj): ____/____/_____
    - Als u positief testte, wie was de vermoedelijke bron van de besmetting?
        - □ patiënt
        - □ medewerker
        - □ gezinslid
        - □ andere, namelijk
        - ……..

28. Hoeveel gezinsleden zijn behandeld voor (vermoeden van) COVID-19, uzelf inbegrepen? ____
    - Als u bent behandeld, welke behandeling was dat?
        - □ symptomatische behandeling van pijn, koorts en andere klachten
        - □ hydroxychloroquine
        - □ antibiotica
        - □ andere, namelijk ……..
29. Hoeveel gezinsleden zijn opgenomen in het ziekenhuis voor (vermoeden van) COVID-19, uzelf inbegrepen? ____
    - Als u bent opgenomen, hoe lang was u in het ziekenhuis? ____ dagen
    - Als u bent opgenomen, hoe lang bent u op intensieve zorg behandeld? ____ dagen

<u>Risicofactoren voor COVID-19</u>

30. Ben u sinds de uitbraak steeds blijven werken?
    - □ ja
    - □ nee
31. Hebt u sinds de uitbraak fysiek contact gehad met patiënten met bevestigde COVID-19?
    - □ ja, met hoeveel?
        - □ 1- 5
        - □ 6 – 10
        - □ 11 – 15
        - □ 16 – 20
        - □ > 20
    - □ nee
32. Had u sinds de uitbraak soms geen beschermingsmateriaal ter beschikking?
    - □ ja, welk? (meerdere antwoorden mogelijk)
        - □ Handschoenen
        - □ Chirurgisch mondmasker
        - □ Ander mondmasker (FFP2 of FFP3)
        - □ veiligheidsbril
        - □ Schort/lichaamsbescherming
        - □ Ander, namelijk ……..
    - □ nee
33. Indien beschikbaar, welk beschermingsmateriaal gebruikt u bij patiënten met (vermoeden van COVID-19)? (meerdere antwoorden mogelijk)
    - □ Handschoenen
    - □ Chirurgisch mondmasker
    - □ Ander mondmasker (FFP2 of FFP3)
    - □ veiligheidsbril
    - □ Schort/lichaamsbescherming
    - □ Ander beschermingsmateriaal, namelijk ……..

34. Indien beschikbaar, welk beschermingsmateriaal gebruikt u bij uw andere patiënten? (meerdere antwoorden mogelijk)
    - □ Handschoenen
    - □ Chirurgisch mondmasker
    - □ Ander mondmasker (FFP2 of FFP3)
    - □ Veiligheidsbril
    - □ Schort/lichaamsbescherming
    - □ Ander beschermingsmateriaal, namelijk ……..
35. Hebt u meegewerkt aan de COVID triage van patiënten?
    - □ ja, hoeveel patiënten hebt u fysiek onderzocht die nadien COVID-19 positief bleken?
        - □ 0
        - □ 1 – 5
        - □ 6 – 10
        - □ 11 – 15
        - □ 16 – 20
        - □ > 20
    - □ nee

<u>Opvattingen</u>

Geef aan in welke mate u het eens bent met volgende stellingen (1=helemaal oneens; 5= helemaal eens):

	1	2	3	4	5
36. Ik ben er zeker van dat ik al besmet ben met COVID-19					
37. Ik zal zeker besmet worden met COVID-19 tijdens deze epidemie					
38. Ik vrees dat ik mijn familieleden besmet					
39. Ik vrees dat ik zal sterven van COVID-19 in de komende maanden					
40. De richtlijnen voor huisartsen werden duidelijk gecommuniceerd					
41. De richtlijnen voor huisartsen zijn wetenschappelijk onderbouwd					
42. Het Belgisch systeem is sterk genoeg om deze epidemie goed op te vangen					
43. De testcapaciteit in België is voldoende					
44. De maatregelen die de regering oplegt zijn voldoende					
45. Iedereen moet een masker dragen indien hij/zij zich buitenhuis begeeft					
46. Ik heb alle vertrouwen in de wetenschappelijke COVID-19 ‘task force’					
47. De meeste van mijn patiënten houden zich aan de regels van ‘social distancing’					
48. De meeste van mijn patiënten houden zich aan de regels voor hygiëne					
49. De meeste van mijn symptomatische patiënten houden zich aan zelf-quarantaine					
50. Deze periode is meer stressvol dan tijdens een drukke griepperiode					

APPENDIX 5: FOLLOW-UP QUESTIONNAIRE (DUTCH VERSION)

Gelieve deze vragenlijst zelf en volledig in te vullen met informatie die nieuw is sinds het vorige meetmoment.

1. Uw studiecode: __ __ __ __
2. U dient dit formulier in als:
    - Huisarts
    - Andere zorgverlener, bv. verpleegkundige
    - Andere medewerkers, bv. secretariaatsmedewerker
3. U werkte sinds het vorige meetmoment ook (meerdere antwoorden mogelijk):
    - □ Als CRA
    - □ In een ziekenhuis
    - □ In een instelling (bv. psychiatrie, gehandicaptenzorg, ...)
    - □ Ergens anders, namelijk
      ……..
4. Datum waarop u de sneltest uitvoerde? (dd/mm/jjjj): ____/____/_____
5. Resultaat van uw sneltest?
   IgM
   □ positief
   □ negatief
   □ onduidelijk
   IgG
   □ positief
   □ negatief
   □ onduidelijk
   □ ongeldig
6. Datum waarop u deze vragenlijst invult? (dd/mm/jjjj): ____/____/_____
7. Hoeveel gezinsleden hebben sinds het vorige meetmoment klachten gehad die bij COVID-19 passen, uzelf inbegrepen? ____
    - Als u klachten had, welk klachten waren dat dan?
      □ hoest
      □ hoofdpijn
      □ keelpijn
      □ koorts
      □ kortademigheid
      □ neusloop
      □ spierpijn
      □ verlies van geur
      □ verlies van smaak
      □ algemene zwakte/vermoeidheid
      □ misselijkheid/braken
      □ diarree
      □ andere, namelijk
      ……..
8. Zijn er sinds het vorige meetmoment gezinsleden getest voor COVID-19, uzelf inbegrepen?
    - □ Ja
    - □ Nee

COVID-19 test - details

9. Hoeveel gezinsleden uit uw huishouden zijn sinds het vorige meetmoment getest voor COVID-19, uzelf inbegrepen (testen voor onderzoeksdoeleinden niet meegerekend)? ____
    - Als u zelf bent getest, wanneer was dat dan? (dd/mm/jjjj): ____/____/_____
    - Als u zelf bent getest, op basis van welk staalmateriaal?
        - □ Nasopharyngeale wisser
        - □ Gecombineerde keel-neus wisser
        - □ Bloedname
        - □ Andere, namelijk ……..
    - Als u zelf bent getest, met welke test(en)?
        - □ Virusdetectie
        - □ Antilichaamdetectie
        - □ Andere, namelijk ……..
10. Hoeveel gezinsleden testten sinds het vorige meetmoment positief voor COVID-19, uzelf inbegrepen? ____
    - Als u positief testte, wie was de vermoedelijk bron van de besmetting?
        - □ Patiënt
        - □ Medewerker
        - □ Gezinslid
        - □ Andere, namelijk ……..

COVID-19 behandeling - details

11. Hoeveel gezinsleden zijn sinds het vorige meetmoment behandeld voor (vermoeden van) COVID-19, uzelf inbegrepen? ____
    - Als u bent behandeld, welke behandeling was dat?
        - □ Symptomatische behandeling van pijn, koorts en andere klachten
        - □ Hydroxychloroquine
        - □ Antibiotica
        - □ Andere, namelijk ……..
12. Hoeveel gezinsleden zijn sinds het vorige meetmoment opgenomen in het ziekenhuis voor COVID-19, uzelf inbegrepen? ____
    - Als u bent opgenomen, hoe lang was u in het ziekenhuis? ____ dagen
    - Als u bent opgenomen, hoe lang bent u op intensieve zorg behandeld? ____ dagen
13. Ben u sinds het vorige meetmoment steeds blijven werken?
    - □ ja
    - □ nee
14. Hebt u sinds het vorige meetmoment fysiek contact gehad met patiënten met bevestigde COVID-19?
    - □ ja, met hoeveel?
        - □ 1- 5
        - □ 6 – 10
        - □ 11 – 15
        - □ 16 – 20
        - □ > 20
    - □ nee

15. Had u sinds het vorige meetmoment soms geen beschermingsmateriaal ter beschikking?
    - □ ja, welk? (meerdere antwoorden mogelijk)
        - □ Handschoenen
        - □ Chirurgisch mondmasker
        - □ Ander mondmasker (FFP2 of FFP3)
        - □ Veiligheidsbril
        - □ Schort/lichaamsbescherming
        - □ Ander, namelijk
        - ……..
    - □ nee
16. Indien sinds het vorige meetmoment beschikbaar, welk beschermingsmateriaal gebruikt u bij patiënten met (vermoeden van**)** COVID-19? (meerdere antwoorden mogelijk)
    - □ Handschoenen
    - □ Chirurgisch mondmasker
    - □ Ander mondmasker (FFP2 of FFP3)
    - □ Veiligheidsbril
    - □ Schort/lichaamsbescherming
    - □ Ander beschermingsmateriaal, namelijk
    - ……..
17. Indien sinds het vorige meetmoment beschikbaar, welk beschermingsmateriaal gebruikt u bij uw andere patiënten?
    - □ Handschoenen
    - □ Chirurgisch mondmasker
    - □ Ander mondmasker (FFP2 of FFP3)
    - □ Veiligheidsbril
    - □ Schort/lichaamsbescherming
    - □ Ander beschermingsmateriaal, namelijk
    - ……..
18. Hebt u sinds het vorige meetmoment meegewerkt aan de COVID triage van patiënten?
    - □ ja, hoeveel patiënten hebt u fysiek onderzocht die nadien COVID-19 positief bleken?
        - □ 0
        - □ 1- 5
        - □ 6 – 10
        - □ 11 – 15
        - □ 16 – 20
        - □ > 20
    - □ nee

Opvattingen

In welke mate u het eens bent met volgende stellingen? (1=helemaal oneens; 5= helemaal eens)

	1	2	3	4	5
19. Ik ben er zeker van dat ik al besmet ben met COVID-19					
20. Ik zal zeker besmet worden met COVID-19 tijdens deze epidemie					
21. Ik vrees dat ik mijn familieleden besmet					
22. Ik vrees dat ik zal sterven van COVID-19 in de komende maanden					
23. De richtlijnen voor huisartsen werden duidelijk gecommuniceerd					
24. De richtlijnen voor huisartsen zijn wetenschappelijk onderbouwd					
25. Het Belgisch systeem is sterk genoeg om deze epidemie goed op te vangen					
26. De testcapaciteit in België is voldoende					
27. De maatregelen die de regering oplegt zijn voldoende					
28. Iedereen moet een masker dragen indien hij/zij zich buitenhuis begeeft					
29. Ik heb alle vertrouwen in de wetenschappelijke COVID-19 ‘task force’					
30. De meeste van mijn patiënten houden zich aan de regels van ‘social distancing’					
31. De meeste van mijn patiënten houden zich aan de regels voor hygiëne					
32. De meeste van mijn symptomatische patiënten houden zich aan zelf-quarantaine					
33. Deze periode is meer stressvol dan tijdens een drukke griepperiode					

APPENDIX 6: ONLINE REGISTRATION FORM

https://surveys.sciensano.be/index.php/748475

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