Prevalence, incidence and longevity of antibodies against SARS-CoV-2 among primary healthcare providers in Belgium: a prospective cohort study with 12 months of follow-up

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ABSTRACT

Objectives To estimate the prevalence, incidence and longevity of antibodies against SARS-CoV-2 among primary healthcare providers (PHCPs).

Design Prospective cohort study with 12 months of follow-up.

Setting Primary care in Belgium.

Participants Any general practitioner (GP) working in primary care in Belgium and any other PHCP from the same GP practice who physically manages (examines, tests, treats) patients were eligible. A convenience sample of 3648 eligible PHCPs from 2001 GP practices registered for this study (3044 and 604 to start in December 2020 and January 2021, respectively). 3390 PHCPs (92.9%) participated in their first testing time point (2820 and 565, respectively) and 2557 PHCPs (70.1%) in the last testing time point (December 2021).

Interventions Participants were asked to perform a rapid serological test targeting IgM and IgG against the receptor binding domain of SARS-CoV-2 and to complete an online questionnaire at each of maximum eight testing time points.

Primary and secondary outcome measures The prevalence, incidence and longevity of antibodies against SARS-CoV-2 both after natural infection and after vaccination.

Results Among all participants, 67% were women and 77% GPs. Median age was 43 years. The seroprevalence in December 2020 (before vaccination availability) was 15.1% (95% CI 13.5% to 16.6%), increased to 84.2% (95% CI 82.9% to 85.5%) in March 2021 (after vaccination availability) and reached 93.9% (95% CI 92.9% to 94.9%) in December 2021 (during booster vaccination availability and fourth (delta variant dominant) COVID-19 wave). Among not (yet) vaccinated participants the first monthly incidence of antibodies against SARS-CoV-2 was estimated to be 2.91% (95% CI 1.80% to 4.01%). The longevity of antibodies is higher in PHCPs with self-reported COVID-19 infection.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ Prospective cohort study with good response during 12 months of follow-up.
⇒ Rapid serological test (RST) measuring the presence of antibodies against SARS-CoV-2 after infection and vaccination, without distinction.
⇒ Timely and comparable estimates of the prevalence of antibodies against SARS-CoV-2 among primary healthcare providers.
⇒ Large sample size permitting precise estimates at national and regional level.
⇒ Convenience sample, missing data points and potentially lower actual RST accuracy limiting the study validity.

Conclusions This study confirms that occupational health measures provided sufficient protection when managing patients. High uptake of vaccination resulted in high seroprevalence of SARS-CoV-2 antibodies in PHCPs in Belgium. Longevity of antibodies was supported by booster vaccination and virus circulation.

Trial registration number NCT04779424.

INTRODUCTION

As of 8 June 2022, SARS-CoV-2 has caused over 530 million infections worldwide (4 164 698 in Belgium) and caused over 6.3 million deaths from coronavirus disease (COVID-19) worldwide (over 31 000 in Belgium).1 COVID-19 can be a lethal respiratory tract infection (RTI), but often presents with mild symptoms or remains asymptomatic.

Since the start of the COVID-19 pandemic, SARS-CoV-2 seroprevalence estimates have provided essential information about population exposure to infection and helped predict
the early course of the epidemic.\textsuperscript{2,3} When setting up this study, seroprevalence studies in Iceland\textsuperscript{4} and Spain\textsuperscript{5} 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 is associated with, for example, illness severity, age and comorbidities.\textsuperscript{6-8} Meanwhile, other seroprevalence studies showed antibody positivity lasting up to 9 months.\textsuperscript{9,10} Additionally, after vaccination, longevity of antibody positivity could differ depending on the type of vaccination and vaccination regime.\textsuperscript{11,12} For Belgium, Sciensano (the Belgian national institute of public health, www.sciensano.be) performs national seroprevalence studies of SARS-CoV-2 antibodies in the general population\textsuperscript{13} and several relevant populations including school-aged children and school staff,\textsuperscript{14} hospital staff,\textsuperscript{15} nursing homes residents and their staff.\textsuperscript{16,17} These results are publicly available and regularly updated on an online dashboard.\textsuperscript{18}

This article focuses on the seroprevalence among primary healthcare providers (PHCPs).\textsuperscript{19} PHCPs manage the vast majority of patient contacts, including COVID-19 patients, and therefore, play an essential role in the efficient organisation of healthcare.\textsuperscript{20,21} 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.\textsuperscript{22} In Belgium, this is particularly concerning given that the GP workforce consists of mainly older adults and is therefore at higher risk for COVID-19-related morbidity and mortality.\textsuperscript{23} In Italy, GPs represented up to 38% of the physicians who died from COVID-19 early in the epidemic.\textsuperscript{24}

Before the start of this study (December 2020), data on how many PHCPs in Belgium had been infected by SARS-CoV-2 was not readily available,\textsuperscript{25} and effective vaccines for PHCPs were not anticipated to be available in the near future.

During the COVID-19 crisis rapid serological tests (RSTs) have been developed to identify the presence of antibodies to SARS-CoV-2. Compared with laboratory tests, a valid easy-to-use RST could speed up the availability of the test results for both the participants and the national health authorities.\textsuperscript{25} Furthermore, by using RSTs in this study, PHCPs got the opportunity to become more familiar with this type of technology.

Sciensano has validated five RSTs using finger prick blood, identifying one test with appropriate sensitivity (92.9%) and specificity (96.3%) for use in seroprevalence studies.\textsuperscript{26} We used this RST for this study. It targets IgM and IgG against the receptor binding domain (RBD) of SARS-CoV-2 and could therefore also provide valuable information in a vaccinated population.

Given the availability of vaccines for PHCPs soon after the start of this study, we now report on the prevalence of antibodies against SARS-CoV-2 among a cohort of PHCPs in Belgium followed-up for 12 months, and on the incidence and longevity of those antibodies both after natural infection and after vaccination.

**METHODS**

This study was a prospective cohort study. Data collection was performed according to the publicly available protocol, providing more details on the study methods.\textsuperscript{19}

**Study population**

Any GP working in Belgium (including those in professional training) working in primary care and any PHCP from the same GP practice in a clinical role (clinical examination, testing or treating patients) were eligible if they were able to comply with the study protocol and provided informed consent to participate in the study. Staff hired on a temporary (interim) basis were excluded as follow-up over time would be compromised. Administrative staff or technical staff without any prolonged (longer than 15 min) face-to-face contact with patients and PHCPs who were not professionally active during the inclusion period were not eligible either.

PHCPs were recruited between 15 November 2020 and 15 January 2021. GPs working in clinical practice in Belgium were invited to register online for participation in this national epidemiological study and were asked to invite the other PHCPs in their practice to do the same. We emphasised that PHCPs who had already been diagnosed with COVID-19 were also eligible. Information about the study was disseminated to GPs and PHCPs via professional organisations (Domus Medica and Collège de Médecine Générale), university networks across the country and through professional media channels. We checked our convenience sample for representativeness in terms of geographic and demographic characteristics.\textsuperscript{23}

To assess the geographical representativeness of our sample, we compared the distribution by region and by province of active GPs in Belgium in 2020 (source www ima-aim.be) with the distribution of participating GPs.

**Data collection**

On inclusion in the study, participants were assigned a unique study code by the researchers and received testing material at their workplace through regular mail. At their first testing time point they received an invitation by email inviting them to autocollect a capillary blood sample and analyse it using the RST (OrientGene) and to complete a baseline questionnaire available in Dutch, French and English via a personalised link through a secured online platform hosted by Sciensano (Limesurvey). The invitation email included links to both written and video instructions to perform the RST on yourself and on someone else.

The baseline questionnaire at the first testing time point asked for written informed consent and for information about the result of the RST, basic sociodemographic data (age, gender, composition
of household—eg, presence of school-aged children in the house), professional data (practice patient size), health status (pre-existing health conditions, regular medication use, presence of symptoms since the start of the epidemic, previous positive test results for COVID-19), professional exposure (contact with confirmed cases, use of infection prevention and control measures and the availability of personal protective equipment (PPE)) and practice organisational aspects (delayed care for non-urgent conditions) (see online supplemental file 1). A follow-up questionnaire was sent for each of the subsequent testing time points. In addition to the RST result, it collected information on the health status, including the presence of symptoms, COVID-19 testing and results, vaccination status (date of vaccination, type of vaccine, number of doses, presence of side effects) and professional exposure (contact with confirmed cases, use of infection prevention and control measures) (see online supplemental file 2).

Follow-up
The study lasted 12 months, from December 2020 to December 2021, and included eight testing time points. Compared with the study protocol, the testing time point at the fifth month was skipped because of limited additional epidemiological value based on progressive insights from studies with similar protocols conducted by Sciensano that longer interval than 4 weeks between testing time point are suitable.

Sample size
This study aimed to include 5000 PHCPs with a ratio of 4 GPs to 1 other PHCP. The sample size considerations regarding the different objectives of the proposed study are described in more detail in the study protocol. For the objectives reported here, even half the sample size aimed for would allow for precise estimates of the prevalence, incidence and longevity of antibodies against SARS-CoV-2.

Data analysis
In the analysis, we included all PHCPs who provided informed consent and reported RST results at the testing time points. If in the questionnaire the entry for the date the RST was performed was missing or implausible, the date of completing the questionnaire was used instead. All analyses were conducted using R V.4.1.0 (www.R-project.org).

Prevalence
To assess the prevalence of antibodies against SARS-CoV-2, we calculated among the valid RST the proportion (95% CI) of positive RST for IgG and/or IgM, and for IgG and IgM separately (crude seroprevalences). In addition, we calculated the proportion (95% CI) of PHCPs that self-reported testing positive for SARS-CoV-2 (no test specified, so this includes both virus or antibody detection) since the outbreak of the COVID-19 pandemic (February 2020) and the proportion (95% CI) of PHCPs with any positive test, either a positive study RST or testing positive since the outbreak at their first testing time point. For any subsequent testing time points, we asked the participants to specify if self-reported testing positive for SARS-CoV-2 since the previous testing time point concerned virus or antibody detection.

We also estimated the prevalence of antibodies against SARS-CoV-2 (IgG and/or IgM) taking into account clustering of PHCPs within their practice as well as the distribution of PHCPs across the districts in Belgium (adjusted seroprevalences). Weights were calculated based on the differences between the actual distribution of GPs across districts and the distribution of participating GPs with RST results across districts. These weights were then extrapolated to all other PHCPs. The estimates are based on generalised estimating equations assuming a binomial distribution for the RST result, an identity link function and an independent working correlation matrix. In a similar way, we also estimated the adjusted prevalence of self-reported positive testing for SARS-CoV-2 since the start of the COVID-19 pandemic and the adjusted prevalence of these two tests results combined, either a positive study RST or testing positive since the outbreak for the first two testing time points.

Incidence
To assess the incidence of antibodies against SARS-CoV-2 (IgG and/or IgM) among participants not (yet) vaccinated, first we produced a Kaplan-Meier plot including participants providing a valid negative RST result at their first testing time point and not testing positive before, considering a positive RST during follow-up as event and censoring on vaccination or lost to follow-up. Second, we assessed the monthly incidence of antibodies against SARS-CoV-2 due to natural infection in those not yet vaccinated, by analysing the data collected during the testing time points after the first testing time point. We included participants providing valid RST results both at the testing time point assessed and the preceding testing time point. We excluded participants reporting a positive RST at the preceding time point or already vaccinated with a first dose. In addition, we corrected the estimates for clustering of participants in general practices.

To assess the incidence of antibodies against SARS-CoV-2 (IgG and/or IgM) due to vaccination in those vaccinated, we calculated the proportion of participants with antibodies against SARS-CoV-2 less than 7 days and 7 days or more after the first, the second and the third dose of a COVID-19 vaccine, respectively, and stratified by self-reported history of COVID-19 infection.

Longevity
To assess the longevity of antibodies against SARS-CoV-2 (IgG and/or IgM) among participants not (yet) vaccinated, first we produced a Kaplan-Meier plot including...
of third dose) or lost to follow-up (midpoint and interval censoring).

Vaccination
The start of the vaccination of PHCPs during the study follow-up provided the opportunity to monitor its progress.

Patient and public involvement
Neither patients (or PHCPs in this specific study) nor the public were involved in the design of the study. During the study, the information shown in figure 1 was shared with the participants and the general population through the publicly available website of the Belgian health authorities (Sciensano) shortly after each testing—time point both for Belgium and its three regions, Brussels, Flanders and Wallonia.

RESULTS
Description of the study cohort
In total, 3648 eligible PHCPs from 2001 practices registered and were asked to provide informed consent of whom 3044 and 604 PHCPs were sent personal study materials to be able to collect data for their first testing time point starting on 24 December 2020 and 25 January 2021, respectively. A total of 3390 PHCPs participated in their first testing time point by completing the baseline questionnaire, among which 2597 GPs, 386 GPs in training and 407 other PHCPs (table 1).

Our sampling procedure resulted in the participation of a reasonably geographically representative sample of GPs at the level of the provinces (online supplemental table S1). At the level of the regions, there is about 8% overrepresentation of GPs in Flanders and corresponding underrepresentation of GPs in Wallonia.

Participant characteristics
Table 1 presents the characteristics of the 3390 PHCPs who participated in their first (baseline) testing time point. These PHCPs, mainly GPs, were relatively young, more often female and working more often in (large) group practices than in solo or duo practices. Table 2 shows in how many testing time points PHCPs participated. A total of 3415 (93.6%) PHCPs participated in at least one testing time point, 2909 (79.7%) participated in 6 and 2141 (58.7%) participated in all 8 testing time points. The number of PHCPs participating per testing time point is presented in online supplemental table S2. While the response rate gradually decreased, still 2557 (77.2% of invited PHCPs) participated in the last testing time point.

Vaccination status
Overall, 3227 participants received a full primary vaccination. 2783 participants received two doses of an m-RNA vaccine (2639 (81.8%) BNT162b2, 144 (4.5%) mRNA-1273 and 2 (0.1%) mRNA-1273 followed by BNT162b2). A total of 437 participants (13.5%) received two doses of
ChAdOx1-S and 5 (0.2%) participants one dose of Ad26.COVA2S.

At the final testing time point, 2211 of the participants had received a booster vaccination. A total of 1879 (85.0%) participants received a booster with BNT162b2 and 267 (12.1%) with mRNA-1273. 1 participant received ChAdOx1-S and another participant Ad26.COV2.S as third dose.

Prevalence

The prevalence of antibodies against SARS-CoV-2 among PHCPs in Belgium from December 2020 to December 2021 is shown in figure 1 and online supplemental table S3. Online supplemental table S3 also gives the number of eligible PHCPs, that is, those testing between the start and end date of the respective testing time point, as well as the regional differences. At the first testing time point (T1), among 2680 eligible PHCPs, 2629 provided valid test results, of which 366 (15.1%) were positive. Afterwards, the prevalence increased substantially up to 84.2% at T4, mainly due to vaccination (see online supplemental table S4). Six months later (T7) the prevalence was substantially lower (70.2%), while during the fourth COVID-19 wave (delta variant dominant) and after booster vaccination became available it increased again to 93.9% (T8).

Incidence

Among not (yet) vaccinated participants

The incidence of antibodies against SARS-CoV-2 among vaccinated PHCPs in Belgium according to their self-reported history of COVID-19 infection is shown in figure 3. The incidence of antibodies is higher in PHCPs with self-reported COVID-19 infection compared with PHCPs with no self-reported COVID-19 infection both less than 7 days and 7 days or more after the first and the

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Characteristics of primary healthcare providers (PHCPs), including general practitioners (GPs), GPs in training and other PHCPs who participated in their first testing time points*</th>
</tr>
</thead>
<tbody>
<tr>
<td>PHCPs n=3390</td>
<td>GPs n=2597</td>
</tr>
<tr>
<td>Age†, median (IQR)</td>
<td>40 (31-54)</td>
</tr>
<tr>
<td>Gender‡, n (%)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1119 (33.0)</td>
</tr>
<tr>
<td>Female</td>
<td>2296 (66.9)</td>
</tr>
<tr>
<td>Not reported</td>
<td>2 (0.1)</td>
</tr>
<tr>
<td>Practice size, n (%)‡</td>
<td></td>
</tr>
<tr>
<td>Solo</td>
<td>618 (33.5)</td>
</tr>
<tr>
<td>Duo</td>
<td>361 (19.6)</td>
</tr>
<tr>
<td>Group (&lt;8 employees)</td>
<td>382 (20.7)</td>
</tr>
<tr>
<td>Large group (&gt;7 employees)</td>
<td>444 (24.1)</td>
</tr>
</tbody>
</table>

*The first testing time point was December 2020 for 2820 and January 2021 for 570 PHCPs, respectively.
†Ages <21 were considered unrealistic and recoded as missing; IQR=IQR range.
‡If numbers do not add up to the column total, this is due to missing data; numbers of practices for PHCPs=1845, GPs=1672, GPs in training=335 and other PHCPs=245.

<table>
<thead>
<tr>
<th>Table 2</th>
<th>The number of testing time points that primary healthcare providers (PHCPs) participated in</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of testing time points participated in</td>
<td>No of PHCPs (%)</td>
</tr>
<tr>
<td>8*</td>
<td>2141 (58.7)</td>
</tr>
<tr>
<td>7</td>
<td>490 (13.4)</td>
</tr>
<tr>
<td>6</td>
<td>278 (7.6)</td>
</tr>
<tr>
<td>5</td>
<td>153 (4.2)</td>
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<tr>
<td>4</td>
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<tr>
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<td>46 (1.3)</td>
</tr>
<tr>
<td>0</td>
<td>233 (6.4)</td>
</tr>
</tbody>
</table>

second dose, less than 7 days after the third dose, but not 7 days or more after the third dose.

**Longevity**

**Among not (yet) vaccinated participants**

The longevity of antibodies against SARS-CoV-2 among not (yet) vaccinated PHPCs in Belgium is shown in figure 4.

For T2 the positivity of antibodies against SARS-CoV-2 was estimated to be 18.54% (95% CI 12.84% to 24.24%; n=178) lower compared with T1, that is, the proportion of participants not yet vaccinated at T1 and testing positive at T1 for SARS-CoV-2 antibodies that tested negative for SARS-CoV-2 antibodies at T2. For T3 and T4 it was estimated to be 19.42% (95% CI 11.76% to 27.07%; n=103) and 12.50% (95% CI 0.99% to 24.01%; n=32), respectively. As of T4, the sample size of eligible participants was too small for precise estimates.

**Among participants after full primary vaccination**

The longevity of antibodies against SARS-CoV-2 among PHCPs in Belgium who have received their full primary vaccination, but not yet a booster vaccination, according to their self-reported history of COVID-19 infection is shown in figure 5. The longevity of antibodies is higher in PHCPs with self-reported COVID-19 infection compared with PHCPs without self-reported COVID-19 infection after full primary vaccination.

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**Figure 2** Kaplan-Meier plot of incidence of antibodies against SARS-CoV-2 among primary healthcare providers in Belgium not yet vaccinated after self-reported COVID-19 infection. Interval censoring is taken into account by assuming that the actual event occurred somewhere between the testing time point of the event and the testing time point before.

**Figure 3** Incidence of antibodies against SARS-CoV-2 among primary healthcare providers in Belgium after vaccination according to self-reported history of COVID-19 infection.

**Figure 4** Kaplan-Meier plot of longevity of antibodies against SARS-CoV-2 among PHCPs in Belgium after self-reported history of COVID-19 infection. Interval censoring is taken into account by assuming that the actual event occurred somewhere between the testing time point of the event and the testing time point before.
DISCUSSION

The prevalence of antibodies against SARS-CoV-2 among PHCPs in Belgium was 15.1% in December 2020, that is, before vaccination had started and right after the second COVID-19 wave that peaked beginning November 2020, and reached 93.9% in December 2021, i.e. after booster vaccination had started and after the fourth Belgian COVID-19 wave in which the Delta variant was dominant and that peaked beginning December 2021.

The incidence of antibodies against SARS-CoV-2 within 2 weeks after COVID-19 vaccination with a first dose was higher in PHCPs with a self-reported history of COVID-19 infection compared with those with no self-reported history of infection. The longevity of antibodies was more pronounced in the former group of PHCPs than in those with no self-reported history of infection.

The seroprevalence in PHCPs before vaccination (15.1%) appeared to be lower than that among the general population (18.7%) and that among hospital healthcare workers (19.7%) in Belgium, in December 2020, when the Belgian healthcare system was approaching the end of the second COVID-19 wave. It should, however, be noted that the accuracy of the RST might be lower when used by many different PHCPs instead of a few trained and experienced staff (for validation) and lower than analysis of a serum sample in the lab (for seroprevalence in the general population and in hospital healthcare workers) using conventional lab-tests. This is suggested by the lower seroprevalence in this study for PHCPs in Flanders compared with that in an earlier prospective cohort study using dried blood spots (DBS) analysed in the lab. Not finding a higher seroprevalence among PHCPs, generally concerned about being at high risk of COVID-19 infections, compared with the general population might be explained by the availability and proper usage of PPE.

Most PHCPs in our study (94.49%) received a first vaccine dose in the period January–March explaining the increase in seroprevalence to 84.1% in April 2021. The monthly incidence of antibodies due to natural infection in those not yet vaccinated in the same time period was estimated to be around 4% in this study. Natural course of infection could, therefore, not have caused a similar rise in seroprevalence.

A gradual decrease in the prevalence of anti-SARS-CoV-2 antibodies among PHCP was observed in the following months leading to a seroprevalence of 70.2% in September 2021. In December 2021 most PHCPs (86.5% of participants in testing time point 8) already received a booster dose of a COVID-19 vaccine resulting in a seroprevalence of 93.1% at the end of the study. Although, also the circulation of Delta variant corona virus might have impacted this increase in seroprevalence. For example, the seroprevalence in mainly unvaccinated schoolchildren in Belgium almost doubled during the fourth COVID-19 wave (26.6% at 8 October 2021 vs 50.9% at 15 December 2021). Natural infection before vaccination did seem to limit waning of antibodies after vaccination. These findings strengthen the accruing evidence base for reduced protection from infection in vaccinated, but previously uninfected participants. The clinical significance is however still to be determined. A reduction in vaccine effectiveness against infection could increase transmission to and the risk of infection among high-risk persons who consult PHCPs, some of whom may have progression to severe disease. In addition, recent studies have shown that vaccination confers more durable protection against severe outcomes of hospitalisation and death than against mild symptomatic and asymptomatic infection.

At this point, studies suggest that a third or booster dose provides additional protection on top of simply reversing previous waning, but that the greatest protection from
the worst clinical outcomes still remains heavily concentrated in the first two doses.32–36

Although studies suggest prolonged protection, it remains unclear to what extent the presence of antibodies (against the RBD) is associated with protection against new variants of the coronavirus.36 37 Neutralising antibody titers measured in the laboratory remain the strongest correlate of protection against symptomatic and severe illness across multiple variants.38 39

This large cohort study with 12 months follow-up provided precise estimates of the prevalence and incidence of antibodies against SARS-CoV-2 among PHCPs at national and regional level. Another strength of this study is the use of RSTs. This substantially improved the timeliness of the test result availability and allowed the PHCPs to immediately check their results, which was not the case in our previous work that used DBS to assess the prevalence and incidence of antibodies against SARS-CoV-2 among PHCPs in Flanders.23 Consequently, the results in PHCPs in Belgium could be compared much faster to that of the general population and other population groups, for example, healthcare workers in hospitals and nursing homes.

In addition, the RST used in this study allowed us to estimate the incidence and longevity of antibodies against SARS-CoV-2 both after natural infection and after vaccination. This, on the other hand, also limits seroprevalence studies like ours and others,16 using an RST not able to distinguish antibodies after natural infection (with new variants) from antibodies after vaccination, to assess virus circulation once the target population is highly vaccinated.

Lost to follow-up or missing data, reduced accuracy of the RST in primary care and the use of a convenience sample could also have limited the validity of the study results. However, overall retention and response of PHCPs in the study was good to excellent, we used the best available RST to avoid under- and overestimation of the presence of SARS-CoV-2 among PHCPs due to imperfect testing methods (imperfect sensitivity and specificity), and the estimates were corrected for clustering and potential geographical misrepresentation of the PHCPs. Still, the RST used is less accurate than the ELISA and missing this reference test’s quantitative aspect.

Selection bias is possible, because the study started at the end of the second COVID-19 wave: if all the most vulnerable PHCPs had 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). Therefore, we explicitly asked for participation regardless of previous SARS-CoV-2 testing and test results.

In conclusion, this national study confirms results from an earlier study at regional level (Flanders only) that for the PHCPs seroprevalence and incidence during the second COVID-19 wave was similar to that of the general population suggesting that the occupational health measures implemented provided sufficient protection when managing patients. A vaccination programme including one booster increased the seroprevalence of antibodies against SARS-CoV-2 leading to a seroprevalence of 93.9% in December 2021. Between primary and booster vaccination, longevity of antibodies was more pronounced in PHCPs with a history of self-reported COVID-19 infection. Therefore, continued monitoring of the seroprevalence in PHCPs after booster vaccination, with longer time intervals, could be relevant, provided that the presence of antibodies is associated with protection.

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Contributors The study concept and design was initiated by SC, NA, BS and ED and finalised with contributions from JYJV, ADS, SH, AVDB, ID, PVD, HG, SC, NA, BS and PVN conducted registration and data collection. Analysis was performed by RB. NA prepared the first draft of the manuscript. All authors (NA, BS, RB, PVN, JYJV, ADS, SH, AVDB, ID, PVD, HG, SC, NA, BS and PVN) contributed equally to this work as first author. NA and BS contributed equally to this work as last author. SC is acting as guarantor.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication Not applicable.

Ethics approval Ethical approval granted at 16 November 2020 (reference number: 20/46/605) by the Ethics Committee of the University Hospital Antwerp/University of Antwerp (Belgian registration number: 3002020000237). Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

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

Dear Participant,

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

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

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

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

The CHARMING study team

There are 74 questions in this survey.

E - Consent

Before giving your consent it is important that you have reviewed the information document about this study available in French here (https://dox.uliege.be/index.php/s/n64T153cp07BOkG) and in Dutch here (https://dox.uliege.be/index.php/s/OYp4clx8oxERBl).
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
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

Your health

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? *

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:

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:

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></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>
<td></td>
<td></td>
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</tr>
<tr>
<td>A temporary ban on non-essential international travel is needed.</td>
<td></td>
<td></td>
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<tr>
<td>I am sure I am already infected with COVID-19.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I will certainly be infected with COVID-19 during this epidemic.</td>
<td></td>
<td></td>
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<tr>
<td>I am afraid I am contaminating my relatives.</td>
<td></td>
<td></td>
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<tr>
<td>The guidelines for primary care are clearly communicated.</td>
<td></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>
<td></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>
<td></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:

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: 

<p>| | |</p>
<table>
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</table>

### 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:

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

Please enter a date:
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

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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
- [ ] 11 - 15 patients
- [ ] 16 - 20 patients
- [ ] > 20 patients
35 Have you been vaccinated against COVID-19? *
Please choose **only one** of the following:
- Yes
- No

36 Which vaccine did you receive? *
Please choose **only one** of the following:
- Pfizer/BioNTech
- Moderna
- Oxford/AstraZeneca
- Other

37 How many doses have you received? *
Please choose **only one** of the following:
- 1 dose
- 2 doses

38 When did you receive the **first** dose of the vaccine (dd.mm.yyyy)? *
Please enter a date:
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>
<thead>
<tr>
<th></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>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A temporary ban on non-essential international travel is still needed.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>The Belgian healthcare system is strong enough to cope with this epidemic.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>The testing capacity in Belgium is sufficient.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rapid diagnostic tests are relevant for general practice.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rapid diagnostic tests for SARS-CoV-2 viral detection are manageable for general practice.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>The measures imposed by the government are sufficient.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Everyone should wear a mask when they work inside with other people.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I have every confidence in the scientific COVID-19 expert committee.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Most of my patients follow the rules of 'social distancing'.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Most of my patients adhere to hygiene rules.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</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:

The CHARMING study team

21.03.2021 – 20:58
Submit your survey.
Thank you for completing this survey.
<table>
<thead>
<tr>
<th>Region/Province</th>
<th>Active GPs n (%)</th>
<th>Participating GPs n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brussels</td>
<td>1,178 (10.01)</td>
<td>239 (9.2)</td>
</tr>
<tr>
<td>Flanders</td>
<td>6,805 (57.83)</td>
<td>1,725 (66.4)</td>
</tr>
<tr>
<td>Wallonia</td>
<td>3,784 (32.16)</td>
<td>633 (24.4)</td>
</tr>
<tr>
<td>Antwerpen-Anvers</td>
<td>1,806 (15.35)</td>
<td>454 (17.5)</td>
</tr>
<tr>
<td>Brussel-Hoofdstad-Bruxelles Capitale</td>
<td>1,178 (10.01)</td>
<td>239 (9.2)</td>
</tr>
<tr>
<td>Henegouwen-Hainaut</td>
<td>1,293 (10.99)</td>
<td>175 (6.7)</td>
</tr>
<tr>
<td>Limburg-Limbourg</td>
<td>943 (8.01)</td>
<td>235 (9.0)</td>
</tr>
<tr>
<td>Luik-Liège</td>
<td>1,125 (9.56)</td>
<td>200 (7.7)</td>
</tr>
<tr>
<td>Luxemburg-Luxembourg</td>
<td>301 (2.56)</td>
<td>78 (3.0)</td>
</tr>
<tr>
<td>Namen-Namur</td>
<td>594 (5.05)</td>
<td>104 (4.0)</td>
</tr>
<tr>
<td>Oost-Vlaanderen-Flandre Orientale</td>
<td>1,556 (13.22)</td>
<td>431 (16.6)</td>
</tr>
<tr>
<td>Vlaams-Brabant-Brabant-Flamand</td>
<td>1,241 (10.55)</td>
<td>317 (12.2)</td>
</tr>
<tr>
<td>Waals-Brabant-Brabant Wallon</td>
<td>471 (4.00)</td>
<td>76 (2.9)</td>
</tr>
<tr>
<td>West-Vlaanderen-Flandre Occidentale</td>
<td>1,259 (10.70)</td>
<td>288 (11.1)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>11,767</strong></td>
<td><strong>2,597 (22.1)</strong></td>
</tr>
</tbody>
</table>

1 The first testing timepoint was December 2020 for 2224 and January 2021 for 373 GPs. PHCPs, respectively.
Table S2. The number of primary healthcare providers (PHCPs) participating per testing timepoint

<table>
<thead>
<tr>
<th>Testing timepoints</th>
<th>Number of PHCPs (%)</th>
<th>Invited (%)</th>
<th>Responding (%)</th>
<th>Responding within the testing timeframe(^1) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3,044</td>
<td>2,820</td>
<td>(92.6%)</td>
<td>2680 (88.0%)</td>
</tr>
<tr>
<td>2</td>
<td>3,648</td>
<td>3,289</td>
<td>(90.2%)</td>
<td>3060 (83.9%)</td>
</tr>
<tr>
<td>3</td>
<td>3,648</td>
<td>3,162</td>
<td>(86.7%)</td>
<td>3018 (82.7%)</td>
</tr>
<tr>
<td>4</td>
<td>3,409</td>
<td>3,043</td>
<td>(89.3%)</td>
<td>3021 (88.6%)</td>
</tr>
<tr>
<td>5</td>
<td>3,409</td>
<td>2,989</td>
<td>(87.7%)</td>
<td>2891 (84.8%)</td>
</tr>
<tr>
<td>6</td>
<td>3,409</td>
<td>2,802</td>
<td>(82.2%)</td>
<td>2750 (80.7%)</td>
</tr>
<tr>
<td>7</td>
<td>3,313</td>
<td>2,819</td>
<td>(85.1%)</td>
<td>2756 (83.2%)</td>
</tr>
<tr>
<td>8</td>
<td>3,313</td>
<td>2,557</td>
<td>(77.2%)</td>
<td>2516 (75.9%)</td>
</tr>
</tbody>
</table>

Table S3. Prevalence of antibodies against SARS-CoV-2 among primary healthcare providers in Belgium at eight testing timepoints from December 2020 to December 2021

<table>
<thead>
<tr>
<th>Testing timepoint</th>
<th>Region</th>
<th>PHCPs n</th>
<th>Valid RST(^2) n</th>
<th>Positive RST(^3) n</th>
<th>Adjusted prevalence(^4) % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>Belgium</td>
<td>2,680</td>
<td>2,629</td>
<td>366</td>
<td>15.08 (13.54-16.62)</td>
</tr>
<tr>
<td></td>
<td>Brussels</td>
<td>234</td>
<td>233</td>
<td>43</td>
<td>18.45 (13.47-23.44)</td>
</tr>
<tr>
<td></td>
<td>Flanders</td>
<td>1,841</td>
<td>1,800</td>
<td>203</td>
<td>11.28 (9.77-12.79)</td>
</tr>
<tr>
<td></td>
<td>Wallonia</td>
<td>605</td>
<td>596</td>
<td>120</td>
<td>20.37 (16.91-23.84)</td>
</tr>
<tr>
<td>T2</td>
<td>Belgium</td>
<td>3,060</td>
<td>2,995</td>
<td>716</td>
<td>25.42 (23.75-27.08)</td>
</tr>
<tr>
<td></td>
<td>Brussels</td>
<td>270</td>
<td>263</td>
<td>55</td>
<td>20.91 (15.98-25.84)</td>
</tr>
<tr>
<td></td>
<td>Flanders</td>
<td>2,024</td>
<td>1,980</td>
<td>389</td>
<td>20.10 (18.29-21.92)</td>
</tr>
<tr>
<td></td>
<td>Wallonia</td>
<td>766</td>
<td>752</td>
<td>272</td>
<td>36.03 (32.46-39.60)</td>
</tr>
<tr>
<td>T3</td>
<td>Belgium</td>
<td>3,018</td>
<td>2,967</td>
<td>2,278</td>
<td>75.70 (74.03-77.37)</td>
</tr>
<tr>
<td></td>
<td>Brussels</td>
<td>274</td>
<td>273</td>
<td>168</td>
<td>61.54 (55.72-67.36)</td>
</tr>
<tr>
<td></td>
<td>Flanders</td>
<td>2,014</td>
<td>1,971</td>
<td>1,615</td>
<td>82.35 (80.63-84.06)</td>
</tr>
<tr>
<td></td>
<td>Wallonia</td>
<td>730</td>
<td>723</td>
<td>495</td>
<td>68.80 (65.26-72.34)</td>
</tr>
<tr>
<td>T4</td>
<td>Belgium</td>
<td>3,021</td>
<td>2,980</td>
<td>2,509</td>
<td>84.17 (82.86-85.48)</td>
</tr>
<tr>
<td></td>
<td>Brussels</td>
<td>279</td>
<td>274</td>
<td>209</td>
<td>76.28 (71.24-81.31)</td>
</tr>
<tr>
<td></td>
<td>Flanders</td>
<td>1,987</td>
<td>1,963</td>
<td>1,706</td>
<td>86.91 (85.42-88.40)</td>
</tr>
<tr>
<td></td>
<td>Wallonia</td>
<td>755</td>
<td>743</td>
<td>594</td>
<td>79.95 (77.07-82.83)</td>
</tr>
<tr>
<td>T5</td>
<td>Belgium</td>
<td>2,891</td>
<td>2,859</td>
<td>2,410</td>
<td>84.07 (82.65-85.48)</td>
</tr>
<tr>
<td></td>
<td>Brussels</td>
<td>274</td>
<td>268</td>
<td>206</td>
<td>76.87 (71.82-81.91)</td>
</tr>
<tr>
<td></td>
<td>Flanders</td>
<td>1,898</td>
<td>1,877</td>
<td>1,622</td>
<td>86.67 (85.09-88.25)</td>
</tr>
<tr>
<td></td>
<td>Wallonia</td>
<td>719</td>
<td>714</td>
<td>582</td>
<td>81.86 (78.97-84.75)</td>
</tr>
<tr>
<td>T6</td>
<td>Belgium</td>
<td>2,750</td>
<td>2,725</td>
<td>2,230</td>
<td>81.57 (80.02-83.12)</td>
</tr>
<tr>
<td></td>
<td>Brussels</td>
<td>252</td>
<td>244</td>
<td>197</td>
<td>80.74 (75.81-85.67)</td>
</tr>
<tr>
<td></td>
<td>Flanders</td>
<td>1,839</td>
<td>1,826</td>
<td>1,514</td>
<td>82.76 (80.97-84.55)</td>
</tr>
<tr>
<td></td>
<td>Wallonia</td>
<td>659</td>
<td>655</td>
<td>519</td>
<td>79.78 (76.59-82.98)</td>
</tr>
<tr>
<td>T7</td>
<td>Belgium</td>
<td>2,756</td>
<td>2,730</td>
<td>1,917</td>
<td>70.17 (68.36-71.97)</td>
</tr>
<tr>
<td></td>
<td>Brussels</td>
<td>238</td>
<td>237</td>
<td>178</td>
<td>75.11 (69.62-80.59)</td>
</tr>
<tr>
<td></td>
<td>Flanders</td>
<td>1,844</td>
<td>1,823</td>
<td>1,271</td>
<td>69.38 (67.20-71.56)</td>
</tr>
<tr>
<td></td>
<td>Wallonia</td>
<td>674</td>
<td>670</td>
<td>468</td>
<td>70.04 (66.46-73.62)</td>
</tr>
<tr>
<td>T8</td>
<td>Belgium</td>
<td>2,516</td>
<td>2,498</td>
<td>2,356</td>
<td>93.91 (92.89-94.93)</td>
</tr>
<tr>
<td></td>
<td>Brussels</td>
<td>222</td>
<td>221</td>
<td>201</td>
<td>90.95 (87.17-94.73)</td>
</tr>
<tr>
<td></td>
<td>Flanders</td>
<td>1,696</td>
<td>1,681</td>
<td>1,607</td>
<td>95.42 (94.36-96.47)</td>
</tr>
<tr>
<td></td>
<td>Wallonia</td>
<td>598</td>
<td>596</td>
<td>548</td>
<td>92.22 (90.02-94.43)</td>
</tr>
</tbody>
</table>

\(^1\) See Table S4 for the proportions of PHCPs partially and fully vaccinated; \(^2\) RST: Rapid Serological Test; \(^3\) IgG and/or IgM positive among the valid RST; \(^4\) Estimates are based on Generalised Estimating Equations taking into account clustering of PHCPs within their practice and distribution of GPs across districts in Belgium; T1: 24/12/2021-8/1/2021, T2: 25-31/1/2021, T3: 22-28/2/2021, T4: 22-31/3/2021, T5: 19-28/4/2021, T6: 14-27/6/2021, T7: 13-26/9/2021, T8: 13-26/12/2021.
### Table S4. Proportions of primary healthcare providers in Belgium with valid rapid serological test results1 vaccinated at eight testing timepoints from December 2020 to December 2021

<table>
<thead>
<tr>
<th>Testing timepoint</th>
<th>Region</th>
<th>Partially vaccinated2 % (95%CI)</th>
<th>Fully vaccinated3 % (95%CI)</th>
<th>Booster vaccinated4 % (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>Belgium</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Brussels</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Flanders</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Wallonia</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>T2</td>
<td>Belgium</td>
<td>57.16 (55.39-58.93)</td>
<td>0.87 (0.54-1.20)</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Brussels</td>
<td>17.49 (12.90-22.08)</td>
<td>1.14 (0.00-2.42)</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Flanders</td>
<td>67.27 (65.21-69.34)</td>
<td>0.30 (0.06-0.55)</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Wallonia</td>
<td>44.41 (40.86-47.97)</td>
<td>2.26 (1.20-3.32)</td>
<td>NA</td>
</tr>
<tr>
<td>T3</td>
<td>Belgium</td>
<td>16.92 (15.57-18.27)</td>
<td>66.23 (64.53-67.93)</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Brussels</td>
<td>50.18 (44.25-56.11)</td>
<td>21.98 (17.07-26.89)</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Flanders</td>
<td>11.72 (10.30-13.14)</td>
<td>76.15 (74.27-78.04)</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Wallonia</td>
<td>18.53 (15.70-21.37)</td>
<td>55.88 (52.26-59.50)</td>
<td>NA</td>
</tr>
<tr>
<td>T4</td>
<td>Belgium</td>
<td>16.88 (15.53-18.22)</td>
<td>78.46 (76.98-79.93)</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Brussels</td>
<td>30.29 (24.85-35.73)</td>
<td>60.22 (54.42-66.01)</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Flanders</td>
<td>11.30 (10.30-13.14)</td>
<td>84.06 (82.44-85.67)</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Wallonia</td>
<td>21.13 (18.20-24.07)</td>
<td>70.39 (67.11-73.67)</td>
<td>NA</td>
</tr>
<tr>
<td>T5</td>
<td>Belgium</td>
<td>15.49 (14.17-16.82)</td>
<td>81.11 (79.68-82.55)</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Brussels</td>
<td>26.46 (22.21-31.78)</td>
<td>66.04 (60.38-71.71)</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Flanders</td>
<td>13.16 (11.63-14.69)</td>
<td>84.06 (82.44-85.67)</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Wallonia</td>
<td>17.51 (15.70-21.37)</td>
<td>55.88 (52.26-59.50)</td>
<td>NA</td>
</tr>
<tr>
<td>T6</td>
<td>Belgium</td>
<td>1.54 (1.08-3.00)</td>
<td>95.93 (95.18-96.67)</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Brussels</td>
<td>2.05 (0.27-3.83)</td>
<td>92.21 (88.85-95.58)</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Flanders</td>
<td>0.82 (0.41-1.24)</td>
<td>98.68 (97.39-98.67)</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Wallonia</td>
<td>3.36 (1.42-5.35)</td>
<td>92.90 (90.63-95.17)</td>
<td>NA</td>
</tr>
<tr>
<td>T7</td>
<td>Belgium</td>
<td>0.51 (0.24-0.78)</td>
<td>97.91 (97.38-98.45)</td>
<td>0.73 (0.41-1.05)</td>
</tr>
<tr>
<td></td>
<td>Brussels</td>
<td>2.53 (0.53-4.53)</td>
<td>94.51 (91.62-97.41)</td>
<td>0.42 (0.00-1.25)</td>
</tr>
<tr>
<td></td>
<td>Flanders</td>
<td>0.11 (0.00-0.26)</td>
<td>99.23 (98.88-99.63)</td>
<td>0.93 (0.49-1.37)</td>
</tr>
<tr>
<td></td>
<td>Wallonia</td>
<td>0.90 (0.18-1.61)</td>
<td>95.92 (93.96-97.09)</td>
<td>0.30 (0.00-0.71)</td>
</tr>
<tr>
<td>T8</td>
<td>Belgium</td>
<td>0.20 (0.02-0.38)</td>
<td>98.72 (98.28-99.16)</td>
<td>84.78 (83.37-86.18)</td>
</tr>
<tr>
<td></td>
<td>Brussels</td>
<td>0.00 (0.00-0.00)</td>
<td>98.64 (97.12-100.00)</td>
<td>72.07 (66.17-77.97)</td>
</tr>
<tr>
<td></td>
<td>Flanders</td>
<td>0.06 (0.00-0.18)</td>
<td>99.46 (99.12-99.81)</td>
<td>89.74 (88.30-91.18)</td>
</tr>
<tr>
<td></td>
<td>Wallonia</td>
<td>0.67 (0.02-1.33)</td>
<td>96.64 (95.20-98.09)</td>
<td>75.42 (71.97-78.87)</td>
</tr>
</tbody>
</table>

1See Table S3 for the number of primary healthcare providers with valid rapid serological test results; 2 Received one out of two doses; 3 Received two doses; 4 Received a third dose. T1: 24/12/2021-8/1/2021, T2: 25-31/1/2021, T3: 22-28/2/2021, T4: 22-31/3/2021, T5: 19-28/4/2021, T6: 14-27/6/2021, T7, 13-26/9/2021, T8: 13-26/12/2021.