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Long-term outcome after SARS-CoV-2 infection in healthcare workers: a single centre cohort study

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Summary

BACKGROUND: Long-term symptoms after acute COVID-19 are highly debated. Nevertheless, data on long-term symptoms of COVID-19 in healthcare workers are scarce.

METHODS: We assessed frequency and risk factors of persisting symptoms in a retrospective cohort of healthcare workers infected with SARS-CoV-2.

RESULTS: Persistent symptoms at 3 and 12 months were reported by 26.5% and 13.5% of participants, respectively. Most commonly reported symptoms were fatigue, impaired sense of taste or smell and general weakness. A history of depression or state of exhaustion, pre-existing lung disease and older age were associated with persisting symptoms.

CONCLUSION: Our study shows that a relevant proportion of healthcare workers with mild COVID-19 report persisting symptoms over 3 and 12 months. Although in the majority of cases symptoms are mild, this study highlights the need for further research into causes and therapy.

Background

Reported rates of persisting symptoms after SARS-CoV-2 infection vary between 2.6% [1] and 76% [2], depending on the individual's disease severity and comorbidity, as well as on the study methodology. A Swiss study reported that at least a third of ambulatory patients present persistent symptoms 30 to 45 days after diagnosis [3]. The most commonly reported symptoms were loss of taste or smell, cough, fatigue and headache. In a Norwegian survey-based study, 47% of female participants and 33% of male participants from a nonhospitalised cohort reported ongoing symptoms 1.5–6 months after COVID-19 [4]. The most commonly reported symptoms were dyspnoea and loss/disturbance of smell or taste.

Healthcare workers worldwide are at the forefront of the fight against the COVID-19 pandemic. They are at a particular risk of infection, acute disease and possible long-term consequences. Nevertheless, data on the long-term effects of COVID-19 on healthcare workers are scarce. In a Swedish study 26% and 15% of healthcare workers reported at least one moderate to severe symptom at 2 and 8 months after diagnosis, respectively [5]. To our knowledge, there are no data about long-lasting symptoms after COVID-19 in Swiss healthcare workers. This study aimed to assess the frequency of persisting symptoms after COVID-19 infection in healthcare workers at a university hospital in Switzerland.

Methods

This retrospective cohort study was conducted from 30 April 2021 to 3 June 2021 at the University Hospital Basel, enrolling employees with a reported SARS-CoV-2 infection between 1 March 2020 and 15 April 2021. The University Hospital Basel is a tertiary care centre in Switzerland with 855 beds, approximately 37,000 admissions per year and 7637 employees. To ensure rapid and adequate infection control measures in the case of in-hospital outbreaks, employees had to report to the Employee Health Service if they tested positive for SARS-CoV-2. Further, the Staff Medical Service screened the hospital's laboratory system on a daily basis for employees with a positive test.

On 30 April 2021, the Staff Medical Service sent a link to an online questionnaire to all employees who had a SARS-Cov-2 infection between 1 March 2020 and 15 April 2021. Seventeen days after the initial email a reminder was sent to all potential participants. The questionnaire could be answered up to 3 June 2021. Participation in the survey was voluntary and fully anonymous with questionnaires not being linked to the email address. To ensure anonymity, we did not collect identifying information such as exact age. The locally responsible Ethics Committee (Ethikkommission Nordwest- und Zentralschweiz) granted a waiver for this online survey.

In the questionnaire, participants were asked about potential comorbidities, approximate date of the positive test,

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suspected place of infection, workdays missed, if admission was required and how long it took them to return to the same level of health as before the illness. Only participants who reported not having regained their usual level of health at the time they completed the survey were asked about their exact symptoms (checkboxes with suggestions and a possibility to insert free text) and what percentage of their pre-disease health they consider themselves to be at. See supplementary appendix for the full original questionnaire (in German) and an English translation.

Data collection and analysis

Data were collected using REDCap electronic data capture tools. The main outcome variable of interest was presence of self-reported symptoms 90 days after COVID-19 diagnosis. The secondary variable of interest was self-reported symptom persistence for more than 12 months in participants for whom the infection took place more than 1 year ago. This was an explorative descriptive study without a specific hypothesis or sample-size determination. To describe the study population, continuous variables were summarised as medians and interquartile ranges (IQRs), categorical variables as counts and proportions. We used uni- and multivariable logistic regression to test for associations between participant baseline characteristics and reported symptom persistence. Due to a limited number of participants with persisting symptoms at day 90 (main variable of interest), we used a forward stepwise selection for the multivariable logistic regression. Baseline characteristics showing an association at a two-sided significance level <0.1 in univariate analysis were included into the multivariable model. Results from logistic regressions are reported in unadjusted odds-ratios (ORs) and adjusted ORs (aORs) with 95% confidence intervals (95% CIs). All analyses were run on STATA version 15.1.

Results

By 31 May 2021, 567 employees were registered in the Staff Medical Service database with a past SARS-CoV-2 infection. Among them 397 (70%) were male, and median age of these employees was 37 years (IQR 28–49). We could not contact 44 because they had changed workplace and thus the email address was not functional any more.

Of the remaining 523, 303 (57.9%) filled in the questionnaire. Six questionnaires were incomplete: four had only minor gaps, two were excluded because the date of the positive test was missing. Of the remaining 301 respondents, 260 had a SARS-CoV-2 infection ≥90 days previously and were included in the analysis (figure 1). The mean age range of these 260 participants was 30–39 years, 196 (75.4%) were female and 167 participants (64.2%) had direct patient contact at work. Only three (1.2%) participants had been hospitalised, none of them in intensive care.

Table 1 displays all baseline characteristics of participants, including the information about missing data.

Sixty-nine (26.5%) participants reported not having regained their usual level of health or having had a symptom duration of more than 3 months. Forty-five participants reported details about their symptoms. Symptoms most commonly reported were fatigue (31 participants, 68.9%), impaired sense of taste or smell (23 participants, 51.1%) and general weakness (21 participants, 46.7%). Table 2 displays all reported symptoms and their frequency among these 45 patients. Twenty-seven participants reported having regained ≥80% of their pre-SARS-CoV-2 level of health and only three participants reported not having regained at least 50% of their pre-COVID-19 level of health. Those with persisting symptoms for over 90 days reported

Figure 1: Study flow chart.

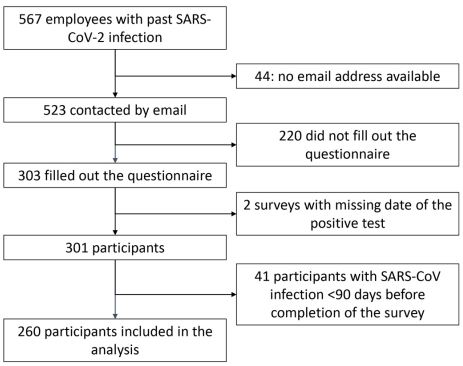

Table 1:
Baseline characteristics of the patients with SARS-CoV-2 infection ≥90 days ago.

		n/N (%) or median (IQR)
Age group	10–19	5/260 (2.3)
	2029	68/260 (26.2)
	3039	66/260 (25.4)
	4049	56/260 (21.5)
	5059	52/260 (20.0)
	6069	12/260 (4.6)
Female gender		196/260 (75.4)
BMI (kg/m^2)		23.8 (21.526.7)
Co-morbidities	Arterial hypertension*	18/ 258 (7.0)
	Asthma°	27/259 (10.4)
	COPD*	2/ 258 (0.8)
	Other lung disease°	0/259 (0)
	Depression*	5/258 (1.9)
	Active cancer*	0/258 (0)
	Hypothyroidosis*	12/258 (4. 7)
History of myocardial infarction or stroke*		1/258 (0.4)
History of depression or state of exhaustion *		23/258 (8.9)
History of cancer*		6/258 (2.3)
Job type	Nursing staff	123/260 (47.3)
	Medical staff	38/260 (14.6)
	Diagnostic staff	14/260 (5.4)
	Therapeutic staff (e.g., physical therapy	7/ 260 (2.7)
	House staff (cleaning, logistics..)	15/260 (5.8)
	Administrative staff	37/260 (14.2)
	Other	26/260 (10.0)
Days between positive test and completion of survey		167.7 (142.7193.1)
Hospitalized for COVID-19		3/260 (1.2)
Hospitalized on ICU for COVID-19		0/260 (0)

IQR: interquartile range: ICU: intensive care unit; BMI: body mass index; COPD: chronic obstructive pulmonary disease. * Value missing for two participants, °value missing for one participant.

1412 cumulative missed workdays (median 15, IQR 10–21, no missing data). The 191 participants with a symptom duration of 90 days or less reported 1801 cumulative missed workdays (median 10 days, IQR 711). Data about lost workdays were missing in 5 of these 191 participants.

Thirty-seven participants reported the diagnosis of SARS-CoV infection to have been made more than 365 days previously. Among these, five (13.5%) reported not having regained their usual level of health. The most common reported symptoms among them were fatigue (5 participants, 100%), general weakness (4 participants, 80%) impaired sense of taste or smell and palpitations (3 participants, 60%). All these participants reported having regained at least 60% of their pre SARS-CoV-2 infection level of health. Those with persisting symptoms over 365 days reported 106 cumulative missed workdays (median 21, IQR 18–21, no missing data). The 32 patients who reported the diagnosis of SARS-CoV infection to have been made more than 365 days ago with a symptom duration of 365 days or less reported 303 cumulative missed workdays (median 10 days, IQR 5–10 days, no missing data).

In the univariate analysis, a history of depression or history of state of exhaustion (OR 4.36, 95% CI 1.64–10.56), older age and any lung disease (OR 3.80, 95% CI 1.70–8.49) were associated with symptom persistence for more than 90 days (table 3). These associations persisted in the multivariable analysis that included age, any lung disease, arterial hypertension and history of depression or of state of exhaustion (table 3).

Gender, function in the hospital, e.g., nurse, physician, administration, and comorbidities did not show a significant association with symptom persistence at 3 months.

Discussion

In this retrospective cohort study at a tertiary care hospital in Switzerland, 26.5% and 13.5% of healthcare workers with a history of mostly mild COVID-19 reported not having regained their usual level of health after 90 and 365 days, respectively. The most commonly reported persisting symptoms were fatigue, loss of sense of taste or smell and general weakness. Older age, history of depression or state of exhaustion and pre-existing lung disease were associated with symptom duration >90 days.

Our results are in line with a recent Swedish study, in which 26% of seropositive healthcare workers reported persisting symptoms 2 months after seroconversion [5]. In a Danish study, however, 40% of the participating healthcare workers reported symptoms at day 90 after diagnosis, although they were not asked about fatigue, which was among the most common symptoms in our study and in the Swedish study [6]. In this study participants were not asked whether they attributed their symptoms to their COVID-19 disease. Other studies showed an even higher prevalence of long-lasting symptoms [2, 7]. The higher proportions in other studies might be explained by the inclusion of more individuals with a severe course of COVID-19 or re-

Table 2:
Reported symptoms of the 45 participants with a symptom duration of more than 3 months who reported their symptoms. Only participants with ongoing symptoms at the time they completed the survey were asked about their symptoms. Participants could report more than one symptom.

Symptom	Number (total = 45)	Percent
Fatigue	31	68.9
Loss/disturbance of smell or taste	23	51.1
General weakness	21	46.7
Concentration problems	20	44.4
Breathing problems	19	42.2
Sleep difficulties	13	28.9
Headache	10	22.2
Dizziness	10	22.2
Chest pain	9	20.0
Muscular pain	9	20.0
Loss of hair	8	17.8
Palpitations	7	15.6
Cough	5	11.1
Joint pain	4	8.9
Other	4	8.9
Feverish feeling	3	6.7
Decreased appetite	3	6.7
Digestive problems	2	4.4

Table 3:
Characteristics of patients with positive test ≥90 days before completion of the survey with and without symptoms at day 90 after diagnosis.

Characteristic		Total n/N (%)	With symptoms N/n (%)	OR (95% CI)	p-value	aOR	Adjusted p-Value
Gender	Male	64/260 (24.6)	14/64 (21.9)	Ref		Ref	
	Female	196/260 (75.4)	55/196 (28.1)	0.72 (0.37–1.40)	0.332		
Age	<30	74 / 260 (28.5)	10/74 (13.5)	Ref		Ref	
	30–49.99	122/260 (46.9)	34/122 (27.9)	2.74 (1.145.37)	0.022	2.83 (1.236.54)	0.015
	≥50	64/260 (24.6)	25/64 (39.1)	4.1 (1.789.45)	0.001	4.13 (1.6410.34)	0.003
Any lung disease		28/260 (10.8)	15/28 (53.6)	3.80 (1.708.49)	0.001	3.78 (1.598.93)	0.003
Arterial hypertension*		18/258 (7.0)	8/18 (44.4)	2.45 (0.936.51)	0.071	1.27 (0.433.75)	0.663
Hypothyroidosis*		12/258 (4.7)	5/12 (41.7)	2.12 (0.656.92)	0.213		
History of depression or state of exhaustion *		23/258 (8.9)	13/23 (56.5)	4.36 (1.8110.49)	0.001	4.16 (1.6410.56)	0.003
History of cancer*		6/258 (2.3)	2/6 (33.3)	n/a	n/a		
Nursing staff		123/260 (47.3)	29/123 (23.6)	0.75 (0.431.30)	0.306		
BMI	<25	166/260 (63.9)	39/166 (23.5)	Ref			
	25–29.99	66/260 (25.4)	20/66 (30.3)	1.42 (0.752.67)	0.284		
	≥30	28/260 (10.8)	10/28 (35.7)	1.81 (0.774.24)	0.173		

OR: odds ratio; aOR: adjusted odds ratio: CI: confidence interval, Ref: reference.

Multivariable model adjusted for: age group, any lung disease, hypertension and history of depression or state of exhaustion.

* Value missing for two participants

porting of symptoms that were already present before the SARS-CoV-2 infection. In our study, the majority of participants with symptoms lasting longer than 3 months or 12 months reported only mild impairment of their perceived health state. Similarly, the median workdays lost are well below the reported symptom duration. This is in line with the Swedish study mentioned above [5] and a British study [8]. In the former, the majority of participants reporting symptoms lasting at least 2 months reported mostly a mild impairment in their work, social and home life using the Sheehan Disability Scale. In the latter, only 2% of healthcare workers who had ongoing symptoms 3–4 months after the suspected infection reported taking sick leave after recovering from the acute illness. Similarly, a large patient, and health insurance registry-based study showed only minor increases in healthcare system use and medication prescription in patients after COVID-19 [9]. However, the comparisons are limited due to differences in methodology and the length of time between the infection and the survey.

In our study, a history of depression or state of exhaustion, pre-existing lung disease and increasing age were associated with persisting symptoms 90 days after diagnosis. Previous studies reported older age and comorbidities including lung conditions – but not history of depression or state of exhaustion – as risk factors for persisting symptoms after COVID-19 [1,2].

Our study has several limitations. The study relied on participants' ability to recall their health state 90 and 365 days after diagnosis. As participants reported events in the past, there is a risk for a recall bias. Although the response rate was good, we do not know whether differences between employees who responded to the survey introduced a selection bias. We asked participants about specific symptoms only if they reported not having reached their usual level of health. However, some subtle symptoms might evade these questions. We did not use a validated questionnaire. As there is no SARS-CoV-2 negative control group in our study, we cannot exclude the possibility that some of the described symptoms or the absence from work might not be related to the SARS-CoV-2 Infection. Finally, compared with all employees with a positive SARS-CoV-2 test, women were overrepresented among the respondents. The strength of our study is the inclusion of a relatively large number of participants from a defined, unselected group of including participants diagnosed more than 365 days previously with COVID-19.

In conclusion, our study shows that a relevant proportion of healthcare workers with mild COVID-19 report persisting symptoms over 3 and 12 months. Although in the majority of cases symptoms are mild, this study highlights the need for further research into causes and therapy.

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Conflict of interest

All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. No potential conflicts of interest were disclosed.

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Appendix

Fragebogen (English translation below)

#	Frage	Antwortoptionen	Wem wird die Frage angezeigt?
1	Wie alt waren Sie zum Zeitpunkt Ihrer Covid-19 Erkrankung?	10-19 Jahre 20-29 Jahre 30-39 Jahre 40-49 Jahre 50-59 Jahre 60-69 Jahre 70 und mehr Jahre Radio (single answer)	Allen Teilnehmern
2	Wie gross sind Sie (in cm)?	text (number, Min: 120, Max: 250)	Allen Teilnehmern
3	Wie schwer sind Sie (in kg)?	text (number, Min: 20, Max: 250)	Allen Teilnehmern
4	Was ist Ihr Geschlecht?	Weiblich Männlich Nicht-binär Radio (single answer)	Allen Teilnehmern
5	Vorerkrankungen Leiden Sie an einer der folgenden Erkrankungen?		Allen Teilnehmern
	Arterielle Hypertonie	Ja/nein	
	Asthma	Ja/nein	
	COPD	Ja/nein	
	Andere Lungenerkrankung	Ja/nein	
	Depression	Ja/nein	
	Aktive Krebserkrankung	Ja/nein	
	Schilddrüsenunterfunktion	Ja/nein	
6	Litten Sie in der Vergangenheit an		Allen Teilnehmern
	Einem Herzinfarkt oder einem Schlaganfall?	Ja/nein	
	einer Depression, einem Burnout oder einem anderen	Ja/nein	

	Erschöpfungszustand? einer Krebserkrankung?	Ja/nein	
7	In welcher Funktion arbeiten Sie?	Pflege Ärztlicher Dienst Diagnostik (BMA, MTRA, ...) Therapien Hausdienst: Reinigung, Logistik, Hotellerie Administration Andere (dropdown, single answer)	Allen Teilnehmern
8	Waren Sie zur Zeit Ihrer Covid-19 Erkrankung als Auszubildende*r angestellt?	Ja/nein	Allen Teilnehmern
9	Wie häufig hatten Sie Kontakt mit Patienten bevor Sie sich angesteckt haben?	Ich hatte bei der täglichen Arbeit regelmässig Patientenkontakt (z.B. Pflege, Ärzte, Therapie) Ich hatte bei der täglichen Arbeit regelmässigen aber keinen engen Patientenkontakt (z.B. Anmeldung, Hotellerie, Reinigung, ...) Ich hatte bei der täglichen Arbeit keinen Patientenkontakt Ich war im Homeoffice. Radio (single answer)	Allen Teilnehmern
10	An welchem Tag wurden Sie positiv auf Covid-19 getestet? (Falls Sie es nicht mehr genau wissen, machen Sie einfach eine ungefähre Angabe.)	text (date_dmy, Min: 2020-01-01, Max: 2021-04-16)	Allen Teilnehmern
11	Ungefähr wieviele Tage vor dem positiven Test begannen Ihre Symptome?	10-20 Tage vor dem Test 5-10 Tage vor dem Test 0-5 Tage vor dem Test Sie begannen erst nach dem Test Ich hatte nie Symptome	Allen Teilnehmern

		Dropdown (single answer)	
12	Wurden Sie aufgrund der COVID-19 Erkrankung hospitalisiert?	Ja/nein	Allen Teilnehmern
13	Wie viele Tage waren Sie wegen der Covid-19 Erkrankung hospitalisiert? (Falls Sie es nicht mehr genau wissen, machen Sie einfach eine ungefähre Angabe.)	text (number, Min: 0, Max: 300)	Nur falls Frage 12=ja
14	Waren Sie während der Hospitalisation wegen Covid-19 auf der Intensivstation hospitalisiert?	Ja/nein	Nur falls Frage 12=ja
15	Wieviel Zeit nach dem Test, fühlten Sie sich wieder genau so gesund wie vor der Covid Erkrankung:	Ich hatte nie Symptome/habe mich immer gut gefühlt 1-5 Tage 5-10 Tage 10-28 Tage 4 Wochen bis 3 Monate Mehr als 3 Monate Ich fühle mich bis jetzt nicht wieder genau so gesund, wie vor der Covid Erkrankung	Allen Teilnehmern
16	Ich leide weiterhin an folgenden Symptomen	Atembeschwerden Druck auf der Brust Husten Fiebriges Gefühlt/Erhöhte Temperatur Müdigkeit Eingeschränkter/nicht vorhandener Geruch/Geschmackssinn Allgemeine Schwäche Schlafprobleme Haarverlust Kopfschmerzen Schwindel Konzentrationsstörungen	Nur falls Frage 15 = Ich fühle mich bis jetzt nicht wieder genau so gesund, wie vor der Covid Erkrankung

		Muskelschmerzen Gelenkschmerzen Herzklopfen Appetitverlust Verdauungsbeschwerden Andere Checkbox (multiple answers)	
17	An welchen anderen Symptomen, die Sie auf die Covid-19 Erkrankung zurückführen, leiden Sie noch?	text	Nur falls Frage 16 = Andere
18	Insgesamt denke ich, dass wenn ich vor der COVID-19 Erkrankung bei 100% Leistungsfähigkeit war, bin ich jetzt bei...	0 % 10 % 20 % 30 % 40 % 50 % 60 % 70 % 80 % 90 % Dropdown (single answer)	Nur falls Frage 15 = Ich fühle mich bis jetzt nicht wieder genau so gesund, wie vor der Covid Erkrankung
19	Wo denken Sie, haben Sie sich mit Covid-19 angesteckt?	Bei der Arbeit von einem Patienten Bei der Arbeit von anderen Mitarbeitenden Ausserhalb des Spitals In der Familie oder bei Bekannten/Freunden Ich habe keine Ahnung	Allen Teilnehmern
20	Wie viele Arbeitstage sind Sie zirka wegen Ihrer Covid-19 Erkrankung ausgefallen?	text (number, Min: 0, Max: 300)	Allen Teilnehmern

English version

#	question	choices	condition
1	How old were you when you developed Covid-19? disease?	10-19 years 20-29 years 30-39 years 40-49 years 50-59 years 60-69 years 70 and more years Radio (single answer)	All participants
2	What is your height (in cm)?	text (number, Min: 120, Max: 250)	All participants
3	What is your weight (in kg)?	text (number, Min: 20, Max: 250)	All participants
4	What is your gender?	Female Male Non-binary Radio (single answer)	All participants
5	Do you suffer from any of the following conditions? Arterial hypertension Asthma COPD Other lung condition Depression Active cancer Hypothyreosis	 Yes/no Yes/no Yes/no Yes/no Yes/no Yes/no Yes/no	All participants
6	Have you suffered in the past from A heart attack or stroke? depression, burnout or any other state of state of fatigue?	 Yes/no Yes/no	All participants

	cancer?	Yes/no	
7	In what function do you work?	Nursing Medical service Diagnostics (BMA, MTRA, ...) Therapies Housekeeping: cleaning, logistics, hotel services Administration Other (dropdown, single answer)	All participants
8	Were you employed as a apprentice at the time of your Covid 19 disease?	Yes/no	All participants
9	How often did you have contact with patients before you became infected?	I had regular patient contact in my daily work. (e.g. nursing, doctors, therapy) I had regular but not close contact with patients (e.g. registration, hospitality, cleaning, ...) I had no patient contact in my daily work I was working from home Radio (single answer)	All participants
10	On which day did you test positive for Covid-19? (If you do not remember exactly, just give an approximate date).	text (date_dmy, Min: 2020-01-01, Max: 2021-04-16)	All participants
11	Approximately how many days before the positive test did your symptoms start?	10-20 days prior to the test 5-10 days prior to the test 0-5 days prior to the test They only started after the test I never had any symptoms Dropdown (single answer)	All participants
12	Have you been hospitalised due to COVID-19 disease?	Yes/no	All participants

13	How many days were you hospitalised because of Covid-19 disease? (If you do not remember exactly, just give an approximate figure).	text (number, Min: 0, Max: 300)	Only if question 12=yes
14	Were you hospitalised in the intensive care unit during the hospitalisation for Covid-19?	Yes/no	Only if question 12=yes
15	How much time after the test, did you feel exactly as healthy as you were before the Covid disease:	I never had symptoms/have always felt well 1-5 days 5-10 days 10-28 days 4 weeks to 3 months More than 3 months I do not yet feel as healthy as I did before the Covid disease	All participants
16	I continue to suffer from the following symptoms	Breathing difficulties Pressure on the chest Cough Feverish feeling/increased Temperature Fatigue Restricted/absent Smell/taste General weakness Sleep problems Hair loss Headaches Dizziness Concentration problems Muscle pain Joint pain Heart palpitations Loss of appetite Digestive problems Other Checkbox (multiple answers)	Only if question 15 = I do not yet feel as healthy as I did before the Covid disease
17	What other symptoms do you suffer from that you attribute to Covid-19?	text	Only if question 16= other

18	Overall, I think that if I was at 100% capacity before the COVID-19 disease, I am now at...	0 % 10 % 20 % 30 % 40 % 50 % 60 % 70 % 80 % 90 % Dropdown (single answer)	Only if question 15 = I do not yet feel as healthy as I did before the Covid disease
19	Where do you think you contracted Covid-19?	When working from a patient When working from other staff members Outside the hospital In the family or with acquaintances/friends I have no idea	All participants
20	Approximately how many days have you been absent from work due to your Covid 19 disease?	text (number, Min: 0, Max: 300)	All participants