Non-occupational and occupational factors associated with specific SARS-CoV-2 antibodies among Hospital Workers – a multicentre cross-sectional study

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ABSTRACT (max 250 words)

Background

Protecting healthcare workers (HCW) from Coronavirus Disease-19 (COVID-19) is critical to preserve the functioning of healthcare systems. We therefore assessed seroprevalence and identified risk factors for Severe Acute Respiratory Syndrome-Coronavirus-2 (SARS-CoV-2) seropositivity in this population.

Methods

Between June 22nd and August 15th 2020, employees from healthcare institutions in Northern/Eastern Switzerland were screened for SARS-CoV-2 antibodies. We recorded baseline characteristics, non-occupational and occupational risk factors. We used pairwise tests of associations and multivariable logistic regression to identify factors associated with seropositivity.

Findings

Among the 4'664 included HCW from 23 healthcare facilities, 139 (3%) were seropositive. Non-occupational exposures independently associated with seropositivity were contact with a COVID-19 positive household (adjusted OR=54, 95%-CI: 31-97) and stay in a COVID-19 hotspot (aOR=2·2, 95%-CI: 1·1-3·9). Blood group 0 vs. non-0 (aOR=0·4, 95%-CI: 0·3-0·7), active smoking (aOR=0·5, 95%-CI: 0·3-0·9) and living with children <12 years (aOR=0·3, 95%-CI: 0·2-0·6) were associated with decreased risk. Occupational risk factors were close contact to COVID-19 patients (aOR=2·8, 95%-CI: 1·5-5·5), exposure to COVID-19 positive co-workers (aOR=2·0, 95%-CI: 1·2-3·1), poor knowledge of standard hygiene precautions (aOR=2·0, 95%-CI: 1·3-3·2), and frequent visits to the hospital canteen (aOR=1·9, 95%-CI: 1·2-3·1).

Interpretation

We identified several modifiable factors associated with SARS-CoV-2 seropositivity among our HCW. Living with COVID-19 positive households showed by far the strongest association. The lower risk among those living with children, even after correction for multiple confounders, is remarkable and merits further study.

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INTRODUCTION

Coronavirus disease 2019 (COVID-19) is currently afflicting healthcare systems around the globe. As of November 1st 2020, over 1.2 million COVID-19 deaths have been reported worldwide[1]. In Switzerland, over 200'000 COVID-19 cases have been reported, almost 9'000 patients have been hospitalized and more than 2'400 have died[2]. Seroprevalence studies among Swiss healthcare workers (HCW) performed in March and April 2020 have shown a low prevalence of 1% in the Eastern part of the country, and a higher prevalence of around 10% in the Western part[3,4]. The recent massive re-emergence of cases in many European countries including Switzerland is putting further strain on healthcare systems and hospital workers. Studies from different countries suggest that HCW are at increased risk to acquire Severe Acute Respiratory Syndrome-Coronavirus-2 (SARS-CoV-2) when compared to the general population. A study among 72 symptomatic HCW from Wuhan showed that working on high-risk wards was associated with increased risk[5]. A seroprevalence study among over 2'000 HCW from a Hospital in Sweden depicted 19% to be seropositive, with higher proportions among those with patient contact and among those caring for COVID-19 patients, suggesting a relevant occupational risk[6]. In the UK, HCW and their household contacts accounted for a sixth of all COVID-19 cases admitted to the hospital for those aged 18-65 years. This risk was increased for HCW involved in patient care[7]. In light of these data it is imperative to better understand risk factors for SARS-CoV-2 acquisition among HCW in order to better protect them from infection[8].

In this multicentre study from Switzerland, we aimed to assess the prevalence of specific antibodies against SARS-CoV-2 among HCW with and without patient contact. In addition, we intended to identify non-occupational and occupational factors associated with seropositivity to inform prevention recommendations for this population.

METHODS

Study design and participants

We initiated a multicentre cross-sectional study between June 22nd and August 15th 2020 in healthcare institutions located in Northern and Eastern Switzerland. Acute care hospitals, rehabilitation clinics, geriatric and psychiatric clinics in the region were asked to participate. Within every participating institution, employees aged 16 years or older were invited to enrol into the study via institutional webpages. Employees registered online and provided electronic consent. The study was approved by the ethics committee of Eastern Switzerland (#2020-00502).

Questionnaire and definitions

We implemented a multi-modular digital baseline questionnaire for institutions and participants. Questions about facility structure were asked in the institutional questionnaire (e.g. type and size of institution, and number of HCW). Participants were asked about place of residence, anthropometric data including body mass index (BMI), and baseline health including presumed risk factors for COVID-19 (i.e. comorbidities, smoking status, number of respiratory tract infections per year, blood group, seasonal influenza and Bacillus Calmette-Guérin [BCG] vaccination) [9,10]. Questions related to non-occupational exposure included household structure (i.e. number, gender and age of household contacts), visits to COVID-19 hotspot regions in bordering countries during February or March 2020 (i.e. Northern Italy, Austrian ski resorts, Alsace), leisure activities (i.e. visits to restaurants and bars, participation in music groups or choirs, fitness centres, sport clubs, religious and cultural activities), number of shopping trips per week, adherence to protective measures, and exposure to non-occupational COVID-19 cases or symptomatic household contacts (i.e. people living in the same household or intimate partners). Questions related to work included type of profession, medical department, employment rate, patient contact in general, contact to COVID-19 patients, close contact to COVID-19 patients (i.e. >15 minutes within 2 meters with or without personal protective measures [PPE]), involvement in aerosol-generating procedures (AGP) defined according to national guidelines[11], exposure to COVID-19 confirmed or symptomatic co-workers, knowledge of standard precautions, use of PPE while caring for COVID-19 patients (in case of multiple events the participants were asked to describe the event with the lowest protection) and frequency of visits to the hospital canteen or cafeteria. Poor knowledge of standard precautions was assumed for those who correctly identified less than 3 measures in a multiple choice question (among a choice of hand hygiene, surgical mask in case of respiratory symptoms, donning gowns in case of potential contamination with body fluids, cough etiquette, and vaccination). Low protection while caring for COVID-19 patients was assumed for those using less than 3 measures out of face masks, gloves, gowns, and goggles. Also, results of previously performed nasopharyngeal swabs for SARS-CoV-2 were asked.

Sample processing

Upon registration, participants provided a venous blood sample at time of inclusion, which was collected at local sites. After obtaining serum by standardized centrifugation, samples were analysed with an electro-chemiluminescence immunoassay (ECLIA, Roche Diagnostics, Rotkreuz, Switzerland, detection of total antibodies directed against the nucleocapsid-(N)-protein of SARS-CoV-2) run on a COBAS 6000 instrument, as described elsewhere[12]. These antibodies have been shown to provide constant antibody levels for a median of 150 days after initial diagnosis of COVID-19 infection [Schaffner A et al. Sustained SARS-CoV-2 nucleocapsid antibody levels in nonsevere COVID-19: a population-based study. Clin Chem Lab Med 2020; In press]. A subgroup of samples with a positive signal in the ECLIA (at a cut-off index, COI, $\geq$ 1) were also tested with an Enzyme-linked Immunosorbent Assay (ELISA, Euroimmune, Germany, detection each of IgG and IgA antibodies against S1 domain of the spike-(S)-protein including the immunologically relevant receptor binding domain) [13]. Cut-offs for seropositivity were applied as recommended by the manufacturers. Seropositivity was defined as positive result in the ECLIA followed by confirmation in the ELISA (either positive IgA or IgG).

Statistical analysis

Baseline information of institutions and participants was characterized using descriptive statistics. The relative frequency of participants with ELISA confirmed positive and negative serology was compared between levels of baseline characteristics, non-occupational risk factors and occupational risk factors. Fisher's exact test was used for dichotomous factors or factors with a reference level, comparing each level to the reference. Logistic regression was used for numeric and ordinal variables. Age, sex, BMI, smoking status, comorbidities as well as non-occupational and occupational risk factors expected to influence seropositivity were entered into a multivariable logistic regression model to evaluate the effect of each risk factor after adjusting for all other factors in the model. For sensitivity analysis, we fitted two additional models including place of residence (7 predefined regions) and institution either as fixed effects or as random effects to assess whether spatial proximity or clustering of observations confounded the effects of the risk factors. Analyses were performed with R statistical software, version 4.0.2.

RESULTS

Baseline characteristics

We included 17 institutions on 23 sites across Northern and Eastern Switzerland, thereof 19 inpatient sites (14 acute care; 1 geriatric clinic; 1 rehabilitation clinic; 3 psychiatric clinics) and 4 outpatient clinics (3 psychiatric facilities; 1 blood donation centre). The total of represented patient beds was 3'523 (thereof 106 ICU beds) (**Table 1**).

Of the 17'060 potentially eligible HCW, 4'664 (27%) participated in the study. Median age was 38 years (range 16-73); 3'654 (78%) were female. The majority were nurses (n=2'126; 46%) followed by physicians (n=776; 17%); 3'676 (79%) reported having patient contact (**Table 2**).

Seropositivity and self-reported PCR results

Overall, seropositivity was 3·0% (139/4'664). Among these 139, 88 (63%) were also tested with the confirmatory ELISA and all 88 samples had either positive IgA or IgG. On the institutional level, seropositivity ranged between 0·5% and 4·2% for inpatient, and 0% and 2·3% for outpatient facilities (**Table 1**). Seropositivity by district (only districts with at least 10 participants) ranged from 0% to 13%. Seropositivity was lower in regions located in Eastern compared to Northern Switzerland (**Figure 1**).

A previous PCR result was reported by 864 of 4'664 (18·5%) participants. Of the 72 participants with positive PCR, 66 (92%) were also seropositive. On the other hand, 17/792 (2·2%) participants with negative PCR had a positive serology. Overall, 23/864 (2·7%) self-reported PCR results were discordant to serology results. Seroprevalence among those without previous PCR was 1·5% (56/3'800).

Non-occupational factors associated with seropositivity

Exposure to COVID-19 confirmed (55·7% vs. 2·1%, p<0·001) or symptomatic, not confirmed household contacts (5·5% vs. 1·9%, p<0·001) was strongly associated with seropositivity. Also, having visited a known COVID-19 hotspot in Austria (but not in Italy or France) was clearly associated with seropositivity (6·8% vs. 2·8%, p=0·002). Seroprevalence was lower among those with blood group 0 vs. non-0 (1·8% vs· 3·5%, p=0·002) and for those living with children aged 12 or younger (1·7% vs. 3·4%, p=0·002). The proportions of seasonal influenza vaccination 2019/2020 and previous BCG vaccination were not different between seropositive and seronegative participants (**Table 2**).

Occupational factors associated with seropositivity

Nurses had a higher (3·9%), physicians a lower (1·0%) seropositivity rate; no differences according to medical speciality were noted. Seroprevalence was higher among those with patient contact (3·1% vs. 1·7%, p=0·037), particularly for those with contact to confirmed COVID-19 patients (4·1% vs. 1·7%, p<0·001). Workers indicating low protection while caring for COVID-19 patients (5·8% vs. 3·5%, p=0·019) and those with poor knowledge of hygiene standards had higher seropositivity (4·1% vs. 2·6%, p=0·018) (**Figure 2, panels A and B**). The number of unprotected contacts to COVID-19 confirmed or symptomatic co-workers was associated with seropositivity (**Figure 2, panel C**). Also, workers who never or only occasionally visited the hospital canteen had a lower seroprevalence compared to those with weekly or daily visits (1·9% vs. 3·5%, p=0·004) (**Figure 2, panel D**). This effect was consistent across institutions and professions (**Table S1**). HCW visiting bars and restaurants other than the hospital canteen did not have an increased risk for seropositivity (**Table 2**).

Multivariable analyses

In multivariable analysis, exposure to a COVID-19 positive household member remained the strongest risk factor for seropositivity with an adjusted odds ratio (aOR) of 54 (95% CI 31-97) (**Figure 3, Table S2**). Stay in a COVID-19 hotspot was associated with increased risk (aOR 2·2, 95% CI 1·1-3·9), whereas blood group 0 (aOR 0·4, 95% CI 0·3-0·7), active smoking (aOR 0·5, 95% CI 0·3-0·9) and living with children <12 years (aOR 0·3, 95% CI 0·2-0·6) were all associated with decreased risk after correcting for multiple confounder variables. The number of respiratory tract infections per annum was only marginally significant (aOR 1·6, 95% CI 1·0-2·5).

Significant occupational factors included close contact with a COVID-19 patient (aOR 2·8, 95% CI 1·5-5·5), exposure to a COVID-19 positive co-worker (aOR 2·0, 95% CI 1·2-3·1), poor knowledge of standard precautions (aOR 2·0, 95% CI 1·3-3·2), as well as having weekly/daily (vs. rarely/never) meals in the hospital canteen (aOR 1·9, 95% CI 1·2-3·1). Low protection while caring for COVID-19 patients was marginally not significant. Both models in the sensitivity analysis did not show any relevant impact of geographic region or institution on the significance level of the variables in the original model (**Table S2**).

DISCUSSION

In this cross-sectional study including 4'664 HCW from Northern and Eastern Switzerland, 3% of participants had specific SARS-CoV-2 antibodies. Our main findings are that exposure to a COVID-19 positive household member is by far the strongest risk factor for seropositivity, and that living with children under the age of 12 - even after correction for multiple confounders - is clearly associated with decreased risk. Furthermore, we identified several exposures associated with seropositivity which might serve as leverage to further decrease the risk of SARS-CoV-2 acquisition among HCW.

We confirm findings from other studies showing that COVID-19 positive household contacts are probably the main source of SARS-CoV-2 infection for HCW[14,15]. Our findings are also in line with a Dutch study analysing viral genomes of HCW and patients from the same hospital. The authors concluded that nosocomial transmissions seemed rather uncommon and that multiple hospital introductions from the community are probably responsible for the large part of COVID-19 cases among patients and HCW, at least in a low prevalence setting[16]. Of course, this association might be overestimated given that the directionality of virus transmission cannot be definitely assessed with our study design. It therefore must be assumed that a certain proportion of household contacts was in fact infected by the HCW, and not vice versa.

An important finding of our study is that participants living with children under the age of 12 were clearly less likely to be seropositive. A large study among over 300'000 HCW households from Scotland has recently found a similar association[17]. In contrast to the Scottish study, we corrected our result for important confounders, including age of HCW, full-time working, and leisure activities. An intriguing hypothesis for this finding is that certain childhood infections, particularly those with endemic coronaviruses such as HCoV-OC43 or HCoV-HKU1, might confer partial immunity (i.e. cross-immunity) to SARS-CoV-2. In line with this hypothesis, adults aged 15 to 44 years (having presumably an increased probability of living with young children) have been shown to have higher antibody titers against the HCoV-OC43 N protein than older adults[18]. Also, supporting the notion of a rather immunological than a purely epidemiological phenomenon, a German study among over 4’000 COVID-19 patients suggested a less complicated disease course for those with frequent contact to children[19]. This hypothesis was partially confirmed by a recent study that demonstrated pre-existing humoral immunity (including neutralizing antibodies) to be particularly prevalent in children and adolescents[20]. This should be confirmed in prospective studies using immunologic assays that demonstrate humoral and cellular immunity against endemic coronaviruses and evaluate their protective role against SARS-CoV-2. If proven to be protective, this could represent a paradigm change for COVID-19 preventive measures in daycare, primary schools and in contact with grandparents.

We specifically asked the participants in our study about staying in geographic regions and places with high COVID-19 activity. Interestingly, stay in an Austrian ski resort where at least one COVID-19 superspreading event had occurred in February/March 2020 was indeed an independent risk factor for seropositivity[21]. Several studies have by now identified an association between the AB0 blood group system and acquisition of COVID-19. Quite consistently, blood group 0 is considered to have a protective effect as shown in our study, whereas people with a non-0 blood group (mostly A) seem to carry an increased risk[22–26]. Whether the blood group also determines the course of the disease is less clear[24,27]. We also observed a lower seroprevalence among active smokers, confirming findings of other studies, including a living rapid review and meta-analysis[28,29]. Possible explanations for this observation include biological effects of tobacco smoke on virus receptors on epithelial cells, or increased physical distancing from people who actively smoke. However, although susceptibility for SARS-CoV-2 might indeed be reduced in this population, the disease course seems to be negatively impacted by smoking[28].

An important question is whether HCW caring for COVID-19 patients are in fact at increased risk for acquiring the disease themselves. Digital surveillance data from the UK and the US indicate that frontline HCW are at increased risk for (self-reported) COVID-19 compared to the general population[30]. Also, frontline HCW in Denmark showed higher seroprevalence than other HCW[31]. Our study confirms these findings, at least for those with close contact to COVID-19 patients. A lower level of protection was not significantly associated with seropositivity in multivariable analysis, probably because of our restrictive definition of low protection. Due to the cross-sectional study design we cannot draw valid conclusions regarding the individual benefit of single protective measures such as gloves, gowns or goggles. However, participants performing AGPs as well as those working in intensive care or emergency rooms did not have an increased risk for COVID-19, suggesting that current safety measures are sufficient for these high-risk HCW. Of note, poor knowledge of standard hygiene precautions was associated with detection of SARS-CoV-2 antibodies, supporting efforts to continuously educate HCW regarding basic infection prevention concepts.

Apart from COVID-19 patients, we identified several easily modifiable occupational factors which might place HCW at increased risk for COVID-19. Exposure to ill co-workers is a known risk factor for respiratory illness in HCW, not only for COVID-19 but also for other respiratory viral diseases[32]. Although this signal was not evident in other HCW cohorts in countries with similar disease burden[14], it is well conceivable that basic hygiene principles, such as physical distancing or hand hygiene are being neglected in contact with co-workers.

Across all participating institutions, we identified visits to the hospital canteen as potential risk factor for seropositivity, even after correction for multiple confounder variables. Visiting restaurants other than hospital canteens has previously been shown to be potentially associated with higher risk of SARS-CoV-2 acquisition[33,34]; however, this was not the case in our data. This discrepancy could be explained by the fact that i) the visitor turnover of hospital canteens is much higher than in other eating places and ii) that the probability of a HCW being infectious is higher than for an average visitor to other restaurants. We therefore suggest that hospitals should revisit and potentially reinforce the safety concepts of their canteens and food courts. This might include limiting the number of people in the area, limiting the duration of stay for each individual, or increasing distances between tables, but also increase adherence to hand washing recommendations before eating.

Our study has several limitations. First, causality cannot be inferred between exposures and seropositivity. Second, sampling bias (both on the institutional and on the individual level) may have arisen given that study participation was non-mandatory. Third, we relied on mostly self-reported data in our questionnaire which is subject to recall and other bias. For this exact reason, we decided not to include self-reported PCR results for the definition of positive and negative participants, thereby accepting a certain number of false negative serology results. Fourth, because of the low disease prevalence we have to assume that a certain proportion of our serology results might also be false positive. However, the reported specificity of >99% for the ECLIA[35], the positive confirmatory results in our tested subsample and the overall low proportion of discordant results between PCR and serology supports the validity of our testing approach.

Strengths of the study are its large sample size, the inclusion of different types of healthcare institutions across a large geographic area, and consideration of not only occupational but a broad range of non-occupational risk factors. In particular the latter differentiates our study from most other seroprevalence studies performed among HCW.

To conclude, having a COVID-19 positive household member was by far the strongest predictor for SARS-CoV-2 seropositivity among our HCW. Furthermore, we identified several modifiable variables associated with seropositivity, including contact to COVID-19 co-workers, poor knowledge of standard hygiene precautions, and possibly frequent visits to the hospital canteen. Living with children below 12 years of age in the same household was independently associated with decreased risk, an extraordinary finding suggesting an increased role of cross-immunity.

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AUTHORS CONTRIBUTION

All authors contributed to the concept and conduct of the study. CRK, PV, and PK were responsible for funding. CRK, MS, PV and PK conceived and planned the study, CRK and PK directed the study. CRK, OL, TE and PK created the electronic database. TE was responsible for communication between study centers. SG performed the data analysis and prepared the figures. CRK, RP and PK interpreted the results and prepared the manuscript, which was critically revised and approved by all authors.

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TABLES

Table 1. Characteristics of institutions (n=15) including size, number of study participants and seropositivity.

	Sites (n)	Beds (n)	ICU beds (n)	HCW (n)	HCW in study (n)	HCW in study (%)	Seropositive HCW (n)	Seropositive HCW (%)
TOTAL	**23**	**3'523**	**106**	**17'060**	**4664**	**27%**	**139**	**3·0%**
Inpatient facilities								
Acute care	3	765	36	5930	1074	18%	37	3·4%
Acute care	1	370	10	2245	1023	46%	39	3·8%
Acute care	3	304	7	1367	534	39%	9	1·7%
Acute care	1	74	0	362	109	30%	3	2·8%
Acute care	1	46	0	178	66	37%	1	1·5%
Acute care	1	246	9	749	169	23%	7	4·1%
Acute care	1	310	12	740	171	23%	3	1·8%
Acute care	1	330	18	1788	448	25%	18	4·0%
Acute care	1	129	6	525	159	30%	4	2·5%
Acute care	1	100	8	632	109	17%	3	2·8%
Geriatric acute care	1	98	0	265	123	46%	3	2·4%
Rehabilitation clinic	1	135	0	510	168	33%	7	4·2%
Psychiatric clinic	1	242	0	360	190	53%	1	0·5%
Psychiatric clinic	1	150	0	391	108	28%	1	0·9%
Psychiatric clinic	1	224	0	780	98	13%	1	1·0%
Outpatient facilities								
Psychiatry	3	-	-	178	88	49%	2	2·3%
Blood donation	1	-	-	60	27	45%	0	0·0%

Table 2. Baseline, non-occupational and occupational factors by serostatus.

	Total n	Seropositive (n and %)	Seronegative (n and %)	OR with 95% CI	p-value
BASELINE					
Gender					
Female	3654	105 (2·9%)	3549 (97·1%)	ref	-
Male	983	34 (3·5%)	949 (96·5%)	1·21 (0·79 - 1·81)	0·343
Age, median (IQR), OR per 10y	38·3 (29·7-49·5)	35·5 (26·8-46·8)	38·4 (29·7-49·6)	0·83 (0·71 - 0·96)	0·012
BMI, median (IQR), OR per unit	23·4 (21·3-26·2)	24·2 (22·2-27·1)	23·4 (21·3-26·1)	1·03 (1·00 - 1·07)	0·078
Smoking status					
Never	2891	96 (3·3%)	2795 (96·7%)	ref	-
Active	822	27 (2·8%)	924 (97·2%)	0·58 (0·32 - 0·99)	0·049
Former	951	16 (1·9%)	806 (98·1%)	0·85 (0·53 - 1·33)	0·525
Comorbidity					
No	3021	80 (2·6%)	2941 (97·4%)	ref	-
Yes	1643	59 (3·6%)	1584 (96·4%)	1·37 (0·96 - 1·95)	0·072
Blood group (OR: one group vs all others)					
A	1396	51 (3·7%)	1345 (96·3%)	1·37 (0·95 - 1·97)	0·090
AB	161	6 (3·7%)	155 (96·3%)	1·27 (0·45 - 2·91)	0·482
B	354	14 (4·0%)	340 (96·0%)	1·38 (0·72 - 2·43)	0·254
0	1383	25 (1·8%)	1358 (98·2%)	0·51 (0·32 - 0·80)	0·002
I don't know	1305	41 (3·1%)	1264 (96·9%)	1·08 (0·73 - 1·58)	0·701
Influenza vaccine 2019/2020					
No	3159	102 (3·2%)	3057 (96·8%)	ref	-
Yes	1416	35 (2·5%)	1381 (97·5%)	0·76 (0·50 - 1·13)	0·189
BCG vaccine					
No	1586	55 (3·5%)	1531 (96·5%)	ref	-
Yes	1908	49 (2·6%)	1859 (97·4%)	0·73 (0·49 - 1·11)	0·134
I don't know	1104	34 (3·1%)	1070 (96·9%)	0·88 (0·56 - 1·39)	0·661
No of respiratory tract infections/year					
0 or 1	3862	105 (2·7%)	3757 (97·3%)	ref	-
2 to 4	776	31 (4·0%)	745 (96·0%)	1·49 (0·96 - 2·26)	0·062
5+	26	3 (11·5%)	23 (88·5%)	4·66 (0·88 - 15·8)	0·034
NON-OCCUPATIONAL EXPOSURES					
No of persons in household					
1 (OR per person)	814	17 (2·1%)	797 (97·9%)	0·94 (0·82 - 1·08)	0·383
2	1660	64 (3·9%)	1596 (96·1%)		
3	778	22 (2·8%)	756 (97·2%)		
4	957	29 (3·0%)	928 (97·0%)		
5+	455	7 (1·5%)	448 (98·5%)		
No of children ≤12 years					
0 (OR per person)	3526	120 (3·4%)	3406 (96·6%)	0·70 (0·52 - 0·90)	0·010
1	492	6 (1·2%)	486 (98·8%)		
2	509	12 (2·4%)	497 (97·6%)		
3+	137	1 (0·7%)	136 (99·3%)		
Confirmed COVID-19 case in household					
No	4585	95 (2·1%)	4490 (97·9%)	ref	-
Yes	79	44 (55·7%)	35 (44·3%)	59·1 (35·4 - 99·9)	< 0·001
Symptomatic household contact					
No	3269	62 (1·9%)	3207 (98·1%)	ref	-
Yes	1395	77 (5·5%)	1318 (94·5%)	3·02 (2·12 - 4·32)	< 0·001
Visit to a COVID-19 hotspot					
No	4413	122 (2·8%)	4291 (97·2%)	ref	-
Yes	251	17 (6·8%)	234 (93·2%)	2·55 (1·42 - 4·35)	0·002
Leisure activities (currently; OR for with vs without activity)					
Visit to restaurant/bar	2783	84 (3·0%)	2699 (97·0%)	1·03 (0·72 - 1·49)	0·930
Sport club	833	28 (3·4%)	805 (96·6%)	1·17 (0·74 - 1·79)	0·499
Fitness/yoga classes	1462	49 (3·4%)	1413 (96·6%)	1·20 (0·82 - 1·73)	0·309
Theater/concerts	112	4 (3·6%)	108 (96·4%)	1·21 (0·32 - 3·27)	0·577
Cinema	290	14 (4·8%)	276 (95·2%)	1·72 (0·90 - 3·05)	0·071
Religious gatherings	228	6 (2·6%)	222 (97·4%)	0·87 (0·31 - 1·99)	1·000
Singing in choir	59	2 (3·4%)	57 (96·6%)	1·14 (0·13 - 4·41)	0·695
Active group musician	110	4 (3·6%)	106 (96·4%)	1·24 (0·33 - 3·33)	0·570

No of leisure activities above					
0 (OR per activity)	1045	25 (2·4%)	1020 (97·6%)	1·13 (0·95 - 1·34)	0·169
1	1875	55 (2·9%)	1820 (97·1%)		
2	1320	46 (3·5%)	1274 (96·5%)		
3	342	9 (2·6%)	333 (97·4%)		
4+	82	4 (4·9%)	78 (95·1%)		
No of shopping trips per week (currently)					
0 (OR per trip)	34	2 (5·9%)	32 (94·1%)	1·03 (0·87 - 1·21)	0·753
1	1212	34 (2·8%)	1178 (97·2%)		
2	1631	46 (2·8%)	1585 (97·2%)		
3	963	33 (3·4%)	930 (96·6%)		
4+	650	19 (2·9%)	631 (97·1%)		
OCCUPATIONAL EXPOSURES					
Profession (OR: one profession vs all others)					
Nurse	2257	88 (3·9%)	2169 (96·1%)	1·87 (1·31 - 2·71)	< 0·001
Physician	776	8 (1·0%)	768 (99·0%)	0·30 (0·13 - 0·61)	< 0·001
Administration/Secretary	472	8 (1·7%)	464 (98·3%)	0·53 (0·22 - 1·09)	0·087
Physiotherapist	181	7 (3·9%)	174 (96·1%)	1·33 (0·52 - 2·87)	0·498
Other	769	16 (2·1%)	753 (97·9%)	0·65 (0·36 - 1·11)	0·130
Speciality (OR: one speciality vs all others)					
Internal Medicine	995	31 (3·1%)	964 (96·9%)	1·06 (0·68 - 1·61)	0·753
Surgery/Orthopedics	475	14 (2·9%)	461 (97·1%)	0·99 (0·52 - 1·74)	1·000
Intensive care	289	5 (1·7%)	284 (98·3%)	0·56 (0·18 - 1·35)	0·280
Emergency department	272	9 (3·3%)	263 (96·7%)	1·12 (0·50 - 2·23)	0·712
Other	585	18 (3·1%)	567 (96·9%)	1·04 (0·59 - 1·73)	0·896
Employment rate					
> 80%	2690	90 (3·3%)	2600 (96·7%)	ref	-
≤ 80%	1974	49 (2·5%)	1925 (97·5%)	0·74 (0·51 - 1·06)	0·098
Patient contact					
No	719	12 (1·7%)	707 (98·3%)	ref	-
Yes	3676	115 (3·1%)	3561 (96·9%)	1·23 (0·85 - 1·77)	0·263
Involved in AGP					
No	3228	90 (2·8%)	3138 (97·2%)	ref	-
Yes	1436	49 (3·4%)	1387 (96·6%)	1·90 (1·04 - 3·81)	0·037
No of correct standard precaution measures					
0 or 1	434	20 (4·6%)	414 (95·4%)	ref	-
2 to 4	2868	79 (2·8%)	2789 (97·2%)	0·59 (0·35 - 1·02)	0·048
5	1362	40 (2·9%)	1322 (97·1%)	0·63 (0·35 - 1·14)	0·093
Adherence to standard precautions					
almost always	2829	76 (2·7%)	2753 (97·3%)	ref	-
if I remember	1227	37 (3·0%)	1190 (97·0%)	1·13 (0·73 - 1·70)	0·604
often not possible	320	10 (3·1%)	310 (96·9%)	1·17 (0·53 - 2·30)	0·589
poorly	43	2 (4·7%)	41 (95·3%)	1·77 (0·20 - 7·02)	0·327
no answer	245	14 (5·7%)	231 (94·3%)	2·19 (1·13 - 3·99)	0·015
Caring for COVID-19 patients					
No	2348	40 (1·7%)	2308 (98·3%)	ref	-
Yes	2062	85 (4·1%)	1977 (95·9%)	2·48 (1·68 - 3·73)	< 0·001
Physical contact with COVID-19 patient					
No (only distant contact)	732	16 (2·2%)	716 (97·8%)	ref	-
Yes	1329	69 (5·2%)	1260 (94·8%)	2·45 (1·39 - 4·56)	0·001
Exposure to coughing or sneezing by COVID-19 patient					
No	1544	52 (3·4%)	1492 (96·6%)	ref	-
Yes	517	33 (6·4%)	484 (93·6%)	1·96 (1·21 - 3·12)	0·005
Protection during close contact (n = 1329); OR for with vs without each protection					
Any face mask	1275	59 (4·6%)	1216 (95·4%)	0·21 (0·10 - 0·50)	0·000
Gloves	1125	49 (4·4%)	1076 (95·6%)	0·42 (0·24 - 0·76)	0·003
Gown	979	41 (4·2%)	938 (95·8%)	0·50 (0·30 - 0·86)	0·008
Goggles	931	39 (4·2%)	892 (95·8%)	0·54 (0·32 - 0·91)	0·015
None	47	8 (17·0%)	39 (83·0%)	4·10 (1·58 - 9·40)	0·002
No of protection measures above					
0 (OR per measure)	44	8 (18·2%)	36 (81·8%)	0·73 (0·61 - 0·87)	< 0·001
1	147	12 (8·2%)	135 (91·8%)		
2	116	6 (5·2%)	110 (94·8%)		
3	157	8 (5·1%)	149 (94·9%)		

4	865	35 (4·0%)	830 (96·0%)		
Contacts with COVID-19 positive co-worker					
No answer / don't know	1212	31 (2·6%)	1181 (97·4%)	1·15 (0·71 - 1·82)	0·564
None	2548	57 (2·2%)	2491 (97·8%)	ref	-
1-2 times	474	25 (5·3%)	449 (94·7%)	2·43 (1·44 - 4·01)	0·001
3 or more times	176	12 (6·8%)	164 (93·2%)	3·20 (1·53 - 6·17)	0·001
Frequency of meals in staff canteen					
never	765	10 (1·3%)	755 (98·7%)	ref	-
occasionally	659	17 (2·6%)	642 (97·4%)	2·00 (0·86 - 4·92)	0·083
weekly	1184	45 (3·8%)	1139 (96·2%)	2·98 (1·47 - 6·68)	0·001
daily	2027	66 (3·3%)	1961 (96·7%)	2·54 (1·29 - 5·57)	0·004

FIGURES

Figure 1. SARS-CoV-2 seropositivity by district in Northern and Eastern Switzerland (in grey: no seroprevalence indicated for districts with less than 10 participants).

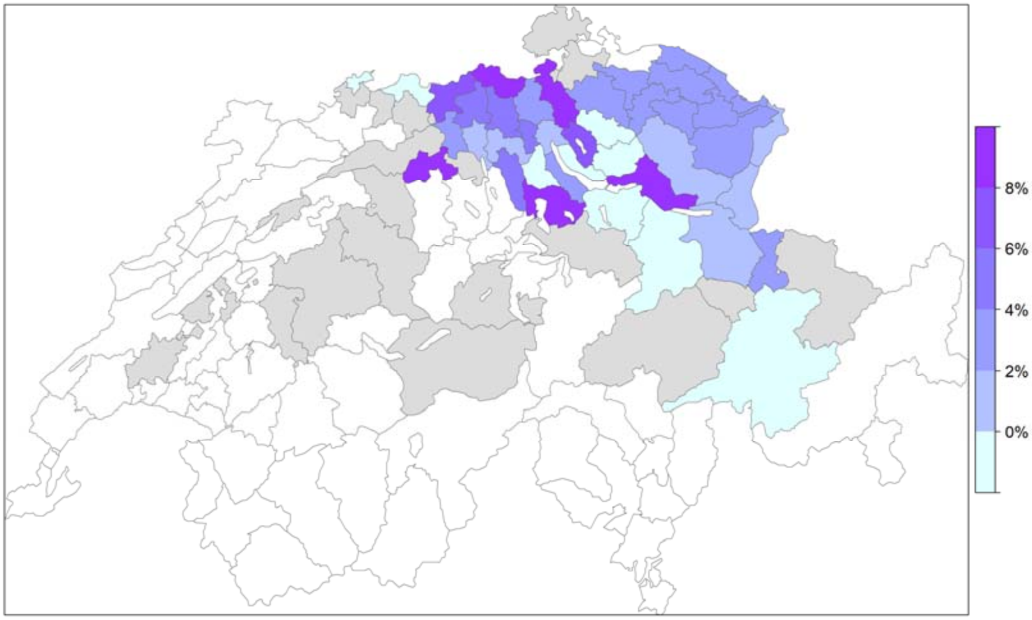

Figure 2. Figure shows (A) number of protective measures used (among face mask, gown, gloves, goggles) while caring for COVID-19 patients; (B) number of correctly identified elements of standard precautions (among hand hygiene, cough etiquette, mask in case of respiratory symptoms, vaccinations, donning of gowns if potential contact with body fluids); (C) number of contacts with COVID-19 positive co-workers; (D) frequency of meals in the hospital canteen

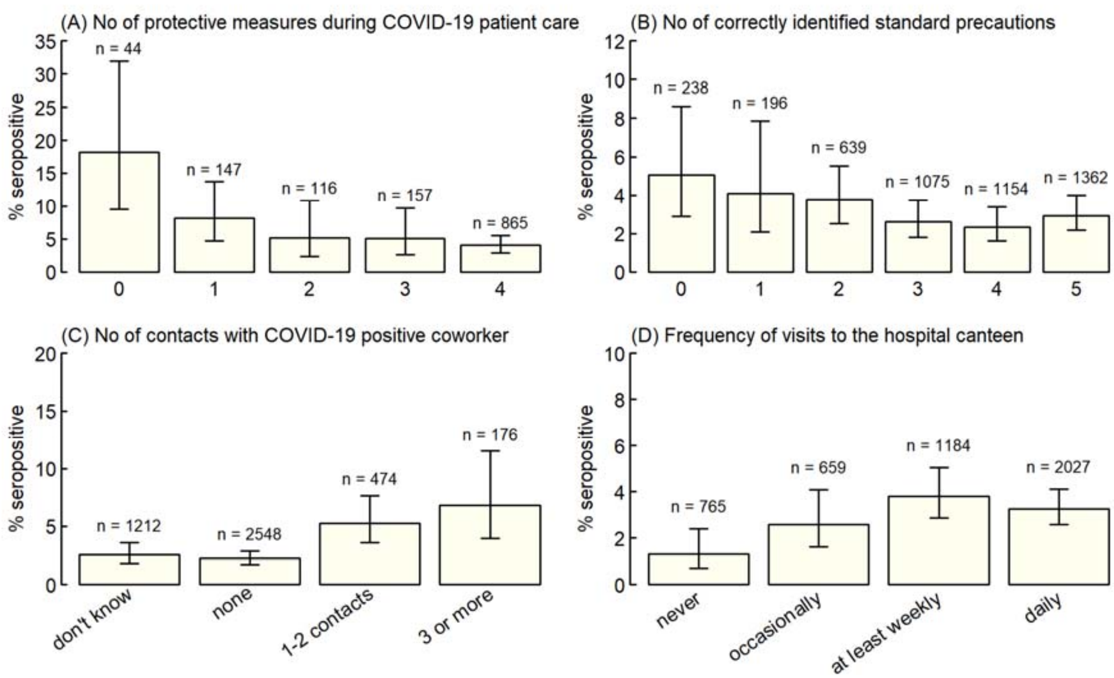

Figure 3. Forest plot showing independent association of baseline, occupational and non-occupational risk factors with seropositivity based on multivariable logistic regression analysis.