Prospective Assessment of SARS-CoV-2 Antibodies in Ontario Healthcare Workers During the First Wave of the Pandemic

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Abstract (250 words)

Background: Healthcare workers (HCWs) have a critical role in the pandemic response to SARS-CoV-2 and may be at increased risk of infection. The objective of this study was to assess the seroprevalence of SARS-CoV-2 IgG antibodies among HCWs during the first wave of the pandemic.

Methods: We conducted a prospective multi-center cohort study of HCWs in Ontario, Canada to detect anti-SARS-CoV-2 antibodies. Blood samples and self-reported questionnaires were obtained at baseline, 6 weeks and 12 weeks. Hospital sites, both academic and community, enrolling participants from April 1 to September 23, 2020 were included in this first wave analysis. Predictors of seropositivity were evaluated using a multivariable logistic regression.

Results: Among the 1,062 HCWs, median age was 40 years and 80% were female. Overall, 53 (5%) were seropositive at any time point (2.2% when participants with prior PCR-confirmed infection were excluded). Seroprevalence was higher amongst those who had a known unprotected exposure to a patient with COVID-19 ($p<0.001$) and those who had been contacted by public health because of a non-hospital exposure ($p=0.002$). Providing direct care to COVID-19 patients or working on a unit with a COVID-19 outbreak were not associated with higher seroprevalence. In multivariable logistic regression, presence of symptomatic contacts in the household was the strongest predictor of seropositivity (aOR 7.61, 95% CI 6.16, 9.41, $p<0.001$), adjusting for clustering by hospital site.

Conclusion: HCWs exposed to household risk factors had higher seroprevalence than those not exposed, and importantly direct care of COVID-19 patients was not associated with increased seropositivity.

Background:

Healthcare workers (HCWs) have a critical role in the pandemic response to COVID-19, potentially increasing the risk for infection as a consequence.[1-3] It is important to understand risk factors that may predispose HCWs to COVID-19 infection and guide targeted interventions or improved direct health and safety measures. Understanding risk and preventative measures is significant to both ensure a healthy essential workforce and protect patients as well as HCWs from potential nosocomial transmission.

Estimates of SARS-CoV-2 infection using only molecular diagnostic tests can lead to substantial testing bias and may underestimate the prevalence of infection.[4] In contrast to molecular tests, which primarily detect acute infection, serologic testing can assist in assessing prior infection and identifying cases that may not have had acute diagnostic testing. As such, serologic assays targeting SARS-CoV-2 antibodies is a useful tool to understand the epidemiology of COVID-19 within a population and the burden of previous mild or asymptomatic infection.[5] Serology tests typically have a high sensitivity for previous SARS-CoV-2 infection when testing occurs >14 days after the onset of symptoms.[6,7]

Studies assessing whether COVID-19 seropositivity in HCW is elevated compared to the general population report mixed results.[8-12] In addition to risk factors shared with the general population, such as age, ethnicity, household exposure with COVID-19, and burden of COVID-19 in the residing communities, there are potential risk factors specific to the hospital including direct care of COVID-19 patients and working on a COVID-19 ward.[8,11-14] It is therefore critical to place the risk of HCWs acquiring COVID-19 in a local clinical context, which addresses hospital safety practices and also community disease prevalence.

The purpose of this study was to assess the overall seroprevalence of SARS-CoV-2 IgG antibodies in a population of HCWs within Ontario over the course of the first wave of the pandemic, and explore factors associated with seropositivity. Further, the durability of SARS-CoV-2 specific antibodies over time was explored.

Methods:

Study setting:

We conducted a prospective multi-center cohort study of HCWs in Ontario, Canada to detect anti-SARS-CoV-2 antibodies. Sites with data from April 1 to September 23, 2020 were included in this first wave analysis. Three hospitals from three Ontario regions[15] participated during this period including 1) The Hospital for Sick Children (SickKids), a tertiary care pediatric hospital in Toronto, Ontario (Toronto Region), 2) London Health Sciences Centre (LHSC), an academic center in London, Ontario consisting of two hospitals including a combined pediatric/adult hospital (South West Region) and 3) Markham Stouffville Hospital (MSH), a community hospital in Markham, Ontario (Central East Region). Over the study period, each hospital saw over 100 patients with COVID-19. Infection Prevention and Control guidelines were the same across hospitals and aligned with provincial guidelines including use of Droplet and Contact precautions for routine care of patients with suspect or confirmed COVID-19, with N95 respirators used for aerosol-generating medical procedures (AGMPs).[16]

Research ethics approval was obtained by Clinical Trials Ontario Research Ethics Board, with local site approvals as required. All participants provided informed consent.

Study participants:

HCWs invited to participate included health care professionals (physicians, nurses, nurse practitioners), allied health workers and other workers who may have had contact with patients, their body fluids or their environments (auxiliary health workers as defined by WHO).[17] HCWs from presumptive high-risk areas were specifically targeted for recruitment through directed communication from clinical directors including those who worked in emergency departments, COVID-19 wards/units, intensive care units and those involved with AGMPs (anesthesia, respiratory therapy).

Study Design and Procedures:

Blood samples and self-reported questionnaires were obtained from all enrolled participants at baseline, 6 weeks and 12 weeks. Blood samples were separated by centrifugation and serum stored frozen at -80ºC. Questionnaires asked about potential COVID-19 risk factors and mitigation strategies including travel history, care of COVID-19 positive patients, known exposure (occupational or otherwise) to a confirmed case of COVID-19, perceived adherence to physical distancing measures and the routine use of personal protective equipment (PPE) during patient encounters. In addition, all participants were emailed weekly requesting that they report any new symptoms.

Outcome:

The anti-SARS-CoV-2 IgG enzyme immunoassay (ELISA) from EUROIMMUN (Lubeck, Germany)[18] was utilized for testing in accordance with the manufacturer's directions on the EUROIMMUN Analyzer I. This Health Canada approved semiquantitative assay detects a recombinant S1 protein of SARS-CoV-2. Interpretation was based on the index values (signal to cut-off ratios) of <0.8 reported as negative, ≥0.8 to <1.1 as borderline, and ≥1.1 as positive.[18] This assay has a reported sensitivity of >90% and specificity of >98% in patients ≥15 days post-symptom onset.[19] All testing was performed at the Microbiology Laboratory at SickKids.

Statistical Analysis:

We reported continuous variables using the mean and standard deviation for normally distributed variables, and the median and range for non-normally distributed data. We reported numbers and percentages for dichotomous outcomes. Proportion of samples seropositive at each time point (baseline, 6 weeks and 12 weeks) was calculated overall and stratified by whether participants had a known COVID-19 infection prior to enrollment. Statistical significance between sites was assessed using chi-squared tests. Spaghetti plots were used to display antibody responses over time.

Detailed information on several potential predictors will be studied in a larger longitudinal study that is ongoing. Due to the few numbers of seropositive participants, we focused this analyses on potential hospital risk factors and household exposure. We targeted the univariable analyses to hospital risk factors (working on a COVID-19 outbreak unit, providing care for COVID-19 patients, unprotected COVID-19 exposure) and non-hospital risk factors (symptomatic household contacts as defined by participant, contacted by public health about exposure) and evaluated the relationship with seropositivity using the chi-square or Fisher's exact test. Multivariable logistic regression model included predictors identified *a priori* including age, sex, race/ancestry, a non-hospital risk factor (symptomatic contacts in the household) and a hospital risk factor (care of COVID-19 positive patients). Generalized estimating equations (GEE) with an exchangeable correlation structure were used to adjust for clustering at the site. A sensitivity analysis was conducted removing patients with known infection at baseline.

All estimates are presented with 95% confidence intervals (95% CI). A p value < 0.05 was considered statistically significant. All analyses were conducted using R (R Core Team, 2020)

Results:

A total of 1,062 HCWs were enrolled. Participants from 2 sites still have ongoing follow–up, thus, only data from participants up to September 23 are included. This resulted in a total of 1062 baseline tests, 1001 6-week samples and 344 12-week samples (Figure 1. participant flow diagram). Median age of HCWs was 40 years (interquartile range 32, 51) and 80% were female (Table 1). Participants were predominantly nurses from inpatient units, critical care and the emergency department. Most participants racially self-identified as White, followed by Asian, with less than 3% self-identifying as Black or Inuit, First Nations or Métis.

Overall, 53/1062 (5%) of HCWs were seropositive at any time point, of which 31 (59%) had a history of confirmed COVID-19 infection by PCR prior to enrollment. An additional 9 participants had previous confirmed COVID-19 infection but were seronegative. Of the 1022 HCW with no confirmed COVID-19 infection prior to enrolment (i.e. excluding those with known recruitment bias), 22 (2.2%) were seropositive at any time point over the study (Table 2). Seroprevalence varied minimally by month (Figure 2), and there was no statistically significant difference in seroprevalence by site (p=0.08).

Of the 53 HCWs with positive serology at any time over the course of the study, 48 (91%) were positive at baseline testing and only 5 (9%) seroconverted during the study. Of the 5 that seroconverted, 1 had a confirmed COVID-19 infection and had baseline testing prior to 15 days. Of the remaining 4 without previous confirmed infection, 3 (6%) were only transiently positive at the 6-week collection and 1 had more than one positive but at a relatively low antibody index value. Figure 3a shows the antibody responses in the 22 participants that were antibody positive but had no history of confirmed COVID-19 infection by PCR. Antibody responses of the 31 participants with positive serology and history of previous PCR confirmed infection are shown in Figure 3b (by month) and Figure 3c (days since positive PCR test).

Comparison of demographics, clinical and possible exposures by detectable antibody status are summarized in Table 3 (additional factors are described in Supplemental Appendix, Table 1). Seroprevalence was higher amongst those who had a known unprotected exposure to a patient with COVID-19 (p<0.001), those who had been contacted by public health because of a non-hospital exposure (p=0.002) and in those with confirmed infection prior to enrollment (p<0.001). Working on a unit with a COVID-19 outbreak was not associated with higher seroprevalence (p=0.5). In the multivariable model (Table 4), presence of symptomatic contacts in the household was the strongest predictor of seropositivity (aOR 7.61, 95% CI 6.16, 9.41, p<0.001). When HCWs with known infection

at baseline were removed, several other predictors were identified. Presence of symptomatic contacts in the house remained a strong predictor (aOR 8.17, 85% CI 4.30, 15.53, p<0.001). Younger age by year (aOR 0.95, 95% CI 0.93, 0.98, p < 0.001) and non-white race (aOR 3.02, 95% CI 1.14, 7.98, p=0.03) were also found to be statistically significant. Of note, providing direct care to patients with COVID-19 was found to be associated with a lower odds of infection (aOR 0.34, 95% CI 0.20, 0.60, p<0.001).

Only 48% (n=23) of HCWs with positive serology at baseline reported a history of symptomatic illness (52% asymptomatic). The most reported symptoms included cough (n=17, 35%), myalgias (n=17, 35%) and fatigue (n=17, 35%) (Supplemental Appendix, Table 2). Those with symptoms documented at least 2 symptoms (n=22), with only one HCW with isolated anosmia.

Discussion:

Among the HCWs sampled across multiple Ontario hospital sites, including a community hospital, tertiary care pediatric hospital and a combined adult/pediatric academic health center, seroprevalence of SARS-CoV-2 antibodies was 5%. The prevalence was even lower at 2.2% taking into account recruitment bias of prior infection before enrolment. Among HCWs, risk factors identified for seroprevalence were outside of the hospital (household / community exposure), unless they had a known unprotected healthcare exposure.

Our finding of 2-5% prevalence of seropositivity depending on prior infection is consistent with several other seroprevalence studies in HCWs that range from 0 – 44%, depending on the jurisdiction.[8,9,11,13,20-31] Since the start of the pandemic given the experience with SARS-CoV-1[32-34] and studies of SARS-CoV-2 showing environmental contamination[35] and occasionally, but not consistently, presence in air samples, there was a concern of higher prevalence of infection in HCWs.[36,37] Not surprisingly, we found higher seroprevalence among healthcare workers from jurisdictions with higher community rates. Overall, seroprevalence in the two hospitals from the Greater Toronto Area, where community rates and seroprevalence are higher,[15,38] at 6.4% (2.5% excluding knowns positives) and 5.8% (2.5% excluding known positives), respectively, while in southwestern Ontario, a community where incidence and seroprevalence was lower, it was 2.9% (1.5% excluding known positives).

In addition to variation in COVID-19 disease burden by region,[9,13,27,30] studies with higher seroprevalence amongst HCWs attributed these estimates to availability of personal protective equipment (PPE)[26,31] and delayed implementation of public health measures in the hospital (i.e. universal masking).[27,28] Shortages of PPE, and episodes lacking any facial coverings while caring for

patients with COVID-19 (defined as lack of surgical mask, or N95 respirator, or powered air purifying respirator [PAPR]), was associated with seropositivity in a multicenter US-based serosurvey.[23] This is in line with our findings of a higher odds of infection in HCWs who had unprotected exposures with COVID-19 patients. Across our hospitals, like across Canada, medical masks are used as part of Droplet and Contact precautions for routine care of patients, with N95 respirator or PAPRs recommended only for use in AGMPs. This approach differs from the United States where an N95 respirator or PAPR is recommended for all encounters with patients with COVID-19, while acknowledging that medical masks are an acceptable alternative.[39] While further studies are needed, our results demonstrating a lack of substantially different seroprevalence in our HCWs compared to either the general Ontario population or other HCW seroprevalence studies in other countries, is reassuring that our current infection prevention and control practices appear to be effective.

We found that the exposure to a symptomatic household member was a strong predictor of positive serology and providing direct care to patients with COVID-19 or working on a unit with a COVID-19 outbreak was not significant. Evidence supporting household exposure as potentially contributing more to infection risk than the healthcare environment has been previously described. Wilkins et al. found that exposure outside of hospital was strongly associated with seropositivity in a large HCW seroprevalence study in Chicago[12] and Steensels et al. found that having a suspected COVID-19 household contact was strongly associated with seropositivity.[11] Additionally younger age and non-white race were significant predictors of seropositivity, a finding described in other studies[40,41] and consistent with community risk factors.[42]

Only about half of the HCWs with antibodies reported signs or symptoms of COVID-19. Similar prevalence of asymptomatic or pauci-symptomatic HCWs with positive serology were documented in other studies[9,22-27,43] and highlight the need for low threshold for testing among HCWs as well as ensuring health and safety measures are followed consistently in hospitals and the community.

The longitudinal collection of samples allowed for the evaluation of the durability of the antibody response. Present evidence suggests that measurable antibody responses may decrease over time with decline potentially related to disease severity.[44-46] In this study, it was surprising that a decline in antibody levels that resulted in a change of serostatus from positive to negative was rare, occurring in only 6% of HCWs in contrast to the significant decline of more than 50% of seen by over a 60-day period in HCWs in another study.[44]

Limitations of this study include the convenience sampling of HCWs, a recruitment bias towards HCW with previous confirmed COVID-19 infection and modest sample size. Ongoing recruitment at additional hospital sites has also focused increasing the number of high-risk workers. The study had low power to detect differences between seropositive and seronegative groups. In addition, the serologic response to SARS-CoV-2 can cross-react with antibodies following infections with SARS-CoV-1, MERS-CoV and other seasonal coronaviruses in circulation.[47] Two individuals with previous exposure to SARS-CoV-1 or MERS-CoV were tested with one being seropositive. While orthogonal testing with an alternative target antigen was not performed, following patient status over time was used as a mitigation strategy, with 87% of participants positive on multiple blood collections. False negative results may have also occurred due to the failure of the assay to detect a measurable antibody response due to a limitation in the assay sensitivity.[48-50] Additionally, false negative results may occur if a participant did not mount a robust antibody response. [51,52]

In conclusion, we found HCWs with community risk factors such as household or community exposure had a higher seroprevalence, and direct care of COVID-19 patients was not associated with an increased seropositivity.

Figure 1. Participant inclusion flow diagram.

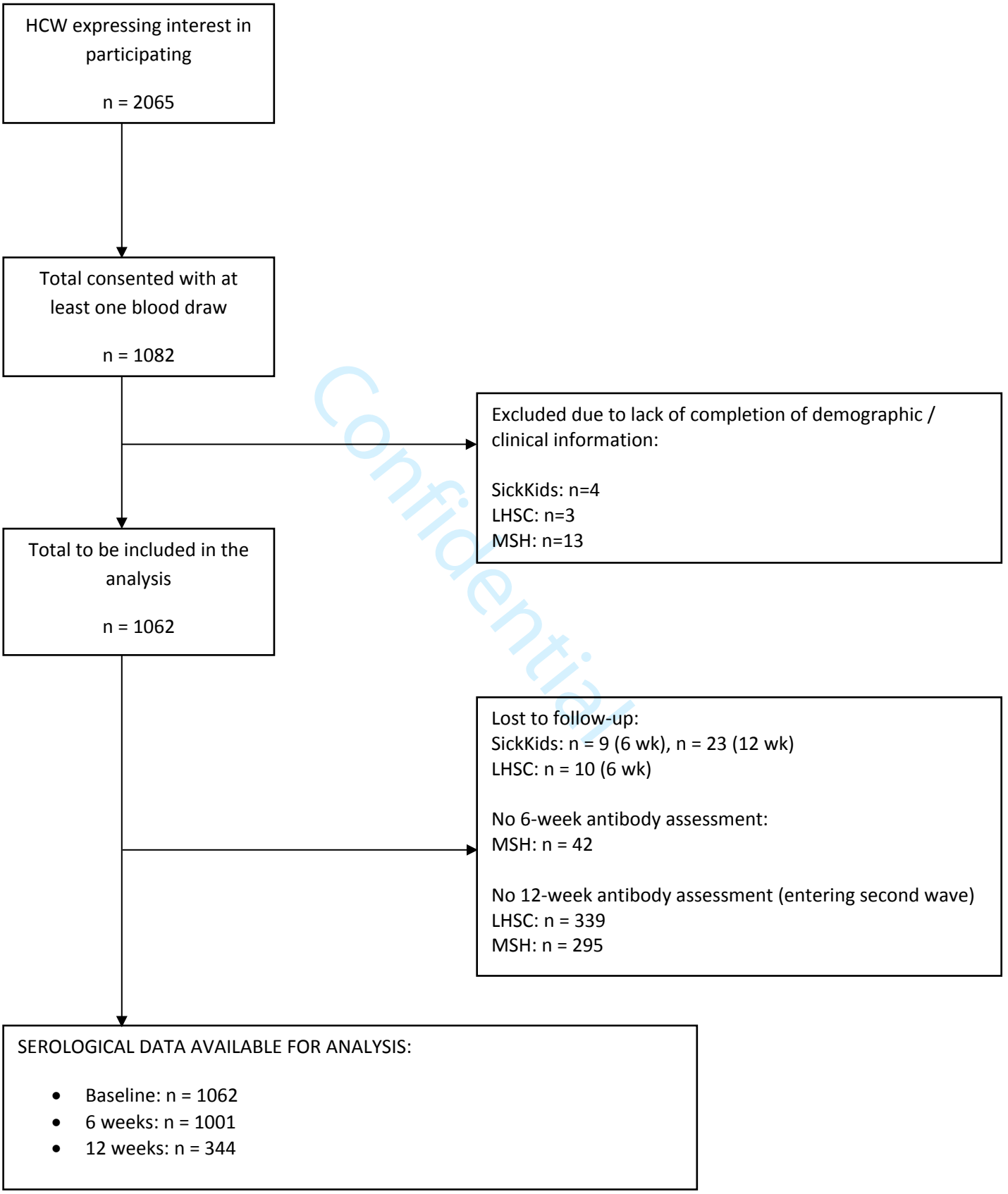

Figure 2. Percentage of participants with positive serology for SARS-CoV-2 by month and by site. Horizontal lines represent the baseline, 6-week, or 12-week collection period mean percent positivity.

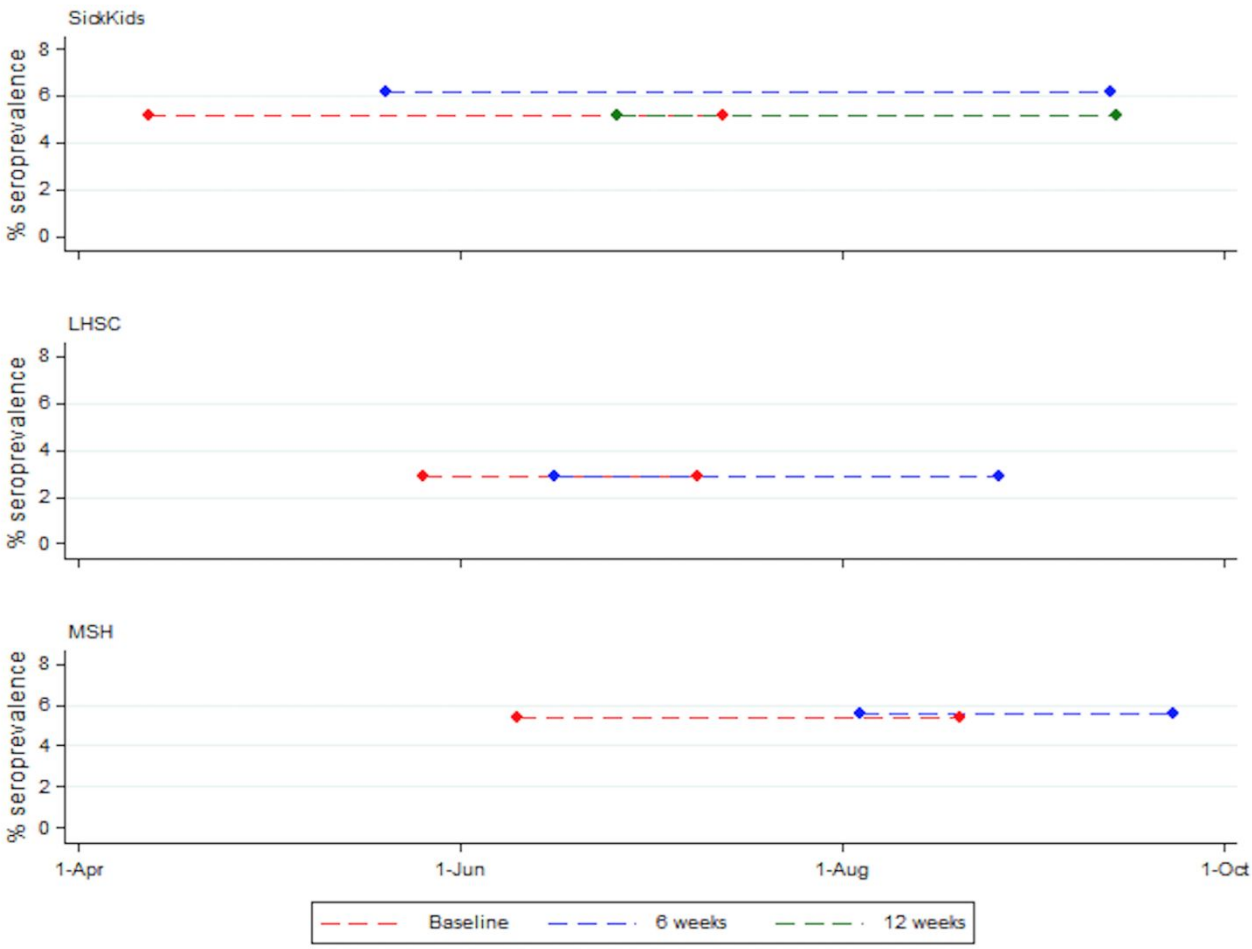

Figure 3a. Antibody responses of the 53 participants who tested positive for SARS-CoV-2 antibodies at any time point during the study. Points above the dashed red line represent a positive antibody result.

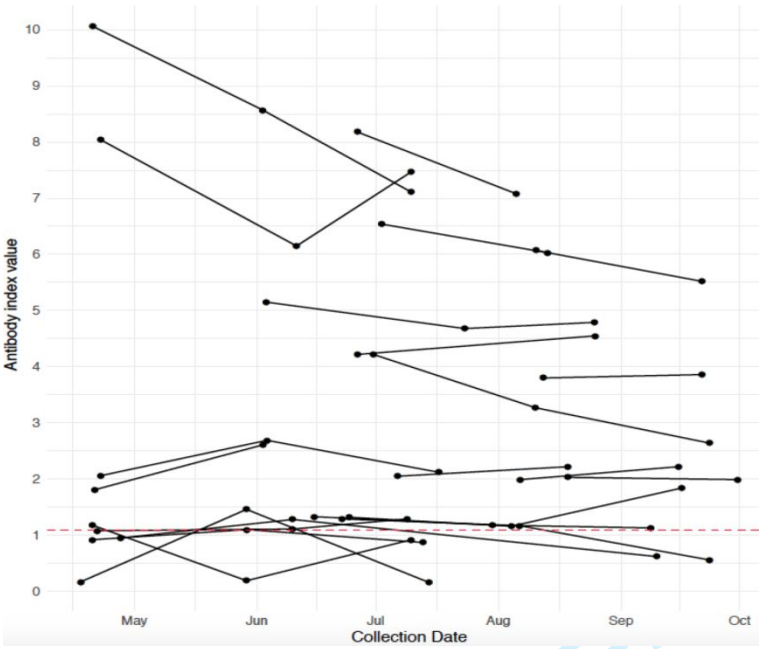

Figure 3b. Antibody responses of the 31 participants who had confirmed SARS-CoV-2 infection by PCR testing and tested positive for SARS-CoV-2 antibodies at any time point during the study by collection time. Points above the dashed red line represent a positive antibody result.

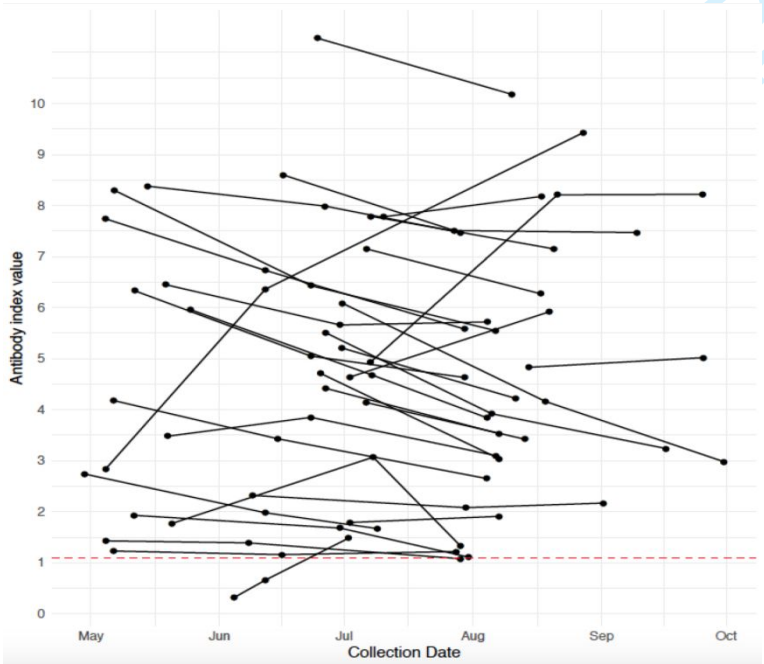

Figure 3c. Antibody responses of the 31 participants who had confirmed SARS-CoV-2 infection by molecular testing and tested positive for SARS-CoV-2 antibodies at any time point during the study expressed as a time from their positive PCR result. Points above the dashed red line represent a positive antibody result.

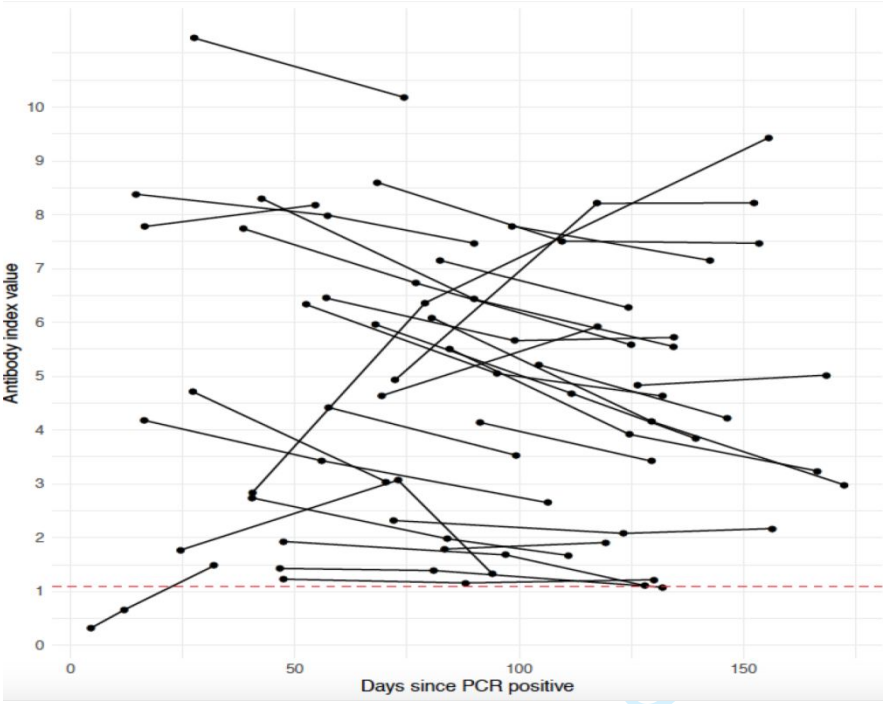

Table 1. Baseline participant characteristics and potential risk factors for SARS-CoV-2 infection

	Total (n=1062)	SickKids (n=376)	London (N=349)	MSH (n=337)
Age, median (IQR)	40 (31.5,51)	38 (31,49)	39 (31,52)	42 (33,51)
Sex, female (%)	834 (80)	272 (76)	283 (81)	279 (83)
Role, n (%)				
Physician	237 (22)	121 (32)	66 (19)	50 (15)
Nurse Practitioner	15 (1)	5 (1)	3 (1)	7 (2)
Nurse	446 (42)	135 (36)	195 (56)	116 (34)
Allied Health Workers	159 (15)	34 (9)	47 (14)	78 (23)
Respiratory Therapy	52 (5)	15 (4)	20 (6)	17 (5)
Auxiliary Health Workers	76 (7)	41 (11)	16 (5)	21 (6)
Other	115 (11)	39 (10)	16 (0.5)	60 (18)
Work Place, n (%)				
Emergency Department	306 (29)	102 (27)	129 (37)	75 (22)
Critical Care	245 (23)	70 (19)	125 (36)	50 (15)
Hospital Ward	373 (35)	121 (32)	128 (37)	124 (37)
Perioperative Services / Surgical Ward	157 (15)	60 (16)	49 (14)	48 (14)
COVID-19 Assessment Center	37 (4)	8 (2)	5 (1)	24 (7)
Other (None of the listed above)	257 (24)	99 (26)	51 (15)	107 (32)
Number of individuals in household				
Median (IQR)	3 (2,4)	3 (2,4)	3 (2,4)	4 (2,4)
Household reporting 3 or more individuals in the house (including the HCW)	602 (58.3)	178/359 (51)	182/349 (52.1)	242/335 (72.2)
Number with children in the household (< 18 yrs)	401 (37.8)	122 (32.4)	121 (34.7)	158 (46.9)
Underlying medical conditions	386 (36)	124 (33)	135 (39)	127 (37)
Race / Ancestry				
Inuit, First Nations, Métis	3 (0.3)	0 (0)	1 (0.3)	2 (0.5)
White	734 (72)	243 (71)	296 (86)	195 (59)
Black	16 (2)	9 (3)	3 (1)	4 (1)
Hispanic	14 (1.4)	10 (3)	3 (1)	1 (0.3)
Asian	172 (16)	52 (14)	25 (7)	95 (28)
Middle Eastern	31 (3)	8 (2)	12 (4)	11 (3)
Other	55 (5)	21 (6)	7 (2)	27 (8)
Unknown / unspecified	40 (4)	33 (9)	3 (1)	4 (1)
Travel since January 1, 2020	402 (38)	159 (42)	138 (40)	105 (31)
Worked on a unit with COVID outbreak	120 (11)	3 (1)	93 (27)	24 (7)
Provided direct care patient with COVID-19	439 (42)	29 (8)	230 (67)	180 (54)
Known unprotected occupational exposure with direct patient care)	41 (9)	4 (14)	24 (10)	13 (7)
Known SARS-COV-2 positive by PCR prior to enrolment	40 (4)	17 (5)	7 (2)	16 (5)
Positivity proportion				
Overall (at any time point)	53 (5.0)	24 (6.4)	10 (2.9)	19 (5.8)
Baseline	49 (4.6)	20 (5.2)	10 (2.9)	19 (5.4)
6 weeks	50 (4.7)	23 (6.2)	10 (2.9)	17 (5.6)
12 weeks		18 (5.2)	n/a	n/a

Table 2. Seroprevalence at study collection time points overall and by confirmed SARS-CoV-2 infection confirmed by PCR

Serology status	Prior PCR status		Total number of samples positive and negative at each time point (n, %)
	Positive	Negative	
Positive (n)			**53 / 1062 (5.0)**
Baseline	30 / 40	18 / 1022	48 / 1062 (4.5)
6 weeks	29 / 38	20 / 963	49 / 1001 (4.9)
12 weeks	14 / 17	4 / 327	18 / 344 (5.2)
At any point	31 / 40	22 /1022	53 / 1062 (5.0)
Negative (n)			**1009 / 1062 (95.0)**
Baseline	10 / 40	1004 / 1022	1014 / 1062 (95.5)
6 weeks	9 / 38	943 / 963	952 / 1001 (95.1)
12 weeks	3 / 17	323 / 327	326 / 344 (94.8)
At any point	9 / 40	1000 / 1022	1009 / 1062 (95.0)
Total	**40**	**1022**	**1062**

Table 3. Factors associated with having detectable SARS-CoV-2 antibodies

	SARS-CoV-2 Serology Positive (n= 53)	SARS-CoV-2 Serology Negative (n= 1009)	p-value
Symptomatic contacts in the household	7 / 49 (14)	25/975 (3)	< 0.001
Provided direct care to COVID patients	25 (47)	414 (41)	0.4
Unprotected occupational exposure to a COVID-19 case	8 (32)	33 (8)	< 0.001
Worked on a COVID-19 outbreak unit	4 (8)	116 (12)	0.5
Contacted by public health to indicate exposure	9 (17)	54 (5)	0.002
Known positive PCR test at baseline	31 (59)	9 (0.9)	< 0.001

Table 4. Multivariable model for predictors of having SARS-CoV-2 antibodies

Variable	All HCW (n=1062) Odds Ratio (95% confidence interval)	HCW excluding those with previously confirmed COVID-19 infection (n=1022) Odds Ratio (95% confidence interval)
Age by year	0.99 (0.97, 1.01)	0.95 (0.93, 0.98)
Female sex	1.69 (0.71, 4.00)	1.22 (0.43, 3.43)
White vs. non-white race*	1.13 (0.40, 3.21)	3.02 (1.14, 7.98)
Symptomatic household exposure	7.61 (6.16, 9.41)	8.17 (4.30, 15.53)
Direct care of patients with COVID-19	1.51 (0.80, 2.84)	0.34 (0.20, 0.60)

*Participants indicating unknown ancestry were excluded

References

1. Kampf G, Bruggemann Y, Kaba HEJ, et al. Potential sources, modes of transmission and effectiveness of prevention measures against SARS-CoV-2. *J Hosp Infect* 2020; **106**(4): 678-97.
2. Reynolds MG, Anh BH, Thu VH, et al. Factors associated with nosocomial SARS-CoV transmission among healthcare workers in Hanoi, Vietnam, 2003. *BMC Public Health* 2006; **6**: 207.
3. Schwartz J, King CC, Yen MY. Protecting Healthcare Workers During the Coronavirus Disease 2019 (COVID-19) Outbreak: Lessons From Taiwan's Severe Acute Respiratory Syndrome Response. *Clin Infect Dis* 2020; **71**(15): 858-60.
4. Havers FP, Reed C, Lim T, et al. Seroprevalence of Antibodies to SARS-CoV-2 in 10 Sites in the United States, March 23-May 12, 2020. *JAMA Intern Med* 2020.
5. Loeffelholz MJ, Tang YW. Laboratory diagnosis of emerging human coronavirus infections - the state of the art. *Emerg Microbes Infect* 2020; **9**(1): 747-56.
6. Xiang F, Wang X, He X, et al. Antibody Detection and Dynamic Characteristics in Patients With Coronavirus Disease 2019. *Clin Infect Dis* 2020; **71**(8): 1930-4.
7. Zhao J, Yuan Q, Wang H, et al. Antibody Responses to SARS-CoV-2 in Patients With Novel Coronavirus Disease 2019. *Clin Infect Dis* 2020; **71**(16): 2027-34.
8. Iversen K, Bundgaard H, Hasselbalch RB, et al. Risk of COVID-19 in health-care workers in Denmark: an observational cohort study. *Lancet Infect Dis* 2020; **20**(12): 1401-8.
9. Houlihan CF, Vora N, Byrne T, et al. Pandemic peak SARS-CoV-2 infection and seroconversion rates in London frontline health-care workers. *Lancet* 2020; **396**(10246): e6-e7.
10. Lai X, Wang M, Qin C, et al. Coronavirus Disease 2019 (COVID-2019) Infection Among Health Care Workers and Implications for Prevention Measures in a Tertiary Hospital in Wuhan, China. *JAMA Netw Open* 2020; **3**(5): e209666.
11. Steensels D, Oris E, Coninx L, et al. Hospital-Wide SARS-CoV-2 Antibody Screening in 3056 Staff in a Tertiary Center in Belgium. *JAMA* 2020; **324**(2): 195-7.
12. Wilkins J, Gray EL, Wallia A, et al. Seroprevalence and Correlates of SARS-CoV-2 Antibodies in Healthcare Workers in Chicago. *medRxiv* 2020: 2020.09.11.20192385.
13. Moscola J, Sembajwe G, Jarrett M, et al. Prevalence of SARS-CoV-2 Antibodies in Health Care Personnel in the New York City Area. *JAMA* 2020; **324**(9): 893-5.
14. Nguyen LH, Drew DA, Joshi AD, et al. Risk of COVID-19 among frontline healthcare workers and the general community: a prospective cohort study. *medRxiv* 2020.
15. Ontario Agency for Health Protection and Promotion (Public Health Ontario). Epidemiologic summary: COVID-19 in Ontario – January 15, 2020 to December 20, 2020. Toronto, ON: Queen's Printer for Ontario; 2020. Available at: https://www.publichealthontario.ca/-/media/documents/ncov/epi/2020/covid-19-daily-epi-summary-report.pdf?la=en.
16. Ontario Agency for Health Protection and Promotion (Public Health Ontario). IPAC recommendations for use of personal protective equipment for care of individuals with suspect or confirmed COVID-19. Toronto, ON: Queen's Printer for Ontario; 202. Available at: https://www.publichealthontario.ca/-/media/documents/ncov/updated-ipac-measures-covid-19.pdf?la=en.
17. World Health Organization. Protocol for assessment of potenital risk factors for 2019-novel coronavirus (COVID-19) infection among health care workers in a health care setting. Available at https://who.int/publications-detail/protocol-for-assessment-of-potential-risk-factors-for-2019-novel-coronavirus-(2019-ncov)-infection-among-health-care-workers-in-a-health-care-setting.
18. EUROIMMUN Medizinische Labordiagnostika AG. SARS-CoV-2 ELISA test systems from EUROIMMUN [Internet]. [cited 2020 Apr 1]. Available from: https://www.coronavirus-diagnostics.com/antibody-detection-tests-for-covid-19.html.

19. Theel ES, Harring J, Hilgart H, Granger D. Performance Characteristics of Four High-Throughput Immunoassays for Detection of IgG Antibodies against SARS-CoV-2. *J Clin Microbiol* 2020; **58**(8).
20. Jeremias A, Nguyen J, Levine J, et al. Prevalence of SARS-CoV-2 Infection Among Health Care Workers in a Tertiary Community Hospital. *JAMA Intern Med* 2020.
21. Barrett ES, Horton DB, Roy J, et al. Prevalence of SARS-CoV-2 infection in previously undiagnosed health care workers at the onset of the U.S. COVID-19 epidemic. *medRxiv* 2020.
22. Stubblefield WB, Talbot HK, Feldstein L, et al. Seroprevalence of SARS-CoV-2 Among Frontline Healthcare Personnel During the First Month of Caring for COVID-19 Patients - Nashville, Tennessee. *Clin Infect Dis* 2020.
23. Self WH, Tenforde MW, Stubblefield WB, et al. Seroprevalence of SARS-CoV-2 Among Frontline Health Care Personnel in a Multistate Hospital Network - 13 Academic Medical Centers, April-June 2020. *MMWR Morb Mortal Wkly Rep* 2020; **69**(35): 1221-6.
24. Korth J, Wilde B, Dolff S, et al. SARS-CoV-2-specific antibody detection in healthcare workers in Germany with direct contact to COVID-19 patients. *J Clin Virol* 2020; **128**: 104437.
25. Godbout EJ, Pryor R, Harmon M, et al. COVID-19 seroprevalence among healthcare workers in a low prevalence region. *Infect Control Hosp Epidemiol* 2020: 1-8.
26. Mansour M, Leven E, Muellers K, Stone K, Mendu DR, Wajnberg A. Prevalence of SARS-CoV-2 Antibodies Among Healthcare Workers at a Tertiary Academic Hospital in New York City. *J Gen Intern Med* 2020; **35**(8): 2485-6.
27. Grant JJ, Wilmore SMS, McCann NS, et al. Seroprevalence of SARS-CoV-2 antibodies in healthcare workers at a London NHS Trust. *Infect Control Hosp Epidemiol* 2020: 1-3.
28. Rudberg AS, Havervall S, Manberg A, et al. SARS-CoV-2 exposure, symptoms and seroprevalence in healthcare workers in Sweden. *Nat Commun* 2020; **11**(1): 5064.
29. Eyre DW, Lumley SF, O'Donnell D, et al. Differential occupational risks to healthcare workers from SARS-CoV-2 observed during a prospective observational study. *Elife* 2020; **9**.
30. Galan I, Velasco M, Casas ML, et al. SARS-CoV-2 SEROPREVALENCE AMONG ALL WORKERS IN A TEACHING HOSPITAL IN SPAIN: UNMASKING THE RISK. *medRxiv* 2020: 2020.05.29.20116731.
31. Chen Y, Tong X, Wang J, et al. High SARS-CoV-2 antibody prevalence among healthcare workers exposed to COVID-19 patients. *J Infect* 2020; **81**(3): 420-6.
32. Varia M, Wilson S, Sarwal S, et al. Investigation of a nosocomial outbreak of severe acute respiratory syndrome (SARS) in Toronto, Canada. *CMAJ* 2003; **169**(4): 285-92.
33. Masur H, Emanuel E, Lane HC. Severe acute respiratory syndrome: providing care in the face of uncertainty. *JAMA* 2003; **289**(21): 2861-3.
34. Fowler RA, Guest CB, Lapinsky SE, et al. Transmission of severe acute respiratory syndrome during intubation and mechanical ventilation. *Am J Respir Crit Care Med* 2004; **169**(11): 1198-202.
35. Ye G, Lin H, Chen S, et al. Environmental contamination of SARS-CoV-2 in healthcare premises. *J Infect* 2020; **81**(2): e1-e5.
36. Guo ZD, Wang ZY, Zhang SF, et al. Aerosol and Surface Distribution of Severe Acute Respiratory Syndrome Coronavirus 2 in Hospital Wards, Wuhan, China, 2020. *Emerg Infect Dis* 2020; **26**(7): 1583-91.
37. Li YH, Fan YZ, Jiang L, Wang HB. Aerosol and environmental surface monitoring for SARS-CoV-2 RNA in a designated hospital for severe COVID-19 patients. *Epidemiol Infect* 2020; **148**: e154.
38. Ontario Agency for Health Protection and Promotion (Public Health Ontario). COVID-19 Seroprevalence in Ontario: March 27, 2020 to June 30, 2020. Toronto, ON: Queen's Printer for Ontario; 2020. Available at: https://www.publichealthontario.ca/-/media/documents/ncov/epi/2020/07/covid-19-epi-seroprevalence-in-ontario.pdf?la=en.
39. Centers for Disease Control and Prevention. Interim Infection Prevention and Control Recommendations for Healthcare Personnel During the Coronavirus Disease 2019 (COVID-19) Pandemic. Updated Dec 14. Available at: https://www.cdc.gov/coronavirus/2019-ncov/hcp/infection-control-recommendations.html.

40. Rosser JI, Roltgen K, Dymock M, et al. SARS-CoV-2 Seroprevalence in Healthcare Personnel in Northern California Early in the COVID-19 Pandemic. *Infect Control Hosp Epidemiol* 2020: 1-27.
41. Ebinger J, Botwin GJ, Albert CM, et al. SARS-CoV-2 Seroprevalence Across a Diverse Cohort of Healthcare Workers. *medRxiv* 2020: 2020.07.31.20163055.
42. Ontario Agency for Health Protection and Promotion (Public Health Ontario). COVID-19 in Ontario - A Focus on Diversity: January 15, 2020 to May 14, 2020 Toronto, ON: Queen's Printer for Ontario; 2020. Available at: https://www.publichealthontario.ca/-/media/documents/ncov/epi/2020/06/covid-19-epi-diversity.pdf?la=en.
43. Garcia-Basteiro AL, Moncunill G, Tortajada M, et al. Seroprevalence of antibodies against SARS-CoV-2 among health care workers in a large Spanish reference hospital. *Nat Commun* 2020; **11**(1): 3500.
44. Patel MM, Thornburg NJ, Stubblefield WB, et al. Change in Antibodies to SARS-CoV-2 Over 60 Days Among Health Care Personnel in Nashville, Tennessee. *JAMA* 2020.
45. Seow J, Graham C, Merrick B, et al. Longitudinal observation and decline of neutralizing antibody responses in the three months following SARS-CoV-2 infection in humans. *Nat Microbiol* 2020; **5**(12): 1598-607.
46. Roltgen K, Powell AE, Wirz OF, et al. Defining the features and duration of antibody responses to SARS-CoV-2 infection associated with disease severity and outcome. *Sci Immunol* 2020; **5**(54).
47. Lisboa Bastos M, Tavaziva G, Abidi SK, et al. Diagnostic accuracy of serological tests for covid-19: systematic review and meta-analysis. *BMJ* 2020; **370**: m2516.
48. Van Elslande J, Houben E, Depypere M, et al. Diagnostic performance of seven rapid IgG/IgM antibody tests and the Euroimmun IgA/IgG ELISA in COVID-19 patients. *Clin Microbiol Infect* 2020; **26**(8): 1082-7.
49. Manthei DM, Whalen JF, Schroeder LF, et al. Differences in Performance Characteristics Among Four High-Throughput Assays for the Detection of Antibodies Against SARS-CoV-2 Using a Common Set of Patient Samples. *Am J Clin Pathol* 2020.
50. Beavis KG, Matushek SM, Abeleda APF, et al. Evaluation of the EUROIMMUN Anti-SARS-CoV-2 ELISA Assay for detection of IgA and IgG antibodies. *J Clin Virol* 2020; **129**: 104468.
51. Plebani M. Antibody responses in mild COVID-19 hospital staff. *EBioMedicine* 2020; **59**: 102940.
52. Ibarrondo FJ, Fulcher JA, Goodman-Meza D, et al. Rapid Decay of Anti-SARS-CoV-2 Antibodies in Persons with Mild Covid-19. *N Engl J Med* 2020; **383**(11): 1085-7.

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STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1,2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4,11
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	4
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5
Bias	9	Describe any efforts to address potential sources of bias	8,9
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	4
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5
		(*b*) Describe any methods used to examine subgroups and interactions	5
		(*c*) Explain how missing data were addressed	6
		(*d*) If applicable, explain how loss to follow-up was addressed	6
		(*e*) Describe any sensitivity analyses	5
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6, 10(Figure1)
		(b) Give reasons for non-participation at each stage	10(Figure 1)
		(c) Consider use of a flow diagram	10
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6, 14 (table1)
		(b) Indicate number of participants with missing data for each variable of interest	Tables
		(c) Summarise follow-up time (eg, average and total amount)	11
Outcome data	15*	Report numbers of outcome events or summary measures over time	6-7

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (*b*) Report category boundaries when continuous variables were categorized (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	6
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	6-7
Discussion			
Key results	18	Summarise key results with reference to study objectives	7-8
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	9
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	7-9
Generalisability	21	Discuss the generalisability (external validity) of the study results	7-9
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	1

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

Supplemental Appendix

Table 1. Comparison of SARS-CoV-2 seropositivity by predictor

	SARS-CoV-2 Serology Positive (n= 53)	SARS-CoV-2 Serology Negative (n= 1009)
Age, median (IQR)	39 (31,50)	40 (32,51)
Sex, female n (%)	44 (86)	790 (79)
Any Comorbidity / underlying conditions	16 (30)	370 (37)
Hospital Site		
SickKids	24 (45)	352 (35)
London	10 (19)	339 (34)
MSH	19 (36)	318 (31)
Role		
HCP	38 (72)	672 (67)
Allied Health	4 (8)	155 (15)
Auxiliary	3 (6)	73 (7)
Other	8 (15)	2 (0.5)
HCP Role		
Nurse	23 (43)	423 (42)
Physician	14 (26)	223 (22)
Nurse Practitioner	1 (2)	14 (1)
Allied Health Role	2 (4)	50 (5)
Auxiliary Health Role	0 (0)	13 (1)
Work place		
COVID-19 Assessment Center	8 (15)	29 (3)
Emergency Department	15 (28)	291 (29)
Critical Care	8 (15)	237 (24)
Travel after Jan 1 (outside of Canada)	18 (34)	384 (38)
Household reporting 3 or more individuals in the house (including the HCW)	602 (59)	25 (51)
Number with children in the household (< 18 yrs)	383 (38)	18 (34)
Worked on a COVID-19 outbreak unit	4 (8)	116 (12)
Diagnosed with SARS-CoV-1 / MERS	1 (2)	1 (0.5)
How often do you leave the house per week outside of work? > 5 times vs. other	18 (37)	302 (31)
When leave the house, wear facemask all the time vs. most of the time/sometimes/never	22 (42)	326 (33)
When leave the house, physical distancing always vs. most of the time/sometimes/never	27 (55)	542 (56)

Table 2. Clinical Symptoms of HCW testing positive for SARS-CoV-2 antibodies at baseline (? Appendix)

Symptom	Number of seropositive HCW reporting symptoms(%) (n = 48)
Asymptomatic / No symptoms	25 (52)
Isolated Symptom	1 (2)
>=2 symptoms	22 (46)
Fever	12 (25)
Chills	11 (23)
Cough	17 (35)
Shortness of Breath	11 (23)
Sore Throat	4 (8)
Fatigue	17 (35)
Muscle Aches	17 (35)
Runny nose	11 (23)
Chest Pain	5 (10)
Abdominal Pain	1 (2)
Diarrhea	7 (15)
Vomiting	3 (6)
Loss of appetite	6 (13)
Headache	10 (21)
Ageusia	7 (15)
Anosmia	7 (15)
Joint pains	6 (13)
Rash	1 (2)