SARS-CoV-2 Antibodies in Ontario Healthcare Workers During and Following the First Wave of the Pandemic: a Cohort Study

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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 and following 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 enrolment, 6 weeks and 12 weeks. A community hospital, tertiary care pediatric hospital and a combined adult/pediatric academic health center enrolled participants from April 1 to November 13, 2020. 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, 57 (5.4%) were seropositive at any time point (2.5% 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 ($p=0.003$). 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 7.15, 95% CI 5.42, 9.41, $p<0.001$), adjusting for clustering by hospital site.

Interpretation: HCWs exposed to household risk factors had higher seroprevalence than those not exposed, highlighting the need to emphasize the importance of public health measures outside the hospital.

Background:

Healthcare workers (HCWs) have a critical role in the pandemic response to coronavirus disease 2019 (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, the use of 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]

Some studies assessing whether COVID-19 seropositivity in HCW is elevated compared to the general population have reported higher seroprevalence.[8-10] 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 general inpatient care, direct care of COVID-19 patients and working on a COVID-19 ward.[8,11-15] 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 during and immediately following 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 Design:

We conducted a prospective multi-center cohort study of HCWs in Ontario, Canada to detect anti-SARS-CoV-2 antibodies. The study was proposed to hospitals across Ontario through an infection prevention and control community of practice with representation from over 30 hospitals. After review and approval of the protocol, interested sites obtained research ethics and legal approvals leading to variable start dates. The sites that completed recruitment during and immediately following the first wave (April 1 to November 13, 2020) were included in this analysis.

Study setting:

Three hospitals from three Ontario regions[16] participated during this study 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). 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).[17] Information on the number of COVID-19 patients treated during the study period was collected from each hospital.

Study participants:

HCWs invited to participate included health care professionals, defined as physicians, nurses and nurse practitioners; allied health workers, defined as phlebotomists, respiratory therapists, socials workers, dieticians, diagnostic imaging staff, physiotherapists, occupational therapists, and dentistry staff; and auxiliary HCW (as defined by the World Health Organization as workers who may have had contact with patients, their body fluids or their environments[18]), including environmental services, patient transport and laboratory personnel, and ward clerical workers. Recruitment tools included posters, all-staff emails from leadership, computer screen savers and a website (http://cancovid19plasma.ca/healthcare-worker-serology/) that provided general information about the study and contact information for the study coordinators. In addition, we specifically recruited HCW who worked in emergency departments, COVID-19 wards/units, intensive care units and those involved with AGMPs (anesthesia, respiratory therapy) through directed communication at departmental meetings or emails by clinical directors, as these groups may have had a higher risk of COVID-19 exposure.

Study Procedures:

Blood samples and self-reported questionnaires were obtained from all enrolled participants at baseline (i.e. enrolment), 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 type of personal protective equipment (PPE) used during patient encounters (all patients and suspect/confirmed COVID-19 patients) (See supplemental Appendix 1, Baseline Survey). In addition, all participants were emailed weekly requesting that they report any new symptoms.

Our proposed sample size of at least 1000 HCW would allow us to determine seropositivity at baseline with an 80% probability that the confidence interval has a precision of ±1.5%, assuming a seroprevalence of 5% (80% power, alpha of 0.05).

Outcome:

The anti-SARS-CoV-2 IgG enzyme immunoassay (ELISA) from EUROIMMUN (Lubeck, Germany)[19] 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.[19] This assay has a reported sensitivity of >90% and specificity of >98% in patients ≥15 days post-symptom onset.[20] All testing was performed at the Microbiology Laboratory at SickKids.

Statistical Analysis:

We reported continuous variables using the mean and standard deviation or median and interquartile range as appropriate. 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. The proportions with seropositive results at each time point were compared between sites using chi-square 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 and included only 5 predictors in the multivariable model using the 10-events per variable rule of thumb. 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. All analyses were based on the baseline questionnaire responses. 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, Vienna, Austria)

Ethics Approval:

Research ethics approval was obtained by Clinical Trials Ontario Research Ethics Board (Project ID 3182), with local site approvals as required. All participants provided informed consent.

Results:

This analysis represents data from the first three hospitals recruited to participate in our study. A total of 2,065 HCWs contacted the study team to learn more about the study and 1082 consented to participate. Of those who consented, 1,062 HCWs had baseline information available and bloodwork completed and were included in the study from SickKids (n=376), LHSC (n=349) and MSH (n=337). This resulted in a total of 1062 baseline tests, 1042 6-week samples and 966 12-week samples (Figure 1. participant flow diagram). Over the study period, each hospital saw over 100 patients with COVID-19. The range of timing of recruitment and sample collection at each site are shown in Figure 2. 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 Seropositivity:

Overall, 57/1062 (5.4%) of HCWs were seropositive at any time point, of which 31 (54%) 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), 26 (2.5%) were seropositive at any time point over the study (Table 2). Seroprevalence varied minimally by timepoint (Figure 2), and there was no statistically significant difference in seroprevalence by site (p=0.15).

Antibody Responses:

Of the 57 HCWs with positive serology at any time over the course of the study, 48 (84%) were positive at baseline testing and only 9 (16%) seroconverted during the study. Of the 9 that seroconverted, 1 had a confirmed COVID-19 infection and had baseline testing prior to 15 days. Of the remaining 8 without previous confirmed infection, 3 (6%) were only transiently positive at the 6-week collection, 1 had more than one positive but at a relatively low antibody index value and the remaining 4 were positive only on the 12-week sample with a low antibody index value; none of the participants had confirmed infection over the course of the study. Figure 3a shows the antibody responses in the 26 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).

Predictors of Seropositivity:

Comparison of demographics, clinical and possible exposures by detectable antibody status are summarized in Table 3 (additional factors are described in Supplemental Appendix 2, Table 1). Seroprevalence was higher amongst those who had a known unprotected exposure to a patient with COVID-19 (30% vs. 8%, p<0.001), those who had been contacted by public health because of a non-hospital exposure (16% vs. 5%, p=0.003) and in those with confirmed infection prior to enrollment (54% vs. 1%, p<0.001). Working on a unit with a COVID-19 outbreak was not associated with higher seroprevalence (9% vs. 11%, p=0.5). In the multivariable model (Table 4), presence of symptomatic contacts in the household was the strongest predictor of seropositivity (aOR 7.15, 95% CI 5.42, 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 7.22, 95% CI 3.65, 14.3, p<0.001). Younger age by year (aOR 0.94, 95% CI 0.91, 0.98, p =0.002) and non-white race (aOR 2.85, 95% CI 1.36, 5.98, p=0.006) 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 0.50, 95% CI 0.36, 0.70, p<0.001).

Symptom history:

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%) and fatigue (n=17, 35%) (Supplemental Appendix 2, Table 2). Those with symptoms documented at least 2 symptoms (n=22), with only one HCW with isolated anosmia.

Interpretation:

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 5.4%. The prevalence was even lower at 2.5% 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.[8,9,11,12,21-33] Since the start of the pandemic given the experience with SARS-CoV-1[34-36] and studies of SARS-CoV-2 showing environmental contamination[37] and occasionally, but not consistently, presence in air samples, there was a concern of higher prevalence of infection in HCWs.[38,39] 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,[16,40] was higher at 6.4% (2.5% excluding knowns positives) and 6.2% (3.1% excluding known positives), respectively, while in southwestern Ontario, a community where incidence and seroprevalence was lower, it was 3.4% (2.0% excluding known positives).

In addition to variation in COVID-19 disease burden by region,[9,12,28,31] studies with higher seroprevalence amongst HCWs attributed these estimates to availability of personal protective equipment (PPE)[27,32] and delayed implementation of public health measures in the hospital (i.e. universal masking).[28,29] 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]), were associated with seropositivity in a multicenter US-based serosurvey.[24] 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.[41] 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 the strongest 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[13] 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[42,43] and consistent with community risk factors.[44]

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[9,23-28,45] 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.[46-48] This decline has been observed in assays utilizing the SARS-CoV-2 S protein, including the one utilized for this study.[49] 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% seen over a 60-day period in HCWs in another study.[46]

Limitations:

Limitations of this study include the convenience sampling of HCWs and modest sample size. Due to logistical difficulties in bringing on study sites mid-pandemic, only three sites were included in this analysis, which focuses on the first wave. In addition, given the passive and broad nature of recruitment, it is difficult to know the exact number of HCWs notified about the study at each site to obtain an accurate recruitment rate. Ongoing recruitment at additional hospital sites has also focused on increasing the number of high-risk workers. The study had low power to detect differences between seropositive and seronegative groups. Furthermore, as commonly seen in studies assessing seroprevalence, there may have been a recruitment bias towards HCWs who suspected previous infection and were interested in their antibody response (e.g. history of undiagnosed respiratory symptoms or previous confirmed infection). In terms of the risk factor assessment, questionnaires were self-completed. However, antibody testing was batched, and questionnaires completed before results were available, so the results should not have biased the responses. 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.[50] 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.[51-53] Additionally, false negative results may occur if a participant did not mount a robust antibody response or if the antibody response waned prior to recruitment. [54,55] Additionally, the assay utilized was not quantitative and instead signal to cut-off ratios were utilized as a surrogate for antibody titres.

Conclusions:

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.

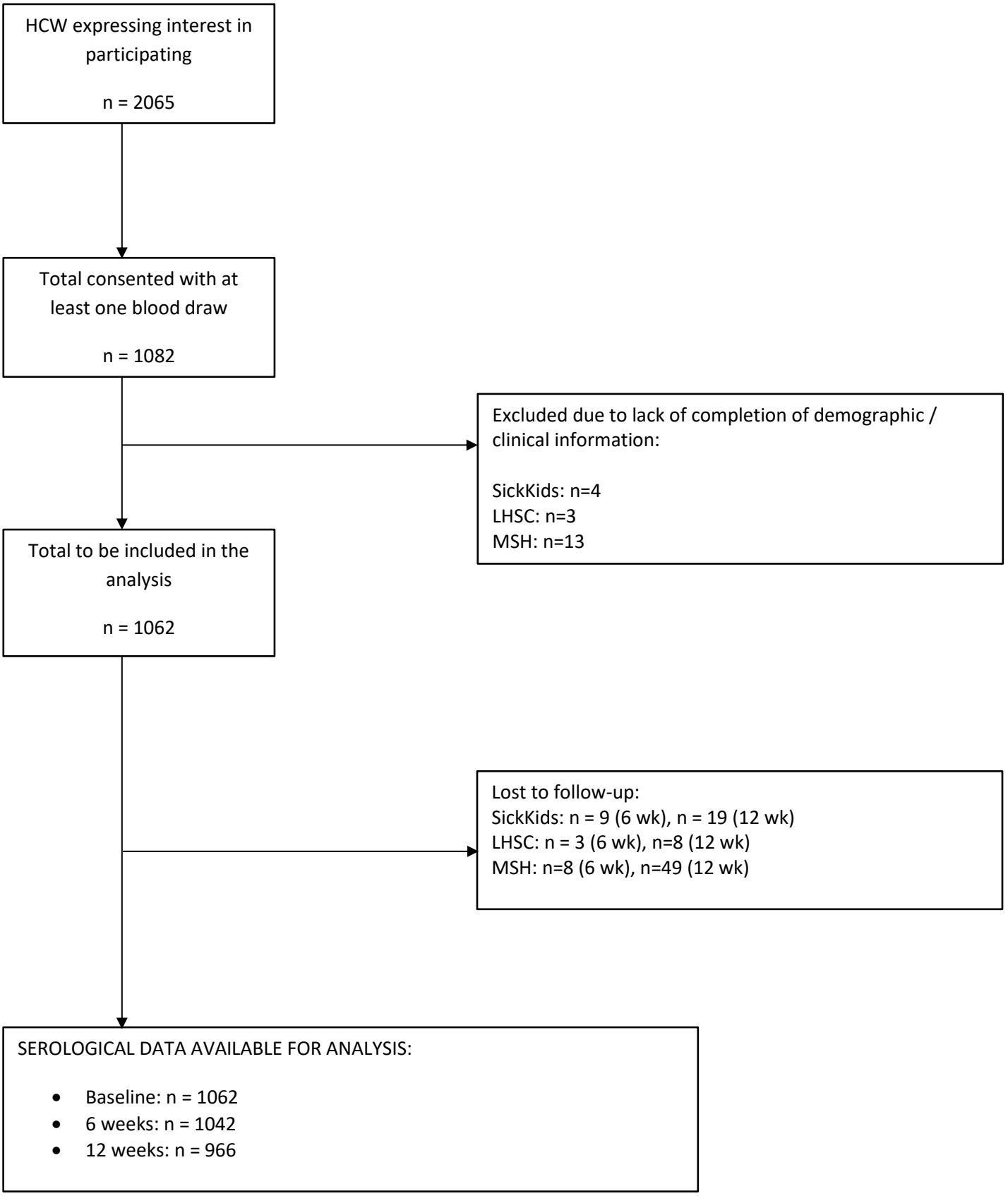

Figure 2. Percentage of participants with positive serology for SARS-CoV-2 by month and by site. Horizontal lines represent the enrolment, 6-week, or 12-week collection period mean percent positivity.

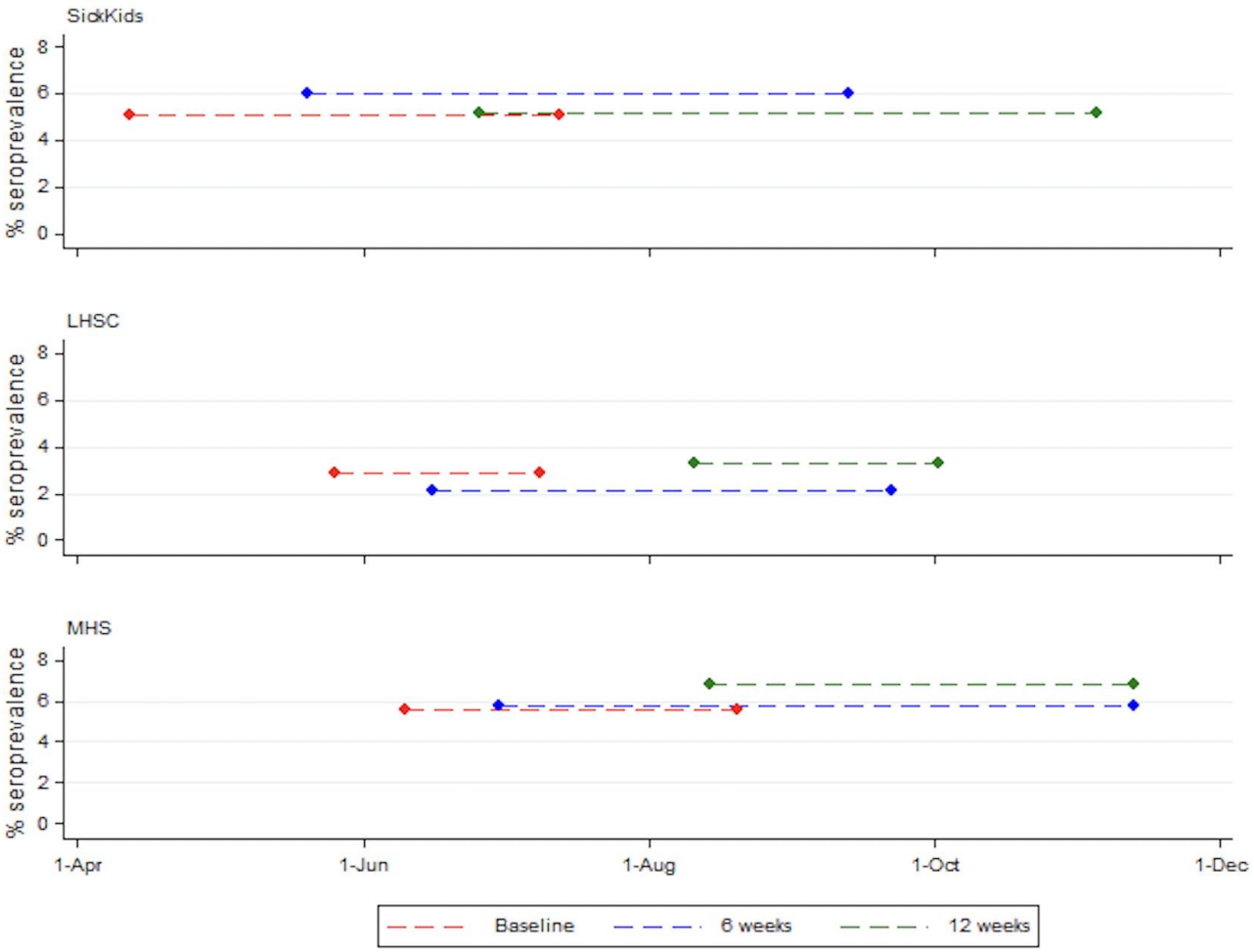

Figure 3a. Antibody responses of the 26 participants who had no history of confirmed SARS-CoV-2 infection and tested positive for SARS-CoV-2 antibodies at any time point during the study. Points above the dashed red line represent a positive antibody result.

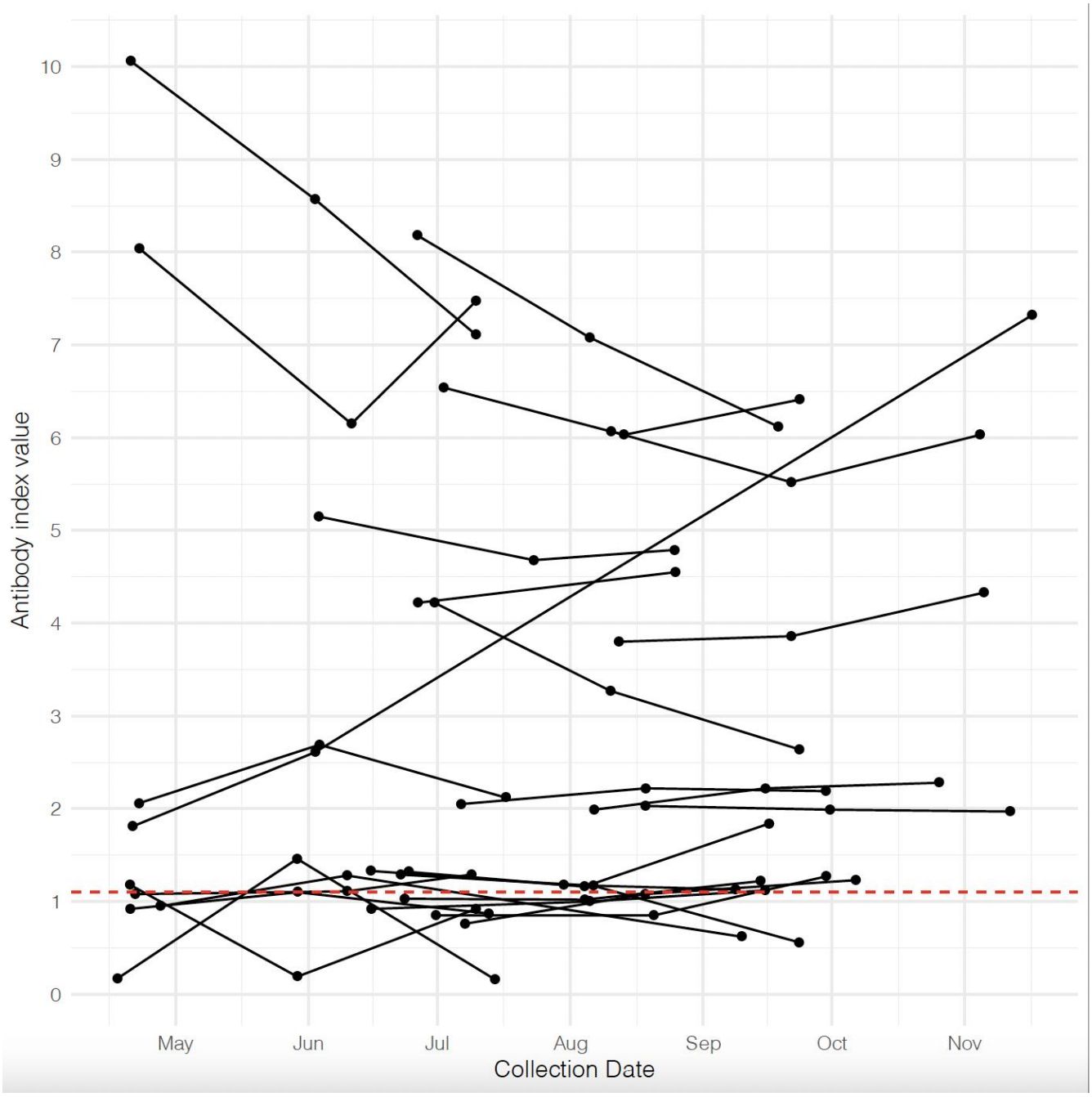

Figure 3b. Antibody responses of the 31 participants who had confirmed SARS-CoV-2 infection by PCR testing and tested positive for SARS-CoV-2 antibodies at any time point during the study by collection time. Points above the dashed red line represent a positive antibody result.

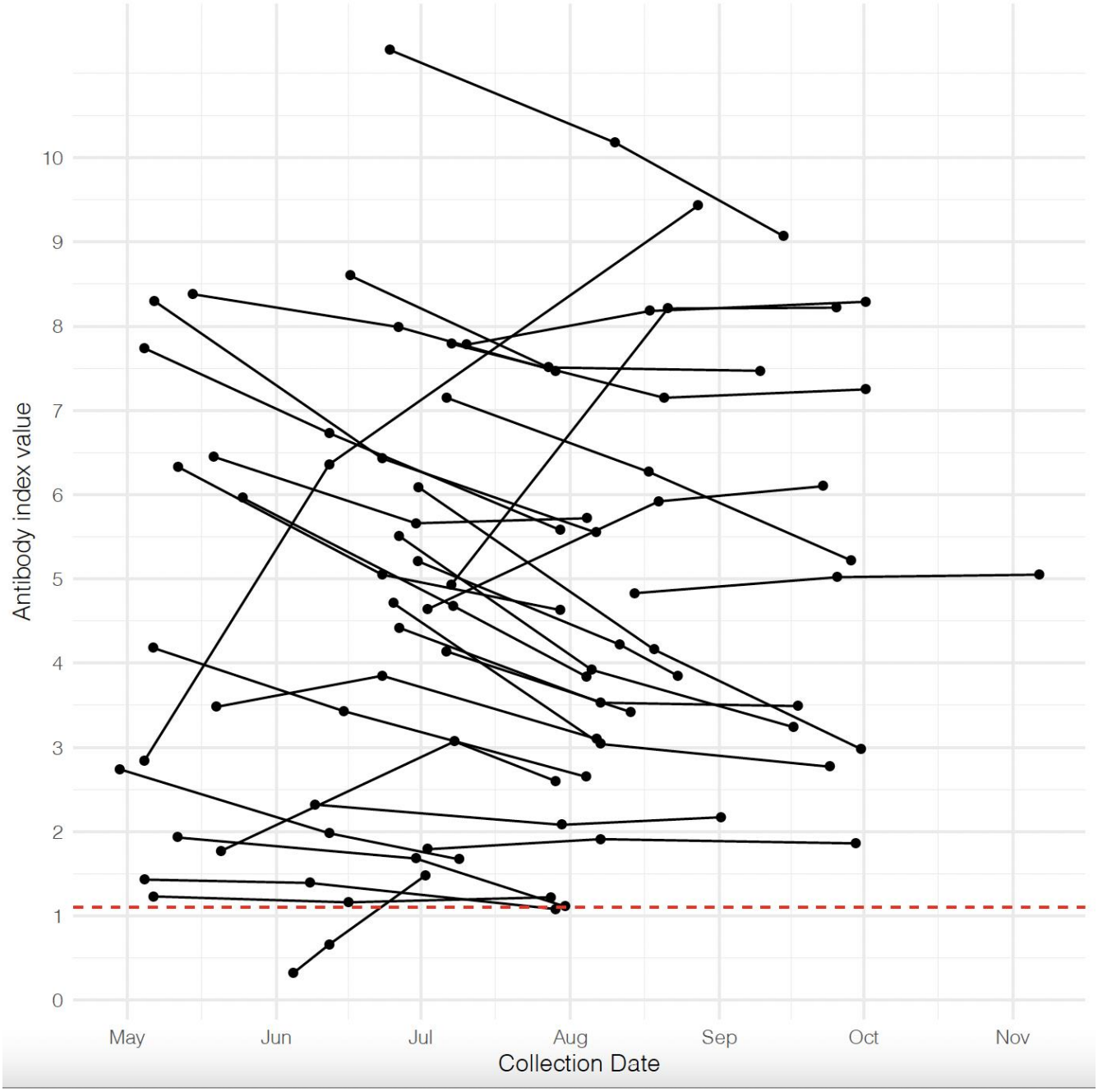

Figure 3c. Antibody responses of the 31 participants who had confirmed SARS-CoV-2 infection by molecular testing and tested positive for SARS-CoV-2 antibodies at any time point during the study expressed as a time from their positive PCR result. Points above the dashed red line represent a positive antibody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

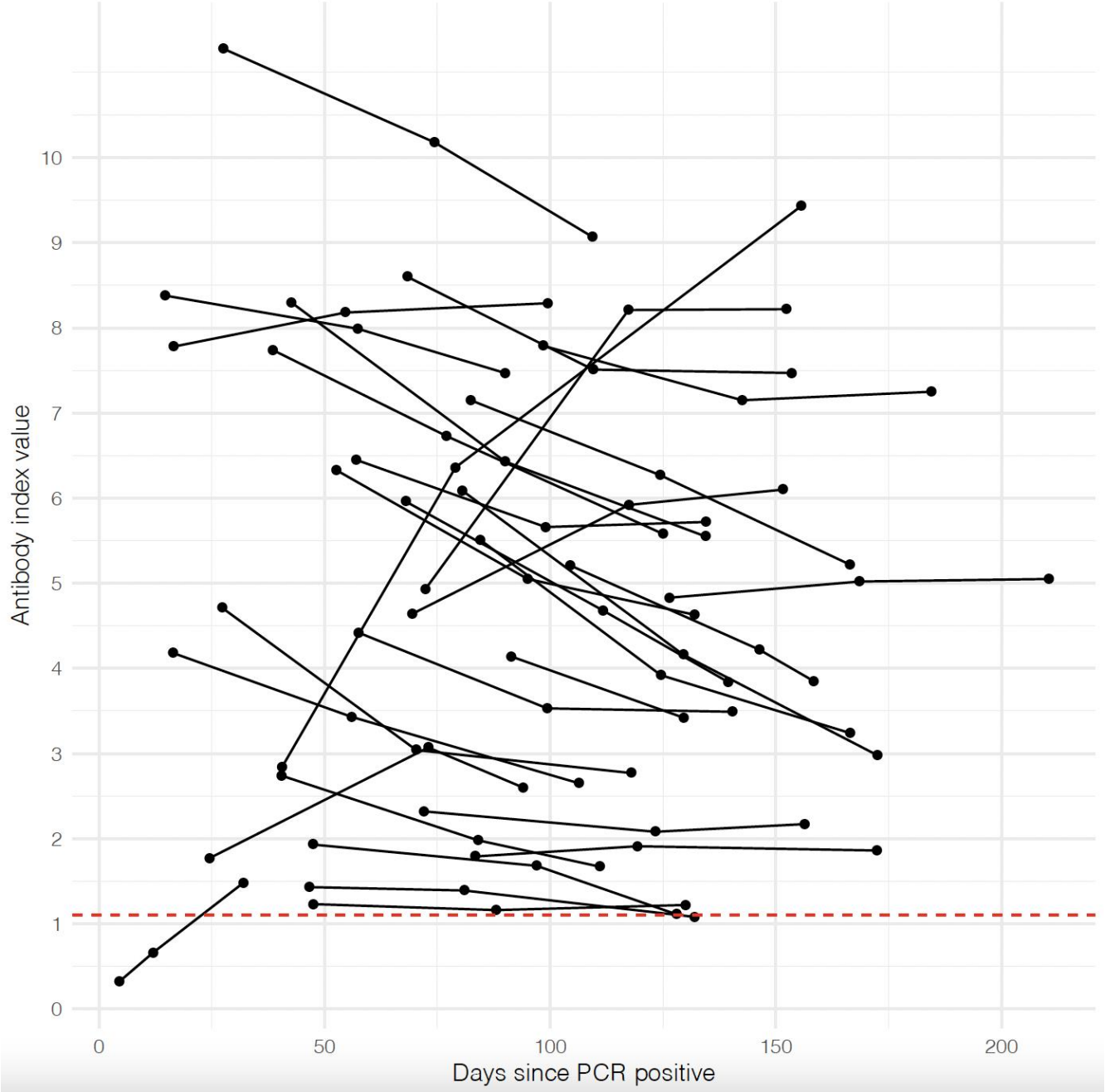

Table 1. Baseline participant characteristics and potential risk factors for SARS-CoV-2 infection

	Total (n=1062)	SickKids (n=376)	London Health Sciences (N=349)	Markham Stouffville (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)	14 (4)	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)	178/359 (51)	182/349 (52)	242/335 (72)
Number with children in the household (< 18 yrs)	401 (38)	122 (32)	121 (35)	158 (47)
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)	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)	57 (5.4)	24 (6.4)	12 (3.4)	21 (6.2)
Baseline (At enrolment)	48 (4.5)	19 (5.1)	10 (2.9)	19 (5.6)
6 weeks	53 (5.1)	22 (6.0)	10 (2.1)	19 (5.8)
12 weeks	48 (5.0)	18 (5.2)	11 (3.3)	19 (6.8)

* included roles such as Midwife, child life specialist, research coordinators, paramedic / transport, speech and language therapists, counselors.

** included work places such as diagnostic imaging, IV team / phlebotomy, labour and delivery/midwife, infection prevention and control and research.

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)			**57 / 1062 (5.4)**
Baseline	30 / 40	18 / 1022	48 / 1062 (4.5)
6 weeks	30 / 39	21 / 1003	51 / 1042 (4.9)
12 weeks	29 / 38	19 / 928	58 / 966 (6.0)
At any point	31 / 40	26 /1022	57 / 1062 (5.4)
Negative (n)			**1005 / 1062 (94.6)**
Baseline	10 / 40	1004 / 1022	1014 / 1062 (95.5)
6 weeks	9 / 39	982 / 1003	991 / 1042 (95.1)
12 weeks	9 / 38	909 / 928	918 / 966 (95.0)
At any point	9 / 40	996 / 1022	1005 / 1062 (94.6)
Total	**40**	**1022**	**1062**

Table 3. Factors associated with having detectable SARS-CoV-2 antibodies (Univariable comparisons)

	SARS-CoV-2 Serology Positive (n= 57)*	SARS-CoV-2 Serology Negative (n= 1005)*	p-value
Symptomatic contacts in the household n (%)	7/53 (13)	25/971 (3)	< 0.001
Provided direct care to COVID patients n (%)	27 (47)	412/995 (41)	0.5
Unprotected occupational exposure to a COVID-19 case n (%)$^{\phi}$	8/27 (30)	33/411 (8)	< 0.001
Worked on a COVID-19 outbreak unit n (%)	5 (9)	115/996 (12)	0.67
Contacted by public health to indicate exposure n (%)	9 (16)	54/985 (5)	0.003
Known positive PCR test at baseline n (%)	31 (54)	9 (1)	< 0.001

*The denominator of each outcome variable is the total in the column heading unless otherwise stated

ϕ Only those HCW who indicated they had direct patient contact were asked this question.

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

Variable	All HCW (n=1008) Odds Ratio (95% confidence interval)	HCW excluding those with previously confirmed COVID-19 infection (n=971) Odds Ratio (95% confidence interval)
Age by year	0.98 (0.96, 0.99)	0.94 (0.91, 0.98)
Female sex	1.86 (0.72, 4.78)	1.60 (0.48, 5.35)
Non-white race*	1.26 (0.46, 3.52)	2.85 (1.36, 5.98)
Symptomatic household exposure	7.15 (5.42, 9.41)	7.22 (3.65, 14.3)
Direct care of patients with COVID-19	1.33 (0.72, 2.47)	0.50 (0.36, 0.70)

*Participants indicating unknown ancestry were excluded

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Data Sharing: The data set from this study are held securely in coded form at the Hospital for Sick Children. As subsequent analyses will be conducted following the completion of the larger study, an anonymized subset of data may be made available beginning 3 months and ending 5 years after publication to researchers who provide a methodologically sound proposal. Proposals should be directed to: michelle.science@sickkids.ca or aaron.campigotto@sickkids.ca. REB approval and a data access agreement will need to be signed to gain access to the data

Supplemental Appendix 1, Baseline Survey

General Information:

1. Age
2. Postal code: first three digits
3. Household information: How many individuals are in your household? What are their ages?
4. What Ethnic group best describes you: European, South Asian, East/Southeast Asian, West Central Asian/ Middle Eastern, West Indian/ Caribbean, African, Latin/ Central/ South American, Aboriginal/ Indigenous, Multi-Ethnic, Canadian/ American, Other
5. What group best describes your ancestry? White/Black/Hispanic/East Asian/Pacific Islander/South Asian, Middle Eastern/Central Asian/Other
6. Any other HCWs in the household? Yes / No
7. Years of employment
8. Gender: Male, female, prefer not to specify
9. Number of shifts (or days worked) in the past 14 days
10. Work Place: ER/Urgent Care, ICU, Inpatient, Outpatient, Surgery/Perioperative care, COVID-19 Assessment Centre, Short stay/Dialysis, Other
11. Role:

a. Healthcare care professionals (physicians, nurses, nurse practitioner)

b. Allied health worker (phlebotomists, respiratory therapists, social workers, dieticians, diagnostic imaging technician/ physicians physiotherapists, occupational therapists, and dentistry)

c. Auxiliary (environmental services personnel, patient transport/ porter, laboratory personnel and ward clerical workers)

12. What PPE do you wear for all patient encounters (i.e for asymptomatic patients not in other precautions)? Check all that apply – face mask, N95 respirators, gown, gloves, eye protection (goggles or face mask)
13. What PPE do you wear for the routine care of suspect or confirmed COVID-19 patients? Check all that apply - face mask, N95 respirators, gown, gloves, eye protection (goggles or face mask)

Health Information:

14. Self-reported weight
15. Self-reported height
16. Current smoker (vaping included): Yes / No
17. Pregnancy: Yes / No / Unknown; If yes, specify trimester: first, second, third, unknown
18. Underlying Medical Conditions:

a. Cancer: yes / no

b. Diabetes: yes / no

i. Has a doctor ever told you that diabetes has affected your eyes; or that you have diabetic retinopathy or have you ever received laser eye therapy for your diabetes?

ii. Are you currently taking insulin? Y/N

iii. Do you currently take diabetes pills (oral agents or oral hypoglycemic agents) to lower your blood sugar. Y/N

c. Immune Deficiency/ HIV: yes / no

i. Have you ever received a transplant of an organ other than kidney (e.g. bone marrow, heart, lung, liver or pancreas)?

d. Heart disease: yes / no

i. Has a doctor or other health professional ever told you that you have coronary/ artery disease (heart attack, angina)? Y/N

ii. Have you ever had prior revascularization of your heart/ blood vessels by balloon angioplasty? Y/N

iii. Have you ever had a prior revascularization of your heart /blood vessels by coronary stenting? Y/N

iv. Have you ever had a prior revascularization of your heart blood vessels by coronary bypass surgery? Y/N

v. Has a doctor or other health professional ever told you that you have heart failure? Y/N

vi. Has a doctor or other health professional ever told you that you have atrial fibrillation or atrial flutter (an irregular heart rhythm)? Y/N

vii. Have you ever had any procedure to open the blood vessels of the neck (carotid endarterectomy)? Y/N

viii. Has a doctor or other health professional ever told you that you have hypertension or high blood pressure? Y/N

e. Asthma (requiring medication): yes / no

i. Have you ever been hospitalized for your asthma? Y/N

ii. Do you use an inhaler? Y/N

f. Chronic lung disease (non-asthma): yes / no

i. Have you ever been hospitalized for COPD? Y/N

ii. Do you use an inhaler? Y/N

g. Chronic liver disease: yes / no

i. Has a doctor or other health professional ever diagnosed or treated you for hepatitis (B or C) infection? Y/N

h. Chronic hematologic (blood) disease (e.g. sickle cell disease, hemoglobinopathies): yes / no

i. Chronic kidney disease: yes / no

j. Chronic neurological disease / impairment: yes / no

i. Were you ever told by a physician that you had a stroke? Y/N

ii. Were you ever told by a physician that you had a transient ischemic attack (TIA), ministroke? Y/N

k. Inflammatory Diseases: Yes/No

l. Has a doctor or other health professional ever diagnosed or treated you for rheumatoid arthritis? Y/N

m. Has a doctor or other health professional ever diagnosed or treated you for gout? Y/N

n. Other pre-existing condition: yes / no, if yes, specify

19. Medications

a. Have you ever had a vaccination for Covid-19?

i. If yes, how many doses?

ii. Please indicate the date each dose was received

iii. Please indicate the vaccine manufacturer if able

b. Do you currently take prescribed medication for your hypertension or high blood pressure? Y/N

c. Do you currently take prescribed medication for your high blood cholesterol?

d. Have you ever received treatment with immunosuppressive drugs such as Cyclophosphamide, Cytoxan, Steroids, Prednisone, Cellcept, or Cyclosporine within the past 6 months. Y/N

e. Any other medication? Y/N. Specify.

20. Any illness or symptoms in the last 3 months: yes / no, if yes, specify

21. Have you ever had any specimens collected for COVID-19 testing (ie NP Swab, Saliva, etc)?: yes / no; if yes, was it positive? Yes / no; if yes, specify date

22. Any history of blood transfusion or immunoglobulin in the last year? Yes / No; if yes, specify date

Exposure history:

23. Any sick contacts in the household in the last 3 months? Yes / no; if yes, what are the ages of sick contacts? have they been tested for COVID-19? Yes/no; if yes, was the result positive? Yes / no / unknown

24. Have you provided direct care to a patient with COVID-19? Yes / No; if yes, how often? Daily, 2-3 times per week, weekly, rarely

25. If yes to 23, have you had any unprotected exposures (i.e within 2 m of the patients without appropriate PPE)? Yes / No; if yes, please specify date(s) and describe exposure(s)

26. If yes to 23, did you perform any aerosol generating medical procedures? (link to PHO list to specify) Yes / No, if yes; list procedure

27. Have you worked on a unit where a COVID-19 outbreak has been declared (during the outbreak period)? if yes, how often? Daily, 2-3 times per week, weekly, rarely

28. Have you been diagnosed by SARS or MERS? Yes / No; if yes, please specify date:

29. Have you been contacted by Public Health to indicate you may have been exposed to someone with COVID-19? Yes / No

30. Have you ever been notified by the COVID Alert App that you may have been exposed to someone with COVID-19?

31. In the last two weeks, how often have you left the house per week (excluding work)? 1 time, 2-4 times, 3-5 times, > 5 times

32. When leaving the house, did you adhere to physical distancing (staying > 2 m away from non-household contacts); always, most of the time, sometimes, never

33. When leaving the house, did you wear a facemask? Always, most of the time, sometimes, never

34. Any travel in the last 4 months? Yes / No, specify country (drop down list) and dates

35. Any other important information we should know related to COVID-19 exposure or risk?

Supplemental Appendix 2

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

	SARS-CoV-2 Serology Positive (n= 57)	**SARS-CoV-2 Serology Negative (n= 1005)**
Age, median (IQR)	36 (30,48)	40 (32,51)
Sex, female n (%)	48 (87)	786 (79)
Any Comorbidity / underlying conditions	16 (30)	370 (37)
Hospital Site		
SickKids	24 (42)	352 (35)
London	12 (21)	337 (34)
MSH	21 (37)	316 (31)
Role		
HCP	40 (70)	670 (67)
Allied Health	5 (9)	154 (15)
Auxiliary	3 (5)	73 (7)
Other	9 (16)	106 (11)
HCP Role		
Nurse	25 (44)	423 (42)
Physician	14 (25)	223 (22)
Nurse Practitioner	1 (2)	14 (1)
Respiratory Therapy	2 (4)	50 (5)
Environmental Services	0 (0)	13 (1)
Work place		
COVID-19 Assessment Center	8 (14)	29 (3)
Emergency Department	17 (30)	289 (29)
Critical Care	8 (14)	237 (24)
Travel after Jan 1 (outside of Canada)	18 (32)	384 (38)
Household reporting 3 or more individuals in the house (including the HCW)	27 (51)	575 (59)
Number with children in the household (< 18 yrs)	19 (33)	382 (38)
Worked on a COVID-19 outbreak unit	5 (9)	115 (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 (34)	302 (31)
When leave the house, wear facemask all the time vs. most of the time/sometimes/never	23 (40)	325 (33)
When leave the house, physical distancing always vs. most of the time/sometimes/never	27 (51)	542 (56)

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

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	10 (21)
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)