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Seropositivity of SARS-CoV-2 in an unvaccinated cohort in British Columbia, Canada: a cross-sectional survey with dried blood spot samples

C Sarai Racey,[1,2] Amy Booth,[1,2] Arianne Albert,[2] Laurie W Smith ,[2,3] Mel Krajden,[4] Melanie C M Murray,[2,5] Hélène C F Côté,[2,6] Anna Gottschlich,[1,2] David M Goldfarb,[6] Manish Sadarangani,[7,8] Liisa A M Galea,[2,9] Angela Kaida,[2,10] Lori A Brotto,[2,11] Gina S Ogilvie [1,2,4]

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For numbered affiliations see end of article.

Correspondence to
Dr Gina S Ogilvie;
gina.ogilvie@cw.bc.ca

ABSTRACT

Objectives Gathering population-based data on prevalence of SARS-CoV-2 infection is vital to the public health response and planning. Current seroprevalence data in BC are limited with respect to considerations of how socioeconomic and demographic factors, such as age, sex, gender, income, identifying as a visibility minority and occupation, are related to SARS-CoV-2 antibody detection due to infection-acquired immunity. We aimed to estimate the SARS-CoV-2 seropositivity in a cohort of British Columbians, using at-home self-collected dried blood spot (DBS) samples.

Design This cross-sectional study included online surveys that collected sociodemographic and COVID-19 vaccine receipt information, and an at-home DBS collection kit.

Setting British Columbia (BC), Canada.

Participants Eligible participants were aged 25–69 years and residents of BC.

Primary outcome measure SARS-CoV-2 anti-spike IgG antibody detection in unvaccinated individuals. Adjusted incidence rate ratios (aIRR) explored factors associated with seropositivity.

Results SARS-CoV-2 serology was performed on a total of 4048 unvaccinated participants 25–69 years of age who submitted DBS samples taken from November 2020 to June 2021. A total of 118 seropositive cases were identified, for an estimated overall seropositivity of 2.92% (95% CI 2.42% to 3.48%). Participants identifying as a visible minority had a higher seropositivity, 5.1% vs 2.6% (p=0.003), compared with non-visible minority participants. After adjustment by age and sex, identifying as a visible minority (aIRR=1.85, 95% CI 1.20 to 2.84) remained the only significant factor associated with SARS-CoV-2 antibody detection in this cohort of unvaccinated individuals.

Conclusions SARS-CoV-2 seropositivity in the BC population due to infection-acquired immunity was low. Seropositivity indicated that among those unvaccinated, visible minority communities have been most impacted. Continued monitoring of SARS-CoV-2 serology due to both infection-acquired and vaccine-acquired immunity will be vital in public health planning and pandemic response.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ Collection of an abundance of demographic variables allowed for a thorough investigation of factors associated with COVID-19 seropositivity.
⇒ Large sample size.
⇒ Recruiting participants from pre-existing research cohorts allowed for rapid recruitment during an emergent public health crisis, producing large amounts of useful data quickly.
⇒ Sample had over-representation of participants who were female, women, from high-income households and from urbanised areas in the lower mainland of BC.
⇒ The seropositivity estimate is for self-reported unvaccinated participants only. We were unable to verify vaccination status.

INTRODUCTION

SARS-CoV-2, which causes COVID-19, was declared a pandemic on 11 March 2020 by the WHO.[1] By July 2021, the virus had caused more than 187 million confirmed cases of COVID-19 and 5 million deaths worldwide, which has climbed to 306 million cases and 5.5 million deaths since the beginning of 2022.[2] In Canada, 1.4 million confirmed cases and 26 000 deaths had been reported by July 2021, which grew to 2.2 million cases and 30 000 deaths by 1 Jan 2022.[3] Given the virus is transmitted via aerosols and droplets produced by symptomatic and asymptomatic people,[4] the true proportion of infected individuals exceeds the confirmed case counts to date.

Many current estimates of population prevalence of SARS-CoV-2 have relied on PCR testing; however, PCR testing as surrogate for seropositivity is biased due to variations in testing recommendations and variability in population testing behaviour. Testing

guidelines and availability have varied by jurisdictions and over time. In British Columbia (BC), Canada, asymptomatic testing has not been recommended,[5] and in the earliest phase of the pandemic, PCR-based testing was limited. Therefore, past and current prevalence estimates based on PCR test positivity under-report mild and asymptomatic cases, and individuals who were not tested while sick.

Seroepidemiological studies can provide more accurate information on the proportion of a population that has been infected with SARS-CoV-2 and has developed antibodies to the virus. Multiple studies report that more than 90% of individuals infected with SARS-CoV-2 will develop an antibody response, which is usually detectable approximately 14–28 days post infection, and has been shown to last as long as 10 months.[6 7] Higher population levels of antibodies from both infection-acquired and/or vaccine-acquired immunity, may correlate with protection from subsequent SARS-CoV-2 infection.[8–10]

A Canada-wide estimate of SARS-CoV-2 prevalence was released by Statistics Canada in July 2021,[11] and based on approximately 11 000 dried blood spot (DBS) samples, found 2.6% of the population had antibodies due to infection-acquired immunity. Similar seroprevalence has been estimated from Canadian blood service donors[12]; however, these estimates are limited with respect to sociodemographic data. Given the current seroprevalence data and the dynamic nature of both the pandemic and the public health control measures, there is an ongoing need for surveillance of SARS-CoV-2 antibodies in the general population. To date, seroprevalence data in BC are also limited with respect to considerations for how socioeconomic and demographic factors, such as age, sex, gender, education, income, location and occupation, are related to SARS-CoV-2 antibody detection due to infection-acquired immunity. Therefore, accurate estimates of SARS-CoV-2 seropositivity can help inform policy-makers on evolving pandemic responses.

The objective of this study was to estimate SARS-CoV-2 antibody prevalence due to infection-acquired immunity, using self-collected DBS, in a population-based cohort in BC, and socioeconomic and demographic factors associated with SARS-CoV-2 antibody detection.

METHODS

The Rapid Evidence Study of a Provincial Population Based COhort for GeNder and SEx (RESPPONSE) was an investigation lead by the Women's Health Research Institute of Vancouver, BC, evaluating the impact of the COVID-19 pandemic in BC, Canada.

Patient involvement

Patient partners from the existing research cohorts were consulted during the conceptualisation of the study. Patient partners were involved in the survey pilot testing. Peer research associates from specific patient groups helped administer the survey to participants who were unable to complete the survey on their own. Regular research updates have been communicated to patient groups.

Study design and recruitment

The study, described previously,[13–15] included an invitation to participate in an online survey and the opportunity to provide an at-home self-collected DBS sample via a finger prick, for SARS-CoV-2 antibody testing. Recruitment for the online survey was from 20 August 2020 to 4 August 2021, with collection of DBS samples from November 2020 to June 2021.

Participants were recruited from existing large research cohorts in BC, comprised of individuals who had provided consent to be contacted for future research, in addition to general public recruitment through social media, patient research networks, as well as stakeholder and community websites (index participants). Eligible participants were those 25–69 years of age who were current residents of BC. To increase representation of diverse sex and gender participants, respondents were able to identify another adult household member of a different gender to participate (household participants). All participants from pre-existing research cohorts were sent an initial email invitation with up to three reminders, and an opportunity to enter a draw for a gift card. Participants were stratified into nine 5-year age strata with a targeted recruitment of 750 per stratum, based on an estimated population seroprevalence of 2% (±1, 95% CI).

Survey design

The survey comprised multiple modules all based on self-reported information, which have been analysed separately.[13–15] Demographic information was collected for age, sex, gender, indigenous ancestry, visible minority status (identifying as non-white), education, income, household composition, employment as a healthcare worker (HCW), other essential worker, or an as non-essential worker, geographic region of residence assigned to one of the five provincial health authorities (assessed via the first three digits of postal code). Health information on existing chronic disease conditions and self-reported history of COVID-19 was also collected. The survey was tested for face validity and pilot tested. At the completion of the survey, participants could opt-in to receive the at-home self-collected DBS kit.

COVID-19 vaccination status was self-reported through a second survey specific to vaccine status, which was sent to all participants who submitted a DBS sample, on receipt of their DBS sample at the processing lab. COVID-19 vaccine information collected included date of first dose and vaccine product information. All surveys were distributed using the Research Electronic Data Capture (REDCap) online platform.[16]

Serology

All survey participants who opted-in for SARS-CoV-2 antibody testing were mailed an at-home DBS self-collection

kit. The at-home self-collection kit was compiled by the research team using commercially available products, which included a protein saver card with five blood spot collection circles, lancets, alcohol swab, gauze, and pictorial and descriptive instructions (online supplemental material). Participants were asked to record the date of sample collection and to mail their sample within 12 hours of collection using a prepaid envelope to the BC Center for Disease Control Provincial Laboratory, which performed all SARS-CoV-2 antibody research serology testing.[17]

Following best practices at the time of study completion, SARS-CoV-2 antibody testing was measured by DBS using Meso Scale Discovery's (MSD) quantitative multiplex anti-immunoglobulin G (IgG) electrochemiluminescence assay (V-PLEX COVID-19 Coronavirus Panel 2 (IgG) Kit). The MSD assay was validated for research purposes for SARS-CoV-2 anti-spike (S) immunoglobin G (IgG) reactivity,[17] which achieved a sensitivity of 79% and specificity of 97% compared to paired serum samples in an unvaccinated population. MSD assay was not approved by health agencies for diagnostic testing at the time of the study. Participants were categorised as SARS-CoV-2 serology positive based on the anti-S result, with a positive threshold cut-off defined as S≥75 AU/mL.[17]

Statistical analysis

SARS-CoV-2 seropositivity was estimated in a cohort that reported being unvaccinated at the time of DBS self-collection (figure 1). Those who self-reported as receiving a COVID-19 vaccine prior to DBS collection, as well as those with unknown vaccination status, were excluded from the seroprevalence estimate. Sensitivity analysis was also done, which included those with unknown vaccination status as unvaccinated.

Generalised estimating equations with a Poisson link were used to estimate the bivariable and multivariable incidence rate ratios (IRR), controlling for clustering due to index and household participants. Multivariable adjustment was based on bivariate analysis ($p<0.10$) associated with SARS-CoV-19 infection, in addition to a priori variables associated with SARS-CoV-2 infection: age, sex, being an essential worker and identifying as a visible minority. All analyses were performed in R v. 4.0.2.[18]

RESULTS

Participant characteristics

Between 20 August 2020 and 4 August 2021, a total of 5470 participants completed the online survey and requested a DBS at-home collection kit. A total of 5402 DBS at-home collection kits were mailed to participants, of which

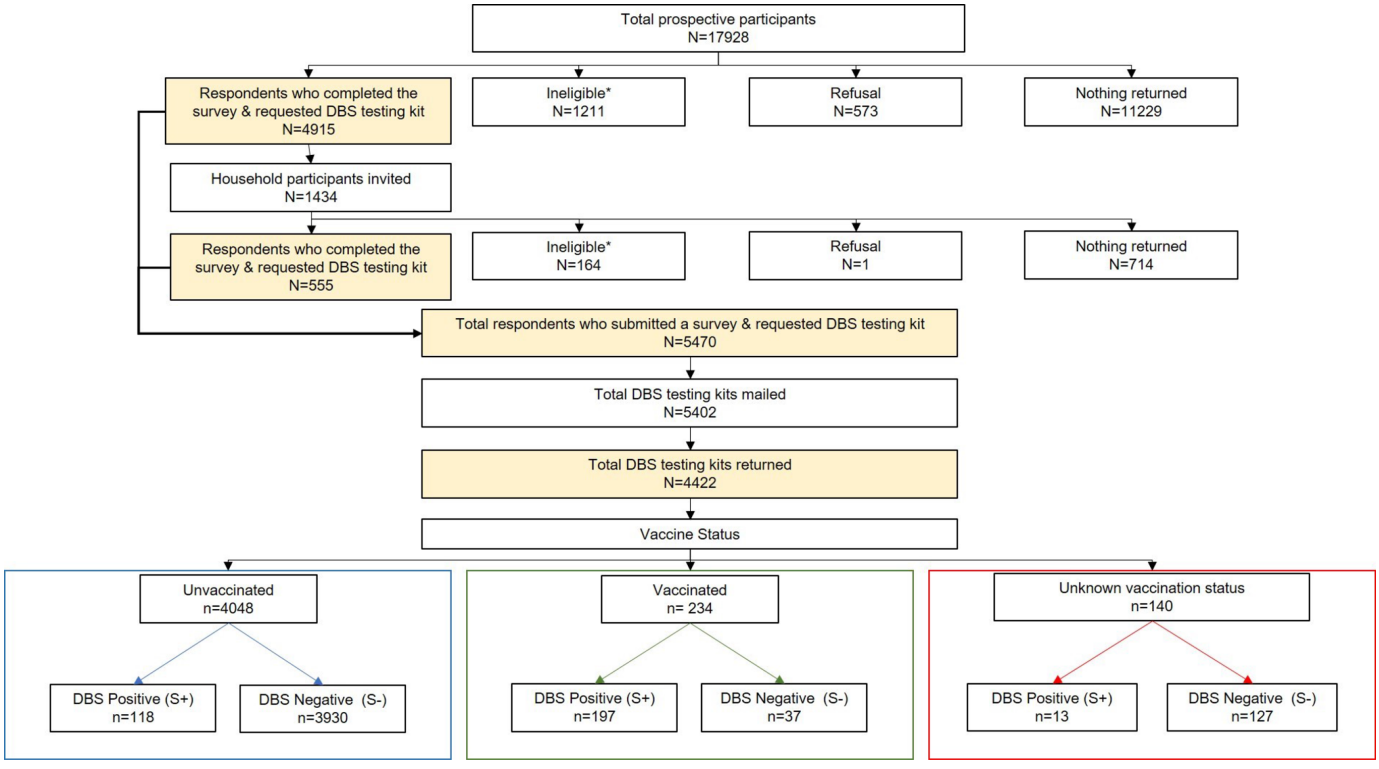

Figure 1 Participants included in this seroprevalence analysis based on recruitment. Categorisation of participants based on self-reported COVID-19 vaccination status (at least 1 dose) and SARS-CoV-2 antibody testing in British Columbia, Canada, on at-home dried blood spot (DBS) samples from November 2020 to June 2021. *Ineligible denotes participants who did not submit the survey, which was required to be able to prompt the request for a DBS testing kit. Note: Participants were categorised as SARS-CoV-2 antibody positive based on the anti-Spike (anti-S) result, with a positive threshold cut-off defined as anti-S >75 AU/mL.[17]

4422 participants submitted a DBS sample for analysis, which included 3981 (90.0%) index participants and 441 (10.0%) household participants (figure 1). There were 234 (5.3%) vaccinated participants and 140 participants with an unknown vaccine status that were removed from analysis, resulting in a total of 4048 participants included in this main analysis. The DBS collection period for those included in the analysis was from November 2020 to June 2021.

The majority of participants identified as female (88.0%), and 87.2% identified as women, with 1% of participants identifying as gender diverse. Overall, 13.0% identified as a visible minority, and HCWs comprised 11.2% of participants (table 1).

DBS self-collection took place between 10 November 2020 and 6 July 2021, during the second wave of the pandemic, with the last DBS sample included in this analysis collected on 2 June 2021 (figure 2). The daily new infection incidence rate in BC during the same time frame ranged from 5 per 100 000 at the beginning of wave 2 to more than 20 per 100 000 at the peak of wave 3 (figure 2).

A total of 118 positive cases were reported for a seropositivity estimate of 2.92% (95% CI 2.42% to 3.48%). There was a significant association between ethnicity and seropositivity, with those identifying as a visible minority having a seropositivity of 5.1% vs 2.6% (p=0.003) among non-visible minority participants. Participants were also asked if they thought they had COVID-19 at any point since the start of the pandemic and survey completion. There was a significantly higher seropositivity in those who reported thinking that they had COVID-19 (7.7% vs 2.1%). There were 16 participants who reported receiving a positive COVID-19 test result, of which 15/16 (93.8%) were also seropositive. The one participant who was seronegative reported a positive COVID-19 test result from August 2020 and completed DBS collection January 2021.

There was a delay in the distribution of DBS collection kits, relative to demographic survey completion; as a result, those who completed the survey earlier had a longer lag time between survey completion and DBS collection. The mean time lag between survey completion and DBS collection was 112 days (SD=35), and there was no difference in lag time between those that tested positive (mean=109 days) or negative (mean=112 days) (p=0.5). The secondary vaccination status survey was automatically sent to a participant when their DBS sample arrived at the laboratory for processing.

Bivariable and multivariable associations with SAR-CoV-2 seropositivity

In bivariable analysis, identifying as a visible minority (IRR 1.98, 95% CI 1.30 to 3.01), an HCW (IRR 1.63, 95% CI 1.01 to 2.64) and thinking you had COVID-19 (IRR 3.6, 95% CI 2.48 to 5.22) were significantly associated with seropositivity (table 2). Age, sex, gender, level of education, income, number of adults living in the household, having a chronic health condition and geographical location of residents (based on health authority) were not significantly different between those who were positive or negative on serology (table 2).

The multivariable adjusted for age and sex, however, only identifying as a visible minority (adjusted IRR (aIRR)=1.85, 95% CI 1.20 to 2.84) remained significantly associated with seropositivity, while being an HCW did not (aIRR=1.49, 95% CI 0.92 to 2.43) (table 2).

Sensitivity analysis with unknown vaccine status

In a sensitivity analysis, the 140 participants excluded from the main analysis due to unknown vaccination status were included as unvaccinated. Of the 140 excluded, 13 had antibodies detected. There was no significant change in the factors associated with seropositivity, apart from essential HCWs, where the effect size increased from aIRR=1.49 (95% CI 0.92 to 2.43) to aIRR=1.89 (95% CI 1.23 to 2.91).

DISCUSSION

In this BC cohort of adults from the general population, the SARS-CoV-2 seropositivity was estimated to be 2.92% (95% CI 2.42% to 3.48%) among unvaccinated individuals for samples collected between November 2020 and June 2021, measuring seropositivity throughout the second wave of the pandemic in BC (figure 2).

A Canadian-wide StatsCan estimate reported that 3.6% of Canadians had antibodies to SARS-CoV-2, with 2.6% having antibodies due to infection-acquired immunity, and 1% due to vaccine-acquired immunity, during a similar time frame from November 2020 to April 2021,[11] which is an increase compared with Canadian seroprevalence estimates of 0.7%–1.7% from May to July 2020 (first wave).[19 20] However, seroprevalence estimates from after the second wave have varied by location. The StatsCan report found that after the second wave, Alberta had the highest seroprevalence at 4.0%, followed by central Canada, ranging from 2.5% to 2.9%, with BC estimated at 1.6% and Atlantic Canada estimated at 0.5%.[11] A second study estimated seroprevalence after the second wave to be as high as 7.0% in the Prairie provinces, 6.4% in BC and as low as 3.3% in the Atlantic provinces.[21] Our study cohort seropositivity as measured throughout the second wave was 2.92%, which was between the afore-mentioned population estimates of 1.6% (StatsCan) and 6.4%[20] for seroprevalence in BC after the second wave.

Globally, geographic estimates of SARS-CoV-2 seropositivity in populations are extremely varied, depending on location, population size, testing guidelines and access, and dynamics of the pandemic. In a meta-analysis of 241 studies, the global pooled SARS-CoV-2 antibody prevalence was 9.5%, and ranged from 1.6% in South-eastern Asia and 22.9% in Southern Asia.[22–24] In countries with a similar socioeconomic profile as Canada, the estimated seroprevalence has varied widely, with 0.1% seroprevalence in New Zealand at the end of 2020, 5.6% in England in October–November 2020, 20.2% in the USA from July

Table 1 Overall participant characteristics by research serology for SARS-CoV-2 antibodies in a population cohort in British Columbia, Canada, with at-home dried blood spot samples from November 2020 to June 2021

		Serology result (IgG anti-Spike)		
	Total N=4048	Negative n=3930	Positive n=118	P value*
Mean age (SD)	49.9 (±11.8)	49.9 (±11.7)	48.4 (±13.0)	0.21
Age				
25–29	223 (5.5%)	213 (95.5%)	10 (4.5%)	0.05
30–39	693 (17.1%)	668 (96.4%)	25 (3.6%)	
40–49	961 (23.7%)	930 (96.8%)	31 (3.2%)	
50–59	1116 (27.6%)	1096 (98.2%)	20 (1.8%)	
60–70	1055 (26.1%)	1023 (97.0%)	32 (3.0%)	
Sex				
Female	3563 (88.0%)	3460 (97.1%)	103 (2.9%)	1
Male	480 (11.9%)	466 (97.1%)	14 (2.9%)	
Missing	5 (0.1%)	4 (80.0%)	1 (20.0%)	
Gender				
Woman	3528 (87.2%)	3425 (97.1%)	103 (2.9%)	1
Man	478 (11.8%)	464 (97.1%)	14 (2.9%)	
Gender diverse	42 (1.0%)	41 (97.6%)	1 (2.4%)	
Indigenous identity				
Indigenous	93 (2.3%)	89 (95.7%)	4 (4.3%)	0.55
Not indigenous	3771 (93.2%)	3658 (97.0%)	113 (3.0%)	
Prefer not to answer	27 (0.7%)	27 (100.0%)	0 (0.0%)	
Missing	157 (3.9%)	156 (99.4%)	1 (0.6%)	
Visible minority				
Visible minority	527 (13.0%)	500 (94.9%)	27 (5.1%)	**0.003**
Non-visible minority	3502 (86.5%)	3411 (97.4%)	91 (2.6%)	
Missing	19 (0.5%)	19 (100.0%)	0 (0.0%)	
Visible minorities				
White	3460 (85.5%)	3369 (97.4%)	91 (2.6%)	**0.048**
Black	17 (0.4%)	17 (100.0%)	0 (0.0%)	
East Asian	271 (6.7%)	257 (94.8%)	14 (5.2%)	
Hispanic/Latinx	49 (1.2%)	48 (98.0%)	1 (2.0%)	
Other	167 (4.1%)	161 (96.4%)	6 (3.6%)	
South Asian	61 (1.5%)	56 (91.8%)	5 (8.2%)	
Southeast Asian	23 (0.6%)	22 (95.7%)	1 (4.3%)	
Education				
More than high school	3530 (87.2%)	3425 (97.0%)	105 (3.0%)	0.67
High school or less	509 (12.6%)	496 (97.4%)	13 (2.6%)	
Missing	9 (0.2%)	9 (100.0%)	0 (0.0%)	
Household income				
US$100k+	2048 (50.6%)	1991 (97.2%)	57 (2.8%)	0.51
≤US$49k	427 (10.5%)	411 (96.3%)	16 (3.7%)	
US$50k–US$100k	1048 (25.9%)	1019 (97.2%)	29 (2.8%)	
Missing	525 (13.0%)	509 (97.0%)	16 (3.0%)	
Occupation group†				

Continued

Table 1 Continued

	Total N=4048	Serology result (IgG anti-Spike) Negative n=3930	Positive n=118	P value*
Non-essential worker	2875 (71.0%)	2797 (97.3%)	78 (2.7%)	0.14
Yes, healthcare worker	452 (11.2%)	432 (95.6%)	20 (4.4%)	
Yes, other essential worker	715 (17.7%)	695 (97.2%)	20 (2.8%)	
Missing	6 (0.1%)	6 (100.0%)	0 (0.0%)	
Number of adults in household				
One	923 (22.8%)	898 (97.3%)	25 (2.7%)	0.89
Two	2276 (56.2%)	2209 (97.1%)	67 (2.9%)	
Three or more	838 (20.7%)	812 (96.9%)	26 (3.1%)	
Missing	11 (0.3%)	11 (100.0%)	0 (0.0%)	
Geographical location				
Region 1	1118 (27.6%)	1086 (97.1%)	32 (2.9%)	0.29
Region 2	147 (3.6%)	144 (98.0%)	3 (2.0%)	
Region 3	41 (1.0%)	40 (97.6%)	1 (2.4%)	
Region 4	1391 (34.4%)	1347 (96.8%)	44 (3.2%)	
Region 5	818 (20.2%)	804 (98.3%)	14 (1.7%)	
Missing	533 (13.2%)	509 (95.5%)	24 (4.5%)	
Chronic health conditions‡				
None	2006 (49.6%)	1951 (97.3%)	55 (2.7%)	0.57
One or more	2033 (50.2%)	1971 (97.0%)	62 (3.0%)	
Missing	9 (0.2%)	8 (88.9%)	1 (11.1%)	
Do you think you had COVID-19				
No	3490 (86.2%)	3415 (97.9%)	75 (2.1%)	**<0.0001**
Yes	556 (13.7%)	513 (92.3%)	43 (7.7%)	
Missing	2 (0.0%)	2 (100.0%)	0 (0.0%)	
COVID-19 diagnosis				
I have not received the results yet	1 (0.9%)	1 (100.0%)	0 (0.0%)	**<0.0001**
Negative PCR test	94 (84.7%)	87 (92.6%)	7 (7.4%)	
Positive PCR test	16 (14.4%)	1 (6.2%)	15 (93.8%)	

Bolded values in the Table indicate a signifance of >0.05.
*Missing values or prefer not to answer were not included in p value calculations.
†When healthcare workers were compared with all other workers combined, the seropositivity was 4.4% vs 2.7%, p=0.053.
‡Chronic health disease options included: asthma, Chronic obstructive pulmonary disease, emphysema, chronic lung disease, diabetes, hypertension, heart disease, coronary artery disease, myocardial infarction, heart failure, atrial fibrillation, stroke, deep vein thrombosis, pulmonary embolism, peripheral vascular disease, high cholesterol, liver disease, liver cirrhosis, renal problem, autoimmune disorder, pneumonia and chronic neurological or neuromuscular disorder.

2020 to May 2021, and 17% between March and August 2021 in unvaccinated Belgian adults.[25–28]

The factors significantly associated with seropositivity in this cohort included identifying as a visible minority and working as an essential heath care worker. Both of these factors have been identified in other jurisdictions as being highly associated with COVID-19.[29–31]

Participants identifying as a visible minority had a higher seropositivity (5.1%) compared with non-visible minorities (2.6%). In this cohort, the visible minority groups of East Asian, South Asian and Southeast Asian represented 67.4% of participants who identified as a visible minority. Identifying as a visible minority had the largest effect size for having SARS-CoV-2 antibodies, even after adjustment for other key demographic factors associated with COVID-19 infection. The elevated risk and overall higher proportion of SARS-CoV-2 infection among visible minority Canadians has been identified across the country.[12 32] Within the same RESPPONSE cohort, future COVID-19 vaccine intention was lower among those who identified as a visible minority.[13] Our findings suggest there is a need to identify strategies to

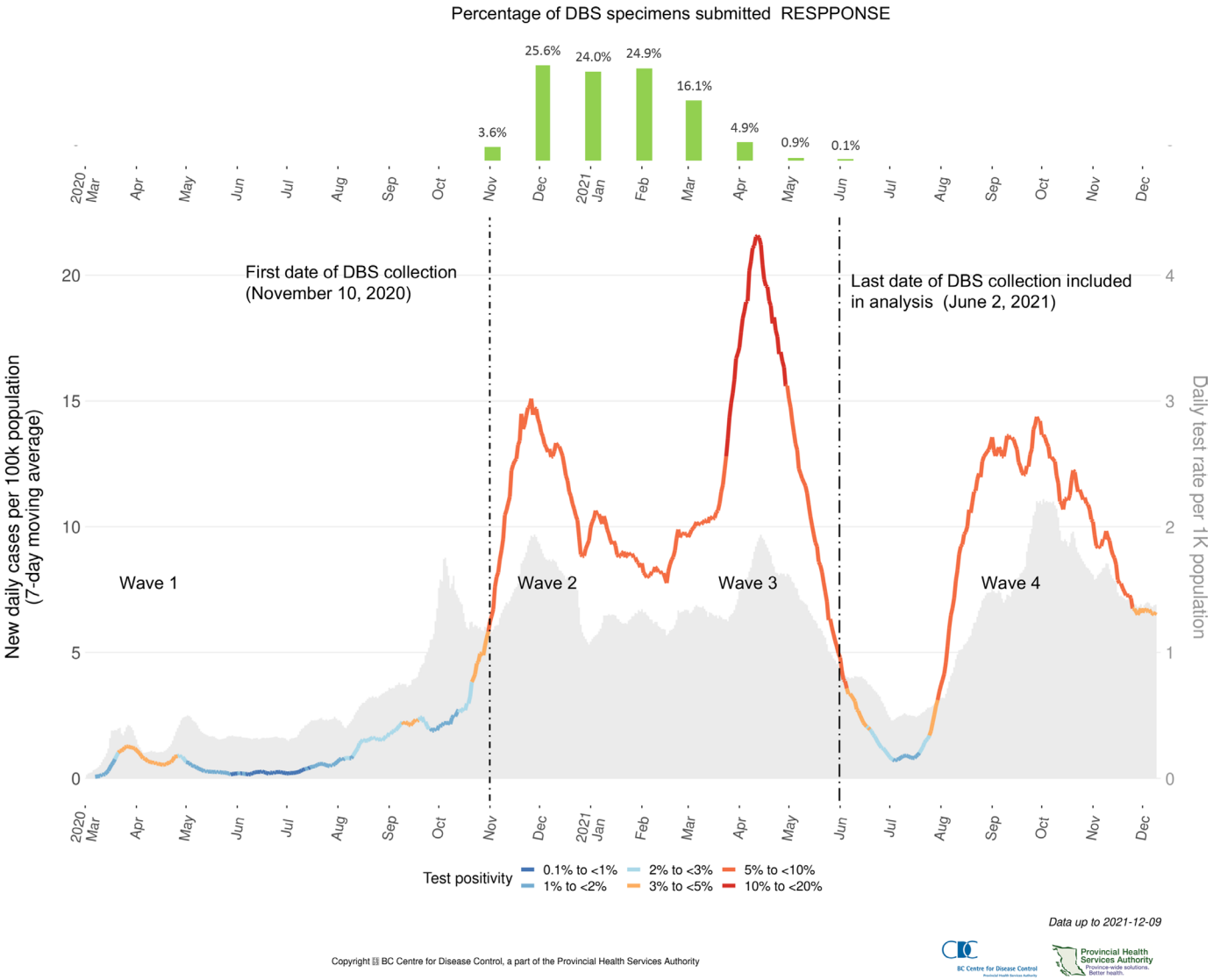

Figure 2 Rapid Evidence Study of a Provincial Population Based COhort for GeNder and SEx (RESSPONSE) dried blood spot (DBS) collection relative to recorded daily case counts per 100 000 and test positivity in British Columbia (BC) (March 2020 to December 2021). Top: DBS collection period from November 2020 to June 2021, and % of DBS samples collected per month of the study period (n=4048). Bottom: Epidemiological curve of cases per 100k population for BC March 2020 to December 2021 as per left-hand y-axis. Test positivity is indicated with colour scale, with daily test rate (PCR tests) per 1k population in the shaded area as per the right-hand y-axis (Adapted from BCCDC Dec 2021[5]).

mitigate both infection risk and support communities for immunisation.

Those working as HCWs had an IRR of 1.63 (95% CI 1.01 to 2.64), indicating an elevated risk for being seropositive compared with non-essential workers; however, after adjusting for age, sex and being a visible minority, the increased risk was no longer significant. Increased risk in HCWs has been previously observed in data from other jurisdictions.[29 30] We estimated the seroprevalence in unvaccinated HCWs to be 4.4%, which is lower than previous national estimates by the national COVID-19 surveillance system, which reported the seropositive cases by occupation in a healthcare setting, and found the prevalence in HCWs has been declining over time from May to September 2020, with estimate of 6.5% from 1 September to 14 September 2020.[33]

The elevated seropositivity in HCWs, compared with non-essential workers, is an important finding, but one that should be interpreted with caution. The exclusion of those who had received the vaccine prior to obtaining a blood sample likely resulted in the exclusion of HCWs based on the COVID-19 vaccine programme roll-out in BC at the time of the study, for which priority eligibility was given to HCWs. In the sensitivity analysis of the 140 participants with unknown vaccination status, they were included as unvaccinated. The overall findings were very similar, except for an increase in the seropositivity among HCWs, which increased from 4.4% (vs 2.7%, p=0.14) to 5.7% (vs 2.8%, p=0.006); however, it is unknown if antibody detection was due to infection-acquired or vaccine-acquired immunity. We felt the elevated seropositivity in the sensitivity analysis was likely due in large part to

Table 2 Bivariable and multivariable analysis of research serology for SARS-CoV-2 antibodies in a population cohort in British Columbia, Canada, with at-home dried blood spot samples from November 2020 to June 2021

	Unadjusted			Adjusted*		
Predictors	**Incidence rate ratios (IRR)**	**95% CI**	**P value**	**Adjusted IRR**	**95% CI**	**P value**
Age	0.99	0.97 to 1.01	0.206	0.99	0.98 to 1.01	0.488
Sex						
Female	Reference			Reference		
Male	1.01	0.59 to 1.73	0.976	1.04	0.60 to 1.79	0.89
Occupation						
Non-essential worker	Reference			Reference		
Essential worker—healthcare Worker	1.63	1.01 to 2.64	**0.047**	1.49	0.92 to 2.43	0.109
Essential worker—other essential worker	1.03	0.63 to 1.68	0.902	1	0.61 to 1.63	0.984
Visible minority						
Non-visible minority	Reference			Reference		
Visible minority	1.98	1.30 to 3.01	**0.001**	1.85	1.20 to 2.84	**0.005**
Income						
US$100k+	Reference					
US$50k–US$100k	0.99	0.64 to 1.55	0.98			
≤US$49k	1.35	0.78 to 2.33	0.288			
Education						
More than high school	Reference					
High school or less	0.86	0.49 to 1.52	0.601			
Geographical location						
Region 1	Reference					
Region 2	0.71	0.22 to 2.29	0.569			
Region 3	0.85	0.12 to 6.09	0.873			
Region 4	1.11	0.70 to 1.74	0.665			
Region 5	0.6	0.31 to 1.15	0.122			
Health status						
No chronic health conditions	Reference					
One or more chronic health conditions	1.11	0.78 to 1.59	0.559			
Number of adults in the household						
One adult	Reference					
Two adults	1.09	0.69 to 1.70	0.717			
Three or more adults	1.15	0.67 to 1.97	0.623			
Think they had COVID-19						
No	Reference					
Yes	3.6	2.48 to 5.22	**<0.001**			

Bolded values in the Table indicate a signifance of >0.05.
*n= 4018; adjusted model included age, sex, occupation and visible minority.

misclassification of HCWs' vaccination status as opposed to infection-acquired immunity, again based on the vaccine programme's priority eligibility of HCWs at the time of the study. Given the overall findings from the sensitivity analysis were similar, participants with unknown vaccine status were excluded from the main analysis. Overall, our findings indicate that among unvaccinated HCWs at the time of sample collection, the seropositivity was higher compared with non-essential workers and other essential workers.

We did not find a significant association between being positive for SARS-CoV-2 antibodies and other participant

characteristics, namely age, sex, gender, level of education, income, number of adults living in the household, having a chronic disease or geographical location of residence based on provincial health authority. Recent population-based seroprevalence studies have had similar findings, although small associations with increased seroprevalence have been observed in younger adults and those living in multifamily dwellings.[31 34 35] In our cohort, younger adults (25–29 years) had higher seroprevalence (4.5%) compared with the other age groups; however, the difference was not significant. We did not see a significant association between seroprevalence and sex (with 2.9% of males and 2.9% of females being seropositive), which may have been due to the sample being 88% female; however, other Canadian seroprevalence data likewise has not found a significant association between infection-acquire immunity and reported sex.[11]

We did not observe an association between seropositivity and household density, as measured by the number of adults in the household, where 20% of participants in our study reported living in households of three or more adults. In a large meta-analysis exploring household transmission, findings indicated that households were an important source of transmission; however, transmission was associated more with the types of relationships within the household, rather than number of adults in the household.[36]

In our cohort, over half the study population reported having one or more chronic diseases; however, we did not find an association between having a chronic disease and SARS-CoV-2 serology status. Chronic disease comorbidities have been associated with increased disease severity with COVID-19[37]; however, the evidence is limited for chronic disease comorbidity as risk factor for infection itself.[34 38] The lack of association between chronic diseases and SARS-CoV-2 antibodies in our study may be due to the public health messaging around the risk for severe disease associated with chronic diseases, where individuals may have made efforts to limit their exposure through increased precaution measures. This may have included participants working from home, given that 70% of the cohort reported as non-essential workers.

Limitations

This study has limitations. First, RESPPONSE study participants were primarily recruited from pre-existing general population research cohorts, which yielded a sample with over-representation of females, women, and high-income households, in addition to participants residing in predominately urbanised areas in the lower mainland of BC, compared with the provincial population of BC. Second, there was the potential for response bias, in that those who were concerned about COVID-19, or wished to access serology testing, may have been more likely to participate regardless of their actual risk to having acquired COVID-19, which may further limit the generalisability of our findings. Third, our seropositivity estimate is only among unvaccinated participants based on self-reported vaccination status based on the vaccine status survey, which was electronically sent to them when their DBS sample was received at the lab. Those with self-reported vaccination and those with unknown vaccination status (incomplete vaccine status survey) were removed from the main analysis to limit the potential for misclassification, due to the inability to discern between infection-acquired or vaccine-acquired immunity. Those who self-reported vaccination prior to DBS collection date were assigned as vaccinated, regardless of the time between vaccination and DBS collection, which may further bias our findings to the null, given those who were vaccinated within close proximity prior to their DBS collection were classified as vaccinated, even though vaccine-acquired antibodies may not have been detectable.

We must also acknowledge the limitation of DBS for serology testing compared with other whole blood serum samples. However, DBS has a number of advantages to consider, including self-collection, transportation, and storage when conducting population and surveillance serological studies.[17]

CONCLUSION

SARS-CoV-2 antibody seropositivity due to infection-acquired immunity remained low in BC during the second wave of the pandemic. Seropositivity indicated that among those unvaccinated, visible minority communities have been disproportionally impacted. Continued monitoring of SARS-CoV-2 serology due to both infection-acquired and vaccine-acquired immunity will be vital in public health planning and ongoing pandemic response.

Author affiliations
[1]School of Population and Public Health, The University of British Columbia, Vancouver, British Columbia, Canada
[2]British Columbia Women's Hospital and Health Centre, Women's Health Research Institute, Vancouver, British Columbia, Canada
[3]Cancer Control Research, BC Cancer Agency, Vancouver, British Columbia, Canada
[4]BC Centre for Disease Control, Vancouver, British Columbia, Canada
[5]Faculty of Medicine, The University of British Columbia, Vancouver, British Columbia, Canada
[6]Pathology and Laboratory Medicine, The University of British Columbia Faculty of Medicine, Vancouver, British Columbia, Canada
[7]Department of Pediatrics, The University of British Columbia, Vancouver, British Columbia, Canada
[8]Vaccine Evaluation Center, BC Children's Hospital Research Institute, Vancouver, British Columbia, Canada
[9]Department of Psychology, The University of British Columbia, Vancouver, British Columbia, Canada
[10]Faculty of Health Sciences, Simon Fraser University, Burnaby, British Columbia, Canada
[11]Department of Obstetrics & Gynaecology, The University of British Columbia, Vancouver, British Columbia, Canada

Twitter Melanie C M Murray @DrMelanieMurray

Contributors All authors contributed significantly to the study. All authors received and approved this manuscript. CSR: Methodology, formal analysis, manuscript drafting. AB: Project administration, data collection, formal analysis, manuscript drafting. AA: Study conceptualisation, methodology, formal analysis. LWS: Study conceptualisation, project administration, data collection. MK: Methodology,

data collection. MCMM: Study conceptualisation, methodology. HCFC: study conceptualisation, methodology. AG: Methodology. DMG: Study conceptualisation, methodology. MS: Study conceptualisation, methodology. LAMG: Study conceptualisation, methodology, project administration. AK: Study conceptualisation, methodology, project administration. LAB: Study conceptualisation, methodology, project administration, data collection. GSO: Guarantor, Study conceptualisation, methodology, project administration, data collection, formal analysis, manuscript drafting.

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Ethics approval This study involves human participants and was approved by the University of British Columbia Research Ethics Board #H20-01421. Participants gave informed consent to participate in the study before taking part.

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ORCID iDs
Laurie W Smith http://orcid.org/0000-0002-9463-1713
Gina S Ogilvie http://orcid.org/0000-0001-5783-4493

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