Canadian COVID-19 Population Serological Survey Utilizing Antenatal Serum Samples

September 27, 2022 Report

Preamble

In August 2020, the COVID-19 Immunity Task Force approved support for the Antenatal Serostudies Project – Phase One to utilize existing, residual antenatal serum across the country to ascertain the Canadian SARS-CoV-2 seroprevalence. Initially, time points were chosen to provide an immediate cross-sectional assessment of seroprevalence and to go back retrospectively to assess seroprevalence during the time when the virus was not expected to circulate in the community.

By March 2022, residual antenatal serum stored in ten provincial laboratories over three time periods were tested: February 3-21 2020 (sample period A), August 24-September 11 2020 (sample period B) and November 16-December 4 2020 (sample period C). Age and postal code administrative data were included to allow comparison with concurrent PCR-positivity rates from StatsCan and regional distribution of SARS-CoV-2 spread.

The seropositivity rates were 1.5 to 10 fold higher than the documented concurrent PCR positive rates in these jurisdictions. Detection of seropositivity as early as February in all jurisdictions reflects the extent of SARS-CoV-2 transmission in the early phases of virus emergence, prior to pandemic declaration. Overall, anti-Spike (pre-vaccine era) seropositivity was below 6%, indicating widespread vulnerability to SARS-CoV-2 prior to the advent of vaccination in Canada. During the time periods sampled, PCR testing-based public health tracking systems in all provinces were underreporting infections by 4-fold on average.

Utilizing the existing infrastructure developed in phase one, phase two was designed to complete cross-sectional serosurveillance studies to examine immune response via natural infection and/or vaccination **and** to monitor the ongoing pandemic as existing variants of concern change or new variants of concern emerge. Four Canadian provinces are participating in the first cross-sectional time period being November 15 – December 3, 2021 (sample period D). Participating provinces were to test all samples on both anti-nucleocapsid assays and anti-spike in order to capture natural infection versus vaccination.

BC, AB, NL, and PEI tested a combined 6407 samples in this time period with raw anti-nucleocapsid seroprevalence per province ranging from 1.1%- 15.0%. Age-adjusted anti-nucleocapsid seroprevalence ranged from 0.60% to 11.8%. Despite varying provincial PCR testing protocols and provisions, these findings of higher seroprevalence in comparison to PCR test results demonstrate an important level of undetected SARS-CoV-2 spread. This suggests a useful mechanism for public health monitoring of the pandemic that overcomes the significant cost and variable availability of PCR testing.

British Columbia – ongoing data:

Serostatus data from British Columbia is available on an ongoing basis. A representative sample set of 100-200 samples per week (February-March 2022), then moving to 300 samples per week (April 2022-ongoing) are pulled across all health authorities in BC and across all childbearing age groups (18-58). In addition, samples were captured from discreet November 2021, December 2021 and January 2022 baseline time points (100 samples/time point).

To examine weekly seroprevalence, the BCCDC uses a multiplex serology assay, V-Plex SARS-CoV-2 Panel 2 (IgG), offered by MesoScale Discovery (MSD), that can be used to measure IgG antibodies to nine important

coronavirus antigens, including SARS-CoV-2 nucleocapsid, spike and receptor-binding domain (RBD). Other antigens include the spike protein of circulating seasonal coronaviruses and SARS-CoV-1 Spike.

Antibody levels are detected via electrochemiluminescence using the MESO QuickPlex SQ 120 plate reader. Using MSD software and pre-determined antibody level cut-offs, samples are analyzed for anti-SARS-CoV-2 nucleocapsid, spike and RBD reactivity, with respect to both qualitative status to individual targets (seropositive or seronegative), as well as antibody levels (in binding antibody units per ml (AU/ml). Based on antibody reactivity, the overall status of the individual can be determined using the following criteria:

- Individuals that are seropositive against antigens nucleocapsid + spike and/or RBD, are likely to have gone through **natural infection,** with or without vaccination.
- Individuals who are seropositive against spike and RBD, but not nucleocapsid are likely to be **vaccinated** and uninfected; other possible scenarios for this phenotype are vaccination with breakthrough infection that did not elicit an anti-nucleocapsid response or a remote natural infection with anti-nucleocapsid response that has waned
- Individuals seropositive for only 1 of the SARS-CoV-2 targets or none of them, are considered **unexposed**

Results: The figures below were developed by the British Columbia Centre for Disease Control Public Health Laboratory (BCCDC PHL) Team.

A total of 8601 samples were collected between November 15, 2021 and September 11, 2022, and tested using the MSD V-PLEX assay. Preliminary results show an increase in natural infections from November 2021 until the end of February 2022 (Figure 1). This data coincides with the emergence of the Omicron variant, which was first detected on November 25, 2021 in British Columbia.

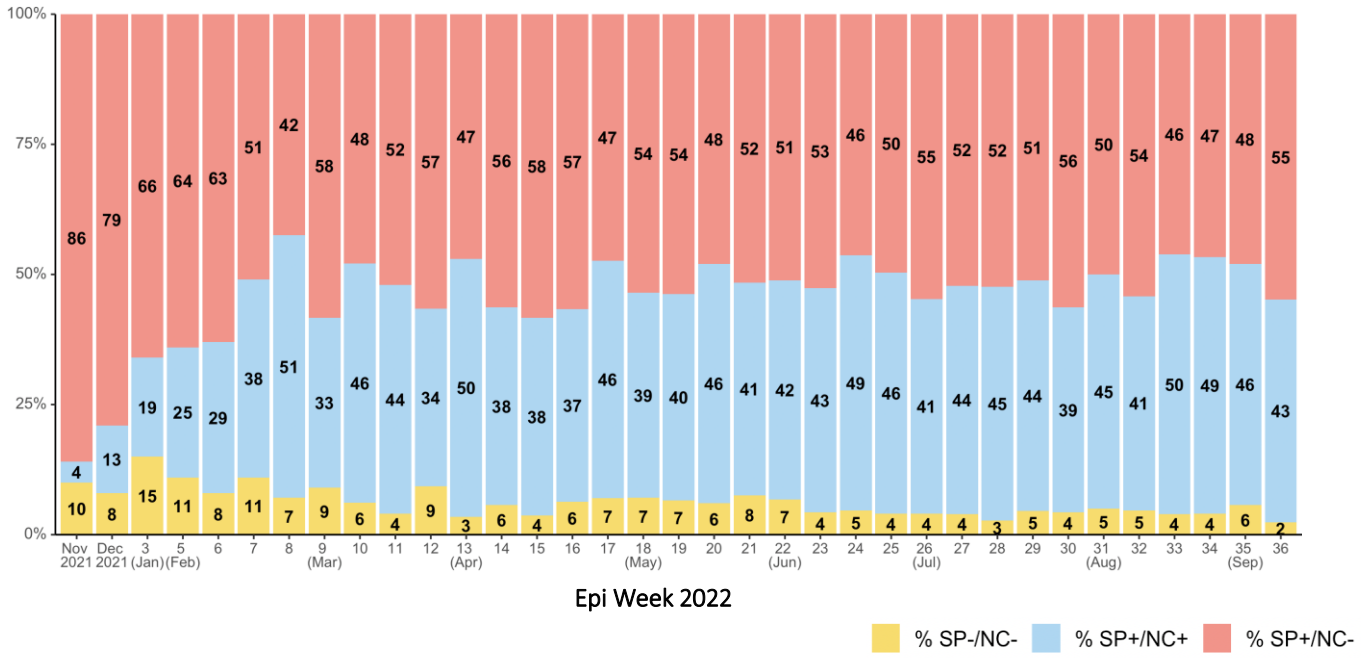

Figure 1: British Columbia antenatal samples tested for spike (SP) and nucleocapsid (NC) proteins to determine natural infection and vaccination status. Data represents prenatal samples collected from women residing in Vancouver Coastal Health, Fraser Health and Interior/Northern/Island Health Authorities.

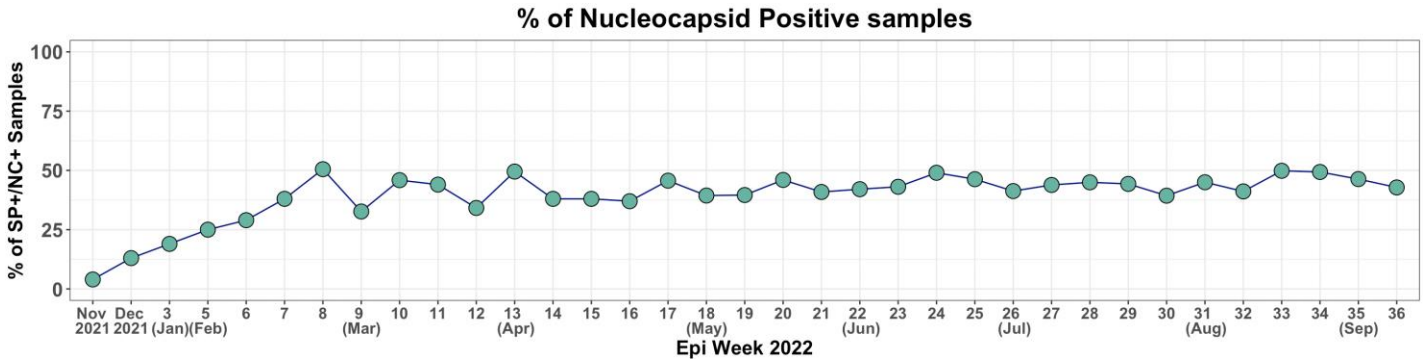

Figure 2: The % of nucleocapsid positive samples (i.e. infected population) over time, showing peaks of infections in March and April 2022. The data represents all health authorities (Vancouver Coastal Health, Fraser Health and Interior/Northern/Island Health Authorities).

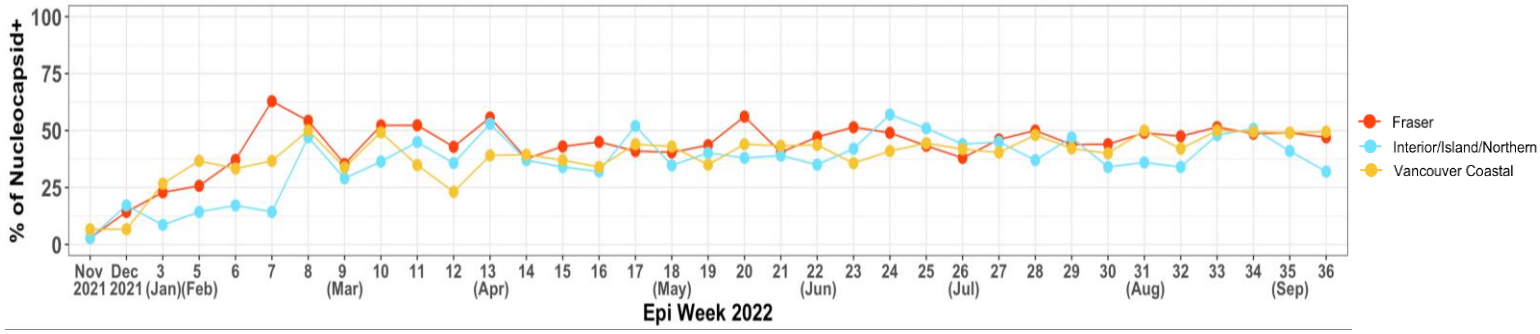

Figure 3: Breakdown of antenatal sera testing by BC health authority. The first omicron cases in Fraser Health authority were detected week of Nov 21-27, 2021, whereas the first omicron cases in Vancouver Coastal and Interior/Northern/Island Health authorities were detected week of Nov 28-Dec 4, 2021.

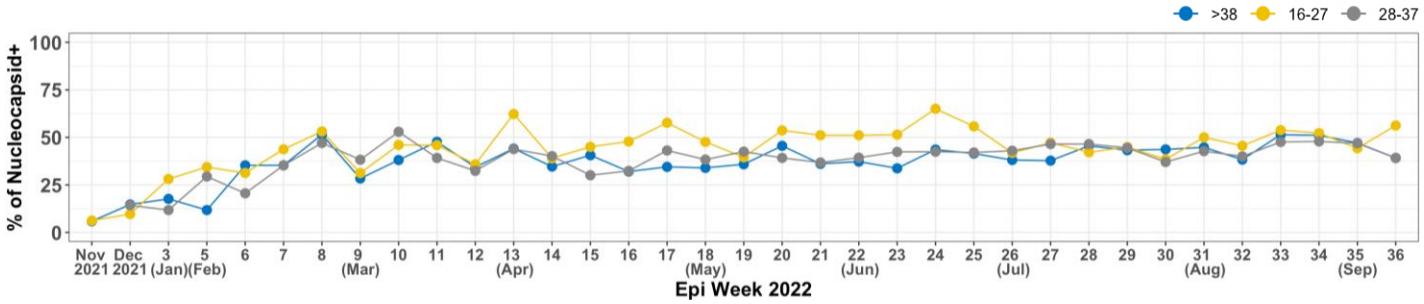

Figure 4: The percentage of nucleocapsid positive samples (infected population) by age group over time.

The BCCDC has been able to measure anti-spike protein antibodies in samples to examine differences associated with fluctuations over time (Figure 5) and population age (Figure 6). Results show an overall increase of the anti-spike antibodies after December, in older age groups, after infection as well as vaccination.

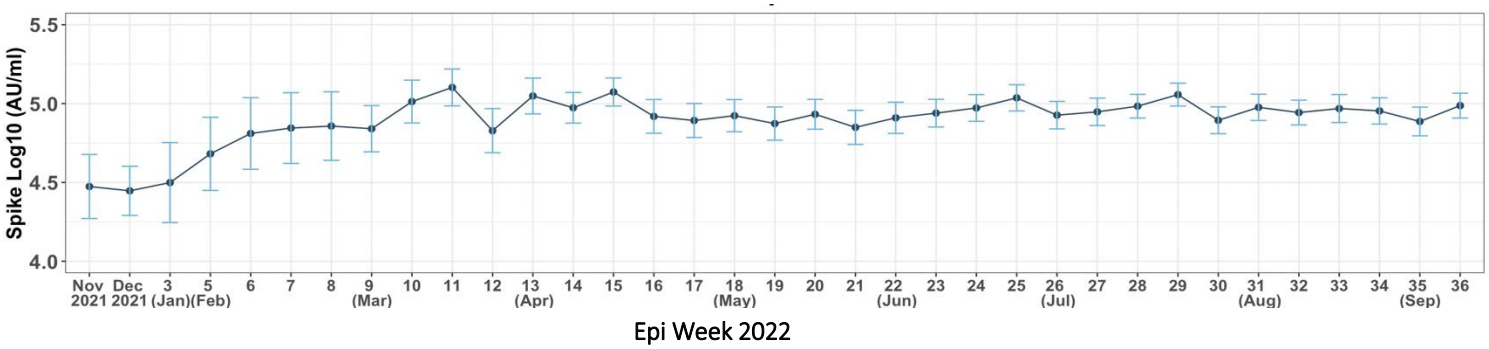

Figure 5: The level of SARS-CoV-2 Anti-Spike protein increase dramatically from January 2022 until March 2022. Error bars represent 95% Confidence intervals. No statistical differences were noted between November and December.

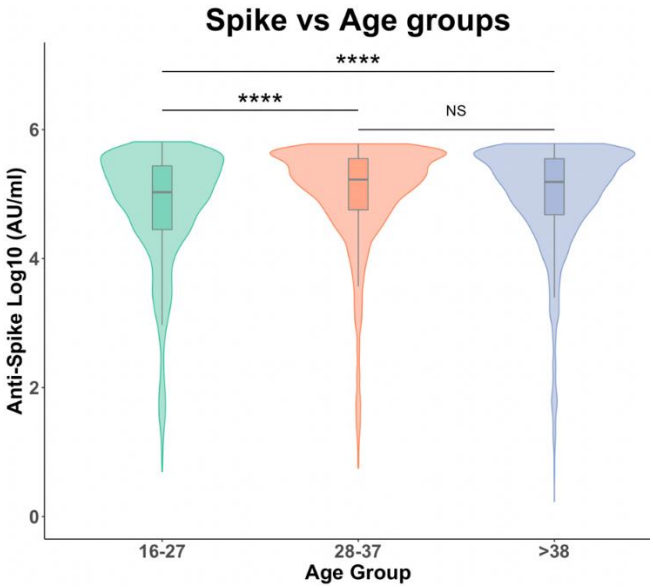

Figure 6: The level of SARS-CoV2 are significantly higher in age groups 28-37 and >38, as compared to ages 16-27. Statistical significance was determined using Kruskal-Wallis test followed by a Wilcoxon test (* $p \leq 0.05$; ** $p \leq 0.01$; *** $p \leq 0.001$; ****, $p < 0.0001$).

Linkage between PCR positive tests and vaccination history will be reported on monthly when made available. Previous linkage of a subset of MSD data to PCR testing data has shown that 987 women were PCR tested. A total of 112 women tested positive prior to antenatal sera collection. 75% (84/112) were positive for nucleocapsid showing a strong correlation between MSD-determined serostatus and PCR data. The vaccination status of these 112 PCR confirmed individuals is shown in Table 1 below:

Table 1: Vaccination status of 112 PCR + women

No vaccination history	7 (6%)
1	3 (3%)
2	59 (53%)
3	43 (38%)

Of those that tested positive by PCR, 91% were fully vaccinated (at least 2 doses) indicating breakthrough infections.

Also, while 25% of the PCR confirmed women were negative for nucleocapsid, 42% of this group were infected 6 months or more prior to prenatal testing demonstrating anti-nucleocapsid antibody waning, or they were infected within 3 weeks of prenatal testing and might not have had enough time to seroconvert. Therefore, overall, 11% of the PCR confirmed individuals with serum samples collected within a suitable time frame from infection failed to seroconvert.

In conclusion, this report demonstrates ongoing high levels of infection in this antenatal population and high levels of vaccine uptake since the onset of the Omicron wave in BC. Limitations to these data include potentially reduced sensitivity in detecting asymptomatic/mild infections by serological testing, as well as reduced sensitivity in detecting those with remote infections and waning antibodies. Also, the MSD assay detects antibodies against proteins reflecting the original wild-type SARS-CoV-2 virus, not the most recent circulating SARS-CoV-2 strains.

References:

1. Meso Scale Diagnostics. Retrieved Apr 5, 2022. Available from https://www.mesoscale.com/products/covid-19-coronavirus-panel-2-igg-k15369u/
2. Li et al. A novel multiplex electrochemiluminescent immunoassay for detection and quantification of anti-SARS-CoV-2 IgG and anti-seasonal endemic human coronavirus IgG. J Clin Virol. 2022 Jan;146:105050. doi: 10.1016/j.jcv.2021.105050.
3. Whitaker et al. Nucleocapsid antibody positivity as a marker of past SARS-CoV-2 infection in population serosurveillance studies: impact of variant, vaccination, and choice of assay cut-off. Preprint.
4. Marquez et al. Validation of saline gargle samples for the detection of anti-SARS-CoV-2 antibodies using an electrochemiluminescence multiplex immunoassay. CACMID 2022 abstract.

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