COVID-19 IMMUNITY TASK FORCE

GROUPE DE TRAVAIL SUR L'IMMUNITÉ FACE À LA COVID-19

Seroprevalence against SARS-CoV-2 due to infection in Canada

Results from the Government of Canada's COVID-19 Immunity Task Force and other partners' funded studies through to May 31, 2022

July 5, 2022

Introduction

When the Omicron wave emerged in mid-December 2021, its magnitude quickly overwhelmed PCR-based testing for acute infection in all Canadian jurisdictions. The resulting lack of PCR testing data has made it difficult to estimate the magnitude and nature of SARS-CoV-2 infection across the country.

One way to shed light on the extent of infection, independent of data from clinical testing, is to assess population seropositivity: the proportion of people with antibodies to SARS-CoV-2 in their blood. Infected individuals respond to the virus by making antibodies against different proteins in the virus, including the nucleocapsid and the spike proteins. In North America, all vaccines currently approved and in use are based on the spike protein, so people can develop antibodies to the spike protein following either past infection or vaccination. In contrast, people only develop antibodies to the nucleocapsid protein following an infection. So, having antibodies to nucleocapsid protein can be interpreted as a sign of past infection, and the proportion of people with antibodies to nucleocapsid protein can be used to track the magnitude of the omicron wave.

Methods and Data

This analysis uses the presence of antibodies to the nucleocapsid protein as an indication of past infection and the presence of anti-spike antibodies to represent the overall seroprevalence representing both vaccine-induced and infection-acquired antibodies.

The seroprevalence estimates presented in this report are from three different sources: 1) Blood donors from Canadian Blood Services and Héma-Québec; 2) anonymized discarded or residual blood samples from provincial laboratories; and 3) participants in CITF-funded research cohorts.

This report includes data received from partners **up to May 31, 2022**. The data are assumed to provide an assessment of seroprevalence reflecting infection approximately 14 days earlier than their collection date, given the time it takes on average for infected individuals to develop measurable IgG antibodies in response to infection.

Main Findings

- Overall, infection-acquired seroprevalence in Canada increased significantly between August 2021 and May 31, 2022: from 5.1% (95% confidence interval [CI]: 4.3–6.0) in the pre-Delta wave to **55.7% (95% CI: 50.7–65.3) after 5 months of the Omicron wave** (Figure 1). This rise in seroprevalence during the Omicron wave corresponds to 17.5 million (95% CI: 15.8–20.8) newly or recently infected Canadians between December 15, 2021, and May 15, 2022. This increase is equivalent to more than 100,000 infections per day, which is more than 10 times the number of daily cases seen during previous peaks of SARS-CoV-2 waves over the last 2 years.

- Seroprevalence due to infection increased steeply during the Omicron wave across all provinces of Canada between December 2021, and May 2022 (Figure 2). By the end of May, infection-acquired seroprevalence was approximately 50-60% in the Western and Central provinces (BC, AB, SK, MB, ON, QC) Although Atlantic Canada (NB, NS, PEI, NL) retained the lowest seropositivity due to infection in the country, it had the largest relative increase, reaching a seroprevalence of over 35%.

- Seroprevalence due to infection increased steeply in all ages during the Omicron wave but the increase was steeper amongst younger Canadians than older Canadians (Figure 3): the highest levels of seropositivity due to infection were observed in **young adults**, with about 65% seropositive. The seroprevalence tended to decrease with increasing age: 25-39 (56%), 40-59 (47%), and 60+ (29%).

Figures

Figure 1. Anti-nucleocapsid seroprevalence (infection-acquired seropositivity) for all Canadian provinces for all age groups, combined by region

Each point represents a seroprevalence estimate from a project at the mid-point of a sample collection period. The black line represents the average seroprevalence weighted by sample size. The grey bands represent the 95% bootstrap confidence intervals, respectively. See the methods section for details of the statistical model.

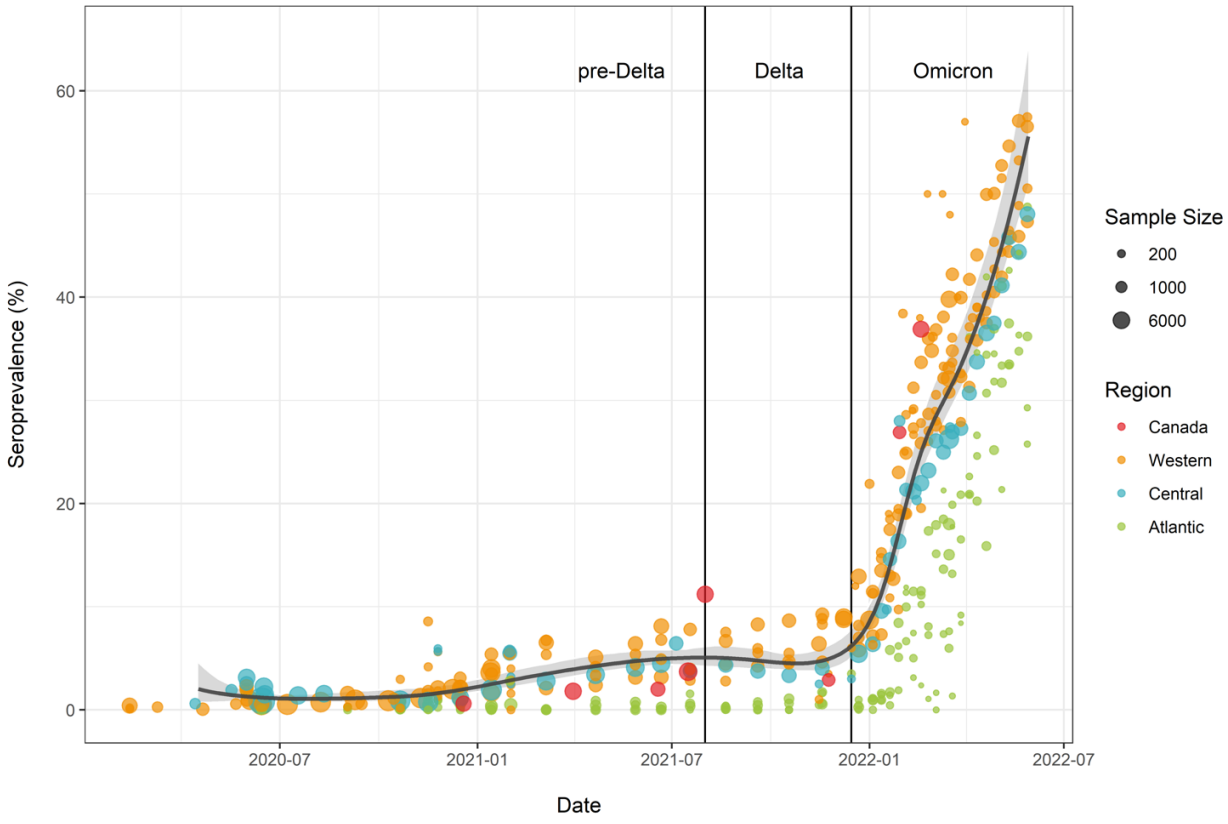
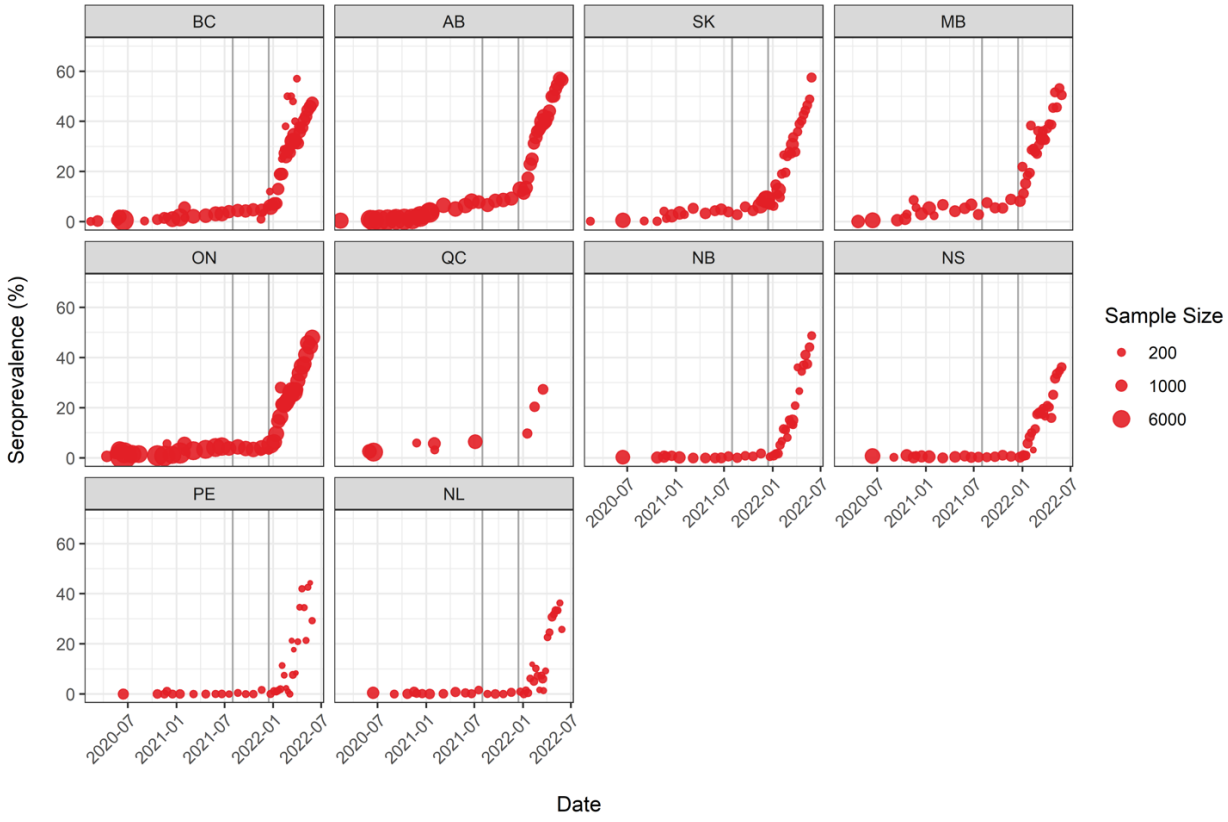
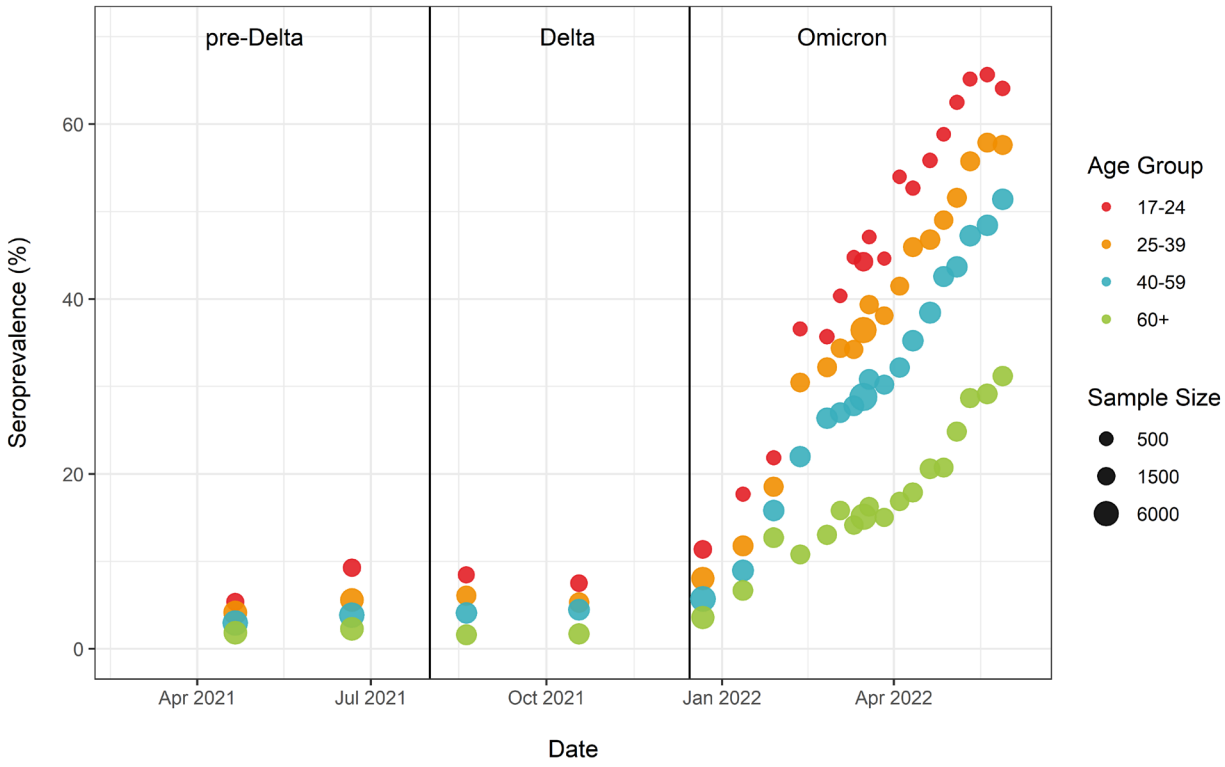


Figure 2. Anti-nucleocapsid seroprevalence (infection-acquired seropositivity) estimates by province



*No seroprevalence estimates for Territories

Figure 3. Anti-nucleocapsid seroprevalence (infection-acquired seropositivity) estimates by median age



Further details on methods

SOURCES OF DATA

Data were drawn from projects funded by the Government of Canada through its COVID-19 Immunity Task Force (CITF) and from CITF partners. The funded projects and engaged partners reflect efforts by the CITF to assess seroprevalence of SARS-CoV-2 antibodies across Canada, as per its mandate beginning in April 2020. The types of projects collecting the data include provincial serosurveys and pan-Canadian studies of the general population, studies focusing on specific age-groups, special, and/or vulnerable subpopulations, and studies in COVID-19 "hotspots", such as in occupational cohorts. Many of these projects have sampled blood from the same participants on multiple occasions, allowing them to assess changes in seropositivity prior to, and during, the Omicron wave due to infection and vaccination.

This report includes data received from funded studies and partners up to May 31, 2022.

ASSAYS USED TO DETECT SARS-COV-2 ANTIBODIES

The measurement of antibodies against the spike (S), receptor binding domain (RBD), and nucleocapsid (N) proteins was performed by provincial laboratories, blood operators, and academic research laboratories. The assays used by provincial labs were Health Canada approved commercial ELISAs (Enzyme linked Immunosorbent Assay), including:

- Anti-nucleocapsid IgG assay – Abbott Laboratories
- Anti-nucleocapsid Total Ig antibodies – Roche Laboratories
- Anti-spike Total Ig antibodies – Roche Laboratories
- Anti-spike IgG antibodies – Diasorin
- Anti-SARS-CoV-2 antibodies – MesoScale Discovery multiplex assay

Academic laboratories used both commercial assays and assays that they developed. These laboratory-developed assays used constructs of the SARS-CoV-2 proteins produced at the National Research Centre in Ottawa or by other reputable, commercially available sources.

Antibody detection was done via ELISA or high-throughput chemiluminescence assays. The development of global standards to help calibrate SARS-CoV-2 IgG

assays, Biological Arbitrary Units, has helped to decrease heterogeneity and facilitated comparison of and combination of results. For the nucleocapsid assays, the threshold for prior infection was at the manufacturer's predetermined cut-off for the assay.

ANALYSIS

This report describes population estimates of SARS-CoV-2 seroprevalence measured across the course of the pandemic, within three distinct phases based on the predominant variant of concern at the time:

- Pre-Delta: before August 1, 2021;
- Delta: August 1 to December 14, 2021; and
- Omicron: December 15, 2021, to May 31, 2022.

Only seroprevalence data for infection-acquired antibodies were analyzed. Anti-spike protein seropositivity can result from vaccination or infection. However, anti-nucleocapsid protein seropositivity only occurs following infection and does not occur following administration of any of the vaccines approved for use in Canada. Therefore, pre-vaccination (prior to Dec 15, 2020) evidence of infection-acquired antibodies includes anti-spike or anti-nucleocapsid seropositivity. After Dec 15, 2020, only anti-nucleocapsid seropositivity is taken as evidence of infection-acquired antibodies.

Seroprevalence results were summarized or presented by:

- Geography: Canada and by provinces (no data are available for Canada's three territories).
- Age group: 17-24 years; 25-39 years; 40-59 years; 60+ years (data for children and teens less than 17 are available but not presented here)

The data from all projects were pooled to allow estimation of an average seroprevalence, weighted by the sample size of each project. The statistical model used was a generalized linear model with log-linear link, Poisson distributed errors, and natural splines for the time predictor. The confidence intervals were obtained by the parametric bootstrap method. To estimate the number of newly (re)infected people in the Omicron era, the change in seroprevalence obtained from the model was scaled to all age groups in the Canadian population.

In plots, data were stratified by age, province, and pandemic phase.

LIMITATIONS

The data were heterogeneous, with different assays using different measurement units. By reporting the proportion of positive samples (seropositivity), we avoid the need to standardize different measurement units. However, it should be noted that different assays have different inherent characteristics (sensitivity, specificity, thresholds), which affect how positive samples are determined. Further, using the nucleocapsid antibody to indicate prior infection has limitations.

These limitations include: the wane in antibody levels over time; that some individuals do not develop antibodies after infection; that it is not possible to know exactly when infection occurred as there is a lag of one- to two-weeks for maximal antibody generation; and it is not possible to differentiate between the first and recurrent infections. Given these limitations, estimates of seroprevalence should not generally be interpreted as direct measures of cumulative infections over the course of a pandemic that has lasted more than 2 years. However, absolute increases in anti-N seroprevalence over short intervals (e.g., a few months) are likely to accurately represent increases in infections over the relevant interval.

Acknowledgements

This report could not have been prepared without the valuable contributions of the CITF network, the Government of Canada and other partners who funded these studies since the beginning of the pandemic. In particular, the willingness of projects to rapidly share data has made it possible to prepare a timely report.

PROJECTS THAT HAVE CONTRIBUTED INFORMATION FOR THIS REPORT

Projects that have provided unpublished data:

- Canadian Blood Services (C. Pambrun)
- CanPath: Canadian Partnership for Tomorrow's Health (P. Awadalla)
- Héma-Québec (M. Germain)
- Canadian Antenatal Serosurvey (D. Money)
- Manitoba Seroprevalence (D. Stein)
- Saskatchewan Seroprevalence (M. Anderson)

References for publicly available data:

- Ab-C: Action to Beat Coronavirus (X. Tang; P. Jha) DOI: 10.1001/jamanetworkopen.2021.46798, DOI: 10.1056/NEJMc2202879
- Alberta Precision Laboratories (C. Charlton) DOI: **10.1128/Spectrum.00291-21**
- BCCDC (D. Skowronski, funded by the BCCDC) DOI: 10.1101/2020.07.13.20153148
- CCAHS-1: Canadian COVID-19 Antibody and Health Survey (R. Gravel) **https://www150.statcan.gc.ca/n1/daily-quotidien/210706/dq210706a-eng.htm#statsinbrief**
- Public Health Ontario (S. Bolotin, funded by PHO) DOI: 10.2807/1560-7917.ES.2021.26.50.2001559

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