COVID-19 IMMUNITY TASK FORCE

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

DEC 2021 EDITION

CITF Immunity Monitoring: Technical Report

Summary

Motivation and methods

Serosurveys measure the proportion of people with antibodies to SARS-CoV-2, the virus causing COVID-19. These seroprevalence estimates provide evidence of the true extent of SARS-CoV-2 infection and humoral immunity and are therefore crucial for public health decision-making. Many Canadian studies have reported seroprevalence estimates to date, but these results must be synthesized to produce regular, comparable estimates of SARS-CoV-2 seroprevalence in Canada.

To this end, the COVID-19 Immunity Task Force (CITF) is synthesizing seroprevalence estimates for Canada and publishing the results each month. The objective for this December 2021 edition was to estimate the cumulative incidence of seroconversion (i.e., development of antibodies to SARS-CoV-2) due to SARS-CoV-2 infection in Canada up until November 30th, 2021. Seroprevalence estimates from Canadian serosurveys of the general public (catalogued by **SeroTracker**) were modelled using Bayesian statistical analysis. This edition uses a model aimed at accommodating pre-vaccine era and vaccine era changes. Specifically, confirmed cases, not deaths, are used as the main predictor of seroprevalence.

Findings

153 seroprevalence estimates from 8 research groups for studies that included the general public and blood donors were included in the analysis. The synthesized estimate of seroprevalence due to SARS-CoV-2 infection in Canada on November 30th, 2021 was 7.76% (95% credible interval [CrI]: 6.94, 8.60). Seroprevalence by region ranged from 1.61% (95% CrI: 1.38, 1.97) in the Atlantic Provinces to 12.5% (95% CrI: 10.7, 14.3) in Alberta.

These results indicate that at the end of November 2021, after multiple epidemic waves of COVID-19 infection, the cumulative incidence of SARS-CoV-2 seroconversion due to infection remained low in Canada; less than 1 in 12 on average. These findings suggest that pandemic control in Canada remains dependent on mass vaccination of many people. However, given emerging evidence about the virus and its variants, it may be challenging to vaccinate enough people to effectively block SARS-CoV-2 transmission in the Canadian population, as we have done for other vaccine-preventable infectious diseases.

Next steps

Future editions will include estimates of seropositivity from infection and vaccination by including seroprevalence of anti-spike antibodies, new seroprevalence studies, and time series data on vaccinations administered in each province and territory.

Suggested citation: *CITF Immunity Monitoring Report Cumulative SARS-CoV-2 seropositivity in Canada: December 2021 edition / Rapport de surveillance de l'immunité du GTIC la séropositivité cumulative au SRAS-CoV-2 au Canada: numéro de decembre.* COVID-19 Immunity Task Force. December 2021.

Motivation

Implementing public health measures to control COVID-19 in Canada requires accurate estimates of the proportion of the population protected against infection. Protection against infection (or re-infection) can result from vaccination or a past infection. However, the true number of infections is underestimated by the reported number of confirmed cases (Giattino, 2020). Many infections are undocumented due to limited diagnostic testing capacity, imperfect contact tracing, and asymptomatic infections. In addition, confirmed cases do not provide a clear measure of how antibodies are accumulating in the population as a result of past infections.

Seroprevalence surveys (serosurveys) measure the proportion of subjects in a study with antibodies to SARS-CoV-2. Antibodies provide evidence of past SARS-CoV-2 infection or vaccination. Serosurveys that measure antibodies to the nucleocapsid virus protein, specifically, can provide a cross-sectional "snapshot" of the cumulative incidence of infections over an interval prior to the serosurvey. Having antibodies to the spike virus protein before vaccines were available is also a reliable measure of past infection.

Serosurveys alone cannot inform public policy because serosurveys are only conducted periodically and provide delayed estimates of seroprevalence. However, serosurvey data can be combined with regularly reported epidemiologic data such as confirmed cases to estimate seroprevalence between serosurveys, since the last serosurvey was conducted, and to synthesize estimates of seroprevalence across serosurveys.

Arora *et al.* (in progress), proposed a relatively simple Bayesian statistical model that exploits sporadic serosurveys and the relationships between infections, case detection and testing rates, and seroconversion. The method produces meta-analytic estimates of seroprevalence over time.

Findings

Main seroprevalence results

We estimated that seroprevalence in Canada from infection, on November 30th, 2021, was 7.76% (95% CrI: 6.94, 8.60) (**Figure 1**). This estimate was based on 153 seroprevalence results from 8 research groups.

Provincial seroprevalence estimates ranged from 1.61% (95% CrI: 1.38, 1.97) in the Atlantic Provinces to 12.5% (95% CrI: 10.7, 14.3) in Alberta. **Figure 2** shows the seroprevalence meta-estimates by province or region along with the individual serosurvey results.

Figure 1. Estimated cumulative proportion of Canadians seropositive for SARS-CoV-2 due to infection from March 1, 2020, to November 30, 2021. Includes all provinces and territories. The dashed line represents confirmed cases as percent of the Canadian population. The solid line, light teal band, and dark teal band represent the median, 50% credible interval, and 95% credible interval estimates, respectively, of the proportion seropositive over time.

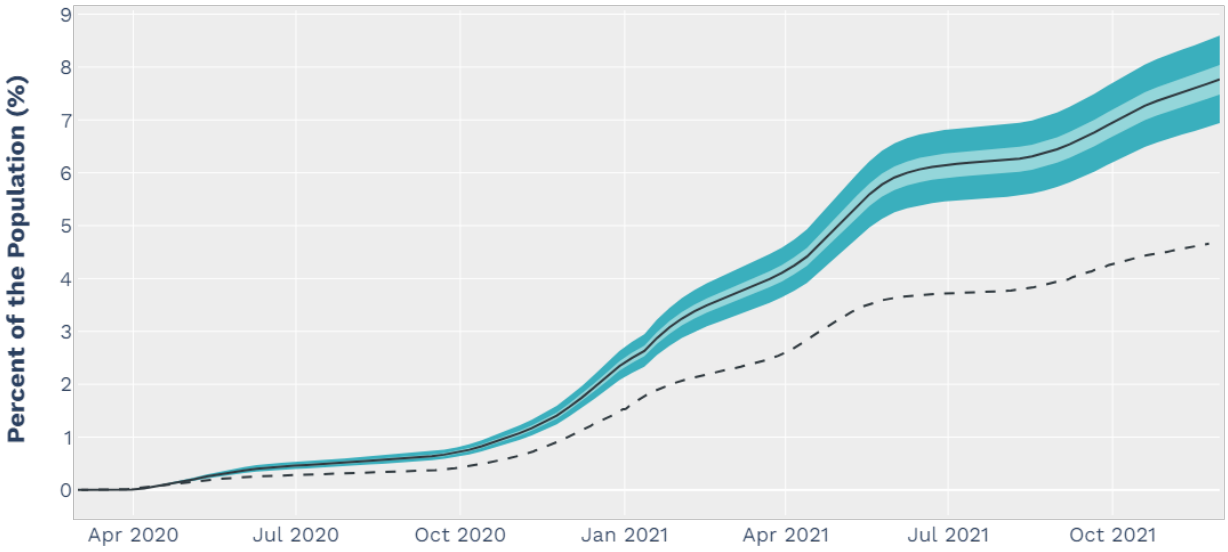
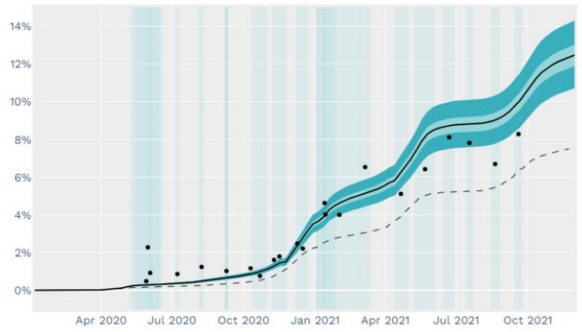
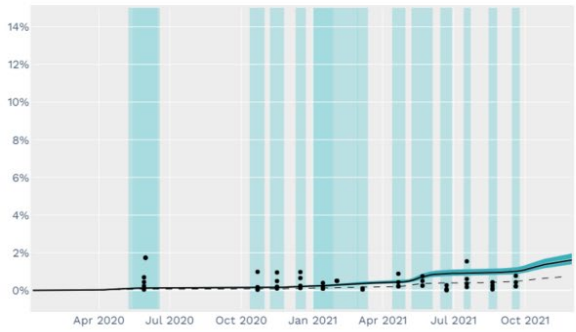


Figure 2. Estimated proportion of the provincial or regional population seropositive for SARS-CoV-2 due to infection from March 1, 2020, to November 30, 2021. Excludes the territories. The dashed line represents confirmed cases as percent of the Canadian population. The solid line, light teal band, and dark teal band represent the median, 50% credible interval, and 95% credible interval estimates, respectively, of the proportion seropositive over time. Black dots represent seroprevalence estimates in a given province or region, with the shaded areas representing the dates on which participants in that seroprevalence study were sampled.

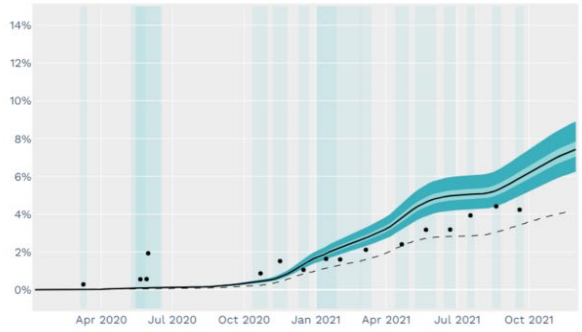
Alberta



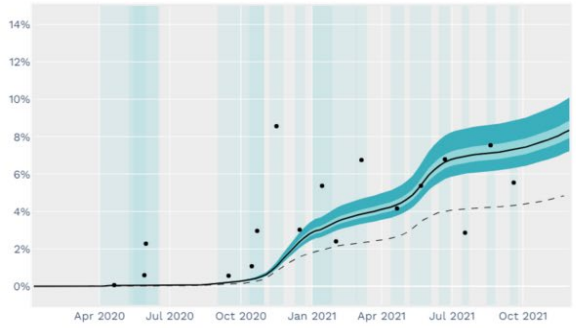
Atlantic Provinces



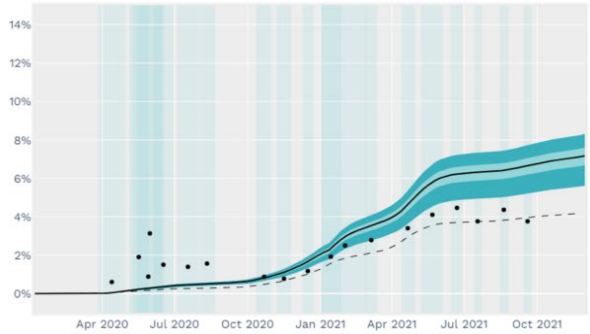
British Columbia



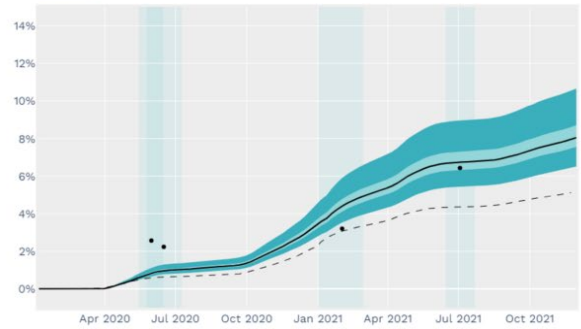
Manitoba



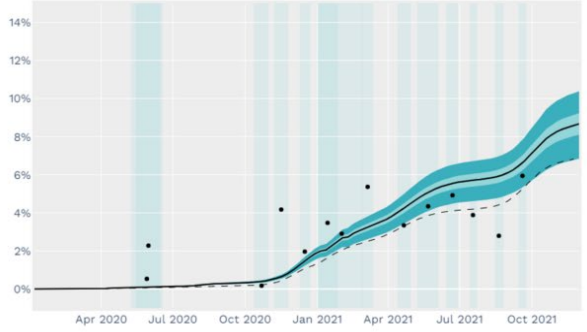
Ontario



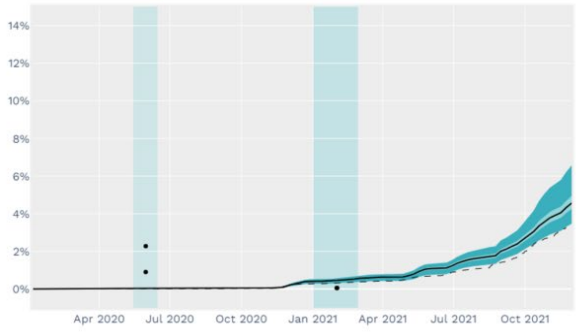
Quebec



Saskatchewan



Territories



Interpretation

In Canada overall and across all regions, immunity to COVID-19 disease from infection, as measured by seroprevalence, remained low after multiple epidemic waves: 12% or less.

For Canada, seroprevalence due to infections, as estimated by the model, was 1.67 times higher than the number of reported cases (1.27 to 2.16 times for provincial totals). This suggests that, on average, there were nearly two true infections for every confirmed case (**Table 1**).

Table 1. Reported COVID-19 cases and estimated seroprevalence.

1. Population estimates for 2021 downloaded from Statistics Canada
2. Cumulative incidence of confirmed cases on Nov 24, 2021, downloaded from the COVID-19 Canada Open Data Working Group (CCODWG; date accessed: Nov 30, 2021).
3. Estimate for November 30, 2021.

Region	Total population [1]	Cumulative Cases [2]	Cumulative Cases as % of population	Model Estimated Seroprevalence % (95% CI) [3]	Number of True Infections per Confirmed Case
Canada	38246108	1782296	4.66	7.76 (6.94, 8.6)	1.67
Alberta	4442879	333466	7.51	12.47 (10.72, 14.3)	1.66
Atlantic Provinces	2466151	18417	0.75	1.61 (1.38, 1.97)	2.16
British Columbia	5214805	216334	4.15	7.42 (6.25, 8.9)	1.79
Manitoba	1383765	67092	4.85	8.34 (7.23, 10.09)	1.72
Ontario	14826276	620874	4.19	7.17 (5.61, 8.31)	1.71
Quebec	8604495	441344	5.13	8.04 (6.51, 10.67)	1.57
Saskatchewan	1179844	80571	6.83	8.67 (6.84, 10.38)	1.27
Territories	127893	4185	3.27	4.56 (3.47, 6.57)	1.39

Limitations

The current version of the statistical model has known limitations, mainly related to simplifications or assumptions. One important such simplification is that the fading or loss of antibodies is not modelled. Another limitation is that age is not included explicitly in the model, so results are not available by age group and the current results should be considered as an average across all ages. Other limitations include the lack of explicit modelling of measurement error in the serosurvey results, although as discussed below, efforts are made to adjust serosurvey results before they are included in the model.

Methods

Data sources

EPIDEMIOLOGIC INDICATORS: CASES AND TESTS

The daily number of confirmed COVID-19 cases and nucleic acid tests for each province or territory, between January 1, 2020, and November 24, 2021, were downloaded from the Canadian COVID-19 Open Data Working Group API (CCODWG; date accessed: Nov 30, 2021). The definition of a confirmed case of COVID-19 differs between provinces and territories and can be found in the CCOWG Technical Report. Test positivity rate was calculated as the number of cases divided by the number of tests.

SEROPREVALENCE

Seroprevalence estimates were downloaded from SeroTracker (Arora, 2021) on Nov 30, 2021. We used results from studies of the general population, which include household and community surveys, studies of blood donors, and studies using residual sera from routine laboratory testing (Appendix **Table A1**). Because we were interested in the seroprevalence due to SARS-CoV-2 infection for this report, we used SARS-CoV-2 seroprevalence estimates measuring only anti-nucleocapsid antibodies after the start of vaccine roll out in December 2020; prior to December 2020, we used both anti-nucleocapsid and anti-spike seroprevalence estimates. Some additional serosurvey estimates for studies supported by CITF but not catalogued in SeroTracker were included (Appendix **Table A1**).

To reduce bias in seroprevalence estimates, we used seroprevalence estimates adjusted for non-representative sampling and corrected for test sensitivity and specificity, by the authors. Where only uncorrected results were available, SeroTracker adjusted published seroprevalence estimates to account for assay

performance by using sensitivity and specificity data from independent evaluations (Bobrovitz, 2021).

Statistical analysis

SEROPREVALENCE LIKELIHOOD

We estimated cumulative seroprevalence with a Bayesian hierarchical beta regression model. Seroprevalence in region *g* at time *t* was the proportion of the population in region *g* with SARS-CoV-2 antibodies due to past infection (detectable anti-nucleocapsid IgG). Using a Bayesian beta regression model, the expected seroprevalence μ_T in region *g* at *T* was estimated from the cumulative proportion who had seroconverted due to infection by the midpoint of the interval t_{min}, t_{max}, the sampling date range of the study. The variance κ was assumed common and unknown.

In this initial version of the model, parameter ρ_t is the discrepancy between cumulative cases and seroprevalence, which, apart from error, we assume is explained by under-ascertainment and seroreversion. In future work we aim to estimate ascertainment and seroreversion separately.

$$S_{gT} \sim Beta(\mu_{gT}, \kappa)$$

$$\mu_T = \frac{\sum_{t=1}^{T} C_t * \rho_t}{N}$$

$$\rho_{gt} = a_g + b * TPR'_{gt}$$

$$TPR'_t = logit(TPR_t) - logit(median(TPR_t))$$

Variable	Values	Definition
Indices		
t	integer+	time, in weeks
T	integer+	midpoint of serosurvey, ISO week
g	factor	province or region
Inputs		
N	integer+	population of region
S_T	[0, 1]	seroprevalence point estimate at T
C_t	integer+	confirmed COVID-19 cases
T_t	integer+	number of COVID-19 tests performed
TPR_t	[0, 1]	test positivity rate, C_t / T_t
Parameters and estimated quantities		
α	real	intercept for combined ascertainment and seroreversion
β	real	coefficient for predictor(s) of combined ascertainment and seroreversion
ρ_t	[1, inf)	combined ascertainment and seroreversion
μ_T	[0, 1]	expected seroprevalence
κ	real+	seroprevalence variance

About this report

Written by the CITF modelling group under the supervision of David Buckeridge, Scientific Lead of Data Management. Special thanks to SeroTracker, PHAC and the CCODWG, Canadian Blood Services and Hema Quebec.

References

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Giattino, Charlie. 2020. "How Epidemiological Models of COVID-19 Help Us Estimate the True Number of Infections." Edited by Our World in Data. Our World in Data. **https://ourworldindata.org/covid-models**.

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COVID-19 Canadian Open Data Working Group. 2021. "Epidemiological Data from the COVID-19 Outbreak in Canada: Technical Report 3.0." Canadian COVID-19 Open Data Working Group. **https://drive.google.com/file/d/10WX-4MiRpwJvpduBmsj18rNFUOhYKE7R/view**

Appendix

Table A1. Serosurveys: Sources, dates, and regions. Unless otherwise stated, estimates were extracted from SeroTracker (date last pulled: Nov 25, 2021).

Authors	Regions	Sampling Dates
Skowronski	British Columbia	Mar/2020, May/2020
Bolotin	Ontario	Apr/2020, May/2020, Jun/2020, Jul/2020, Aug/2020
Stein	Manitoba	Apr/2020*, Sep/2020*, Oct/2020*
Canadian Blood Services	British Columbia, Saskatchewan, Newfoundland and Labrador, Prince Edward Island, Nova Scotia, Ontario, New Brunswick, Alberta, Manitoba	May/2020*, Oct/2020, Nov/2020, Dec/2020, Jan/2021, Mar/2021, Apr/2021, May/2021, Jun/2021, Jul/2021, Aug/2021*, Sep/2021
Xuyang Tang	Saskatchewan, Manitoba, Yukon, Northwest Territories, British Columbia, Québec, Ontario, Nova Scotia, Newfoundland and Labrador, Alberta, Prince Edward Island	May/2020
Charlton	Alberta	Jun/2020, Jul/2020, Aug/2020, Sep/2020, Oct/2020, Nov/2020, Dec/2020, Jan/2021
Héma-Québec	Québec	Jun/2020, Jul/2021*
Statistics Canada	New Brunswick, Nova Scotia, Ontario, British Columbia, Prince Edward Island, Newfoundland and Labrador, Québec, Manitoba, Yukon, Northwest Territories, Alberta, Saskatchewan, Nunavut	Feb/2021*

* Estimates shared with CITF prior to publication.