Canadian Population Serological Survey Utilizing Antenatal Serum Samples

Protocol Version Date **November 16, 2020**

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Supported By: **Public Health Agency of Canada**
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SUMMARY

Title	Canadian Population Serological Survey Utilizing Antenatal Serum Samples
Goal	Assess the Canadian SARS-CoV-2 seroprevalence in a representative population of reproductive age women using antenatal serum samples to inform the public health response to the COVID-19 pandemic.
Objectives	1. Provide an immediate cross-sectional assessment of the seroprevalence of antibodies to SARS-CoV-2 in Canada. 2. Assess the retrospective evolution of SARS-CoV-2 prevalence; antenatal serology can be assessed going back one year thereby providing an opportunity to go back to where 0% prevalence is detected. 3. Plan to perform periodic future seroprevalence based on the level of seroprevalence on the first cross-sectional assessment. 4. Compare seroprevalence between Canadian provinces and territories.
Timeline	July 2020 – December 2021, to be adjusted based on Canadian and global epidemiology
Project design	This serological surveillance, quality assurance project is to inform the public health response to the COVID-19 pandemic. The project will include retrospective and future time points.
Inclusion criteria	• Samples collected from pregnant women as part of routine screening from December 2019 until December 2021
Data collection and time points	• 3 weeks within Fall/Winter 2020 (approx. Nov 16 – Dec 4) • June 2020 time point • Dec 2019 time point • Future time points to be informed by the results of the above three time points

1.0 BACKGROUND

1.1 Epidemiology of SARS-CoV-2

In December 2019, a novel coronavirus, termed Severe Acute Respiratory Syndrome associated Coronavirus-2 (SARS-CoV-2) was identified in Wuhan, China. On March 11, 2020, the WHO declared Coronavirus Disease 19 (COVID-19), the respiratory illness caused by SARS-CoV-2 infection, an official global pandemic. As of October 4, 2020, SARS-CoV-2 has infected >34,804,000 people and caused over 1,030,738 deaths globally.[1] In the same time frame, Canada has reported having 168,960 confirmed cases and 9,504 deaths.[1]

1.2 Study Rationale

Pregnant women are representative of generally healthy adults from ages 18-45 years from all socio-economic and cultural backgrounds. There are approximately 374,000 live births across Canada per year.[2] Pregnant women in Canada undergo routine blood screening as part of prenatal care, with well over 95% of women with pregnancies that proceed to delivery participating in screening. This is conducted for the purposes of assessing antibody status to rubella, HIV, Hepatitis B and syphilis. They are typically taken at 8-12 weeks gestation but in women who access minimal prenatal care they are opportunistically taken at any time point in pregnancy. In addition, there is a second serosample taken for syphilis in some provinces. In many provinces and territories, this serology is done centrally and stored for up to one year. However, in some provinces, the serosampling is privatized and conducted in many laboratories in the province. For this reason, the alternative antenatal blood sample is the biochemical based screening for biomarkers of aneuploidy which is taken up by more than 75% of pregnant women and conducted in the first and second trimester. These blood samples are archived, in many cases stored for one year, and readily accessible from all regions of Canada, including rural/remote areas.

As such, antenatal blood samples represent an opportunity to leverage existing sample collection to answer key questions about the serological prevalence of SARS-CoV-2 antibodies in healthy pregnant women throughout every province and territory and for all women of all sociodemographic and geographic areas.

It is critical that this work is conducted using a surveillance approach so that we may capture all samples collected to provide an unbiased representation of the population to best inform the Canadian and Provincial/Territorial public health response to the COVID-19 pandemic.

2.0 OBJECTIVES

1. Provide an immediate cross-sectional assessment of the seroprevalence of antibodies to SARS-CoV-2 in Canada.
2. Assess the retrospective evolution of SARS-CoV-2 prevalence; antenatal serology can be assessed going back one year thereby providing an opportunity to go back to where 0% prevalence is detected.
3. Plan to perform periodic future seroprevalence based on the level of seroprevalence on the first cross-sectional assessment.
4. Compare seroprevalence between Canadian provinces and territories.

3.0 STUDY DESIGN

This serological surveillance, quality assurance project is to inform the public health response to the COVID-19 pandemic. The survey contains both retrospective and future time points in order to monitor seroprevalence of SARS-CoV-2 within pregnant women going back to a time point where seroprevalence equals 0%. This pan-Canadian, observational, surveillance program will utilize existing serology testing procedures and public health databases.

Each province/territory will receive support by central coordination and data management through the Women's Health Research Institute (WHRI) at BC Women's Hospital and Health Centre, a University of British Columbia Research Centre, Vancouver, British Columbia.

4.0 PROTOCOL

4.1 Achieving Objectives

Objective 1 will be a cross-sectional assessment of prenatal screening blood samples routinely collected by each province and territory. This will be a specified 3-week time period for each province/territory – planned for November 16-December 4, 2020. For those provinces and territories that are less populous, a greater time period will be used as indicated below within each centre specific protocol (see appendices). Findings from objective 1 will be used to tailor the sampling strategy for objectives 2 and 3 in terms of the size and frequency of serologic assessments. This will allow us to generate more refined and policy-relevant seroprevalence findings.

Objective 2 will be a retrospective assessment of seroprevalence using aneuploidy blood samples. These samples are drawn and kept for one year allowing up to one year retrospective assessment.

Objective 3, as in objective 1, will leverage incoming real-time prenatal serology samples for periodic future assessment of seroprevalence. The frequency and number of samples will be determined based on findings from objective 1.

4.2 Laboratory Methods:

Retrospective and real time samples from each province and territory will be tested using validated serological assays. We have reviewed all of the available serotests in Canada with the experts laboratory expert sub-group of our investigator team. After full review of all available assays in Canada at the time of this version of the protocol, it is concluded that an the Ortho Total assay against the anti-spike protein of SARS-COV-2 is the most sensitive, and although not every lab in the country has this platform, there are mechanisms to adjust analysis using cross-validation studies that have been conducted in Canada. Hence, the majority of laboratories will use the Ortho Total. The remaining laboratories will use the Roche assay, which also targets anti-spike antibody while Newfoundland will use the Abbott assay as that is what is available to them. These assays will be procured by the Public Health Agency of Canada for this project and assay choice is subject to change in future and retrospective serological surveys. Data will be reported in absolute levels and the possible positive cut off will potentially be adjusted using manufacturer's recommendations to account for antibody waning over time.

4.3 Administrative Data

Administrative data to be linked to serosamples where available:

Age
Postal code (all 6 characters)

Where available:
Ethnicity
Prenatal serology results (rubella, syphilis, HIV, hepatitis B, hepatitis C, as available)
Income quintile
Vaccination data (flu vaccine in the past 12 months, history of other routine vaccines)
SARS-CoV-2 NAT results
Hospitalization for COVID-19
Gestational age at sampling date
Substance use in pregnancy
Maternal comorbidities

4.4 Provincial and Territorial Protocols

Protocols are currently under development and will be attached to this document as an appendix as each site-specific protocol is confirmed**.**

In brief:

British Columbia
British Columbia has approval to proceed with laboratory testing using a quality improvement/quality assurance (QI/QA) mandate. Research ethics approval, including waiver of consent, is being sought to pipe data from the QI/QA database into a parallel

REDCap research database to allow for pan-Canadian data compilation.
Nov-Dec 2020: 3000 samples

Yukon
As all samples from the Yukon are centrally processed within BC, public health approval to proceed with laboratory testing of the samples in BC is being sought. Yukon will have a siloed data access group within the central REDCap database at the coordinating centre.
Nov-Dec 2020: 28 samples

Alberta
Alberta has approval to proceed with laboratory testing using a quality improvement/quality assurance (QI/QA) mandate. Research ethics approval, including waiver of consent, is being sought to pipe data from the QI/QA database into a parallel REDCap research database to allow for pan-Canadian data compilation.
Nov-Dec 2020: 3173 samples

Northwest Territories
As all samples from the Northwest Territories are centrally processed within Alberta, public health approval to proceed with laboratory testing of the samples in AB is being sought. Northwest Territories will have a siloed data access group within the central REDCap database at the coordinating centre.
Nov-Dec 2020: 40 samples

Saskatchewan
Saskatchewan has approval to proceed with laboratory testing using a quality improvement/quality assurance (QI/QA) mandate. Research ethics approval, including waiver of consent, is being sought to pipe data from the QI/QA database into a parallel REDCap research database to allow for pan-Canadian data compilation.
Nov-Dec 2020: 750 samples

Manitoba
Manitoba requires research ethics approval and permissions are in progress. Upon consent, provincial team members will directly enter data including laboratory testing results into a Manitoba data access group on REDCap.
Nov-Dec 2020: 840 samples

Ontario
Ontario has approval to proceed with prospective laboratory testing using a quality improvement/quality assurance (QI/QA) mandate at Public Health Ontario. Research ethics approval, including waiver of consent, is being sought to pipe data from the QI/QA database into a parallel REDCap research database to allow for pan-Canadian data compilation. Retrospective work will be completed using aneuploidy samples that are tested in three laboratories within the province.
Nov-Dec 2020: 4000 samples

Quebec
The civil code in Quebec prohibits the use of blood samples for secondary purposes without explicit consent. At present, provincial collaborators are seeking the best opportunity

forward to obtain consent from an optimally representative sample.
Nov-Dec 2020: Not participating

Newfoundland
In development.
Nov-Dec 2020: 231samples

New Brunswick
In development.
Nov-Dec 2020: 369 samples

Nova Scotia
Nova Scotia requires research ethics approval and permissions are in progress for utilization of aneuploidy samples. Upon consent, provincial team members will directly enter data including laboratory testing results into a provincial data access group on REDCap.
Nov-Dec 2020: 480 samples

Prince Edward Island
In development.
Nov-Dec 2020: 75 samples

Nunavut
In development.

4.5 REDCap Database

A REDCap (Research Electronic Data Capture) database permits local access to local data and to provide premium case tracking software to regional sites. REDCap is a uniquely designed program, which allows for multi-site entry and automatic blocking or separation of personally identifiable information as per privacy standards.

4.6 Data Management / Stewardship

Data management will be performed by the coordinating centre, Reproductive Infectious Diseases Team, Women's Health Research Institute, a University of British Columbia Faculty of Medicine Centre at BC Women's Hospital and Health Centre in Vancouver, BC.

Collected data will be entered into a REDCap database. Each case will be assigned a unique identification number (ID#). No direct personal identifiers will be included in the national database. All centre/provincial/territorial leads will be given site-specific access to the REDCap database so they may electronically retrieve their jurisdiction's data, if desired. In cases where provinces prefer to use existing infrastructure for added efficiency, they may do so and will liaise with the central coordinating team to ensure inclusion of all necessary data elements. We will then collate all provincial data after permissions obtained to assess national data.

4.7 Statistical Analysis and Metrics

Data from each province and territory will be shared with the coordinating centre in Vancouver and pre-planned descriptive statistics will be used to summarize findings for reporting to the COVID-19 Immunity Task Force. We will report the seropositivity of SARS-CoV-2 antibodies in all samples. Seroprevalence estimates will be corrected for test specificity and sensitivity and will be age standardized according to the distribution of ages of pregnant women within each province or territory. 95% confidence intervals will be calculated using the method in Tiwari et al.[3] The data nationally will be used to calculate national levels of age-adjusted seroprevalence. Level of antibody response will be measured as geometric mean titer of antibodies, and stratified by age (<20, 20-24, 25-29, 30-34, 35-39, >39). Both seroprevalence and antibody response will be reported by ethnicity where possible and health regions within provinces.

We will use generalized linear modelling to investigate age-adjusted longitudinal trends in seroprevalence and antibody levels including both retrospective and future periodic samples. Breakpoint regression analysis will be used to estimate the time in the past at which seroprevalence and antibody levels were undetectable. As above, results will be stratified by health region, province, and also reported on a national level.

National reporting and analysis will be provided at regular intervals by the coordinating centre to fulfill COVID-19 Immunity Task Force reporting guidelines as well as provincial/territorial public health needs. Findings will be reported regularly and will include summary statistics and no individual information. Data suppression rules will be applied to all stages of analysis, which stipulate no variable with less than 5 cases can be reported to maintain confidentiality. For those provinces and territories with exceptionally small numbers, we will attempt to bundle sites together in order to maintain the highest level of anonymity. Summary statistics and project updates will also be posted on our team's University of British Columbia, Reproductive Infectious Diseases Program website.

5.0 REFERENCES

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