McMaster University | HEALTH FORUM

Rapid Evidence Profile

Examining the use of serosurveillance approaches to monitor diseases and conditions and inform policy decisions

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Context

- During the COVID-19 pandemic, serosurveillance became a useful tool to understand disease outbreak dynamics, track disease transmission and immunity, and guide policy decision-making.
- Hundreds of SARS-CoV-2 serological studies were conducted globally to provide estimates of infection rates and antibody levels within populations as public-health strategies were developed.(1)
- However, challenges with the limitations of common study methodologies (e.g., one-time assessments) and uncoordinated approaches to carrying out studies and sharing results at the regional and global level point to the need for improvements to existing serosurveillance infrastructure.(2)
- To prepare for future disease outbreaks and maximize the health investments made in serosurveillance, it is important to assess the serosurveillance approaches that have been used to monitor diseases and conditions and inform policy decisions.

+ Global evidence drawn upon

Evidence syntheses selected based on relevance, quality, and recency of search

+ Forms of domestic evidence used (🍁 = Canadian)

Evaluation

Qualitative insights

+ Other types of information used

Jurisdictional scan (nine countries: AU, CA, DK, DE, IL, KR, NL, UK, US)

*** Additional notable features**

Prepared in three-business days using an 'all hands on deck' approach

Questions

1) How are serosurveillance approaches structured and used to monitor diseases and conditions and inform public-health decisions?
2) What are the features of existing national or sub-national serosurveillance approaches?
3) How are COVID-19 serosurveillance approaches in other countries being adapted?

High-level summary of key findings

- We identified two highly relevant evidence syntheses and 17 primary studies that described serosurveillance approaches as well as five commentaries that offered thoughtful insights about key considerations for developing serosurveillance systems.
- Residual blood collected from donors or from clinical samples were found to be the most common form of biological specimens collected for serosurveillance during the COVID-19 pandemic and other diseases outbreaks across regions and demographic subgroups.
- Several primary studies emphasized the usefulness of serosurveillance in supporting disease modelling to predict trends, improving the efficacy of vaccination policies, and informing decision-making.

- With the exception of South Korea, we identified some publicly available information about serosurveillance approaches in each of the selected jurisdictions (Australia, Denmark, Germany, Israel, Netherlands, U.K., and the U.S) and Canadian provinces and territories.
- We found that serosurveillance approaches are typically led by national research institutes and public health agencies in collaboration with a network of sub-national governments, academic institutions, hospitals, blood services, and laboratories.
- Many jurisdictions leveraged their existing serosurveillance approaches and networks during the COVID-19 pandemic.
- Key gaps that could be the focus of future primary studies and evidence syntheses could include developing multi-pathogen serosurveillance, strengthening the use of biobanks, on adapting serosurveillance approaches for other priority populations, and ensuring clear descriptions of equity and ethical considerations in serosurveillance.

Framework to organize what we looked for

- Category of disease or condition
  - Emerging diseases
  - Infectious diseases
  - Chronic diseases
  - Vector-borne diseases
  - COVID-19
- What is collected
  - Patient-level information
    - Demographic variables (e.g., age, sex, place of residence, ethnic group)
    - Socioeconomic variables (e.g., occupation, educational level, income level)
    - Household conditions
    - Vaccination history (e.g., doses administered)
    - Travel history
    - History of illness or related symptoms
  - Biological specimens collected
    - Residual blood from donation
    - Residual blood from clinical sample
    - Antenatal blood
    - Oral fluid
    - Other
- Who conducts and analyzes the surveillance
  - Internal to a public health agency which oversees a national or sub-national population
  - External to a public health agency (i.e., contracted out)
- How data is collected and linked

    - Surveys
    - Administrative databases
    - Other
- Types of analyses to inform public-health actions
    - Estimating past/accumulated burden of an infectious disease or health condition in a population
    - Identifying groups at increased risk of acquiring the disease (e.g., age, gender, geographic location, etc.)
    - Identifying population trends in past accumulative exposure to an infection over time
    - Monitoring and evaluating the impact of vaccination programs and informing immunization policy
    - Conducting disease modelling (e.g., for the prediction of potential outbreak, projections of illness or hospitalization)
    - Examining trends in immunity over time
    - Monitoring emerging diseases (e.g., in relation to climate change)
- How is serosurveillance shared
    - Not disseminated publicly (i.e., internal-use only)
    - Summary of key indicators provided publicly
    - Summary of all indicators provided publicly
- Adaptations to serosurveillance systems following the COVID-19 pandemic
    - Bio-banking samples
    - Adapting assays for different (or greater specificity for) antigens
    - Creating integrated serosurveillance for multiple conditions
- Equity considerations (derived from PROGRESS-Plus)
- Ethics considerations (e.g., when is individual patient consent required, when REB is sought, and whether requirements differ for anonymous samples vs. linked to administrative/survey data)

Box 1: Approach and supporting materials

At the beginning of each rapid evidence profile and throughout its development, we engage a subject matter expert, who helps us to scope the question and ensure relevant context is taken into account in the summary of the evidence.

We identified evidence addressing the question by searching Health Evidence, Health Systems Evidence and PubMed. All searches were conducted on 20 November 2023. We identified jurisdictional experiences by hand-searching government and stakeholder websites for information relevant to the question from Australia, Denmark, Germany, Israel, Netherlands, South Korea, U.K., and the U.S.), as well as all Canada (nationally and all provinces and territories). The search strategies used, including which websites were searched for the jurisdictional scan, are included in Appendix 1.

In contrast to synthesis methods that provide an in-depth understanding of the evidence, this profile focuses on providing an overview and key insights from relevant documents.

We searched for full evidence syntheses (or synthesis-derived products such as overviews of evidence syntheses), protocols for evidence syntheses and single studies. We also selectively included commentaries for this rapid evidence profile where they provided a thoughtful historical review and/or insight about key priorities for serosurveillance.

We appraised the methodological quality of evidence syntheses that were deemed to be highly relevant using AMSTAR. AMSTAR rates overall quality on a scale of 0 to 11, where 11/11 represents a review of the highest quality. The AMSTAR tool was developed to assess reviews focused on clinical interventions, so not all criteria apply to evidence syntheses pertaining to delivery, financial or governance arrangements within health systems or to broader social systems.

A separate appendix document includes:
1) methodological details (Appendix 1)
2) details about each identified synthesis (Appendix 2)
3) details about each identified single study (Appendix 3)
4) details about each identified commentary (Appendix 4)
5) details from jurisdictional scans (Appendices 5 and 6)
6) documents that were excluded in the final stages of review (Appendix 7).

This rapid evidence profile was prepared in the equivalent of three days of a 'full-court press' by all involved staff.

What we found

Key findings from evidence documents

We identified two highly relevant evidence syntheses and 17 primary studies that described serosurveillance approaches, as well as five commentaries that offered thoughtful historical insights about key priorities for serosurveillance. Below we describe findings from the highly relevant evidence documents as well as some medium-relevance documents that provided additional insights on monitoring diseases through serosurveillance.

Serosurveillance during the COVID-19 pandemic

According to the evidence documents identified, residual blood collected from donors or from clinical samples were found to be the most common form of biological specimens collected for serosurveillance to identify trends in exposure to the SARS-CoV-2 coronavirus strain that causes COVID-19 across regions and demographic subgroups. Two primary studies described estimates of SARS-CoV-2 antibody prevalence that were derived from blood-donor specimens in Melbourne, Australia during the second COVID-19 epidemic wave in 2020 and in numerous jurisdictions across the United States between March and August 2020.(3; 4) The U.S.-based study highlighted the potential bias of blood donations as donors tend to be primarily white, healthy, and in better financial standing, and suggested adapting assays to have sufficient sensitivity to detect asymptomatic or mild symptoms in order to reduce bias. Collecting demographic information at blood centres that can be compared against normative population statistics can also assist with the interpretation of serological data.(5)

Several primary studies emphasized the usefulness of clinical blood samples in providing reliable estimates of COVID-19 transmission and supporting disease modelling to predict trends and inform decision making.(6-8) One study described how serosurveillance of SARS-CoV-2 was conducted in Canada by collecting bio-banking blood samples and adapting assays of different variants in internal public health agencies and external organizations.(9) Another study used a combination of data from blood samples and data on human-bat contact and range distributions for known bat SARS-related coronavirus (SARSr-CoV) hosts in Southeast Asia to estimate the number of people in the region who are infected with SARSr-CoVs annually.(10) However, seroprevalence results derived from blood samples may be hampered by the performance of rapid tests used to conduct surveillance testing, as demonstrated by a Danish study that described a national COVID-19 surveillance survey in 2020.(11)

One medium-quality evidence synthesis that captured a global analysis of SARS-CoV2 surveillance publications concluded that the slower release of peer-reviewed and preprint articles about SARS-CoV-2 seroprevalence made them less useful for public health decision-making during the COVID-19 pandemic than studies on other publication platforms and government or institutional reports.(12) The synthesis highlighted that more timely reporting of seroprevalence data from publications with low or moderate risk of bias can improve their usefulness for surveillance.

Serosurveillance during other disease outbreaks

Similar to the evidence findings on serosurveillance during the COVID-19 pandemic, blood donations were used to estimate the disease burden and identify population trends of the Zika and dengue virus in a medium-quality evidence synthesis.(13) The authors concluded that the seroprevalence of Zika and dengue virus through blood donations was higher than other surveillance tools, possibly because blood donations are able to capture incidence rates of asymptomatic people. One primary study used nucleic acid tests to identify transfusion-transmitted infections among blood donors to demonstrate that standardized surveillance data from multiple U.S. donor blood systems can be combined and analyzed for changes to policies affecting donor suitability.(14)

Results of a primary study assessing serum bank data collected over the year before a measles outbreak in northern Vietnam in 2014 revealed a significant discrepancy between levels of protection from serology and vaccine-coverage

estimates of UNICEF's Multiple Indicator Clustered Surveys.(15) The study's authors suggested that small-scale serosurveillance could improve the efficacy of vaccination policies from low- to high-incidence settings. However, there may be limited added value to the use of blood samples for the surveillance of emerging diseases (e.g., tick-borne diseases) if the sampling size is not large enough to detect differences in risk groups or risk areas.(16)

Additional considerations

In addition to the evidence syntheses and primary studies, we identified several highly relevant commentaries that provided recommendations on key priorities and considerations for serosurveillance. First, leveraging existing infrastructure for data collection, handling and storage of samples and specimens to develop baseline surveys was recommended in two commentaries.(17; 18) Another commentary highlighted that establishing a serosurveillance platform requires consideration of biomarkers, data-collection strategies, ethical considerations (including consent), and dissemination techniques.(19) The platform should be continuously monitored and evaluated to determine its utility in monitoring infection and informing public health decisions. Looking ahead to the future of serosurveillance in disease monitoring, the Public Health Collaborator on Serosurveillance for Pandemic Preparedness and Response recommended the use serological studies to guide vaccination strategies, shift toward multi-pathogen monitoring, build a repository of serosurveillance studies, and strengthen national and regional biobanks for the development of tests for novel pathogens and biomarkers.(2)

Key findings from jurisdictional scan

International jurisdictions

With the exception of South Korea, we identified some publicly available information about serosurveillance approaches in each of the selected jurisdictions (Australia, Denmark, Germany, Israel, Netherlands, U.K., and the U.S). Generally, publicly available information about serosurveillance approaches was limited. From what we found, these approaches are typically led by national research institutes and public health agencies in collaboration with a network of sub-national governments, academic institutions, hospitals, blood services, and laboratories. In Australia, the National Centre for Immunisation Research and Surveillance (NCIRS) provides technical expertise to inform policy and planning for vaccine-preventable diseases, including surveillance, monitoring of vaccination coverage, vaccination program evaluations, and vaccine safety monitoring. The Robert Koch Institute in Germany, the U.K. Health Security Agency (previously Public Health England), The Statens Serum Institut in Denmark, the Public Health Services Unit in Israel, the National Institute for Public Health and the Environment of the Netherlands, and the U.S. Centers for Disease Control and Prevention have developed serosurveillance approaches for different diseases and health conditions to inform public-health decisions. The types of data and how they are collected or linked was seldomly described across the jurisdictions.

We identified features of serosurveillance approaches across some jurisdictions, including:

- The National Centre for Immunisation Research and Surveillance (NCIRS) in Australia, funded by the Federal government and the government of New South Wales, uses consent-based blood donation surveys and residual sera from the public and hospitalized individuals to examine trends of immunity over time, understand the impact of vaccination programs, identify groups at risk, estimate the burden of specific vaccine-preventable diseases, predict potential outbreaks, and identify new or emerging pathogens to inform policies and disease modelling
- The Statens Serum Institut in Denmark, funded by Novo Nordisk Foundation and the Ministry of Science, Technology and Innovation, houses the Danish National Biobank which contains more than 30.6 million biological samples (residual blood from donations and clinical samples and antenatal blood) that are all linked with administrative databases containing information of all Danish residents to conduct public-health research
- The Robert Koch Institute in Germany collect information from blood donations under the Transfusion Act, where donation institutions must report the number of samples tested, and they must record demographic

information and mode of infection if a sample is confirmed with a positive infection marker (these findings are typically disseminated through the Federal Health Gazette)

- The National Institute for Public Health and the Environment of the Netherlands has had a nationwide serosurveillance program since 1995, where they use population-based random sampling strategies, population-based serum banks, multiplexing techniques, and surveys to study the prevalence of vaccine-preventable diseases among the Dutch population
- The U.K. Health Security Agency and the Seroepidemiology Network inform policy decisions and have further expanded their serological testing to include diseases such as pertussis and influenza

Many jurisdictions leveraged their existing serosurveillance approaches and networks during the COVID-19 pandemic. In Australia, the National Centre for Immunisation Research and Surveillance co-lead the Australian COVID-19 Serosurveillance Network to measure prevalence of SARS-CoV-2-specific antibodies and conduct serosurveys among Australian blood donor population. In Germany, nationwide COVID-19 antibody monitoring was conducted from 2020 to 2022, including studying COVID-19 in daycares through blood samples. The Netherlands leveraged their existing serosurveillance program to examine blood samples to identify prevalence and immunity across different regions, racial backgrounds and gender during COVID-19 since 2020. In the U.K., the Healthy Security Agency collected serological samples from adult blood donors supplied by the National Health Service, samples from routine blood tests at participating Royal College of General Practitioners, and residual sera provided by participating laboratories across England. In the U.S., the Centers for Disease Control and Prevention conducted COVID-19 antibody seroprevalence studies based on data collected from nationwide commercial laboratories and blood donations. With surveys collected every eight weeks from nationwide commercial laboratories, the U.S. CDC was able to estimate the infection-induced antibody seroprevalence of adults and pediatric age groups (ages six months to 17 years). In addition to infection-induced seroprevalence, the U.S. CDC estimated the seroprevalence of vaccination-induced antibodies among pediatric age groups. Related to blood donations, the U.S. CDC worked with the National Heart, Lung, and Blood Institute Recipient Epidemiology and Donor Evaluation Study-IV-Pediatric (REDS-IV-P) program to use monthly blood donation specimens from 17 metropolitan regions to estimate both infection- and vaccination-induced antibody seroprevalence from 2020 to 2021. In 2022, the U.S. CDC collaborated with Vitalant Research Institute, American Red Cross, and Westat to conduct antibody seroprevalence from de-identified blood samples. These seroprevalence approaches ended in December 2022.

Canadian jurisdictions

We found limited publicly available information about serosurveillance approaches, structures and features across the Canadian provinces and territories. The BC Centre for Disease Control monitors seroprevalence changes for COVID-19, Influenza A and other emerging pathogens with support from LifeLabs for residual serological surveillance, blood donor screening with Canadian Blood Services, and antenatal serological surveillance. Alberta uses a serosurveillance system to monitor emerging infections such as COVID-19 and West Nile Virus. In a 2007 report, Alberta Health and Wellness conducted a seroprevalence study by recruiting residents by a telephone survey and collection of blood samples. Nova Scotia is part of the Canadian HIV Strain and Drug Resistance Surveillance Program, where they send archived diagnostic sera samples of those newly diagnosed with HIV for subtype analysis, genotyping, and testing for recency of infection. This information is sent to the Public Health Agency of Canada to describe trends in reports of HIV diagnoses.

Related to serosurveillance approaches during the COVID-19 pandemic, Canada leveraged partnerships to conduct relevant serosurveys. In April of 2020, seroepidemiologic work was funded by PHAC through the COVID-19 Immunity Task Force (CITF). This was a large, coordinated effort involving external researchers, national blood donor agencies and Statistics Canada, that produced over 120 individual studies related to seroprevalence as well as immunity science, optimization of immunologic testing, vaccine surveillance, pediatric vaccination, boosters, and population immunity modelling. The CITF generated monthly national seroprevalence estimates during the pandemic by pooling estimates from 25 individual studies, the largest component of which came from Canadian

Blood Services donors. The findings on infection and vaccination rates, and population trends are publicly available on the COVID-19 Immunity Task Force webpage. National seroprevalence estimates were also produced through the Canadian COVID-19 Antibody and Health Survey (CCAHS) carried out by Statistics Canada, CITF, and PHAC. These surveys evaluated active COVID-19 infections and COVID-19 antibody prevalence using self-reported data from a representative population survey and dried blood spot (DBS) testing, producing national seroprevalence estimates for two time periods: November 2020-April 2021 and April 2021-August 2022. The most recent cycle (April 2021-August 2022) concluded that nearly all Canadian adults (98%) had antibodies against SARS-CoV2 during that period of time. These antibodies were acquired through vaccination, a previous infection, or both.

Seroprevalence estimates were also conducted in specific jurisdictions, often with the support of CITF. In provinces, data collection largely included blood donors from Canadian Blood Services and Héma-Québec, biobanks, anonymized discarded, or residual blood samples from provincial laboratories, or participants from research cohorts. Another example of a serosurveillance approach is Public Health Ontario's serosurveillance program that was established earlier in the COVID-19 pandemic by collecting and analyzing anonymized residual specimens (e.g., blood, serum or plasma) to understand the proportion of Ontario's population that had COVID-19 antibodies and support the government in evaluating the effectiveness of its pandemic response. The residual specimens were selected based on a distribution of age groups, sex, and residence of each health region in Ontario. Public Health Ontario is currently focusing on validating new methods for measuring antibody response to COVID-19 and investigating vaccine protection from COVID-19. We found limited to no information about the territories. The Government of the Northwest Territories collected residents' discarded samples from routine health tests dating back to 1 April 2022 to test for antibodies and whether the antibodies resulted from immunization or infection. The samples were sent to Canadian Blood Services' research laboratory for analyzing prevalence, which will not have any personal information from residents.

Next steps

The following are key gaps identified that could be the focus of future primary studies and/or evidence syntheses:

- antibody measurements, correlates of protection (e.g., seroconversion and waning of antibodies), and multi-pathogen serosurveillance to test different pathogens or biomarkers
- how to strengthen biobank infrastructures to use as baseline measurements or as negative controls for a novel pathogen and biomarker testing for chronic disease
- how serosurveillance can be tailored to focus on priority populations (e.g., those who are immunocompromised and older adults)
- equity and ethical considerations in serosurveillance
- serosurveillance approaches, structures, and features of Canadian provinces and territories.

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